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)

Actions from the meeting

Action	Action given by	Action taken by	Date for delivery
Review Australian study pairings on mental health effects to check if Williamstown is the outlier	Dr Hajioff	Dr Hajioff	ASAP

Post meeting note – Dr Hajioff completed his action to check if Williamstown is the outlier in the mental health effects and confirmed that it is the same place. Therefore, he agrees with Dr Fletcher's assessment that the physical effects seen are as a result of the comparator being unusually healthy, as this effect is borne out in the mental health data as well.