# Second Report of the Independent PFAS Scientific Advisory Panel for Jersey – An Assessment of the Impact on PFAS Exposure on Health.

November 2024

PSAP
PFAS Scientific Advisory Panel

# Executive summary

## Background and Context

Per- and polyfluoroalkyl substances (PFAS) are a group of over 14,000 synthetic chemicals known for their widespread use in consumer products and industrial applications. These substances are valued for their chemical stability and resistance to degradation, properties that have unfortunately led to persistent environmental contamination and potential health risks. PFAS have been used since the 1960s in products such as firefighting foams, non-stick cookware, water repellents, and food packaging. The main concern in Jersey stems from the historical use of PFAS-containing aqueous film-forming foams (AFFF) at Jersey Airport. This has resulted in contamination of groundwater, impacting local borehole water supplies.

## Response and Investigation

In response to public concern and potential health implications, the Government of Jersey commissioned the Independent PFAS Scientific Advisory Panel in 2023. The panel, comprising international experts and supported by the local public health team, was tasked with assessing the current PFAS situation in Jersey. Their work included hearing evidence from affected Islanders, interviewing subject matter experts from around the world, reviewing scientific literature, and evaluating the likelihood of potential health impacts. The evidence base is evolving, and this report is based on current understanding.

## Key Findings

### Cardiovascular Health

The panel found a consistent association between exposure to certain PFAS and elevated cholesterol levels, particularly low-density lipoprotein (LDL), known as "bad cholesterol." Elevated LDL levels are typically associated with increased risk of cardiovascular diseases, such as ischaemic heart disease and strokes. However, despite the increased cholesterol levels, evidence of a corresponding increase in cardiovascular diseases among PFAS-exposed populations (particularly PFOA) was less clear. The panel hypothesized that factors such as increased high-density lipoprotein (HDL) levels (good cholesterol) and indications of lower inflammation in the body might mitigate some effect of LDL on cardiovascular risk. Nevertheless, the panel took a precautionary approach; they recommended that individuals with elevated cholesterol due to PFAS exposure should follow standard management practices, including diet, exercise, and possibly lipid-lowering medications.

### Cancer Risks

There is evidence suggesting a probable increase in the incidence of kidney and testicular cancers among populations exposed to certain PFAS. The panel also noted some evidence indicating an increased risk of bladder cancer, though this was less clear. In contrast, common cancers such as breast, colon, and prostate cancers did not show a significant increase in incidence across the most relevant research studies, providing some reassurance. Nevertheless, a link not having been clearly found does not mean that a link is not there. The panel noted that there were also concerns expressed by Islanders about rarer cancers and concluded that, although there is not yet evidence to give a clear answer on rare cancers, there is also insufficient evidence to rule out any potential risk from PFAS exposure.

### Immune System and Autoimmune Diseases

Exposure to certain PFAS has been associated with a reduced antibody response to childhood vaccinations, which could theoretically lower the effectiveness of immunisations. While the panel was of the view that it is very likely that there is an effect on antibodies after childhood vaccination, the studies to date do not show an increase in vaccine-preventable or other infectious diseases. There was not consistent evidence linking PFAS exposure to a higher

incidence of autoimmune diseases, such as rheumatoid arthritis, ulcerative colitis, or lupus. The panel suggested that enhanced public health efforts to maintain high vaccination coverage should help protect vulnerable populations, including those potentially affected by PFAS.

### Endocrine and Metabolic Disorders

The evidence linking PFAS exposure to endocrine disorders, including thyroid dysfunction and metabolic issues like obesity and type 2 diabetes, was found to be inconsistent. While some studies indicated potential associations, these were not uniformly supported across different populations and settings. The panel acknowledged the complexity of these potential health effects and were of the view that further research to clarify these associations and inform public health recommendations is needed.

### Mental Health and Wellbeing

The psychological impact of environmental contamination, including stress, anxiety, and depression, was identified in the scientific literature. The panel recognized that these concerns may be impacting in Islanders' lives and recommended providing mental health support to those affected by PFAS exposure. This includes access to talking therapies and other mental health services as needed.

### Reproductive Health

While the only concern raised by the community was fertility, subject matter experts brought up a broader range of issues. These included potential complications like intrauterine growth retardation, reduced birth weight, high blood pressure during pregnancy, and breastfeeding challenges. Studies on birth weight are inconsistent. Some research suggested a possible reduction in birth weight associated with maternal PFAS exposure, but others not. The panel noted that the studies showing a connection often relied on measurements taken later in pregnancy, potentially introducing bias. With regard to pregnancy-associated hypertension and polycystic ovarian syndrome (PCOS). While some studies, like the C8 study, reported an association between PFAS exposure and hypertension in pregnancy and there was a report of increased PCOS cases in a high-exposure area like Ronneby, the panel did not find sufficient evidence across other studies to establish a clear link. This was also no clear evidence of reduced fertility. Overall, the panel was not persuaded that PFAS exposure been demonstrated to have impacts on most reproductive health outcomes, except for some evidence pointing to challenges with breastfeeding. They strongly recommended that mothers, even those exposed to PFAS, should breastfeed, emphasizing that the considerable benefits are likely outweigh any potential risks from PFAS transfer during breastfeeding.

### Other Health Concerns

Additional health concerns explored included some gastrointestinal issues for which there was not good evidence, and changes in liver enzyme levels. The panel noted that while changes in liver enzymes were observed, they generally fell within normal ranges and were unlikely to be clinically significant or associated with poor health outcomes. The panel also looked at neurodevelopmental issues (such as speech and language delay), but the evidence in that area was also not yet clear. With regard to potential impacts on the musculoskeletal system, like osteoporosis and an increased risk of fractures the evidence was also not yet sufficiently clear. The panel was of the view that further research was needed in these areas in order to ascertain whether any risks can be corroborated across studies and what the magnitude of those risks might be.

### Interactions between Services and Islanders:

Islanders reported concerns about the level of understanding and information provided by healthcare professionals regarding PFAS-related health risks. This has contributed to worry and left them with a lack of clarity on appropriate measures to take. GPs in Jersey expressed a need

for up-to-date information and expertise on PFAS. The panel suggests establishing a knowledgeable human resource and a written resource to assist healthcare professionals in addressing PFAS-related concerns.

## Recommendations

While this report is primarily to provide information about the health effects of PFAS, the panel made the following recommendations to government and to health professionals in Jersey:

- PFAS-exposed persons found to have elevated serum cholesterol should have their cholesterol managed in the usual way (e.g. diet, statins).
- When PFAS-exposed people exhibit symptoms which are consistent with kidney cancer or testicular cancer , clinicians should have a higher level of suspicion of cancer than in unexposed populations.
- Regular testicular self-examination should be considered in PFAS-exposed populations.
- Childhood vaccination should be promoted across the whole population to ensure that those less likely to mount a strong vaccine response (such as those exposed to PFAS) are protected through herd immunity.
- Breastfeeding has significant health benefits and should be promoted in PFAS-exposed populations as it is in the wider population.
- Health professionals should have access to accurate information to help manage any concerns about breastfeeding in PFAS-exposed populations.
- Where a person is at increased risk of osteoporosis and is also PFAS-exposed, clinicians should consider a lower threshold for investigating whether osteoporosis is present.
- People who live in communities with increased PFAS exposure should be offered access to talking therapies to support their psychological health and wellbeing.
- A health professional with particular expertise in PFAS and health should be made available to clinicians in Jersey to offer technical support in caring for PFAS-exposed patients.
- A concise knowledge-based resource on PFAS exposure and health should be made available to the public and health professionals in Jersey.

# Non-technical summary

## What are PFAS?

PFAS stands for per- and polyfluoroalkyl substances. These are chemicals made by humans, not found naturally. There are over 14,000 different types of PFAS. They are useful for a lot of things because they don't get damaged by strong chemicals and don't break down easily. This means that they last a long time in the environment and our bodies. PFAS are used in many everyday products like:

- **Firefighting foam**: Helps put out fires quickly.
- **Non-stick cookware**: Pots and pans that food doesn't stick to.
- **Water-resistant clothes**: Jackets and shoes that keep you dry.
- **Food packaging**: Like fast food wrappers and microwave popcorn bags.

These chemicals have been used in more than 200 separate uses since the 1950s. But, because they don't break down, they can build up in water, soil, and even our bodies. This has made people worried about their health.

## Why are PFAS a Problem in Jersey?

In Jersey, there's a problem with PFAS getting into the water. This happened because, at the Jersey Airport, they used firefighting foam that contained PFAS. When this foam was used (mostly when they practiced putting out fires), the PFAS soaked into the ground and mixed with the groundwater. Groundwater is a source of drinking water for many people, so this contamination affects the water some people drink from wells or boreholes.

## What Did the Experts Do?

To understand the PFAS problem better, the Government of Jersey asked a group of experts to look into it in 2023. These experts included scientists and health professionals. They did several things to learn more about the situation:

- **Talked to People Affected**: They listened to stories from people living in Jersey who are worried about PFAS.
- **Reviewed Scientific Studies**: They read a lot of research papers to see what other scientists have discovered about PFAS.
- **Consulted Other Experts**: They talked to other specialists from around the world to get more information.

## What Did They Find Out?

### Heart Health

PFAS can increase the amount of "bad" cholesterol in the blood, known as LDL. High levels of LDL can lead to heart problems like heart disease or strokes. While the experts didn't always find a big increase in these diseases among people exposed to PFAS, they agreed to be careful anyway.

### Cancer Risks

There is some evidence that people exposed to PFAS might have a higher chance of getting kidney and testicular cancers. The experts also looked into bladder cancer, but the evidence was not as strong. For other common cancers like breast or prostate cancer, the studies did not show a significant increase in risk. This doesn't mean there's no risk, but it's not clear yet.

### Immune System and Vaccines

PFAS might affect how well vaccines work. Vaccines help protect us from diseases by boosting our immune system. Some studies suggest that PFAS could lower the effectiveness of vaccines, especially in children. However, there wasn't a clear increase in diseases among people with PFAS exposure. The experts suggested that everyone should still get vaccinated to stay protected.

### Hormones and Metabolism

Some studies suggested that PFAS could lead to problems with hormones and metabolism, such as thyroid issues, being overweight, or having diabetes. But the evidence was mixed, meaning not all studies agreed. So, it's not certain if PFAS cause these problems.

### Mental Health

The experts also found that people worried about PFAS contamination might feel stressed, anxious, or depressed. It's important to offer mental health support to those feeling this way, as stress can impact overall well-being.

### Reproductive Health

There were concerns about PFAS affecting reproductive health, like having trouble getting pregnant, lower birth weights in babies, or high blood pressure during pregnancy. However, the evidence wasn't strong or consistent. For breastfeeding, the experts said that the benefits of breastfeeding are much greater than the possible risks from PFAS.

### Other Health Issues

The experts looked at other possible health problems, like stomach issues, changes in liver function, bone health (like osteoporosis), and development issues in children. The evidence wasn't strong or clear in these areas either, so more research is needed.

### What Do People in Jersey Think?

Many people in Jersey are worried because they don't know much about the risks of PFAS. Some doctors and healthcare workers also said they need more up-to-date information to help their patients.

### What Should Be Done?

The experts made several recommendations to help protect people's health and provide better information:

- **Cholesterol Management**: People with high cholesterol from PFAS should follow normal treatments like a healthy diet or taking tablets.
- **Cancer Awareness**: Doctors look more closely for the signs of cancers like kidney and testicular cancer in people exposed to PFAS.
- **Self-Exams**: Regular self-checks for new lumps on the testicles should be encouraged for those exposed to PFAS.
- **Vaccination**: Everyone, especially those affected by PFAS, should keep up with their vaccinations to stay protected from diseases.
- **Breastfeeding Support**: Mothers should be encouraged to breastfeed, even if they are exposed to PFAS, because the benefits are really important.
- **Accurate Information**: Doctors and healthcare workers need good information about PFAS to help their patients.

- **Mental Health Support**: People worried about PFAS should have access to mental health services.
- **Expert Support**: Jersey should have an expert on PFAS to help local doctors and healthcare workers.
- **Public Information**: Make easy-to-understand resources about PFAS for the public and healthcare workers.

These steps can help keep people informed and healthy while we learn more about the effects of PFAS.

# Contents

# Table of figures

# 1 Background

Per- and polyfluoroalkyl substances (PFAS) comprise a group of over 14,000 synthetic chemicals (this total number is evolving all the time and differs in various reports) used in a wide range of consumer product and industrial applications around the world including, from the 1960s, in fire-fighting foams, the manufacture of non-stick cookware, water repellents, and food packaging (Glüge et al., 2020). Their chemical stability and resistance to degradation (Cousins et al., 2020), which has led to long-term environmental contamination and the toxicological profiles of certain PFAS (*Toxicological Profile for Perfluoroalkyls*, 2021) have driven concerns regarding possible human health effects (Buck et al., 2011).

The main source of concern in Jersey relates to the historical use of PFAS-containing aqueous film-forming foams (AFFF) used in firefighting. PFAS-containing AFFFs have been effective in extinguishing liquid fuel fires but have been identified as a significant source of environmental contamination (Prevedouros et al., 2006). These foams were in use at Jersey Airport and its on-site training facility in the parish of Saint Peter. Groundwater near the airport and, as a consequence, some water supplies became contaminated with PFAS. In 2006, mains water was extended to the area, and therefore the initial exposure from the airport is believed to have been markedly reduced for those households that switched to using mains water, although there will be some ongoing exposure from secondary sources and recirculation of PFAS. While AFFF use and consequent exposure started some years ago; before potential environmental and human health risks from PFAS had become known; the persistence of PFAS in the environment and in the human body mean that there are still concerns today.

In response to the concerns that had been raised, a company called Arcadis were commissioned in 2018 to survey private water supplies for the presence of certain PFAS, and an Officer Technical Group (drawing its membership from several directorates across Infrastructure and Environment, Public Health, Jersey Water and others) was established by the Government in 2019 (*PFAS in Jersey*, 2023).

In 2022, a programme of blood testing was arranged for people who had regularly used borehole water supplies in the affected area as a source of drinking water and had symptoms consistent with conditions that have been associated with PFAS exposure.

In 2023, the Government of Jersey made provision, through the public health team, to commission an independent group of scientists to assess the current situation in Jersey, with regard to PFAS, and make recommendation for actions to be taken. The Independent PFAS Scientific Advisory Panel has three standing members and a standing observer from the public health team. They have regular, publicly livestreamed, meetings where they hear from subject matter experts from around the world, as well as from affected people in Jersey (experts by experience). The key issues brought to light by these contributors as well as those from the scientific literature are explored. The standing Panel members are:

- PFAS Scientific Advisory Panel Chair, Dr Steve Hajioff

  Steve Hajioff is an experienced leader with over 30 years as a practicing doctor and more than two decades in leadership roles in the health sector and public health practice: including being Director of Public Health in the London Borough of Hillingdon - an area with two international airports and other environmental challenges. He has worked for a variety of organisations including the WHO, World Bank, EU, international governments, UK government departments, the Greater London Authority (where he co-led the health impact assessment of the nine mayoral strategies), several NHS bodies, and has advised BMJ, Elsevier, British Standards Institute, Reuters, and many others. He is experienced at chairing scientific panels, having chaired two high-profile guideline development groups for NICE, and also at chairing groups with a high level of political and media engagement; he chaired the Representative Body of the British Medical Association for several years and several scientific fora, regional, national, and international. Steve has also served in Chief Medical Officer roles for a variety of biotechnology businesses and has been involved in many clinical trials.

- PFAS and health expert, Dr Tony Fletcher

  Tony Fletcher PhD is an environmental epidemiologist with over 40 years' work in occupational and environmental epidemiology and risk assessment, with experience of studies of exposure, biomonitoring, and health impacts such as cancer, respiratory disease, and metabolic disorders. He has been researching the health effects of PFAS – Perfluorinated Substances – since 2005, as a member of the C8 Science Panel which led a major investigation on potential health effects of PFOA polluted drinking water in West Virginia and Ohio. More recently he has been working in epidemiology programmes in PFAS-contaminated communities in Ronneby, Sweden and Veneto, Italy. He is currently Associate Professor at the London School of Hygiene and Tropical Medicine, where he has been since 1992, and has held jobs in the past at Public Health England, UKHSA, the International Agency for Research on Cancer (IARC) in Lyon, France, Birmingham University, the MRC Environmental Epidemiology Unit, Southampton and Aston University. He was Adjunct Research Professor in Environmental Health in the School of Public Health, Boston University, Massachusetts, and President of International Society for Environmental Epidemiology.

- PFAS and environment expert, Professor Ian Cousins

  Professor Ian Cousins is Professor of Environmental Organic Chemistry at the Department of Environmental Science at Stockholm University. Professor Cousins leads a research group focusing on understanding the sources, transport, fate, and exposure of organic contaminants and is particularly well known for his research on PFAS. Professor Cousins has extensive PFAS research experience, dating back over 20 years to 1999. Some notable career highlights include being a keynote speaker at international PFAS workshops on multiple occasions and receiving several best paper awards for his research. In recent years, Ian has coordinated a large European multidisciplinary project, PERFORCE3, which focuses on PFAS. He was also chair of the recent international conference, FLUOROS 2023, where the world's leading experts on PFAS gathered. Ian's research currently focuses on better understanding uses of PFAS and investigating suitable alternatives, using analytical approaches to measure PFAS in consumer products and environmental samples, and investigating the transport and fate of PFAS in the environment.

- Standing observer and Deputy Director of Public Health, Grace Norman
  Grace Norman is the Deputy Director of Public Health for Jersey. She began working in Jersey in 2021, and took on the role of Deputy Director in 2022. In the latter role, she has responsibility for health protection, which is the branch of public health which deals with infectious disease and environmental hazards, including PFAS. Grace led the work to arrange PFAS blood testing in 2022 and commissioning the Scientific Advisory Panel. Grace is a standing observer so that she can contribute to the discussion, bringing the island perspective and knowledge from the work already undertaken.

The Panel will be producing five reports over the course of its work programme to provide best available evidence and evidence-based recommendations to the Government of Jersey, other key stakeholders like health services and Jersey Water and to wider society across Jersey and, potentially, beyond.

The five reports are:

1. An interim report on the appropriateness and feasibility of the use of therapeutic phlebotomy to lower PFAS body burden in affected individuals in Jersey.
2. A report on the current state of knowledge about the health effects of PFAS on people and an evaluation of which groups of people may be at increased risk.
3. A review of the range of interventions which may reduce PFAS body burden in those with elevated PFAS levels and the expected impacts, along with recommendations on the nature and extent of serum PFAS testing in both the affected community and the wider population of Jersey.
4. A systematic review of the technologies and methods that may be used to manage PFAS in the environment, along with key strategies for environmental monitoring.
5. An update report taking into account new and emerging evidence from the previous report areas, as well as progress made and any emergent results in the environment or population of Jersey.

All the reports will take due account of the balancing of risks and benefits and also of opportunity cost, including any potential consequences of impacts on services, and will pay particular attention to ensuring that people at greater risk are given additional consideration. The overall approach the Panel will take is:

- Being led by evidence
- Working through consensus
- Involving input from experts by experience and subject matter experts
- Public involvement throughout the process
- Default to meetings being in public
- Ability to work in private where there is a need for confidentiality
- Regular engagement with key stakeholders in addition to Panel meetings
- No surprises

Each report will follow a similar process, with an initial draft scope being agreed within the Panel and consulted on with stakeholders (including Islanders) before a final scope is developed. There will then be a series of systematic reviews of the available, relevant scientific literature and the consideration of evidence from subject matter experts and experts by experience. These draft reviews and meeting summaries will be shared in advance of the publicly accessible Panel meetings,

where they will be discussed, and draft inferences and recommendations arrived at. A draft report will be prepared, integrating the various workstreams and will be shared with Government of Jersey through public health (the commissioners of the process) and with the public for consultation and comment. The consultation findings will be reviewed by the panel and, where appropriate, the report revised. The final report will be shared with the Government to consider the findings and launched through one or more public meetings. The Panel meets normally once a month online and the public can observe and email in comments, the agenda and minutes of the meetings are publicly available on the Jersey Government website: PFAS in Jersey (gov.je)

In order to optimise the use of time, there may be some time overlap between consecutive reports, with reports processes starting before the previous report has been finalised.

# 2 Introduction and approach

The assessment and quantification of any effects resulting from environmental contamination is a complex process. Even if there is sufficient high-quality evidence to quantify a risk, translating a population level risk to the health of an individual or group of individuals is difficult. In a similar way, the appraisal and evaluation of scientific studies is a complex matter, and several criteria are crucial to that assessment. It is not uncommon that a scientific study appears, on face value, to say something very clear, but does not really to have strong evidence that it is the case. Even if there is strong evidence in a particular study, different places and people have distinct characteristics that can make such findings less relevant.

Because of that level of complexity, the Panel has decided to explain some of those concepts, techniques, and caveats here; better to offer context to the discussion of specific findings.

## 2.1 Terms used to describe the evidence in this report

In this report, we will be reviewing the evidence from a variety of sources and describing what we have found. There are two key factors which we need to address. Firstly, we must assess whether research has looked at a particular condition or situation at all. If there is no research on a particular illness in the context of PFAS exposure, it would not be appropriate for us to say that there is likely to be a link. It would be equally inappropriate for us to say that there is no link as an absence of evidence does not constitute evidence of absence. In such a situation it might be appropriate to refer to refer to any link between a condition and PFAS exposure as “unknown” or to say that there is no evidence of a link. This conclusion should never be interpreted as the panel saying that such a link does not exist, merely that we do not have the evidence to conclude one way or another.

The second factor is, where there is evidence, whether that evidence is reliable, relevant, and consistent. If there is evidence from a range of relevant, high-quality studies that a particular condition is linked to prior PFAS exposure, then we may refer to the link as “likely” or “probable”. It is unusual for scientists to refer to a link as “proven” unless there really is a lot of consistent evidence. In practice, there is no difference in the sort of response the panel would recommend to a “probable” or “likely” link versus a “proven” link. In these situations, there is enough evidence to act as though the link were proven and take a precautionary approach for public health risks.

There is also the situation where there is some evidence pointing to a link between a condition and PFAS exposure, but there is more, or better quality, or more relevant evidence that does not find a link. These situations require careful judgement. For example, a link may be described as being “unlikely” when the link is judged to be more likely to have been found by coincidence, the study is reporting a different type of PFAS exposure, or has poor study design, and the studies that have not found a link are big and robust.

It should also be noted that the evidence base continues to evolve and the likelihood of a particular outcome may change as more research is published.

## 2.2 Key concepts in environmental epidemiology

Environmental epidemiology is the study of how factors in the lived environment can affect the health and wellbeing of people and communities(Pearce, 1996). The scope of environmental epidemiology is broad and many different things that people might be exposed to (known as “exposures”) are considered. This ranges from chemicals; either synthetic or naturally occurring; to

noise, radiation, or climate, the range of exposures environmental epidemiologists study is very broad (Nieuwenhuijsen, 2005).

### 2.2.1 Measurement of exposure

In order to undertake any analysis, it is necessary to assess and to measure the nature of the exposure. There are different approaches that can be taken, some are more reliable, some are easier to do and some of which are particularly suited to a specific type of exposure. These can include things like monitoring the air, the water or the soil, measuring the amount of something in people, plants or animals, using interviews or questionnaires within communities or the use of mapping tools (GIS) to compare known characteristics about a place with who is in or near that place ("Exposure Assessment in Environmental Epidemiology," 1997). Using these tools, the extent and magnitude of the exposure can be quantified.

### 2.2.2 Assessing impacts on populations

#### *2.2.2.1 Types of study*

Because environmental epidemiology is dealing with potentially harmful things that people have been exposed to, it would not be ethical to expose people to them and look for the outcomes. Therefore, “observational studies” are appropriate. There are several different types of observational studies, each having different strengths, weaknesses, and ethical considerations. Observational studies are designed to observe and analyse individuals in their natural settings without any intervention by the researchers. They aim to identify associations between certain variables, such as exposures or other risk factors and health outcomes. There are several types, but of particular value are those where contrasts in levels of exposure or differences in relevant risk factors can be identified. Those most relevant to environmental epidemiology are:

- **Cohort Studies**: Cohort studies follow a group of people over a specific period, tracking their exposure to risk factors and monitoring their health outcomes. This type of study can help to identify potential causes or risk factors for diseases. They can also be useful for looking at whether different levels of exposure within a community are associated with different health outcomes and for identifying new patterns of health outcome as time passes and the duration of exposure gets longer.
- **Case-Control Studies**: In case-control studies, researchers compare people with a particular health outcome (cases) to those without it (controls). By analysing past exposures or characteristics, researchers can determine potential associations between risk factors (including exposures) and diseases or health states.
- **Cross-sectional Studies**: Cross-sectional studies collect data at a specific point in time to assess the prevalence or frequency of a condition or exposure in a population. They provide a snapshot of the population and help generate hypotheses for further investigation.
- **Ecological Studies**: Ecological studies look at potential associations between exposures and health outcomes across populations as a whole, rather than per individual person. They are particularly useful when individual level data is difficult or impractical to get (*What types of studies are there?*, 2016).

Each of these study types has different strengths and weaknesses. Cohort studies provide strong insights, but they can take a very long time to get results from and may need a very large number of people to show meaningful results so they can be impractical in many situations. Case control studies can be a good compromise if the expected health outcomes are known, but are less useful where there are many different potential health impacts. Because cross sectional studies are a snapshot in

time, they may not give a clear understanding of what causes what (causality). They are, nevertheless, often more straightforward, and quicker to conduct than some of the other study types. Ecological studies are particularly prone to a bias known as ecological fallacy; this is discussed below.

#### *2.2.2.2 Outcome measures*

There are several different ways of assessing impact of exposure, with two main measures. The first is a group of ratio measures which compare the risk of disease in (for example) exposed versus unexposed as the ratio of the risk, or likelihood or incidence rate in one group relative to the other. These may be called relative risk, rate ratio, hazard ratio or risk ratio. In case control studies this is derived differently. One starts with whether someone with the health outcome or not (i.e. a case or a control), has the exposure of interest. The ratio is then the ratio between the likelihood or odds that a person with the condition had been exposed in the past and the likelihood that someone without the condition had been exposed. Conveniently this ratio, called the odds ratio, is quite similar to the relative risk.

Secondly, impact can be shown with difference measures, sometimes called the Attributable Risk. This is calculated as the difference in the rate (or risk or prevalence) of a condition between an exposed group and the unexposed. It therefore gives an indication of how many cases of the condition are potentially a result of the exposure (assuming the observed risk is causal) and, therefore, the potential benefit from any reduction to that exposure(Rothman et al., 2008).
More information about outcome measures can be found in the section on understanding risk, later in the document.

### 2.2.3 Challenges in environmental epidemiology research

As in most areas of scientific research there can be challenges in interpreting the outcome data and sometimes those challenges can affect how robust the authors' conclusions are.

#### *2.2.3.1 Bias*

In epidemiological studies, several types of bias can affect the reliability and validity of research findings.

- **Selection bias** occurs when the participants included in the study are not representative of the target population, potentially due to the way they were recruited or chose to participate.
- **Information bias** arises from systematic errors in the way data on exposure or outcome is collected or measured, which can misclassify study variables.
- **Confounding bias** happens when the observed effect of an exposure on an outcome is changed by another variable that influences both the exposure and the outcome, but is not controlled for in the analysis (Vandenbroucke et al., 2007) For example, in a study exploring the impact of coffee consumption on heart disease, stress could be a confounding factor, as individuals who drink more coffee might also experience higher stress levels, which independently increase the risk of heart disease.
- **Ecological fallacy** (also known as aggregation bias) occurs when assumptions about individual outcomes or exposures are incorrectly inferred from data collected at the group or population level. This can lead to misleading conclusions(Rothman et al., 2008). All these types of bias can affect how well the study's findings reflect the truth of what is being studied and can result in either over- or under-estimations of the factors being explored. This is why it is important that scientific findings are reviewed by experts in their field when considering the implications and making recommendations.

#### *2.2.3.2 Chance association*

Chance association in epidemiological studies refers to the possibility that observed associations between an exposure and an outcome are due to random variation rather than a true causal relationship. This can occur due to the inherent variability in data, particularly when sample sizes are small or when multiple comparisons are made. Statistical tests, such as p-values and confidence intervals, help assess whether observed associations are likely to be real or simply due to chance. However, these tests are not foolproof, and even statistically significant results can sometimes be attributed to chance, especially if they are not consistent with other findings (Porta, 2016)

#### *2.2.3.3 Association or causation?*

An association indicates a relationship or correlation between two variables, meaning that changes in one variable correspond with changes in another. Such an association, however, cannot reliably be assumed to represent a causal relationship. Demonstrating causation requires a stronger body of evidence than demonstrating association and often involves considering criteria like temporality, strength of association, consistency across studies, specificity, dose response and biological plausibility (Hill, 1965).

### 2.2.4 Mitigation of challenges in epidemiological research

Many of the challenges outlined above can be effectively manage through robust study design, careful data collection, data triangulation (assessing and drawing upon evidence from different types of study) and additional data collection or data analysis. Techniques like stratification or matching on the basis of potentially confounding variables, multivariate analysis, nested studies and triangulation with other studies and other types of research all have an important role in managing bias and better understanding the real-world relevance of associations(Vandenbroucke et al., 2007).

While it is rare to see a scientific study that has no shortcomings, even studies with a degree of compromise are still very important in growing the scientific knowledge base.

## 2.3 Understanding risk

Risk is a complex concept that permeates many disciplines, from finance and engineering to pharmacology to public health and environmental science. While the nuances of risk might vary depending on context, certain foundational principles, and concepts, can be identified. At its core, risk refers to the possibility of an adverse or unfavourable outcome. In other contexts, risk is quantified as the product of the probability of an event occurring and the consequences or impact of that event consistently (Kaplan & Garrick, 1981). In the context of PFAS, it might refer to the likelihood of a particular adverse health outcome with a given pattern of exposure.

### 2.3.1 Risk perception

Risk perception is the subjective judgment that individuals make about the severity and probability of a risk. This can be influenced by the extent to which the risk is in the control of the person, their cultural beliefs, and media exposure as well as how they understand and interpret scientific data. It is important to note that, perceived risk often differs markedly from actual risk, which can impact decision-making and behaviours (Slovic, 1987). An example of this is where a person might believe air travel (a low-risk activity) to be very dangerous but be comfortable with smoking cigarettes (a higher risk activity).

### 2.3.2 Risk assessment

Risk assessment is a systematic process to identify potential hazards, evaluate their likelihood, and determine any potential consequences. It typically involves hazard identification, dose-response assessment, exposure assessment, and risk characterisation ("Risk Assessment in the Federal Government: Managing the Process," 1983).

### 2.3.3 Total risk and attributable risk

**Total risk** refers to the overall probability or chance of an individual developing a disease or experiencing an adverse event within a specified time frame. It gives a broad perspective on the disease burden in a particular population or subgroup (Rothman et al., 2008). In contrast, **attributable risk** (often termed "risk difference" or "attributable risk among the exposed") quantifies the portion of the total risk that can be attributed to a specific exposure. Essentially, it measures the difference in risk between those exposed and those not exposed to a particular factor. It provides insight into how much of the disease burden might be reduced if the exposure were eliminated, assuming a causal relationship between the exposure and the disease (Levin, 1953). Attributable risk is particularly useful in public health as it helps in prioritising interventions by determining the potential benefits of addressing specific risk factors.

### 2.3.4 Absolute or relative risk

In medical and epidemiological studies, absolute risk denotes the probability of an event happening in a specific group, while relative risk is a ratio comparing the risk in two different groups. A relative risk of one implies equal risk in both groups, greater than 1 indicates increased risk, and less than 1 denotes decreased risk in the exposed or intervention group (Rothman et al., 2008).

### 2.3.5 Population and individual risk

Population risk refers to the overall risk of a disease or adverse event in a specified population over a given period. It provides a broad perspective on the disease burden and can be instrumental in guiding public health interventions and resource allocation (Rose, 1992). On the other hand, individual risk denotes the probability that a specific individual will develop a disease or experience an adverse event in a given time frame. Factors that influence individual risk can include genetics,

lifestyle, and specific exposures, among others (Khoury et al., 2013). It is important to note that an individual's risk might differ substantially from the overall population risk because people have different combinations of risk factors.

### 2.3.6 Risk factors or risk markers

Risk factors and risk markers are terms frequently employed in epidemiology and medical research to describe variables or attributes associated with the probability of disease occurrence. However, their implications are distinct. Risk factors are attributes or exposures that have been shown to directly influence the likelihood of disease occurrence. They often carry a causal relationship with the disease. For example, smoking is a well-established risk factor for lung cancer, given that there's substantial evidence suggesting smoking can cause lung cancer (Doll & Peto, 1978). On the other hand, risk markers (or risk indicators) are attributes that are associated with an increased probability of disease but are not necessarily causative. They can serve as indicators of a higher risk of disease but do not directly result in the disease. Elevated resting heart rate, for example can be a risk marker for having a heart attack in the future, but it does not cause heart disease, so it is not a risk factor. Likewise, weight loss as a symptom is associated with an increased likelihood of having cancer, so is a risk marker (Nicholson et al., 2018).

### 2.3.7 Uncertainty

Uncertainty is an inherent aspect of risk. It acknowledges the limitations and variability in data, methods, or understanding. Distinguishing between variability (natural differences) and true uncertainty (lack of knowledge) is crucial for making informed decisions (Morgan & Henrion, 1990) but this can be difficult, especially with lower quality evidence. It is particularly important to acknowledge uncertainty in areas where there is limited or complex evidence.

### 2.3.8 Risk communication

Effective risk communication conveys information about risks to the public, stakeholders, or decision-makers. It is crucial in shaping perceptions, alleviating unnecessary fears, and highlighting genuine risks, and guiding informed decisions. It involves clarity, transparency, and often requires tailoring messages to different audiences (Fischhoff et al., 1993).

### 2.3.9 Risk management

Once risks are assessed and understood, risk management comes into play. It involves decisions and actions taken to mitigate, transfer, avoid, or accept the identified risks. Factors considered include the magnitude and nature of the risk, cost of intervention, and the values and preferences of stakeholders (Haimes, 2009). Where appropriate, risk treatment or mitigation plans are developed. These can involve accepting, transferring, avoiding, or reducing the risk ("ISO 31000:2018. Risk management — Guidelines," 2018). Continuous monitoring and review are essential to ensure that risk strategies remain effective. Effective risk management often requires a combination of approaches, tailored to the specific context and nature of the risks involved (Williams et al., 2017).

## 2.4 Critical appraisal of scientific evidence

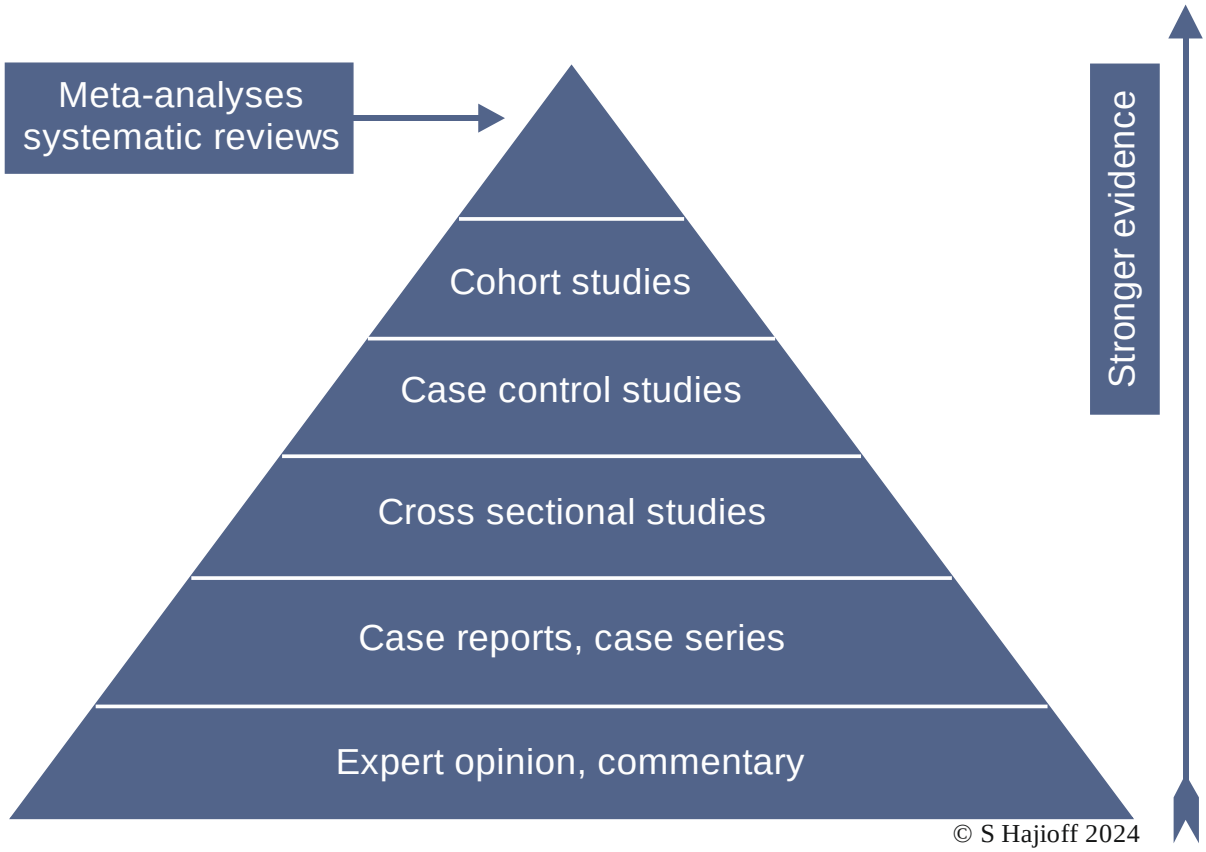
Critical appraisal is a structured process where scientific studies are evaluated to assess how truly robust the researchers' findings are and whether any conclusions that are drawn can really be supported by the evidence.

### 2.4.1 Key factors to consider in critical appraisal

#### *2.4.1.1 Study type and the evidence ladder*

The evidence ladder is used to rank different types of research according to their potential for bias. This aids researchers and clinicians in evaluating the quality and trustworthiness of evidence, guiding better-informed decisions in public health and clinical practice(Sackett et al., 2005).

*Figure 1: The evidence ladder for environmental exposure studies (RCTs omitted)*




The strongest types of study, in terms of evidence, are systematic reviews and meta-analyses. Because they have already synthesised data from multiple studies and looked at how consistent the findings are, they are the least prone to bias.

Interventional studies, like randomised controlled trials (RCTs), are, potentially very strong, but it is not ethical to conduct interventional studies on humans with potentially harmful exposures. Therefore, they are usually unsuitable for epidemiological research on environmental toxins. Interventional toxicological studies in animals, however, can be a useful adjunct to epidemiological evidence and can also give an indication of appropriate research questions for future epidemiological studies.

Among observational studies, cohort studies are usually considered the least prone to bias, followed by case control studies followed by cross-sectional studies, but there are, of course, practicability

considerations. For example, descriptive studies which provide general patterns of disease incidence based on registries, but little information on exposures, tend to be less informative.

At the base of the hierarchy are case reports and expert opinions, which, while insightful, are considered weak forms of evidence due to the high potential for subjective bias.

Some studies are referred to as “registry studies”. In these studies, one or more data sources (such as electronic medical records) are used to conduct the study. This can be done as a cohort study, a case control study, or a cross-sectional study. The registry is the tool used for the study, and so registry studies are not considered a different study type for critical appraisal purposes.

#### *2.4.1.2 Sampling*

The method used to select participants, the sample size, and the response rate can influence study validity and generalisability.

#### *2.4.1.3 Confounding*

The previous section discussed bias (including confounding) and what tools may be used to minimise that bias. A key component of critical appraisal is assessing the extent to which those tools and methods have been employed by the researchers. When assessing the risk of confounding, looking at whether stratification, multivariate analysis or matching has taken place, can be important.

#### *2.4.1.4 Reliability*

Reliability refers to the consistency and repeatability of a measurement tool or method. A reliable study produces comparable results when replicated under the same conditions (Norman & Cairney, 2015).

#### *2.4.1.5 Validity*

Validity addresses the accuracy of a study, ensuring that the tool or method measures what it intends to measure. It is often categorized into different types, such as internal validity (extent to which a study is free from biases) and external validity (generalisability of study results to wider populations or settings)(Rothman et al., 2008).

#### *2.4.1.6 Setting*

The setting of the study is also crucial, as it provides context to the conditions under which the study was conducted, influencing its generalisability. For example, research done on people in a working environment cannot always be generalised to people in their homes.

#### *2.4.1.7 Applicability*

Applicability (or relevance) ensures that the evidence is pertinent to the specific population, compounds, or exposure type of interest. Applicability considers whether the study's participants, interventions, and outcomes align with the scenario where the findings will be used(Guyatt et al., 2015).

#### *2.4.1.8 Statistical significance*

Statistical significance is a fundamental concept in research that helps to differentiate between outcomes likely due to genuine effects and those that are more likely to have arisen by chance. When a result is deemed statistically significant, it suggests that the observed association or effect is unlikely to have occurred randomly. In hypothesis testing, this is often determined by comparing the p-value (a measure of probability) to a predetermined significance level, commonly set at 0.05. If the p-value is less than 0.05, the result is typically considered statistically significant. However, it is crucial

to understand that statistical significance is not the same as a cutoff between evidence of harm or safety. It helps to provide a guide to the strength of evidence, but a non-significant result may reflect the study being simply too small to detect the risk. Conversely, a small “significant p-value" may be found in a large study but related to a small effect. Thus, significance does not necessarily equate to practical importance. A result can be statistically significant but have minimal real-world impact. Additionally, with larger sample sizes, even trivial differences can become statistically significant, emphasizing the need to consider effect size and clinical relevance alongside p-values. It should also be noted that even if an association is found to be statistically significant with a p-value of 0.05, it could have happened by chance; at that significance level you would expect a spurious association 5% of the time (Sullivan & Feinn, 2012).

### 2.4.2 In summary

Extracting the most important and useful content from the academic literature and interpreting it appropriately is a complex and time-consuming task. Studies often disagree with each other, and some might appear useful, but for technical reasons explained above may be misleading when applied to the specific context in Jersey.

## 2.5 The chemistry of PFAS

This is a summary of a presentation given by Professor Cousins at the Panel meeting on 4/3/24. Further detail is available in the minutes of the meeting.

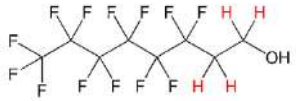
Per- and polyfluorinated alkyl substances (PFAS) represent a group of chemically related substances used across a wide array of applications due to their unique properties. This section clarifies the terminology, chemical structure, and regulatory aspects surrounding PFAS, with an emphasis on their environmental and health implications.

### 2.5.1 Definition and classification

PFAS are broadly categorized based on their chemical structure:

- **Perfluorinated**: These compounds have carbon chains fully saturated with fluorine atoms, replacing all hydrogen atoms.

- **Polyfluorinated**: In these substances, not all hydrogen atoms in the carbon chain are replaced by fluorine.



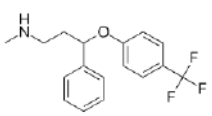
- **Alkyl Substances**: This term refers to compounds containing fully saturated chains of carbon atoms, and not rings of unsaturated carbon atoms.

There is no single globally approved definition of PFAS. The Organisation for Economic Co-operation and Development (OECD) defines PFAS as "fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (OECD, 2021). This definition encompasses substances with at least one $-CF_2-$ or $-CF_3-$ group, including molecules that have a ring of unsaturated carbon atoms elsewhere, expanding the number of substances defined as PFAS compared to the previous narrower definition. This broad OECD definition includes both alkyl substances and those containing rings of unsaturated carbon atoms, which can be confusing because the name “PFAS” implies that only alkyl substances should be included in the definition. The UK regulators have their own less broad definition of PFAS than that proposed by the OECD (i.e. “fluorinated substances that contain at least one fully fluorinated methyl carbon atom (without any hydrogen, chlorine, bromine or iodine atom attached to it), or two or more contiguous perfluorinated methylene groups ($–CF_2–$).”) (*Regulatory management option analysis (RMOA)*, 2023).

### 2.5.2 Types of PFAS and their properties

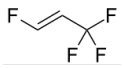
The extensive variety of PFAS includes compounds in various forms—solids, liquids, gases; and with diverse properties—reactive, inert, soluble, insoluble, volatile, non-volatile, mobile, immobile, and ranging from highly toxic to relatively non-toxic. Structurally, they can be long or short-chained, linear, or branched, anionic, cationic, or zwitterionic. Examples include:

- **Fluoxetine (Prozac)**: An antidepressant fitting the PFAS definition.



- **Polytetrafluoroethylene (PTFE, Teflon)**: A fluoropolymer used in non-stick cookware.

- **Hydrofluoroolefin**: Employed as a refrigerant and air conditioning agent.



This diversity demonstrates the ubiquity and functional versatility of PFAS in modern society.

Research is generally focused on specific subsets of PFAS, such as:

- **Perfluoroalkyl carboxylic acids (PFCAs)**: Ranging from C2 to over C20 in carbon chain length. Examples include (with 4 to 12 carbons):
    - perfluorobutanoic acid (PFBA)
    - perfluoropentanoic acid (PFPeA)
    - perfluorohexanoic acid (PFHxA)
    - perfluoroheptanoic acid (PFHpA)
    - perfluorooctanoic acid (PFOA
    - perfluorononanoic acid (PFNA)
    - perfluorodecanoic acid (PFDA)
    - perfluoroundecanoic acid (PFUnDA)
    - perfluorododecanoic acid (PFDoDA)
- **Perfluoroalkane sulfonic acids (PFSAs)**: Typically, C4, C6, C8, or C10, although other lengths are present:
    - perfluorbutanesulfonic acid (PFBS)
    - perfluorohexanesulfonic acid (PFHxS)
    - perfluorooctanesulfonic acid (PFOS)
    - perfluordecanesulfonic acid (PFDS)

These compounds form anions when their terminal carbons in the acidic functional groups lose hydrogen atoms. They are, or were, used widely due to their effective surfactant properties, as a result of having a hydrophobic “tail” and a hydrophilic “head”. PFCAs and PFSAs belong to the group of PFAS known as perfluoroalkyl acids (PFAAs). They have been used in the manufacture of fluoropolymers like PTFE and in firefighting foams, and were also present as impurities in textiles, carpets, and food packaging materials. Much of the research has focused on these PFAS because of their widespread presence in the environment, wildlife, and humans and because they have established toxicity data and there are analytical methods available to measure them.

### 2.5.3 Precursors

Precursors, such as perfluoroalkyl sulphonamides and fluorotelomer alcohols, are PFAS which degrade in the environment and in organisms to form other (more stable) PFAS (usually the abovementioned PFAAs). This complicates environmental management and monitoring. For example, fluorotelomer alcohols degrade in the environment and within organisms to form PFCAs. While precursors can degrade to form PFAAs, PFAAs are highly stable and do not degrade into other PFAAs in the environment or in the human body (e.g. PFHxS cannot transform into PFOA) (Cousins et al., 2020; Prevedouros et al., 2006).

### 2.5.4 Aqueous Film Forming Foams (AFFF) and chemical fingerprints

Aqueous Film Forming Foams (AFFF) used for firefighting prominently incorporate PFAS because of the ability of these strong surfactants to spread an aqueous film over fuel fires and thus effectively extinguish the fire. Over the years, however, concerns over the bioaccumulation and environmental persistence (discussed below) of the PFAS in the AFFF have led to shifts in chemistries of AFFF. Historically the 3M PFAS-based foams containing PFSAs (especially PFOS and PFHxS) and PFCAs (notably PFOA) dominated the market. Since 3M discontinued the manufacture of AFFF in 2002, there has been a shift to other PFAS-based foams made by other manufacturers (so called fluorotelomer-based AFFF) and eventually towards fluorine-free alternatives in many countries and regions; Sweden, for example.

The complex mixtures of substances in AFFF are unique to a particular product. Understanding the "chemical fingerprints" of these products in environmental samples, which include the presence of specific isomers or breakdown products, is crucial for tracking and mitigating environmental contamination.

The only AFFF products which have PFOS and PFHxS as markers are 3M Lightwater AFFF products. These were initially used in the US, from 1967, and were also used in Jersey and elsewhere. The presence of those specific PFAS in Jersey, suggest that it is these products, rather than something else, that are the primary source of PFOS and PFHxS contamination. Most users transitioned away from 3M Lightwater to fluorotelomer-based products in the early 2000s when 3M discontinued manufacture of AFFF in 2002. Some later transitioned to fluorine-free foams (3F). PFOA is a marker of both 3M Lightwater AFFF products and fluorotelomer-based AFFF products. A unique marker of fluorotelomer-based foams is 6:2 fluorotelomer sulfonate.

### 2.5.5 Bioaccumulation

The tendency of PFOS, PFHxS and PFOA to bioaccumulate in biological tissues raises concerns about their long-term health impacts. Regulatory bodies have identified long-chain PFAAs as particularly bioaccumulative (as they bioaccumulate in humans), emphasizing the need for stringent regulatory controls for PFAAs with eight carbons and greater (i.e. with 7 or more perfluorinated carbons) and PFSAs with six carbons and greater (i.e. with 6 or more perfluorinated carbons). So PFOA and PFCAs with longer perfluorinated carbon chains are bioaccumulative and PFHxS and PFSAs with longer perfluorinated chains are also bioaccumulative. PFSAs are relatively more bioacculative than PFCAs with equivalently long perfluorinated chains because of the special effect of the sulfonate functional group (Brunn et al., 2023; Buck et al., 2011).

### 2.5.6 Environmental Accumulation

The chemical stability of PFOS, PFOA, and PFHxS due to strength of the carbon-fluorine bonds leads to their persistence in the environment, posing significant challenges for remediation. Efforts to monitor and reduce environmental levels of these pollutants are ongoing, but their inert nature complicates effective degradation and removal strategies (Cousins et al., 2020; Prevedouros et al., 2006). This will be explored in more detail in Report 4.

### 2.5.7 Regulatory and environmental concerns

PFAS are notably persistent in the environment, which complicates their management and regulation. In response, Denmark, Germany, the Netherlands, Norway, and Sweden have proposed a REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) restriction for all PFAS meeting the OECD definition. It is recognized that PFAS have diverse properties (e.g. different toxicities), but they are all highly persistent in the environment. Additionally, there is an ongoing

restriction proposal specifically targeting PFAS in firefighting foams, with a proposed 10-year phase-out, which is also currently under consideration at the European Commission.

PFAS encompass a broad and complex category of chemicals that pose significant challenges due to their persistence, bioaccumulation, and widespread use. Ongoing research and regulatory efforts aim to better understand and mitigate their health and environmental impacts. Looking forward, enhanced analytical methods and comprehensive toxicological data are increasingly important for guiding effective policy and industry practices.

# 3 Evidence from experts by experience

To understand better the context and lived experience of Islanders who live or have lived in the plume area, or with elevated levels of PFAS in their bodies, the Panel invited members of the public to give evidence on how they feel that PFAS exposure has affected their health. This was done either by a discussion with the panel or by written testimony, which was collected in November and December 2023. The panel refers to PFAS exposed persons who may have health problems they attribute to the PFAS exposure as "experts by experience". Because of the sensitive nature of personal health information, people were offered a choice; either to meet the Panel in a public meeting or a private meeting. All written testimonies were treated as confidential. While the public meetings were all open meetings, the Panel, when writing the minutes, did not associate any specific medical condition with a given individual. The reason for this is because, even if a person is happy for their personal health information to be public now, that view may change over time. In addition, the identification of named individuals would not make a difference to the Panel's findings. Finally, in the case of rarer diseases or disease types, we have captured them in the minutes and in this report in very general terms, so as not to inadvertently identify any individuals. Overall, the panel formally received evidence from thirteen Islanders.

The purpose of hearing these testimonies is to gain insights into several areas. We wanted to ensure that we had looked at specific conditions that were of concern to people, even though they were not necessarily the subject of high-quality research. This was in order to offer as much information and reassurance to potentially affected Islanders as the scientific literature would allow. Secondly, we wanted to gain insight into what the affected Islanders' care journeys were like; were healthcare professionals knowledgeable about PFAS? Were healthcare professionals engaged with how the Islanders felt about their illness and their PFAS exposure? How was the journey through the government PFAS testing programme? Finally, and most importantly, to understand the impacts of illness and PFAS exposure on Islanders' social and emotional wellbeing, and what their specific concerns are for the future.

In addition to these, anticipated, benefits to the Panel's work, we also were able to be aware of other related beliefs and concerns; for example, a belief that it was possible for one PFAS to become another in the body (this is not possible). These insights allowed us to offer clarifications and explanations and, in this case, build some additional content on the chemistry of PFAS into the report.

## 3.1 Health issues of concern

A wide range of conditions were discussed as well as some additional matters relating to how services supported the affected Islanders and to impacts on the person's wider health, wellbeing, and family life. Those issues are summarised below.

### 3.1.1 Cancer

Islanders mentioned concerns about several cancers. These included some of the more common cancers, such as breast cancer, prostate cancer, and cancer of the bowel, as well as some that were less common. Cancers of the blood (these are things like lymphomas or leukaemias and related conditions) came up in the discussion, as did cancers of the urinary system (the organs from, and including, the kidney, down to and through the bladder and to the point where urine leaves the body), cancers of the uterus (womb), the skin and the mouth.

#### 3.1.2 Elevated cholesterol

This was brought up by a few people, and there were also discussions about the potential impacts of high cholesterol.

#### 3.1.3 Gastrointestinal problems

More than one Islander brought up issues to do with the stomach and the intestines, ranging from indigestion and oesophageal reflux and related symptoms to unusual bowel habit.

#### 3.1.4 Sexual health and fertility

Issues around sexual health and fertility were raised a couple of times as well.

#### 3.1.5 Autoimmune disease

Diseases where the body's immune system attacks parts of the body (like rheumatoid disease and lupus) were also brought up.

#### 3.1.6 Psychological and emotional wellbeing

In addition to the conditions outlined above, several Islanders talked about mental health consequences from PFAS exposure and PFAS-attributed illnesses. Some of the themes highlighted were anxiety and worry, moral injury, or feelings of guilt over children being exposed to PFAS, moral injury over children being exposed to traumatising medical conditions and environments, and financial concerns. Mistrust was also a theme that featured.

#### 3.1.7 Interaction with health services

Several themes were highlighted here. Most health professionals with whom the Islanders interacted did not seem to have significant expertise in PFAS which undermined reassurance. Islanders also expressed that healthcare professionals often had different views on whether their condition is attributable to PFAS than they do themselves. This contributed to their concerns.

### 3.2 Discussion

Several important issues have been highlighted by this process. The health conditions identified are being given additional attention during the reviews of the scientific literature and add to the richness of the report. The issues around psychological wellbeing also suggest potential areas to prioritise in the Panel's recommendations. This is also the case for those issues identified in interaction with healthcare and related services.

# 4 Evidence from subject matter experts

This section summarises the opinions expressed by the subject matter experts who presented at the Panel's meetings. These views will form part of the panel's deliberations but do not necessarily directly reflect the Panel's views. In addition, some of the views expressed relate to matters to be considered in future reports. That material will be used by the panel during the development of those reports. It should be noted that not all the PFAS that are highlighted by the experts in their research are present in Jersey, nevertheless they help illustrate the issues related the breadth of PFAS exposure and related issues internationally.

The subject matter experts with whom the panel met are:

**Professor Jane Hoppin** is a professor at North Carolina State University, an Environmental Epidemiologist, and currently runs a large study of PFAS exposed people in North Carolina. She was also a panel member on US (United States) National Academies of Science, Engineering and Medicine that made recommendations for health care and follow up of PFAS exposed people. Most recently served on the International Agency for Research on Cancer (IARC) Panel that evaluated PFOA and PFOS for carcinogenicity.

**Dr Gloria Post** is a human health toxicologist and risk assessor in the State of New Jersey Department of Environmental Protection (NJDEP). Dr Post has worked in the NJDEP Division of Science and Research, since 1986, with responsibility for developing health-based guidelines for contaminants found in New Jersey's environment. She is also a member of the New Jersey Drinking Water Quality Institute (DWQI), an advisory group which recommends drinking water standards to the Commissioner of NJDEP Also, she was a member of a National Academies of Science and Medicine committee that planned a workshop on human health PFAS research for the federal government, the USEPA (United States Environmental Protection Agency) Science Advisory Board panel that reviewed the scientific basis for the proposed federal drinking water standards for PFAS, and the International Agency for Research on Cancer (IARC) recent evaluation of PFOA and PFOS.

**Dr Jamie DeWitt** is a professor of Environmental Molecular Toxicology at Oregon State University and Director of their Environmental Health Science Centre. She has worked with PFAS in the laboratory since around 2005, looking at what PFAS does to laboratory models and investigating the immune system response. Dr DeWitt has served in several different advisory capacities (as have Professor Hoppin and Dr Post) and serves as an expert witness for plaintiffs (*a person who brings a case to court)*. Most of her work includes looking at laboratory models, and she supports different organisations in decision making.

**Dr Sue Fenton** is a reproductive endocrinologist, having worked for 11 years in the USEPA (*United States Environmental Protection Agency)* specifically focused on PFAS and other environmental contaminants and their health effects. Dr Fenton then moved to the National Institute of Environmental Health Sciences for 14 years and expanded her work specifically looking at development and targeting the effects of chemicals such as PFAS. She is now the Director of the Center for Human Health and the Environment at North Carolina State University.

**Dr Christel Nielsen** is an environmental epidemiologist from Lund University in Sweden. Dr Nielsen works on health effects in children and pregnant women in Ronneby, Sweden, which also has PFAS contamination because of exposure from firefighting foam.

The sections below represent summaries of the salient points of the presentations given by the experts to the Panel. These are the views expressed by those experts and do not necessarily reflect the views of the panel. A fuller account of those presentations is available in the minutes of the panel meetings.

## 4.1 What are the Human Health Effects of AFFF (aqueous film forming foam) & other PFAS by Professor Jane Hoppin

Professor Hoppin has been involved with a study of the contamination of Cape Fear River basin in North Carolina, which is the largest river in North Carolina on the East Coast of the USA. Cape Fear River basin supplies more than 1.5 million people with drinking water. The study (*Gen X Exposure Study*, 2024) followed 3 different communities: 1) those at the mouth of the river, who were drinking water downstream from a chemical manufacturing site, 2) those living near where a chemical manufacturing plant discharged into the river, and 3) a community upriver of the plant, to understand PFAS exposure .

Per- and polyfluoroalkyl substances (PFAS) comprise a large class of chemicals, encompassing over 14,000 substances. In the United States and other populations, four specific PFAS are commonly measured: perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA). Research on PFAS is complicated by the fact that individuals are typically exposed to mixtures of multiple PFAS rather than a single type, and these mixtures vary across different populations. This variability makes it challenging to identify the specific role of each contaminant and complicates efforts to gather comprehensive exposure data and establish clinical follow-up recommendations.

The study involved a cohort of 1,000 individuals in North Carolina with high levels of PFAS exposure. The health effects of PFAS were reviewed, drawing on the findings from the National Academies' report "Potential Health Effects of PFAS | Guidance on PFAS Exposure Testing and Clinical Follow-Up." (National Academies of Sciences & Medicine, 2022)

### 4.1.1 Established associations between PFAS and health

Evidence suggests that PFAS exposure is associated with several adverse health outcomes with varying degrees of certainty.

### 4.1.2 Sufficient Evidence of Association:

- **Decreased Antibody Response**: Both adults and children exhibit reduced antibody responses.
- **Dyslipidemia**: Elevated levels of cholesterol and other fats in the blood are observed in both adults and children.
- **Decreased Infant and Fetal Growth**: Exposure during pregnancy is linked to reduced growth rates in infants and fetuses.
- **Increased Risk of Kidney Cancer**: There is a noted increased risk of kidney cancer in adults.

### 4.1.3 Limited Suggestive Evidence of Association:

- **Increased Risk of Breast Cancer**: PFAS exposure may be linked to a higher risk of breast cancer in adults.
- **Increased Risk of Testicular Cancer**: There is a potential association with testicular cancer in adults.
- **Liver Enzyme Alterations**: Both adults and children show changes in liver enzyme levels.

- **Increased Risk of Pregnancy-Induced Hypertension**: Conditions such as gestational hypertension and preeclampsia are more prevalent.
- **Increased Thyroid Disease and Dysfunction**: Adults may experience higher rates of thyroid-related issues.
- **Increased Risk of Ulcerative Colitis**: There is a suggestive link to ulcerative colitis in adults.

### 4.1.4 Clinical Follow-Up Recommendations

The study aimed to determine appropriate health care follow-up for individuals exposed to PFAS and establish blood level thresholds warranting clinical attention. Data from the German Human Biomonitoring Commission (HBM) work were utilized as a reference for these guidelines, though it was noted that these levels are not yet formally adopted.

1. **Less than 2 ng/mL (nanograms per milliliter) of Summed PFAS**:
   - **Adverse Health Effects**: Not expected.
   - **Recommendation**: Usual standard of care.
2. **2 to Less than 20 ng/mL of Summed PFAS**:
   - **Adverse Health Effects**: Potential for adverse effects in sensitive populations.
   - **Recommendation**: Reduce PFAS exposure; screen for dyslipidemia, hypertensive disorders of pregnancy, and breast cancer, among other conditions.
3. **More than 20 ng/mL of Summed PFAS**:
   - **Adverse Health Effects**: Higher potential for adverse effects.
   - **Recommendation**: Reduce exposure; test for thyroid function, kidney cancer, testicular cancer, and ulcerative colitis. Lipid testing is recommended starting from age 2.

### 4.1.5 Summary of potential health impacts

The presentation highlighted the impact of PFAS on the immune system, including reduced childhood vaccine response and other effects on the body's ability to respond to infections. Key health outcomes influenced, or potentially influenced, by PFAS exposure include:

- **Thyroid Disease**: There seems to be an increased risk, but large sample sizes are needed for greater clarity.
- **Blood Cholesterol Levels**: Elevated levels are noted.
- **Vaccine Response**: Decreased antibody response to childhood vaccines is observed.
- **Fertility in Women**: Decreased fertility rates have been reported.
- **High Blood Pressure and Preeclampsia**: Increased risks are associated with PFAS exposure.
- **Infant Birth Weight and Growth**: Lower birth weights and reduced growth rates in infants and foetuses are linked to exposure.
- **Cancer Risks**: There is some evidence of increased risks for kidney, testicular, and breast cancers, as highlighted by studies such as those by the International Agency for Research on Cancer (IARC) (Shelia Zahm et al., 2024).

The potential health effects of PFAS are diverse and can affect individuals across their lifespan. Continued research and updated clinical guidelines are necessary to better understand and mitigate these risks.

## 4.2 New Jersey and other US Drinking Water Guidelines for PFAS by Dr Gloria Post

This presentation provided an overview of New Jersey's regulatory efforts and the associated health concerns related to per- and polyfluoroalkyl substances (PFAS) in drinking water. It should be noted that the views expressed here are do not necessarily represent the policies of the New Jersey Department of Environmental Protection or the views of all policy advisers there.
New Jersey has been a forerunner in establishing stringent drinking water standards for PFAS, beginning with the detection of perfluorooctanoic acid (PFOA) in drinking water near an industrial source in 2005. Over the years, New Jersey has developed Maximum Contaminant Levels (MCLs) for various PFAS, reflecting the state's proactive approach to addressing PFAS contamination.

### 4.2.1 Regulatory framework

New Jersey has a history of setting drinking water standards for contaminants since the 1980s. Key milestones in the state's PFAS regulation include:

- **2007**: Drinking water guidance (non-regulatory) for PFOA set at 40 parts per trillion (ppt), significantly lower than other states' guidance at the time.
- **2018**: Established the first MCL for any PFAS in the United States, setting the PFNA level at 13 ppt.
- **2020**: MCLs established for PFOA at 14 ppt and PFOS at 13 ppt (NJDEP, 2024).

### 4.2.2 PFAS in Drinking Water: Concerns and Implications

The presence of PFAS in drinking water is a significant concern due to several factors:

- **Persistence**: PFAS do not break down in the environment and persist for long periods.
- **Bioaccumulation**: Some PFAS (such as PFOA, PFOS, PFNA, PFHxS) have long human half-lives (ranging from approximately 2 to over 8 years), meaning they remain in the body for years after exposure ends.
- **Toxicity**: Various animal studies have demonstrated toxicity at low doses.
- **Human Health Effects**: There is evidence of health effects at low exposure levels typical of the general population.
- **Exposure Pathways**: Drinking water can be a major source of PFAS exposure, especially compared to other sources like food packaging and consumer products.
- **Infants and Susceptible Subgroups**: Infants, particularly those who are breastfed, are at higher risk due to higher exposure levels relative to body weight.

Given these concerns, minimizing exposure to PFAS from drinking water with significant PFAS contamination is crucial.

### 4.2.3 Health Effects and Evidence

New Jersey's development of MCLs for PFAS was informed by consistent findings across different populations and concordance with animal toxicology studies.
A more recent evaluation that included newer studies concluded that key health outcomes associated with PFAS exposure include:

- **Increased Cholesterol Levels**: PFAS exposure is linked to higher cholesterol levels in humans.
- **Kidney Cancer**: There is evidence of an increased risk of kidney cancer.
- **Liver Enzyme Alterations**: Elevated levels of the liver enzyme ALT have been observed.
- **Decreased Vaccine Response**: PFAS exposure is associated with a reduced antibody response to vaccinations.
- **Decreased Birth Weight**: Lower birth weights have been noted in infants exposed to PFAS in utero.

In a 2022 review, the Drinking Water Quality Institute (DWQI) aligned with the United States Environmental Protection Agency (USEPA) in concluding that human data are appropriate for use in risk assessments of PFOA and PFOS. The DWQI also agreed that PFOA is likely carcinogenic to humans. Consequently, the DWQI supported setting health-based drinking water levels below the current New Jersey analytical limits of 6 ppt for PFOA and 4 ppt for PFOS.

### 4.2.4 Drinking Water Exposure Assessment

Drinking water exposure assessments consider the concentration of PFAS in water, the volume of water ingested, and the body's clearance factor, which varies for different PFAS. For example, continuous ingestion of water containing 10 ppt of PFOA would lead to an estimated increase in blood serum levels of approximately 1000 ppt (1 ppb). The current New Jersey MCLs are set at 13 ppt for PFNA, 14 ppt for PFOA, and 13 ppt for PFOS. Further reductions in these levels are not yet committed.

### 4.2.5 Conclusion

New Jersey's proactive measures in regulating PFAS in drinking water highlight the importance of addressing these persistent environmental contaminants. The state's stringent standards and ongoing research into the health effects of PFAS exposure underscore the need for continued vigilance and adaptation of public health policies.

## 4.3 Effects of PFAS exposure on the immune system by Dr Jamie DeWitt

This presentation explored the impact of per- and polyfluoroalkyl substances (PFAS) on the immune system, based on Dr DeWitt's work and related studies.
The immune system is crucial for maintaining health, protecting against pathogens, aiding in injury repair, and eliminating mutated cells that could develop into tumours. Imbalances in the immune system, whether through suppression or inappropriate stimulation, can lead to significant health issues.

### 4.3.1 Functions and Dysfunctions of the Immune System

The immune system performs several essential functions:

- Maintaining overall health.
- Protecting against pathogens such as viruses, bacteria, fungi, and other invaders.
- Repairing the body after injuries.
- Recognizing and eliminating mutated cells to prevent cancer.

Imbalances in the immune system can manifest as:

- **Immune Suppression**: A reduced ability to respond to challenges, which can increase the risk of infections and certain cancers.
- **Inappropriate Immune Stimulation**: Abnormal immune responses to common substances (e.g., allergies) or self-antigens (autoimmunity).

### 4.3.2 Effects of PFAS on the Immune System

PFAS exposure can affect various bodily systems, including the immune system. Key implications include:

- **Decreased Vaccine Response**: This serves as a marker of immune suppression, increasing susceptibility to infections and potentially certain cancers. Both human and laboratory model studies indicate that higher levels of PFOA/PFOS in blood correlate with reduced vaccine efficacy.
- **Inappropriate Immune Stimulation**: PFAS can cause the immune system to overreact to common substances, leading to conditions such as allergic hypersensitivity.

### 4.3.3 Case Study: Cape Fear River

Dr DeWitt's research included a study on the Cape Fear River, focussed on several compounds found there. [While these specific compounds are not found in the AFFF exposure in Jersey, the health effects they researched are like those found in the more common PFAS] They looked at the following compounds:

- **PFMOAA** (perfluoro-2-methoxyacetic acid): Dominant short-chain PFAS detected at high concentrations in the river but not in human blood.
- **Nafion Byproduct 2**: A longer-chain compound detected at low concentrations in the river and in human blood.
- **PFO5DoA** (perfluoro-3,5,7,9,11-pentaoxadodecanoic acid): Not detected in the river but found in human blood of those drinking from the river.

Some PFAS have a short half-life in the body and therefore may not have been detected.

#### *4.3.3.1 Laboratory Findings*

Animal studies were conducted over a 30-day exposure period, adhering to harmonized test guidelines acceptable to WHO and other agencies. Key findings include:

- **Liver Toxicity**: Signs of liver toxicity varied depending on the specific PFAS compound and concentration.
- **Vaccine Response**: High doses of PFAS altered vaccine responses in laboratory models, although not all changes were statistically significant.

The overall potency of PFAS compounds was evaluated based on their impact on liver markers and vaccine response suppression. PFO5DoA was identified as the most potent, while PFMOAA was the

least potent, likely due to differences in carbon chain length, functional groups, and biological half-life.

#### 4.3.4 Regulatory Perspectives

The European Food Safety Authority (EFSA) established a tolerable weekly intake (TWI) for food at 4 ng/kg/day for PFOA, PFOS, PFNA, and PFHxS, based on decreased vaccine responses (Chain et al., 2020). The US Environmental Protection Agency (EPA) used decreased vaccine responses, among other health effects, to set protective levels for drinking water, including a proposed limit of 4 ppt for PFOA based on cancer risk (National Academies of Sciences & Medicine, 2022).

#### 4.3.5 Immunosuppression as a Public Health Risk

Exposure to PFOA and PFOS is expected to cause mild to moderate immune suppression, posing a public health risk. However, the risks associated with less studied PFAS compounds remain unclear. Immunosuppression is indicated by reduced vaccine responses but is not necessarily a direct risk factor.

#### 4.3.6 Challenges in PFAS Toxicity Data

Interpreting PFAS concentrations in the blood is challenging due to limited toxicity data from environmental studies. The complexity of PFAS exposure, including internal transformations and varying elimination rates, complicates assessments.

#### 4.3.7 Conclusion

PFAS exposure impacts the immune system, necessitating continued research to fully understand these effects and develop appropriate regulatory standards. Reduced vaccine responses indicate potential immunosuppression, underscoring the need for further investigation into the health risks of both well-studied and emerging PFAS compounds.

## 4.4 PFAS health effects in a mouse model: Early life exposure and later life effects by Dr Sue Fenton

This presentation provided an overview of research on both legacy and new PFAS compounds, with a focus on their health impacts as studied through mouse models. Dr Fenton's work, particularly in North Carolina, highlights the widespread presence of PFAS and the associated health risks. The chapter also discusses regulatory and scientific efforts to understand and mitigate these risks.

### 4.4.1 PFAS in North Carolina

PFAS contamination is detected throughout the USA, with the highest concentrations in the northeastern regions. In North Carolina, industrial PFAS exposure sources include a fluorochemical manufacturer producing novel products such as GenX (a replacement for PFOA), an Air Force base, fire training sites, and landfills and biosolid waste fields that drain into waterways in the eastern half of the state contaminating the Cape Fear River basin. PFAS contamination was discovered in the region's water supply about ten years ago, with 650 personal wells currently known to be contaminated with novel PFAS compounds.

#### *4.4.1.1 Exposure Pathways*

PFAS exposure in North Carolina occurs through various pathways including ingestion, inhalation, dermal contact from:

- Industrial sites
- Fire training and firefighting facilities
- Landfills
- Wastewater treatment plants and biosolids
- Consumer products and dust
- Food items (e.g., vegetables, fish, and shellfish)
- Food packaging

### 4.4.2 Health Effects of PFAS Exposure

Both animal and human studies have identified several health effects associated with PFAS exposure:

- **Immune Function**: Changes leading to reduced vaccine response and increased susceptibility to infections.
- **Thyroid Function**: Disruption, potentially leading to thyroid disease.
- **Liver Disease and Cancer**: Including non-alcoholic fatty liver disease, which is rising globally.
- **Metabolic Dysfunction**: Including obesity, glucose intolerance, and insulin resistance.
- **Kidney Disease and Cancer**: Increased risk due to PFAS exposure.
- **Reproductive and Developmental Outcomes**: Delays or shortened duration of lactation, among other issues.

### 4.4.3 2023 PFAS Report to Congress

Dr Fenton contributed to a 2023 PFAS report to Congress, which focused on:

- Removal and safe destruction or degradation of PFAS from the environment.
- Development of safer and more environmentally friendly PFAS alternatives.
- Identification of sources and pathways of human exposure.
- Understanding the toxicity of PFAS to humans and animals through epidemiological evidence, laboratory animal models, and ecotoxicology studies.

The report highlighted gaps in knowledge regarding PFAS health effects, such as obesity, metabolic disease, and pregnancy complications, emphasizing the need for further research and funding.

### 4.4.4 Comparative Study of PFOA and GenX

A comparative study was conducted on PFOA and its replacement, GenX, using mouse models. The study aimed to determine if GenX is a safer alternative to PFOA. Findings indicated that GenX, despite its shorter half-life, has similar adverse health effects as PFOA. These effects included

placental lesions, increased maternal weight gain, adverse liver features, and metabolic disease in offspring. The study concluded that both PFOA and GenX are similarly potent, despite GenX's shorter half-life. It was noted that GenX has not been found in Jersey.

### 4.4.5 Future Research Directions

Dr Fenton emphasized the need to study numerous other PFAS compounds present in the environment. Future research aims to predict pathways for emerging PFAS and analyse their effects, particularly on foetal growth restriction (FGR) and other adverse outcomes.

### 4.4.6 Conclusion

In utero exposure to PFAS sets the stage for a lifetime of increased disease susceptibility. Key health concerns include:

- **Transplacental Transfer**: PFAS crossing into the placenta, leading to lower birth weight.
- **Hypertensive Disorders of Pregnancy**: Increased risk.
- **Reduced Immune Function**: Impaired response to infections and vaccines.
- **Disruptions in Puberty and Fertility**: Menstrual issues and reduced fertility.
- **Elevated Cholesterol and Reduced Kidney Function**: Increased risks.
- **Thyroid Hormone Disruption and Cancer**: Potential for various cancers.

Protecting pregnant women and babies from PFAS effects is crucial. Dr Fenton also highlighted the need for more research on PFAS in AFFF (Aqueous Film Forming Foam) used in firefighting, noting the challenges in testing due to the complex mixture of substances.

## 4.5 High exposure to PFAS in Ronneby, Sweden – effects on child health and development by Dr Christel Nielsen

This presentation provided an in-depth exploration of the health impacts resulting from PFAS exposure in Ronneby, Sweden, as researched by Dr Nielson and her team. Ronneby, a small town with a population of 28,000, experienced significant contamination in its municipal drinking water due to the use of Aqueous Film Forming Foam (AFFF) at a nearby airfield. The presentation discussed the discovery of the contamination, subsequent research initiatives, and the maternal and child health impacts observed in the affected population.

### 4.5.1 Discovery of Contamination

PFAS contamination in Ronneby was discovered in December 2013 during routine environmental monitoring, facilitated by leftover budget funds and awareness of upcoming EU drinking water regulations. This discovery was pivotal, as PFAS contamination around airfields was becoming a recognized issue. Extensive sampling of the Bredåkradeltat reservoir, located in the Kallinge area of Ronneby, revealed high levels of PFAS. The municipal water treatment plant in the exposure area showed a sum PFAS concentration of 10,380 ng/L, in stark contrast to 47.6 ng/L in another waterworks and less than 5 ng/L in a neighbouring municipality. The contamination was traced to AFFF used in fire training exercises, leading to the immediate closure of the contaminated waterworks.

### 4.5.2 Population Exposure and Initial Response

The Brantafors reservoir, serving about a third of Ronneby's households, had been a source of PFAS exposure for over 30 years, as suggested by military procurement records from the mid-1980s. Following the discovery of contamination, blood testing was offered to the local population in 2014. The initiative included open samplings at approximately 20 locations, with tests provided free of charge. Despite a participation rate of only 13%, the results were significant, showing elevated serum concentrations of PFAS in all tested individuals, including those not residing at exposed addresses. Other contaminants were not found to be elevated.

The 2014 first results revealed that median blood serum concentrations in Ronneby were significantly higher than those in the reference population, with PFHxS levels at 280 ng/mL and PFOS levels at 303 ng/mL, compared to 0.5 ng/mL and 2.9 ng/mL respectively in the reference population.

### 4.5.3 The Ronneby PFAS Research Programme

In response to the contamination, the Ronneby PFAS Research Program was established as a joint venture between Lund and Gothenburg Universities. The programme focuses on the health impacts of PFAS in the Ronneby population. The research encompasses several key areas:

#### *4.5.3.1 Pregnancy Health and Birth Outcomes:*

- **Transplacental Transfer**: Studies showed that at birth, infants can have 30-60% of their mother's PFOS levels.
- **Breastfeeding**: While breastfeeding is an exposure source for infants, it also offers numerous health benefits. Research indicated a lower transference of PFAS through breast milk compared to in utero exposure.
- **Pregnancy Complications and Birth Weight**: No increased risk of pregnancy complications was found. A study on pregnancy blood pressure is ongoing. However, there were small, sex-specific effects on birth weight.

#### 4.5.3.2 *Impaired Breastfeeding:*

- **Establishment of Breastfeeding**: Although numbers were small, exposed mothers seemed to have a three times higher risk of failing to establish breastfeeding compared to background-exposed populations.
- **Breastfeeding Duration**: More mothers ceased breastfeeding by six months, potentially due to delayed mammary gland development from PFAS exposure.

#### 4.5.3.3 *Neurodevelopment:*

- **Developmental Language Disorder**: Girls from the highly exposed area had a 1.6 times higher risk of being diagnosed with a developmental language disorder, although no effect was observed in boys.

### 4.5.4 Detailed Data Collection and Analysis

Sweden's comprehensive population registers, which include healthcare and socio-economic data, support the extensive PFAS studies. The national birth register enabled researchers to examine background PFAS exposure, pregnancy complications, and birth weight within the county.

Studies found no increased risk of pregnancy complications and only minor effects on birth weight, which differed between girls and boys. Breastfeeding decisions in the population before 2013 were not influenced by PFAS exposure awareness. Additionally, highly exposed mothers seemed to have a higher likelihood of not establishing breastfeeding and were less likely to breastfeed at six months, possibly due to delayed lactation.

### 4.5.5 Ongoing and Future Research

Dr Nielson emphasized the need for continued research to:

- **Understand Early-Life Exposure**: Further studies are needed to determine how early-life PFAS exposure affects health from a life-course perspective.
- **Investigate Thyroid and Endocrine Disruption**: Research is required to explore the impact of PFAS on thyroid function and other endocrine systems.
- **Assess Dose-Response Relationships**: There is a need to understand PFAS health risks at different levels of exposure.

### 4.5.6 Conclusions from Ronneby Research

- **Pregnancy Complications**: No increased risk was found. In-depth studies are ongoing.
- **Birth Weight**: Small, sex-specific effects were observed.
- **Breastfeeding Ability**: Impaired breastfeeding was noted.
- **Neurodevelopment**: An increased risk of developmental language disorder was found in girls. This is a new finding that warrants verification by further epidemiologic studies.
- **Health Benefits of Breastfeeding**: Despite PFAS exposure, the overall health benefits of breastfeeding might outweigh the risks. This should be a prioritized area for future research.
- **Exposure Levels and Health Risks**: Higher PFAS exposure did not correlate with proportionately higher health risks, indicating a complex dose-response relationship.

### 4.5.7 Recommendations from Ronneby

Given the findings, it was recommended to:

- **Continue Promoting Breastfeeding**: The benefits of breastfeeding are significant, and current evidence does not support advising against it due to PFAS exposure.
- **Enhance Monitoring and Research**: Ongoing studies and continued monitoring are crucial to fully understand the long-term health effects of PFAS.

## 4.6 Other issues identified in plenary discussions with the subject matter experts

This is a summary of two plenary discussions with subject matter experts on the health effects of PFAS exposure, highlighting key points on environmental contamination, health impacts, and ongoing research challenges. It covers various themes including toxicity testing, exposure pathways, health impacts on immune function and breastfeeding, and the need for further research.

### 4.6.1 Cost and Implementation of Water Quality Standards

The implementation of strict water quality levels in various jurisdictions involves considerable cost and methodological challenges.

### 4.6.2 Environmental Contamination and Toxicity Testing

- **Limited Toxicity Data**: There is a lack of comprehensive toxicity testing data for environmental PFAS contaminants. This poses a challenge in interpreting blood concentration levels without comparable toxicity data.

### 4.6.3 Exposure Pathways

- **PFAS Degradation and Travel**: Different PFAS compounds degrade and travel differently in the environment, making it difficult to identify primary sources of exposure. The primary contaminant source may not be the main PFAS exposure source for individuals.
- **Serum Levels and Local Exposure**: Variations in PFAS serum levels can often be explained by local exposure, such as drinking water sources and duration of residence. Serum levels in communities can help establish exposure concerns.

### 4.6.4 Health Impacts

It was noted that studies are not consistent on which health impacts occur and which do not. This may be a function of the different PFAS involved in different exposures.

#### *4.6.4.1 Immune Function:*

PFAS exposure is linked to immune system changes, including reduced childhood vaccine response, which serves as an indicator of potential immune suppression. This reduction appears to be a risk marker rather than a direct risk factor for population health.

- **Age-Related Immune Decline**: After age 59, the immune system's competence naturally declines, necessitating comparisons with data from immunosuppressed individuals or the elderly in exposed communities.
- **Childhood Infections**: Current evidence does not strongly link PFAS exposure to increased rates of common childhood infections.

#### *4.6.4.2 PFAS Potency and Health Effects:*

- **Elimination Rates**: Different PFAS compounds have varying elimination rates, affecting their relative potency and health impacts.
- **Threshold Levels**: Some health effects have been observed at PFAS levels below 20 ng/mL, indicating that the level of 20 ng/ml cannot really be considered a threshold below which no health effects may be expected. In the USA, approximately 8% of the population exceeds 20 ng/mL, with most individuals having levels between 2 and 20 ng/ml. More research is needed to understand if a threshold can be established.

#### *4.6.4.3 Breastfeeding and PFAS*

- **Data Collection Challenges**: Collecting data on breastfeeding volumes is difficult, though Sweden has biomonitoring data for one-year-olds. Studies are ongoing to determine if lower breastfeeding rates are associated with PFAS exposure, potentially due to delayed lactation.
- **Health Benefits vs. Risks**: There is insufficient evidence to suggest that the health benefits of breastfeeding are significantly offset by PFAS exposure. Promoting breastfeeding remains important due to its overall benefits.

### 4.6.5 Further steps highlighted by subject matter experts

- **Implement Protective Measures**: Efforts should be made to reduce PFAS exposure, particularly in vulnerable populations such as pregnant women and infants.
- **Thyroid Effects**: Further study is needed on the thyroid effects of PFAS, which may influence other health areas.
- **Saturation Point**: Increasing PFAS exposure does not always correlate with greater health risks, or put another way, the incremental increase of risk with increasing exposure seems much less at higher exposures, suggesting a potential saturation point.
- **Animal Studies**: Further animal studies are needed to explore PFAS impacts. For human studies, due to widespread PFAS presence in water, it is challenging to find comparison groups with zero exposure for comparison.
- **Placental Glycogen Deficit**: Research shows a glycogen deficit in the placentas of animals exposed to novel PFAS, which may impact insulin resistance and survival at birth. Collecting similar data in humans is challenging but crucial.

# 5 Evidence from the scientific literature

## 5.1 PFAS in the human body

### 5.1.1 Exposure routes and pathways

The presence of organic fluorine in human blood was first detected by the dental researcher Donald Taves in the 1960s (Taves, 1968). In 2024, it is now known that virtually all humans on the planet have certain PFAS in their bodies at low microgram per litre levels(Sunderland et al., 2019). Human blood concentrations of long-chain perfluoroalkyl acids (PFAAs) such as PFOS, PFHxS and PFOA, peaked in the late 1990s/early 2000s in the general population of most countries and have declined since the 3M industrial phase-out of long-chain PFAS chemistries (the phase-out was between the years 2000 and 2002).(Sunderland et al., 2019).

For humans, exposure to PFAS occurs by three routes, namely: ingestion, inhalation, and dermal absorption, as described below. Some special exposure routes for prenatal stages and infants are discussed further down this section.

1. Ingestion exposure of PFAS for humans occurs via consumption of contaminated food, water, and other beverages. Exposure by ingestion also occurs via the intentional or inadvertent non-dietary ingestion of soil, dust, or chemical residues on surfaces or objects that are contacted via hand-to-mouth or object-to-mouth activity (especially important for young children).
2. Inhalation exposure of PFAS for humans results from breathing air that is contaminated with fine particulate matter or gas-phase volatile PFAS. Individuals can be exposed via the inhalation route during a variety of activities, both outdoors and indoors. Individuals indoors could also be exposed to outdoor air contaminants that infiltrate the indoor environment.
3. Dermal exposure of PFAS by humans results from skin contact with PFAS-containing consumer products and contaminated environmental media, including water (e.g., during bathing, washing, swimming), bottom sediments in surface waters (e.g., while wading, fishing), outdoor soil or dust (e.g., during recreational and gardening activities), and indoor dust that has settled on carpets, floors, clothing, counter tops, or other surfaces.

The relative importance of the many different PFAS exposure pathways (e.g. dietary ingestion, versus dust ingestion, versus gaseous inhalation, etc.) has been estimated in multiple studies (e.g.(Gebbink et al., 2015)) and these have been reviewed in the literature.(De Silva et al., 2021; Sunderland et al., 2019). There is general agreement that for PFOS, PFHxS and PFOA, and other long-chain PFAAs, dietary intake is the dominant exposure pathway for the general population compared to air inhalation or dermal contact(Sunderland et al., 2019). Furthermore, it is known that protein-rich foods such as eggs, meat and fish make the largest contribution to dietary exposure for the long-chain PFAAs(Vestergren et al., 2012).

In areas such as the plume area in Jersey where drinking water levels of PFAS have been substantially elevated due to contamination with AFFF, drinking water ingestion is the dominant exposure pathway for PFOS, PFHxS and PFOA(Li et al., 2018b) (AECOM, 2016; Yiyi Xu et al., 2021). In some areas (e.g. in Oakey, Australia) where contaminated water has been used for watering livestock or irrigating crops, substantial additional exposure can be derived from consumption of local produce.(AECOM, 2016).

A further complication to understanding exposure to PFAS is that humans can be exposed to the so-called precursors, which are substances that transform to PFAAs either in organisms (including in the

human body) or in the environment(Vestergren et al., 2008). Precursors are sometimes, but not always, measured when analysing exposure media for PFAS, which means that human exposure to certain PFAS is likely underestimated. Although these precursors certainly make an additional contribution to human exposure to PFAS, the extent of this contribution, and which precursors contribute, has been debated among scientists(Vestergren et al., 2008).

Toxicokinetics is the study of the absorption, distribution, metabolism, and excretion of a chemical within an organism. Within the following sections we review the current knowledge of toxicokinetics of PFAS with particular focus on PFOS, PFHxS and PFOA. The chemical structure (e.g. chain length, functional groups, branching of the carbon chains) all impact the toxicokinetics. An exhaustive review of toxicokinetics for all PFAS is not possible here and we therefore aim to summarize the key points.

### 5.1.2 Absorption of PFAS into the body

The absorption behaviour of PFAS has been studied in laboratory animals (e.g., rodents and monkeys),(Gannon et al., 2011) but not typically in humans due to ethical considerations. Absorption of PFOS, PFHxS and PFOA via ingestion has been determined in animal experiments and it has been shown that 66–100% is absorbed into the body(OECD, 2002, OCA.0029.0001.0063) (Gannon et al., 2011) (Kudo & Kawashima, 2003; Sundström et al., 2012). Animal studies also suggest that PFOA is easily absorbed via the lungs(Kennedy et al., 2004). Due to the high absorption of PFAS in animal studies, the absorption of PFOS, PFHxS and PFOA is typically set to 100% as a conservative assumption in human exposure modelling studies(Trudel et al., 2008) (Gebbink et al., 2015; Vestergren et al., 2008). These reported absorption efficiencies for PFAS are higher than for other well studied hydrophobic organic contaminants (such as polychlorinated biphenyls)(Schlummer et al., 1998). Given this near consensus on very high levels of absorption, these are likely to be the primary routes in the bulk of cases.

Absorption through the skin, however, is more complex. Experimental studies on dermal absorption are scarce. *In vitro* exposure studies using rat and human skin replicates conducted by Fasano et al. in 2005 have shown that PFOA can penetrate the skin, albeit with a low absorption efficiency (1.44% and 0.048% of PFOA absorbed through the rat and human skin, respectively, after 48 h of exposure)(Fasano et al., 2005). A more recent study by Franko et al. in 2012(Franko et al., 2012) suggested that PFOA is readily absorbed by human and mouse skin, but on close examination this only occurred at unrealistically low pH (2.25) when PFOA was in its acidic neutral form. Franko et al., admitted in their study that PFOA will most likely be ionized on the skin surface. Interestingly, Franko et al. achieved similarly low absorption as in the 2005 Fasano study when PFOA was in its ionized form. These observations are consistent with the pH-partition hypothesis,(Shore et al., 1957) which suggests that the passive transport of charged chemical species across biological membranes is small, owing to their poor solubility in lipids.

Abraham and Monien (Abraham & Monien, 2022) investigated the dermal absorption of $^{13}C_4$-perfluorooctanoic acid ($^{13}C_4$-PFOA) mixed into a sunscreen that was applied on the skin of a volunteer. The blood concentrations of $^{13}C_4$-PFOA were monitoring over 115 days after application. After application, $^{13}C_4$-PFOA blood levels increased continuously with a maximum level measured 22 days after application. The fraction absorbed was estimated to be 1.6 % of the dose, which is still relatively low compared to ingestion and inhalation. The study of Abraham & Monien could be considered an extreme exposure scenario given that that the contaminated suncream is rubbed into the skin.

Ragnarsdóttir et al (Ragnarsdóttir et al., 2024) used 3D human skin equivalent models (multilayered laboratory grown tissues that mimic the properties of normal human skin) to study the dermal absorption of 17 PFAS including PFOS, PFHxS and PFOA. Of the 17 PFAS assessed, 15 substances were shown to absorb by at least 5% of the exposure dose, which is higher than observed in the previous abovementioned studies. It is unclear, however, if the artificial skin models represent the dermal absorption of PFAS compounds behaviour of real human skin, even if the authors claim that it does.

There are few dermal contact studies for PFAS but based on the existing studies it seems reasonable to assume that dermal absorption of PFAS is relatively low compared to ingestion and inhalation absorption. In exposure modelling studies,(Gebbink et al., 2015) it is typically assumed that dermal absorption is less than 1% for PFOS, PFHxS and PFOA based on animal experiments for PFOA and typical exposure scenarios, and these exposure models provide good estimations of human serum levels of PFAS.

### 5.1.3 Distribution of PFAS in the human body

As discussed above, PFAS are readily absorbed into the human body via ingestion and inhalation routes, and to a much lesser extent via the dermal route. Once absorbed, PFAS are distributed throughout the body both in the blood and into extravascular tissues (i.e. in tissues other than the blood vessels)(De Silva et al., 2021). In the tissues, PFAS bind to both phospholipids and proteins (e.g. in the blood serum to a protein called human serum albumin (HSA)) and also to fatty acid binding-proteins (FABPs)(De Silva et al., 2021). It has long been considered that the blood, liver, and kidneys are the main tissues of distribution for PFAAs in humans(De Silva et al., 2021). A recent study measured the distribution of PFAAs between liver, kidneys, lungs, spleen, brain, and the whole blood of 19 deceased adult humans(Nielsen et al., 2024). The highest extravascular tissue PFAA concentrations were in the liver, lungs, and kidneys with concentrations in the brain and spleen being much lower. PFOS was particularly high in the liver compared to other organs. PFHxS was the only PFAA that showed higher concentrations in the kidney than in the liver, while PFOA was higher in the lungs than in the liver. Extravascular PFAA tissue concentrations were generally well-correlated with those in the blood and in reasonable agreement with the partitioning predicted by theoretical models. The differing accumulation of PFAAs in various tissues has been associated with their relative binding affinities to phospholipids and proteins (e.g. HSA and FABPs)(De Silva et al., 2021). Higher binding affinities to HSA and FABPs have been observed for long-chain PFAAs compared with short-chain PFAAs(Fischer et al., 2024).

### 5.1.4 Metabolism

PFAAs are not chemically modified or metabolised within the human body due to their chemical inertness (Wang et al., 2017). However, and as mentioned above, there are precursor substances which can metabolize to form PFAAs within the human body(Vestergren et al., 2008).

### 5.1.5 Elimination

Some long-chain PFAAs are primarily eliminated slowly via urine(Cui et al., 2010) with others predominantly via the faeces(Ma et al., 2020). Women have some additional elimination pathways discussed below. Previous studies have shown relatively long human elimination half-lives (the time it takes for the amount of PFAS in the body to be reduced by 50 percent) of long-chain PFAAs. For example, average serum half-lives for PFOS, PFHxS and PFOA, of 2.9-8.5, and 2.9-7.3, 1.8-3.5 years, respectively, have been reported in different studies(Xu et al.) (Li et al., 2018b; Olsen et al., 2007). Shorter human serum half-lives have been observed for short-chain PFAAs (e.g. perfluorobutane sulfonate (PFBS) of 44 days, and perfluoropentane sulfonate (PFPeS) of 230 days).(Xu et al.) However,

elimination half-lives are not only dependent on the length of the perfluoroalkyl chain. The head group (sulfonate versus carboxylate) and degree of branching in the perfluoroalkyl chain also impacts elimination rates of PFAAs.(Xu et al.)

Some of the differences in elimination half-lives for individual PFAAs between studies can be due to differing exposure histories. For example, the half-lives in retired fluorochemical workers (PFOS average elimination half-life of 8.5 years)(Olsen et al., 2007) are much higher compared to residents of contaminated communities who have received historical exposure via contaminated drinking water (PFOS half-life of 2.9 years).(Xu et al.) Additionally, elimination half-lives have also been reported to be highly variable between individuals and the reasons for this variability remain unknown.(Xu et al.)

Women between 12.5 and 50 years old have been shown to have lower blood serum levels of PFOS than men and this is thought to be primarily because women eliminate PFOS (and other long-chain PFAAs) more rapidly than men due to their additional elimination pathway of monthly menstrual blood loss (Upson et al., 2022). Women can also eliminate PFAS from their bodies by transfer to the child to some extent, during pregnancy, childbirth, and breast feeding (Wong et al., 2014).

The long elimination half-lives of long-chain PFAAs in humans is thought to be due to their ability to be reabsorbed by organic anion transporters (OATs) in the kidneys and due to their uptake from the gut via enterohepatic circulation (Niu et al., 2023). Therefore, renal elimination/reabsorption in the kidneys is a critical process in determining the elimination of PFAAs. However, the interactions between PFAAs and the renal transporters (i.e. OATs) are not fully understood (Niu et al., 2023). The active transport processes differ between different PFAAs and possibly also can explain differences in elimination between individuals. It is further possible that kidney disease can alter the expression of the renal transporters and further influence renal elimination of PFAS (Niu et al., 2023). However, little is currently known about how altered kidney function affects elimination rates of PFAS; this is an area of ongoing research.

### 5.1.6 Transmission

#### *5.1.6.1 In-utero transfer*

It has been shown that PFAS can pass the placental barrier from mother to child during pregnancy (Beesoon et al., 2011; Gützkow et al., 2012; S. Kim et al., 2011; Liu et al., 2011; Monroy et al., 2008; Pan et al., 2017). These studies have measured serum concentrations of PFAS in maternal and cord blood, or new-born blood samples directly after birth. The transplacental transfer efficiency (TTE) can be calculated for each individual mother-child pair as the ratio of foetal to maternal blood or serum concentrations, and these data have been reviewed and summarised (Winkens et al., 2017). TTEs vary significantly within and between the different studies. Strong positive correlations between maternal and foetal serum concentrations have generally been observed for PFOS, PFOA and other long-chain PFAAs. A comparison of TTEs for different PFAAs suggests a negative relationship with the perfluoroalkyl chain-length and a slightly lower transfer efficiency for sulfonates compared to carboxylates.

#### *5.1.6.2 Breastfeeding*

PFAS have been measured in human breast milk and they are thus transmitted through lactation (Kärrman et al., 2007; S.-K. Kim et al., 2011; Liu et al., 2010; Llorca et al., 2010; So et al., 2006; Sundström et al., 2011; Tao, Kannan, et al., 2008; Tao, Ma, et al., 2008; Thomsen et al., 2010; Völkel et al., 2008). Breastfeeding is therefore an additional elimination pathway for breastfeeding mothers.

Breastfeeding gradually reduces the mothers' concentration of PFOA and PFOS in serum and breast milk (Fei et al., 2010; Mondal et al., 2014; Thomsen et al., 2010). For PFOA and PFOS, a common 3% reduction has been observed per month of breastfeeding, whereas for PFNA and PFHxS a 2 and 1% reduction, respectively, per month of breastfeeding has been observed (Mondal et al., 2014). This is in accordance with the finding that primiparous women have the highest loads of PFOS and PFOA in their breast milk (Fei et al., 2010; Tao, Kannan, et al., 2008).

Breastfeeding is the dominant exposure pathway for PFAS for infants who are breastfed (Mogensen et al., 2015; Verner et al., 2016). Early-life longitudinal studies have shown a consistent increasing trend of both PFOS and PFOA during the first six months of life and this has been attributed to intake via breastfeeding (Fromme et al., 2010; Gyllenhammar et al., 2016; Koponen et al., 2018; Mogensen et al., 2015). The level of exposure to an infant depends on several circumstances, principally the level of PFAS in the mother, the amount of PFAS that transfers to her breast milk, and the duration of breastfeeding (Winkens et al., 2017).

## 5.2 Groups at increased risk

As discussed earlier, there are a very wide range of PFAS compounds, which seem to differ in their physiological effects, their persistence, and their route of elimination. It should be noted that patterns of exposure can be complex, and that elimination can vary from person to person.

Whilst there is not strong evidence in every area, there are indications of some groups who may potentially be more vulnerable. This may be through higher exposure risk, different patterns of elimination and different physiological effects.

### 5.2.1 Age

#### *5.2.1.1 Children*

Children, particularly neonates and infants, are potentially more susceptible to PFAS exposure due to their developmental stage. PFAS can cross the placental barrier, exposing the foetus during critical periods of development. Postnatally, infants can absorb PFAS through breast milk and contact with consumer products containing these chemicals (Fromme et al., 2009). Exposure during these formative years has been associated with vaccine resistance, developmental delays, and metabolic disorders (Fei et al., 2007; Grandjean et al., 2012).

#### *5.2.1.2 Older people*

While it is well-established that older people, on average, have reductions in kidney function (and the functions of some other organs and that they are more likely to have developed comorbidities, be taking medications and have accumulated risk factors), it is not clear if these have any impact on PFAS absorption, PFAS elimination or any physiological effects from PFAS exposure. Nevertheless, frailty may render certain conditions and symptoms more serious in an older person.

The elderly may experience more severe effects from PFAS exposure due to age-related decreases in renal function, which can slow the excretion of PFAS from the body. This slower clearance rate can lead to higher cumulative body burdens of PFAS. Moreover, the elderly often have multiple chronic conditions, which may be exacerbated by PFAS exposure, complicating their medical care, and adversely affecting their quality of life.

### 5.2.2 Additional exposure

#### *5.2.2.1 Lived environment and diet*

It is important to note that PFAS from all sources of exposure contribute to the body burden in an individual person. Consumption of water from contaminated supplies will increase levels, as will consumption of seafood from contaminated water. Fruit and vegetables irrigated with contaminated ground water or grown in contaminated soils may also be contributory factors (Sunderland et al., 2019). A diet rich in these sources in a contaminated area could be associated with increased risk of elevated body burden.

#### *5.2.2.2 Occupational*

Workers in industries where PFAS are produced, used, or disposed of including chemical manufacturing, firefighting, and environmental cleanup, face additional potential exposure. Firefighters, for example, are exposed to PFAS through firefighting foams and gear. These occupational groups often have elevated levels of PFAS in their blood, and are associated with higher rates of some health conditions (Lau et al., 2007).

#### *5.2.2.3 Socioeconomic disadvantage*

Socioeconomic status has been suggested as being relevant to PFAS risk. People from more disadvantaged backgrounds may lack the resources to avoid exposure or mitigate its effects, such as accessing clean water or medical services. Poorer communities are also more likely to be located near industrial zones or waste disposal sites where PFAS contamination is higher, compounding their risk of exposure and subsequent health problems (Burningham & Thrush, 2003).

### 5.2.3 Pregnancy

In addition to the potential for risk to the developing foetus, pregnant people may also be at increased risk. PFAS exposure has been linked to preeclampsia, high cholesterol, and reduced birth weight (Manzano-Salgado et al., 2015). In addition, because there are, in effect, two persons at potential risk, additional precautions may be appropriate in pregnancy.

### 5.2.4 Comorbidities

Individuals with certain genetic backgrounds or pre-existing health conditions may experience more severe effects from PFAS exposure. In addition, some kidney or liver diseases may affect PFAS elimination (although it is not yet clear if that would result in higher or lower body burdens). The interaction between PFAS and lipid metabolism may be particularly relevant to individuals with comorbid conditions like high cholesterol, obesity, or metabolic syndrome. PFAS exposure could affect cholesterol and exacerbate these conditions, increasing the theoretical risk of cardiovascular diseases. Similarly, people with weakened immune systems, disrupted hormonal systems or at increased risk of certain cancers might, theoretically, have their risk of adverse consequences increased by PFAS exposure (Fitz-Simon et al., 2013; Grandjean et al., 2012; Knox et al., 2011).

## 5.3 The health effects of PFAS, findings from the literature

### 5.3.1 Introduction

A number of recent reviews of the potential risks have published lists of associated health risks which are not always consistent. These inconsistent conclusions can be a confusing as they are in general drawing on the same body of research. Some have been from regulatory bodies such as the US Environmental Protection Agency (EPA), some have been specially constituted expert committees such as the World Health Organisation (WHO) International Agency for Research on Cancer (IARC), and then there are smaller academic teams publishing reports or journal articles. Most reviews have focussed on single substances, especially PFOA and PFOS, some conducted an overview of the set of more common PFAS compounds. Review documents have in general not addressed the complex mixture of exposures from AFFF contamination, although the EU has done so recently.

In June last year, the European Chemicals Agency (ECHA) announced a proposed ban in relation to AFFF: ECHA's Committee for Socio-Economic Analysis (SEAC) has adopted its final opinion supporting a gradual ban on per- and polyfluoroalkyl substances (PFAS) in firefighting foams.(ECHA, 2023) The restriction could reduce PFAS emissions into the environment by around 13 200 tonnes over 30 years in Europe. This policy proposes, if implemented, to ban all PFAS compounds from AFFF, and is justified by the environmental persistence and adverse health effects associated with several of the individual PFAS to be found in AFFF. They cross reference the reviews of individual PFAS undertaken by EPA and European Food Standards Authority (EFSA).

In assessing the potential health effects of mixed PFAS exposure coming from AFFF pollution, it may be the mixture itself that is important or it may be that specific compounds each have an effect. This review therefore considers first the evidence from specific studies of communities exposed to AFFF contaminated drinking water, and supplements that evidence with conclusions made by some of the authoritative systematic reviews principally on PFOS, PFHxS and PFOA.

For studies of AFFF exposure there are many recorded pollution episodes next to airports and fire stations where the run-off has led to pollution of groundwater and drinking water, but in most cases the population affected is too small to be informative for epidemiological study or has not been studied for health outcomes. However, there are two large populations which have been exposed to AFFF-derived drinking water contamination and have been studied. These are in Sweden and Australia and results are summarised below.

### 5.3.2 The range of epidemiological studies of PFAS

Most epidemiological studies of individual or mixtures of PFAS, can be divided into three exposure scenarios. First the workplace, where workers (usually quite small numbers) making or using specific PFAS have been studied. Blood measurements reported in the workplace have been among the highest found.

Secondly, samples of the general population with no known particular sources of exposure, but with measurable PFAS levels in blood, who have been studied. This can be in the form of cross-sectional studies linking blood measurements to information such as cholesterol levels taken at the same time, or followed up over time, linking them to mortality or disease registries to study for example cancer incidence. There are very many studies of this nature, especially cross sectional. Contrasts in

exposure indicated by differing levels of serum concentration tend to be quite small, as average serum concentrations are quite low.

Thirdly populations near a specific exposure source, with much higher exposure (and serum) levels than the average background, and these have been the source of some of the more solid epidemiological evidence because there are clear contrasts of exposure from high to low levels. Where the populations are large, they can investigate the relative risks of even quite rare diseases in relation to exposure. Four large populations stand out in this type of study. Two are exposed to factory emissions, one the "C8 study" population of about 80,000 exposed in the USA to PFOA from a plant making a fluoropolymer (polytetrafluoroethylene (PTFE) or, as it was a DuPont factory "Teflon™" well known for its use in non-stick cookware). The other is an Italian population of about 120,000 in Veneto, near a PFAS manufacturing facility, exposed to a mix of PFAS but primarily PFOA.

The C8 studies in the US were the first to highlight a number of diseases which the C8 Science Panel research team concluded were probably linked to PFOA exposure (Steenland et al., 2020): high cholesterol, ulcerative colitis, thyroid disease, testicular cancer, kidney cancer, and pregnancy-induced hypertension.

Two other scenarios are large populations with significant exposure to AFFF run-off from military airfields, and which have been studied. These populations are one in Ronneby in Sweden and one in Australia and both are described in the following sections.

### 5.3.3 Ronneby Sweden

Potential health effects have been studied in detail in Ronneby, Sweden. As well as reviewing many published papers from the research team there, we have benefitted from two Subject Matter Experts, Dr Kristina Jakobsson and Dr Christel Nielsen, presenting to our Panel meetings.

This broad research programme has investigated several potential health effects of AFFF/PFAS exposure, and a report summarising all this work (in English) has recently been made available on their project website(Jakobsson & Nielsen, 2024). In some cases, their epidemiological studies have confirmed previous findings observed at background levels and/or in the C8 studies with high PFOA exposure. These include elevated cholesterol levels and to an extent, increased risk of kidney and testicular cancers. In other cases, their findings suggest no risk for some associations reported in prior PFAS studies. This applies to impacts on ulcerative colitis, pre-eclampsia during pregnancy, thyroid disease, and birth weight.

#### *5.3.3.1 The Ronneby exposure*

In late autumn 2013, high levels of PFAS were detected in soil and groundwater in Ronneby, Sweden. It soon became clear that the drinking water was very heavily contaminated in one of the municipality's two waterworks. The contamination had come from AFFF use in the fire training area at the nearby military airfield, which had been using PFAS containing AFFF since the 1980s. The population was informed, and the contaminated water was promptly disconnected on December 16, 2013. Soon after, it was agreed to investigate human exposure level in the municipality and a pilot study first examined children from a school in the centre of the area with contaminated drinking water and a school in a clean area for comparison.

The study, released in March 2014, showed large differences for several different PFAS levels in their blood between the children, based on which school they attended. This led to all Ronneby residents

being offered PFAS blood testing free of charge. This was followed by setting up a research programme to investigate how PFAS exposure could have affected the health of the exposed population, led by the universities of Lund and Gothenburg with input from Panel member Tony Fletcher. It remains the place where the largest set of studies of the particular mix of PDAS in AFFF exposure has been epidemiologically studied. For this reason, it has particular relevance to Jersey.

#### *5.3.3.2 Key epidemiology findings from Ronneby*

They have not reported findings on every outcome of interest, but they have looked at a wide range and from this work have found some adverse effects related to exposure and some clear absences of associations with other conditions. For some of the adverse effects, these are new findings which need confirming through further research of other exposed populations: they may be chance associations which are not causal. For other adverse effects, they have already been noted in other studies so the combined weight of evidence means that they can be considered causal.

The Ronneby research has indicated the following outcomes raised in relation to exposure to the PFAS mixture: An increased incidence of type 2 diabetes, an increased risk of fractures associated with osteoporosis, an increased risk of elevated blood cholesterol levels, an increased risk of language impairment (among girls, but not among boys) and an increased risk of a shortened breastfeeding period. They found an increased risk of polycystic ovary syndrome (PCOS) but not an increased risk of endometriosis. They found a moderately increased risk of kidney cancer and testicular cancer.

They did not find an increased risk of common cancers such as breast cancer, prostate cancer, and bowel cancer. They did not find an indication of increased risk of thyroid disease, pregnancy complications, inflammatory bowel diseases such as ulcerative colitis and Crohn's disease, nor of impaired antibody response after vaccination against COVID 19 in adults.

These results are summarised in turn in the following sections.

#### *5.3.3.3 Exposure levels in Serum samples of the Ronneby Population*

Those exposed to the contaminated drinking water who participated in the community sampling showed elevated levels of, in particular, PFOS and PFHxS, and to a lesser extent PFOA(Y. Xu et al., 2021). The following table summarises the average (geometric mean) serum levels for those PFAS compared to another Swedish population Karlshamm in the same region but far from the contaminated area. The paper also summarised the age and sex differences in the serum levels. Levels tend to be higher in males than the females and the serum levels tend to rise with age, probably a reflection of longer cumulative exposure.

*Figure 2: Levels of different PFAS in Ronneby vs control area*

| | PFHXS (NG/ML) | PFOS (NG/ML) | PFOA (NG/ML) |
|---|---|---|---|
| **RONNEBY (N=3293)** | 114 | 135 | 4.5 |
| **KARLSHAMN (N=219)** | 0.84 | 3.9 | 1.5 |

The population was further subdivided depending on where in the town they were living. For those living most recently in the part of town provided with the contaminated water, serum levels were higher, averaging 210, 239 and 13 ng/ml for PFHxS, PFOS and PFOA, respectively.

In the same population, repeated measurements were made following the end of exposure. From these repeated measurements, the rate of fall in serum concentration was measured. This is expressed as the half-life – the time it takes for the serum levels to fall by half(Y. Li et al., 2022; Li et al., 2018a). There was quite a wide variability between individuals and the reasons for this are unknown, perhaps genetic, dietary, other exposures may play a role. On average the half-life found for PFHxS was 5.3 years, PFOS 3.4 years and PFOA 2.7 years.

#### *5.3.3.4 Childhood immunisations*

There are no published studies to date on childhood vaccinations from the Ronneby study of the AFFF exposed community, nor in other heavily exposed communities. However, there are multiple studies of impacts on childhood vaccinations in relation to serum concentrations measured in the mother, indicating exposure during pregnancy or children themselves. These studies have been conducted in the general populations exposed to PFAS in the general environments. These have been summarised and critically assessed in two recent panel reviews by EFSA for PFAS and by the US EPA for PFOS and PFOA specifically (EFSA et al., 2020; EPA, 2024a, 2024c). Both the EFSA and the EPA reviews conclude that the evidence supports PFOS and PFOA resulting in reduced antibody levels following routine childhood immunisations against infections such as diphtheria and tetanus (and for PFOS rubella). There are some studies reporting associations between PFOA or PFOS exposure and increased childhood infections, but others not showing such associations, so the evidence overall is not so convincing for common infections in children. For PFHxS a draft review for EPA (which is not yet finalised) concluded on a more limited range of studies that an association with childhood immunisation was “likely”. (EPA, 2023)

#### *5.3.3.5 Osteoporosis fractures*

PFAS can accumulate in bone tissue. Some studies in population groups with background PFAS exposure have suggested a risk of reduced bone density (osteoporosis), but evidence is still very limited and there is a lack of data from highly exposed groups. Reduced bone density can result in an increased risk of fracture. As osteoporosis is common among the elderly in Sweden, the risk of osteoporosis fractures was investigated in Ronneby.(Xu et al., 2023a)

Data on the diagnosis of osteoporosis-related fractures (vertebrae, upper arm, forearm/wrist, and hip) were obtained from the Swedish national patient register. The study included over 63,000 persons who were registered in the municipality at some point during the period 1985-2013. Their residential addresses were used to classify exposure to PFAS-contaminated water. They found that the risk of osteoporosis-related fractures was increased in the group with the high PFAS exposure, notably hip fractures and upper arm fractures.

#### *5.3.3.6 Cancer epidemiology*

The Swedish population register includes details of residence and the entire population were classified by whether they lived in the area of Ronneby served by contaminated drinking water, and how long they resided there. Data on 35 different cancer diagnoses during the period 1985-2016 were retrieved from the Cancer Registry for over 60,000 persons, who were registered in Ronneby at some point in 1985-2013. Their PFAS exposure was based on annual address and drinking water

distribution data. Comparisons of cancer incidence among adults were compared to rates in the rest of Blekinge county(H. Li et al., 2022).

The table below, reproduced from the paper, gives an overview of the overall risk comparing those in the exposed area to those in the unexposed area. For nearly all results, the confidence interval includes 1, which means the excesses and deficits are plausibly due to chance alone. There was no increased risk of all cancers combined, nor was there an increased risk of the most common cancers (prostate and breast cancer), among those who had ever lived at an address with contaminated drinking water. The only result showing a confidence interval excluding 1 is prostate cancer with a relative risk of 0.83 which implies a 17% lower risk in the exposed population. Among the excesses, there is a modest excess for kidney cancer (1.27), testicular cancer (1.38) and bladder cancer (1.30).

*Figure 3: Internal comparisons of cancer risk between groups with respect to exposure to PFAS-contaminated drinking water at their home.*

| Cancer | Never-high [a] | Ever-high [b] | | |
|---|---|---|---|---|
| | *N* | *N* | HR | 95% CI |
| Overall | 4,320 | 1,325 | 1.02 | 0.96, 1.09 |
| Stomach | 119 | 37 | 1.14 | 0.79, 1.66 |
| Colon | 326 | 93 | 0.98 | 0.78, 1.23 |
| Rectum | 190 | 73 | 1.25 | 0.95, 1.64 |
| Gall bladder, bile duct | 43 | 13 | 1.15 | 0.62, 2.15 |
| Pancreas | 77 | 16 | 0.71 | 0.41, 1.22 |
| Trachea, lung | 277 | 93 | 1.14 | 0.9, 1.45 |
| Breast [c] | 525 | 156 | 0.95 | 0.79, 1.13 |
| Cervix [c] | 55 | 15 | 0.91 | 0.51, 1.61 |
| Uterus [c] | 113 | 31 | 0.9 | 0.6, 1.34 |
| Ovarian [c] | 68 | 25 | 1.24 | 0.78, 1.96 |
| Prostate [c] | 712 | 181 | 0.83 | 0.71, 0.98 |
| Testicle [c] | 31 | 14 | 1.38 | 0.73, 2.61 |
| Kidney | 89 | 33 | 1.27 | 0.85, 1.91 |
| Bladder | 200 | 74 | 1.30 | 0.99, 1.69 |
| Skin (melanoma) | 218 | 77 | 1.09 | 0.84, 1.41 |
| Skin (non-melanoma) | 225 | 67 | 0.99 | 0.75, 1.3 |
| Brain | 109 | 42 | 1.24 | 0.86, 1.77 |
| Thyroid | 46 | 19 | 1.36 | 0.79, 2.33 |
| Bone, cartilage | 39 | 15 | 1.33 | 0.73, 2.42 |
| Non-Hodgkin | 149 | 41 | 0.94 | 0.67, 1.34 |
| Myeloma | 69 | 20 | 0.95 | 0.58, 1.57 |
| Chronic lymphocytic leukaemia | 52 | 13 | 0.84 | 0.46, 1.54 |

[a] 'Never-high' comprises subjects who resided in Ronneby, but never resided at an address supplied by the highly contaminated waterworks (including those who had their own well) between 1985 and 2013.

[b] 'Ever-high' comprises subjects who resided in Ronneby, at an address supplied by the highly contaminated waterworks, at any time between 1985 and 2013.

[c] Analyses were limited to the relevant sex.

*The results are presented as hazard ration (HR) from Cox proportional hazard model. All analyses were adjusted for age and sex.*

To investigate these patterns further, the researchers checked whether those exposed more recently (when concentrations were likely higher) or living in the exposure area for longer, showed higher risk.

They found a pattern of higher risk for people with longer exposure in the case of kidney, testicular and bone cancers. This work is still ongoing.

#### *5.3.3.7 Inflammatory bowel disease (IBD)*

There have been suspicions that PFAS entering the gastrointestinal tract could affect the gut lining and ultimately lead to inflammatory bowel disease. In the C8 study there was a significantly increased risk of ulcerative colitis in relation to PFOA reported (Steenland et al., 2020). To investigate whether the PFAS-contaminated drinking water has led to an increased incidence of inflammatory bowel disease in Ronneby, a large register study was carried out, which included over 63,000 persons who had been registered in the municipality at some point during the period 1985-2013.(Xu et al., 2020d). Data on diagnoses of inflammatory bowel disease (ulcerative colitis, Crohn's disease, and unspecified colitis) were obtained from the national patient register. The registry study showed no association between exposure to PFAS in drinking water and increased risk of inflammatory bowel disease.

#### *5.3.3.8 Gynaecological diseases*

Several persistent environmental pollutants have been shown to affect the reproductive hormone system in women, including PFAS. They therefore investigated the prevalence of the gynaecological diseases including polycystic ovarian syndrome (PCOS, ovarian cysts and elevated testosterone levels), uterine leiomyoma (muscle nodules in the uterus, also known as fibroids) and endometriosis (growth of endometrium outside the uterus) (Hammarstrand et al., 2021).

The study covered disease diagnoses during the period 1987-2013 among about 29,000 women who lived in Ronneby anytime between 1985 and 2013. For endometriosis, no increased risk was seen and for uterine leiomyoma there was a small increase that was not statistically significant. For women aged 20 to 50 years, one outcome was raised in the exposed versus unexposed population polycystic ovarian syndrome (PCOS), with a disease about two-fold higher for those in the exposed area.

#### *5.3.3.9 Pregnancy complications*

Pregnancy complications such as pre-eclampsia, high blood pressure and gestational diabetes can pose risks to mother and child, both during and after pregnancy. Previous research has linked PFAS to an increased risk of developing pregnancy complications, specifically the C8 study of preeclampsia in relation to PFOA. (Steenland et al., 2020) but the association has never been studied following high exposure to PFOS and PFHxS.

Women were identified who were registered in Blekinge at some time between 1990 and 2013, and who gave birth in 1995-2013 (27,292 pregnancies). They were linked to diagnostic data from the Medical Birth Register. (Ebel et al., 2023) The study considered other factors that affect the risk of pregnancy complications such as age, smoking habits, country of birth, level of education and number of previous pregnancies. This very extensive study found no evidence of any increase in the risk of gestational diabetes, nor high blood pressure or preeclampsia.

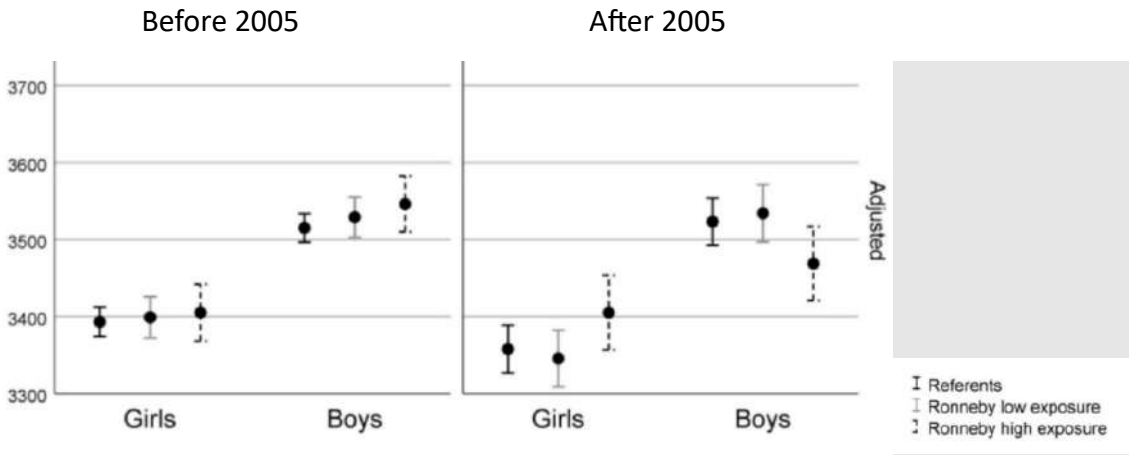
#### *5.3.3.10 Birth weight in relation to maternal exposure*

PFAS are transferred from the mother to the foetus during pregnancy. Several studies have reported that birth weight is slightly lower with increased levels of PFASs in the mother's blood, but these studies have only been conducted at low exposure levels.

All children born in Blekinge between 1995 and 2013 were identified in the Medical Birth Register which has data on birth weight, length of pregnancy and confounding factors such as the child's sibling order, the mother's level of education and smoking. (Engstrom et al., 2022)

PFAS exposure was classified by where the mother lived during the five years before the birth; in Ronneby with contaminated water (high exposure, n=823), in Ronneby without contaminated water (lower exposure, n=3,452) or in the rest of the county with no local exposure (n=9,692). Since PFAS levels were estimated to have increased over time, the authors distinguished between children born before and after 2005. Significant differences were found in average birthweight for recent births and either the earlier births prior to 2005 or births in a non-exposed area:

*Figure 4: Mean birth weight with 95% confidence intervals stratified for infant sex and period (before or after 2005). Adjusted models include gestational age, parity, and maternal age, civil status, smoking habits, and BMI in early pregnancy*




Boys born after 2005 weighed on average 54 g less than boys from the rest of Blekinge if the mother had contaminated water in the home. On the other hand, for girls born after 2005 they weighed on average 47 g more than girls from the rest of Blekinge if the mother had contaminated water in the home. While significant, the observed effect of PFAS exposure on birth weight per ng/ml of PFAS, is much smaller than previously observed in studies among women with background exposure and so is being further investigated by the researchers. Although the cumulative exposure was expected to be higher post 2005, there were still large differences in exposure before then, thus the absence of an effect in the pre-2005 data is surprising. Thus, it may be that the difference in birth weight after 2005 cannot be simply attributed to contrasts in average exposure. The opposite directions of effect between boys and girls is also surprising.

#### *5.3.3.11 Breastfeeding*

Breastfeeding has positive health benefits for both mother and baby. Effective breastfeeding depends on both complex social factors and complex hormonal processes. As PFASs are endocrine disruptors, there is a suspicion that exposure could interfere with the development of the mammary glands and ultimately the mother's ability to produce enough breast milk. Animal studies have supported this suspicion, and some studies of women with background exposure to PFASs point in the same direction. However, it is not known how breastfeeding is affected by high PFAS exposure.

The researchers conducted a study based on information about breastfeeding from the local records for 2079 children born in Ronneby municipality between 1999 and 2009, along with records from a

comparison group of 295 children from Karlshamn. (Nielsen et al., 2022) Information on other factors that may affect breastfeeding was also obtained from the records and was used to make adjusted risk estimates. Women's PFAS exposure was based on residential addresses and water distribution data. They were divided into three groups: Background exposure (comparison group): Women who have lived in Blekinge county but never in Ronneby during five years before giving birth; Medium exposure: Women living in Ronneby, but never with contaminated water at their home address during five years before giving birth; High exposure: Women living in Ronneby, with contaminated water at their home address at some point during the five years before giving birth.

They found that it was more common among highly exposed mothers in Ronneby to fail to establish effective breastfeeding than in the comparison group from Karlshamn: 5% compared to 2%. Furthermore, a lower proportion of highly exposed first-time mothers were breastfeeding at six months, 54%, compared to 65% in Karlshamn (they were 1.6 times more likely have stopped breastfeeding at 6 months, adjusted for confounding factors). They were also more likely to have started complementary feeding at three months of age. There was no increased risk of a shortened breastfeeding period among multiparous women, i.e., not first-time mothers.

#### *5.3.3.12 Thyroid disease*

The thyroid gland is one of the most important hormone-producing organs in the body. Its various hormones affect almost all body functions by regulating metabolism, i.e. how the body converts food into energy. Both overproduction and underproduction of thyroid hormone can lead to ill health. During the foetal period, the mother's thyroid hormones are needed for the development and growth of the foetus.

Experimental animal studies have shown that PFAS can adversely affect hormonal balance, but many epidemiological studies have given quite different results. Almost all these studies have been conducted at background exposure. In this study, the relationship between PFAS exposure and thyroid disease was examined in three different ways.

i. A registry study covering more than 63,000 persons who have lived in Ronneby at some point. Data on disease diagnoses and medication use were obtained from national healthcare registers.(Andersson et al., 2019)
ii. A study of the prescribing pattern for drugs used in thyroid disease at the different medical centres in Ronneby and Karlshamn during the period 2009-2016. (Andersson et al., 2019)
iii. A biomarker study investigating the relationship between thyroid hormones and PFAS levels in the blood among 3397 persons from Ronneby and 226 from Karlshamn (representing background exposure levels).(Li et al., 2021)

PFAS exposure was estimated by measured PFAS levels (the hormone level studies), and by address-based classification of drinking water occurrence in the home (diagnoses). There was no evidence of any increased risk of thyroid disease or increased thyroid-related medication use among those with the highest exposure to PFAS in drinking water, either among women or men. Among middle-aged and elderly, there was no pattern of correlation between the levels of the different thyroid hormones in the blood and the levels of PFAS in the blood. Among children and young persons, the results were more difficult to interpret, but there were no consistent findings in either direction. The health centre in the highly contaminated water district (Kallinge) did not have a higher prescription of medicines for thyroid disease than the other health centres in Ronneby or in Karlshamn. The overall

result from the three different studies did not been demonstrate any adverse impact on thyroid function or disease.

#### *5.3.3.13 Type 2 diabetes*

PFAS substances have been suspected of increasing the risk of metabolic diseases, including type 2 diabetes. However, epidemiological studies examining large groups of persons with background levels of PFAS exposure have produced contradictory results.

More than 55,000 adults who ever were registered in Ronneby during the period 1985-2013, were followed up (Xu et al., 2023b). Information on diagnosed type 2 diabetes was obtained from the national patient register and the pharmaceutical register. The persons' residential addresses were used to classify their exposure to PFAS-contaminated water.

There was some evidence of increased type 2 diabetes with an 18% increase in disease rate in the exposed compared to the non-exposed (Hazard rate as a measure of relative risk 1.18, 95% CI 1.03-1.35). The increased risk was most evident at younger ages, and the prescription of medicines for the treatment of type 2 diabetes was more common in the area with heavily contaminated drinking water than in the other health centres.

#### *5.3.3.14 Language development*

Given some animal experiments indicating that foetal exposure to PFASs may adversely affect brain development, but there is very little epidemiological data, a study was designed to address this hypothesis. Language ability is a good marker of brain development, and all children in Sweden have long been examined at the child health services in a standardised way. If a problem in language development is suspected, children are referred to a speech therapist for further assessment.

The study includes all children in Blekinge born between 1998 and 2013. (Stubner, Ebel, et al., 2023).

They were divided into three groups: Background exposure (comparison group): Women who have lived in Blekinge county but never in Ronneby during five years before giving birth; Medium exposure: Women living in Ronneby, but never with contaminated water at their home address during five years before giving birth; High exposure: Women living in Ronneby, with contaminated water at their home address at some point during the five years before giving birth.

They calculated the risk of referral to a speech and language pathologist after screening at the child healthcare centre and the risk of a language disorder diagnosis after at least two clinical assessments by a speech and language pathologist. The analyses were adjusted for the mother's age, level of education and smoking as well as the child's gender and sibling order. These factors are of great importance for children's language development.

Highly exposed children in Ronneby showed an increased risk of being referred to a speech therapist compared to the background group. Highly exposed girls (but not boys) had an increased risk of being diagnosed with a language disorder. The medium exposure group in Ronneby had no increased risk of referral or diagnosis compared to children from the rest of Blekinge.

In a review of published studies of PFAS exposure and neurodevelopment, linked to this project, the authors found no systematic effect of early-life PFAS exposure on language and communication development. (Stubner, Nielsen, et al., 2023) This study is the first study showing increased risk of

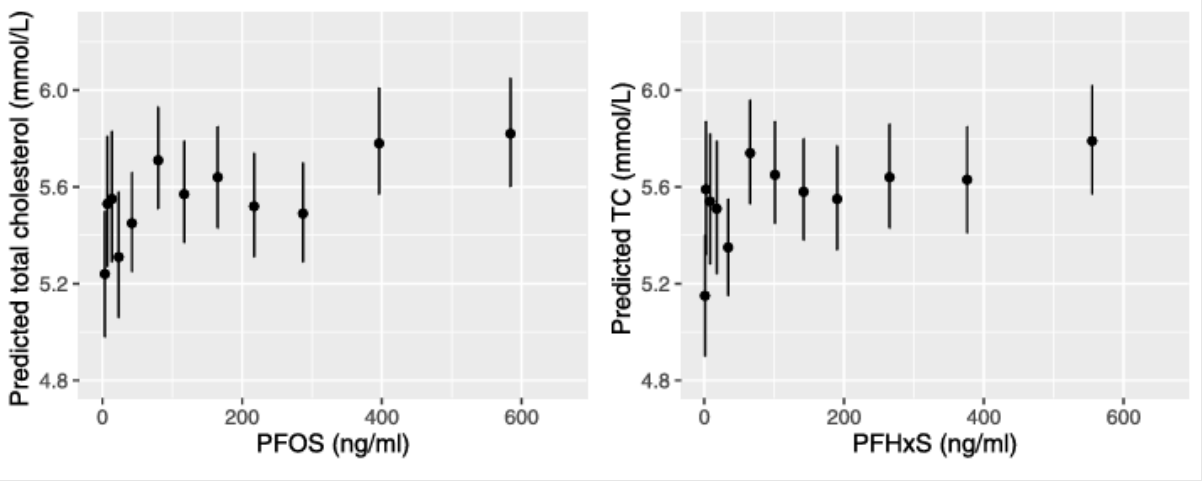
developmental language disorders in association with prenatal exposure to elevated levels of PFOS and PFHxS, and thus more studies are needed.

#### *5.3.3.15 Blood lipids (including cholesterol)*

An association between exposure to PFAS and elevated levels of blood lipids, especially cholesterol, has been observed in many epidemiological studies, mainly in the general population with background exposure. This study, in Ronneby, was the first one to also be able to study large contrasts in PFHxS exposure.

1,815 persons aged 20-60 years who participated in the open sampling in Ronneby in 2014-16 and 130 persons from Karlshamn (control area without PFAS-contaminated drinking water) were included in the study.(Li et al., 2020). The associations between PFAS levels and blood lipids were calculated adjusting for age, gender, and BMI, which also affect blood lipid levels. The figure from the paper shows the relationship between total cholesterol and decile groups of PFOS and PFHxS, respectively.

*Figure 5: Adjusted means for total cholesterol in PFAS centile (up to the 20th percentile) and deciles. The means were adjusted with age, sex, and BMI in quartiles.*




The study found a tendency for cholesterol to increase with serum concentration for both PFOS and PFHxS. The risk increase appeared to level off at the highest PFAS levels. This has also been seen in studies of high exposure to PFOA. At the group level comparing people living in high and low towns, 7-9% increases in total cholesterol and LDL were seen among participants from Ronneby compared to participants from Karlshamn. The authors concluded that the findings reinforce the evidence that there is a causal link between PFAS exposure and blood lipids, especially cholesterol.

We were informed of preliminary findings from the Ronneby study team of the associations with heart diseases. These are not yet published but suggest a small elevated risk. This is a comparison of 4 heart disease categories comparing the population living in the exposed area of Ronneby with the comparison area with no direct contamination. The results for risk of disease and 95% confidence intervale were as follow Hypertension 0.99 (0.94 – 1.05), Acute Myocardial Infarction 1.10 (1.01 – 1.21), Ischemic Stroke 1.07 (0.96 – 1.20) and Hemorrhagic Stroke 1.11 (0.86 – 1.44). Thus there is a suggestion of 7 to 10% excess risks for stroke and heart attacks, comparing the high vs low exposure areas, however they generally do not reach “statistical significance” so may be explained by chance.

#### *5.3.3.16 Antibody formation after COVID-19 vaccination*

PFASs have been shown in animal studies to affect the immune system negatively, and observations of reduced antibody levels after childhood vaccinations have formed the basis for developing guidelines for maximum permitted levels of PFASs in drinking water. Data from adults have been sparse and difficult to interpret. The COVID-19 pandemic - a new disease and a new vaccine - provided a unique opportunity to conduct a vaccine study among adults. During the summer of 2021, 319 persons from Ronneby and 48 persons from Karlshamn with only background exposure to PFAS participated in a study of vaccination responses after two doses of an mRNA vaccine. (Andersson et al., 2023). All participants obtained a good vaccination response.

The results indicated no difference between the exposure groups, either for antibody levels or cellular immune response. There was also no relationship between measured PFAS content and vaccination response. Those exposed to PFAS during early childhood did not have a reduced vaccination response compared to those exposed only in adulthood. The authors suggested that the difference compared to childhood vaccine studies is explained by the maturation of the immune system in adulthood.

### 5.3.4 Australian Exposure

In Australia, exposure to AFFF from some military airports contaminated drinking water supplies. Three sites in different states, were identified in the period 2013 to 2017 and this prompted a major intervention to reduce exposure and conduct surveillance and research. The research included sampling residents from each of the contaminated areas with blood samples to assess PFAS and clinical markers, and to consider rates of cancer and some other diseases in the affected areas(Law et al., 2023; Lazarevic, Smurthwaite, D'Este, et al., 2023). For both studies, non-exposed comparison areas were set up, one in each state, selected in each case as having similar sociodemographic profiles based on available census data.

Serum levels of contamination were somewhat lower than for the Ronneby Sweden situation, but the period for follow up since exposure was thought to have stopped, was longer. For the three contaminated areas, median PFOS levels were 5.2 to 5.7 ng/ml compared to 2.7 to 3.6 in the comparison areas(Lazarevic, Smurthwaite, D'Este, et al., 2023), and for PFHxS average serum levels were 2.8 to 3.7, compared to 0.8 to 1.3 ng/ml in the comparison areas. Contrasts were lower for PFOA. For the sum of median levels of PFOS, PFHxS and PFOA, they were 10.3 to 10.4 ng/ml in the three areas compared to 4.7 to 6.3 in the comparison areas. So, the serum levels for the sum of these three PFAS averaged 4 to 6 ng/ml higher than background. The serum sampling was conducted during 2016 to 2020, a few years since the problem was discovered.

#### *5.3.4.1 Mortality study*

Populations were identified who had lived in each of the areas judged contaminated by PFAS, Katherine (NT), Williamstown (NSW) and Oakey (Qld). There were a total of 54,343 people who had lived in an exposure area and 264,544 people frequency matched for age, sex, year of arriving to area and ethnicity, who had lived in a comparison area between 1983 and 2019. Cancer cases were identified for the years 1982-2017 and mortality for 1980 to 2019. The SIR (Standardised Incidence Ratio for cancer registrations, or deaths from some causes, age and sex adjusted) was calculated for exposed vs comparison areas in each state and for each cancer site. There were a few apparent excesses, but not consistently across the three areas. Prostate cancer was raised in one location

(SIR=1·76, 95 % confidence interval (CI) 1·36–2·24) in Katherine but not in the other two; laryngeal cancer (SIR=2·71, 95 % CI 1·30–4·98), kidney cancer (SIR=1·82, 95 % CI 1·04–2·96) and coronary heart disease (CHD) mortality (SIR=1·81, 95 % CI 1·46–2·33) were raised in Oakey; and lung cancer (SIR=1·83, 95 % CI 1·39–2·38) and CHD mortality (SIR=1·22, 95 % CI 1·01–1·47) in Williamstown. SIRs for all other outcomes and overall cancer were similar across exposure and comparison areas. The authors concluded that "Our study found no overall increased risk of cancer, and limited evidence for increased risk of any specific cancer or cause-specific death in three Australian communities with PFAS exposure from firefighting foams."

The apparent raised incidence of lung cancer in one area, Williamstown, along with coronary heart disease mortality (and also excesses in bladder and pancreatic cancers) may be confounded by smoking. The smoking rate was lowest in the comparison area for Williamstown, which might make the risk in the exposed area (compared to the comparison area) seem raised as a consequence. Also, the authors looked at some "control diseases" which they considered very unlikely to be caused by PFAS (e.g., death from intentional self-harm), and they too were raised in the Williamstown comparison, supporting the argument that the comparison area may have not been so well matched for other risk factors.

Summing the observed and expected numbers across all three areas, there was a modest overall increased risk of kidney cancer 47/39, an SIR of 1.21. For testicular cancers, numbers were small, and the presented ratios were all close to 1. They concluded that there was limited evidence to support an association between living in a PFAS exposure area and risks of cancers or cause-specific deaths.

#### *5.3.4.2 Cross sectional study*

The Australian researchers also took blood samples to assess the effect of PFAS on various clinical markers, with 881 adult volunteers who provided blood samples from the three communities and a similar number from the comparison communities(Lazarevic, Smurthwaite, D'Este, et al., 2023). There was inconsistency in the results from the three areas despite them having similar average levels of PFAS contamination, however there were significant associations between higher PFAS and higher total cholesterol (or LDL cholesterol) in one of the areas, but little evidence for clinical markers of liver function in any area.

### 5.3.5 Other reviews of the evidence on PFAS and health

#### *5.3.5.1 Australian review*

The Australian team who studied the PFAS problem in the three states with military airfields, also conducted a review of available literature at that time (Kirk M, 2018). They concluded that only one outcome had sufficient evidence of being affected by PFOA and PFOS: raised cholesterol. They judged that there was limited evidence of higher levels of blood PFAS being associated with raised uric acid, reduced kidney function, chronic kidney disease and lower levels of antibodies following vaccination. For kidney and testicular cancer, the evidence of association with PFAS was also judged to be limited.

For the other outcomes they addressed, they concluded that the evidence of any adverse effect related to PFAS, was inadequate. These included: neonatal, infant, and maternal outcomes; Reproductive outcomes; Other metabolic outcomes; Thyroid outcomes; Neurodevelopmental and neurophysiological outcomes; Diabetes; Cardiovascular outcomes; Overweight and outcomes; Skeletal outcomes; and Respiratory outcomes.

#### 5.3.5.2 ATSDR review

The US *Agency for Toxic Substances and Disease Registry* (ATSDR) published a review of PFAS and health in 2021. (ATSDR, 2021)They concluded that the available epidemiological studies suggest associations between perfluoroalkyl exposure and several health outcomes, however, cause-and-effect relationships have not been established for these outcomes: Pregnancy-induced hypertension/pre-eclampsia (PFOA, PFOS); Increases in serum hepatic enzymes, particularly alanine aminotransferase (ALT), and decreases in serum bilirubin levels (PFOA, PFOS, PFHxS); Increases in serum lipids, particularly total cholesterol and low-density lipoprotein (LDL) cholesterol (PFOA, PFOS, PFNA, PFDA); Decreased antibody response to vaccines (PFOA, PFOS, PFHxS, PFDA); Small (<20-g or 0.7-ounce decrease in birth weight per 1 ng/mL increase in either PFOA or PFOS blood level) decreases in birth weight (PFOA, PFOS); They noted an earlier conclusions from the International Agency for Research on Cancer (IARC 2017) that PFOA is possibly carcinogenic to humans (Group 2B), and EPA (2016e, 2016f) which concluded that there was suggestive evidence of the carcinogenic potential of PFOA and PFOS in humans.

They also noted suggestive evidence for associations between perfluoroalkyls and other health outcomes. These health outcomes include osteoarthritis in women under 50 years of age (PFOA, PFOS) and decreased antibody response to vaccines (PFNA, PFUnA, PFDoDA). Additionally, associations between serum PFOA and PFOS and decreases in glomerular filtration rate and increases in serum uric acid levels and between serum PFOA, PFOS, PFHxS, and PFNA and increased risk of early menopause have been observed. They noted that these effects may be due to reverse causation, where the effect (disease) causes the change in serum perfluoroalkyl levels (exposure) because weaker kidneys could lead to less reabsorption and so a faster decrease in PFAS.

#### 5.3.5.3 EFSA review

The European food agency published a detailed review of toxicology and epidemiology for the four most widespread persistent PFAS in blood samples PFOA, PFOS, PFHxS and PFNA, concluding with a recommended limit in terms of a tolerable weekly intake for the sum of these four PFAS.(EFSA et al., 2020). This was an update to a report two years earlier which had only looked at PFOA and PFOS. (EFSA et al., 2018)

They concluded that PFOS and PFOA are associated with reduced antibody response to vaccination, observed in several studies. Further they noted that there are some studies suggesting that serum levels of PFOS and PFOA are associated with increased propensity for infection, but that studies provide insufficient evidence to conclude on associations between exposure to PFASs and asthma and allergies. The evidence for other PFASs was considered to be weaker.

They concluded that there was clear evidence for an association between exposure to PFOS, PFOA and PFNA and increased serum levels of cholesterol. But for PFOS and PFOA, epidemiological studies provide insufficient evidence to conclude on associations between exposure to other PFASs and increased risk of cardiovascular disease.

Epidemiological studies provide evidence for an association between exposure to PFASs and increased serum levels of the liver enzyme alanine transferase (ALT). The magnitude of the associations was small (~ 3%), however, and few studies found associations with ALT outside the reference range. There were no associations with liver disease. There is therefore insufficient

evidence for associations between exposure to PFASs and diabetes, obesity, and metabolic syndrome.

They consider that “there may well be” a causal association between PFOS and PFOA and reduced birth weight, but no evidence for an adverse association for other PFAS and birth weight. There were no associations between other PFASs and fertility and other reproductive outcomes in either males or females. Epidemiological studies provide insufficient evidence for associations between exposure to PFASs and neurodevelopment outcomes, growth in infancy or childhood, neurobehavioural, neuropsychiatric, cognitive outcomes or thyroid function. Epidemiological studies provide insufficient evidence for associations between exposure to PFASs and changes in kidney function or serum levels of uric acid, as well as low bone mineral density or osteoporosis. They concluded that epidemiological studies provide insufficient support for carcinogenicity of PFOS and PFOA in humans. Limited information was identified for other PFASs.

Considering critical effects, in the previous opinion(EFSA et al., 2018), four endpoints were selected as potential critical effects for PFOS and/or PFOA. These were (i) increased serum total and LDL cholesterol (risk factor for cardiovascular disease), (ii) increased ALT levels (indicating effects on liver cells), (iii) reduced birth weight and (iv) effects on the immune system as shown by decreased antibody response to vaccines. Although the association with increased cholesterol was observed in many studies, the EFSA panel considers in the later report that the uncertainty regarding causality to be larger.

These were revised in the 2020 assessment and only effects on the immune system, which were observed at the lowest serum PFAS levels in both animals and humans, were judged critical for the risk assessment. They concluded that for the other outcomes, evidence of causality was weaker, or the data were too uncertain to establish a tolerable limit.

The findings of a decreased immune response were considered robust since they were consistently observed for the two studied PFASs in rodents (PFOA, PFOS) and in humans. They noted that this is not the case for effects on mammary gland development, which are observed at similar low serum levels in mice but have not been studied in other animal models or humans. Therefore, EFSA decided to base the latest assessment on PFASs on effects on the immune system.

#### *5.3.5.4 IARC*

Recently a comprehensive review of cancer risk was published on PFOA and PFOS by IARC (S. Zahm et al., 2024), and they concluded that there was sufficient evidence for the carcinogenicity of PFOA, whereas PFOS was possibly carcinogenic. Subdividing this into types of evidence, the evidence of carcinogenicity from epidemiology was judged limited for PFOA and inadequate for PFOS. For PFOA they highlighted the two specific cancer sites with data from several studies and for which the evidence was limited – kidney and testicular, for all other sites the data was judged “inadequate”. The data was also judged “inadequate” for any site for PFOS. They assembled all the evidence from animal tests and studies of potential carcinogenic mechanism, and for both PFOA and PFOS, there was “strong” mechanistic evidence for carcinogenicity in exposed humans. Based on all the evidence together they concluded that overall, there was sufficient evidence of carcinogenicity (category 1) for PFOA and classified PFOS as Category 2b, meaning it is possibly carcinogenic. There are no studies of cancer among people only exposed to PFHxS, and the only cancer study with significant exposure to PFHxS along with PFOS is the Ronneby study mentioned above.

#### 5.3.5.5 EPA Reviews

EPA have completed three recent reviews finalised for PFOA, PFOS and in draft for PFHxS.

Conclusions about which diseases were associated were very similar for both PFOA and PFOS. (EPA, 2024a, 2024b). PFOA and PFOS are “Likely to Be Carcinogenic to Humans” via the oral route of exposure. Epidemiological studies provided evidence of bladder, prostate, liver, kidney, and breast cancers in humans, although evidence was limited or mixed for some cancer types.

PFOA and PFOS were related to hepatic, immunological, cardiovascular, and developmental effects in humans given sufficient exposure conditions. For hepatic effects, the primary support is evidence of increased serum liver enzyme levels (i.e., alanine transaminase (ALT) in humans. For immunological effects, the primary support is evidence of developmental immunosuppression in humans, specifically decreased antibody response to vaccination against tetanus, diphtheria, and rubella in children. For cardiovascular effects, the primary support is evidence of increased serum lipids levels in humans, and for developmental effects, the primary evidence is decreased birth weight in human infants.

For PFHxS they have published a review for consultation, and this is the only major review focussed on PFHxS.(EPA, 2023). Overall, the conclusions were cautious, but they indicated that the available evidence indicates that PFHxS exposure is likely to cause thyroid and developmental immune effects in humans, given sufficient exposure conditions. Evidence primarily from epidemiological studies suggests, but is insufficient, to infer that PFHxS exposure might affect foetal development, specifically resulting in decreased birth weight. In addition, evidence from human and animal studies suggests, but is insufficient, to infer that PFHxS exposure may cause hepatic, neurodevelopmental, and cardiometabolic effects in humans. Lastly, although evidence from humans and or animals was also identified for hematopoietic, reproductive, renal, and carcinogenic effects, the currently available evidence is inadequate to assess whether PFHxS exposure may be capable of causing these health effects in humans, and these outcomes were not considered for use in deriving toxicity values.

### 5.3.6 Overview of findings

Considering the specific studies of AFFF exposed populations, and the various reviews summarised above, our conclusions of the categories of disease potentially associated with AFFF contaminated drinking water are:

*Figure 6: Summary of findings from literature review*

| | |
|---|---|
| Most likely | Increased cholesterol |
| | Reduced vaccination efficiency in children |
| | Reduced duration of breastfeeding in exposed mothers |
| Probably | Kidney Cancer |
| | Testicular Cancer |
| | Liver function |
| Possibly | Type 2 diabetes |
| | Osteoporosis linked fractures |
| | Polycystic Ovarian Syndrome (PCOS) |
| | Reduced birthweight |
| | Learning and development issues |
| | Bladder cancer |
| | Thyroid Disease |
| Unlikely | Ulcerative Colitis |
| | Pregnancy induced hypertension |

It should be noted that this assessment only includes conditions where research has been done, there may be other conditions linked to PFAS exposure for which there is no research to draw upon.

## 5.4 Environmental issues and mental health, findings from the literature

The Panel were concerned that there might be mental health consequence from living in areas where there are concerns about environmental pollution and reviewed the scientific literature on the subject. Whilst there initially appeared to be thousands of studies, most related to Covid-19 and were therefore not relevant to this report. Once those were removed, nineteen studies remained.

It is important, in this analysis, to distinguish between physiological effects on mental health from a particular substance (where the substance changes the biological function of the brain) and psychological effects on mental health as a consequence of learning that a person or community has been exposed. While physiological effects (as long as they relate to PFAS) are interesting and important, they are more relevant to the wider review and not to this section of the report.

Several studies have looked for associations between environmental contamination and adverse mental health impacts, and many of them are discussed in detail below. We have focused on papers where there appears to be a clear impact on the person's overall mental health and not where it looks more at worry or concern about the contamination without using validated clinical tools to assess the psychological impact. The key areas where evidence was found are discussed below.

### 5.4.1 Overall mental health

A systematic review and meta-analysis of several papers showed weak to moderate associations between chronic environmental contamination and several mental health challenges, including anxiety symptoms, stress, symptoms of depression and symptoms of PTSD. This study mostly drew on cross sectional surveys and so it is not necessarily clear the extent to which confounding factors have been controlled for. It is also not clear that physiological mechanisms have been excluded. Many of the papers that were reviewed in this study are discussed individually below (Schmitt et al., 2021).

One study looked at community impact and support service development after a containment failure of toxic waste from a quarry near a chemical plant in the northwest of England. This necessitated the evacuation of several households and was heavily covered in the local and national media. This coverage was often strongly worded, with one new outlet referring to the community as the "Village of the Damned". There were also biochemical markers of toxicity found in residents, which normalised after the contamination was mitigated. There was also an impact on home values and many people moved away, leaving the remaining residents isolated. While there were considerable impacts on stress, with a small number experiencing psychological distress, a qualitative analysis found that it was the decline of the community and the loss of social interactions, rather than health anxiety that were the main drivers (Barnes et al., 2005).

Four other studies looked at associations between background pollutants (not PFAS) and mental health, but they are cross-sectional surveys and so may well be heavily confounded. They also seem to relate to physiological responses to those pollutants, rather than psychological responses to the knowledge of exposure (Rahman et al., 2022), (Eum et al., 2012), (Xu et al., 2023), (Wu et al., 2022).

Another paper looked more widely at mental health and exposure to potentially toxic compounds, and, while it was not a cross-sectional survey and potentially confounded, it too took a physiological, rather than a psychological approach (Genuis, 2009).

### 5.4.2 Psychological distress, somatisation, and anxiety

Two papers, one quantitative and one qualitative, looked at psychological distress in three PFAS exposed communities in Australia. They were contrasted with, in the quantitative work, three

sociodemographically similar communities which did not have any known environmental PFAS contamination.

The quantitative study (Lazarevic, Smurthwaite, Batterham, et al., 2023) was through a cross-sectional survey and the administration of standard assessment tools for general psychological distress, generalised anxiety disorder and also an assessment of somatisation (which is where mental health issues manifest as physical symptoms in the affected person). Participants were also asked how concerned they were about their health. The study looked both at living in a PFAS exposed community, and also at serum concentrations of PFOS, PFOA and PFHxS. Several potentially confounding variables were also considered. Having adjusted for confounding factors, the study found a higher prevalence of psychological distress, somatisation, and anxiety in each of the exposed communities as against the prevalence in the matched control communities without known exposure.

For somatisation, the findings were statistically significant for each of the three matched pairs of communities and the prevalence ratio varied from 3.65 times in the highest matched pair to 1.82 times in the lowest.

Two measures were used to assess psychological distress, one of which was statistically significant across all three pairings and the other of which only reached statistical significance with one of the three pairings.

With regard to anxiety, the increased prevalence in exposed communities reached statistical significance in two out of three community pairings.

Notwithstanding the variability in statistical significance, the consistent effect, with increased prevalence of all three mental health states in exposed communities versus unexposed community is clear.

Looking at the serum concentrations of the three PFAS and assessing the mental health indicators on the basis of doubling of the serum PFAS level did not appear to show any increase in the prevalence of psychological distress, somatisation, or anxiety with an increase in levels of any of the 3 PFAS investigated. On this basis, it is unlikely that the findings in this study relate to a physiological effect, and they are more likely to be explainable on the basis of a psychological effect, i.e. it was the participants being aware of being exposed rather than actual level of chemicals in their blood which prompted the anxiety.

The study also drilled down into individual characteristics and found that people who had worked with AFFF and people who used bore-hole water supplies were more likely to display psychological distress, somatisation, or anxiety than those who had not, but none of these associations were statistically significant. Having moved away did not appear to be associated with a different prevalence.

The qualitative study (Banwell C, 2021) is across the same communities as the previous paper, and several themes emerged. There was significant mistrust around the measurement of PFAS levels in the environment, the approach to water treatment, advice with regard to the continued use of borehole water for irrigation and livestock and perceived discrepancies between the scientific literature and the people's own lived experience, including their own illnesses. The uncertainty around whether illnesses could be attributed to exposure and also the contradictory nature of

different parts of the scientific literature were sources of stress to residents. The study also identified feelings of guilt and moral injury around the exposure their children have had.

Much of the stress, anxiety, and anger that people experienced, they attributed to their physical health, their fears around longer-term impacts on their physical health, and disruption to their financial and social situations.

Because of the established distrust of government (a government agency was responsible for the contamination and the initial response) the willingness to trust others also diminished. A programme of testing that was offered to residents seemed, paradoxically, to increase concern, rather than decrease it. This was found to be partly because of a lack of clear information on the meaning of findings, partly because of confusion between the different units used for biological and environmental sampling, and partly because there was not a correlation at hyperlocal level between degree of land contamination and serum levels.

Stigmatisation of areas and communities affected was also a stressor, with uncertainty around the potential impact on tourism and other economic activities.

Finally, they highlighted the disparity of views within the affected community as a source of significant stress, with a consensus that something should be done but discord as to what the specific actions might be.

### 5.4.3 Perinatal mental health

A study from San Francisco looked at perinatal depression in US born and migrant women. It found a stronger association between PFAS exposure and depression in the migrant women than the US born population. While the study was relatively small and, therefore, difficult to draw strong conclusions from, given that it is unlikely that there would be neurophysiological differences in women based upon country of birth, this finding is suggestive of there being some psychological process. However, given the potential for confounding factors, the suggestion is a weak one (Aung et al., 2023).

One study looked at PFAS alongside a different group of substances and, while it found an association between the other substances and postpartum depression, it did not for PFAS. This was a relatively small study, so it is difficult to draw any inferences about PFAS. Furthermore, given the design of the study, it is likely that it was looking at physiological, rather than psychological responses (Vuong et al., 2020). This contrasts with another study on postpartum depression from China looking only at twin pregnancies, which did find an association, but again, it is unclear if the study was looking at physiological, rather than psychological effects (Hu et al., 2024). A further review study, looking at perinatal mental health and a wide variety of pollutants, including PFAS, appeared to be focussed on physiological mechanisms (Surace et al., 2023).

### 5.4.4 Depression

A large study in The Netherlands (Roberts et al., 2021) looked at a variety of neighbourhood characteristics, including perceived environmental disturbance and the association with depression. It found an association between environmental disturbances and depression in both working and stay-at-home populations and an even stronger association with stress. This does appear to show a psychological connection between environmental disturbance and depression, potentially by way of stress. In this study, however, environmental disturbance related to perceived air quality and perceived noise levels. It is not clear whether these exposures are comparable with water contamination in terms of potential adverse psychological impacts.

Another cross-sectional study of NHANES data found a lower risk of depressive symptoms in those exposed to PFAS with a dose response, however it is important not to overinterpret the finding as, being a cross sectional study, it is prone to confounding factors and furthermore, it is it is also unclear whether findings relate to physiological, rather than psychological responses (Sun et al., 2023).

A further cross-sectional analysis of NHANES data (Yi et al., 2023), using different ways of assessing depression found a bimodal association with a decreased likelihood of depression below 39.66 ng/ml serum PFAS and an increased likelihood above that level. Again, it is important not to overinterpret due to potential confounding and lack of clarity whether findings may relate to physiological, rather than psychological processes.

### 5.4.5 In summary

While there appears to have been fewer high-quality studies on the mental health and wellbeing impacts of environmental concerns than is ideal, there have been some. Bringing the findings together, while none of the evidence is particularly strong, there does seem to be a reasonable indication that stress, psychological distress, and anxiety are associated with environmental contamination and some indication for depression, perinatal depression, and PTSD. Worry about short and long-term physical health, mistrust and lack of clear and unifying evidence seem to be key factors.

# 6 Discussion and conclusions

This section brings together evidence from experts by experience, from subject matter experts and from reviews of the published literature by panel members and synthesises it all into where the current state of the evidence is, in the context of the type of PFAS exposure that has happened in Jersey. It should be noted that much of the evidence is unclear and that the absence of clear evidence does not mean that links do not exist. For ease of use for healthcare professionals, we have recorded our discussions and conclusions by the body function that has potentially been affected.

## 6.1 Comparability of exposure

The places in the world where people have been exposed to the same mixture of chemicals as some in the area around the airport in Jersey have been, and research into potential health effects has been conducted, are Ronneby in Sweden and parts of Australia. In panel meetings, potential differences in median levels between the places were noted, but it became clear that the time between primary exposure and testing was different and so also a factor in assessing whether the primary exposures were similar in extent between the places.

At first sight, serum levels seem quite different, in the different populations. Let us take the levels of PFOS for example, using available data on medians or geometric means (which are quite similar, and either is a useful measure of the “average” level in each population). The average across all the population samples in Ronneby was 135 ng/ml, in the Australian contaminated area 5.5 ng/ml and for the Jersey residents the median PFOS was 10.9 ng/ml. Each population had levels higher than average population levels with no local AFFF contamination source, which is assumed to be about 3 ng/ml.

However, the timing between exposure and when blood testing was undertaken was quite different. The Swedish samples were taken a shorter time since primary exposure was identified and stopped, between 6 months and 2 years. The Australian samples were taken about 4 years since the contaminated ground water was identified and alternative sources were used for the mains water. In Jersey, people were provided with piped alternatives to the most contaminated water supplies in 2006, some 16 years prior to the serum data being collected.

The average level in the Australian population was clearly much lower than for the population of Ronneby. The half-life for PFOS is about 3 years, so the Australian serum levels might have been about twice as high when the exposures were identified and controlled. It is likely that a smaller subset of the Australian population relying on private wells near to the airfields would have had much higher exposures and serum levels than these averages, however the mortality study was conducted in the larger population and the reported averages are appropriate for considering the population exposure.

To compare the level of serum in the Ronneby population to the Jersey sample, we can estimate by extrapolation what the average levels Ronneby would be expected to be 16 years since exposure stopped instead of less than 2 years. An additional 14 years is 4.7 half-lives, and so the serum levels would be expected to fall by then to about 10 ng/ml. Comparable calculations for PFHxS would indicate the measured level of 114 ng/ml falling to about 14 ng/ml if followed for an equivalence time, around 3 half-lives. These values are quite similar to those measured in Jersey for both these PFAS.

These extrapolations are considering only the time of sampling in relation to the when the contamination was dealt with, however in all places the type of AFFF contamination varied over time. It should be noted that the move away from the PFAS-containing Lightwater firefighting foam happened before the move away from borehole supplies, but this is true in all three places. We also do not have information on how the contamination moved in the groundwater and how persistent PFAS are in the various aquifers. The panel also discussed that there is not necessarily clarity on the duration of the primary exposure in any of the locations nor on the degree of ongoing exposure after the discontinuation of borehole supply through other routes.

After lengthy discussion, the panel came to the consensus view that while there are uncertainties, it is reasonable to assume that Ronneby exposure is reasonably analogous to the situation in Jersey and therefore a valuable source of evidence for possible health effects. The exposure profile for Australian population contributing to epidemiology there was likely somewhat lower.

## 6.2 PFAS and cardiology

Elevation of serum cholesterol was highlighted by affected Islanders, subject matter experts and in the evidence in the scientific literature as being associated with PFAS exposure. In addition to this, the literature also contained evidence of an increase in low density lipoprotein (LDL) also known as “bad cholesterol”. These are strong findings that have been corroborated in many studies. Elevated cholesterol, particularly LDL, is usually associated with an increase in diseases of the circulatory system, such as ischaemic heart disease, cerebrovascular disease, heart attacks and strokes. Not all of the studies in PFAS exposed populations that show the increase in cholesterol appear to show a clear increase in diseases of the circulatory system or in people dying from those diseases. For example, in the large (PFOA-exposed) C8 studies, there was a clear association with increased cholesterol, but a follow up analysis of cardiovascular incidence failed to identify any increased risk of cardiovascular disease. On the other hand, the Ronneby study of an AFFF exposed population suggests a modest increase in some cardiovascular disease categories. A small number of other studies (Steenland et al., 2009; Winquist & Steenland, 2014), however, have found an increase, so the panel took the view that it would be unwise to assume that the elevated cholesterol in PFAS exposed persons was less likely to be associated with cardiovascular disease than in the general population.

There was some discussion about why any relationship between PFAS-exposed persons’ elevated cholesterol and cardiovascular conditions was not as clearly defined as in the general population and a few hypotheses were discussed. The first of these related to the finding in a few studies that there is an elevation of high-density lipoprotein (HDL); commonly known as “good cholesterol” in PFAS-exposed persons. It was hypothesised that this might, to some degree, balance the elevation in LDL and so the net increase in risk might be small or even not exist at all. The second hypothesis discussed related to findings in the C8 study where PFAS-exposed persons appeared to have a lower c-reactive protein (CRP). This is a blood marker of inflammation anywhere in the body. Given that one of the factors in the development of cardiovascular disease can be inflammation in the body, it may be that, if PFAS are reducing inflammation in the body, that effect might offset some of the risk from elevated cholesterol.

In oral evidence, one of the subject matter experts who gave evidence to the panel also suggested that other lipids (fats in the blood) over and above cholesterol may be elevated by PFAS exposure. While there was not clear evidence to support this in the epidemiological literature, it cannot be

ruled out as a possibility. It should be noted, however, that many of the measures that are used to manage living with elevated cholesterol may also help if other lipids are elevated.

In summary, the panel came to the view that elevation of total cholesterol is highly likely to occur in PFAS-exposed populations, and, while the evidence was not as clear for cardiovascular disease as a potential consequence, the panel adopted a precautionary approach.

The panel briefly discussed testing for cholesterol in PFAS-exposed people but noted that this is a matter that will be considered in Report 3 and so deferred further discussion until the matter is considered for that report.

Because there was no evidence found to suggest that managing cholesterol in PFAS-exposed persons should be either more stringent or less stringent than in the general population who have elevated cholesterol, the Panel resolved to recommend that normal management of elevated cholesterol (diet, exercise, lipid-lowering drugs, management of other risk factors) should be undertaken in the PFAS-affected populations.

## 6.3 PFAS and cancer

Affected Islanders highlighted several different types of cancer which they were concerned might be related to PFAS exposure. These included breast, prostate, bowel and uterine (womb) cancer as well as cancers of the urinary system (kidney, bladder) and blood cancers such as leukaemias, lymphomas and myeloma. Among the subject matter experts who gave evidence to the panel there was felt to be strong evidence to support an additional risk of kidney cancer in PFAS-exposed populations and that there was some evidence of lesser strength for breast and testicular cancers. They also highlighted evidence from animal experiments showing an increased likelihood of liver cancer and of thyroid cancer.

The International Agency for Research on Cancer (IARC) has assessed some PFAS species for cancer risk and has determined PFOA has sufficient evidence to suggest that it is likely to cause cancer. They also assessed PFOS, but found insufficient evidence at this time: the mechanistic evidence was there, but there was not sufficient epidemiological evidence at the time of assessment. PFHxS has not yet been assessed by IARC because insufficient evidence has been generated hitherto.

In Ronneby, which has a similar chemical mix to that to which people in Jersey were exposed, there appeared to be an increase in the rates of kidney cancer, bladder cancer and testicular cancer. Neither prostate, colon nor lung cancers were found it be increased, indeed prostate cancer appeared to be reduced, but that may be a chance finding. Studies in Australia only found an increase in kidney cancer, but, for the reasons discussed above in the section on comparability of exposure, those studies did not include as many highly exposed persons as those in Ronneby. Looking at the data from Ronneby, there appears to be a 20% increase in the chance of getting kidney or testicular cancers. The increase in bladder cancer was similar although there is less corroborating evidence from other studies and so that may be a chance finding. The panel noted that neither of these are common cancers; unlike breast, colon, or prostate cancers for example, and so a 20% increase in risk does not mean that an individual is likely to get those cancers, but, across large populations, the additional risk could be detected. Clearly, if someone has one of those cancers, it is a very important matter, but the panel wanted to reassure the public that the chances of developing those diseases still remains low.

The panel discussed further the IARC findings; that there was a reasonable mechanistic case for both PFOA and PFOS causing cancer, even if the epidemiological evidence so far only indicates that PFOA is likely to cause a small number of cancer types. The mechanisms IARC highlighted are common to the genesis if many or most types of cancer, and so it would be unwise to say that PFOA (and possibly PFOS) only increase the risk of kidney and testicular cancers. There is plausibly an effect on the other cancer types that have been highlighted by the Islanders with whom the panel had discussions and, potentially, others too.

The panel noted that the Swedish medical records data linkage is among the most comprehensive in the world and so patterns of disease increase are relatively easy to spot. Some of the cancers that have been highlighted (such as the blood cancers, for example) are sufficiently rare that it would be very difficult to spot an increase even if the risk in PFAS-exposed populations were much higher than that in the wider population. However, among the common cancers; like breast, colon, and prostate cancers; we would have expected to see clear evidence of an increase in the number of cases in the exposed population if there was a PFAS related risk, unless the additional risk was very small. This provides some reassurance, but does not exclude the potential for PFAS to have some influence on the common cancers. For the rarer cancers, there really is not enough evidence in the literature to conclude one way or another.

In summary, the panel came to the view that an increase in kidney and testicular cancer in PFAS exposed populations was highly likely, and increase in bladder cancer was possible, that an increase in common cancers such as breast, lung and colon was less likely and that there was not sufficient evidence to make a judgement about rare cancers, but it is plausible that there may be an effect.

The panel briefly discussed whether some sort of screening for kidney and testicular cancers might be feasible and, while it was felt that that would be unlikely given the low overall risk of these illnesses even in PFAS-exposed populations, the panel resolved that this matter should be given a fuller consideration in Report 3.

The panel gave some consideration to whether to advise regular testicular self-examination but was not convinced that there was a case over and above general population advice on the matter.

While the panel did not believe that there was enough evidence to recommend a change to normal clinical practices, in terms of cancer detection in PFAS-exposed persons, it was recommended that, when clinicians see a PFAS-exposed person with symptoms consistent with kidney, testicular or bladder cancer, they should have a higher level of suspicion that the symptoms might be cancer related, and should manage the person's care accordingly.

## 6.4 PFAS and the immune system

Islanders who gave evidence to the panel expressed concerns about autoimmune diseases. These are conditions where the body's immune system attacks the body, and include conditions such as rheumatoid disease and systemic lupus erythematosus (SLE) – commonly known as lupus. The subject matter experts who gave evidence to the panel highlighted two potential areas: antibody response to childhood vaccinations and susceptibility to infections and infectious diseases. They also mentioned another autoimmune disease called ulcerative colitis.

The panel considered the literature on autoimmune diseases in PFAS-exposed populations. The data from Ronneby does not show an increase in autoimmune disease. The C8 study looked specifically at lupus and ulcerative colitis, an inflammatory disease of the bowel, and did find an increase for the

latter, but this has not been replicated in further studies and is likely to represent a chance association. The panel discussed these findings further and felt that autoimmune disease is often associated with an increased antibody response in the body. Given that there is stronger evidence of a reduced antibody response in the body, in the context of childhood vaccinations, which are discussing below, the panel found it difficult to see a mechanism where there might also be an increased antibody response as a result of PFAS exposure. In the light of this, and the limited evidence, the panel felt that any increased risk of autoimmune disease was unlikely.

While the evidence for reduced antibody response to childhood vaccines was seen by the panel as strong, there does not seem to be a consistent concomitant increase in vaccine-preventable diseases in the literature. This may be because these diseases are generally rare and because vaccination in the wider population creates herd immunity, which offers protection to those PFAS-exposed children with a reduced antibody response to those vaccines. Looking at more common childhood infections, some studies show a modest increase and others do not. There also does not appear to be an increase in exacerbations of childhood asthma, which are often triggered by respiratory infections.

There is limited evidence on adult vaccinations, with the team at Ronneby having looked at immunisation against SARS CoV-2 (the virus responsible for COVID-19) and antibody titres. This did not show a reduction with PFAS exposure, but the panel were of the view that the difference between childhood and adult immune systems could easily account for the apparent discrepancy. The panel also discussed another paper that appeared to show a difference in COVID-19 severity between PFAS-exposed persons and the general population, but this was with one PFAS moiety that is not part of the exposure in Jersey and could also be explainable by confounding or chance association.

In summary, the panel were of the view that an effect on antibody titres after childhood vaccination in PFAS-exposed children was highly likely, but there is not clarity if that has implications for infectious disease. An increase in autoimmune diseases or a reduction in adult vaccine responses was judged to be unlikely. It should be noted that this reduction of antibody response could be indicative of wider compromise of the immune system. For that reason, it has been important in setting the regulations for PFAS exposure in several countries.

The panel discussed childhood immunisations as a potential area for recommendation and came to the consensus that the most effective approach would be to recommend high uptake across the population so that those who might have a lesser immune response (such as those exposed to PFAS) might be afforded additional protection through herd immunity.

## 6.5 PFAS and the hormonal system

This was not an area where the Islanders who gave evidence to the panel highlighted concern, but some potential areas of concern were highlighted by the subject matter experts who gave evidence to the panel. Subject matter experts highlighted two areas, thyroid dysfunction, and metabolic dysfunction: including obesity and type 2 diabetes mellitus.

In the literature there are several studies looking at circulating hormones, thyroid hormones, oestrogen, testosterone. Some of these have found associations with circulating PFAS. These findings, however, are not consistent and, because these are cross-sectional studies, it is difficult to draw any inferences about causality. On this basis, such evidence is not usually viewed as robust evidence. While thyroid dysfunction did come up in the C8 study, the more relevant Ronneby study did not find an association. The panel also noted that a change in the levels of some thyroid

hormones, even if it were clearly supported by the evidence, may not be clinically important if it is not associated with a disease state. It is important to focus primarily on the health and wellbeing of the person and not the specific numbers from a blood test.

Type 2 diabetes was not found to be increased in the C8 study, but did show an increase with PFAS exposure in the study at Ronneby. The panel came to the view that the inconsistency meant that evidence was not strong and that the Ronneby findings could be explained by chance association. On the other hand, if other studies corroborate the finding, it may be clinically important.

For obesity, there are both positive and negative studies in relation to childhood exposure and obesity developing in childhood but not clear evidence. The C8 study did not show an association with adult obesity and found an inverse relationship between PFOS and obesity in childhood. The panel therefore came to the view that there was insufficient evidence to demonstrate an association between PFAS exposure and obesity. The panel also discussed a potential effect of PFAS on the gut microbiome. This mixture of microscopic organisms in the gut is associated with poorer health if it becomes disrupted. A disrupted microbiome can be associated with an increased risk of obesity and of several other disorders. Microbiomal disruption may also impact on PFAS reabsorption in the body and therefore PFAS levels in the serum. This could potentially be a confounding factor for some apparent health effects.

In summary, the panel came to the view that an association with thyroid disease was unlikely, although it was possible that there may be some effect on hormone levels. Increases in type 2 diabetes and in obesity were also possible, although the evidence was not yet strong or consistent enough to make a determination.

The panel considered whether any recommendations were appropriate in these areas but, in the light of the conflicting nature of the evidence, chose not to make any at this time.

## 6.6 PFAS and the nervous system

While the islanders who gave evidence to the panel did not raise any issues of this type, the subject matter experts interviewed referred to effects of PFAS on developmental language disorder, which only seems to be apparent with girls, and also a potential association with neurodevelopmental disorders. Looking to the literature, the C8 study found an association with ADHD, and a meta-analysis across several studies was suggestive of a link, especially in girls, but was not statistically significant, so it is difficult to draw any inferences. The Ronneby study found an association between PFAS exposure and delayed language learning (only in girls) but that has not been replicated elsewhere and may be a chance association. The panel were of the view that more research was needed before any conclusions or recommendations in this area can be drawn.

## 6.7 PFAS and the gastrointestinal system

The Islanders who gave evidence to the panel highlighted gastrooesophageal reflux symptoms and change in bowel habit as areas of concern for them. The subject matter experts highlighted alterations in liver enzymes (they also highlighted ulcerative colitis, an autoimmune disease of the bowel, but that is discussed in the section on PFAS and immunity).

The literature contains several studies which find an association between changes in liver enzymes (particularly ALT), but these are, overwhelmingly, changes within the normal range. The panel was of the view that blood test results moving within the normal range were interesting but are unlikely to be associated with any risk of harm to the health and wellbeing of affected persons. There is some,

weaker, evidence on an association with non-alcoholic fatty liver disease (NAFLD) but it was not clear and, given the lack of a current standard of care treatment for that condition, is not suitable for recommendation at this time.

As discussed elsewhere in this report, the lack of scientific literature on gastro-oesophageal reflux or change in bowel habit related to PFAS does not mean that those Islanders who have experienced those effects might have had another cause (although that is a possibility), rather it simply shows that research has not yet been done in this area.

While, as discussed, the variation on ALT is unlikely to be clinically important, there was not a basis on which the panel could make a recommendation at this time.

## 6.8 PFAS and the urinary system

Islanders did not highlight any urinary issues, in discussion with the panel but subject matter experts did highlight reduces kidney function as an area for further scrutiny. Looking at the literature, however, the panel came to the view that the association is probably an example of reverse causality, and appears because of the role the kidney has in excreting (and reabsorbing) PFOA. No other conditions (apart from cancers that are discussed elsewhere) showed an association in the literature.

## 6.9 PFAS and reproductive health (including foetal and infant growth and lactation and breastfeeding)

This is a broad topic, ranging from fertility and conception, pregnancy and potential complications of pregnancy, foetal growth, infant growth, first year of life and also breastfeeding and lactation. While the only issue raised by the Islanders who met with the panel was fertility, the subject matter experts who gave evidence to the panel raised a range of issues including intrauterine growth retardation, reduced birth weight, high blood pressure in pregnancy, difficulties with the commencement and continuation of breast feeding and some concerns around puberty. Subject matter experts took pains to stress the importance of breastfeeding, even in PFAS-exposed populations.

The literature contained several studies showing a reduction in the duration of breastfeeding in PFAS-exposed populations and some relating to breastfeeding initiation difficulties. The panel took the view that, given the profound and widespread benefits of breastfeeding, it was highly likely that those benefits would greatly outweigh any risks from the PFAS that might be passed on to the child during breastfeeding.

Regarding birthweight, the studies are contradictory. Some studies reported a reduction, but they did not report serious consequences and other studies find no reduction at all. For example one recent review highlighted that although there are many studies suggesting an association between reduced birthweight and maternal serum PFAS, these studies which rely on measurements made later in pregnancy may be at risk of bias, as the studies where the PFAS exposure clearly precedes the pregnancy show on average little or no impact on birthweight (Steenland et al., 2018). Overall, the panel was not convinced that this was established as a risk.

While the C8 study did find an association with pregnancy associated hypertension, Ronneby (where there was a higher level of exposure) and other studies did not. The C8 findings may have been a chance association.

The literature review did not find clear evidence on puberty difficulties or fertility challenges per se, but the study in Ronneby did find an increase in polycystic ovarian syndrome (PCOS); a condition

which can lead to suboptimal fertility. Because this has not been found in other studies yet, the panel was not persuaded that this is a probable health effect with the current level of evidence. It needs further research.

Overall, the panel were unconvinced that many of the health impacts (other than breastfeeding challenges) had evidence that was sufficiently robust to draw conclusions or make recommendation. On breastfeeding, however, the panel was convinced of significant net benefit from breastfeeding, even among those with PFAS exposure, and recommended that PFAS-exposed mothers do breast feed.

## 6.10 PFAS and the musculoskeletal system

While nothing in this area, (other than autoimmune joint disease, which is discussed in the section on PFAS and the immune system) was raised by Islanders or by the invited experts, the literature showed evidence of an increased likelihood of fractures linked to osteoporosis. This finding was borne out by studies showing reduced bone density in PFAS exposed persons, adding to the biological plausibility of the findings with regard to fractures.

On this basis, the panel made a recommendation about having a higher index of suspicion in people who have risk factors for osteoporosis and have been exposed to PFAS in the past.

## 6.11 Environment and Mental Health

During the meetings with Islanders, several referred to stress and worry at having been exposed to PFAS and to moral injury or guilt both by living in a place where their children had been exposed to PFAS and also through them having to witness their parent's ill-health journey.

Although the number of high-quality studies on the mental health and wellbeing impacts of environmental concerns is limited, some research has been conducted. When combining these findings, the evidence, while not particularly strong, reasonably indicates that environmental contamination is associated with stress, psychological distress, and anxiety. There are also indications of links to depression, perinatal depression, and PTSD. Key factors include worries about short- and long-term physical health, mistrust, and the lack of clear, unifying evidence.

The panel also discussed the experience in Australia, with falling property prices in the affected area driving financial worry in addition to broader concerns, but was reassured that overall, the property market in Jersey is buoyant and Public Health were not aware of any local variation.

In the light of these discussions, the panel decided to recommend that talking therapies be available to people with a history of PFAS exposure.

## 6.12 Interactions between services and Islanders

Islanders raised a series of issues regarding their interactions with health services. They did not feel that health professionals understood PFAS and the health risks of PFAS well and this made any reassurance they received less effective. They also sometimes received contradictory advice from different health professionals, which makes them feel uncomfortable.

General practitioners (GPs) in Jersey also expressed concerns that they did not have access to the latest information on PFAS and health effects and voiced the need for a resource in Jersey with up-to-date knowledge on the health effects of PFAS. The panel took the view that a summary of this report could be a useful point of care resource for GPs and other clinicians. The panel also discussed the suggestion from Jersey GPs that there be at least one person with detailed knowledge on PFAS and

health to whom GPs might refer and/or from whom they might seek advice and guidance. The panel, however acknowledged that they are not experts on how healthcare is delivered in Jersey and that, for that reason, believes that to specify exactly who that resource should be is inappropriate.

In the light of the discussion, the panel resolved to recommend both a human resource with expertise in PFAS and health and a written resource, summarising the findings of this report.

# 7 Recommendations

While this report is primarily informational, the panel made the following recommendations to government and to health professionals in Jersey:

- PFAS-exposed persons found to have elevated serum cholesterol should have their cholesterol managed in the usual way (e.g. diet, statins).
- When PFAS-exposed people exhibit symptoms which are consistent with kidney cancer or testicular cancer , clinicians should have a higher level of suspicion of cancer than in unexposed populations.
- Regular testicular self-examination should be considered in PFAS-exposed populations.
- Childhood vaccination should be promoted across the whole population to ensure that those less likely to mount a strong vaccine response (such as those exposed to PFAS) are protected through herd immunity.
- Breastfeeding has significant health benefits and should be promoted in PFAS-exposed populations as it is in the wider population.
- Health professionals should have access to accurate information to help manage any concerns about breastfeeding in PFAS-exposed populations.
- Where a person is at increased risk of osteoporosis and is also PFAS-exposed, clinicians should consider a lower threshold for investigating whether osteoporosis is present.
- People who live in communities with increased PFAS exposure should be offered access to talking therapies to support their psychological health and wellbeing.
- A health professional with particular expertise in PFAS and health should be made available to clinicians in Jersey to offer technical support in caring for PFAS-exposed patients.
- A concise knowledge-based resource on PFAS exposure and health should be made available to the public and health professionals in Jersey.

## References


Abraham, K., & Monien, B. H. (2022). Transdermal absorption of 13C4-perfluorooctanoic acid (13C4-PFOA) from a sunscreen in a male volunteer – What could be the contribution of cosmetics to the internal exposure of perfluoroalkyl substances (PFAS)? *Environment International*, *169*, 107549. https://doi.org/https://doi.org/10.1016/j.envint.2022.107549

AECOM. (2016). *Stage 2C Environmental Investigation - Human Health Risk Assessment, Army Aviation Centre Oakey 01/09/2016*. https://publications.aecom.com/pfas/solutions/pfas-contamination-investigation

Andersson, A. G., Lundgren, A., Xu, Y., Nielsen, C., Lindh, C. H., Pineda, D., Cederlund, J., Pataridou, E., Sogaard Tottenborg, S., Ugelvig Petersen, K., Fletcher, T., Lagging, M., Bemark, M., Jakobsson, K., & Li, Y. (2023). High Exposure to Perfluoroalkyl Substances and Antibody Responses to SARS-CoV-2 mRNA Vaccine-an Observational Study in Adults from Ronneby, Sweden. *Environ Health Perspect*, *131*(8), 87007. https://doi.org/10.1289/EHP11847

Andersson, E. M., Scott, K., Xu, Y., Li, Y., Olsson, D. S., Fletcher, T., & Jakobsson, K. (2019). High exposure to perfluorinated compounds in drinking water and thyroid disease. A cohort study from Ronneby, Sweden. *Environ Res*, *176*, 108540. https://doi.org/10.1016/j.envres.2019.108540

ATSDR. (2021). *Toxicological profile for perfluoroalkyls - release May 2021. Agency for Toxic Substances and Disease Registry.* https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf

Aung, M. T., Eick, S. M., Padula, A. M., Smith, S., Park, J.-S., DeMicco, E., Woodruff, T. J., & Morello-Frosch, R. (2023). Maternal per- and poly-fluoroalkyl substances exposures associated with higher depressive symptom scores among immigrant women in the Chemicals in Our Bodies cohort in San Francisco. *Environment International*, *172*, 107758. https://doi.org/https://doi.org/10.1016/j.envint.2023.107758

Banwell C, H. T., Smurthwaite K, Trevenar S, Walker L, Todd K, Rosas M, Kirk M (2021). Health and social concerns about living in three communities affected by per- and polyfluoroalkyl substances (PFAS): A qualitative study in Australia. *PLoS One*, *14;16(1):*.

Barnes, G. J., Litva, A., & Tuson, S. (2005). The social impact of land contamination: reflections on the development of a community advocacy and counselling service following the Weston village incident. *J Public Health (Oxf)*, *27*(3), 276-280. https://doi.org/10.1093/pubmed/fdi036

Beesoon, S., Webster Glenys, M., Shoeib, M., Harner, T., Benskin Jonathan, P., & Martin Jonathan, W. (2011). Isomer Profiles of Perfluorochemicals in Matched Maternal, Cord, and House Dust Samples: Manufacturing Sources and Transplacental Transfer. *Environmental Health Perspectives*, *119*(11), 1659-1664. https://doi.org/10.1289/ehp.1003265

Brunn, H., Arnold, G., Körner, W., Rippen, G., Steinhäuser, K. G., & Valentin, I. (2023). PFAS: forever chemicals—persistent, bioaccumulative and mobile. Reviewing the status and the need for their phase out and remediation of contaminated sites. *Environmental Sciences Europe*, *35*(1), 20. https://doi.org/10.1186/s12302-023-00721-8

Buck, R., Franklin, J., Berger, U., Conder, J., Cousins, I., de Voogt, P., Jensen, A., Kannan, K., Mabury, S., & van Leeuwen, S. (2011). Perfluoroalkyl and polyfluoroalkyl substances in the environment: Terminology, classification, and origins. *Integr Environ Assess Manag*, 513-541.

Burningham, K., & Thrush, D. (2003). Experiencing Environmental Inequality: The Everyday Concerns of Disadvantaged Groups. *Housing Studies*, *18*(4), 517-536. https://doi.org/10.1080/02673030304244

Chain, E. Panel o. C. i. t. F., Schrenk, D., Bignami, M., Bodin, L., Chipman, J. K., del Mazo, J., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L., Leblanc, J.-C., Nebbia, C. S., Nielsen, E., Ntzani, E., Petersen, A., Sand, S., Vleminckx, C., Wallace, H., Barregård, L., Ceccatelli, S.,…Schwerdtle, T. (2020). Risk to human health related to the presence of perfluoroalkyl substances in food. *EFSA Journal*, *18*(9), e06223. https://doi.org/https://doi.org/10.2903/j.efsa.2020.6223

Cousins, I. T., DeWitt, J. C., Glüge, J., Goldenman, G., Herzke, D., Lohmann, R., Ng, C. A., Scheringer, M., & Wang, Z. (2020). The high persistence of PFAS is sufficient for their management as a chemical class. *Environ. Sci.: Processes Impacts*, *22*(12), 2307-2312.

Cui, L., Liao, C.-y., Zhou, Q.-f., Xia, T.-m., Yun, Z.-j., & Jiang, G.-b. (2010). Excretion of PFOA and PFOS in Male Rats During a Subchronic Exposure. *Archives of Environmental Contamination and Toxicology*, *58*(1), 205-213. https://doi.org/10.1007/s00244-009-9336-5

De Silva, A. O., Armitage, J. M., Bruton, T. A., Dassuncao, C., Heiger-Bernays, W., Hu, X. C., Kärrman, A., Kelly, B., Ng, C., Robuck, A., Sun, M., Webster, T. F., & Sunderland, E. M. (2021). PFAS Exposure Pathways for Humans and Wildlife: A Synthesis of Current Knowledge and Key Gaps in Understanding. *Environmental Toxicology and Chemistry*, *40*(3), 631-657. https://doi.org/https://doi.org/10.1002/etc.4935

Doll, R., & Peto, R. (1978). Cigarette smoking and bronchial carcinoma: dose and time relationships among regular smokers and lifelong non-smokers. *J Epidemiol Community Health (1978)*, *32*(4), 303-313. https://doi.org/10.1136/jech.32.4.303

Ebel, M., Rylander, L., Fletcher, T., Jakobsson, K., & Nielsen, C. (2023). Gestational hypertension, preeclampsia, and gestational diabetes mellitus after high exposure to perfluoroalkyl substances from drinking water in Ronneby, Sweden. *Environ Res*, *239*(Pt 1), 117316. https://doi.org/10.1016/j.envres.2023.117316

ECHA. (2023). *Restricting the use of per- and polyfluoroalkyl substances (PFASs) in fire-fighting foams*. https://echa.europa.eu/registry-of-restriction-intentions/-/dislist/details/0b0236e1856e8ce6

EFSA, Knutsen, H. K., Alexander, J., Barregard, L., Bignami, M., Bruschweiler, B., Ceccatelli, S., Cottrill, B., Dinovi, M., Edler, L., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L. R., Nebbia, C. S., Oswald, I. P., Petersen, A., Rose, M., Roudot, A. C., Vleminckx, C.,…Schwerdtle, T. (2018). Risk to human health related to the presence of perfluorooctane sulfonic acid and perfluorooctanoic acid in food. *EFSA J*, *16*(12), e05194. https://doi.org/10.2903/j.efsa.2018.5194

EFSA, Schrenk, D., Bignami, M., Bodin, L., Chipman, J. K., Del Mazo, J., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L. R., Leblanc, J. C., Nebbia, C. S., Nielsen, E., Ntzani, E., Petersen, A., Sand, S., Vleminckx, C., Wallace, H., Barregard, L., Ceccatelli, S.,…Schwerdtle, T. (2020). Risk to human health related to the presence of perfluoroalkyl substances in food. *EFSA J*, *18*(9), e06223. https://doi.org/10.2903/j.efsa.2020.6223

Engstrom, K., Axmon, A., Nielsen, C., & Rignell-Hydbom, A. (2022). High in Utero Exposure to Perfluoroalkyl Substances from Drinking Water and Birth Weight: A Cohort Study among Infants in Ronneby, Sweden. *Int J Environ Res Public Health*, *19*(4). https://doi.org/10.3390/ijerph19042385

EPA. (2023). *IRIS Toxicological Review of Perfluorohexanesulfonic Acid (PFHxS) and Related Salts (Interagency Science Consultation Draft, 2023), Environmental Protection Agency. (EPA/635/R-23/148a External Review Draft)*. https://cfpub.epa.gov/si/si_public_pra_view.cfm?Lab=CPHEA&dirEntryID=355410

EPA. (2024a). *FINAL Human Health Toxicity Assessment for Perfluorooctane Sulfonic Acid (PFOS) and Related Salts. Environmental Protection Agency. (Document No. 815R24007)*. https://www.epa.gov/system/files/documents/2024-05/final-human-health-toxicity-assessment-pfos.pdf

EPA. (2024b). *FINAL Human Health Toxicity Assessment for Perfluorooctanoic Acid (PFOA) and Related Salts. Environmental Protection Agency. (Document No. 815R24006)*. https://www.epa.gov/system/files/documents/2024-05/final-human-health-toxicity-assessment-pfoa.pdf

EPA. (2024c). *FINAL Human Health Toxicity Assessment for Perfluorooctanoic Acid (PFOA) and Related Salts. Environmental Protection Agency. (Document No. 815R24006)*.

https://www.epa.gov/system/files/documents/2024-05/final-human-health-toxicity-assessment-pfoa.pdf

Eum, K. D., Korrick, S. A., Weuve, J., Okereke, O., Kubzansky, L. D., Hu, H., & Weisskopf, M. G. (2012). Relation of cumulative low-level lead exposure to depressive and phobic anxiety symptom scores in middle-age and elderly women. *Environ Health Perspect*, *120*(6), 817-823. https://doi.org/10.1289/ehp.1104395

Exposure Assessment in Environmental Epidemiology. (1997). In *Use of the Gray Literature and Other Data in Environmental Epidemiology*. National Research Council (US) Committee on Environmental Epidemiology; National Research Council (US) Commission on Life Sciences. https://doi.org/10.17226/5804

Fasano, W. J., Kennedy, G. L., Szostek, B., Farrar, D. G., Ward, R. J., Haroun, L., & Hinderliter, P. M. (2005). Penetration of Ammonium Perfluorooctanoate Through Rat and Human Skin In Vitro. *Drug and Chemical Toxicology*, *28*(1), 79-90. https://doi.org/10.1081/DCT-39707

Fei, C., McLaughlin, J. K., Lipworth, L., & Olsen, J. (2010). Maternal concentrations of perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) and duration of breastfeeding. *Scandinavian Journal of Work, Environment & Health*(5), 413-421. https://doi.org/10.5271/sjweh.2908

Fei, C., McLaughlin, J. K., Tarone, R. E., & Olsen, J. (2007). Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. *Environ Health Perspect*, *115*(11), 1677-1682. https://doi.org/10.1289/ehp.10506

Fischer, F. C., Ludtke, S., Thackray, C., Pickard, H. M., Haque, F., Dassuncao, C., Endo, S., Schaider, L., & Sunderland, E. M. (2024). Binding of Per- and Polyfluoroalkyl Substances (PFAS) to Serum Proteins: Implications for Toxicokinetics in Humans. *Environmental Science & Technology*, *58*(2), 1055-1063. https://doi.org/10.1021/acs.est.3c07415

Fischhoff, B., Bostrom, A., & Quadrel, M. J. (1993). Risk perception and communication. *Annu Rev Public Health*, *14*, 183-203. https://doi.org/10.1146/annurev.pu.14.050193.001151

Fitz-Simon, N., Fletcher, T., Luster, M. I., Steenland, K., Calafat, A. M., Kato, K., & Armstrong, B. (2013). Reductions in serum lipids with a 4-year decline in serum perfluorooctanoic acid and perfluorooctanesulfonic acid. *Epidemiology*, *24*(4), 569-576. https://doi.org/10.1097/EDE.0b013e31829443ee

Franko, J., Meade, B. J., Frasch, H. F., Barbero, A. M., & Anderson, S. E. (2012). Dermal Penetration Potential of Perfluorooctanoic Acid (PFOA) in Human and Mouse Skin. *Journal of Toxicology and Environmental Health, Part A*, *75*(1), 50-62, OCA.0025.0001.0938. https://doi.org/10.1080/15287394.2011.615108

Fromme, H., Mosch, C., Morovitz, M., Alba-Alejandre, I., Boehmer, S., Kiranoglu, M., Faber, F., Hannibal, I., Genzel-Boroviczény, O., Koletzko, B., & Völkel, W. (2010). Pre- and Postnatal Exposure to Perfluorinated Compounds (PFCs). *Environmental Science & Technology*, *44*(18), 7123-7129. https://doi.org/10.1021/es101184f

Fromme, H., Tittlemier, S. A., Völkel, W., Wilhelm, M., & Twardella, D. (2009). Perfluorinated compounds--exposure assessment for the general population in Western countries. *Int J Hyg Environ Health*, *212*(3), 239-270. https://doi.org/10.1016/j.ijheh.2008.04.007

Gannon, S. A., Johnson, T., Nabb, D. L., Serex, T. L., Buck, R. C., & Loveless, S. E. (2011). Absorption, distribution, metabolism, and excretion of 1-C-14 -perfluorohexanoate ( C-14 -PFHx) in rats and mice [Article]. *Toxicology*, *283*(1), 55-62. https://doi.org/10.1016/j.tox.2011.02.004

Gebbink, W. A., Berger, U., & Cousins, I. T. (2015). Estimating human exposure to PFOS isomers and PFCA homologues: The relative importance of direct and indirect (precursor) exposure. *Environment International*, *74*, 160-169. https://doi.org/10.1016/j.envint.2014.10.013

*Gen X Exposure Study*. (2024). North Carolina State University. Retrieved 10/5 from https://genxstudy.ncsu.edu/

Genuis, S. J. (2009). Toxicant exposure and mental health--individual, social, and public health considerations. *J Forensic Sci*, *54*(2), 474-477. https://doi.org/10.1111/j.1556-4029.2008.00973.x

Glüge, J., Scheringer, M., Cousins, I. T., DeWitt, J. C., Goldenman, G., Herzke, D., Lohmann, R., Ng, C. A., Trier, X., & Wang, Z. (2020). An overview of the uses of per- and polyfluoroalkyl substances (PFAS). *Environ. Sci.: Processes Impacts*, *22*(12), 2345-2373.

Grandjean, P., Andersen, E. W., Budtz-Jørgensen, E., Nielsen, F., Mølbak, K., Weihe, P., & Heilmann, C. (2012). Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *Jama*, *307*(4), 391-397. https://doi.org/10.1001/jama.2011.2034

Gützkow, K. B., Haug, L. S., Thomsen, C., Sabaredzovic, A., Becher, G., & Brunborg, G. (2012). Placental transfer of perfluorinated compounds is selective – A Norwegian Mother and Child sub-cohort study. *International Journal of Hygiene and Environmental Health*, *215*(2), 216-219. https://doi.org/https://doi.org/10.1016/j.ijheh.2011.08.011

Guyatt, G., Rennie, D., Meade, M. O., & Cook, D. J. (2015). In *Users' Guides to the Medical Literature: A Manual for Evidence-Based Clinical Practice, 3rd ed*. McGraw-Hill Education. jamaevidence.mhmedical.com/content.aspx?aid=1147669501

Gyllenhammar, I., Benskin, J. P., Lignell, S., Kärsrud, A.-S., Sandblom, O., & Glynn, A. (2016). *Temporal trends of poly- and perfluoroalkyl substances (PFASs) in serum from children at 4, 8, and 12 years of age, in Uppsala 2008-2015*. http://urn.kb.se/resolve?urn=urn:nbn:se:naturvardsverket:diva-6707

Haimes, Y. Y. (2009). *Risk modeling, assessment, and management* (3rd ed.). John Wiley & Sons. Table of contents only http://www.loc.gov/catdir/toc/ecip0821/2008026773.html

Hammarstrand, S., Jakobsson, K., Andersson, E., Xu, Y., Li, Y., Olovsson, M., & Andersson, E. M. (2021). Perfluoroalkyl substances (PFAS) in drinking water and risk for polycystic ovarian syndrome, uterine leiomyoma, and endometriosis: A Swedish cohort study. *Environ Int*, *157*, 106819. https://doi.org/10.1016/j.envint.2021.106819

Hill, A. B. (1965). The Environment and Disease: Association or Causation? *Proc R Soc Med*, *58*(5), 295-300. https://www.ncbi.nlm.nih.gov/pubmed/14283879

Hu, L., Mei, H., Cai, X., Song, L., Xu, Q., Gao, W., Zhang, D., Zhou, J., Sun, C., Li, Y., Xiang, F., Wang, Y., Zhou, A., & Xiao, H. (2024). Prenatal exposure to poly- and perfluoroalkyl substances and postpartum depression in women with twin pregnancies. *Int J Hyg Environ Health*, *256*, 114324. https://doi.org/10.1016/j.ijheh.2024.114324

ISO 31000:2018. Risk management — Guidelines. (2018). In: International Organization for Standardization.

Jakobsson, K., & Nielsen, C. (2024). *Ronneby PFAS Research Programme: A summary of research 2014 - 2023*. https://pfas.blogg.lu.se/report-summary-of-research-in-ronneby-2014-2023/

Kaplan, S., & Garrick, B. J. (1981). On The Quantitative Definition of Risk. *Risk Analysis*, *1*(1), 11-27. https://doi.org/https://doi.org/10.1111/j.1539-6924.1981.tb01350.x

Kärrman, A., Ericson, I., van Bavel, B., Darnerud Per, O., Aune, M., Glynn, A., Lignell, S., & Lindström, G. (2007). Exposure of Perfluorinated Chemicals through Lactation: Levels of Matched Human Milk and Serum and a Temporal Trend, 1996–2004, in Sweden. *Environmental Health Perspectives*, *115*(2), 226-230. https://doi.org/10.1289/ehp.9491

Kennedy, G. L., Butenhoff, J. L., Olsen, G. W., O'Connor, J. C., Seacat, A. M., Perkins, R. G., Biegel, L. B., Murphy, S. R., & Farrar, D. G. (2004). The toxicology of perfluorooctanoate [Review]. *Critical Reviews in Toxicology*, *34*(4), 351-384. https://doi.org/10.1080/10408440490464705

Khoury, M. J., Janssens, A. C., & Ransohoff, D. F. (2013). How can polygenic inheritance be used in population screening for common diseases? *Genet Med*, *15*(6), 437-443. https://doi.org/10.1038/gim.2012.182

Kim, S.-K., Lee, K. T., Kang, C. S., Tao, L., Kannan, K., Kim, K.-R., Kim, C.-K., Lee, J. S., Park, P. S., Yoo, Y. W., Ha, J. Y., Shin, Y.-S., & Lee, J.-H. (2011). Distribution of perfluorochemicals between sera

and milk from the same mothers and implications for prenatal and postnatal exposures. *Environmental Pollution*, *159*(1), 169-174. https://doi.org/https://doi.org/10.1016/j.envpol.2010.09.008

Kim, S., Choi, K., Ji, K., Seo, J., Kho, Y., Park, J., Kim, S., Park, S., Hwang, I., Jeon, J., Yang, H., & Giesy, J. P. (2011). Trans-Placental Transfer of Thirteen Perfluorinated Compounds and Relations with Fetal Thyroid Hormones. *Environmental Science & Technology*, *45*(17), 7465-7472. https://doi.org/10.1021/es202408a

Kirk M, S. K., Bräunig J, Trevenar S, D'Este C, Lucas R, Lal A, Korda R, Clements A, Mueller J, Armstrong B. The PFAS Health Study: Systematic Literature Review. (2018). *The PFAS Health Study: Systematic Literature Review*. https://nceph.anu.edu.au/files/PFAS%20Health%20Study%20Systematic%20Review_1.pdf

Knox, S. S., Jackson, T., Javins, B., Frisbee, S. J., Shankar, A., & Ducatman, A. M. (2011). Implications of early menopause in women exposed to perfluorocarbons. *J Clin Endocrinol Metab*, *96*(6), 1747-1753. https://doi.org/10.1210/jc.2010-2401

Koponen, J., Winkens, K., Airaksinen, R., Berger, U., Vestergren, R., Cousins, I. T., Karvonen, A. M., Pekkanen, J., & Kiviranta, H. (2018). Longitudinal trends of per- and polyfluoroalkyl substances in children's serum. *Environment International*, *121*, 591-599. https://doi.org/https://doi.org/10.1016/j.envint.2018.09.006

Kudo, N., & Kawashima, Y. (2003). TOXICITY AND TOXICOKINETICS OF PERFLUOROOCTANOIC ACID IN HUMANS AND ANIMALS. *The Journal of Toxicological Sciences*, *28*(2), 49-57. https://doi.org/10.2131/jts.28.49

Lau, C., Anitole, K., Hodes, C., Lai, D., Pfahles-Hutchens, A., & Seed, J. (2007). Perfluoroalkyl acids: a review of monitoring and toxicological findings. *Toxicol Sci*, *99*(2), 366-394. https://doi.org/10.1093/toxsci/kfm128

Law, H. D., Armstrong, B. K., D'Este, C., Hosking, R., Smurthwaite, K. S., Trevenar, S., Lucas, R. M., Lazarevic, N., Kirk, M. D., & Korda, R. J. (2023). Relative rates of cancers and deaths in Australian communities with PFAS environmental contamination associated with firefighting foams: A cohort study using linked data. *Cancer Epidemiol*, *82*, 102296. https://doi.org/10.1016/j.canep.2022.102296

Lazarevic, N., Smurthwaite, K. S., Batterham, P. J., Lane, J., Trevenar, S. M., D'Este, C., Clements, A. C. A., Joshy, A. L., Hosking, R., Gad, I., Lal, A., Law, H. D., Banwell, C., Randall, D. A., Miller, A., Housen, T., Korda, R. J., & Kirk, M. D. (2023). Psychological distress in three Australian communities living with environmental per- and polyfluoroalkyl substances contamination. *Sci Total Environ*, *874*, 162503. https://doi.org/10.1016/j.scitotenv.2023.162503

Lazarevic, N., Smurthwaite, K. S., D'Este, C., Lucas, R. M., Armstrong, B., Clements, A. C., Trevenar, S. M., Gad, I., Hosking, R., Law, H. D., Mueller, J., Braunig, J., Nilsson, S., Lane, J., Lal, A., Lidbury, B. A., Korda, R. J., & Kirk, M. D. (2023). Liver and cardiometabolic markers and conditions in a cross-sectional study of three Australian communities living with environmental per- and polyfluoroalkyl substances contamination. *Environ Res*, *226*, 115621. https://doi.org/10.1016/j.envres.2023.115621

Levin, M. L. (1953). The occurrence of lung cancer in man. *Acta Unio Int Contra Cancrum*, *9*(3), 531-541. https://www.ncbi.nlm.nih.gov/pubmed/13124110

Li, H., Hammarstrand, S., Midberg, B., Xu, Y., Li, Y., Olsson, D. S., Fletcher, T., Jakobsson, K., & Andersson, E. M. (2022). Cancer incidence in a Swedish cohort with high exposure to perfluoroalkyl substances in drinking water. *Environ Res*, *204*(Pt C), 112217. https://doi.org/10.1016/j.envres.2021.112217

Li, Y., Andersson, A., Xu, Y., Pineda, D., Nilsson, C. A., Lindh, C. H., Jakobsson, K., & Fletcher, T. (2022). Determinants of serum half-lives for linear and branched perfluoroalkyl substances after long-term high exposure-A study in Ronneby, Sweden. *Environ Int*, *163*, 107198. https://doi.org/10.1016/j.envint.2022.107198

Li, Y., Barregard, L., Xu, Y., Scott, K., Pineda, D., Lindh, C. H., Jakobsson, K., & Fletcher, T. (2020). Associations between perfluoroalkyl substances and serum lipids in a Swedish adult population with contaminated drinking water. *Environ Health*, *19*(1), 33. https://doi.org/10.1186/s12940-020-00588-9

Li, Y., Fletcher, T., Mucs, D., Scott, K., Lindh, C. H., Tallving, P., & Jakobsson, K. (2018a). Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occup Environ Med*, *75*(1), 46-51. https://doi.org/10.1136/oemed-2017-104651

Li, Y., Fletcher, T., Mucs, D., Scott, K., Lindh, C. H., Tallving, P., & Jakobsson, K. (2018b). Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. *Occupational and Environmental Medicine*, *75*(1), 46-51. https://doi.org/10.1136/oemed-2017-104651

Li, Y., Xu, Y., Fletcher, T., Scott, K., Nielsen, C., Pineda, D., Lindh, C. H., Olsson, D. S., Andersson, E. M., & Jakobsson, K. (2021). Associations between perfluoroalkyl substances and thyroid hormones after high exposure through drinking water. *Environ Res*, *194*, 110647. https://doi.org/10.1016/j.envres.2020.110647

Liu, J., Li, J., Liu, Y., Chan, H. M., Zhao, Y., Cai, Z., & Wu, Y. (2011). Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. *Environment International*, *37*(7), 1206-1212. https://doi.org/https://doi.org/10.1016/j.envint.2011.05.001

Liu, J., Li, J., Zhao, Y., Wang, Y., Zhang, L., & Wu, Y. (2010). The occurrence of perfluorinated alkyl compounds in human milk from different regions of China. *Environment International*, *36*(5), 433-438. https://doi.org/https://doi.org/10.1016/j.envint.2010.03.004

Llorca, M., Farré, M., Picó, Y., Teijón, M. L., Álvarez, J. G., & Barceló, D. (2010). Infant exposure of perfluorinated compounds: Levels in breast milk and commercial baby food. *Environment International*, *36*(6), 584-592. https://doi.org/https://doi.org/10.1016/j.envint.2010.04.016

Ma, J., Zhu, H., & Kannan, K. (2020). Fecal Excretion of Perfluoroalkyl and Polyfluoroalkyl Substances in Pets from New York State, United States. *Environmental Science & Technology Letters*, *7*(3), 135-142. https://doi.org/10.1021/acs.estlett.9b00786

Manzano-Salgado, C. B., Casas, M., Lopez-Espinosa, M.-J., Ballester, F., Basterrechea, M., Grimalt, J. O., Jiménez, A.-M., Kraus, T., Schettgen, T., Sunyer, J., & Vrijheid, M. (2015). Transfer of perfluoroalkyl substances from mother to fetus in a Spanish birth cohort. *Environmental Research*, *142*, 471-478. https://doi.org/https://doi.org/10.1016/j.envres.2015.07.020

Mogensen, U. B., Grandjean, P., Nielsen, F., Weihe, P., & Budtz-Jørgensen, E. (2015). Breastfeeding as an Exposure Pathway for Perfluorinated Alkylates. *Environ Sci Technol*, *49*(17), 10466-10473. https://doi.org/10.1021/acs.est.5b02237

Mondal, D., Weldon Rosana, H., Armstrong Ben, G., Gibson Lorna, J., Lopez-Espinosa, M.-J., Shin, H.-M., & Fletcher, T. (2014). Breastfeeding: A Potential Excretion Route for Mothers and Implications for Infant Exposure to Perfluoroalkyl Acids. *Environmental Health Perspectives*, *122*(2), 187-192. https://doi.org/10.1289/ehp.1306613

Monroy, R., Morrison, K., Teo, K., Atkinson, S., Kubwabo, C., Stewart, B., & Foster, W. G. (2008). Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. *Environmental Research*, *108*(1), 56-62. https://doi.org/https://doi.org/10.1016/j.envres.2008.06.001

Morgan, M. G., & Henrion, M. (1990). Uncertainty: A Guide to Dealing with Uncertainty in Quantitative Risk and Policy Analysis.

National Academies of Sciences, E., & Medicine. (2022). *Guidance on PFAS Exposure, Testing, and Clinical Follow-Up*. The National Academies Press. https://doi.org/doi:10.17226/26156

Nicholson, B. D., Hamilton, W., O'Sullivan, J., Aveyard, P., & Hobbs, F. R. (2018). Weight loss as a predictor of cancer in primary care: a systematic review and meta-analysis. *Br J Gen Pract*, *68*(670), e311-e322. https://doi.org/10.3399/bjgp18X695801

Nielsen, C., Li, Y., Lewandowski, M., Fletcher, T., & Jakobsson, K. (2022). Breastfeeding initiation and duration after high exposure to perfluoroalkyl substances through contaminated drinking

water: A cohort study from Ronneby, Sweden. *Environ Res*, *207*, 112206. https://doi.org/10.1016/j.envres.2021.112206

Nielsen, F., Fischer, F. C., Leth, P. M., & Grandjean, P. (2024). Occurrence of Major Perfluorinated Alkylate Substances in Human Blood and Target Organs. *Environmental Science & Technology*, *58*(1), 143-149. https://doi.org/10.1021/acs.est.3c06499

Nieuwenhuijsen, M. J. (2005). Design of exposure questionnaires for epidemiological studies. *Occup Environ Med*, *62*(4), 272-280, 212-274. https://doi.org/10.1136/oem.2004.015206

Niu, S., Cao, Y., Chen, R., Bedi, M., Sanders, A. P., Ducatman, A., & Ng, C. (2023). A State-of-the-Science Review of Interactions of Per- and Polyfluoroalkyl Substances (PFAS) with Renal Transporters in Health and Disease: Implications for Population Variability in PFAS Toxicokinetics. *Environ Health Perspect*, *131*(7), 76002. https://doi.org/10.1289/ehp11885

NJDEP. (2024). *Per- and Polyfluoroalkyl (PFAS)*. New Jersey Department of Environmental Protection. Retrieved 05/14 from https://dep.nj.gov/pfas/

Norman, G., & Cairney, J. (2015). *Health Measurement Scales: A Practical Guide To Their Development and Use* (Vol. 117). https://doi.org/10.1093/acprof:oso/9780199231881.003.0006

OECD. (2002, OCA.0029.0001.0063). *Cooperation on existing chemicals: Hazard assessment of perfluorooctane sulfonate (PFOS) and its salts, env/jm/rd(2002)17/final*.

OECD. (2021). *Reconciling Terminology of the Universe of Per-and Polyfluoroalkyl Substances: Recommendations and Practical Guidance*. Organisation for Economic Co-operation and Development

Olsen, G. W., Burris, J. M., Ehresman, D. J., Froehlich, J. W., Seacat, A. M., Butenhoff, J. L., & Zobel, L. R. (2007). Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environmental Health Perspectives*, *115*(9), 1298-1305, OCA.0032.0001.0018. https://doi.org/10.1289/ehp.10009

Pan, Y., Zhu, Y., Zheng, T., Cui, Q., Buka, S. L., Zhang, B., Guo, Y., Xia, W., Yeung, L. W. Y., Li, Y., Zhou, A., Qiu, L., Liu, H., Jiang, M., Wu, C., Xu, S., & Dai, J. (2017). Novel Chlorinated Polyfluorinated Ether Sulfonates and Legacy Per-/Polyfluoroalkyl Substances: Placental Transfer and Relationship with Serum Albumin and Glomerular Filtration Rate. *Environmental Science & Technology*, *51*(1), 634-644. https://doi.org/10.1021/acs.est.6b04590

Pearce, N. (1996). Traditional epidemiology, modern epidemiology, and public health. *Am J Public Health*, *86*(5), 678-683. https://doi.org/10.2105/ajph.86.5.678

*PFAS in Jersey*. (2023). https://www.gov.je/Environment/ProtectingEnvironment/Water/Pages/PFAS.aspx

Porta, M. (2016). *A Dictionary of Epidemiology*. Oxford University Press. https://doi.org/10.1093/acref/9780199976720.001.0001

Prevedouros, K., Cousins, I. T., Buck, R. C., & Korzeniowski, S. H. (2006). Sources, Fate and Transport of Perfluorocarboxylates. *Environmental Science & Technology*, *40*(1), 32-44.

Ragnarsdóttir, O., Abou-Elwafa Abdallah, M., & Harrad, S. (2024). Dermal bioavailability of perfluoroalkyl substances using in vitro 3D human skin equivalent models. *Environment International*, *188*, 108772. https://doi.org/https://doi.org/10.1016/j.envint.2024.108772

Rahman, H., Niemann, D., & Munson-McGee, S. (2022). Association among urinary polycyclic aromatic hydrocarbons and depression: a cross-sectional study from NHANES 2015–2016. *Environmental Science and Pollution Research*, *29*. https://doi.org/10.1007/s11356-021-16692-3

*Regulatory management option analysis (RMOA)*. (2023). Health and Safety Executive. Retrieved 1/8 from https://www.hse.gov.uk/REACH/rmoa.htm

Risk Assessment in the Federal Government: Managing the Process. (1983). In. National Research Council. https://doi.org/10.17226/366

Roberts, H., van Lissa, C., & Helbich, M. (2021). Perceived neighbourhood characteristics and depressive symptoms: Potential mediators and the moderating role of employment status. *Social Science & Medicine*, *268*, 113533. https://doi.org/https://doi.org/10.1016/j.socscimed.2020.113533

Rose, G. A. (1992). *The strategy of preventive medicine*. Oxford University Press. Publisher description http://www.loc.gov/catdir/enhancements/fy0636/92008612-d.html

Table of contents only http://www.loc.gov/catdir/enhancements/fy0636/92008612-t.html

Rothman, K. J., Greenland, S., & Lash, T. L. (2008). *Modern epidemiology* (3rd ed.). Wolters Kluwer Health/Lippincott Williams & Wilkins. Publisher description http://www.loc.gov/catdir/enhancements/fy0743/2007036316-d.html

Table of contents only http://www.loc.gov/catdir/enhancements/fy0828/2007036316-t.html

Sackett, D., Richardson, W., Rosenberg, W., & Haynes, b. m. c. (2005). Evidence-Based Medicine. How to Practice and Teach EBM. Evidence-Based Medicine. *Churchill Livingston*, *2*.

Schlummer, M., Moser, G. A., & McLachlan, M. S. (1998). Digestive tract absorption of PCDD/Fs, PCBs, and HCB in humans: mass balances and mechanistic considerations. *Toxicol Appl Pharmacol*, *152*(1), 128-137. https://doi.org/10.1006/taap.1998.8487

Schmitt, H. J., Calloway, E. E., Sullivan, D., Clausen, W., Tucker, P. G., Rayman, J., & Gerhardstein, B. (2021). Chronic environmental contamination: A systematic review of psychological health consequences. *Science of The Total Environment*, *Volume 772*.

Shore, P. A., Brodie, B. B., & Hogben, C. A. (1957). The gastric secretion of drugs: a pH partition hypothesis [Article]. *The Journal of pharmacology and experimental therapeutics*, *119*(3), 361-369. https://www.scopus.com/inward/record.uri?eid=2-s2.0-0001152155&partnerID=40&md5=beeffa3503f4d5623ffb107f29814210

Slovic, P. (1987). Perception of risk. *Science*, *236*(4799), 280-285. https://doi.org/10.1126/science.3563507

So, M. K., Yamashita, N., Taniyasu, S., Jiang, Q., Giesy, J. P., Chen, K., & Lam, P. K. S. (2006). Health Risks in Infants Associated with Exposure to Perfluorinated Compounds in Human Breast Milk from Zhoushan, China. *Environmental Science & Technology*, *40*(9), 2924-2929. https://doi.org/10.1021/es060031f

Steenland, K., Barry, V., & Savitz, D. (2018). Serum Perfluorooctanoic Acid and Birthweight: An Updated Meta-analysis With Bias Analysis. *Epidemiology*, *29*(6), 765-776. https://doi.org/10.1097/ede.0000000000000903

Steenland, K., Fletcher, T., Stein, C. R., Bartell, S. M., Darrow, L., Lopez-Espinosa, M. J., Barry Ryan, P., & Savitz, D. A. (2020). Review: Evolution of evidence on PFOA and health following the assessments of the C8 Science Panel. *Environ Int*, *145*, 106125. https://doi.org/10.1016/j.envint.2020.106125

Steenland, K., Tinker, S., Frisbee, S., Ducatman, A., & Vaccarino, V. (2009). Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. *Am J Epidemiol*, *170*(10), 1268-1278. https://doi.org/10.1093/aje/kwp279

Stubner, C., Ebel, M., Jakobsson, K., Gillberg, C., Nielsen, C., & Miniscalco, C. (2023). Developmental language disorders in preschool children after high exposure to perfluoroalkyl substances from contaminated drinking water in Ronneby, Sweden. *Environ Epidemiol*, *7*(1), e233. https://doi.org/10.1097/EE9.0000000000000233

Stubner, C., Nielsen, C., Jakobsson, K., Gillberg, C., & Miniscalco, C. (2023). Early-Life Exposure to Perfluoroalkyl Substances (PFAS) and Child Language and Communication Development: A Systematic Review. *Int J Environ Res Public Health*, *20*(24). https://doi.org/10.3390/ijerph20247170

Sullivan, G., & Feinn, R. (2012). Using Effect Size—or Why the P Value Is Not Enough. *Journal of graduate medical education*, *4*, 279-282. https://doi.org/10.4300/JGME-D-12-00156.1

Sun, X., Yang, X., Zhang, Y., Liu, Y., Xiao, F., Guo, H., & Liu, X. (2023). Correlation analysis between per-fluoroalkyl and poly-fluoroalkyl substances exposure and depressive symptoms in adults: NHANES 2005–2018. *Science of The Total Environment*, *906*, 167639. https://doi.org/10.1016/j.scitotenv.2023.167639

Sunderland, E. M., Hu, X. C., Dassuncao, C., Tokranov, A. K., Wagner, C. C., & Allen, J. G. (2019). A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects. *Journal of Exposure Science & Environmental Epidemiology*, *29*(2), 131-147. https://doi.org/10.1038/s41370-018-0094-1

Sundström, M., Chang, S.-C., Noker, P. E., Gorman, G. S., Hart, J. A., Ehresman, D. J., Bergman, Å., & Butenhoff, J. L. (2012). Comparative pharmacokinetics of perfluorohexanesulfonate (PFHxS) in rats, mice, and monkeys. *Reproductive Toxicology*, *33*(4), 441-451. https://doi.org/https://doi.org/10.1016/j.reprotox.2011.07.004

Sundström, M., Ehresman, D. J., Bignert, A., Butenhoff, J. L., Olsen, G. W., Chang, S.-C., & Bergman, Å. (2011). A temporal trend study (1972–2008) of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in pooled human milk samples from Stockholm, Sweden. *Environment International*, *37*(1), 178-183. https://doi.org/https://doi.org/10.1016/j.envint.2010.08.014

Surace, T., Quitadamo, C., Caldiroli, A., Capuzzi, E., Colmegna, F., Nosari, G., Borroni, E., Fedrizzi, L., Bollati, V., Pesatori, A. C., Carugno, M., Clerici, M., & Buoli, M. (2023). Air Pollution and Perinatal Mental Health: A Comprehensive Overview. *J Clin Med*, *12*(9). https://doi.org/10.3390/jcm12093146

Tao, L., Kannan, K., Wong, C. M., Arcaro, K. F., & Butenhoff, J. L. (2008). Perfluorinated Compounds in Human Milk from Massachusetts, U.S.A. *Environmental Science & Technology*, *42*(8), 3096-3101. https://doi.org/10.1021/es702789k

Tao, L., Ma, J., Kunisue, T., Libelo, E. L., Tanabe, S., & Kannan, K. (2008). Perfluorinated Compounds in Human Breast Milk from Several Asian Countries, and in Infant Formula and Dairy Milk from the United States. *Environmental Science & Technology*, *42*(22), 8597-8602. https://doi.org/10.1021/es801875v

Taves, D. R. (1968). EVIDENCE THAT THERE ARE 2 FORMS OF FLUORIDE IN HUMAN SERUM. *Nature*, *217*(5133), 1050-&. https://doi.org/10.1038/2171050b0

Thomsen, C., Haug, L. S., Stigum, H., Frøshaug, M., Broadwell, S. L., & Becher, G. (2010). Changes in Concentrations of Perfluorinated Compounds, Polybrominated Diphenyl Ethers, and Polychlorinated Biphenyls in Norwegian Breast-Milk during Twelve Months of Lactation. *Environmental Science & Technology*, *44*(24), 9550-9556. https://doi.org/10.1021/es1021922

*Toxicological Profile for Perfluoroalkyls*. (2021). https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=1117&tid=237

Trudel, D., Horowitz, L., Wormuth, M., Scheringer, M., Cousins, I. T., & Hungerbuhler, K. (2008). Estimating consumer exposure to PFOS and PFOA [Review]. *Risk Analysis*, *28*(2), 251-269, KCA.0028.0001.0029. https://doi.org/10.1111/j.1539-6924.2008.01017.x

Upson, K., Shearston, J. A., & Kioumourtzoglou, M. A. (2022). An Epidemiologic Review of Menstrual Blood Loss as an Excretion Route for Per- and Polyfluoroalkyl Substances. *Curr Environ Health Rep*, *9*(1), 29-37. https://doi.org/10.1007/s40572-022-00332-0

Vandenbroucke, J. P., von Elm, E., Altman, D. G., Gøtzsche, P. C., Mulrow, C. D., Pocock, S. J., Poole, C., Schlesselman, J. J., Egger, M., & for the, S. I. (2007). Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and Elaboration. *PLOS Medicine*, *4*(10), e297. https://doi.org/10.1371/journal.pmed.0040297

Verner, M.-A., Ngueta, G., Jensen, E. T., Fromme, H., Völkel, W., Nygaard, U. C., Granum, B., & Longnecker, M. P. (2016). A Simple Pharmacokinetic Model of Prenatal and Postnatal Exposure to Perfluoroalkyl Substances (PFASs). *Environmental Science & Technology*, *50*(2), 978-986. https://doi.org/10.1021/acs.est.5b04399

Vestergren, R., Berger, U., Glynn, A., & Cousins, I. T. (2012). Dietary exposure to perfluoroalkyl acids for the Swedish population in 1999, 2005 and 2010 [Article]. *Environment International*, *49*, 120-127. https://doi.org/10.1016/j.envint.2012.08.016

Vestergren, R., Cousins, I. T., Trudel, D., Wormuth, M., & Scheringer, M. (2008). Estimating the contribution of precursor compounds in consumer exposure to PFOS and PFOA. *Chemosphere*, *73*(10), 1617-1624. https://doi.org/10.1016/j.chemosphere.2008.08.011

Völkel, W., Genzel-Boroviczény, O., Demmelmair, H., Gebauer, C., Koletzko, B., Twardella, D., Raab, U., & Fromme, H. (2008). Perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA) in human breast milk: Results of a pilot study. *International Journal of Hygiene and Environmental Health*, *211*(3), 440-446. https://doi.org/https://doi.org/10.1016/j.ijheh.2007.07.024

Vuong, A., Yolton, K., Braun, J., Sjodin, A., Calafat, A., Xu, Y., Kim, N., Lanphear, B., & Chen, A. (2020). Polybrominated diphenyl ether (PBDE) and poly- and perfluoroalkyl substance (PFAS) exposures during pregnancy and maternal depression. *Environment International*, *139*, 105694. https://doi.org/10.1016/j.envint.2020.105694

Wang, Z., DeWitt, J. C., Higgins, C. P., & Cousins, I. T. (2017). A Never-Ending Story of Per- and Polyfluoroalkyl Substances (PFASs)? *Environmental Science & Technology*, *51*(5), 2508-2518. https://doi.org/10.1021/acs.est.6b04806

*What types of studies are there?* (2016). https://www.ncbi.nlm.nih.gov/books/NBK390304/

Williams, T. A., Gruber, D. A., Sutcliffe, K. M., Shepherd, D. A., & Zhao, E. Y. (2017). Organizational Response to Adversity: Fusing Crisis Management and Resilience Research Streams. *Academy of Management Annals*, *11*(2), 733-769. https://doi.org/10.5465/annals.2015.0134

Winkens, K., Vestergren, R., Berger, U., & Cousins, I. T. (2017). Early life exposure to per- and polyfluoroalkyl substances (PFASs): A critical review. *Emerging Contaminants*, *3*(2), 55-68. https://doi.org/https://doi.org/10.1016/j.emcon.2017.05.001

Winquist, A., & Steenland, K. (2014). Modeled PFOA exposure and coronary artery disease, hypertension, and high cholesterol in community and worker cohorts. *Environ Health Perspect*, *122*(12), 1299-1305. https://doi.org/10.1289/ehp.1307943

Wong, F., MacLeod, M., Mueller, J. F., & Cousins, I. T. (2014). Enhanced Elimination of Perfluorooctane Sulfonic Acid by Menstruating Women: Evidence from Population-Based Pharmacokinetic Modeling. *Environmental Science & Technology*, *48*(15), 8807-8814. https://doi.org/10.1021/es500796y

Wu, Y., Song, J., Zhang, Q., Yan, S., Sun, X., Weizhuo, W., Pan, R., Cheng, J., Xu, Z., & Su, H. (2022). Association between organophosphorus pesticide exposure and depression risk in adults: A cross-sectional study with NHANES data. *Environmental Pollution*, *316*, 120445. https://doi.org/10.1016/j.envpol.2022.120445

Xu, B., Mei, S., Wu, W., Liu, Q., & Xie, K. (2023). Association of formaldehyde concentration with depression risk in US adults: a population-based epidemiology study. *Environ Sci Pollut Res Int*, *30*(43), 98261-98270. https://doi.org/10.1007/s11356-023-29290-2

Xu, Y., Fletcher, T., Pineda, D., Lindh Christian, H., Nilsson, C., Glynn, A., Vogs, C., Norström, K., Lilja, K., Jakobsson, K., & Li, Y. Serum Half-Lives for Short- and Long-Chain Perfluoroalkyl Acids after Ceasing Exposure from Drinking Water Contaminated by Firefighting Foam. *Environmental Health Perspectives*, *128*(7), 077004. https://doi.org/10.1289/EHP6785

Xu, Y., Hansson, E., Andersson, E. M., Jakobsson, K., & Li, H. (2023a). High exposure to perfluoroalkyl substances in drinking water is associated with increased risk of osteoporotic fractures - A

cohort study from Ronneby, Sweden. *Environ Res*, *217*, 114796. https://doi.org/10.1016/j.envres.2022.114796

Xu, Y., Jakobsson, K., Harari, F., Andersson, E. M., & Li, Y. (2023b). Exposure to high levels of PFAS through drinking water is associated with increased risk of type 2 diabetes-findings from a register-based study in Ronneby, Sweden. *Environ Res*, *225*, 115525. https://doi.org/10.1016/j.envres.2023.115525

Xu, Y., Li, Y., Scott, K., Lindh, C. H., Jakobsson, K., Fletcher, T., Ohlsson, B., & Andersson, E. M. (2020d). Inflammatory bowel disease and biomarkers of gut inflammation and permeability in a community with high exposure to perfluoroalkyl substances through drinking water. *Environ Res*, *181*, 108923. https://doi.org/10.1016/j.envres.2019.108923

Xu, Y., Nielsen, C., Li, Y., Hammarstrand, S., Andersson, E. M., Li, H., Olsson, D. S., Engstrom, K., Pineda, D., Lindh, C. H., Fletcher, T., & Jakobsson, K. (2021). Serum perfluoroalkyl substances in residents following long-term drinking water contamination from firefighting foam in Ronneby, Sweden. *Environ Int*, *147*, 106333. https://doi.org/10.1016/j.envint.2020.106333

Xu, Y., Nielsen, C., Li, Y., Hammarstrand, S., Andersson, E. M., Li, H., Olsson, D. S., Engström, K., Pineda, D., Lindh, C. H., Fletcher, T., & Jakobsson, K. (2021). Serum perfluoroalkyl substances in residents following long-term drinking water contamination from firefighting foam in Ronneby, Sweden. *Environment International*, *147*, 106333. https://doi.org/https://doi.org/10.1016/j.envint.2020.106333

Yi, W., Xuan, L., Zakaly, H. M. H., Markovic, V., Miszczyk, J., Guan, H., Zhou, P. K., & Huang, R. (2023). Association between per- and polyfluoroalkyl substances (PFAS) and depression in U.S. adults: A cross-sectional study of NHANES from 2005 to 2018. *Environ Res*, *238*(Pt 2), 117188. https://doi.org/10.1016/j.envres.2023.117188

Zahm, S., Bonde, J. P., Chiu, W. A., Hoppin, J., Kanno, J., Abdallah, M., Blystone, C. R., Calkins, M. M., Dong, G.-H., Dorman, D. C., Fry, R., Guo, H., Haug, L. S., Hofmann, J. N., Iwasaki, M., Machala, M., Mancini, F. R., Maria-Engler, S. S., Møller, P.,…Schubauer-Berigan, M. K. (2024). Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid. *The Lancet Oncology*, *25*(1), 16-17. https://doi.org/10.1016/S1470-2045(23)00622-8

Zahm, S., Bonde, J. P., Chiu, W. A., Hoppin, J., Kanno, J., Abdallah, M., Blystone, C. R., Calkins, M. M., Dong, G. H., Dorman, D. C., Fry, R., Guo, H., Haug, L. S., Hofmann, J. N., Iwasaki, M., Machala, M., Mancini, F. R., Maria-Engler, S. S., Moller, P.,…Schubauer-Berigan, M. K. (2024). Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid. *Lancet Oncol*, *25*(1), 16-17. https://doi.org/10.1016/S1470-2045(23)00622-8

## Glossary

| | |
|---|---|
| AFFF | Aqueous film-forming foams; used in firefighting, particularly where liquid fuel may be involved. Can contain PFAS. |
| ALT (Alanine Aminotransferase) | An enzyme found in the liver and blood, often measured to assess liver health. |
| Anaemia | A condition where there is a lower-than-normal number of healthy blood cells. This can reduce oxygen availability and lead to shortness of breath and fatigue. |
| Anionic | Refers to PFAS molecules that carry a negative charge in aqueous solutions. Anionic PFAS are commonly found in industrial applications and consumer products, often as surfactants due to their ability to lower surface tension. |
| ATSDR (Agency for Toxic Substances and Disease Registry) | A federal public health agency within the United States Department of Health and Human Services. The ATSDR is responsible for assessing the health effects of exposure to hazardous substances and providing guidance on preventing or reducing harmful exposures. It conducts public health assessments, health consultations, and studies to evaluate the impact of environmental contaminants on human health, offering recommendations and support to communities, health professionals, and policymakers |
| Attributable risk | The difference in the rate of a condition between an exposed population and an unexposed population, attributable to a specific risk factor |
| Autoimmune diseases | Conditions where the immune system mistakenly attacks the body's own cells |
| Bioaccumulative, bioaccumulation | The accumulation of chemicals in an organism over time due to the rate of intake exceeding the rate of excretion. |
| Biological plausibility | The logical relationship between a cause and an effect based on existing biological or medical knowledge |
| BMJ | British Medical Journal. |
| Body burden | Describes the amount of a chemical in the human body at a given time. |
| bwt | Bodyweight. |
| C8 | the name given to the surfactant PFOA in some commercial contexts, the name deriving from it having 8-carbons in its chemical structure. Also the name used for the research programme on health effects in the USA near a DuPont plant. |
| Cationic | Refers to PFAS molecules that carry a positive charge. These cationic PFAS are less common than the anionic ones but can be used in specific industrial applications, such as coatings and textile treatments, where they help bind the PFAS to surfaces, and in some types of AFFF. |
| Causality (Causal relationship) | The relationship between cause and effect, where one event (the cause) directly influences another event (the effect). |
| Causation | The action of causing something; a relationship where one event causes another. |
| CDC | Centers for Disease Control, a national public health body in the US. |
| Cerebrovascular disease | Disorders affecting the blood vessels in the brain, which can lead to strokes. |
| Chance association | A relationship between two variables that occurs randomly rather than through a causal link. |
| Confounding (Confounding bias) | A distortion in the perceived relationship between an exposure and an outcome caused by a third variable that is associated with both the exposure and the outcome. |
| C-reactive protein (CRP) | A substance produced by the liver in response to inflammation, used as a marker in blood tests. |

| | |
|---|---|
| Data triangulation | The use of multiple data sources or methods to validate research findings and ensure accuracy. |
| Decile groups | Statistical divisions that split a population into ten equal parts, often used in data analysis to compare different groups. |
| Degradation | The breakdown or decay of substances. |
| Dyslipidemia | An abnormal amount of lipids (e.g., cholesterol and/or fat) in the blood. |
| Ecological fallacy | The error of making inferences about individuals based on aggregate data for a group. |
| EFSA (European Food Safety Authority) | An agency of the European Union that provides independent scientific advice on food-related risks. |
| Endometriosis | A condition where tissue similar to the lining inside the uterus grows outside of it, causing pain and potential fertility issues. |
| Endometrium | The mucous membrane lining the uterus, which thickens during the menstrual cycle. |
| Enterohepatic circulation | The circulation of substances from the liver to the bile, absorbed by the intestine, and returned to the liver. |
| EPA | Environmental Protection Agency, the federal agency in the US responsible for protecting the environment. |
| EQ5D-5L | European 5 dimension, 5 level, quality of life assessment. A commonly used tool to assess health related quality of life. |
| EU | European Union. |
| Experts by experience | Individuals who provide expertise based on personal experiences rather than formal qualifications. |
| Exposure media | The different environments (e.g., air, water, soil) through which individual humans and wildlife can be exposed to substances. |
| FDA | Food and Drug Administration, the regulator of medicines in the US. |
| Gastrooesophageal reflux | A condition where stomach acid frequently flows back into the tube connecting the mouth and stomach, causing heartburn. |
| Gen X | Refers to a specific type of PFAS developed as a replacement for older, longer-chain PFAS (specifically to replace PFOA used in the manufacture of Teflon by DuPont). The term "Gen X" in this context is used both to describe the chemical process and the resulting products, which are marketed as having a lower bioaccumulation potential and lower toxicity compared to traditional PFAS like PFOA and PFOS. However, concerns remain about the environmental and health impacts of these substances. |
| Gut microbiome | The community of microorganisms living in the digestive tracts of humans and other animals. |
| Haematoma | Localised collection of blood outside blood vessels. |
| Half-life | The time it takes for the concentration of a substance in the body or in the environment to reduce to half its initial value. |
| HBM | Human Biomonitoring Committee of the German Environmental Agency. |
| Herd immunity | The resistance to the spread of a contagious disease within a population, achieved when a high proportion of individuals are immune. |
| High-density lipoprotein (HDL) | Known as "good" cholesterol, it helps remove other forms of cholesterol from the bloodstream. |
| IARC (International Agency for Research on Cancer) | An agency of the World Health Organization that conducts and coordinates research on the causes of cancer. |

| | |
|---|---|
| Immunosuppression | The reduction of the activation or efficacy of the immune system, which can occur naturally or be induced by medication or disease. |
| Information bias | Bias arising from measurement errors or misclassification in the data collection process. |
| Intrauterine growth retardation | A condition where a foetus is smaller than expected for the number of weeks of pregnancy, due to various factors. |
| Ischaemic heart disease | A condition characterized by reduced blood supply to the heart, often due to clogged arteries. |
| kg | Kilograms. |
| Leiomyoma | A benign smooth muscle tumour, often found in the uterus (uterine fibroids). |
| low density lipoprotein (LDL) | A type of cholesterol known as "bad" cholesterol because high levels can lead to plaque buildup in arteries. |
| Mean (Arithmetic mean) | A statistical average where all values are added up and divided by the number of readings. |
| Median | A statistical measure where the middle value of a list of findings is used. |
| MeFOSAA | N-Methylperfluorooctanesulfonamidoacetic acid. A so-called “precursor” which can break down and transform to both PFOS and PFOA. |
| Millilitre (ml) | One thousandth of a litre. |
| ml/y | Millilitre per year. |
| Moral injury | Psychological distress resulting from actions that violate one's moral or ethical code. |
| Nanogram (ng) | One billionth of a gram. |
| Neurodevelopment | The process of brain development, often focusing on growth and maturation from birth through adolescence. |
| ng/ml | nanogram per millilitre. |
| NHS | National Health Service. |
| NICE | The National Institute of Health and Care Excellence, the national clinical guidelines organisation in England. |
| OECD | The Organisation for Economic Cooperation and Development, an international organisation comprising the countries with advanced economies. |
| Osteoporosis | A condition characterized by weakened bones, increasing the risk of fractures. |
| PCOS (Polycystic Ovary Syndrome) | A hormonal disorder causing enlarged ovaries with small cysts on the outer edges. |
| PFAS | per- and polyfluoroalkyl substances. |
| PFCAs | perfluoroalkyl carboxylic acids or perfluoroalkyl carboxylates. |
| PFDA | perfluorodecanoic acid. |
| PFHpS | perfluoroheptane sulfonic acid. |
| PFHxS | perfluorohexane sulfonic acid. |
| PFNA | perfluorononanoic acid. |
| PFOA | perfluorooctanoic acid. |
| PFOS | perfluorooctane sulfonic acid. |
| PFPeS | perfluoropentane sulfonic acid. |
| PFSAs | perfluoroalkane sulfonic acids or perfluoroalkane sulfonates. |
| PFUnDA | perfluoroundecanoic acid. |
| Plasma | The liquid portion of the blood. |
| Plume | The geographical area over which a contaminant spreads. |

| | |
|---|---|
| Precursors | Substances which break down and transform into stable PFAS such as PFOS, PFOA and PFHxS either in the environment or within organisms. |
| Primiparous | Referring to a woman who has given birth for the first time. |
| PTFE (Polytetrafluoroethylene) | A synthetic fluoropolymer, commonly known by the brand name Teflon™ (although Teflon refers strictly only to the products made by DuPont/Chemours and there are many other manufacturers of PTFE), used in non-stick cookware and other products. |
| REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) | A European Union regulation governing the use of chemicals to protect human health and the environment. |
| Reliability | The consistency and stability of a measurement or test over time. |
| Reverse causality | A situation where the direction of cause and effect is opposite to what is presumed. |
| Rheumatoid disease | Refers to autoimmune conditions like rheumatoid arthritis, where chronic inflammation affects joints and other parts of the body. |
| Risk factors | Characteristics or variables associated with an increased risk of a disease or condition. |
| Saturated | Refers to organic compounds where all the carbon atoms are fully bonded with hydrogen atoms (and in the case of PFAS, fluorine atoms), with no double or triple bonds present. Full fluorination of the carbons in a carbon chain (i.e. saturated carbons) contributes to the stability and low reactivity of PFAS under normal conditions. |
| Saturation Point | The level above which a further increase in the level of PFAS does not lead to any additional increase in risk of a particular health condition. This may apply in some instances but is not yet proven. |
| Scotchgard | A waterproofing and stain proofing treatment developed by 3M containing PFAS. |
| Selection bias | A type of bias caused by the non-random selection of participants, leading to unrepresentative samples. |
| Serum | The liquid that is left when blood has clotted, often used for doing medical tests. |
| Somatisation | The manifestation of psychological distress through physical symptoms. |
| Specificity | The extent to which a particular exposure leads to a specific outcome, used to help establish causal relationships. |
| Systemic Lupus Erythematosus (SLE) | A chronic autoimmune disease affecting multiple organ systems, including the skin, joints, and kidneys. |
| Teflon | A brand name for PTFE, known for its non-stick properties. DuPont developed the Teflon brand name, but it is now owned by Chemours (a spinoff company of DuPont). |
| Temporality | The timing of exposure relative to the occurrence of an outcome, important in establishing causality. |
| Therapeutic phlebotomy | Withdrawal of blood to prevent or cure disease. |
| Total risk | The overall risk of an outcome occurring in a population or study group, encompassing all possible contributing factors. |
| Toxicokinetics | The study of how a substance enters, moves through, and exits the body. |
| Toxicologist | A scientist who studies the effects of chemicals on living organisms. |
| UK | United Kingdom. |

| | |
|---|---|
| Validity | The extent to which a measurement or test accurately represents the concept it is intended to measure. |
| Venesection | Taking blood. |
| Volume of Distribution (Vd) | The theoretical volume into which an amount chemical or drug would be dispersed to result in the observed concentration in serum or plasma. Usually expressed in volume per body weight ml/kg. |
| WHO | World Health Organization, the United Nations agency devoted to health and health protection. |
| Zwitterionic | Molecules with both positive and negative charges in different parts of the molecule. Zwitterionic PFAS are also present in some kinds of AFFF. |

## Appendix 1 – Islander input comments and Panel responses

Below are the responses received in the Islander input process. They have been grouped by topic or condition in order to make it easier for the reader to see the themes highlighted.

| | **Comment** | **Response** |
|---|---|---|
| **Cancer** | | |
| | Could you please take a look again at the bladder cancer information and check you're happy with it? Bladder cancer wasn't included in the table anywhere, but from what you explained at the time, that seems to be an oversight. | Thank you for your comments. Addressing bladder cancer explicitly was an oversight and will be remedied in the final report. |
| | The report mentions increased risks of kidney and testicular cancers, but it downplays these findings by emphasising the rarity of these cancers and suggesting that the overall risk is not significant. This overlooks the fact that, with widespread PFAS exposure and long latency periods for many cancers, these risks are much more concerning on a population level.<br>Research has shown a clear link between PFAS exposure and increased cancer risks, especially for kidney and testicular cancers. The International Agency for Research on Cancer (IARC) classifies PFOA, a common PFAS, as a Group 2B carcinogen (possibly carcinogenic to humans). (reference appended) | Thank you for your comments. We are concerned that you may not have understood the nuance of our findings with regard to cancers. We took some pains in the text of the report to point out that, even though research to date has not clearly and directly shown an increase in cancers other than kidney and testicular cancers, that does not mean that they are not, potentially, more likely in PFAS exposed populations. This is especially true for rarer cancers. We will review the text of the report to ensure that that is clear.<br>We are puzzled at the comment that we are downplaying the risks; at no point do we state that cancer risk is not significant. Cancer latency is important, and the studies we have focused on are constructed in such a way as to pick up a lot of cancers and account for a significant latency interval, but we recognise that, as more years pass, further cancers may come to light. It will be important to continue research.<br>Thank you for highlighting the IARC report. We do cite that report in several places, and in fact Dr Fletcher participated in the panel that made the determination and we refer to it in several places in the document (Group 1 for PFOA and Group 2B for PFOS). |

| | Comment | Response |
|---|---|---|
| | The panel noted that there were also concerns expressed by Islanders about rarer cancers and concluded that, although there is not yet evidence to give a clear answer on rare cancers, there is also insufficient evidence to rule out any potential risk from PFAS exposure.<br>The fact that it is stated 'there is insufficient evidence to rule out any potential risk from PFAS exposure' clearly indicates there is risk and grave risk of both the more common cancers and of the rare. | Thank you for your comments. We felt that it was very important to highlight that, just because there wasn't scientific evidence yet that a particular cancer was more likely in PFAS exposed people, doesn't mean that such evidence wouldn't come to light in the future. The purpose of this is to ensure that people don't jump to concusions that are not supported by science. At this point science does not know one way or another if there is a link between PFAS exposure and developing other cancers or not. It is also important to point out that we have only talked about the risks of getting cancer. The harms that having a cancer can do to a person and their family are also extremely important, but not in the scope of this report. |
| **Vaccines and infectious diseases** | | |
| | If the impact is island wide the proposal to "promote" childhood vaccines needs to help with herm immunity must be reconsidered. If all children are impacted by local water contamination not just those who live in St Ouen this would be pointless and in fact counter intuitive suggestion. | Thank you for your comment. By recommending universal promotion of childhood immunisations, we anticipate two benefits. The first is that PFAS-exposed children, wherever they live, would get the maximum possible protection from vaccine preventable diseases by being fully vaccinated. The second benefit is that, the more non-PFAS exposed children are fully vaccinated, the less likely they are to pass on a disease to a PFAS exposed child whose vaccine isn't working quite so well. |

| | Comment | Response |
|---|---|---|
| | A more detailed island wide impact to the extent of the levels of PFAS in all island water must be undertaken before any suggestion to vaccinate all other children to safeguard those with elevated PFAS levels when we are not certain of the extent of the issue amongst the entire population, although based on the 104 islanders who self funded blood testing, it would suggest the issue is widespread. | Thank you for your comments. The first part, on wider PFAS testing, is out of scope for Report 2 and is being considered in Report 3. We have already made a recommendation in Report 1 for assessing the background PFAS levels in people outside the plume area.<br><br>We can see no reason why vaccinating children to reduce their risk of contracting serious, vaccine-preventable, diseases should be delayed pending further PFAS testing. We have seen no evidence that vaccines are harmful to PFAS exposed children. Vaccines are beneficial in disease prevention whether or not they are also exposed to PFAS. |
| | I would also like to understand the impact of children with high levels of PFAS toxicity in their bodies with vaccinations - what is the impact and effects to a child. Has this been tested and researched? Are there any negative health consequences to a child who receives vaccination when they already have high levels of PFAS either immediately or longer term. Has this been considered or studied? | Thank you for your comment. We can see no reason why vaccinating children to reduce their risk of contracting serious, vaccine-preventable, diseases should be avoided in children who may have been PFAS exposed. We have seen no evidence that vaccines are harmful to PFAS exposed children or are associated with any negative health outcomes. |

| | Comment | Response |
|---|---|---|
| | The report acknowledges that PFAS exposure reduces the antibody response to vaccines but downplays this by saying there has not been a noticeable rise in infectious diseases. This conclusion overlooks the potential long-term immune system suppression that could become apparent in specific contexts, like during pandemics. Studies have shown that PFAS exposure can weaken the immune response to vaccinations, posing serious risks, especially for children. (reference appended) | Thank you for your comment. The research evidence shows a decrease in vaccine antibody response in PFAS exposed children (not adults) but has not found conclusive indications of an increase in either vaccine-preventable disease or other infectious disease. We are puzzled how the reporting of facts can be characterised as "downplaying". It is our view that it is not decreased vaccine efficacy that has the most potential for concern, but the presence of immunomodulation for which reduced vaccine antibody response is just a marker. It is on the basis of this interpretation that most of the current guidance on PFAS exposure is based. As stated in sections 2.2 and 2.4 of the report, the evaluation of research papers and their stated findings is more complicated than it might seem on face value and it is important to take a structured approach. It is important to be certain that the dose, the type of PFAS and the affected populations are similar, that measurement and classification of diseases has been carried out in a manner that accords with standard clinical practices and that the data analyses and inferences drawn are in accordance with good research practice. In this review, we focused on studies where the PFAS to which people were exposed were similar to those people in Jersey were exposed to. We also looked at existing reviews of the literature. This is the best way to use the most appropriate evidence |

| | Comment | Response |
|---|---|---|
| | The panel suggested that enhanced public health efforts to maintain high vaccination coverage should help protect vulnerable populations, including those potentially affected by PFAS. This suggestion does not protect anyone from PFAS toxicity and the risks we know it poses. | Thank you for your comment. One of the best described effects of PFAS exposure is reduced vaccine antibody response in PFAS-exposed children. By recommending universal promotion of childhood immunisations, we anticipate two benefits. The first is that PFAS-exposed children, wherever they live, would get the maximum possible protection from vaccine preventable diseases by being fully vaccinated. The second benefit is that, the more non-PFAS exposed children are fully vaccinated, the less likely they are to pass on a disease to a PFAS exposed child whose vaccine isn't working quite so well. |
| **Cardiovascular disease** | | |
| | Where PFAS levels are deemed elevated their cholesterol should also be looked at together with any other health consequences and suitable recommendations for lowering. It does not seem sensible to suggest that any child should be put on a medical treatment to lower this. What are suitable solutions for children? | Thank you for your comment. We are recommending that elevated cholesterol in people who have been exposed to PFAS be managed in the same way as it is managed in people who have not been exposed to PFAS. While many doctors are experienced in helping lower cholesterol in adults, few have experience of treating children. It would be important, if a child has elevated PFAS and elevated cholesterol, for them to be seen by a doctor who is experienced in managing high cholesterol in children (usually a paediatrician). This may or may not involve medication. It would not be approriate for the panel to suggest specific treatments. |

| | Comment | Response |
|---|---|---|
| | The report acknowledges that PFAS exposure is linked to higher LDL cholesterol, but then downplays the significance by saying there is no clear evidence linking this to cardiovascular disease in affected populations. This ignores the fact that high LDL is a well-known risk factor for heart disease, and given the persistence of PFAS in the body, the long-term risks are likely more serious than the report suggests. Studies clearly show that PFAS exposure leads to elevated cholesterol levels, which are linked to heart disease. The European Food Safety Authority (EFSA) review supports this, highlighting cardiovascular risks over time. (reference appended) | Thank you for your comments. The report is clear that PFAS exposure is associated with an increase in LDL cholesterol. We also noted that there is evidence from large studies which did not show an increase in cardiovascular disease as would usually be expected from such an increase in LDL cholesterol. However some more recent data has come to light showing that there is evidence in some research of increasing cardiovascular disease in relation to the PFAS. The report has been updated to reflect that. Also In the report, we discuss that any absence of increased cardiovascular disease risk in relation to PFOA could be explained as related to the concomitant increase in HDL cholesterol, which has a protective effect. We nevertheless, take a precautionary approach and recommend that raised cholesterol should be treated, with the same treatment for a PFAS-exposed person with elevated total and/or LDL cholesterol as would apply to a non PFAS-exposed person. |
| **Autoimmune disease** | | |
| | No comments received | N/A |
| **Endocrine and metabolic disorders** | | |
| | The report frequently mentions inconsistent evidence linking PFAS to thyroid problems, obesity, and diabetes, but by focusing on this inconsistency, it underplays the growing scientific consensus that PFAS disrupts the endocrine system.<br>Research increasingly shows that PFAS exposure affects thyroid function and other metabolic processes. (list of references appended) | Thank you for your comment. We are focussing on the evidence of specific disease in order to offer the maximum clarity and benefit to PFAS-exposed people and the clinicians involved in their care. In the areas of diabetes, obesity and thyroid disorders, we find some studies seeing an effect and some not and there is not sufficient evidence, on balance, to say that these are or aren't actual PFAS effects. We are well aware of data from animal and other models that show mechanisms for |

| | Comment | Response |
|---|---|---|
| | | endocrine disruption and find this interesting, but these sorts of data are not sufficient to draw conclusions about the impact on human health unless accompanied by good, consistent human evidence. |
| **Reproductive health** | | |
| | The report minimises concerns about reduced birth weight and pregnancy complications, stating that the evidence is mixed. This downplays the potential risks, as environmental pollutants like PFAS often have complex mechanisms that may not consistently show effects across all studies.<br>A number of studies, including meta-analyses, have found PFAS exposure linked to lower birth weight and complications like preeclampsia (reference appended) | Thank you for your comment. We are focussing on the evidence of specific disease in order to offer the maximum clarity and benefit to PFAS-exposed people and the clinicians involved in their care. In the areas of pregnancy-induced hypertension, low birth weight and intrauterine growth retardation, we find some studies seeing an effect and some not and there is not sufficient evidence, on balance, to say that these are or aren't actual PFAS effects. As stated in sections 2.2 and 2.4 of the report, the evaluation of research papers and their stated findings is more complicated than it might seem on face value and it is important to take a structured approach. It is important to be certain that the dose, the type of PFAS and the affected populations are similar, that measurement and classification of diseases has been carried out in a manner that accords with standard clinical practices and that the data analyses and inferences drawn are in accordance with good research practice. In this review, we focused in particular on studies where the PFAS to which people were exposed were similar to those people in Jersey were exposed to. We also looked at existing reviews of the literature. This is the best way to use the most appropriate evidence. |

| | Comment | Response |
|---|---|---|
| **Children** | | |
| | In addition, consideration is future health consequences of younger generations being impacted by PFAS. How do we safeguard the children generally from the negative future health consequences that may follow? | Thank you for asking this important and challenging question. Much of what you are looking for will be considered in the part of report 3 that looks at strategies to lower PFAS in the body, and Report 4, where it looks at PFAS in the environment. We have also made some recommendation in this report about how to mitigate potential harms to PFAS-exposed children. None of these give a full answer, and it will be this consideration that needs to be foremost in the minds of those setting policy going forward. |
| | My own 15 year old son was tested and has been found to have elevated levels even though he is not living in the plume area and never has! He has ADHD symptoms which are also linked to PFAS.<br>Given that my son was born and raised exclusively in Jersey but has never lived in the impacted plume area. Until 4 years ago he was drinking unfiltered tap water, upon realising that there was something not right with the water we changed this immediately. He was living for the first nine months of life in a house that was on bore hole, again not drinking filtered water.<br>Given that my son has grown up in Jersey but never lived in the impacted area, this leads to the consideration of the wider island impact from the mains water.<br>For context, I have included a snip of my sons blood results. He is 15 years old. He should not have levels this high. They are higher than some individuals who live in the plume area! This is very worrying indeed to us as a family, all of us have high levels but we | Thank you for your comments, and we hope that your son is getting all the care and support that he needs from health and education services to navigate life with ADHD, it is a challenging condition to live with. While the evidence we have reviewed does not show a clear and unambiguous link between PFAS and ADHD, that does not help you.<br><br>You raise some very important points about sampling people and sampling the environment island-wide and measures to reduce PFAS in water. While we have already made a recommendation in Report 1 to test baseline PFAS levels in people outside the plume area, we will be reviewing human testing overall in Report 3 and will discuss the pros and cons of testing people outside the plume area. In Report 4, we will also look at testing water outside the plume area. We will also be considering the use of domestic filtration systems to reduce PFAS, particularly for those on borehole supplies, in Report 4 (subject to consultation). |

| | Comment | Response |
|---|---|---|
| | don't live in the impacted area. It needs wider focus!<br>I would therefore strongly suggest that specific considerations are given to the impact to children island wide. The children of Jersey are our future and need to be given adequate care and consideration.<br>Currently most families are completely unaware and are still drinking from the tap putting themselves, their children and babies at risk. | |
| **Panel approach** | | |
| | Thank you for the opportunity to read through the draft report 2. I have spent hours reading through the report and made countless notes.<br>Statements such as potential harm or possible health implications are misleading and should no longer be used. PFAS causes harm to health. Any one person who researches PFAS knows this is the truth. It is about time the scientific community stopped pandering to the immorality of giant chemical companies and apathetic Government bodies; I realise that this is not possible though as most funding for research is from less than ethical misanthropists.<br>The facts being presented in report two are an extremely conservative view of the literature on PFAS and should be noted as such. The literature on PFAS is so vast that perhaps an A.I. programme to review all conclusions from PFAS scientific research would give humanity a better understanding of the harm individual PFAS cause with the knowledge available to date. For | Thank you for your comments. We understand that you might be happier with more categorical assertions, but science does not do that, even with much stronger evidence than exists for PFAS. We have described the potential risk in the light of the strength of the available evidence, this is set out in section 2.1 on page 20.<br>While your description of research funding does not correspond in any way to our experience, thank you for your views.<br><br>As stated in sections 2.2 and 2.4 of the report, the evaluation of research papers and their stated findings is more complicated than it might seem on face value and it is important to take a structured approach. It is important to be certain that the dose, the type of PFAS and the affected populations are similar, that measurement and classification of diseases has been carried out in a manner that accords with standard clinical practices and that the data analyses and inferences drawn are in accordance with good research practice. In this review, we focused on studies where the PFAS to which people were exposed were similar to those people in Jersey were exposed to. We |

| | Comment | Response |
|---|---|---|
| | example; there are, as of today's date, 83,900 research papers on the affects of PFAS and the human immune system. It is not possible for any one research group to read such vast amounts of literature and come to a truly informed conclusion.<br>Report two suggests there are levels of ambiguity among the scientific community, therefore, prevention and risk control should be at the forefront of islanders health. | also looked at existing reviews of the literature. This is the best way to use the most appropriate evidence.<br><br>The subject of artificial intelligence that you bring up is interesting, particularly to Dr Hajioff, who has worked extensively in the field. Unfortunately, the panel is not aware of any AI tool that is sufficiently thorough and robust to critically appraise research literature at this time. |
| | Please attach the clinicians guide from PFAS Research, Education, and Action for Community Health (as attached to this email). Last week I sat with a local doctor that was still clueless as to the affects PFAS have on a persons health.<br><br>"Can the science panel make a recommendation to Public Health that the attached clinicians guide from PFAS Research, Education, and Action for Community Health be given to all medical practitioners locally in Jersey so that they may better understand | Thank you for your comments. We have recommended that a concise knowledge-based resource on PFAS exposure and health should be made available to the public and health professionals in Jersey and will support the Public Health team in the production or sourcing of any such guide. The guide you have highlighted is interesting and easy to read, however the evidence has moved on since that guide was published and it largely relates to PFAS exposure very different from that in Jersey. Your comment has been shared with the Public Health team. |

| | Comment | Response |
|---|---|---|
| | the additional care/screening required for their patients?" | |
| | To that order, please review the attached clinicians guide from PFAS Research, Education, and Action for Community Health. I find it interesting that a number of the laboratory tests suggested for the victims of PFAS poisoning are noted in report two as 'unlikely' to affect health. Breast cancer is not even noted. | Thank you for your comments. We have recommended that a concise knowledge-based resource on PFAS exposure and health should be made available to the public and health professionals in Jersey and will support the Public Health team in the production or sourcing of any such guide. The guide you have highlighted is interesting and easy to read, however the evidence has moved on since that guide was published and it largely relates to PFAS exposure very different from that in Jersey. Your comment has been shared with the Public Health team.<br><br>The matter of biomonitoring for potential risks form PFAS exposure is being reviewed in Report 3. |
| | I have significant concerns about the current draft of the Independent PFAS Scientific Advisory Panel report. This report downplays the significant health risks related to PFAS exposure. Below, I have taken pains to show specific points where the report does not fully reflect the seriousness of the available scientific evidence. | Thank you for your comments, we have dealt with the specific matters you raise in the sections that relate to those comments, you will see them elsewhere in this table. We have managed it this way so that readers can see all the comments related to a particular condition or theme together. On your wider point, we understand that you might be happier with more categorical assertions, but science does not do that, even with much stronger evidence than exists for PFAS. We have described the potential risks in the light of the |

| | Comment | Response |
|---|---|---|
| | | strength of the available evidence, this is set out in section 2.1 on page 20, thank you for your views. |
| | I feel the report is misleading and unfair to the people of Jersey, who deserve a transparent presentation of the facts - facts that we can all find for ourselves if we spend a few minutes searching the available information online. It pains me to wonder why Jersey is feeling the need to reinvent the science on this, as we watch other countries bring down their PFAS levels in drinking water in response to the emerging science on its harms. We have the opportunity to lead the way on this matter, the UK is significantly lagging behind other countries and I hope we will not take the UK as our guiding light. Denmark would be a good model to follow. | Thank you for your comments. As stated in sections 2.2 and 2.4 of the report, the evaluation of research papers and their stated findings is more complicated than it might seem on face value and it is important to take a structured approach. It is important to be certain that the dose, the type of PFAS and the affected populations are similar, that measurement and classification of diseases has been carried out in a manner that accords with standard clinical practices and that the data analyses and inferences drawn are in accordance with good research practice. In this review, we focused on studies where the PFAS to which people were exposed were similar to the PFAS mixtures people in Jersey were exposed to. We also looked at existing reviews of the literature. This is the best way to use the most appropriate evidence.<br><br>On your comments on drinking water standards, this will be an important part of Report 4, which we hope to start working on in the next few months. |

| | Comment | Response |
|---|---|---|
| | My feedback is that I am very concerned about the cautious language used in the report, when discussing the health implications of PFAS exposure. This language has the effect of downplaying the risks, which I know we are all well aware of. The report acknowledges that certain PFAS are "associated" with elevated cholesterol and "probable" increases in kidney and testicular cancers, and it frequently over emphasises the absence of conclusive evidence for a range of other potential health impacts. Researching elsewhere tells a completely different story. It feels like it was written by a politician, not someone motivated to protect our health. | Thank you for your comments. We understand that you might be happier with more categorical assertions, but science does not do that, even with much stronger evidence than exists for PFAS. We have described the potential risk in the light of the strength of the available evidence, this is set out in section 2.1 on page 20. The way that we have described the data is in accordance with normal practice among epidemiologists, clinicians and other scientists. |
| **Matters that relate to other reports** | | |
| | In terms of lowering PFAS levels in children and younger generations, will Phlebotomy be an option for under 18's, if so what ages would be permitted? | Thank you for your question. While we only recommended phlebotomy for over 18s in Report 1, we are considering a wider range of strategies to lower PFAS in the body in Report 3. For any of these options, it would be a matter for the treating clinician to determine whether a person is suitable based on factors such as body weight, age, PFAS levels, general health etc. |
| | As your panel continues to "assess the risks associated with PFAS exposure", I would like to remind the Panel and the Government and our Public Health Department and Jersey Water of the precautionary principle. Given the persistent nature of PFAS in the environment and the growing body of scientific evidence indicating potential long-term health risks, it is crucial that action is taken to protect the | Thank you for your comments, we will be looking at PFAS levels in water and allowable thresholds in Report 4. |

| | Comment | Response |
|---|---|---|
| | population's health, even in the face of (what is clearly a very diminishing) "scientific uncertainty". | |
| | We know the risks have been considered high enough for other countries to drastically reduce their limits - why are we shedding any doubt on the need to do that here? Does Jersey need to reinvent the scientific interpretation of the current body of knowledge in PFAS?<br><br>Please, let's look to progressive countries on this topic and follow their lead. Denmark allow 4 ng/L in their tap. I'm currently drinking a total of 38 ng/L, and quite likely so are you and your family. | Thank you for your comments, we will be looking at PFAS levels in water and allowable thresholds in Report 4. |

| | Comment | Response |
|---|---|---|
| | Whilst I appreciate the steps that have been taken to look at the matter of our water quality, I feel the report underplays the seriousness of the contamination. Wouldn't it be great if Jersey made positive steps to filter the water polluted by many sources across the Island? The report dances around the facts concerning the impacts on our health. Is there anything more important than the health of the children of Jersey?<br>The UK directives are not the ones we should be listening too. Look ahead, look abroad and yes look at spending the money in filtration.<br>In your report you fail to mention how chemicals were diluted across multiple reservoirs. Why is this not stated? Why is this being hidden from the Islanders? Why are you not telling the whole story? Was this or was this not an attempt to fix a problem?<br>The report really does fall short and the only real thing it suggests is to appoint an expert for doctors to talk too. Why isn't the report looking at addressing the quality of water at source? Instead managing Islanders who are ill from drinking it. Obviously that is important but why why why aren't you looking at the problem itself?<br>After last nights news that Nitrate levels have been bent yet again, sadly I hold no faith that anything constructive and progressive will result from your independent study. This saddens me. Please help prove me wrong and HELP Jersey. | Thank you for your comments, we will be looking at PFAS levels in water and allowable thresholds in Report 4. We will also be looking at filtration and other technologies to reduce PFAS in water. |

| | Comment | Response |
|---|---|---|
| | Whilst I appreciate these findings have not made local headline news so as to not cause island wide hysteria, the resources and funds for 'enhanced public health efforts' could be used in a far better way i.e. island wide testing of water and community blood testing. | Thank you for your comments, we will be looking at blood testing for PFAS in Report 3, and PFAS levels in water and allowable thresholds in Report 4. We recommended blood testing for background levels outside the plume area in Report 1 |
| **Suggestions for government** | | |
| | My concerns are not limited to the ones mentioned above. We know PFAS is carcinogenic and what carcinogens cause. Public Health & Environmental Health should be working with Jersey Water to make sure people are more well informed. This could include memos on the panels progress being sent out with billing to ensure the public are aware and information is having a wider reach. Islanders can then make an informed decision on whether they wish to consume the water in its current unknown state. | Thank you for your comment, we will share it with the Public Health and Environmental Health teams. |

# Appendix 2 – Minutes of PFAS panel public meetings

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 10.00 – 12:00 on 16 November 2023

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Professor Ian Cousins – PFAS and Environment member

Joined by Islanders: Mr Graeme Farmer and Mr Joseph Farmer

In attendance: Grace Norman – Deputy Director Public Health

Sarah Tyler – Senior Policy Officer

Anita De La Cour – Executive Assistant

**Welcome:**

The Chair welcomed everyone to the Panel meeting, and reminded people the meeting was being recorded.

The Chair recapped in the meeting that the Panel would be producing a series of five reports:

1. **The 1st report is an interim report on the feasibility of therapeutic phlebotomy as a way of supporting people who have elevated PFAS levels in their serum and assessing whether phlebotomy helps them. The report is now finalised.**
2. **The 2nd report is more detailed, on the health impacts of PFAS exposure and particular groups of the population that might be at increased risk or reduced risk. Today's discussions will inform this report.**
3. **The 3rd report is more detailed and will look at all potential treatments for people who have been exposed to PFAS, and the evidence on how effective those treatments are as well as looking at testing.**
4. **The 4th report focuses on PFAS in the environment, how to reduce exposure, environmental interventions, and how to help manage PFAS in environment.**
5. **The 5th report is an update to first 4 reports, and any further information and evidence as the science is fast moving.**

***The Panel can be emailed via PFASpanel@gov.je.***

**Introductions:**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental challenges.

Dr Tony Fletcher, PFAS and Health Panel Member: Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of studies on the health effects of PFAS in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby.

Tony Fletcher commented that he was aware of a cancer research study, due to be published in the next 2 weeks, which may be of interest to this report.

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Grace Norman, Deputy Director of Public Health for the Government of Jersey, the commissioner of this work, and a standing observer at these meetings.

Support staff for programme management and administration were also in attendance.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

The minutes of the last meeting were agreed. No matters arising.

**Additional findings since the last meeting**

Exploring the Bradford Hill viewpoints is on the agenda, however, the Chair decided to move this item to another meeting as the main function of this meeting is to hear from experts by experience.

Update on report 1: The potential for an interim therapeutic phlebotomy service

The final version of report 1 has been sent to Ministers and a public meeting will be held on 1 December where Ministers will give their response to the report.

**Introducing the experts by experience and the purpose of the meeting**

Steve Hajioff explained that there were subject matter experts on PFAS, and global experts will be invited to give evidence at future meetings. There are also experts by experience, who are people from the Island who have experiences that they want to share, and this can inform areas that the Panel may explore. In the report, the Panel can also reflect on what this looks like in the real world and reflect on the case studies they have heard. This information may also help inform how doctors support people in the future.

The plan was to hear from 3 people this morning, but unfortunately one person could not attend, and they will be invited to the next meeting. Later today the Panel will also meet with 2 other affected Islanders who wish to give their testimonies in private.

A reminder was given to stay on topic and that this discussion is specifically for report 2, assessment of the impact of PFAS exposure on health. In addition, the Panel cannot give individual health advice. The Panel hope to support a resource for clinicians in the future to support discussions with people regarding PFAS.

**Experts by experience personal stories**

Mr Graeme Farmer and Mr Joseph Farmer gave testimonies which described the places they had lived, on island and off island, the years they had drank water from a private supply, and their respective medical histories.

The Panel then asked some clarification questions regarding the testimonies.

The Panel agreed to ensure that a range of health conditions will be reviewed.

The Chair thanked Graeme and Joe for their testimonies and acknowledged the difficulties they had faced.

**Broader discussion**

The meeting then went on to have a broader discussion of the implications on their lives, and what else the Panel might need to investigate, in terms of the report.

Steve Hajioff mentioned that raised cholesterol can be difficult to pinpoint the cause for, as cholesterol can run in families, however the Panel are aware of an association between PFAS and cholesterol and will look into it.

Steve Hajioff enquired regarding whether Islanders had conversations with clinicians about PFAS, and how have they engaged with you?

Graeme Farmer commented that clinicians were not helpful when we got the blood results and did not know how to interpret it.

Joe Farmer commented that his doctors did not want to comment on PFAS.

Steve Hajioff commented that this is interesting to note. This tells us there is a learning need.

Grace Norman commented that Public Health engaged with GPs ahead of the blood testing, and sent information and GPs had separate briefing. This was to enable them to have information to support giving people their results. Grace apologised that people had a negative experience with their results and said that the patient leaflet will be added to the PFAS web page.

Ian Cousins said that PFAS results can be very difficult for doctors to interpret, and the Panel will consider how the information can be communicated in the future.

Tony Fletcher commented on exposure and said we do not know how much ongoing exposure may be nor the background levels in the general population. The average half-life is 5 years but there is a big variation between different types of PFAS and between individuals, for example it can range from two or ten years. Depending on your individual half-life, you may have a faster or slower rate of decline. There is not good data on estimating the chance of each condition based on PFAS levels.

Steve Hajioff commented that the Panel will look at the literature for a dose response, it may be hard to find anything definitive. There is also some data on the distribution of PFAS in different body tissues, e.g.is it different in bone marrow and blood.

Tony Fletcher mentioned that there is some research on endocrine disrupting chemicals as a broader category. In some reviews PFAS are included in the category of endocrine disrupting chemicals.

Environmental issues were raised, and Steve Hajioff reminded people that the Panel will look at the environment in report 4.

**Additional questions**

Graeme Farmer commented that the Panel has settled people's minds and feeling much happier about the independence of the Panel. Steve Hajioff responded by saying that the Panel wants to continue to be open, this improves relationships, and dispels mistrust. Grace Norman commented that she was pleased to hear this feedback as it is important that the Panel is independent, and that Islanders understand that. Steve Hajioff continued by saying that some people are more comfortable to meet in private and gave reassurance that this will be anonymous, and all identifiers removed so it cannot be traced back to an individual.

Steve Hajioff thanked Graeme and Joe for the discussion and confirmed that for those wishing to meet in private, their testimonies will be anonymous, and once information has been used, all correspondence will be destroyed. Only the Panel and a minute taker will be present at the private meetings, and those attending will be asked if they are comfortable with someone attending and taking notes. It will be optional, if people are happy, for Grace Norman to attend.

Steve also re-confirmed that people can meet in public, private or submit written information, and that the Panel needs consent to use the information given. If consent is not given, the Chair has offered to meet people and has met regularly with some Islanders but cannot use their information in the report without consent. The Chair will email people who did not give consent and repeat this offer.

Steve Hajioff asked Joe and Graeme to email after the meeting regarding whether they are comfortable for the recording to be shared and will be asked to check their section of the notes for accuracy.

It was agreed the default position for minutes regarding people testimonies should be brief with headlines only. Detailed notes would be available for the Panel only for the writing of the report.

**Any other business**

The Chair reminded people that there is a meeting with Ministers on 1 December regarding their response to report 1.

**Date of next meeting**

7 December. This is currently 10am to 1pm however the timing may change to suit other experts by experience. Times to be confirmed.

The Chair thanked Graeme and Joe for sharing their experiences and helping the Panel with the process of this report.

There being no further business, the meeting was closed.

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 16:00 on 7 December 2023

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Professor Ian Cousins – PFAS and Environment member

Joined by Islanders: Joan Renouf and Lorna King

In attendance: Grace Norman – Deputy Director of Public Health

Sarah Tyler – Senior Policy Officer

**Welcome:**

The Chair welcomed everyone to the Panel meeting, and reminded people the meeting was being recorded.

**Introductions:**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental challenges; and getting science into policy.

Dr Tony Fletcher, PFAS and Health Panel Member: Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of studies on the health effects of PFAS in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby,

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Grace Norman, Deputy Director of Public Health for the Government of Jersey, the commissioner of this work, and a standing observer at these meetings.

Support staff for programme management and administration were also in attendance.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

The minutes of the last meeting are not yet available as the last meeting included hearing from experts by experience (EBE). The minutes from these meetings take longer and EBE will see first what goes on public record. There may be a delay in the minutes of this meeting due to the same reason.

**Additional findings since the last meeting**

There are two issues to note:

Firstly, there was a meeting with Ministers about the response to report 1, the potential for an interim therapeutic phlebotomy service. The public event with the Chief Minister, Environment Minister and Minister for Health and Social Services with Islanders was held on 1 December. The Chair commented that this was a useful meeting, and some interesting questions were raised by the public. The Chair was pleased to say that government has taken on the Panel recommendations in full.

Secondly, the International Agency for Research on Cancer (IARC) have recently published a Monograph: Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid. This research can be found at Volume 135: Perfluorooctanoic acid and perfluorooctanesulfonic acid – IARC Monographs on the Identification of Carcinogenic Hazards to Humans (who.int)

Tony Fletcher presented a summary of the research.

There were four working groups:

1. Exposure of people to PFOA and PFOS

2. Evidence of cancer in humans

3. Evidence of cancer in experimental animals

4. Mechanisms of action or key characteristics of carcinogenic activity

They were only investigating PFOS and PFOA.

Based on the criteria for classification at IARC they concluded the following:

PFOA epidemiology evidence is limited for humans.

PFOS epidemiology evidence is inadequate for humans.

Overall conclusions were:

PFOA carcinogenic to humans (categorised as Group 1 carcinogenic) based on:

• sufficient evidence for cancer in experimental animals

• strong mechanistic evidence that PFOA exhibits key characteristics of carcinogens in exposed humans

• There was limited evidence in humans for cancer of the testis and for renal cell carcinoma

PFOS possibly carcinogenic to humans (categorised as Group 2B possibly carcinogenetic) based on:

• limited evidence for cancer in experimental animals

• strong mechanistic evidence

• There was inadequate evidence for cancer in humans for PFOS

Following the presentation, Ian Cousins commented that it is difficult to look at one PFAS at a time when they are interrelated. Tony Fletcher commented that animal experiments are carried out with single substances. The chemical classifications are always one substance at a time.

Steve Hajioff commented that this report is relevant for the report 2, an assessment of the impact of PFAS exposure on health, currently being developed by the Panel.

**Introducing the experts by experience (EBE) and the purpose of the meeting**

Steve Hajioff explained that it is important to hear from EBE and to help explore issues raised against the scientific literature. In the report, the Panel can also reflect on what this looks like in the real world and reflect on the case studies they have heard.

The Panel thanked EBE today and those from the last meeting for engaging with the process.

A reminder was given that the Panel cannot give individual health advice. The Panel may not be able to reach conclusions around whether individual conditions were caused by PFAS exposure. The Panel will hear from two experts by experience (EBE), then will ask questions for clarification.

Usually, the recordings for these meetings are made available, however where the Panel are speaking to EBE the recording will not be made available to a wider audience. This is to respect people's privacy. The notes of the meeting will be shared with the EBE and published when agreed. After report 2 is complete, transcripts and recordings will be destroyed.

**Experts by experience personal stories**

Joan Renouf and Lorna King gave testimonies which described the places they had lived, on island and off island, the years they drank water from a private supply, and their respective medical histories.

The Panel then asked some clarification questions regarding their testimonies.

The Panel agreed to ensure that a range of health conditions will be investigated as part of Report 2, informed by Islander testimonies.

**Wider discussion**

Joan said that because her PFAS water levels were low, she was told she could still drink the water. Joan is still using bore water for washing, showering etc and is concerned about this. PFAS water levels are below WHO (World Health Organization) levels, but she is still concerned.

Steve Hajioff explained that the Panel is looking at different ways that PFAS gets into and out of the body and the impacts of this. The Panel have not formally investigated showering and bathing and its impact.

Ian Cousins said that dermal intake (ie. through the skin) is considered to be low risk for PFAS and so washing should not be a source of exposure). The exposure intake routes for the general global population are generally food, particularly fish, meat, eggs. In general, for someone living in a contaminated area, the primary intake is likely to be drinking contaminated water *(where there is significant contamination of the water system that is being consumed).* There is further evidence on exposure pathways of PFAS.

Steve Hajioff asked about home-grown food and keeping animals for food. Ian Cousins said this has been a concern in other countries using contaminated water for irrigating crops and feeding animals or home produce. In some areas around the world people had been advised not to use home grown produce. If you have been using bore water for irrigating produce, there may be additional exposure. There may be some additional exposure from consumption of produce.

*Post meeting note: A point of clarification was raised at the 8 February meeting where these notes were agreed. To clarify that in areas where there is not a direct source of PFAS contamination, then foods like meat fish and eggs are important for PFAS levels, but where there is a source of contamination from water, then this is the primary factor for exposure.*

*There are variances between types of PFAS. For example, PFOS in the general population (not specific exposed populations) then PFOS in fish is an important factor.*

Steve Hajioff asked whether the mains water is metered or a fixed cost in Jersey, as if it is metered then that may have an impact on people's use of bore hole water. Grace Norman commented that water is both metered and not metered across Jersey.

Ian Cousins asked is gastroenteritis a general diagnosis. Steve Hajioff commented that this is usually caused by a virus or bacteria. However, the symptoms can look like other conditions. It is possible that chemical exposure could cause symptoms like gastroenteritis and a GP may just put it down for food poisoning and not do wider testing. Steve Hajioff will check if there are similar cases like this and feedback in the future if there is any evidence found.

Grace Norman asked if the experts by experience (EBE) had any issues regarding engaging with their GPs at the time of obtaining their PFAS blood results and what was their experience at the time. Grace Norman also checked if the EBE had received the leaflet which helped people understand their PFAS blood results at the time. She commented that this has been updated and is now available online, for future reference. Steve Hajioff mentioned that one of the recommendations from the Panel will be to develop information for clinical staff. It is not unusual for GPs not to know about PFAS. Report 2 will help to increase the understanding of PFAS.

The Chair thanked Joan and Lorna for their testimonies, commenting that these are valuable for the Panel and also that a number of areas have been highlighted for report 2 and report 4 (on the environment) which will be considered.

Joan and Lorna thanked the Panel and staff.

**Any other questions**

None.

**Any other business**

None.

**Date of next meeting**

The 18 January meeting is currently advertised as 10am to 1pm (held online) however the timing may change due to subject matter experts being in different time zones across the world. This meeting is likely to be held in the afternoon and the time is to be confirmed shortly.

*Post meeting note: the meeting time is 3pm to 5:30pm.*

The Chair thanked Lorna and Joan for sharing their experiences and helping the Panel with the process of this report. Thanks, were also extended to the Panel and supporting staff for their valued work.

Steve Hajioff wished everyone a Merry Christmas and a Happy New Year.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 3:00pm – 5:30pm on Thursday 18 January 2024

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Prof Ian Cousins – PFAS and Environment member

Subject Matter Experts present: Prof Jane Hoppin, North Carolina State University

Dr Gloria Post, New Jersey Department of Environmental Protection

Dr Jamie DeWitt, Professor, Oregon State University

In attendance: Grace Norman – Deputy Director Public Health *from 420pm*

Sarah Tyler – Senior Policy Officer

**Welcome**

The Chair welcomed everyone and briefly outlined the running order of the meeting as per the agenda.

**Introductions**

Steve Hajioff is the Panel Chair – and has a background as a physician and a public health expert, in economics, and a retired Director of Public Health in an area of London with two major international airports and a variety of other environmental hazards. Steve Hajioff is not a PFAS expert and has worked in pharmaceuticals and supported policy makers to make evidenced based policy.

Tony Fletcher is the Health Panel Member – An Environmental Epidemiologist from London School of Hygiene and Tropical Medicine, and member of the Panel with experience of studies on the health effects of PFAS in several polluted communities.

Ian Cousins is the Environment Panel Member – A Professor in Environmental chemistry at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and human exposure of PFAS.

The Chair mentioned the meeting is usually joined by Grace Norman, Deputy Director of Public Health for the Government of Jersey, the Commissioner for this work, and a standing observer at these meetings and that she will join later.

Support staff, for programme administration and minute taking, were also in attendance.

**Declarations of Interest**

None.

**Minutes of last meeting**

There were no minutes to approve as the last meeting heard from Islanders and to ensure their clinical confidentiality is protected and the information is captured, the process takes longer than normal.

**Additional findings from the last meeting**

Discussions had been had between Government officers from Infrastructure & Environment and the Panel on the topic of potatoes being irrigated with water from within the plume area.

**Subject Matter experts**

The Chair asked the subject matter experts to introduce themselves to the meeting.

**Professor Jane Hoppin** is a professor at North Carolina State University, an Environmental Epidemiologist, and currently runs a large study of PFAS exposed people in North Carolina. She was also a panel member on US (United States) National Academies of Science, Engineering and Medicine that made recommendations for health care and follow up of PFAS exposed people. Most recently served on the International Agency for Research on Cancer (IARC) Panel that evaluated PFOA and PFOS for carcinogenicity.

**Dr Gloria Post** is a human health toxicologist and risk assessor in the State of New Jersey Department of Environmental Protection (NJDEP). Dr Post has worked in the NJDEP Division of Science and Research, since 1986, with responsibility for developing health-based guidelines for contaminants found in New Jersey's environment. She is also a member of the New Jersey Drinking Water Quality Institute (DWQI), an advisory group which recommends drinking water standards to the Commissioner of NJDEP  Also, she was a member of a National Academies of Science and Medicine committee that planned a workshop on human health PFAS research for the federal government, the USEPA (United States Environmental Protection Agency) Science Advisory Board panel that reviewed the scientific basis for the proposed federal drinking water standards for PFAS, and the International Agency for Research on Cancer (IARC) recent evaluation of PFOA and PFOS.

**Dr Jamie DeWitt** is a professor of Environmental Molecular Toxicology at Oregon State University and Director of their Environmental Health Science Centre. She has worked with PFAS in the laboratory since around 2005, looking at what PFAS does to laboratory models and investigates the immune system response.  Dr DeWitt has served in several different advisory capacities (as have Professor Hoppin and Dr Post) and serves as an expert witness for plaintiffs (*a person who brings a case to court)*.  Most of her work includes looking at laboratory models, and she supports different organisations in decision making.

**Presentations from subject matter experts**

The Chair invited subject matter expert guests to present to the meeting to contribute to report 2 on the health effects of PFAS.

Professor Jane Hoppin

Professor Jane Hoppin gave a presentation entitled "What are the Human Health Effects of AFFF (aqueous film forming foam) & other PFAS". For further details of the project see GenX Exposure Study - GenX Exposure Study (ncsu.edu)

Summary notes from the presentation:

Professor Hoppin has been involved with a study of the contamination of Cape Fear River basin in North Carolina, which is the largest river in North Carolina on the East Coast of the USA. Cape Fear River basin supplies more than 1.5 million people with drinking water. The study followed 3 different communities: 1) those at the mouth of the river, who were drinking water downstream from a

chemical manufacturing site, 2) those living near where a chemical manufacturing plant discharged into the river, and 3) a community upriver of the plant, to understand PFAS contamination and the baseline.

The study involved a group of 1,000 highly exposed people in North Carolina.

Professor Hoppin began by presenting some context about PFAS. PFAS is a large class of chemicals of more than 14,000 substances. In the US and other populations, 4 PFAS are commonly measured, PFOS, PFHxS, PFOA, and PFNA.

A factor which makes PFAS research challenging is that people are exposed to mixtures of multiple PFAS, and not to single type of PFAS, and each population is exposed to a different mixture of PFAS. Therefore, it is difficult to identify the role of each contaminant and different populations have different chemical profiles. Additionally, there is not good data on who has been exposed, or who should be tested, or for when clinical follow up is recommended. The work outlined by Dr Hoppin focused on health effects more broadly, focusing on PFOS, PFHxS, PFOA, and PFNA, which are all types of PFAS.

Jane Hoppin's presentation included what conclusions had been drawn on the health effects of PFAS – referenced in 3 Potential Health Effects of PFAS | Guidance on PFAS Exposure, Testing, and Clinical Follow-Up | The National Academies Press

Professor Hoppin reported that there are health effects which are outlined in the National Academies research above to have 'sufficient' evidence of an association between exposure and health:

- Decreased antibody response (in adults and children)
- Dyslipidemia (in adults and children)
- Decreased infant and fetal growth
- Increased risk of kidney cancer (in adults)

She also reported that there are other health effects where the research deemed that there is 'Limited suggestive evidence' of an association:

- Increased risk of breast cancer (in adults)
- Increased risk of testicular cancer (in adults)
- Liver enzyme alterations (in adults and children)
- Increased risk of pregnancy-induced hypertension (gestational hypertension and preeclampsia)
- Increased thyroid disease and dysfunction (in adults)
- Increased risk of ulcerative colitis (in adults)

The research also sought to identify what health care follow up could be required for people exposed to PFAS and identified blood levels that would warrant a health follow up, although noting that data for this was limited.

In the general population, PFAS in blood is reducing over time. The German HMB (human biomonitoring) work was used as a guide in this research to determine whether individuals should receive clinical follow up, as follows.

- Less than 2 ng/mL (nanograms per milliliter in blood) summed PFAS – adverse health effects are not expected and is recommended that people receive usual standard of care
- 2 to less than 20 ng/mL summed PFAS – HBM and this research determined that there is the potential for adverse effects in sensitive populations. Recommendations are to reduce PFAS exposure, screen for dyslipidemia, hypertensive disorders of pregnancy, and breast cancer, among other conditions
- More than 20 ng/mL of summed PFAS – A higher potential of adverse effects so the recommendations were to reduce exposure and test for thyroid function, kidney cancer, testicular cancer, and ulcerative colitis. Lipid test could start from age 2

To note these levels are not formally adopted, however they have been used in other research across the world.

The presentation went on to cover the evidence on reduced vaccine response and other effects on the immune system and how the body responds to infections. The potential health effects of PFAS are many and health outcomes change throughout the life course.

Human studies suggest PFAS exposure may:

- Increase risk of thyroid disease (noting that thyroid disruption would need a large sample size to test this further)
- Increase blood cholesterol levels
- Decrease the body's response to vaccines
- Decrease fertility in women
- Increase risk of high blood pressure and pre-eclampsia
- Lower infant birth rate
- Decrease fetal and infant growth
- Increase the risk of kidney, testicular and breast cancer (some or limited evidence for these, for example see IARC study)

Professor Jane Hoppin provided some resources and the Guidance on PFAS Exposure, Testing, and Clinical Follow-Up. National Academies of Sciences, Engineering, and Medicine, 2022. Full report here:

Front Matter | Guidance on PFAS Exposure, Testing, and Clinical Follow-Up | The National Academies Press

The Chair thanked Professor Hoppin and clarified that the US uses different units than Jersey for cholesterol levels.

Ian Cousins asked a clarification question about why PFOS was the predominant contaminant in the exposed communities around Cape Fear River, when would it normally be PFOA? Professor Hoppin indicated that further work was to be done on this. The Cape Fear River had been used as an industrial river since before the Civil War, there were nearby airports, textile manufacturers (contributing PFOA) and the largest military base in US was nearby (Fort Liberty). It is not understood why they have elevated PFAS levels. However, people with private well water supplies also had elevated levels compared to other areas in the US.

Dr Gloria Post

Dr Gloria Post gave a presentation entitled "New Jersey and other US Drinking Water Guidelines for PFAS." As a disclaimer, Dr Post said her presentation did not necessarily reflect the views of her department.

Dr Post gave an overview of New Jersey's PFAS work. New Jersey has developed drinking water standards (called Maximum Contaminant Levels = MCLs) for many types of containments since the 1980s.

PFOA was first reported in New Jersey's drinking water near an industrial source in 2005.

In 2007, the New Jersey drinking water guidance for PFOA was set at 40 parts per trillion (ppt), which was much lower than other US states' guidance at the time. In 2018, the New Jersey Maximum Contaminant Level (MCL) for PFNA of 13 ppt was established as the first drinking water standard for any PFAS in the United States. In 2020, New Jersey established MCLs for PFOA at 14 ppt and PFOS at 13 ppt

From Dr Post's work in New Jersey, she outlined why PFAS in drinking water is a concern.

· There is widespread occurrence of PFAS in drinking water throughout the state of New Jersey, and elsewhere in the US and worldwide.

· PFAS do not break down; they persist in the environment

· Some have long human half-lives (~2 to > 8 years), so they remain in body for many years after exposure ends

· Multiple types of animal toxicity, some at low doses

· Evidence for human health effects at low (general population) exposures

· Greater exposure from relatively low drinking water levels than from other common sources (food & packaging, consumer products)

· Drinking water is not commonly a major source for other persistent, bioaccumulative, and toxic chemicals, for example PCBs (polychlorinated biphenyls)

· Exposure is higher in infants, who are a susceptible subgroup, particularly those who are breastfed

· In conclusion, there is a need to minimize exposure to PFAS from drinking water

Dr Post presented detailed information on PFAS drinking water guidelines in the US, which vary among states.

The notable conclusions about the human data reviewed as part of the development of the New Jersey MCLs for PFAS were:

· There is consistency of results in different populations for some health effects

· There is concordance with effects in animal toxicology studies

· Serum concentrations can be used as a measure of internal exposure

· Although limitations precluded use of human data available at the time the NJ PFAS MCLs were developed, the human data justified concern for the increase in PFAS blood levels from drinking water exposure

In a more recent 2022 review that evaluated newer information, the DWQI agreed with the current USEPA (United States Environmental Protection Agency) conclusion that human data should be used for risk assessment of PFOA and PFOS. The DWQI concluded that the strongest human evidence was for increased cholesterol, increased risk of kidney cancer, increases in the liver enzyme ALT, decreased antibody response to vaccination, and decreased birth weight. The DWQI also agreed with USEPA that PFOA is likely to be carcinogenic to humans. In summary, the DWQI concluded that there are multiple lines of evidence to support health-based drinking water levels below the current New Jersey analytical limits of 6 ppt for PFOA and 4 ppt for PFOS.

Dr Post shared a list of publications for further information which included the NJDEP website about PFAS, available here: https://dep.nj.gov/pfas/

The Chair thanked Dr Post for her presentation and asked whether drinking water is the most important source of exposure to PFAS. Dr Post commented that it depends on the drinking water concentration and that there is a factor called a 'clearance factor' that relates the PFAS dose received (ng per kg body weight per day) to the PFAS concentration in the blood serum (ng per ml). The PFAS dose (ng per kg body weight per day) can be estimated from the PFAS drinking water concentration (ng per liter) and the average water ingestion (liters per kg body weight per day). The clearance factor is different for PFOA and PFOS. For PFOA, with ongoing ingestion of 10 ppt (part per trillion) in drinking water, there would be an increase in the blood serum level of about 100 times this, so the increase in PFOA in blood serum can be estimated to be 1000 ppt from ongoing exposure to 10 ppt PFOA in drinking water.

Ian Cousins asked about the methods and costs for the strict water quality levels in New Jersey. Dr Post commented that the levels used now in New Jersey are PFNA (13 ppt), PFOA (14 ppt), and PFOS (13 ppt), and that nothing regarding lower levels has been committed to in New Jersey.

Dr Jamie DeWitt

Dr Jamie DeWitt gave a presentation entitled, "Effects of PFAS exposure on the immune system".

Dr DeWitt outlined the basic functions of the immune system which performs many tasks in the body:

- Helping to keep the body healthy
- Protecting the body from pathogens like viruses, bacteria, fungi, and other things that want to invade
- Helping the body to repair itself when injured

- Recognising and killing mutated cells that could become tumors/cancers

When the immune system is out of balance, it may lead to (a) immune suppression which is a reduced ability of the immune system to respond to a challenge from a level considered normal, regardless of whether clinical disease results, and (b) inappropriate immune stimulation which is inappropriate immune responses to common substances, e.g., allergic hypersensitivity, or responses to self-antigens, i.e., autoimmunity.

PFAS affects many bodily systems, and one implication to the immune system is a decreased response to vaccines, which is a marker of immune suppression. Immune suppression can, in turn, increase the risk of infections (for example, the flu) and certain types of cancers. Decreased responses to vaccines have been seen in people who have higher levels PFOA/PFOS in their blood and laboratory model studies also support this finding. However, PFAS can also lead to an imbalance where the immune system responds too strongly (inappropriate immune stimulation) to things like pollen. It can be challenging to study the effects of PFAS exposure on the immune system because of the basic role of the immune system in overall health, but "challenging" the immune system with a vaccine, for example, can give important clues.

Dr DeWitt also worked on the study in Cape Fear River, and she explained some of the compounds found there:

**PFMOAA - $C_3HF_5O_3$**

- perfluoro-2-methoxyacetic acid
- (mono-ether carboxylic acid)
- Dominant short-chain PFAS detected in Cape Fear River in 2018 at high concentrations and not in human blood

**Nafion Byproduct 2 – $C_7H_2F_{14}O_5S$ a longer chain compound**

- Perfluoro-4-methoxybutanoic acid
- (di-ether sulfonic acid)
- PFEA detected in Cape Fear River in 2018 at low concentrations and detected in human blood

**PFO5DoA – $C_7HF_{13}O_7$**

- Perfluoro-3,5,7,9,11-pentaoxadodecanoic acid
- (multi-ether carboxylic acid)
- PFEA not measured in Cape Fear River in 2018 and was detected in human blood of people drinking water from the river

Some PFAS have a shorter half-life in the body, so they are not always detected.

In Dr DeWitt's work, laboratory administered compounds were given to laboratory models (*Mice used)* over a 30-day period of exposure (as per harmonized test guidelines which is a guide acceptable to the WHO and other agencies across the world).

Animal studies on changes in a liver marker: Signs of toxicity were detected in liver markers, all tests elicited effects at the administered concentrations, effects which varied depending on the compound.

Changes in vaccine response: Changes were seen to vaccine response at the highest doses administered for all models, however not all changes were statistically significant, although raised some concern that these compounds were changing the ability of the immune system to do its job.

In summary, the overall potency based on the liver and the ability to suppress the vaccine response (and changes seen in the liver in the lab) is that PFO5DoA is the most potent and PFMOAA least potent. This could be due to the carbons and length of the chain, or the functional group, or how structure affects the biological half-life in organisms. *(Half-life is the time it takes for the concentration of a substance in the body or in the environment to reduce to half its initial value).*

The European Food Safety Authority (EFSA) calculated a tolerable weekly intake (TWI) for food for four PFAS (PFOA, PFOS, PFNA, PFHxS) of 4 ng/kg/day (nanograms per kilogram per day) based on decreased vaccine responses. The US Environmental Protection Agency used decreased vaccine responses as a health effect (also used cardiovascular and developmental effects) to calculate health protective levels, although the proposed limit of 4 ppt (parts per trillion) for PFOA in drinking water was based on risks of cancer.

Immunosuppression can therefore be seen as a public health risk. PFOA and PFOS exposure are expected to cause mild to moderate immune suppression, but they are well studied, so it is known humans will be at risk if exposed. For other PFAS that have not been as well studied, the risks are not as well known.

The Chair thanked Dr DeWitt for the presentation and asked whether there are effects on other immune response pathways (cellular immunity). Dr DeWitt mentioned a range of studies to note in this regard. Dr Post commented that the IARC study identified some human data for carcinogens.

Ian Cousins asked Dr DeWitt to clarify what laboratory models are for the purposes for the public listening. Dr DeWitt explained that in her presentation she referred to studies on mice, and she noted that the compounds that she discussed are related to the US exposure relevant to North Carolina and not raised in relation to the Jersey context.

A broader discussion then followed, of which a summary of the headlines from the discussion are as follows:

In terms of health effects and contaminants present in the environment, there is limited toxicity testing data available from the environment. It is a challenge to interpret concentrations in the blood when there is no toxicity data to compare it with.

A study was referred to, an AFFF (A*queous Film-Forming Foams)* dosing study using AFFF measuring different PFAS compounds in the formulation and administered in lab testing on mice. They found that the formulation was different to what was found in blood serum, showing internal transformation in different PFAS compounds. From the different compounds they could measure (in blood) there was no toxicological data from the environment. Therefore, it is difficult to determine which compound to study.

Exposure profiles were discussed, including the degradation of products and the changes in exposure in different areas. Different PFAS will degrade and travel differently in the environment. The primary source of contaminant is not necessarily the main source of PFAS the person is exposed to.

Variables in PFAS in serum could be explained by the level of local exposure e.g. in the USA example mentioned they were drinking the same water source and so researchers could see the exposure levels based on how long they had resided in the area and whether they had a water filter. Serum levels in the community can be useful to establish the exposure of concern.

There could be an issue in using reduced vaccine response as evidence of risk in the population, but this is an indicator that something may be happening to the immune system in general and may not be linked directly to PFAS. It is noteworthy that reduced vaccine response is a risk *marker* not a risk *factor*, (the factor is worth looking at but will not necessarily be a risk factor).

Regarding studies on common childhood infections being affected by the presence of PFAS in the blood, the evidence does not appear to be strong.

To note that after age 59 the human immune system competence declines naturally. Data in people who are immunosuppressed, or the elderly can be explored to compare data in exposed communities to see the level of immunosuppression in the exposed population.

There are many variables and factors which can make comparisons between populations difficult to understand and interpret, for example general viruses and colds and there are changes in virus profiles across communities. It can be difficult to measure the impact of PFAS on vaccines due to numerous factors.
Examples in Ronneby were mentioned along with the exposure and profile of this population.

The potency of PFAS was explored and the regulations in the USA set for individual PFAS. Different PFAS have different elimination rates. The relative potency of PFAS varies and lots of factors can affect this.

Some health effects have been seen in people with PFAS levels below 20 ng/mL (nanograms per millilitre) therefore this is not a totally robust threshold. The challenge in determining the numbers is where to start given the lack of thresholds. In a USA study, people would have high PFAS levels 20 years ago and they would be lower today. In general, PFAS levels in blood are coming down. In the USA, about 8% of the population exceed 20 ng/mL. Most of the population will be between 2 to 20 ng/mL. There is more work to do in the scientific community to understand these numbers and what the numbers should be.

The Chair then brought the discussion to a close.

**Any other business**

None.

**Date of next meeting**

8 February, 3pm.

**Thank you and close**

The Chair thanked the Panel, the expert guests, and the supporting staff.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 3pm – 5pm on Thursday 8th February 2024

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Prof Ian Cousins – PFAS and Environment member

Subject Matter Experts present: Dr Sue Fenton – Director, Center for Human Health and the Environment, North Carolina State University

Dr Christel Nielsen – Occupational & Environmental Medicine, Lund University, Sweden

In attendance: Grace Norman – Deputy Director of Public Health

Sarah Tyler – Senior Policy Officer

Anita De La Cour – Executive Assistant (minutes)

**Welcome**

The Chair welcomed everyone and briefly outlined the running order of the meeting as per the agenda.

**Introductions**

Steve Hajioff is the Independent Panel Chair, with a background as a physician and a public health expert, in health economics, and a retired Director of Public Health in an area with two major international airports and a variety of other environmental hazards. Steve is not a PFAS expert.

Tony Fletcher is the health Panel Member. An Environmental Epidemiologist from London School of Hygiene and Tropical Medicine.

Ian Cousins is the environment Panel Member. A Professor in Environmental chemistry at Stockholm University, an expert on PFAS, whose expertise is on the sources, transport, fate, and human exposure of PFAS.

The Chair mentioned that the meeting is also joined by Grace Norman, Deputy Director of Public Health, who commissioned this work and is a standing observer.

Support staff, for programme management and administration were also in attendance.

The Chair reminded people that the meeting is being recorded and a copy of the recording can be requested by emailing publichealth@gov.je.

**Declarations of Interest**

None.

**Minutes of the last meetings**

The minutes of the November meeting are not yet available, as final sign off was needed by those experts by experience who attending that meeting. It was anticipated that they would be available for agreement and sign off at the next meeting on the 4th of March.

The minutes of the meeting of 18th January 2024 were also not yet available due to the wide ranging and detailed presentations by subject matter experts needing to be captured, which was taking longer than normal to complete.

The minutes of the meeting of 7th December 2023 were agreed, subject to adding in a post meeting point of clarification as follows:

- On page 3 of the minutes: To clarify that in areas where there is not a direct source of PFAS contamination, then foods like meat fish and eggs are important for PFAS levels, but where there is a source of contamination from water, then this is the primary factor for exposure

There are variances between types of PFAS. For example, PFOS in the general population (not specific exposed populations) then PFOS in fish is an important factor

There were no other matters arising.

**Additional findings from the last meeting**

No additional findings.

**Subject Matter Experts**

The Chair asked the subject matter experts to introduce themselves to the meeting, after which they would each present to the Panel.

Dr Sue Fenton is a reproductive endocrinologist, having worked for 11 years in the USEPA (*United States Environmental Protection Agency)* specifically focused on PFAS and other environmental contaminants and their health effects. Dr Fenton then moved to the National Institute of Environmental Health Sciences for 14 years and expanded her work specifically looking at development and targeting the effects of chemicals such as PFAS. She is now the Director of the Center for Human Health and the Environment at North Carolina State University.

Dr Christel Nielsen is an environmental epidemiologist from Lund University in Sweden. Dr Nielsen works on health effects in children and pregnant women in Ronneby, Sweden, which has PFAS contamination which also had exposure from firefighting foam.

**Dr Fenton's presentation**

Dr Fenton gave a presentation entitled "PFAS health effects in a mouse model: Early life exposure and later life effects". The work has looked at 'known' or 'legacy' PFAS and comparing them to new PFAS. Mouse models indicating health effects were used to show direct causations to PFAS exposure.

Dr Fenton outlined that PFAS is detected across the USA, with the northeastern areas having the biggest concentration. The presentation focused on PFAS exposure in North Carolina State coming from industrial sites (including a fluorochemical manufacturer, producing a replacement for PFOA, called GenX), an Airforce base, fire training sites and landfill, which were all across the Cape Fear River basin. It was noted that there are also popular tourist areas in this vicinity.

PFAS was discovered in the water about ten years ago, originally there were permits allowing the discharge of waste into the water and then these were revoked, however PFAS by-products had been discharged into the water for about 40 years. It is now known that 650 personal wells in the area are contaminated with 'novel' (*newly researched compounds)* PFAS.

There are many PFAS exposure pathways in this area (old and new), including:

Ingestion, inhalation, dermal (skin) via:

- industrial sites (point sources)
- fire training / fire-fighting facilities
- landfill
- wastewater treatment plants/biosolids
- consumer products/dust
- food items (e.g., fish/shellfish)
- food packaging

<u>The effects of PFAS on human health</u>

There are health effects associated with PFAS exposure (seen in both animal and human studies), which may include:

- Immune function changes
- Thyroid function/disease
- Liver disease and cancer
- Metabolic dysfunction
- Kidney disease and cancer
- Reproductive and developmental outcomes (a key focus of Dr Fenton's work)
- There is some evidence from several papers on delays or a shortened duration of lactation due to PFAS exposure (and potentially other life factors)

There was a 2023 PFAS Report delivered to Congress, which Dr Fenton contributed to as a subject matter expert, which was a high-level summary focusing of the following areas:

- Removal, safe destruction, or degradation of PFAS from the Environment
- Safer and more environmentally friendly PFAS alternatives
- Sources of PFAS and pathways of human exposure
- Understanding the toxicity of PFAS to humans and animals:
    1. Epidemiology evidence *(a particular exposure causes a particular harm)*
    2. Laboratory animal models *(e.g. mice, rats)*
    3. Ecotoxicology studies *(substances harmful to the environment)*

The report also listed gaps in knowledge of PFAS health effects, which included obesity and metabolic disease, and the assessment of the placenta or pregnancy complications. It was hoped

that this focus would enable direct funding into the understanding of the health effects of PFAS, as this is not currently widely understood.

There has been a lot of focus on non-alcoholic fatty liver disease, which cases are rising globally, and has been linked by some to PFAS exposure in both humans and animal models. This is relevant to Dr Fenton's work as liver disease is on the rise in the United States.

A comparison study between PFOA and its replacement GenX was conducted exposing mice, where the foetuses and subsequently the offspring were studied. PFAS was looked at in the blood, in livers, foetuses, and the placenta. The aim of the comparison between PFOA and GenX was to see if GenX was a safe replacement for PFOA, and this study showed that it may not be.

The results of this study showed that exposure to PFOA and GenX was associated with placental lesions, increased maternal weight gain, an increased embryo to placenta ratio, and a constellation of adverse liver features. These occurred in both the mother *(mouse)* and the liver of the foetus, which suggested that what was happening in the mother was also happening in the offspring.

In the offspring, there were sex specific liver effects, and metabolic disease in both males and females. The female mice had worse liver disease, the males became obese, had glucose intolerance and insulin resistance.

The conclusion from the study is that PFOA and GenX are very similar, with almost identical effects, even though GenX has a much shorter half-life than PFOA. *(Half-life is the time it takes for the concentration of a substance in the body or in the environment to reduce to half its initial value).* The GenX half-life is about one day in a mouse compared with a 3-week half-life in a mouse for PFAS.

Dr Fenton explained that there are numerous other PFAS in our environment, but there is no health data for these. In future, it is hoped to be able to predict pathways for new emerging PFAS, to analyse their effects, including adverse outcome pathways for foetal growth restriction (FDR).

Dr Fenton outlined that the full extent of the work cannot be covered in this short presentation, and in summary in utero PFAS exposure sets the stage for a lifetime of increased disease susceptibility, for example this could include:

- Transplacental transfer- PFAS has been found to cross into the placenta and in mouse models found lower birth weight
- Hypertensive disorders of pregnancy
- Low birth weight
- Reduced immune function
- Disruptions in timing of puberty
- Menstrual issues and reduced fertility
- Elevated cholesterol
- Reduced kidney function
- Thyroid hormone disruption
- Cancer

Dr Fenton felt that protecting pregnant women and babies from PFAS effects was important.

Finally, Dr Fenton talked about PFAS in AFFF (Aqueous Film Forming Foam) which is found in firefighting foam and concluded that there is not a lot of health data on AFFF. It is difficult to know about changes in formulas from the manufacturer unless they make it known or it is discovered via research. In the future Dr Fenton will be looking at genomic signatures and assays to help understand these novel PFAS components quickly, which is important for understanding health impacts.

The Chair thanked Dr Fenton for her fascinating presentation.

The Chair asked for clarification as to whether socio-economic factors were considered with the lactation studies, i.e. mothers from poorer areas are less likely to breastfeed, and more likely to live in areas where exposure is higher (e.g. in industrial areas) which could be a source of confounding. Dr Fenton confirmed these factors were controlled for in the analysis and that socio-economic factors have long been associated with PFAS levels.

Dr Fenton was asked about the fact that that GenX is considered to be a more toxic substance (given its half-life was much shorter than PFOA) yet the results showed same effect in the lab mice. She confirmed that appeared to be the case, and other studies had also shown that lower doses of GenX shows same effects in mice too. GenX appears to be causing metabolic disease.

To clarify for members of the public listening, no GenX had been found in Jersey.

A further discussion followed about testing, what has been tested and what is available to test. There are thousands of mixtures in different PFAS substances, for example AFFF is a complex mixture of substances. This can present challenges in testing as it is difficult to know what to test for.

**Dr Christel Nielsen's presentation**

Dr Nielsen gave a presentation entitled "High exposure to PFAS in Ronneby, Sweden – effects on child health and development".

Dr Nielson gave a brief background summary, notably her interest in public health following PFAS exposure in Ronneby, Sweden. Ronneby is a typical Swedish small town, with a population of 28,000 people, with mostly municipal drinking water from two water plants. Sweden has a strong tradition of drinking tap water, which, in this case, was an important source of exposure.

PFAS contamination was discovered by chance in December 2013 and action was taken as a result of:

- Money was left in the budget for regional environmental monitoring
- There was an awareness of the upcoming EU drinking water directive at the time
- There was new knowledge of PFAS contamination around the airfields

Extended sampling of water was undertaken in Bredåkradeltat, one of Sweden's largest water reservoirs, located in the Kallinge area of Ronneby. High levels of PFAS were found in this reservoir. A municipal water treatment plant was located in the exposure area, and outgoing drinking water was analysed. The results showed the sum PFAS in the contaminated waterworks was 10,380 ng/L (nanograms per litre), compared with Kärragården (47.6ng/L), the other waterworks, and <5ng/L in the neighbouring municipality Karlshamn, which was used as a reference point. The exposure profile

was driven by AFFF (Aqueous Film Forming Foam) contamination. The contaminated waterworks was immediately closed.

In terms of the population exposure, the Brantafors reservoir served a third of the households with water in 2013. The start of the exposure is unknown (there were no saved or banked samples) however military purchase records from the mid-1980s suggested that exposure had taken place for over 30 years.

In 2014, after the water source was closed, blood testing was offered to the local population for PFAS:

- Open samplings at around 20 locations
- Tests were free of charge
- The participation rate was 13% of the population
- This showed elevated serum concentrations in everyone tested in Ronneby (including those not living at exposed addresses)
- Other contaminants measured were not elevated

The 2014 results showed blood serum concentrations were much higher in Ronneby than in the reference population; the PFHxS median was 280ng/mL (nanograms per litre), and PFOS 303ng/mL, compared with the median levels of 0.5ng/mL for PFHxS and 2.9ng/mL for PFOS in the reference population.

In 2013, there was no information about how PFAS impacted human health in terms of comparable data for effects of AFFF, so the Ronneby PFAS research Program was formed. This is a joint venture between Lund and Gothenburg Universities, which Panel member Tony Fletcher is a part of. Together they are looking at health impacts of PFAS in the population.

From this work, 6 areas for research needs in children were identified: pregnancy health; birth outcomes; neuro development; cardio-metabolic health; immunologic effects, and puberty.

In Ronneby, they enrolled mothers during early pregnancy to take part in a study. All pregnant women were invited. Follow up was until the child was one year old. The study involved taking biological samples and completing questionnaires. Pregnancy health and PFAS transfer during pregnancy was explored. This showed that, at birth, an infant can have 30-60% of the mother's level of PFOS. Breast milk concentrations and blood concentrations were also reviewed. The study showed a lower transference through breastmilk. Further studies are underway to find out more.

The changes in breastmilk concentrations over time was researched and in conclusion:

- Transfer efficiencies are not affected by the maternal exposure level
- Transfer during pregnancy is more efficient than the transfer into breastmilk
- Breastfeeding is an exposure source for the infant but is also associated with several health benefits
- If/when possible, female PFAS serum levels should be reduced before pregnancy
- There is a further need to understand how early-life exposure affects child health

- Previously there were no studies regarding high AFFF exposure

Sweden has a comprehensive register of population data which supports PFAS studies. The data collected in Sweden was also outlined and they have a long history of keeping various registers which are useful for these studies, including population characteristics, healthcare data and socio-economic data. There is mandatory participation in this data collection and personal identification numbers are used. For example, they could look at the national birth register and see who had background exposure to PFAS and pregnancy complications and birthweight in the county.

In terms of pregnancy complications, the studies concluded there was no increased risk. For birth weight, there was an effect, but the magnitude was small and different in girls and boys.

It should be noted that the data used was before 2013 so breastfeeding decisions were not based on knowledge of PFAS exposure. It was suggested that breastfeeding mothers had a 3 times higher risk of not establishing breastfeeding than in the non-exposed population. Also, more mothers were not breast feeding at 6 months, which may be indicative of delayed mammary gland development in exposed mothers. Dr Nielsen commented that what we can conclude today, is there is not sufficient evidence to recommend that highly exposed mothers refrain from breastfeeding, given the other benefits breast milk and breastfeeding has for infant health.

The final study Dr Nielsen shared was in relation to neuro development, and developmental language disorder. This research included all pregnancies in the county between 1998-2013 and conditions diagnosed by speech and language pathologist after screening by Child Health Services. Hence, the data is based on clinical diagnosis. The results showed that girls from the highly exposed area had a 1.6 higher risk of being diagnosed with a developmental language disorder *(no effect in boys).* Therefore, Dr Nielsen concluded that there may be an effect on neurodevelopment that warrants further investigation.

Overall, her concluding remarks on health effects in the Ronneby population:

No increased risk of pregnancy complications

- A small and sex-specific effect on birth weight
- Impaired breastfeeding ability was seen
- Increased risk of developmental language disorder in girls (more research needed here)
- Adverse effects on breastfeeding and language development can be intervened on
- A many times higher exposure did not cause many times higher risks (however more research is needed)

Dr Nielsen concluded by letting the meeting know that an English summary of the Ronneby research is published at https://pfas.blogg.lu.se.

The Chair thanked Dr Nielsen for a fascinating presentation.

**Questions and discussion**

The Chair commented that he had previously worked as part of an Infant Mortality Taskforce in England, which looks at deaths of babies in first year of life, and he wanted to stress that one of the most important factors in first year of life is breastfeeding, and whilst there is some exposure to PFAS

by breastfeeding, there is no strong evidence of breastfeeding causing harm. Breastfeeding is extremely important for babies' health and wellbeing. The Chair asked people not to over interpret the studies or change their behaviours with regards to breastfeeding. Dr Fenton echoed this, commenting that breastfeeding gives children the best start in life.

A general discussion then took place, the summary points to note are:

- It is difficult to collect breastfeeding data in terms of volumes of milk consumed (in Sweden they do have biomonitoring data for 1-year olds)
- Studies are ongoing as to whether lower breastfeeding rates could be associated with PFAS exposure, possibly through delayed lactation
- In Sweden, 98% of mothers breastfeed so there are only a small number of mothers who do not breastfeed, meaning that there is greater statistical uncertainty (as displayed by confidence intervals) around non-breastfeeding
- Studies on breastfeeding pathways show higher levels of PFAS intake and levels peak at about 20 months, this maybe when breastfeeding stops
- Transfer during pregnancy is more efficient than transfer into breast milk
- There is not sufficient evidence to suggest that the general health benefits of breastfeeding are significantly offset by PFAS, so it is important to continue to promote breastfeeding because of its additional benefits
- Study design and dose response are important factors in the research and its conclusions
- Ronneby did have a number of immigrants (who don't always have a personal identification number in Sweden yet), however, there is confidence that the majority of people had a personal identification number and therefore have contributed to the evidence
- Thyroid effects of PFAS need further study as this appears important and could be affecting some of the other health areas discussed above
- It is important to understand the threshold effect and dose response in PFAS as there appears to be a saturation point, so it is not necessarily the case that the higher the PFAS exposure leads to a greater health concern, which would normally be assumed to be the case in general toxicology
- There could be differences in the metabolism of peoples or animals, as well as differences in population exposure, which may affect the measurements and data. Some populations therefore would be more vulnerable to internal confounding *(i.e. mixing of effects, which can distort the data)*
- There is a role for further animal studies to explore some of these issues. It is likely that no animal group will have a zero PFAS exposure (which would be used for comparison) due to the presence of PFAS in water
- By looking at gene data a very low level of PFAS can be identified and this has been used in animal models and this can be compared with the serum levels found in human populations

- It could be that wider endocrine disrupting hormones could lead to health effects other than thyroid as there is some evidence of this (thyroid information is being collected from the pregnant women in the Swedish study, so this can be explored further in their research)
- Research showed a glycogen deficit in the placentas of animals exposed to novel PFAS (and their metabolism affected at birth). In animals, if their glycogen deficit is large enough, they cannot survive. This is also important in humans also as it could have implications for insulin resistance, for example. It was noted that it can be difficult to collect this data in humans

In conclusion, the Chair stressed the need to be careful about interpreting numbers, measurements and exposure information quoted in today's presentations and using them out of context. For example, animals have a half-life of about 3 weeks for PFAS and in humans, by comparison, the half-lives are many years, so there are meaningful differences between humans and animals. There has been some PFAS research on larger animals such as sheep and horses to compare exposure, although there are differences such as their food consumption and exposure (noting that animal studies are different to human studies when looking at the effects of PFAS).

The Chair thanked Dr Fenton and Dr Nielsen for their informative presentations, which will be useful for the Panel's report.

**Any other business**

None.

**Date of next meeting**

4th March 2024 at 10.00 am.

**Thank you and close**

The Chair thanked the Panel, the expert guests, and the supporting staff.

A reminder was given that the meeting recording is available on request by emailing publichealth@gov.je.

There being no further business, the meeting was closed.

8 *To note that the Panel can be emailed via PFASpanel@gov.je.*

9

10 *Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams From 10.00am to 12pm on Monday 4 March 2024

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Professor Ian Cousins – PFAS and Environment member

In attendance: Sarah Tyler – Senior Policy Officer

Anita De La Cour – Executive Assistant

Apologies: Grace Norman, Deputy Director Public Health

**Welcome**

The Chair welcomed everyone to the Panel meeting, and reminded people the meeting was being recorded and that the recordings are available afterwards on request (*by emailing publichealth@gov.je).*

**Introductions**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, is the Independent Panel Chair, with a background as a GP and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental challenges. Steve is not an expert in PFAS but has extensive experience in helping turn science into policy. He led the Health Impact Assessment at the Greater London Authority and has chaired policy development groups for a range of organisations.

Dr Tony Fletcher is the PFAS and Health Panel Member, and he is an environmental epidemiologist at the London School of Hygiene and Tropical Medicine, and a long-term researcher on the health effects of PFAS.

Professor Ian Cousins is the PFAS and Environment Panel Member. A Professor at Stockholm University, whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Grace Norman gave apologies for the meeting. Support staff for programme management and administration were also in attendance.

**Declarations of Interest**

None.

**Minutes of the previous meetings**

The minutes of the meeting of 16 November 2023 were agreed, with no matters arising.

The minutes of the meetings of 18 January and 8 February 2024 are still being finalised, due to the complexities of capturing the subject matter expert's content. These meetings were recorded and are available online for people who wish to watch them. Please email publichealth@gov.je to request the recordings.

**Additional findings since the last meeting**

To date, two public meetings had taken place and several private meetings held with Islanders regarding their health experiences, and written testimonies were submitted by Islanders which had identified a list of key conditions to be investigated as part of report 2. Rare conditions had not been included as clinical confidentiality of those concerned could not be guaranteed due to the low numbers involved. These areas will however still be looked at.

Key conditions to be researched:

- A range of cancers
- High cholesterol
- Fertility issues
- Inflammatory of the stomach and gut disorders
- Liver disorders
- Impacts on children
- Impact on mental health, psychological and physiological effects

**Presenting drafts of parts of the literature reviews to inform report 2; An assessment of the impact on PFAS exposure on health**

The Chair explained the running order of the meeting. The Panel will give three presentations on areas they have been working on. Ian Cousins will present on the chemistry of PFAS as it was noted that there was some confusing and seemingly contradictory information about PFAS, and the presentation would seek to clarify some of this information. Tony Fletcher will be speaking about the literature review and preliminary findings, as a starting point for their report. The Chair will then present on the mental health effects of environmental contamination.

**Introduction to the chemistry of PFAS**

Ian Cousins shared a presentation entitled “Introduction to the Chemistry of PFAS”.

A summary of the key points from the presentation are outlined below:

<u>What are PFAS?</u>

PFAS stands for per- and polyfluorinated alkyl substances (also written as PFASs and means the same thing). 'Perfluorinated’ means a fully fluorinated carbon chain and all the hydrogens replaced by fluorine While ‘polyfluorinated’ means that not all of the hydrogens in the chain have been replaced by fluorine. ‘Alkyl’ means substances that contain chains of fully saturated carbon atoms and not unsaturated aromatic rings.

In 2021, the OECD *(Organisation for Economic Co-operation and Development)* made a broad definition of what PFAS is “…the fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom…” i.e. substances are PFAS that have at least one $-CF_2-$ or $-CF_3$ moiety in their structure. This expands the PFAS definition to cover over 10,000 PFAS in use in Europe.

The diversity of PFAS means the group comprises a very wide range of substances, some of which you may not expect, and there are many thousands in use, for example:

- Fluoxetine (better known under the tradename Prozac), is an antidepressant and a type of PFAS
- Polytetrafluoroethylene (PTFE, known under its tradename Teflon), is a fluoropolymer used in non-stick cookware, etc. and meets the PFAS definition due to its structure
- Hydrofluoroolefin is a gas used as a refrigerant and in air conditioning. It also meets the PFAS definition.

There are many thousands of structurally diverse PFAS used in society; solids, liquids and gases, reactive and inert, soluble and insoluble, volatile and involatile, mobile and immobile, high toxic and relatively nontoxic. We don't know the properties and toxicities for most of them. However, they are all highly environmentally persistent themselves or and even when they breakdown they form persistent breakdown products which stay in the environment.

Regulation of PFAS

The authorities of Denmark, Germany, Netherlands, Norway and Sweden published a REACH restriction proposal for all PFAS meeting the OECD definition. There is also a separate restriction proposal on restricting PFAS in firefighting foams which is nearly finalised, which will lead to a 10-year phase out plan for PFAS in firefighting foams.

The PFAS that most people conduct research on are perfluoroalkyl carboxylic acids (PFCAs, also known as carboxylates, from 2 to >20 carbons) and perfluoroalkane sulfonic acids (PFSAs, also known as sulfonates, with typically 4, 6, 8 or 10 carbons, but other chain lengths are also present). When a hydrogen is lost from the sulfonic acid or carboxylic acid groups, the PFAS become negatively charged anions.

There are many acronyms for the different types of PFAS. A typical list of PFCAs and PFSAs which might be analyzed in an environmental include:

**C4 – C12 perfluoroalkyl carboxylic acids (PFCAs) *C =carbon***

perfluorobutanoic acid (PFBA)

perfluoropentanoic acid (PFPeA)

perfluorohexanoic acid (PFHxA)

perfluoroheptanoic acid (PFHpA)

perfluorooctanoic acid (PFOA

perfluorononanoic acid (PFNA)

perfluorodecanoic acid (PFDA)

perfluoroundecanoic acid (PFUnDA)

perfluorododecanoic acid (PFDoDA)

**C4, C6, C8 and C10 perfluoroalkane sulfonates**

perfluorbutanesulfonic acid (PFBS)

perfluorohexanesulfonic acid (PFHxS)

perfluorooctanesulfonic acid (PFOS)

perfluordecane sulfonic acid (PFDS)

The Panel discussed linear and branched structural isomers and the complexities involved; e.g. linear isomers are more bioaccumulative than branched. There are other types of isomers. Steve pointed out that isomers can react differently in the body, for example Thalidomide drugs created in the 1950s/60s were tested, however when it went into manufacture there were 2 isomers and the second isomer caused issues for unborn babies. Ian responded that Steve was mentioning chiral isomers known as enantiomers (mirror images of each other). Ian was talking about the different levels of branching on the alkyl chains which are different types of isomers. There are also chiral isomers of PFAS (e.g. there are chiral isomers of PFOS), but the research on enantiomers of PFOS is very limited.

AFFF (Aqueous Film Forming Foam) is most relevant to the Jersey context, and has a mixture of linear and branched PFAS (e.g. linear and branched PFOS and PFOA).

Other terminology used includes ultra short-chain, short-chain, and long-chain PFCAs and PFSAs:

- Short- and long-chain definitions are based on their ability to bioaccumulate
- Definitions complicated by the fact that PFCAs and PFSAs bioaccumulate to different extents
- For PFCAs, PFOA and all longer chain length PFCAs (>C7) are considered “long-chain” and bioaccumulative
- For PFSAs, PFHxS and all longer chain length PFSAs (>C5) are considered “long-chain” and bioaccumulative
- There are also ultra short-chain PFCAs (1-3 carbons) and PFSAs (1-3 carbons). These have been defined as a special class as they are very mobile in water and difficult and expensive to remove from drinking water

There are no agreed definitions for short- and long-chain PFAS, although the terms are often used in the literature.

**Properties of PFCAs and PFSAs:**

- They are powerful “surfactants” i.e. detergents

*Post meeting note – Surfactants are chemical compounds which decrease surface tension of a liquid in which it is dissolved. They can form foams and help facilitate the detachment of dirt (e.g. non-PFAS surfactants are used in household cleaning products). They are very important chemicals used for a wide variety of purposes and can also be found naturally.*

  - They lower surface tension of liquids; i.e. increase spreading and wetting properties
  - AFFF: rapidly spread aqueous film blanket over fuel fires (used in firefighting foams)
- They have a hydrophobic “tail” and hydrophilic “head”

- They are acids, so they lose a hydrogen from the acid head group and become (anionic) sulfonates and carboxylates with a negative charge.

**Uses of PFCAs and PFSAs:**

- They have been used for their powerful surfactant properties for making fluoropolymers (e.g. PFOA for making Teflon), in fire fighting foams, and other industrial and consumer users (e.g. paints, inks).
- They are impurities in, and break down products of, a wide range of other PFAS (the substances which break down are known as “precursors” which means they can breakdown and form these acids) used in multiple applications, such as in textiles and food packaging
- The long-chain PFCAs and PFSAs, which were more problematic because of being more bioaccumulative and toxic, so they have been phased out (transition between 2002 & 2015) and replaced with shorter-chain alternatives or non-PFAS alternatives.

**Further detail on precursors**

Precursors are substances which break down in the environment or inside organisms to form PFCAs and PFSAs. They are used in products such as waterproof jackets and food packaging. They can degrade in our bodies and in the environment into these acids. The acids are the end degradation products.

- Perfluoroalkyl sulfonamido ethanols (form PFCAs and PFSAs in environment and PFSAs in organisms);
- Perfluoroalkyl sulfonamides (form PFCAs and PFSAs in environment and PFSAs in organisms);
- Fluorotelomer alcohols (form only PFCAs in environment and in organisms)
- PFSAs and PFCAs are not the major surfactants in firefighting foams – there are other, non PFSA and PFCA surfactants in these foams. It is a complex mixture of surfactants. PFSA and PFCA are degradation products of these surfactants.
- There are 40 classes of PFAS (many are “precursors” to PFCAs and PFSAs) in AFFF products

**Why most research focuses on PFCAs and PFSAs:**

- There are reliable analytical methods for them
- They are stable degradation products of many other substances
  - They are unreactive and cannot interconvert, e.g. PFOA cannot transform into PFHxS
  - The many precursors in AFFF ultimately are converted to PFCAs and PFSAs
  - The precursors are released, but ultimately many will not be present in drinking water
- There is toxicity data for them
  - In fact, among all PFAS we have the most extensive and reliable toxicity data for PFOS, PFHxS, PFOA and PFNA

**There are two main types of aqueous film forming foams (AFFFs):**

- 3M Lightwater products have been used since 1967 in the US, and were also used in Jersey. These contained PFSAs (PFOS and PFHxS) and lower levels of PFOA, and also precursors to PFOS, PFHxS and PFOA
- Fluorotelomer-based products (used generally since 1973 onwards)
  - contained PFCAs: PFHxA, PFOA, etc.
  - contained fluorotelomer-based precursors (e.g. fluorotelomer sulfonates) which degrade to PFCAs (and not PFSAs)
  - never contained PFSAs or their precursors
  - always predominantly based on C6 chemistry, but more recent formulations contain less C8 impurities
- Most users transitioned away from 3M Lightwater to fluorotelomer-based products in the early 2000s because 3M stopped making these products in 2002. Some later transitioned to fluorine-free foams (3F). 3F are used widely at commercial airports in Sweden for example

**Chemical "fingerprints" of the two main types of AFFFs:**

*Fingerprinting is a pattern seen in the environment or human plasma which can identify the type of AFFF which has been used (i.e. AFFF products have unique marker substances).*

PFOS and PFHxS are only markers of 3M Lightwater AFFF products

- PFOA is present in, or generated in the environment from precursors present in, both 3M Lightwater and fluorotelomer-based AFFF products
- Fluorotelomer sulfonates (e.g. 6:2 fluorotelomer sulfonate) are unique markers of fluorotelomer-based AFFF products
- Structural isomers (linear versus branched) of PFOA can also be used as markers. If only linear PFOA is present then fluorotelomer-based AFFF has been used.
- Cross-contamination of AFFF products during storage creates a problem for "fingerprinting". If AFFF is stored in old vats which have been previously used for storing other AFFF, then the material can become contaminated from the storage container, introducing uncertainty in fingerprinting during analysis

Fluorotelomer sulfonates are quite stable and can be found in water. These can be analyzed by labs. A key question for report 4 can include a better understanding of fluorotelomer sulfonates. It will indicate if fluorotelomer-based AFFF has been used in Jersey.

The Chair thanked Ian Cousins for his presentation.

**Introduction to Health effects review**

Dr Fletcher then presented an Introduction to Health effects review.

This was the first overview of the approach for health evidence for Report 2, and will cover source data, sources of evidence and most common contaminants. A summary of the main points of the presentation is below:

Sources of evidence

- Epidemiology linking PFAS to health in people
- Animal experiments exposing, for example, mice to specific PFAS
- Mechanistic data on modes of action. Previously assembled information in reports by authoritative bodies, including:
    - The World Health Organization's International Agency for Research on Cancer (IARC) for cancer
    - European Food Safety Authority (EFSA) and European Chemicals Agency (ECHA)
    - Many US bodies – USA Environmental Protection Agency (EPA), State Health Departments, and the National Academy of Science (NAS)

It should be noted there are more than 12,000 PFAS Health/Science publications a year on PubMed, and 10,000 a year on Science Direct, so the Panel need to focus on well-established studies, and are targeting the reviews most relevant to Jersey.

Sources of evidence – Epidemiology 1

Types of study design, such as cross-sectional studies, which are helpful for effects on clinical markers like cholesterol, however not so helpful for disease.

Sources of evidence – Epidemiology 2

Types of exposure situation: for example, the background levels using serum PFAS (a general mix of long chain long half-life PFAS) *(Half-life is the time it takes for the concentration of a substance in the body or in the environment to reduce to half its initial value).*

High level occupationally exposed groups- may be specific PFAS: PFOA, PFOS, Gen-X

Third source is following up in affected communities.

Community exposures in exposed hotspots due to AFFF contamination or factory emissions.

Outcomes of interest

For this report, many health outcomes have been identified as of interest to Jersey, either through published academic literature, input from subject matter experts, and concerns raised by islanders as experts by experience. One topic area that has been of major public interest is cancer related to PFAS exposure.

The sources of evidence include:

- Epidemiological studies of the individual PFAS of concern
- Reviews of the Epidemiology plus other evidence for these same PFAS
- Epidemiological studies targeting the AFFF mixture

Sources of evidence looking at the epidemiology of AFFF exposures. Although AFFF mixtures vary between products and over time, they are characterised by a complex mixture of specific PFAS compounds. Serum levels in people marked with raised PFHxS and PFOS. Follow up studies of AFFF regarding exposed people are particularly informative for health effects of these mixtures. Good examples are some of the work in Ronneby, Sweden, and subject matter experts Kristina Jakobsson and Christel Nielsen have presented some of this work to the Panel previously.

Findings from the Ronneby research suggested there was some evidence for health conditions such as kidney cancer, testicular cancer being linked to PFAS, and less evidence for such as prostate cancer and breast cancer. Tony explained the median serum levels in Ronneby, which had a highly exposed population. The population data was linked to health records and compared the rate of cancer incidents in this population. The conclusion was that kidney cancer was associated with a 20% greater risk in the Ronneby population compared to the wider population. Higher proportions of rare cancers could have other explanations, such as that they could be due to chance. Some association with brain and bone cancers were found in Ronneby but this has not been found in other studies. Therefore, it could be concluded that there is less risk of cancer from AFFF exposure than from the PFOA exposures in other exposure studies.

Tony then mentioned the summary of the IARC PFOA and PFOS classifications of carcinogenicity from December 2023 which, in summary, concluded;

PFOA ***carcinogenic to humans*** **(Group 1)** on the basis of:

- *sufficient* evidence for an association between PFOA and cancer in experimental animals
- *strong* mechanistic evidence that PFOA exhibits key characteristics of carcinogens in exposed humans
- There was limited evidence in humans for cancer of the testis and for renal cell carcinoma.

PFOS ***possibly carcinogenic to humans*** **(Group 2B)** on the basis of

- limited evidence for cancer in experimental animals
- strong mechanistic evidence
- There was inadequate evidence for cancer in humans for PFOS.

Details are summarised on the IARC website and Lancet Oncology article found at Carcinogenicity of perfluorooctanoic acid and perfluorooctanesulfonic acid - The Lancet Oncology

**In conclusion**

There is suggestive evidence of mixed AFFF being associated with several cancers however, none are strongly statistically significant. There is supportive evidence for PFOA for kidney and testicular cancer from other studies but the evidence is inadequate for PFOS. There is no data at all for cancers and PFHxS.

The Panel will summarise the evidence for all health concerns raised with them by Islanders.

The Chair commented that it could be impossible to establish if there is an increased risk of very rare cancers from PFAS as there may not be enough cases to show a statistical difference. It is also difficult

to prove this in just a small increase in the number of cases. There could be risks in other cancers from PFAS exposure, although the research is not yet available.

The Chair gave a health example of smoking regarding population data, where you are twice as likely to get heart disease if you smoke, however, heart disease is very common in the wider population. Therefore, separating the causal factors from other factors presents some challenges. The Panel acknowledged the difficulty of attributing specific cancers to PFAS in a small population such as Jersey, and recognised there was still more research needed.

Dr Fletcher was thanked for his presentation.

**Environmental Contamination and Mental Health**

The Chair gave a presentation on environmental contamination and mental health, a summary of which is below:

A variety of sources were explored for the evidence review. The evidence on mental health and environmental contamination was particularly limited to 23 research papers.

The research focussed on psychological distress and somatisation, which is when a person has physical symptoms in response to a psychological stress. The most interesting study was from Australia on PFAS exposed population with AFFF, and the population's wellbeing was compared to other non-exposed communities. Psychological distress, somatisation and anxiety were higher in the exposed community in this research. Additionally, the research looked at serum concentrations and found that there was not a dose-response relationship between PFAS exposure and blood concentrations, which suggests that the higher levels of distress are likely to be caused by the psychological impact rather than the direct chemical effect on the body.

Reference: Health and social concerns about living in three communities affected by per- and polyfluoroalkyl substances (PFAS): A qualitative study in Australia | PLOS ONE

Depression

A large study in the Netherlands looked at characteristics of neighbourhoods, including pollution, on rates of depression. Depression was associated with pollution in both working and resident populations. However, it was difficult to know how much of this relationship is due to other characteristics, such as poverty which can also have an impact on rate of depression.

Perinatal mental health (depression or anxiety in pregnancy or after giving birth)

There was a Californian study which found that there was an increase in perinatal depression among women exposed to PFAS, especially non-US born mothers. However, this was a small study so it is not appropriate to draw strong conclusions.

In a study from China, researchers found an association between PFAS exposure and postpartum depression in twin pregnancies. Also, a further study looked at postpartum depression in a range of other substances, but not with PFAS.

Stress and post traumatic stress

There are several papers exploring stress, and the strongest findings were found from a Dutch depression study that found pollution was strongly associated with stress. One review found some evidence of symptoms consistent with PTSD *(post-traumatic stress disorder),* however it was not

clear that these were PTSD specific or symptoms of depression and anxiety, which are both features of PTSD.

Qualitative findings

In the Australian study described above, the researchers undertook focus groups to find out what factors were responsible for the increased stress levels.

Key findings included:

- Mistrust of the measurements provided by the military and people did not trust the water treatment was taking place, nor did they trust the Government advice about irrigation and livestock
- There was uncertainty about disease attributability (i.e. would it have happened anyway?) There is also contradictory scientific literature, with thousands of papers, so people were unsure of the facts
- There were feelings of guilt for example parents feeling guilty that their children had been exposed
- Health anxiety, with people thinking will they get better or worse
- A financial anxiety, for example, could their health impact their ability to work
- A stigma at a community level, is the area seen as blighted
- Lack of agreement on what to do to help or improve the situation

In summary, there was less research than the Chair expected about mental health due to environmental contamination. There is reasonable evidence for psychological distress, stress, anxiety, and somatisation in areas of environmental contamination. There is some weaker evidence for depression, perinatal depression, and a potential indication in PTSD however, the evidence was not found to be clear.

The Chair asked if there were questions.

Tony Fletcher commented on the research on risk perception and what it is that underlies people's perception of risk which may be useful to review. Both Tony and Ian were familiar with the Australian case and the subsequent legal cases.

The Panel acknowledged that people in these situations could be stressed and anxious and referenced cases in Australia and in Liverpool *(River Mersey contamination)*.

The Chair commented that the papers found with a link but not relevant to this review would also be explored. The Panel agreed this was thought provoking and needed to be factored into the work in Jersey.

**Any other business**

There was no other business.

**Date of next meeting**

17 April 2024 *at 10.00am.*

The Chair thanked everyone for attending and reminded people they can request the meeting recording.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 10am on 17 April 2024

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Professor Ian Cousins – PFAS and Environment member

In attendance: Grace Norman – Deputy Director of Public Health (until 11.30)

Sarah Tyler – Senior Policy Officer

Julia Head – Senior Policy Officer

Anita De La Cour – Executive Assistant

**Welcome:**

The Chair welcomed everyone to the 17 April meeting of the Scientific Advisory Panel, and reminded people the meeting was being recorded.

**Introductions:**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP for 25 years and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental hazards and challenges. Not a PFAS expert but has done lots of work with National Institute of Care Excellence and other groups about translating science into policy. Dr Hajioff has also worked a lot in the pharmaceutical industry.

Dr Tony Fletcher, PFAS and Health Panel Member: Environmental Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of epidemiological studies on the health effects of PFAS in contaminated communities in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby, and is the health expert on the panel.

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor in Environmental Chemistry at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Grace Norman, Deputy Director of Public Health for the Government of Jersey, the commissioner of this work, and a standing observer at these meetings.

Support staff for programme management and administration were also in attendance.

Dr Hajioff mentioned Sarah Tyler who has been coordinating this programme of work since the beginning and has done an amazing job. This will be Sarah's last meeting and Dr Hajioff thanked her for all the support she has given the Panel, it has been invaluable. Sarah has been wonderful to work with.

Julia Head will be taking over from Sarah and we are looking forward to working with her. Julia has a background in toxicology which may be useful for the panel over and above broader public health experience which her and Sarah shared.

Anita was thanked for minuting the meetings.

Members of the public were also in attendance. The Chair reminded people that the meeting is being recorded and a copy of the recording can be requested by emailing publichealth@gov.je.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

January meeting minutes were discussed and agreed by the Panel to be a true and accurate record of the meeting.

February meeting minutes were shared on screen as they were not sent in advance of the meeting. The Chair apologised that they were not available sooner. The Panel reviewed the minutes in the meeting. Following a question from Tony, the Chair confirmed that the subject matter experts who presented in February meeting have reviewed the minutes and have both agreed they are an accurate representation of the meeting and their presentations. Dr Fletcher suggested that both presentations should be referred to as “fascinating” and the Chair agreed as they both were fascinating. This change will be made in the minutes.

The minutes were agreed by the Panel to be a true and accurate record of the meeting and very well presented. Dr Fletcher congratulated Sarah on the minutes and the Chair agreed. The fact these minutes were not circulated ahead of the meeting was again apologised for by the Chair, indicating that they needed to be reviewed by the subject matter experts for accuracy ahead of sharing which sometimes takes some time.

**Additional findings since the last meeting**

There has been some media around ground water and PFAS levels in water supplies and food internationally. These are interesting and important and will be incorporated into the work in Report 4 on PFAS in the environment but are not directly relevant to this particular report. Therefore, they will not be discussed at present.

The Environmental Protection Agency (EPA) in the United States have released new guidance on PFAS. Prof Ian Cousins noted that the EPA have concluded that there are no safe levels of PFOS and PFOA and set the target values for both at 0 based on them probably causing cancer. The EPA set the drinking water guidelines based on a socioeconomic analysis of what is feasible to achieve, and the levels are set in the low nanogram/L levels. This is very similar to the levels which have been set in Sweden and Denmark, indicating some international agreement on drinking water guidelines with the most stringent ones being set in the low nanogram/L level. Prof. Cousins noted a difference however, as in Sweden the sum of 4 PFAS is set at 4ng/L, but in Denmark the limit is 2ng/L for the sum of 4 PFAS. Sweden and Denmark derive the limits from EFSA guidelines and is based on immunotoxicity endpoint. The US EPA is using a different endpoint, using cancer as a basis of their 0 level. This can be confusing that there are lots of different guidelines using different endpoints.

The Chair reminded the audience that there are lots of things that we come across in our daily lives which are associated with an increased risk of cancer. For example, the nitrites in smoked and processed meats such as sausages. These are not removed from the food chain completely. A factor being associated with an increased risk of cancer doesn't necessarily mean that that risk of cancer is high.

Dr Fletcher indicated that those are health advisory levels, and that the ideal target concentration would be below the regulatory level and are calculated based on the vaccine data endpoints. But whether it is to protect the risk of cancer or impact on the immune system, the target level is a practicable level which is set as a judgement on the feasibility and practicability for measurement. The same applies to regulations in the UK by the Health and Safety Executive or the Environment Agency. At some point the regulatory level is set at a level which is practicable after considering the costs and benefits of reaching that level.

Prof Cousins noted that very low levels of pg/L (picograms per Litre) is totally unachievable from a treatment viewpoint and would be financially and practically unavailable. All the tap water in Stokholm is about 4ng/L (nanograms per Litre) and therefore residents are exposed at levels in the low ng/L all the time. Rain is also at the same level. 80% of exposure comes from food, so even if the water was made to be PFAS-free, most people would continue to have exposure from fish and meat. Prof Cousins commented that it is a difficult message to communicate to the public.

The Chair clarified that the levels of PFAS that the EPA has concluded are safe water levels at 0 PFAS and therefore eliminated in the water are aspirational, and they can only be an aspirational, for several reasons:

1. It is technically not possible to measure absence of PFAS in water
2. It is financially not possible to totally eliminate PFAS from water
3. It would be not cost effective because at very low levels it is assumed that it will not have a significant impact on health outcomes
4. It would make a minimal difference to daily intake of PFAS because exposure from drinking water is typically lower than other routes of exposure, such as food (although this does not apply in places where there has been significant contamination of water supplies)

The Panel agreed to focus on the regulatory levels for now as they apply to Report 2 but will consider the aspirational levels further in Report 4.

The EPA have now set the regulatory level in the USA as 4ng/L (4ppt) (parts per trillion) for either PFOS or PFOA and 10ng/ml for PFHxS and 3 other PFAS. Then there is a risk calculation applied if there are multiple PFAS to result in a maximum risk factor.

Dr Fletcher explained how to calculate the limits for several PFAS in water. He described GenX which is a substitute for PFOA in situations such as manufacturing Teflon and has appeared in recent years. A level has been set at 10ppt for PFHxS and also GenX. The sum should not be more than 10ppt where they have the same limit. A framework has been developed to assess multiple PFAS. As new chemicals are identified which may have different limits, the sums are added together in relation to their limits. For example, PFBS is much less toxic and the limit is 2000ppt. Instead of adding together the individual concentrations, they must be added together relative to their target limits. For example, add together the level of PFHxS / 10ppt, GenX / 10ppt and PFBS / 2000ppt and if each of

those percentage fractions doesn't add up to more than 100%, you are within the limit. But if the sum of those percentage fractions exceeds 100% then the limit has been exceeded.

The Chair reminded the Panel that the three compounds which are of particular interest for Jersey are PFOS, PFOA and PFHxS. GenX does not need to be considered as it was not in the firefighting foam used at the airport.

This will be covered in much more detail in Report 4.

As previously noted, the new EPA set limits for the USA are similar to the Swedish and Danish values and are lower than the UK values which has a tiered system of 10 and 100. It is expected that the UK limits will reduce, and this is being discussed by UK Government. These new EPA set levels in the USA are only slightly stricter than the level of concern of the first tier of UK regulation.

The Chair indicated that this is very helpful and it will have an impact on what we consider in Report 4, but important to have this discussion now as the EPA guidance will be seen by the public and is not easy to understand. This discussion has added clarity.

The Chair congratulated Prof Ian Cousins on two award winning papers recently.

**Update on progress of literature reviews for Report 2 – Health impact of PFAS**

Prof Ian Cousins talked the Panel through his paper about how PFAS gets in and out of the body and is distributed around the body. This will help the Panel to understand where the opportunities and risks are. The paper has been shared in advance of the meeting.

Prof Cousins has looked at different routes for uptake of PFAS and focused on relevant PFAS for Jersey PFOS, PFHxS and PFOA. It has been known that people have had organofluorine [PFAS] in the blood since 1960s but it was not well known until early 2000s. Everyone on the planet is assumed to have PFAS in their blood.

There are 3 main routes for all chemicals entering the body:

- Ingestion (eating food or drinking water, ingesting dust)
- Inhalation (breathing into lungs)
- Dermal (shower products through the skin)

The importance of these routes is studied using animal studies, mostly using rodents and monkeys, although the scientific community have tried to not use animals in recent years. There are lots of historical animal studies with PFAS in 1990s and early 2000s so the relative importance of these routes for uptake is quite well known. For example, if a rat ingests PFAS there is close to 100% absorption into the body through the ingestion route, which is unusual. For other substances such as Polychlorinated biphenyls (PCBs), hydrophobic substances, the absorption through the gut is quite poor.

The studies on absorption through the skin have shown poor absorption for both animals and humans. A study was conducted where PFAS was added to a suntan lotion which was applied on skin and blood levels were measured after exposure. PFAS was recorded in the blood and absorption was calculated as approximately 1% or less, which was very low. This was a very extreme exposure scenario and still resulted in this low exposure. Rat and mice studies also show that dermal is not an efficient route of uptake.

The Chair commented that 100% absorption by inhalation is common based on his experience in the pharmaceutical industry but 100% absorption through ingestion is very unusual though.

Prof Cousins noted that PFAS are quite water soluble compared to PCBs, this is why they get into ground and drinking water. This may be how they are getting through in water from the gut, but the mechanism is not fully defined yet.

Dr Fletcher indicated that there is a theory that they are actively transported via a family of active transporters called OATs – organic anion transporter proteins. The body mistakes PFAS for a nutrient and so absorbs it efficiently because the body treats it as though it is useful for the body. PFAS is efficiently absorbed through the kidney as well.

There are many pathways for ingestion. Humans eat various foods, drink water, and ingest dust. These have been modelled as well as the inhalation and dermal pathways to work out which are the dominant pathways. Which pathway is dominant depends on the population. For the general population who are not affected by contamination events, normal background exposure is from protein rich foods like fish, meat, eggs, milk, cheese because chemicals like PFOS accumulate in the food chains. For the general public, for PFOS, PFOA and PFHxS, ingestion from food is the dominant pathway, although recognising that there is also exposure from water and dust ingestion. This varies if this is broadened if other PFAS are considered - short chain are more dominated by water, long chain more governed by food.

For those who are affected by specific contamination, (e.g. AFFF exposure in areas like Jersey), then drinking water is the predominant route of exposure. This is the same for people who live near the Teflon plant in North America. There are also occupational sources.

The Chair posed a question regarding occupational exposure and queried whether it would be through other routes other than drinking water such as inhalation? Prof Cousins confirmed it would be via routes other than drinking water ingestion. Therefore, the Chair commented that occupational exposures, while important are not the best comparators where the prime route of exposure is drinking water. Dr Fletcher commented that if one is interested in the systemic effects, then the route of exposure is not significant, it does not matter once PFAS is inside the body because blood and fluids are in contact with everything in the body. The advantage of occupational studies is that typically a group of workers would have exposure to one particular chemical dominating exposure which would then be able to help concentrate on effects of one particular chemical. The downside is that the doses and exposure are usually much higher than the general population. It is part of the evidence base of linking particular diseases with health effects though.

The Chair commented that because as there is 100% absorption through ingestion, the other exposure routes do not make a large difference to a person's overall exposure. This is unusual for there to be 100% oral absorption. Additionally, often in pharmacology, there is a first pass metabolism conducted by the liver which can change a compound into something else or break it down. This does not happen with PFAS.

Prof Cousins indicated that for people living in contaminated areas where AFFF has contaminated drinking water supplies, there is evidence that contaminated produce can be an additional exposure. Where contaminated borehole water is used on farms to water crops and animals, there is evidence that there is additional exposure from this use. This is mentioned in the section Prof Cousins has prepared for the report.

There has been a study which reports a distribution of PFAS in human organs in Demark. This study design is rare due to ethical challenges. The findings confirm the theories about how PFAS is distributed in the body and organs. It indicates that PFAS is mostly distributed to the liver, kidney and blood. This confirms the hypotheses regarding the distributions among the organs in the body. PFAS binds quite strongly to the serum albumin protein in the body, among others.

The Chair questioned whether the high levels in the liver and kidney could be related to reabsorption loops with PFAS coming in via the blood supply to the liver and the kidney, and also being reabsorbed. Prof Cousins confirmed this theory could be correct and indicated that slow elimination plays a part in this too. PFAS have long half-lives as a result of this circulation and reabsorption.

There is no evidence that PFOS, PFHxS or PFOA are metabolised in any way to form other compounds and break down within the body.

There are precursors, small fragments of chemicals which can be brought together within the body to potentially form these PFAS compounds. This is another source of exposure to PFAS compounds, by people being exposed to these precursors which are then metabolised in the body to make the PFAS compounds. This complicates matters.

Elimination (also referred to as excretion) is mostly through urine. There is also some evidence of elimination through faeces but urination is thought to be the dominant route. Women have additional elimination pathways through monthly menstruation because PFAS bind strongly to blood proteins. This becomes an important elimination pathway for women. There can also be minor reductions in PFAS due to birth and breastfeeding. Elimination half-lives vary between different PFAS but also between studies and individuals. There is research ongoing to attempt to understand this but at this present time it is not known why this is although one hypothesis is that it might be due to kidney function.

PFAS can also be transferred in-utero through the placenta. An unborn baby will have PFAS in their blood, and a newborn will have similar concentration of PFAS in their body to their mother. Babies receive a high dose of PFAS from breastfeeding, meaning that breastfed babies get a strong exposure to PFAS in their early life. Body burden can be high when breastfeeding ends. There are longitudinal studies showing levels in blood increasing in early months, peaks around 1 year old. As breastfeeding ends and they grow, body burden drops with growth dilution.

The Chair commented that there is lots of evidence that breastfeeding is very helpful, it makes children healthier, and in some cases saves children's lives. There is no evidence yet that that there are any risks from breastfeeding with PFAS exposure which would in any way outweigh those benefits. The studies which have researched the association between PFAS and breastfeeding have still advised breastfeeding as the safer option even where there is a potential risk from PFAS being passed on to the breastfeeding baby. The Chair commented that it is important people are not scared away from breastfeeding which is incredibly beneficial on the basis of the evidence.

Prof Cousins commented that the section could be much longer, but that he feels it is an appropriate length for this report.

Comments were invited, and Dr Fletcher commented that on the issue of excretion, a number of authors, mostly animal toxicologists, claim that the kidney excretion is dominant compared to liver* and gut excretion but there are others that argue the opposite. A Japanese study quoted 20%excretion by the kidney. New data from Dr Fletcher's group examined urinary and faecal samples

from Sweden in participants whose exposure has been stopped. The findings were that there is net excretion, and that for PFOS, 80% of excretion is through faeces and the gut, and only 20% for the urine. It's more balanced for PFHxS. Because there are conflicting statements in the literature, the report should reflect that both routes are significant and should not overemphasise renal excretion. *[* Dr Fletcher mis-spoke and said 'kidney' in the meeting, but he meant liver and apologises for any confusion caused.]*

The Chair agreed that it was a useful point to make because for Report 3, looking at potential treatments, this could include treatments which limit reuptake in the kidney and liver. When considering the specific PFAS molecules, we need to understand which is the most important.

Dr Fletcher also commented on the long half-lives and said that there is lots of variability in individual levels, but most average between 3 and 5 years. PFBS and GenX both have half lives in range of 2-3 months and so they are much more rapidly excreted. The amount of active reabsorption is much less because it is thought that, unlike more well studied PFAS, they are not recognised as potentially good nutrients by the body and so are treated as redundant chemicals, excreted, and not reabsorbed. This mechanism is quite specific to the chemical and the chain length. The consequence of that is that if you ingest complex mixtures of PFAS e.g. AFFF, the ones which are measurable in the serum are the ones with long half-lives. Some will get excreted within a couple of weeks. For situations where exposure is controlled, only the ones with long half-lives will remain. This is why the literature is dominated by these compounds, because the ones in samples are seen after the rapidly excreted ones have gone. Therefore, the literature picture of exposure is primarily of these long half-life chemicals. This is important because your body has them for longer time which is important if they are toxic because they are present for a longer period of time.

The Chair commented that if the short chain, short half-lives ones are more biologically active, then they could be responsible for damage which is being attributed to the ones which have a longer half-life and therefore remain. This is a concern. Dr Fletcher agreed and commented that GenX is just as toxic as PFOA when given in the same concentrations to animals but is presumed to be much less toxic to humans because it has a much more rapid rate of excretion.

Grace noted that the results from the Islanders showed that PFHxS was the compound that was most prevalent at levels above the threshold that we set. She proposed that the potential reason for this is that the half-life is much longer and asked for clarification that this was the case.

Dr Fletcher agreed. If the water had contained PFOA, PFOS and PFHxS at the same concentration, then you would expect to see PFHxS at the highest concentrations in blood because it has the longest half-life. You would expect them to end up at steady state as having the highest concentration in the blood.

The chair asked for additional questions or comments. Dr Fletcher pointed out that this is a challenge because Prof Cousins has gone into a lot of detail which sets a high bar for the level of detail we should be presenting in every section. This is interesting, and Dr Fletcher indicated that he would think about it. The Chair thinks it is not too detailed and indicated that although each of these reports are a standalone piece of work, it is also part of a body of work and this level of detail will be extremely helpful in Report 3 and Report 4. It does not necessarily mean that we need to think about exposure pathways in every potential health effect or biodistribution in ever health effect, but it is useful as a context and it will be very useful when we consider potential treatments and exposure reduction approaches going forward.

Dr Fletcher indicated that studies conducted on individual PFAS compounds to study the different excretion patterns between different PFASs gives a different pattern in the serum than from environmental exposure. This is because the environmental exposure is a mixture of types of PFAS. In studies which look at individual PFAS, the results could be less meaningful in mixtures exposure context such as in Jersey. This clarification is required to be added between this section and the one on health effects. The Chair agreed entirely and said it would also be important when looking at treatments.

The Chair thanked Prof Cousins for the paper, he considers it great and the right level of detail to inform this report and the next two. It has been a useful discussion.

**Agenda item – Health effects data – Dr Tony Fletcher**

Dr Fletcher commented that he is not so advanced in preparing text as Prof Cousins, and so has no document to share. However, Dr Fletcher has been reviewing and preparing sections. He commented that he had spoken previously about the evidence for cancer and that today he will talk about two other outcomes of particular interest which have the strongest evidence:

1. Effects on vaccine efficiency
2. Cholesterol

Vaccine efficiency reduction in children

This was the lead effect which was used to determine a tolerable weekly intake by the EFSA (European Food Safety Authority) review of evidence and it was for the provisional target value for EPA (American Environmental Protection Agency). The final target value set by the EPA in drinking water was 0 because the cancer effect took over, but the provisional one was based on vaccine data.

Data on children's immunisation to common vaccines including diphtheria and typhoid shows that antibody levels are not as high in people with higher levels of PFAS. In other words, the routine titre levels have gone up a bit less as they have been hampered by the presence of PFAS. Not all studies have shown this, but many have repeated this apparent effect which is judged by the scientific community to be a real association. However, there is not evidence which shows that this reduction in individual level immunity is resulting in increases in disease. Diphtheria is a rare disease so even if the population protection against diphtheria was reduced for everyone because of PFAS in the body, it would not be expected to lose the herd immunity.

Dr Fletcher commented that the expectation would be that if reduced vaccine efficacy was a generic effect across vaccines, that it would be also reflected in common infections. There have been a number of studies trying to establish if upper respiratory infections have gone up in populations in relation to contrasting levels of PFAS. A few years ago it seemed there was not much evidence of that but recently the balance of evidence has been shifting somewhat as there are now several studies that are indicating that there is an increased risk of common infections in relation to contrasting levels of PFAS exposure. The evidence is still not overwhelming, but there is more of a coherent patten that both the childhood vaccines which have been studied (diptheria and typhoid) are consistent with a reduced protection against common infections in children.

In adults, a marginal effect was found, a borderline significance, on the protection from flu vaccination for seasonal flu in the PFOA study in the US. Recent work in Sweden looking at whether the antibody levels in response to COVID were affected by quite high PFOA exposure did not find an

effect. This is for adults and is a different type of vaccine and antibody so that doesn't necessarily conflict with the childhood data. It might be that the childhood immune system is inherently more vulnerable. The evidence is still that there is an interference with the immune system and there is consistent data on childhood infections.

Dr Fletcher commented that the animal data that one of the previous subject matter experts talked about is convincing in that you can show experimentally that the immune system in animals is compromised by experimental exposure to individual PFAS chemicals.

The Chair indicated that the immune system is quite important in cancer protection, noting that his experience is in the pharmaceutical industry rather than environmental hazards. There are two ways in which drugs are associated with a risk in cancer. 1) Some drugs cause changes in the DNA, they cause mutations which turn into cancerous cells, and 2) some drugs suppress the immune response which otherwise normally eliminates gets rid of with the lots of small cancers which people get all the time. He questioned whether there had been any thought about whether this immune modulation could be part of, or all of the mechanism to the increased risk of cancers?

Dr Fletcher considered it a good question and indicated that he didn't know at present. There is some indication that the endocrine system affects cell proliferation which affects the later stage of transition from a mutated cell to a cancer cell. This is in addition to the immune protection about cancer cells. Particularly in testicular cancer, the discussion is hinged on whether or not PFAS are endocrine-disrupting chemicals, and would be on a pathway affecting the development of cancer. This would not necessarily apply in kidney cancer. Dr Fletcher agreed and would consider the impact of immune modulation when looking for evidence on kidney cancer.

On epidemiology, there is a quantitative story between childhood vaccines which has been used for setting target values for no affect levels or low affect levels for regulatory purposes and to some extent is reflected in infections. There is supportive toxicological data to underpin that as a real association. This will be summarised quite reasonably for chemicals which are of concern – there is data on PFOS and PFOA. The evidence is a little stronger for PFOS and immune effects but there is not much data on PFHxS.

Dr Fletcher moved on to discussing autoimmune conditions such as Lupus and ulcerative colitis. He described how he found in the C8 analysis of a PFOA-exposed population, ulcerative colitis showed a significant dose response relationship. This is considered to be a rogue result because several autoimmune conditions were considered and that was the only one which came out as significant; there was not a pattern of several other pathway related conditions also being associated. Subsequently, Dr Fletcher looked in some detail whether or not that would also be apparent in the Ronneby (which has an exposure profile more comparable to Jersey because it is an AFFF exposed population) and no effect was found; there was not an increased risk of either colitis generally or ulcerative colitis in particular. Dr Fletcher noted that he will check on the other autoimmune responses. The findings in the C8 analysis was either a false positive or very specific to PFOA at high concentrations, so it is probably not relevant for an AFFF exposed population.

The Chair commented that we have receptors on the surface of our cells called Human Histocompatibility Antigens, HLA types. Some of these are associated with autoimmune disease. Ulcerative colitis is associated with a particular HLA called B27, as is Crohn's disease and ankylosing spondylitis and Systemic Lupus Erythematosus. Rheumatoid arthritis is associated with something completely different. The Chair suggested Dr Fletcher looks at autoimmune diseases to see if it is

associated with that particular HLA, but noted that it wouldn't form part of this current report as it is a large area of study.

Cholesterol

Dr Fletcher continued feeding back his findings. There are multiple cross-sectional studies which have looked at whether there is an association between PFAS in the blood and cholesterol levels. Most indicate there is a consistent association for PFOA, PFOS and especially PFNA comes out very strongly associated with total cholesterol and sometimes HDL and LDL subtypes of cholesterol. The discussion in the literature is divided between those who think that is a real association which is probably causal, and some who think it is not causal and that instead it could be entirely caused by confounding factors or even reverse causality.

Dr Fletcher commented that there are several ways to look at this. One is to look at the potential mechanisms associated with this effect. Dr Fletcher was recently involved in a paper with some toxicologists and looked at a number of different pathways. These included PPAR, CAR, PxR, CYP7 receptors which are affected by PFAS, involved in cholesterol synthesis, metabolism, transport, conversion of bile acids into cholesterol. This could plausibly explain the positive association but it is complicated because in animal tests it looks like the opposite happens- that high exposure to PFAS reduces cholesterol. This is why some researchers do not believe that PFAS causes high cholesterol, because the human findings are contrary to the animal study findings. Dr Fletcher commented that he prefers to focus on the consistency of the epidemiology evidence.

Cross-sectional studies are a weak study design because it is not known whether the change in cholesterol levels or PFAS levels came first. Comparing different water districts in the C8 study where you can see there is an objective ecological difference in average exposure where you can see a difference in cholesterol. The district which has highest exposure of PFAS in the water and the blood also has the highest cholesterol levels. In a follow up study where people had no further major exposure to PFAS and measurements were repeated of PFOA and cholesterol, the ones whose PFAS levels had fallen the most also showed the biggest falls in their cholesterol levels.

All different study designs, cross-sectional, ecological, and longitudinal, suggest that there is a real association between PFAS levels and cholesterol. This is triangulation, using different methods with different vulnerability to bias. If findings show a consistent result across different study designs then there is a more convincing evidence base for causality. Dr Fletcher commented that without knowing the mechanisms, the pattern seems to be that there is a real causal association across multiple studies. The cross-sectional data is partly confounded so it probably overestimates that association.

Dr Fletcher moved on to explaining the consequences of higher cholesterol and noted that the general assumption is that cardiovascular disease could go up. However, he noted that the interesting finding here is that the evidence for increased disease risk is not strong. There is one mortality study which showed an excess of cardiovascular disease in the Italian data. In the follow up analysis with very large numbers in the C8 study, no association was found with any category of cardiovascular disease. Therefore, it looks like the increase in cholesterol is not reflected by an increase in cardiovascular disease. Dr Fletcher noted that this is why some researchers believe that the apparent relationship must be due to confounding and it's not a real association.

American data suggests that part of the explanation for the lack of cardiovascular disease in spite of increases in cholesterol may be because PFAS also increases HDL (i.e. 'good' cholesterol which is

protective for cardiovascular disease). It suggests that overall, the LDL to HDL percentage or ratio doesn't change.

Another phenomenon the Panel noted that is CRP (C reactive protein) which is an indicator of general inflammatory response, seems to be inversely correlated to PFAS in the American C8 population. The people with higher PFAS have in general slightly lower levels of CRP and this finding is also present in the cross-section analysis and this between area analysis. This would be indicative of some kind of protective mechanism relative to cardiovascular disease.

The Chair commented that CRP is also a measure of inflammation and infection in the body. That indicator could also relate to the immune modulation discussed earlier. When someone has an infection their CRP goes up, but if their immune system is underactive, then their CRP will be lower than someone with a more active immune system. The Chair commented that you would expect to have an elevated CRP in ulcerative colitis and rheumatoid arthritis.

Dr Fletcher commented that there are not many studies reported on CRP. He went on to comment that the starting point of a review was to summarise the evidence which indicates that there are associations with cholesterol. The different study designs show consistency underpinning the association being causal. The Panel has observed that it is not just total cholesterol but that there are LDL, HDL and potentially CRP factors which are complicating the interpretation of that increased cholesterol also being reflected with increased mortality, which the evidence suggests it doesn't seem to be.

Dr Fletcher commented that there is a mechanistic discussion including relevant pathways which would help support the theory that these are real associations. This could be covered by referencing the paper which discusses that, as it would not be proportionate to go into mechanistic information for every outcome. The Chair commented that mechanisms are interesting for the Panel to discuss and may speak to biological plausibility where in areas where the evidence is really weak. The Chair agreed that for the purposes of this report, detail around mechanisms is not necessary. This report is about the Panel understanding what the potential health impacts are which are caused by PFAS, and communicating those risks to doctors and other healthcare professionals, and people who may be potentially affected. Knowing the roles of individual mechanisms is not relevant for this purpose as that would be for academic study, not for this report.

Dr Fletcher summarised that PFAS does affect cholesterol and that should be worrying, but it also has other parallel effects which does not increase chance of dying as a result of increasing this cholesterol, and he therefore draws a nuanced conclusion.

The Chair agreed that it is complicated because the relationship between cholesterol and information and cardiovascular disease is not as clear as may be assumed. To an extent, elevated cholesterol could be a marker of inflammation in the vessels for some people, not necessarily just people exposed to PFAS through AFFF. Dr Fletcher noted that he would ensure his written submissions for the Panel are available for the next meeting, and to the rest of the Panel.

The Chair indicated that on the immune side it is almost that we see contradictory findings. Reduced vaccine response suggests a reduced activity in the immune system and the reduced ability of the immune system to respond to antigens, hostile biological compounds or chemicals. If the increase in ulcerative colitis is real or some of the other suggested increases around autoimmune diseases, they are usually associated with an increased response to antigens or things within the body's own make

up that we shouldn't normally react to. He questioned how do we interpret a simultaneous increase and decrease in immune response?

Dr Fletcher commented that it relies on whether the ulcerative colitis effect is real, and that has only been found in one study and not supported by other studies. For that reason, he considers this to be a chance finding. Multiple different disease categories were looked at and there is always a risk that things are found by chance and other findings which are real are not found. There is always a risk to under or over report findings, and that is why it is very important to look at the breadth of evidence from different studies. If there is a new apparent outcome without a strong biological basis to explain it, it could be a chance finding. Chance findings do happen, and we need to be mindful that in the C8 work, 44 different disease categories were considered and just by chance alone, a statistically significant result would be expected, just caused by change, for at least 2 of the disease categories. The C8 group concluded that there should be more than one different study design or different studies to support it. For kidney cancer for example, C8 had a significant finding in the study, and a study with a different design in workers also found a finding. For ulcerative colitis, there was only one study that showed a statistically significant association, so it seemed convincing, but this finding hasn't been found in other studies so Dr Fletcher is comfortable considering that it is a false positive caused by chance.

The Chair summarised that there is some evidence around reduction of immune response which could have some broader implications and is up for discussion. Dr Fletcher agreed with this comment and noted that multiple bigger expert panels have concluded that this is a real effect. However, the Chair noted that the Panel hasn't seen convincing evidence at this point around the impact of PFAS on autoimmune diseases, such as rheumatoid arthritis, Crohn's, ulcerative colitis, and Lupus. The evidence is not there at this point. Dr Fletcher also agreed with this summation.

Prof Cousins noted that he presumes there will be some discussion about the weight of evidence with these effects, and that if there are multiple epidemiological studies, multiple panels agreeing, with dose response and animal studies then all of this can be taken together as strong evidence of this effect. But one epidemiological study on its own linking PFAS exposure with a random disease, even if they do show a statistical association, should not be considered on their own. Methodologically, it would not be appropriate to review single studies in isolation and draw conclusions from them; the evidence needs to be looked at in totality. Dr Fletcher noted that there are scientists taking publicly available NHANES data to look at multiple associations and picking out the significant ones, which is methodologically flawed.

The Chair commented that in epidemiology, 1 in 20 times you will find a chance association at the 95% centile. But finding the true association is much more complicated.

There is an EFSA panel which is producing a guidance document on how to evaluate epidemiology and synthesising evidence in support of determining causality. It was pointed out that in this area of work, it used to be difficult to get an academic paper published if it did not have strong results, meaning that small studies were more likely to be published, and this resulted in publication bias. Now it is much easier to get papers published as there are many more journals. The only barrier is funding, meaning that random findings are more likely to be published if the group can pay the journal fees which makes things harder and introduces a systematic bias. Therefore, the non-positive studies are more likely to be published which means the evidence base should become more robust.

The Chair commented that this problem demonstrates the importance of the approach that the Panel is taking whereby we triangulate results using multiple studies and multiple study types before drawing any conclusions about health effects. That risk of finding one paper which confirms something you already believe continues, and is why it is important to assess all of the available evidence.

Dr Fletcher thanked the panel for their thoughts.

The Chair thanked Prof Cousins and Dr Fletcher for their presentations and thoughts.

**Agenda item – Next steps**

The Chair noted that the next steps are about completing all these reviews as we go through this process of developing this report.

Dr Fletcher questioned timings. The Chair commented that for the next meeting on May 16th we will need draft sections for the report to allow editing into the report. In the June meeting there will be a broader discussion bringing the whole process together and considering recommendations.

**Any other questions**

None.

**Any other business**

None.

**Date of next meeting**

16th May 10am – 1pm by Teams as usual

The Chair thanked the panel members and observers and particularly Sarah, Anita and Julia and the members of the public who have been observing the meeting.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel 10am on 16 May 2024 on Microsoft Teams

**Panel Members present**:

- Dr Steve Hajioff – Independent Chair
- Dr Tony Fletcher – PFAS and Health member
- Professor Ian Cousins – PFAS and Environment member

**In attendance:**

- Julia Head – Senior Policy Officer

**Welcome:**

The Chair welcomed everyone to the 16 May meeting of the Scientific Advisory Panel, and reminded people the meeting was being recorded.

**Introductions:**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP for 25 years and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental hazards and challenges. Not a PFAS expert but has done lots of work with National Institute of Care Excellence and other groups about translating science into policy. Dr Hajioff has also worked a lot in the pharmaceutical industry.

Dr Tony Fletcher, PFAS and Health Panel Member: Environmental Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of epidemiological studies on the health effects of PFAS in contaminated communities in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby, and is the health expert on the panel.

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor in Environmental Chemistry at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Grace Norman, Deputy Director of Public Health for the Government of Jersey, the commissioner of this work, and a standing observer at these meetings. Grace was not able to be present at this meeting. Julia Head will step in with some comments from her which she has prepared.

Support staff for programme management and administration were also in attendance.

Dr Hajioff thanked Julia Head for being present. Julia has a professional background in toxicology which will be useful for us. Julia will raise any important toxicological comments if appropriate.

Members of the public were also in attendance. The Chair reminded people that the meeting is being recorded and a copy of the recording can be requested by emailing publichealth@gov.je.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

Dr Hajioff apologised for the lack of April minutes which are taking longer to prepare due to the complicated nature. March minutes are available to discuss and were shared in advance of the meeting.

Dr Hajioff asked for feedback on each page of the minutes. Edits were made where appropriate.

Prof Cousins noted some small inaccuracies in the chemistry section. Prof Cousins took an action to correct the notes after the meeting.

On page 5:

- Grace asked for clarification around PFAS not being major surfactants in firefighting foam. Prof Cousins clarified the point which was recorded in the minutes.
- The current definition of fingerprinting in the minutes was questioned and changed to be an accurate statement. Dr Hajioff asked if fingerprinting can give a time course as well? Prof Cousins indicated that it is possible, but very complicated due to too much uncertainty and so is not used for this purpose.
- Clarification was provided on the point regarding cross-contamination during storage of AFFF. This will be expanded on in Report 4

On page 7:

- Grace questioned the use of the word “explained” and this was considered to be clear and accepted.
- The sentences regarding brain and bone cancers found in Ronneby vs other studies were clarified by Dr Fletcher.
- The point regarding risk of cancer from AFFF is lower than PFOA in other studies was clarified by Dr Fletcher.

**Matters arising**

Dr Hajioff noted that the panel should plan to have a discussion about how the difference in serum levels in Ronneby vs Jersey is interpreted because there is potentially a different time interval between exposure and assessment. This is to be considered when looking at the data at a later date. Dr Fletcher asked how long the exposure had been going on in Jersey. It was agreed that this topic was not discussed further at this present time but recorded as a point for discussion in the next meeting when discussing interpretation of findings from the literature and subject matter experts.

Dr Fletcher noted that most of the toxicity discussion is around perfluoroalkyl carboxylic acids (PFCAs) and perfluoroalkyl sulfonic acids (PFSAs) because that is what is measured in blood and they are stable and they bioaccumulate. There is some animal toxicological data on precursors to these acids. The European Chemicals Agency (ECHA) report on AFFF mentions a lot of the other

components which have been identified and what toxicological data there is. Dr Fletcher noted that reviewing each of the precursors individually would be very time consuming and asks how we should engage with and summarise data available on other compounds in AFFF. Dr Hajioff noted that precursors is an important matter arising which the Panel will need to consider and have as a key part of discussion regarding the "unknown unknowns". This will allow a communication of uncertainty.

Dr Fletcher notes that precursors also relate to exposure. Prof Cousins mentioned that it would be possible to do a Total Oxidizable Precursor Assay (TOP assay) to get an understanding of the level of precursors. A TOP assay involves analysing the water sample to achieve a concentration of the different acids, then the water sample is oxidised and analysed again. The difference between the two figures is the precursor contribution. Prof Cousins indicated that this would be an interesting assay to perform on water from Jersey to give an idea of precursor contribution, however it does not indicate which precursors are present and that would require additional analysis.

Dr Hajioff noted that understanding the decay curve of precursors would also be useful in Report 4 when environmental clean up is considered by the panel which Prof Cousins agreed with in principle.

Dr Fletcher noted that precursors may be associated with health concerns too, but as Ronneby has similar exposure scenario this will be covered in the epidemiology assessment as the Ronneby population had precursors in their blood.

Prof Cousins noted that TOP assays can theoretically be conducted on blood samples of exposed populations but to his knowledge this analysis has not yet occurred.

Dr Hajioff commented that for the common health conditions, looking at precursors separately probably is not materially meaningful, because the impact of pre-cursors will already be included in the epidemiology evidence that the Panel has reviewed already. But there are two scenarios where it might be useful to look at precursors:

- rare consequences which have not been demonstrated epidemiologically because the disease is so rare and it is difficult to have found it
- if the disease is so common it becomes a rounding error because there are so many other causes that it is difficult to attribute it to any particular cause

Dr Hajioff commented that he does not believe it is necessary to do a deep dive into the literature on precursors in general, but rather the panel should look at them in the context of some of the specific conditions under consideration, the ones highlighted by experts by experience. The panel agreed.

Dr Fletcher noted that since the last meeting he has been made aware of a book published around the Italian experience of PFAS contamination in Veneto by a group of social scientists in Italy. The book is in Italian. Dr Fletcher considers that this book may be relevant as one of the chapters is on the mental effects of the contamination in the area. The details of the book have not been reviewed. There may have been a review and projected what they think might be the stress related hazards in the community, or whether there is some local evidence of that having been demonstrated. There is a full PDF which Dr Fletcher will share with the panel.

Dr Hajioff thanked Dr Fletcher and agreed that there may well be useful information in that book.

**Additional findings since the last meeting**

Prof Cousins noted that there has been a lot of concern recently around trifluoroacetic acid (TFC) – an ultra short chain perfluroalkylacetate (PFA). This compound is being closely considered because the levels of this substance have been going up significantly in the environment. It is a very short version of PFOA with only 2 carbons, a carboxylic group and one carbon which is fully fluorinated. PFA is not very toxic compared to longer chain PFASs, but many researchers are concerned because levels are rising over time and people are flagging it as a concern because eventually everything is toxic if it crosses a threshold. PFA is very persistent, the behaviour of PFA shows what happens when a chemical is persistently released into the environment.

Dr Hajioff asked if trifluoracetic acid is in 3M AFFF? Prof Cousins confirmed that it is, but that it is not the major source. The major source in any substance (for example rain water, surface water, blood, etc) are fluorinated refrigerants. Dr Fletcher asked if it is a metabolic product of breakdown of other PFAS materials? Prof Cousins answered that it may be, because when destroying or breaking down PFAS, you don't always mineralise them [i.e. *convert them to inorganic product*] then they don't break fully down to fluoride, they break down to shorter chain PFA. This breakdown would be a physical process and would not happen naturally in the environment or human body. Prof Cousins noted that PFA is in micrograms per litre levels whereas we are usually talking about nanograms per litre levels, so PFA is present at much, much higher levels. Dr Hajioff asked due to it's short chain, does PFA have any other behaviours? Dr Fletcher commented that it is rapidly excreted, and Prof Cousins added that there is no way to remove it from water except at extremely high cost so in effect it is there forever. Prof Cousins predicts that PFA will be mentioned in the news in the future.

**Health impact of PFAS – Dr Tony Fletcher**

Dr Fletcher presented a verbal report without slides. He gave an overall picture of the health effects of PFAS and noted that the literature on PFAS is enormous.

<u>Exposure</u>

AFFF is a complex exposure dominated in the serum measurements by PFOS and PFHxS and to a lesser extent, PFOA. There is always an inherent mixture and also the possible mixture of precursors which are no longer present when taking and analysing blood serum later. The Ronneby situation in Sweden where there are over 10,000 people exposed to AFFF is different to the Jersey exposure is still comparable and in fact is a more suitable comparison than evidence on single types of PFAS or background exposure to mixed PFAS which much of the literature is reflecting.

<u>Sources of information for the paper:</u>

Dr Fletcher's paper will start with the 20 papers published by Ronneby research teams and summarise the results. This will be supplemented by review papers including those from:

- International Agency for Research on Cancer (IARC) - reviews looking at carcinogenicity of PFOA and PFOS specifically.
- United States Environmental Protection Agency (EPA) – report on PFHxS
- European Chemicals Agency (ECHA) – reviews forming the supporting documents for the banning of AFFF across Europe

- The European Food Safety Authority (EFSA) – summary of 4 most prevalent PFASs, PFOA, PFHxS, PFOS and PFNA and recommended limit for exposure to the sum of those
- Subject Matter Experts – detailed specific studies they have been involved with

Dr Fletcher is writing a report which will be shared ahead of the next meeting.

The overall picture is that there are clear effects on cholesterol, although reassuringly, there does not seem to be an associated cardiovascular disease risk. IARC considers cardiovascular risk as sufficient for PFOA, and possible for PFOS. The EPA are considering PFOA and PFOS as "likely carcinogens" for their risk assessment and Standard setting purposes. There are a number of other health conditions which have been linked to health effects in one or more studies. For example, in the Ronneby studies, they found effects in diabetes, language development in children and polycystic ovarian syndrome (PCOS). Those have not been replicated in other studies and are therefore considered "possible". Replication is very important, as is systematic review. The various reports by IARC, ECHA etc have been prepared using a systematic review process.

When looking at systematic reviews, Dr Fletcher cautioned that the reader must understand the criteria for authors inclusion or rejection of studies due to quality. For example, the EPA have done an in-depth synthesis of the literature on PFHxS and during study of this review, Dr Fletcher noticed that the Ronneby study was classified as low quality in this review and rejected by the authors for synthesis for evidence. This is because the Ronneby study is deemed to be 'uninformative' for PFHxS (even though it has the highest serum levels) because it is a mixed exposure which includes PFOS and PFOA therefore the effect of PFHxS solely cannot be picked out and so the study was excluded from the EPA's review.

Dr Hajioff explained that, on that basis, every epidemiology study would be considered low quality, and yet this is probably the most important data in helping understand the health risks for the population in Jersey.

Dr Fletcher reported that the EPA believe the studies are more reliable where there are individual measurements of serum levels so that they can be simultaneously statistically adjusted for in the analysis, but that excludes some of the most important studies where there is clear contrast of exposure between people who are drinking differing water sources. This is because drinking water sources have mixed PFAS exposures and the studies are reliant on exposure classification based on the water subjects are drinking rather than the serum levels at an individual level.

Dr Hajioff discussed the fact that addressing chemicals individually is also problematic in the light of the point which Professor Kristina Jakobsson brought up in Report 1 around the imperfect dose response for cholesterol. Increasing PFOS beyond a certain level is not associated with a further increase in cholesterol, so how do you correct where it is a non-linear dose response?

Dr Fletcher commented that the panel will come back to non-linear dose response when looking at the general principles of systematic reviews later in the meeting. He continued to note that it is a reviewer's judgement call as to whether the precision of biomarker measurement is believed. If this is ranked as more believable than having a clear contrast of exposure related to mixed exposures, valuable information useful for assessing exposure will be lost. The exposure contrast and the associated results revealed in the Swedish studies are of more value than the individual studies or the systematic reviews trying to separate out individual substances.

Dr Hajioff commented that this really interesting as someone with a background in pharmacology. When trialling a new drug, biomarkers are the lowest value outcome measures. Even though they are easy to measure and are reliable, their real-world implication is seen as irrelevant. Some countries wouldn't register a drug with only biomarker data and without real-world measurements.

Dr Fletcher gave another example. A systematic review of the effect of PFOA on birthweight was conducted showing a significant negative effect of PFOA on birthweight. Associate Professor Christel Neilson, (who previously presented to the Panel) showed there is overall no effect in Ronneby, but this hides a more complex picture. There was a significant increase in the proportion of babies born at low birth weight for one sex, and a decrease for the other. This effect may be real or may be a chance finding because other researchers have not found a sex-specific difference. One of the systematic reviews which concluded there *was* a significant effect of PFAS on birthweight did a quality check on all of the studies.

One of the studies done on the C8 population was rejected as being low quality because they didn't have measured serum levels, they had modelled serum levels because there was a model available which applied across the whole population. The systematic review authors considered measurement more credible than modelling. Dr Fletcher pointed out, however, that measurement can be subject to a bias, for example, where if you have a big baby and a big increase in weight during pregnancy, there is a dilution in the blood levels of PFAS which can confound the association between exposure and effect. There is a tendency to believe the biomarker results as being the measurable and most precise, and due this belief, the authors of this systematic review discounted the largest study which turned out to be non-positive. Therefore, this decision had a big effect on the results of the meta-analysis. This complication forms part of the discussion in the report.

Dr Hajioff noted that Dr Fletcher makes an important point which is about reliability (i.e. getting the same answer repeatedly when the conditions are the same) vs validity (i.e. getting the answer which is technically accurate). Cholesterol is measured because it is important in heart attacks and strokes. This is the only reason we measure it. With PFAS, evidence suggests that there is an increase in cholesterol but there is not a commensurate increase in heart attacks and strokes. This means that the cholesterol measurement is reliable (because it is giving the same answer each time), but it is not valid because it doesn't tell us anything about real world experience. Therefore, it is thought, therefore, to be less relevant to the lives of people who are affected because of not leading to poorer health outcomes.

Dr Fletcher agrees. He is not persuaded that a change in birthweight has strong evidence in relation to PFAS, but others take the opposite view. It is a contested area of discussion. Both sides of the argument will be addressed in the summary prepared by Dr Fletcher.

There are a number of adverse health effects of PFAS which are 'probable', 'possible', and 'definite', and clearly PFAS is an exposure that one would want to avoid. The implications for the situation in Jersey, where there is a small population, is that it will be almost impossible to demonstrate either the presence or absence of a risk caused by PFAS. If the population of exposure is 100 people, then a rare condition such as kidney cancer would not be expected to appear in such a small population, even if the risk is dramatically increased. If the risk went up 10% (comparing the situation to Ronneby), then you would still not expect to find any evidence of harm in such a small population.

Dr Hajioff commented that if there is an unexpected cluster of disease within the small population, for example 8 cases of kidney cancer in an area of PFAS exposure within this population, then the

opposite conclusion can be drawn, that there is a clear indication of risk of exposure is related to disease. But because it is likely there will be none, or maybe one, then it will be difficult to draw that conclusion.

Dr Fletcher commented that if there was one case of kidney cancer within this population and an estimated relative risk of 1.1 was defined by comparing with other similar populations, then it would be hard to say whether that particular case is caused by the exposure. Realistically there is unlikely to be a major attributable health impact in a population because the population is small, and the increased risk identified in other populations are relatively modest. Also, the heath impact would be unlikely to be able to be shown in any health survey within the population. Therefore, we must rely on benchmark standards in systematic reviews. The EPA has documented their estimate of acceptable drinking water levels which is as low as technically feasible rather than based on a quantitative risk assessment. The EFSA recommendations and the target serum levels of sum of 4 PFAS or equivalent tolerable weekly intake would be a suitable benchmark to use. It is not possible to give an estimate of the relative risk of a disease, or say that the effect has gone up by x% in relation to exposure. Instead, the conventional risk assessment approach can be used to compare likely exposure to an established benchmark of exposure. The EFSA benchmark is sufficiently robust to use in this situation.

Dr Fletcher summarised by noting the panel cannot estimate risk quantitively for this population, but the exposure profile can be compared to the EFSA benchmark.

Dr Hajioff agreed that this is a good approach provided we are using the correct benchmarks. Very different exposures could be argued to be not appropriate benchmarks. For example, using a benchmark derived from near the DuPont factory where the mixed exposure is very different to the mixed exposure in Jersey. This would be less valid than AFFF studies like Ronneby. Dr Fletcher commented that the DuPont factory is only releasing PFOA, resulting in an exposure greater than background.

The Ronneby team have had some discussions about whether it is possible to form a quantitative assessment of risk, but there is not yet sufficient evidence to do this. The exposures are reliant on ecological contrasts between high, medium and low exposure areas. These contrasts are not good enough to be able to convert into risk per nanogram per ml blood. The studies which have provided that metric are the studies on childhood vaccination in relation to maternal exposures. These are at low, background population levels.

Dr Hajioff noted that we have seen a difference in antibody responses to childhood vaccination. He questioned as to whether a meta analysis has been done across multiple studies to look at any change in the incidence of the diseases which are vaccinated against, for example, measles, mumps, rubella, pertussis? Is a change in incidence of disease a marker of immune dysfunction, or is it clinically important because it is increasing the risk of these nasty diseases?

Dr Fletcher answered that the diseases which come out strongest are diphtheria and tetanus and these are so rare such that a reduction in the antibody titres is not reflected in a change in the population data on those particular diseases. Epidemiologists assume that if it is a general depression of childhood immune response to those vaccinations then that should be reflected in a general reduction in immunological defence against common infections. The literature is a little unclear. Some studies show no evidence of an increase, some do show an increase in common

childhood infections in relation to PFAS exposure. There is some evidence which is not overwhelming, but not absent either. There is no formal meta analysis of this area.

Dr Hajioff commented that some studies will be on common cold coronaviruses where antibody immunity is much less important. It is a complicated mixture of studies. Dr Fletcher agreed for common cold coronaviruses but not COVID.

Dr Hajioff asked for any comments or questions for Tony but none were received. He thanked Dr Fletcher for his presentation. Dr Fletcher will bring together his findings in a report.

**Draft document on groups at potential increased risk from PFAS exposure**

The panel discussed the document prepared by Dr Hajioff.

Dr Hajioff commented that is important to identify the groups of people who are potentially more vulnerable and potentially might need preferential monitoring or intervention due to the reason why they are more vulnerable. This is work which has been done elsewhere in the world.

Dr Hajioff has summarised the factors in the literature:

- Age – people who are either very old or very young could be at increased risk from PFAS exposure. The very young particularly due to long half-life in the body and because children are in a developmental phase, the potential for a lifelong adverse outcome might be higher. Some of the studies seem to suggest this is the case.
- Those who have greater exposure through occupation or other additional exposure source. This will be investigated in Report 4
- Socioeconomic disadvantage can be a factor. Areas of greater deprivation are more likely to become contaminated, and they may also have poorer access to healthcare
- Pregnancy – if a pregnant person is exposed, then the PFAS will pass through the placenta resulting in higher risk for the foetus
- People with certain diseases and comorbidities. This is complicated and potentially problematic.

Factors do not exist in isolation – someone can have multiple risk factors which makes overall risk higher e.g. a child living in disadvantaged environment and have an illness which makes them more susceptible.

Dr Hajioff asked for comment and suggestions.

Julia requested on behalf of Grace that the panel takes into account multiple exposures and discusses this aspect.

Dr Fletcher questioned why it was important we understood the vulnerable groups and what impact it has on the recommendations we will give? If the main exposure has stopped and there is a population with a body burden related to past exposure, why would we recommend different activities for those who fall into different vulnerability groups?

Dr Hajioff agreed with the point, and indicated that we will talk about this again in Report 3 when considering wider testing and treatment. He countered by saying that if someone has a co-morbidity,

for example, they have an illness that is associated with PFAS exposure, it might be reasonable to recommended to the health care professionals who look after them should be aware of the increased risk, and so take the PFAS increased risk into consideration during treatment of the patient. If we are concerned about low birth weight for other reasons, we could provide additional advice to those who are pregnant and those who care for them about what can be done to mitigate risk of reduced birthweight.

Dr Fletcher still holds the opinion that everyone should be aware of the increased risk situations, and that there shouldn't be extra advice or surveillance advice given to those who are vulnerable. These are general principals about groups at risk, but they don't necessarily translate into advice in a given population. Dr Fletcher considers the co-morbidity is the most important aspect and more care should be taken in the screening and identification of other potential risks. The effect on children, the risk of reduce effectiveness of vaccination, is thought to be related to perinatal or in-utero developing immune system. This is an important reason for protecting everybody, including those individuals.

Dr Hajioff agreed that the Panel shouldn't let the targeted approach undermine the universal approach in terms of advice and support, due to the effect being marginal. There are a couple of caveats and that is additional exposure e.g. working with PFAS and living in a plume area. In this case, there may be a consideration when reporting about testing in Report 3 for additional monitoring.

Dr Fletcher agreed, saying that thinking about multiple routes of exposure is important as these are groups at extra risk of exposure. This should be deferred to Report 3 where the panel are considering exposure. Dr Hajioff agreed.

Socioeconomic disadvantage is a known explanation for comorbidities; usually poorer health is an indicator for disadvantaged socioeconomic status. However, in some cases, higher wealth is actually associated with higher exposure to PFAS, e.g. carpet treatments, waterproofing treated garments, food packaging and more household goods. The more general poverty-related exposure scenarios may not be true in this case, because some of the more PFAS treated products are more expensive. There is some American evidence showing a correlation of higher wealth, more disposable income being positively associated with higher exposure to PFAS compounds. It is not a simple correlation for PFAS.

Dr Hajioff commented that this paper will also be useful for Report 3 and Report 4, and is included in this report as background. This paper will be used to inform later work as well.

**Draft document on key concepts of environmental epidemiology**

Dr Hajioff presented the paper, and explained that measurement of exposure is important, either a direct measurement if possible or modelled exposure in the absence of measurement. There are different pros and cons for those different approaches. It is necessary to have an assessment of exposure before potential outcomes can be evaluated.

Different study designs were noted in the paper, and they were also touched upon in Report 1. The key point is that experimental studies cannot be used in environmental epidemiology due to it not being ethical to expose people to a risk and measure the outcome. Therefore, randomised controlled trials is not an option for measuring the impact of PFAS on humans.

There are 4 basic study types described in the paper. Yellow highlight are words to go into the PFAS glossary.

Outcome measures was discussed reflecting a discussion about biomarkers vs clinical endpoints vs demographic endpoints. For example, is measuring cholesterol or survival the right outcome measure to look at? How is the meaning of these biomarkers assessed? There are different concepts related to risk which have been outlined in the document, including how potential risk from an exposure is measured.

Bias is discussed in the paper including confounding and ecological fallacy. Dr Hajioff reminded the panel that just because factors are associated with each other, does not mean they are causal. An assessment must be done to look at causality. The paper concludes with a note on how to deal with challenges such as confounding and how to correct for ecological fallacy.

Dr Hajioff invited comments and questions on this paper which is designed to help readers understand why the conclusions and recommendations to be drawn in Report 2 have been formed.

Dr Fletcher noted a couple of comments. He considered the paper to be a good summary of a lot of the concepts and language which is used when describing the studies, but thought it may be a bit abstract for the audience. Dr Fletcher suggested illustrating this paper with tangible examples from the PFAS literature of the sorts of studies which are done to help the reader understand. Typically, the two main types of cohort study in PFAS research are 1) linking general population classified by exposure to health outcomes (e.g. Ronneby) or 2) studies using available registers of biomarker databases containing blood measurements and have been followed up over time (e.g. Danish database or NHANES where there is baseline exposure measurement and follow up). He also referred to case control studies, for example looking at cancer cases and linking them to historical exposures, and cross-sectional studies which mainly look at biomarkers. These general descriptions of studies would be made more accessible by providing specific examples. Dr Fletcher would be happy to provide a number of these.

Dr Fletcher continued by speaking about ecological studies. There are studies which the outcome data may not be ecological data, there may be individual data including confounding data on smoking for example, which means it is semi-ecological. He requests that this distinction is made in the paper. For many of the studies in PFAS literature this distinction is not a problem, because there is individual data to do with outcome. However there is a concern that there is some residual ecological confounding in the general socioeconomic status which varies between areas. Dr Fletcher will provide more examples to make the paper more accessible. Dr Hajioff thanked Dr Fletcher for this offer.

Dr Hajioff asked a clarification question. He noted that it is not uncommon in randomised control studies that there is a unit of randomisation which is not a person, it might be a hospital or a GP surgery. There is a statistical correction to apply to deal with how those groups or clusters behave as a single entity rather than as a group of people. Is there a similar process in ecological studies with intra-cluster correlation correction?

Dr Fletcher said yes, it is generally called multi-layer modelling, which is a statistical tool. There may be individual data but then there would be an area classification for say, deprivation index for that area and that allows statistically to cluster for health and/or effect at that level. Dr Fletcher does not recommend getting into that level of detail for this paper.

Prof Cousins noted that epidemiology has not always been accepted for risk assessment in certain jurisdictions, and animal model data has been more important. The combination of animal model data and epidemiological data is quite powerful. For example, if an effect is seen in an animal model, and also in a human population, then the combined evidence is powerful. In her presentation, Jamie DeWitt [previous Subject Matter Expert] often pointed out the different effects that have both epidemiological evidence and data from animal studies and this is powerful evidence.

Dr Hajioff agreed, and noted that the animal data speaks to biological plausibility and helps to triangulate in that way.

Dr Fletcher noted that he has recently been part of an EFSA panel which has drawn up a guidance document on the systematic assessment of epidemiological data and the features to look for and the strengths and weaknesses of different study designs which should be considered when doing a systematic review. The quality of individual studies and how they are judged, and in particular triangulation across several different epidemiological designs to make that more confident assessment of causality going beyond just association is reflected in that EFSA document. Dr Fletcher will share this document with Dr Hajioff. He noted that this overlaps with the next document on critical appraisal which Dr Hajioff agreed with.

**Draft document on Understanding risk**

Dr Hajioff noted that this document is quite important as a broader primer and will be of particular relevance in Report 4. It has been developed to be used across different reports.

The way humans perceive risk is often fundamentally different to the size of the hazard that they face. Dr Hajioff illustrated this using people who smoke (high risk activity) but are afraid of air travel (a much lower risk activity). There is a literature and reason about why the way people perceive risk is different to the magnitude of the hazard itself. It is important to understand this concept. Dr Hajioff explained the concept of locus of control to explain this phenomenon. For example, you are in control as to whether you light a cigarette or not, but you are not in control of flying the aircraft. This is one of the reasons why there is a mismatch between perceived risk and hazard magnitude. The technique to understand the hazard magnitude nature is called risk assessment. There are various approaches to assessing risk.

The overall risk of something happening, for example, developing kidney cancer, is called ‘total risk’ or ‘absolute risk’. ‘Attributable risk’ is the part of that risk that is directly caused by a certain exposure, for example PFAS. There is often a difference in risk between the overall total risk and the extra part of the risk caused by the exposure. Conceptually, Dr Hajioff considers this quite difficult.

He continued to explain about absolute vs relative risk. Absolute risk is the likelihood of developing a condition, but relative risk is how much more likely someone is to develop a condition because of their exposure. Dr Hajioff explained using an example from the smoking literature. People who smoke are twice as likely to have a serious heart event and 13 times more likely to develop lung cancer than people who do not smoke. This is smokers’ ‘relative risk’.

In the total population, heart disease is more common than lung cancer, so it is said that the absolute risk of heart disease is much greater than the absolute risk of lung cancer. Consequently, a small increase to the absolute risk of heart disease will result in much more disease than a small change to the absolute risk of lung cancer. This remains true even though the relative risk for lung cancer (for people who smoking compared to those who don’t) is much higher (13:1) than relative

risk for heart disease (2:1). These are difficult concepts to understand. Even a small increase in risk that is quite common can be more burdensome on a population than a large relative risk increase in something that is very, very rare.

The ecological fallacy is an important concept in epidemiology and was touched upon in the last section. Ecological studies are those which measure health risk and outcome at a whole population level, and one of the issues with this type of study is that some things which are true at a population level are not true at the individual level, which means that generalising from a population to an individual is very difficult and imprecise.

Dr Hajioff continued by highlighting the difference between risk *factors* and risk *markers*. A risk marker is something that doesn't necessarily *cause* the negative outcome, but is *indicative* of the negative outcome. For example, is elevated serum cholesterol a risk factor for heart disease and stroke, or is it a marker of inflammation and a risk marker for heart disease and stroke? Those aspects often need to be unpacked in risk analysis.

The paper introduces uncertainty and risk communication. Dr Hajioff commented that most of the time people do not absolutely understand what risks are. There is a human tendency to want to create certainty for some sort of reassurance when certainty doesn't in fact exist. The Panel recognises the need, when assessing risk properly, to be honest about what is unknown and communicating risk clearly, which is very challenging. The panel spoke previously about the psychological impacts of environmental contamination. One of the impacts which became clear in the Australian qualitative study is that simply the act of instigating a population testing programme increased people's anxiety rather than decreasing it. This was because the nature of risk was not communicated appropriately. People make the connection in their minds that if testing is being provided, it must be important and it must be dangerous. This issue around communication needs to be considered in this work and ensure that risks are communicated in a way that doesn't increase anxiety and worry, and that does provide clarity and a proportional understanding of what that risk is.

Finally, Dr Hajioff introduced risk management as a series of approaches to minimise or optimise risk across a wide range of factors. That can vary from mitigation, transferring risk, avoidance, and other factors, and this will be conditional on how big the actual risk is and the nature of what that risk is. He illustrated by noting that if there is a big risk of a problem with your fingernails, that might be less important than a small risk of someone dying. All of these considerations need to be thought through in the approach to risk management.

Dr Hajioff invited comments on this document.

Prof Cousins considered it a good general overview. He questioned whether the panel introduce the specific examples we have in PFAS, noting that this is not in his professional background. The US EPA have set a maximum contaminant level goal of 0 for various PFAS. He explained that the definition of this is "the level at which no known or anticipated adverse effect on health or persons occur which allows for an adequate margin of safety. Anything above 0 can be a possibility of an effect." However, he questioned what this definition actually means in practical purposes, and noted that he has difficulty understanding it himself. He continued by noting that this level of 0 is based on the fact that they're carcinogenic and that last year it was extremely low levels in the picograms/litre level which were unachievable. This situation is difficult to communicate. He questioned if there is a real risk there if a human is always being exposed to much higher levels than 0 or picograms level; is there a

risk of developing cancer or having an immune response? Prof Cousins questioned the panel about whether there is the need to discuss what being exposed to these higher levels and the achievability of 0 means.

Dr Hajioff noted that he deliberately steered away from that in this paper because that's what the panel should be discussing in Report 4, this section is just to introduce the concepts. He agrees that this is very challenging, when thinking about the unintended consequences of what the US EPA has done in terms of community anxiety. This is because the EPA have not taken the traditional, risk management approach of conducting a low as reasonably practicable risk assessment.

Prof Cousins noted that the EPA did conduct this type of risk assessment afterwards, as they set enforceable limits on a feasibility and economic study resulting in detailing what are the levels which are achievable and enforceable. These levels are much higher. They also set health based limits which are extremely low. For a member of the public, if you see that they are only doing it to the levels which are achievable rather than the health levels, then that will increase anxiety.

Dr Hajioff noted that he is also considering risk shifting. He explained that the more stringent the EPA sets a target in the US, the more manufacturers of certain PFAS requiring processes will move offshore, and people will be exposed in riskier environments like in East or South Asia. More people end up having their health affected because one place has made the rules stricter. Prof Cousins agreed and said that this situation has happened, not just with PFAS but with lots of other chemicals as well.

Dr Fletcher asked for clarification on the fact that the US EPA recommendation is considered technically feasible. Prof Cousins said he was not 100% sure. The enforceable levels are feasible to the point that it is possible to measure those levels and it is possible to treat down to those levels within a reasonable cost. Dr Fletcher asked if they had done a socioeconomic assessment and decided it was a reasonable cost? Prof Cousins answered by indicating that there has been lots of kick back saying these levels set by the US EPA are too high. In this case, the health assessment was done and then the feasibility assessment was done. This is the way it works in lots of jurisdictions.

Dr Hajioff noted that in Europe, the assessment is conducted together to come up with a balanced approach, but Prof Cousins was not sure and needs to look into it. There are so many different levels around the world which are considered to be safe which is very confusing for the public.

Dr Fletcher notes that the UK levels are set at levels using the ALARP principle (As Low As Reasonably Practicable), which takes into account the judgement of whether the cost is proportionate. This is difficult because it depends on who pays. If the polluter pays, then the public actually pay more to reimburse the polluter, so the clean up is still paid for by the public either through water bills or taxes. But that should be taken into account. He cannot confirm off hand whether who pays has been considered.

Prof Cousins read the definition as being "what is the MCL (maximum contaminant level) for the treatment technique which may be achieved with the use of best available technologies taking cost into consideration." Dr Fletcher noted that for the purposes of this report, he would suggest that the panel is very general about the principles of risk management and not get into a level of detail. Dr Hajioff agreed and said that we will need that level of detail in Report 4, but not this one. The panel agreed that this was reasonable.

Dr Fletcher had additional comments on the section on risk factors and risk markers. Dr Fletcher explained that he was expecting a risk marker to be something like a clinical sign that was a predictor of disease like antibody or cholesterol levels. However, Dr Hajioff has introduced risk markers as risk indicators which are more signs of disease, e.g. weight loss. He considers this scenario confusing and suggests deleting that idea, and stick to risk markers being intermediate steps which are predictors of disease in general, like antibody reduction or cholesterol.

Dr Hajioff noted that Dr Fletcher made a good point, and that he had used those examples because he was using previous knowledge on diagnostic risk markers in cancer, and because they are risk markers when the person comes to see a doctor. They are markers which contribute to the predictive risk of that person's health state being as a result of cancer, that is how they are used in diagnostics.

Dr Fletcher considers the terminology to be a clinical doctor definition, in that it sounds more like a symptom, for example, a high temperature is a risk factor for an infection, but an infection is not the only reason for a high temperature.

Dr Hajioff explained that this situation is how risk markers are used diagnostically, with the exception of smoking which is both a risk marker and a risk factor, or asbestos exposure.

Dr Fletcher answered, noting that you would look at DNA damage or epigenetic markers which are considered on the causal pathway of disease, whereas weight loss or high temperature is not on the causal pathway, it's a sign of being sick. He considers it misleading to call it a risk marker, even though in your context of individual diagnosis it is used. He notes that it is a completely different use of the terminology in the context of the rest of this document and requests that it is not used.

Dr Hajioff said he would find different examples to fit Dr Fletcher's definition rather than the clinical diagnostic definition, and thanked Dr Fletcher for his input, noting that it was very helpful.

Dr Fletcher said in terms of general background and context the summary document is good.

Dr Hajioff explained that the idea is that the documents discussed today would all form part of the introduction as a conceptual framework under which decisions and judgements on evidence are made in future reports. He noted that the panel are used to working in this manner in their professional lives, however the general public are not used to this way of working and this not necessarily how most people might understand the literature.

Dr Hajioff thanked the panel for their comments and will edit accordingly.

**Draft document on Critical appraisal and systematic review**

Dr Hajioff introduced this paper explaining that critical appraisal and systematic review are the key tools used in evaluating scientific literature and understanding what that means in the real world. There are many steps in making that assessment. The sorts of questions to ask oneself are:

- Is the study the best sort of study to demonstrate what we are looking at?
- What sort of evidence does it present in terms of outcomes?
- How many people included in the study?
- Is it in a setting which can be generalised to another setting?

- Confounding, has it been thought about and controlled for?
- Reliability vs validity outcome measures
    - Has the study just used something easy to measure (reliability) or have they used something which is really useful (validity)? In the context of PFAS, cholesterol is easy to measure but does it matter in terms of increase heart attacks or strokes, as this would be the impact on someone's quality of life.
- Is it set in an environment that is comparable?
    - E.g. studies done in America under a different health care organisation may be different so studies affected by types of healthcare systems may not be applicable to Europe. Another example is that lung diseases in Spain are defined differently to the UK and so cannot be compared.
- Setting applicability
- Statistical significance – this is basically a measure that we're looking at two different groups, are they really different? Could it be a chance finding? How certain can we be that this increase in this particular problem in one group over another is actually real?
- Clinical importance when we're assessing medicines or risk (not currently mentioned in the document). The size of the impact to the person is very important, and some interventions can have minimal impact. For example, a medication which improves a health outcome by 1% is less clinically important than one which improves health by 20%.

Dr Hajioff concluded by explaining that these are the key points to highlight so that the process of doing the reviews that are elsewhere in the reports can be understood a bit better by readers who don't do that professionally. He opened the floor for comments and questions.

Prof Cousins noted that there is a journal which only publishes systematic reviews called the Journal of Environmental Evidence. He explained the process of getting a systematic review published in that journal, which is long and extremely thorough. This process involves publishing the protocol first, including the criteria used for assessing the various studies that we were looking into, the statistical methods, the search terms etc. The protocol is assessed by a big panel. Researchers all look at the same studies independently and input findings using an online tool and someone evaluated to see if everyone came to same consensus by using pre-determined criteria. He explained that in his experience, for every study, data had to be input into a spreadsheet and it took 3-4 years to do this one assessment. It is well established, but there are strict protocols.

Dr Hajioff said that that process is gold standard, and there are other ways to do it. Every systematic review that he has been involved with has one evaluator and was less onerous. He agreed that the research question must be defined first, the approach and methodology is defined, and what "good" looks like. It is important to note what will be of value in a study and what you will not use. There will always be censorship of study and exclusion of studies which don't meet the criteria. This all needs to be set up *a priori*. This explanation may need to be strengthened in the document.

Prof Cousins described the gold standard systematic review process:

- The methodology must be made very clear beforehand and the team should stick to it, and work in a very methodical way
- The search terms for how the literature would be searched and which search engines would be used should be defined
- Capture all the papers, document all the papers then systematically go through determining whether the paper is relevant
- Once got the final group of papers, assign to different experts who would determine against previously determined criteria
- Cross checked by an independent expert

Dr Hajioff said there are different standards within this, and that a meta analysis as described by Prof Cousins is at the top. These are the principles and it is important to be overt where this has been differed from. This does not mean that the review is not valid, but that there are practical considerations, such as this project at Government of Jersey is time limited and does not have 3 years available to conduct a systematic review. He indicated that the National Institute of Health and Care Excellence (NICE) doesn't go into that level of detail and it is one of the biggest systematic review delivering organisations in Europe. Dr Hajioff noted that the feedback from the panel is really useful and will be used to clarify the text in this report.

Dr Fletcher pointed out that the Panel isn't carrying out a full systematic review of published literature, as the methods are more pragmatic, and it is important that the report is clear about the methodology the Panel have employed so that it is clear.

The Panel had a discussion about how to best describe the methodology of their work and Dr Hajioff confirmed that he would amend the report to be clear about what the Panel has done, and ensure that it does not erroneously suggest that the Panel have undertaken a systematic review of the whole literature.

**Next steps**

Dr Hajioff asked if there was anything outstanding to pick up. The panel indicated that there was not.

**Any other questions**

None.

**Any other business**

Dr Hajioff informed the panel, observers and members of the public that there may need to be an additional panel meeting in June. We are committed to being able to have a public consultation event on a full draft as soon as possible to not delay reports.

Dr Hajioff asked Julia to ensure the technical difficulties is addressed in the video recording to maintain confidentiality.

**Date of next meeting**

6 June 10am – 1pm by Teams as usual.

The Chair thanked the panel members and observers and particularly Julia and the members of the public who have been observing the meeting.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 10am on 6 June 2024

Panel Members present: Dr Steve Hajioff – Independent Chair

Dr Tony Fletcher – PFAS and Health member

Professor Ian Cousins – PFAS and Environment member

In attendance: Julia Head – Senior Public Health Officer

**Welcome:**

The Chair welcomed everyone to the Panel meeting, and reminded people the meeting was being recorded.

**Introductions:**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP for 25 years and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental hazards and challenges. Not a PFAS expert but has done lots of work with National Institute of Care Excellence and other groups about translating science into policy. Dr Hajioff has also worked a lot in the pharmaceutical industry.

Dr Tony Fletcher, PFAS and Health Panel Member: Environmental Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of epidemiological studies on the health effects of PFAS in contaminated communities in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby, and is the health expert on the panel.

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor in Environmental Chemistry at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Support staff for programme management and administration were also in attendance.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

The Chair apologised that the May minutes are not yet available. He confirmed that they will be available for the next meeting.

The draft minutes of the April were agreed to be a true and accurate record and finalised.

**Additional findings since the last meeting**

GP meeting in Jersey

The Chair met with representatives of General practitioners in Jersey on 28 May. The meeting aims were twofold:

To understand from GPs what they currently understand around PFAS, what knowledge and information would be useful and how they want to use that knowledge in practice.

Engage with GPs as a key stakeholder around what GPs are comfortable with from this report and what they want from Report 3 which will be quite relevant to them.

The Chair commented that he felt the meeting went well, that there was quite a lot of interest around some of the technical issues particularly around body burden and body distribution. Health impacts was also discussed including the work which Dr Fletcher has done and which will be discussed later in the meeting, and treatment and wider testing which will be coming in report 3 was also discussed. The Chair felt it was a positive meeting and noted that there will be a follow up meeting with the GPs to ensure there are no surprises amongst this community as well as the general public and policy makers.

Comparability of different exposures

The panel has discussed in private about comparability of different exposures based on serum levels and the Chair noted that this discussion should be held in public as well. The time frame between exposure reducing and testing is a very important characteristic and something that the panel will be exploring.

Dr Fletcher commented that in deciding what is relevant to potential health effects in the Jersey scenario, there are two sorts of evidence. There are a number of reports which usually focus on one specific chemical, PFOA, PFOS and various other PFASs. In Jersey we have a mixture because a mixture is used in firefighting foams. It is not possible to take the given evidence, for example on PFOA and apply it to the other compounds. PFHxS has the least amount of data on it. Dr Fletcher has been looking at the evidence and giving more weight to evidence which has come from specific studies which have looked at exactly this mixture of water contaminated by the mixture in firefighting foams. There are two studies in particular which are of value. One in Ronneby where a significant proportion of a town of 30,000 people was exposed to contaminated drinking water for many years. And another around three communities around airfields, one of which was in New South Wales in Australia. They are relevant in terms of a similar blend of compounds in the AFFF. However, the relative level of exposure must be considered. It is complicated because each of them has measurements of serum, but the time between when the exposure was discovered and stopped, and even before that, when the composition of AFFF changed and so the composition of pollutants going into the drinking waters, and the time between then and when the measurements were made were all different. There is a requirement to extrapolate back to see what might have been the exposure at a comparable time period to the time period we have here in Jersey. So specifically, in the Ronneby area, there were very high levels, an average of 200ng/ml of both PFOS and PFHxS in the blood taken a year or less after the exposure was identified and stopped and clean drinking water was provided. The time difference in Jersey between when some measurements were made and when the emissions of those chemicals into the water is somewhat longer.

The Chair commented that Dr Fletcher summed it up very well. He considers this really important and noted that when the panel were discussing the situation, he believes that this has not been done in this way before, but it is possible to back calculate and simulate like with like in terms of original exposure levels. This will allow some understanding because we know what the different half-lives of the different PFASs are, then can determine whether the exposure levels are similar or not. A formal request will be made to the Public Health team to get an understanding of the median levels for the

different compounds in the serum from the testing conducted in Jersey, so that the like for like comparison can be done.

Dr Fletcher commented that without pre-judging the detail that will be in report 4, it is also necessary to have an initial understanding about when the water concentrations are likely to have been falling because of a change in emissions.

The Chair commented that he believes we have a slightly less of a problem in Jersey than elsewhere because there is a specific date when people were switched from borehole supplies to mains water supplies so this can be used as a proxy about when the primary contamination ended for those individuals. Not everywhere will have this, so this is good information.

Prof Cousins noted that the panel received a comment following the last Panel meeting in public and noted that it is important to note that the panel don't fully understand how the exposure changed over time in Jersey. The comment the panel received last time pointed out that although they were switched to mains water, the exposure didn't stop, there was still exposure and we don't know that much about the level of exposure in the mains water over the last couple of decades. Exposure to PFAS never stops as PFAS are everywhere and we are all exposed to PFAS. There could still have been an elevated exposure even after there was a switch to mains water. We don't have a good history of exposure of the Islanders and it is hard to reconstruct that. Mains water didn't stop the exposure, but it was adjusted in some way and we don't know the extent of this. Borehole water could still have been continued to be used to irrigate homegrown vegetables by Islanders. It is hard to reconstruct this.

The Chair agreed entirely, commented that the comment after last month's meeting was extremely helpful, and clarified the terminology of primary exposure. Even if no one is using the borehole water to irrigate, there is still ongoing exposure through mains water as there is for the whole world, albeit much, much lower levels. However, there is some indication of an endpoint for the primary exposure which could be helpful to us. This will be investigated in Report 4. The panel should consider how long it takes to clean out the PFAS from the pipes; how long it takes to switch between highly contaminated source to lower contamination.

Dr Fletcher commented that when his group was estimating exposure patterns in the C8 study in America, the group was told by the water companies that it happened relatively quickly, contaminants are washed through in a matter of days through normal water usage. PFAS gets washed through fairly quickly, it is not sticky so doesn't stick in the pipes. Residents in the water distribution area is not an issue, it's the residents in the aquafer and especially boreholes.

Prof Cousins indicated that he thought that was not correct, as for when cleaning infrastructure, it is almost impossible to get the PFAS out of the infrastructure. But it could be that in that case, it is raw AFFF which has really contaminated the structure, instead of in this case it is PFAS in water which may flush through quicker. He commented that he doesn't believe that we know this for sure.

The Chair noted that the panel will investigate this in Report 4 and it will be a really important discussion in this report.

Dr Fletcher wished to put the numbers in perspective. There is a reasonable estimate of the biological concentration factor. If contaminated water is drunk at a particular concentration, it takes a while but steady state of blood concentration is achieved. In round terms for PFOA it is about 100. For example, if you are drinking 500ng/L, times by 100 = 50ng/ml in the blood. If the water levels

reduces to 50ng/L, then it is still a significant exposure. That would be reflected by adding on 5ng/ml in the blood. So the expected burden once steady state has been achieved in the blood is a real difference, but it is much smaller.

The Chair commented that in the context of this scenario, it makes the decay calculation it more complicated as looking at the half-life alone may overestimate the serum reduction because there is the ongoing serum reduction, albeit at a lower level. From the panel's point of view, that ongoing exposure would need to be assumed to be similar at the different places where PFAS has been looked at in order to triangulate what the likely initial exposure looked like. This needs further work, but the panel is trying to pragmatically understand whether there is more or less exposure in Jersey than Ronneby or Australia to look at the comparability of the studies to our population. He considers it fair to make that assumption that the amount of exposure that Islanders continue to receive from regular sources (such as mains water, food packaging etc) is similar between countries.

Dr Fletcher commented that the situation in Sweden is that there is almost no use of private wells, it was an urban population which was contaminated through the pipe drinking water. Australia was different, there are number of people on private wells near the airfields and then there was a wider contamination of the wells and therefore their drinking water supply. The key epidemiology in Australia looked at the average incident rate of cancers and cardiovascular diseases in the whole contaminated area, in which the number of people on private water supplies was a low proportion of that. The study didn't pick out and study them because the numbers were so low, so in order to get sufficient numbers to look at relatively rare diseases, they looked at the whole contaminated area. The average serum levels were modestly raised, about twice as high as background. The background levels were about 5 and exposed area was about 10 and so a modest increase. The results are interpreted in the light of that relatively small difference. It is frustrating that the closer parallel which is the few people who had high concentrations because of private drinking water wells which is more similar to Jersey, there is no epidemiology from those people because it is a tiny population.

The Chair commented that this was absolutely correct, and we will come back to that in the main part of your presentation. He noted that this was discussed to establish in the public meeting what we were discussing offline last week that the panel will look at comparability work. This will allow the panel to help understand how the exposure in Jersey compares to those of Ronneby or Australia with different time durations between exposure and serum testing. The panel will be able to say these studies *are* comparable to the experience in Jersey, or they are not. It will mean the panel will be able to provide a best estimate.

Dr Fletcher commented that he believes they will be reasonably comparable. There is a longer time difference between the reduction of contamination and the measurements done in Jersey.

The Chair commented that he believes Dr Fletcher to be correct, but that the panel needs to do the work to ensure that there is confidence in that assessment.

Dr Fletcher raised a caveat to note that the task he is engaged in here is not a risk assessment to work out quantitative risk per unit of exposure. This is hard to do as the data is not robust or consistent enough to do this. Dr Fletcher will be providing a hazard assessment which is a list of things which are probably related, most probably or unlikely to be health problems related to these exposures.

The Chair agreed and indicated that one of the reasons why we are not doing a quantitative risk assessment is because the numbers of people in Jersey to demonstrate health effects would not be possible as there are so few people exposed at this level, it won't be technically feasible.

**Agenda item 5 – Dr Fletcher reviewing health effects.**

Dr Fletcher noted that he started with looking at the two populations for which there is some epidemiology of real-world exposures to AFFF mixtures in drinking water supplies which is Sweden and Australia. The second piece of evidence is that there are 10,000 publications available. These cannot all be looked at, but there are a number of authoritative reviews done by a number of groups including the European Chemicals Agency (ECHA), the Environmental Protection Agency (EPA), and The UK Health Security Agency (UK HSA). These are usually focussed on specific chemicals such as PFOA and PFOS in particular, but sometimes look at PFAS together as a group. They provide a useful resource which can be referenced of peer reviews which put together and assess what are consistent findings.

However, if these review publications are reviewed with the literature, there is often a different list of potential health effects thought to be as a result of PFAS exposure. Some have thyroid disease, some kidney cancer, some neither, some include birthweight. The lists of potential health effects depend on (amongst other factors), the judgement of the relative strength of evidence and the risk of confounding, how sceptical the authors are, how much mechanistic pathways underlying the epidemiology is relied on, whether just the human data or animal test data is used, or how much animal test data to include. These factors influence the interpretation of the data and different scientists interpret the data in different ways. This accounts for the different lists of potential health effects from PFAS. Dr Fletcher commented that whatever the list of health effects he produces looks like, some people will disagree noting that it is too long or too short.

What is clear is that long chain, long half-life PFASs including those in AFFF do have adverse health effects. It is always the case that there are adverse effects which justify avoiding exposure and getting PFAS into the water system where people can be exposed.

Dr Fletcher noted the health effects for which he believes the evidence is strongest:

- Cholesterol increase
- Decrease in vaccination efficiency in childhood vaccinations
- Reduced duration of breastfeeding
- Kidney cancer
- Testicular cancer
- Effects on liver enzymes

The strongest evidence is in particular for an increase in cholesterol and the decrease in vaccination efficiency in childhood vaccinations. Interestingly, the evidence that they lead to serious adverse effects is much weaker. There is very little evidence that there is an associated dose related increase in cardiovascular disease, as would be expected from a rise in cholesterol. Similarly with the decrease in antibody titres, decrease in apparent effectiveness of vaccination, there is one or two positive studies, but generally isn't strong evidence that this is related to an increase in childhood infections. The specific vaccinations (diphtheria and tetanus) are for very rare infections, so we look for a

general reduction in childhood immune protection which doesn't seem to be very strongly evident in childhood infections. The third area where there is rather consistent evidence in a number of studies is the reduced duration of breastfeeding. The higher the exposure, the shorter the average that women choose to stop breastfeeding. The mechanisms are not clear (it could be either through discomfort or because there is a problem in milk production), but the finding has been repeated in several studies.

Dr Fletcher continued to note that there are two cancers (kidney cancer and testicular cancer) for which there is evidence that they are probably linked to PFOA exposure. There is no evidence either way for PFOS or PFHxS. Whether this is a specific PFOA effect or linked to more general PFAS is unclear.

Another area with evidence linking PFAS and health effects is on liver enzymes. Evidence suggests that PFAS may interfere with liver function but the clinical importance of this is not clear. It is not clear whether it is an increase that lies within the normal range or an actual abnormality. It may be related to the mechanism by which cholesterol is increased.

These are the six health effects for which evidence linking health and PFAS is strongest.

Dr Fletcher noted that in the Ronneby research, there are 3 other diseases which have not been shown in other studies where there is an apparent risk in relation to exposure to AFFF. These are Type 2 diabetes, fractures related to osteoporosis (a reduction in bone density), and Polycystic Ovarian Syndrome (PCOS), a condition affecting women's reproductive system. These health effects need further investigation to see if they are replicated in other areas. They might be random positive findings which do not persist or they might be real effects.

There are a number of other associations which have been found in reports in other studies such as the C8 studies in America. This study found evidence of association between PFAS and ulcerative colitis, thyroid disease and pregnancy induced hypertension. Subsequent research has not found consistent evidence for these health effects, and so they are probably not real effects of PFAS exposure, which is rather reassuring. Studies in Ronneby, where there is much clearer knowledge of exposure, these health effects were not found and they will be taken off his preliminary list of conditions probably associated with PFAS.

For birthweight effects, some early studies found a strong effect related to quite small changes in serum levels measured in mothers. The evidence from populations with much clearer contrast in exposure (i.e. knowledge of exposure), for example the C8 study for PFOA, there seems to be a different pattern for boys and girls, but overall there is not a big effect in the Ronneby study. Per unit of exposure, the effect on birthweight is much, much smaller than the initial scary results in the American studies at background exposures. Birthweight effects is either no effect or not large effect of exposure.

Dr Fletcher concluded indicating that this is a verbal summary of the shape of conclusions that he is reacting, grouping health effects into 'probably', 'possibly', and 'probably not' related to PFAS exposure. He commented that it may be a slightly different list to one which may be in one review or another, but it is overlapping with the various list which have been produced.

The Chair thanked Dr Fletcher for his presentation. He asked Dr Fletcher to expand on what he was talking to the panel about this morning about how there are slightly different findings in Australia and that there are potentially issues with that study. He noted that Dr Fletcher touched on the

dilution effect earlier in the meeting because they didn't analyse between private water supply and non-private water supply. Were there other issues with or findings in the Australian study which is important to highlight now?

Dr Fletcher commented that because it is of relevance, he will investigate the methodological detail of the Australian study. He notes that in particular, in the context of cholesterol, whether it is related to cardiovascular disease is very important. This is because we assume an increase in cholesterol is bad for health, but the cohort studies in the US certainly didn't find any association with cardiovascular disease. In Australia, they had 3 different populations in the areas around 3 different contaminated airfields, and for each, they have taken another comparison area within the state and looked at the relative rates of disease in the exposed area compared to the comparison area within the state. They have used census data on household income to get socioeconomic comparable areas. The three exposed areas are similarly contaminated. In one of these, Williamstown, shows a significantly cardiovascular increased cardiovascular event risk, but the others do not. However, when the data are thoroughly examined, it shows that that population also has a significant excess of lung cancer which is not thought to be related to PFAS exposure. The comparison area (control) for the exposed area with the higher cardiovascular disease and lung cancer seems to have a lower rate of smoking in the cross-sectional study. The two things together (bearing in mind the small sample size of 300) points to the fact the reference area is less well matched than the other areas. The reference area is unusually healthy, it has a lower smoking prevalence than the other two control areas. The authors conclude that there is no evidence of an effect on cardiovascular disease in Williamstown, but don't discuss in the paper this significant limitation of not very good matching for the comparison areas.

The Chair notes that interestingly, when the panel looked at the mental health effects of PFAS exposure a few meetings ago, there was one of the Australian pairings which was also an outlier and he will look to see if that is the same one. It might be that the reference population that they used to measure Williamstown against is in many ways different to the general Australian population and that caused some bias in a variety of analysis which were done.

Dr Fletcher commented that he would have expected the study to not only use a local reference point, but use a national one to work out the number of expected cases based on national averages, but they didn't. If a reference population is an outlier, then it is a warning sign that it is not the exposed data which is the outlier, it is the reference group which is unusual. This happens in animal test data too, where a control group is unusually healthy or unhealthy.

Prof Cousins asked if the fact that exposed area in Williamstown is a mining area with metals contamination was discussed, and whether they accounted for that in the study? He noted that that the population is quite angry about the PFAS pollution and were quick to form resistance to the Government which was because they had a bad case of metal contamination a few years ago.

Dr Fletcher answered that he will check in the papers as he could not remember if they discussed metals in them in the meeting. He noted that there is an excess of lung cancer which might be explained being a mining area.

Dr Hajioff agreed that the dust could be associated with increased prevalence of lung cancer from mining, and toxic contaminants could be contributors too and partly explainable.

Dr Fletcher noted that they found a modest excess of kidney cancer, similar to that found in Ronneby. The evidence could be read either way.

Dr Hajioff questioned are heavy metals associated with kidney cancer?

Dr Fletcher answered that no, he was considering the plausibility of the PFAS association. It was not statistically significant but statistical significance is a hard criterion to use when there are 3 towns and 20 different health outcomes to look at. To their credit, the authors also had control outcomes – self harm and common parasitic diseases with the assumption that these are not caused by PFAS. So if these unrelated conditions are showing a difference between areas, that would indicate that there is some health difference unrelated to the PFAS exposure between the populations. They found the highest apparent risk for those two conditions in Williamstown as well. This again suggests that the comparison population is unusually fit and therefore not a fair comparison for Williamstown.

Dr Hajioff commented that self-harm relates to mental health impacts. This was considered in a previous meeting. Dr Hajioff commented that he will review this again to see if Williamstown is the outlier.

Dr Fletcher concluded by noting that there is some evidence but there is not a clear adverse effect. Based on average exposure in large contaminated area they looked at, the contrast is quite small between serum levels in the control area the and exposed area.

The Chair asked Dr Fletcher regarding the “very likely” and the “probably” conditions that he alluded to, do we have information around dose responses for each of these? He wished to understand more about the “so what” – the clinical consequences to an abnormal biometric like cholesterol, and that it may be less significant than it first seems because there isn’t an associated relationship with cardiovascular outcomes. Is there an area where there is a dose response, and areas where it is more equivocal?

Dr Fletcher answered noting that the dose responses between areas are not consistent. The apparent dose response per unit of exposure generally seems much larger in the populations where the background levels mean the contrast between higher and lower exposures is smaller. For example, for kidney cancer – there are two particular studies, the C8 on PFOA and National Cancer Institute (NCI) study. The risk per unit of exposure is enormously different between the two. It is hard to average two results where one is 10 times the other in terms of risk per unit exposure. This is the case for cholesterol as well. Generally speaking, the studies done at lower exposures suggest a steeper slope per unit exposure so it is hard to extrapolate that onto other populations for the reasons explained. It is also very hard to see the burden of disease in a very small population. Estimating this accurately by calculating the risk per unit of exposure would require another piece of work which would be another month or two. It is not practical to do this within this project. In the general literature, no one has calculated the risk per unit of exposure before. It has been done for vaccine response to find a minimal response level to use as a benchmark to define as an acceptable intake and therefore acceptable standards in terms of drinking water levels in the EFSA and EPA reviews. This has been used to define a ‘no effect’ level or ‘minimal effect’ level. However, the two organisations (EFSA and EPA) have come up with numbers which are very different. Dr Fletcher believes that it is not necessary for this small panel to re-do this work.

The Chair commented that the reason for asking the question is to triangulate our position when we get to Report 3 and 4. He noted that the panel are going to need to make recommendations on lowering body burden of PFAS and they will need to look at whether there are health benefits at this stage. This will need to happen for the environment in Report 4 too. He continued to note that it occurs to him that the cholesterol to cardiovascular disease causal pathway may not be proven, so he

can't be sure that it would be proportionate to recommend a change going forward on that one metric alone. Likewise, the vaccine response is case not proven in terms of health effects with the caveat that modulation of the immune system is a worry in itself and may appear in other ways. He continued to note that the third one for him is cancer and that is a more difficult conversation to have. He has been reflecting on the potential association between PFAS and cancer. There are two mechanisms where a compound can be associated with cancer. Compounds can cause mutations by interacting with DNA so that there are more cancer cells formed. This is unlikely with PFAS as they are very inert compounds. Or, compounds can depress the immune system and therefore reduce the body's ability to deal with new cancer cells at an early stage before they develop into tumours, and therefore more tumours develop over time. This seems to be biologically plausible with PFAS because it aligns with what is known about the modulation of vaccines for diphtheria and tetanus. This is possibly the area we need to think about in Report 3 and 4.

Prof Cousins noted that he is feeling uncomfortable with making health based recommendations for how much we clean up the water. As Dr Fletcher alluded to, there are so many differences of opinion in the literature about what is a safe level. In an earlier meeting, the panel discussed the fact that the EPA set 0 as their safe drinking level, and it was nearly 0 before because of the immune response effects. These recommendations have been created by large panels of toxicologists. Prof Cousins believes that the Jersey PFAS panel should not create health based levels of their own. Instead, in Report 4 the panel should recommend ways in which the water can be cleaned up within the technical, practical and economic constraints. He acknowledged that he is jumping ahead, but noted that he is worried about making health-based recommendations.

Dr Hajioff agreed entirely and noted that he may not have explained properly previously. He notes that he is attempting to tease out where the joining up points will be between this report and the next two reports so readers can see where the panel's thinking will go through the next two reports.

Dr Fletcher commented that he agrees with Ian that the panel should not try and reassess those quantitative relationships between PFAS levels and health effects. The advantage for the panel's work is that there are number of benchmarks already defined which can be used. The panel drew on the Agency for Toxic Substances and Disease Registry (ATSDR) numbers of 10 and 20 ng/ml as part of the guidance for eligibly for the phlebotomy option. EFSA have recommended a target serum and use that as a basis for extrapolating the tolerable weekly intake (TWI). He would recommend using those as target values to aim for rather than trying to re-visit estimating another benchmark for use in quantitative risk assessment.

The Chair commented that he does agree, however he thinks the panel needs a narrative about why they are going to make the choices which they are going to make. He suggests that the panel explore in discussions about why one choice is taken over another and why it is potentially useful going forward.

Dr Fletcher agreed. He notes that on the mechanisms of action, the way International Agency for Research on Cancer (IARC) reviewed the evidence for PFOA and PFOS was using the idea of key characteristics of which immune suppression was one, but also epigenetic effects and cell division, production of cytokines, oxidative stress and altering of cell proliferation and key receptors being changed either in human or animal data. There were 6 different characteristics for dose related situations for which they said the evidence was strong for mechanistic plausibility, which upgraded PFOA evaluation to Category 1. There were multiple pathways which were relevant, none of which

help for quantitative risk assessment, but they do help with supporting the plausibility of associations, particularly weak ones being nevertheless causal.

The Chair noted that establishing a biological plausibility and association will help in Report 3 and 4 when discussing further recommendations. Having plausibility will allow the panel to take a more precautionary approach which they may not be able to do otherwise.

Dr Fletcher noted that when considering the relative benefits, it is quite complicated to apportion action now in terms of the relative benefits. If an individual has had exposure for 15 years without intervention to remove PFAS from the blood and the exposure is stopped, serum levels will go down slowly. If the reduction is then accelerated using an intervention, the historical exposure is not impacted, the individual still has the same level of risk for those 15 years without intervention. The risk is reduced for the following years where intervention is in place. By making changes now, hypothetically, the exposure may be reduced by half over the next few years. But as a proportion of the total exposure accumulated over the whole time of being exposed, the total exposure is not being halved, it is only being reduced by a small percentage due to only having the intervention for the past few years and not the entire time of exposure.

Prof Cousins noted that the damage might have already been done, and Dr Fletcher commented that in that situation then reducing exposure is no use whatsoever. He noted that one may overestimate that marginal benefit if you only think about your reduction of exposure between now and when the intervention is stopped. This will need to be explained as a significant source of uncertainty for the potential benefits in Report 3.

Dr Hajioff agreed that this makes sense when talking about a cumulative effect that could lead to a long term condition. There might be a different argument when talking about immune modulation driving cancer.

Dr Fletcher agreed and noted that if it is a promotional intervention, then the long term cumulative risk is irrelevant because the epidemiology has generally been based on using a sum of cumulative exposure as the index of exposure for studying it on the assumption that it has worked for other studies of carcinogens.

The Chair noted that this argument makes sense assuming a mutagenic mechanism of action, but not necessarily as an immunomodulation mechanism of action. Dr Fletcher agrees. The Chair noted that it may be something for the panel to discuss later in the programme of work.

Dr Fletcher raised the point that it might also have an endocrine effect, affecting hormone levels which are relating to late-stage promotion of carcinogenesis. Dr Hajioff agreed and noted that if it is that, then it mostly relates to cumulative exposure and is very interesting.

The Chair requested that the panel consider each of those conditions highlighted by Dr Fletcher and have a high-level discussion in the meeting about potential mechanisms, so that the evidence can be triangulated and understood a bit better. It would be useful to have the discussion in public ahead of the wider discussion and recommendations meeting in a few weeks. The panel has already done this for cancer earlier in the current meeting, and Dr Hajioff requested that the panel considers the other health conditions that have been identified in this manner and that this will be useful. He gave an example that PCOS is to do with sex hormone receptors and response to sex hormones and that endocrine disruption may potentially be the mechanism for that health effect. Potentially testicular cancer might go along the same pathway, although it might also relate to immune modulation. Dr

Hajioff noted that at present, he struggles to see a mechanism for diabetes and duration of breastfeeding, although the latter could be hormonal or endocrine disruption as well.

The Chair notes that the function of this report is largely information as opposed to the other reports we are doing. Report 2 is intended to inform the public and clinicians about health effects of PFAS.

Dr Fletcher commented that he is unsure about being able to be thorough in all of the health effects in scope. He will need to check in particular that if the authors haven't pointed to the relevant mechanistic support for their contention, then it is an enormous job to dig back and establish that.

The Chair clarified that he was suggesting a high-level discussion now rather than drilling down in the report. The panel will be triangulating in the discussion section with what the subject matter experts such as Jamie DeWitt said, as many of them did talk about potential mechanisms.

The Chair questioned the panel if there was something additional to highlight at this stage, so that it is there when the panel address this in a few week's time during the discussion and recommendations meeting? Dr Fletcher thought that he needs to think about mechanisms of action in the context of each of those subject areas, and so it should form a future discussion rather than now.

The Chair noted Dr Fletcher's wishes and asked if there was anything else to highlight from Dr Fletcher?

Dr Fletcher indicated that he thought he had enough evidence to make the case for those examples he has given today and hopefully it will be in fairly good order for the panel to review a first draft next week.

Prof Cousins indicated that he believed there are no further discussion points on Dr Fletcher's work today. He reminded the panel that he was required to leave the meeting slightly early due to Sweden's National Day today.

**Agenda item 6 – Panel discussion and next steps for Report 2**

The Chair set out the next steps for Report 2. The panel will be going through the final literature review over the next couple of weeks and the next panel meeting on 26 June is where the panel will discuss two things in the context of Dr Fletcher's, Prof Cousins' and Dr Hajioff's work as well as experts by experience and subject matter expert presentations. Firstly, the key findings and their implications, synthesising those different information sources. This will be done disease area by disease area in order for things to be clearer. Secondly, making recommendations. The Chair indicated that a lot of the recommendations that will be made in this report, will be for example "a doctor treating a patient with heart disease should be aware of this" etc because this report will primarily be informational in nature. There may be more differences around mental health recommendations which may be more action-orientated.

The discussion about recommendations will be held at the next Panel meeting on June 26. There will then be a very tight turnaround to pull together a draft of the complete report which will be considered at a public meeting to launch public input on the report on the 11 July *[The Chair indicated that the day was 10 July in the meeting, but the correct date is 11 July at 5.30pm at Les Ormes]*. Islander input will be open for a period time after that which has not yet been finalised. The report will then be revised in the light of the input the panel received with a view to launch final

report some time in the autumn. The Chair asked if the panel had any clarifications or things to highlight for the observers?

The Panel indicated that this was clear.

**Any other questions**

None.

**Any other business**

There is a public meeting this evening which is looking at the potential structure and approach which the panel have already discussed for Report 3. This focuses on testing, both re-testing affected people, testing other people in plume area, testing people outside that area for PFAS levels and what is appropriate and what the panel thinks isn't. It will also look at monitoring those who have been PFAS exposed in terms of their health and what is appropriate to test for, cholesterol etc. It will also cover potential interventions to reduce body burden and how important that is in the real world. The panel touched on some of that discussion today, but it will be expanded on tonight in the public meeting. The framework will be amended in light of that discussion, then first Panel meeting on that report will be on 10 July. There will be some overlap between reports to be most efficient and to get the information out to the Islanders.

No other items from panel.

**Date of next meeting**

26th June 2024 – additional meeting recently added to the calendar. It will be held 10am-1pm online.

The Chair thanked everyone for their contributions, those watching the meeting and Julia for her support throughout the whole process. A reminder to the public that this meeting has been recorded and the video will be available online on request by emailing the PFAS mailbox. This will take a couple of days to make sure the observers are anonymised.

There being no further business, the meeting was closed.

*To note that the Panel can be emailed via PFASpanel@gov.je.*

*Details of meeting dates and times can be found at PFAS in Jersey (gov.je)*

## Minutes of public meeting of the PFAS Scientific Advisory Panel on Teams 10am on 26 June 2024

| | |
|---|---|
| Panel Members present: | Dr Steve Hajioff – Independent Chair |
| | Dr Tony Fletcher – PFAS and Health member |
| | Professor Ian Cousins – PFAS and Environment member |
| In attendance: | Grace Norman – Deputy Director of Public Health |
| | Julia Head – Senior Public Health Officer |

**Welcome:**

The Chair welcomed everyone to the Panel meeting, and reminded people the meeting was being recorded.

Dr Hajioff explained that the meeting papers included an incorrect version of the draft literature review, and apologised for the error. This was an old version and should be discarded. The correct version was circulated to Islanders that morning.

The Chair also reminded the audience that Islander input into Report 2 has been postponed due to unforeseen circumstances. The meeting, which was due to be held in July will be moved to September. Dr Hajioff apologised for the delay.

Dr Hajioff reminded Islanders that queries should be send to the pfaspanel@gov.je mailbox so that the whole panel can feed into the response, rather than sending queries to individual panel members please.

Finally, he gave a reminder for offering evidence of experience around PFAS testing or treatments to lower PFAS body burden for Report 3. Please email pfaspanel@gov.je and instructions will be sent.

**Introductions**

The Chair and Panel members introduced themselves.

Dr Steve Hajioff, Independent Panel Chair: A background as a GP for 25 years and a retired Director of Public Health from an area of London with two major international airports and a variety of other environmental hazards and challenges. Not a PFAS expert but has done lots of work with National Institute of Care Excellence and other groups about translating science into policy. Dr Hajioff has also worked a lot in the pharmaceutical industry.

Dr Tony Fletcher, PFAS and Health Panel Member: Environmental Epidemiologist at the London School of Hygiene and Tropical Medicine, working on PFAS since 2006 and member of the panel with experience of epidemiological studies on the health effects of PFAS in contaminated communities in West Virginia in the United States, in the Veneto region, in Italy, and in Ronneby, and is the health expert on the panel.

Professor Ian Cousins, PFAS and Environment Panel Member: A Professor in Environmental Chemistry at Stockholm University, an expert on PFAS, appointed as the environmental expert on this Panel and whose expertise on PFAS is on the sources, transport, fate, and exposure of PFAS.

Support staff for programme management and administration were also in attendance.

**Declarations of Interest**

No additional declarations.

**Minutes of last meeting**

There were two sets of minutes to review, from the 16 May and 6 June meetings.

16 May

The Chair requested any matters of accuracy.

Dr Fletcher requested that the minutes were changed on page 6 to reflect his opinion that he does not believe that a change in birthweight has strong evidence. This has been updated.

The action list was reviewed and considered to be all completed or in hand. The minutes were signed off as a true and accurate record subject to the above change.

6 June

The Chair commented about a matter arising which was also in the action list. In the 6 June meeting, Dr Fletcher had noted that in the Australian evidence there was a pair of locations where the results are different to the two other pairs, likely caused by the comparator area being uncharacteristic of the country in general. Dr Hajioff had said that there was a similar finding in the mental health section. Following the meeting, Dr Hajioff had confirmed that it was the same pair that were the outliers in both papers. He agreed with Dr Fletcher's assessment that the uncharacteristically healthy comparator population was likely to be resulting in the adverse effects appearing more significant, and consequently out of alignment with the other areas studied.

There were no other matters arising and the minutes were signed off as a true and accurate representation.

**Additional findings since the last meeting**

Dr Hajioff noted that there had been a public meeting to launch Report 3 on 6 June in which Islanders were asked to contribute evidence as Experts by Experience for Report 3. Dr Hajioff reminded the public that the deadline is the 5 July 2024, and invited people with experience of using medical intervention to reduce PFAS burden in their body, or those with experience in testing in addition to the Government testing in 2022 to email the Panel. Testimonies can be given in public or private or by written testimony.

Dr Fletcher confirmed that the request for input is for any interventions that Islanders have used to reduce PFAS levels, not just medical interventions. For example, dietary interventions. He noted that there is one paper in the literature indicating that psyllium husk would be useful to manage PFAS body burden, and there is a planned intervention trial in Denmark which has been planned to investigate psyllium husk against placebo and cholestyramine. Although the results of this trial will be too late to include in Report 3, interventions such as these will be investigated during Report 3.

The Chair clarified that it is important to understand the patient experience has been for certain interventions, and also to indicate those which the panel are unaware of currently.

**Agenda item 5 –** Discussion and recommendations for Report 2

The Chair described the process the panel plan to take in forming the Discussion and Recommendation sections for the report in the meeting. Each health area on the agenda will be discussed section by section, each including evidence from Islanders affected by PFAS, evidence from Subject Matter Experts around the world including from animal and laboratory testing and also the results from literature review on various areas of PFAS and health and related issues. Following this discussion, the panel will look to see if a recommendation can be made. The final wording may not be finalised in the meeting but will be discussed offline ahead of the Islander meeting in September. There is the opportunity to change the wording On the basis of Islander input in September.

Summary of draft recommendations

| **Disease area** | **Recommendation** |
|---|---|
| PFAS and cardiology | - Symptoms of high cholesterol should be treated in the usual manner e.g. with statins |
| PFAS and cancer | - Clinicians, GPs in particular, should have a higher level of suspicion of cancer for people with symptoms consistent with kidney and testicular cancer who have been PFAS exposed<br>- Potentially recommend testicular self-examination |
| PFAS and the immune system | - Encourage higher rates of vaccination in childhood immunisation in affected and unaffected populations to ensure that children in the affected populations have adequate protection |
| PFAS and the hormonal system | No recommendation |
| PFAS and the nervous system | No recommendation |
| PFAS and the gastrointestinal system | No recommendation |
| PFAS and the urinary system | No recommendation |
| PFAS and reproductive health | - Breastfeeding is recommended because of wider benefits. If you are concerned then discuss with your healthcare professional. |
| PFAS and musculoskeletal effects | - Clinicians should have a higher index of suspicion of osteoporosis in PFAS exposed and who are otherwise at risk, e.g. with bowel disease, eating disorders, older women. |
| Environment and Mental Health | - Access to talking therapies is recommended. |
| Interactions between services and Islanders | - Ensure that there is a clinician available for Jersey healthcare professionals to contact for support in managing their patients who have concerns about PFAS.<br>- Make a concise knowledge-based resource available to healthcare professionals on the current state of PFAS and health. |

Comparability of exposure

The places in the world where people have been exposed to a similar mixture of chemicals as Jersey has been are Ronneby in Sweden and parts of Australia, but there appear to be different levels of exposure and different time periods between peak exposure and blood testing. This means that while the levels might look higher or lower in those places, there

might not be a real difference in how much PFAS people have been exposed to when those things have been taken into account. Dr Fletcher has looked into this on behalf of the panel.

Dr Fletcher notes that it looked at first sight as if the exposure levels in the Swedish studies were much higher than in the Australian studies. 100ng/ml in the blood measured in the Swedish population in 2014, after the problem had been discovered in 2013. Whereas in the Australian study the levels were for the sum of PFAS were 10ng/ml in the exposed area compared to 5ml in a background area which had general population exposure.

To compare this against the levels in Jersey, Grace provided the medians for PFOA, PFOS and PFHxS. The median for PFHxS is 9.2ng/ml, the median for PFOS is 10.0ng/ml and the median for PFOA is 2.5ng/ml. This is roughly 21ng/ml total across three analytes. To compare, it was 10ng/ml in Australia, and 100ng/ml in Ronneby. When comparing with other areas, especially Ronneby, the differential in time between when the primary exposure ended and testing happened must be accounted for. In Jersey, serum testing was 16 years after mains water was extended to the area, but only one year in Ronneby.

The non-exposed European population average in 2022 was estimated to be 3ng/ml PFOS and 1ng/ml PFOA.  In round numbers, the Jersey exposure level is twice the level reported in the Australian scenario. In the Australian hotspot, residents were moved to mains water in 2015 and had their blood sampled in 2019-2020. The follow up time is relatively short in Australia, which implies the average exposure in Australia was lower than Sweden or Jersey. The PFAS mixtures in the firefighting foam changed much earlier than 2015, but this is expected to also be true in Jersey.

The Chair questioned if the comparatively lower hotspot exposure in Australia could be due to some of the population using contaminated boreholes and some using mains water which was less contaminated, whereas in Ronneby and Jersey, residents only had access to one water supply. This may be why the median serum concentrations are lower because the Australian data have people with lot lower levels included in that median.

Understanding the Australian exposure is important to establish whether their experience is similar enough to Jersey for their health results to be comparable. The affected Jersey population is too small to study epidemiologically. The Australian residents on affected boreholes may have had high levels comparable to Ronneby, but there is not data specifically on these individuals.

Dr Hajioff commented that when comparing Ronneby and Jersey, calculations can be done to estimate what the levels might have been in Jersey when mains water was extended, which would account for the longer time period between what is assumed to be peak exposure and blood testing. The outcome of this is that, had testing happened 2 years after 2006 (when mains was extended) the total PFAS in the affected Islanders is likely to be around 150ng/ml, which is a comparable figure to Ronneby. Dr Fletcher agreed with this rough calculation. Therefore the health outcomes in the affected Ronneby population are particularly relevant to the Jersey affected population. As the Australian levels appear to be quite a lot lower, the Australian disease studies are less helpful, but still contribute to the evidence-base.

Grace commented that in Jersey, there was an eligibility criterion that islanders had to have a health condition they believed to be related to PFAS exposure. This means that there is a systematic difference between the people who were tested in Ronneby and in Jersey, because those less affected in Jersey may not have been eligible for testing.

The Chair commented that in Report 3, the Panel will review whether there should be further PFAS blood testing among other islanders, and the question of comparability with Ronneby will be considered at that point.

The Chair commented that this summary by Dr Fletcher was very useful, and concluded that the exposure scenario in Jersey does seem similar to Ronneby.

Dr Fletcher asked Prof Cousins whether the products that led to exposure are similar. If it can be assumed that the mixtures are comparable, this would be useful in evaluating the evidence. Prof Cousins noted he doesn't know whether the products are the same, but considered that it would be likely that they are similar, although the specific mixture in the blood may be different depending on the movement of water through the environment. Dr Fletcher commented that the same few big companies were marketing fire-fighting foam globally. Prof Cousins noted that other products used in addition to Lightwater AFFF products might mean they are not directly comparable, but the Lightwater AFFF was the only product discharging PFHxS and PFOS, and we have this in both Ronneby and Jersey, suggesting similarities.

The Chair commented that the panel now has a reasonable comparator in Ronneby for the exposure in Jersey. He noted that there is the potential for there to be further work on this matter in future, looking at the relative half-lives of the different PFAS types and applying that to the difference between the levels between Ronneby and Jersey. This could help assess whether the exposure was identical. The panel will consider this for Report 4 but agreed that Ronneby is a good comparator for report 2 and 3.

Prof Cousins noted that is possible that the total cumulative exposure could be different as Sweden had a longer duration of exposure, as the residents continued to drink the affected water until 2013, in comparison to 2006 in Jersey.

Dr Fletcher reminded the panel that the relevance of this discussion is that there are reports from various bodies reaching conclusions on what the health implications may be from different types of PFAS, but studies specifically of the Ronneby population are likely to be more meaningful because the exposures are thought to be similar. The Chair agreed.

<u>PFAS and cardiology</u>

| **Evidence source** | **Summary of health effects reported** |
|---|---|
| Experts by Experience | Elevated cholesterol |
| Subject Matter Experts | Elevated cholesterol<br>Other fats elevated in blood |
| Literature | Elevated total cholesterol and LDL (bad cholesterol) |

Dr Hajioff noted that high cholesterol is only concerning from a health point of view because it is associated with an increased risk of cardiovascular diseases. He asked Dr Fletcher the evidence shows that there are more cardiovascular events (such as strokes and heart attacks) in areas of high PFAS exposure.

Dr Fletcher indicated that there is scientific agreement that PFAS exposure does cause increase in total cholesterol and LDL (bad cholesterol). There are a number of reviews which therefore suggest, given the well-established associations between cholesterol and heart disease, that PFAS causing higher cholesterol should have a negative impact on health. However, the studies examining PFAS exposure and cardiovascular disease do not find a convincing association. Studies do not show an increase in cardiovascular incidence or

mortality with PFAS exposure. This seems like a paradox. This finding may be because the increase in blood cholesterol caused by PFAS is too small to result in increases in cardiovascular disease.

Dr Fletcher hypothesised that this increase in cholesterol could be due to a more complex subcategory of increases in other factors. For example, some studies show increases in HDL as well as LDL, so the impact on the ratio between HDL and LDL is not so big compared to the apparent effect on total cholesterol; i.e. physiological changes may cancel each other out. Another example is in the C8 analysis of PFOA, there is an apparent reduction in C-reactive protein (CRP), a general indicator of inflammation, and generally reduced CRP is associated with reduced cardiovascular disease.

Dr Fletcher commented that the researchers in Sweden have not yet analysed their data on cardiovascular disease. He noted that the Italian data did show an excess of cardiovascular mortality, and the Australian data was not consistent between three areas studied and this inconsistency may be due to one area having a comparator area which is unusually healthy.

Draft Recommendations

- Treat people who have raised cholesterol in the usual manner e.g. with statins.

The panel briefly discussed whether it would be appropriate to recommend screening for high cholesterol in affected Islanders, but agreed to discuss this further when preparing Report 3, which will include a section on human biomonitoring.

PFAS and cancer

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Breast, prostate, bowel, leukaemia, lymphoma, myeloma, kidney, bladder, uterus, skin and mouth cancers |
| Subject Matter Experts | Kidney (good evidence)<br>Breast and testicular (some evidence but not strong)<br>Liver and thyroid cancer (animal models) |
| Literature | IARC – Strongest evidence for PFOA, inadequate for PFOS<br>Ronneby - Small excess for kidney, testicular and bladder.<br>Australia - kidney |

Dr Fletcher explained the literature evidence. He indicated that there are two main sources of evidence. One is a very recent review by the International Agency for Research on Cancer (IARC) on PFOS and PFOA. The evidence is strongest for PFOA which has been classified on balance of probabilities by IARC as carcinogenic to humans (Class 1) with limited evidence in humans of renal cell carcinoma and testicular cancer. For PFOS there is no epidemiological data with IARC considering the available human evidence to be inadequate. The overall conclusion is that PFOS is "possibly" carcinogenic to humans (Group 2B). PFHxS was not investigated, although there is a good paper on PFHxS in the Ronneby study. In Ronneby, researchers found that there was a greater increase in kidney, testicular and bladder cancers, although the differences were small. Prostate cancer incidence was significantly lower than expected. There is evidence that suggests that there's a lower incidence of prostate, colon and lung cancers in Ronneby.

Extrapolating from the Ronneby data, the two cancers which have been highlighted with mixed evidence are kidney and testicular cancer. The researchers concluded there is a 20% increased risk of developing kidney and testicular cancers. Bladder cancer showed a similar increase, but there was less corroboration from other studies. In Sweden, there is an

efficient health record keeping and data linkage system which means that it is expected that the research is a reliable indicator of the actual rates of cancer in that population. Dr Fletcher noted that kidney cancer was higher in one area in Australia, and when averaged across the whole area, it also has a 20% excess.

Dr Hajioff noted that these are fairly rare cancers, and therefore a 20% increase in risk for a rare cancer does not mean that there would be an increase in risk at an individual level, although it does mean that among large populations, more cases would expect to be detectable. He noted that of course, it will be important for those who are affected, but across the whole population the numbers are not large, because the cancers are relatively rare.

Dr Hajioff noted that it is mechanistically plausible that other cancers could be associated with PFAS exposure, particularly as PFOA is a known carcinogen, but there is little evidence of this in the real world currently. Dr Hajioff noted that the IARC review for both PFOA and PFOS found the mechanistic evidence is strong. There are various epigenetic, cell proliferation, and immunological routes which point to a plausible mechanism of cancer and provides some support for the hypothesis that other cancers could be caused by PFOA and PFOS. The panel will discuss screening for cancers in Report 3 including whether ultrasound would be an effective mechanism.

Draft Recommendations

- Clinicians, GPs in particular, should have a higher level of suspicion of cancer for people with symptoms consistent with kidney, bladder and testicular cancer who have been PFAS exposed
- Testicular self examination is a possible recommendation, although would require further review of the literature. This is often recommended in a lot of places anyway.

PFAS and the immune system

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Autoimmune disease such as rheumatoid disease, lupus |
| Subject Matter Experts | Antibody responses to vaccination<br>Increase in susceptibility to infections |
| Literature | Decrease in antibody levels following childhood immunisation in relation to maternal, perinatal exposure indicating the early immune system seems damaged<br>no strong evidence for autoimmune disease<br>equivocal data on COVID-19 |

Dr Fletcher noted that several reviews have concluded that the strongest evidence of harm, and the basis for setting limits in water, is due to childhood vaccination efficacy reduction. This is because that is an indicator of immunomodulation. Any evidence that this correlates with an increase in vaccine-preventable or common childhood infections is weak; some studies find an association, but others do not. The evidence does not link to childhood asthma, and for common respiratory infections evidence is mixed.

There are several studies showing a decrease in antibody levels following immunisation in infants who have had maternal, perinatal exposure to PFAS. Very early programming of the immune system seems to be damaged. There are some preliminary results from Ronneby which do not find an association with reduced antibody levels in children, however this is not yet published. Because this is not perinatal or in utero data, it does not necessarily contradict

the other findings. Jamie DeWitt gave evidence to the PFAS Panel for this report and showed that PFAS is associated with lower immunity in animal studies also. Overall, the evidence suggests that there is a real association between PFAS and immune function, and PFAS does damage the developing immune system.

Dr Fletcher explained that there is some data on adult vaccine response in the Ronneby study, where antibody levels were tested before and after people received the COVID vaccination, which did not show an effect. This study was conducted in a different age group (adults) with a different type of vaccine so this finding doesn't contradict the finding that some childhood vaccines result in a lower immune response among people in PFAS hotspots. The data suggests that PFAS doesn't affect the adult immune system but there is convincing evidence that PFAS does affect the childhood immune system especially in relation to some immunisations.

For autoimmune diseases, the Ronneby data does not show an increased incidence of autoimmune diseases. The Ronneby research group looked at lupus and ulcerative colitis, both of which were also investigated by the C8 group, with an increase found in ulcerative colitis. This has not, however, been replicated in other studies and may be a chance association. Overall, there is no convincing evidence of an effect for any autoimmune diseases.

The Chair commented that is physiologically consistent because the lower effectiveness of vaccinations is due to the body's immune response being under-active, while autoimmune conditions occur because the body's immune response is over-active.

Prof Cousins commented that there have been a number of studies on COVID-19 comparing more vs less severe disease. An early one by Prof Grandjean suggested that PFAS exposure may have some effect on the severity of disease. Prof Cousins also noted that there is also a study in the literature about 3M retirees which did not show an effect of PFAS on risk of COVID diagnosis.

Dr Fletcher noted that these studies compared severe cases of COVID-19 against less severe cases. The authors compared blood levels of PFAS, comparing levels of PFBA grouped as either below the limit of detection (LOD) or above the LOD. This is a crude way of assessing exposure which is not very robust. The study found that there was an association between exposure of PFBA and more severe cases of COVID-19, but there was no association between for the more common types of PFAS (PFOA, PFOS, PFHxS) and severity of COVID-19 infection. Dr Fletcher considers that the authors may have overstated their conclusion, and the finding that COVID-19 infection is increased by PFAS is likely to be a chance finding. Some data from Italy appeared to show an increase in COVID-19 mortality in those exposed to PFOA, but the analysis was potentially confounded.

Draft Recommendations

Encourage high uptake of childhood immunisation in exposed areas and also in whole population to protect those who don't have high protection themselves. A universal recommendation will increase herd immunity by reducing circulating pathogens in the population.

Grace commented that the overall childhood immunisation level is quite high in Jersey, and that there is no downside to encouraging uptake of childhood immunisation.

PFAS and the hormonal system

Dr Hajioff reminded the panel that when considering changes in blood hormones and other blood tests, the concern is for people getting sick, rather than a difference in results of blood tests.

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | None reported |
| Subject Matter Experts | Thyroid dysfunction<br>Metabolic dysfunction – obesity, glucose intolerance, type 2 diabetes, insulin resistance |
| Literature | Studies investigating circulating hormones, thyroid, oestrogen, testosterone. Not strong evidence<br>Thyroid identified in C8 studies as probable link, however may be false positive as not replicated in Ronneby<br>Type 2 diabetes – association in Ronneby data but not C8 data. May be a chance finding<br>Obesity – mixed data in relation to childhood exposure. No positive association found in C8 data, in fact a significant inverse relationship with PFOS discovered instead |

Dr Fletcher summarised the literature. There are a number of cross-sectional studies looking at circulating hormones thyroid, oestrogen, and testosterone. Some of these have found associations with circulating PFAS. However, with cross sectional studies, it is difficult to determine causality so these are not strong evidence. It was also noted that a change in a hormonal level does not necessarily mean hormone-related disease.

Dr Fletcher explained that metabolic issues sometimes are all related to these cross-sectional hormonal measures. He noted that thyroid hormone disruption came up as one of the original things listed in C8 as having a probable link to PFAS exposure, but this effect was not replicated in Ronneby, which is considered to be a more thorough and better quality study and so this is considered to be a false positive result.

For Type 2 diabetes, there was no evidence of an association in the C8 studies, but there was an association found in Ronneby data. As this is a stronger study than the C8 work, this may result in being a robust association. However, as there is not enough evidence on the subject at present, it is not currently considered robust. Further work is required to determine if this is a real or chance association.

For obesity, there are some studies that provide strong positive results, and others that find negative results in relation to childhood exposure of PFAS and subsequent development of obesity, so there is not convincing evidence in either direction. In the C8 studies, the researchers found no evidence of effect for adult obesity, and that PFOS exposure was associated with decreased body weight, rather than increased body weight for children (significant inverse relationship).

While there is not strong evidence of an association, it is biologically plausible that PFAS could affect the gut microbiome, which could have a range of health-related impacts. The gut microbiome has a lot of health benefits if it is in good order with the right balance of bacteria in the gut. This is crucial for good digestion of food, but also effects on immune system and metabolic outcomes, including obesity. It also plausibly also affects excretion rates of PFAS through the gut, which means it would be a strong confounding factor (which masks a true causal relationship) because it affects excretion through the gut. This is a hypothesis and there is not strong evidence yet.

Overall, the Panel concluded that there is not strong evidence that there is a causal association between PFAS and obesity.

Draft Recommendations

For obesity, the Chair commented that if obesity was related to PFAS exposure, it would still be managed in the same way between exposed and non-exposed populations. Therefore, there is no recommendation.

No strong evidence found around thyroid disease therefore no recommendation is required.

For Type 2 diabetes, Dr Hajioff feels there is not enough strong evidence to make a recommendation to clinicians to have a higher level of suspicion in a PFAS exposed person. Dr Fletcher agreed and noted that the type 2 diabetes finding in the Ronneby study may be a chance finding, and he would not recommend an extra effort for screening in this population on this basis. He considers normal screening to be appropriate and therefore there is no recommendation.

PFAS and the nervous system

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | None submitted |
| Subject Matter Experts | Developmental language disorder in girls<br>Neurodevelopmental disorders – not demonstrated causality |
| Literature | ADHD – found in C8 study<br>Sweden – apparent association with language learning – requires replication |

Dr Fletcher commented that ADHD was investigated in the C8 data which did not find any results. The Swedish group (Ronneby) has found an apparent association with language learning in girls which requires replication. Any mechanism here is not clear, it may be related to the involvement of hormones in neurodevelopment, but that is hypothetical.

Dr Fletcher commented that he has not looked at neurodevelopmental effects thoroughly because he was prioritising those which have been highlighted by experts by experience, subject matter experts and findings from the Ronneby studies. It was agreed that ADHD would be investigated more thoroughly in the draft report.

Draft Recommendations

No recommendation to be made.

PFAS and the gastrointestinal system

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Indigestion, reflux symptoms (high in gut)<br>Change of bowel habit (low in gut) |
| Subject Matter Experts | Alterations in liver enzymes<br>Suggestive link with ulcerative colitis – already discussed and not replicated elsewhere |
| Literature | Several strong studies showing effect on liver enzymes, ALT in particular<br>Non alcoholic fatty alcoholic disease – some evidence but not strong |

Dr Fletcher noted that in the literature there are several studies with strong study designs which suggest PFAS could affect liver enzymes, in particular Alanine transaminase (ALT) which suggests that PFAS could be impacting on normal liver function. There is strong evidence for small changes within the normal clinical range in ALT which seem to be associated with PFAS levels in blood tests. There is no strong evidence for symptoms related to this elevation in ALT. It is unclear whether or not the incidence of non-alcoholic fatty alcoholic disease has increased.

He explained that ulcerative colitis was found to be associated with PFAS in the C8 studies, but there have been two studies since which have not replicated that finding, one of which was in Ronneby. Therefore, it was felt that it was unlikely that ulcerative colitis is caused by PFAS.

Dr Hajioff commented that for ulcerative colitis, there is a particular cell antigen which is genetic which is associated with these types of disease which might be a confounding factor. This genetic variation may be present at a high prevalence in the C8 population.

Recommendations

The panel does not consider it appropriate to make a recommendation. If a treating physician finds elevated ALT, it is good for clinicians to be aware that increase in ALT is related to PFAS exposure but there is no formal recommendation.

PFAS and the urinary system

This section excludes urinary cancers they are discussed with other cancers.

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | None reported |
| Subject Matter Experts | Increased risk of reduced kidney function |
| Literature | Reduced kidney function in some studies may be due to reverse causality |

Dr Fletcher explained that the literature shows that the association between kidney function and PFAS is different to other conditions. People who have reduced kidney function do not reabsorb it as quickly as people with functioning kidneys, which would mean that their PFAS blood levels would be lower than someone with the same exposure to PFAS. With most substances, reduced kidney function leads to higher levels.

If people in high and low exposure water districts are compared, there is no difference in kidney function, but within them there is a strong association which is driven by the kidney function affecting excretion.

Dr Hajioff commented that this is an effect which has come up in cross-sectional studies and animal models, but is not replicable epidemiologically because of the reverse causality Dr Fletcher highlighted.

Draft Recommendations

No recommendation to be made.

PFAS and reproductive health

This section includes foetal growth, infant growth, first year of life and also breastfeeding and lactation.

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Fertility issues |
| Subject Matter Experts | Reduced intrauterine growth<br>Increased risk of pregnancy induced hypertension possibility<br>Reduction in birth weight (small and sex specific)<br>Delayed or shortening of lactation<br>Issues around puberty<br>Duration of breastfeeding and establishment of breastfeeding<br>Some impairment of breastfeeding<br>SME experts highlighted benefits of breastfeeding and recommended healthcare professionals continue to promote breastfeeding in exposed populations due to benefits on the infant |
| Literature | |

*Exposure*

Dr Fletcher commented that at birth, the serum levels in the infant will reflect serum levels from the mother. If the mother has a raised body burden, then lactation will result in increased PFAS take up in the child, approximately doubling every 6 months. There are significant health benefits to the infant and mother through breastfeeding. On balance, the benefits of breastfeeding greatly outweigh the additional exposure. This position was put forward by several of the subject matter experts that presented to the Panel. Additionally, the American Centre of Disease Control (CDC) also report that the benefits outweigh the potential risk of PFAS through breastmilk exposure.

The Chair commented that to make any recommendation other than to continue breastfeeding would require evidence to suggest extreme harm from PFAS.

Dr Hajioff commented that not breastfeeding greatly increases risk of death in the first year of life. He considers it unlikely that all the potential risks across all systems with PFAS exposure would come close to outweighing that risk. Breastfeeding also decreases risk for many health conditions, such as diabetes, heart disease, and cancer, later in life too.

The panel are comfortable to reflect the position of the CDC with recommending breastfeeding in all cases, and to encourage discussion with healthcare providers if the mother is concerned.

*Breastfeeding duration*

Dr Fletcher commented that there have been several studies suggesting mothers with high PFAS exposure tend to breastfeed for less time. The mechanisms for this effect are not clear, but the effect has been replicated. He notes that the effect is an observation, and is an average reduction.

Dr Hajioff asked if anyone has looked at pituitary hormone levels in PFAS exposure, as breastfeeding is largely governed by pituitary hormones such as prolactin. He proposed that if pituitary hormones are affected in PFAS exposure then they could be the reason for reduced duration of lactation. He noted that other pituitary hormones affect type 2 diabetes, indicating some sort of endocrine disruption. Dr Fletcher will consult with one of the panel's SME to follow up this question.

*Birthweight*

Dr Fletcher commented that there are some studies suggesting a change in birthweight and others that do not. Overall, he is not persuaded that the evidence indicates an impact on birthweight.

*Pregnancy induced hypertension*

Dr Fletcher commented that for hypertension in pregnancy, there is no evidence of effect in Ronneby. The C8 data did suggest the risk, but it has not been replicated in other studies including in higher exposed populations

*Polycystic Ovarian Syndrome (PCOS)*

Dr Fletcher commented that PCOS is a new finding from Ronneby and needs replication. For this reason, he does not believe that it should be recommended by the panel to be screened for in this population.

Draft Recommendations

Breastfeeding is recommended because of wider benefits. If a mother is concerned then she should discuss with her healthcare professional.

PFAS and musculoskeletal effects

Rheumatoid conditions and lupus which EBE highlighted were discussed along with the other immunity-related issues.

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Rheumatoid, lupus |
| Subject Matter Experts | None reported |
| Literature | Dose related increase in osteoporosis linked fractures |

Dr Fletcher commented that a study linking serum PFAS levels with medical records in the literature found that there was a dose related increase in osteoporosis linked fractures. He noted that this effect has not yet been replicated by other studies. However, there are bone density reduction studies indicating potential biological plausibly of a real effect.

Dr Hajioff commented that he considers this finding interesting as there is a dose response in both the bone density (found by radiology) and also fractures due to weaker or thinner bones. A dose response increases the likelihood that these findings are real.

Draft Recommendations

Clinicians should have a higher index of suspicion of osteoporosis in people who are PFAS exposed and who are otherwise at risk, e.g. those with bowel disease, eating disorders, and postmenopausal women.

Environment and Mental Health

| Evidence source | Summary of health effects reported |
|---|---|
| Experts by Experience | Mental health consequences of their illness journeys as well as how they feel about having been exposed to PFAS.<br>Anxiety and worry, as well as moral injury at having exposed their children to PFAS and their children watching them being ill. |

| | |
|---|---|
| | Financial concerns.<br>Mistrust in the light of what had gone before. |
| Subject Matter Experts | |
| Literature | Psychological distress – reasonable evidence<br>Anxiety around environmental concerns like PFAS<br>Depression, post-natal depression – weaker findings<br>Post traumatic stress disorder (PTSD)<br>Worry about long and short term physical health<br>Mistrust<br>Uncertainty around evidence and interpretation of evidence |

Dr Hajioff commented that he has looked at literature on mental health and environmental concerns and was surprised at how few studies there were. He explained about a qualitative study in Australia which found the affected population felt:

- worry about long and short term physical health
- mistrust
- uncertainty around evidence and people's interpretation of it

Prof Cousins noted the financial implications of PFAS exposure in Australia was large, there was loss of property prices and business such as farmers and fisheries were significantly impacted. He questioned whether this was the case in Jersey as well.

Grace commented that overall, the property market is generally buoyant in Jersey but that she was not aware of more localised differences. It could not be ruled out as something which is affecting the affected Islanders.

Draft Recommendations

Access to talking therapies is recommended.

Grace noted that there are psychological support services available to all Islanders free at the point of use.

Interactions between services and Islanders

| **Evidence source** | **Summary of health effects reported** |
|---|---|
| Experts by Experience | Health professionals do not understand PFAS<br>Islanders are putting less weight on the reassurance they are being given, because their medical professionals do not understand PFAS<br>Hearing different things from different medical professionals which is making people feel uncomfortable |
| Subject Matter Experts | |
| Literature | |

Dr Hajioff commented that in a recent meeting he held with GPs, they commented that they did not have access to the latest information on PFAS and health. They requested a clinical resource with experience in PFAS with whom they could discuss patients where PFAS might be a factor in their health.

Dr Fletcher agreed that it is crucial to have a network of engaged GPs and Prof Cousins noted that GPs need information to help patients who consult them with regard to breastfeeding concerns and queries as the panel previously recommended.

The panel proposed that an evidence summary is provided to help GPs, based on Report 2. The panel discussed how the Government could produce a short summary of the key content from Report 2 and make it available to the GPs and the public. It would then be updated when Report 3 is made available. Dr Fletcher noted that the Executive Summary from the reports could be used as a starting point, and there are also are already resources online that can be drawn on.

Draft Recommendations

- Have a clinical resource available to help GPs around the issues the patients have raised.
- Make a concise knowledge-based resource available to healthcare professionals on the current state of PFAS and health.

**Agenda item 6 – Additional recommendations**

The panel had no additional recommendations to add.

Dr Fletcher commented that there could be fewer recommendations from this report alone, as it would be more relevant to combine recommendations with Report 3. The Chair agreed, and reminded the panel that this is largely an informational report, and recommendations are less important. Report 3 will be an action orientated report.

**Next steps for Report 2**

Dr Hajioff noted that the panel will collate the recommendations from the minutes, construct draft recommendations and then incorporate into the draft report. The report will then be shared as a courtesy with Public Health team once the process is done.

There will be a public event on September 12 where the panel will hear input from Islanders on the draft report and the recommendations, and launch a period of input for interested islanders. All of the input will be considered, and will be presented as an appendix at the back of the report with a response indicating what changes have been made and why, or why changes have not been made. The report and changes will be made public before the final draft goes to Ministers for publication and launch. Publication of Report 2 is likely to be in November.

He explained that Report 3 will be running in parallel. The panel start their work on Report 3 in a public meeting on 11 July. Report 3 is hoped to be published in Q1 2025.

Dr Hajioff reminded the audience that the panel are still calling for Experts by Experience for Report 3 on their experiences on measures to reduce PFAS in their body and testing for PFAS in their body. This evidence can either be in a public or private panel meeting or in writing. All testimonies will be anonymous regardless of method of testimony.

Dr Hajioff sent further apologies that the wrong draft of the literature review was circulated yesterday, and the correct draft was circulated this morning. He asked the audience to discard the previous version.

**Any other business**

Grace noted that Islanders requested an event with the Ministers at the last Islander event and confirmed that this has been arranged for 31 July at 5.30pm at Les Ormes.

**Date of next meeting**

11 July 2024. It will be held 10am-1pm online.

The Chair thanked everyone for their contributions, those watching the meeting and Julia for her support throughout the whole process. A reminder to the public that this meeting has been recorded and the video will be available online on request by emailing the PFAS mailbox. This will take a couple of days to make sure the observers are anonymised.

There being no further business, the meeting was closed.

To note that the Panel can be emailed via PFASpanel@gov.je.

Details of meeting dates and times can be found at PFAS in Jersey (gov.je)