

Procedural Review of Health Reference Values Established by enHealth for PFAS

Introduction

This review was commissioned by the Minister of Health in fulfilment of the Government's commitment to review the interim human health reference values (HRVs) for per- and poly-fluorinated alkyl substances (PFAS) in drinking water. Given the one month allowed for its conduct, the review focuses on a consideration of the approach, and principles, applied by enHealth, EFSA and US EPA and the scientific and pragmatic arguments for selection of one agency's approach over that of the other.

Background – The enHealth Process and Conclusions

In addressing specific public health issues enHealth draws on specialist scientific and medical expertise through the establishment of working groups and or the programming of workshops where the issue can be discussed in detail, applying a multidisciplinary approach. This is normal practice nationally and internationally, but unlike international agencies such as the US EPA, US FDA or EFSA, enHealth is not supported by a specialist scientific secretariat (i.e. a risk assessment group) and therefore relies on members of its scientific workshops and the agencies of the enHealth membership to prepare background papers for consideration by the medical and scientific experts of its workshops.

In April 2016, enHealth convened an expert workshop of science and medical specialists to provide recommendations for the establishment of *interim* HRVs to support jurisdictional responses to environmental contamination with PFAS and to set drinking water limits for these substances, pending a more formal review by FSANZ. Given an immediate need for guidance to State and Territory environment agencies for the management of PFAS contamination, the considerations of the workshop were focussed on the risk assessments of international regulatory agencies of high standing, including EFSA and the US EPA, rather than a *de novo* assessment. The enHealth committee, in conjunction with the workshop participants, identified the EFSA reference values as the most appropriate **as interim values** based on a range of considerations including;

- The EFSA HRVs were established using a methodology typical of most regulatory agencies across the world and typical of the process used in Australia.
- The US EPA reference values were derived using mathematical modelling incorporating a range of assumptions of uncertain validity.
- Because of the exceptionally slow build up and decline of PFAS in humans over periods of years, the systemic (i.e. internal) exposure to PFAS is also determined by exposures over very long periods of time. As lowering of guidance values cannot in isolation therefore, affect internal exposures meaningfully over the short to medium term, and given the steps already taken to reduce exposure in affected communities, selecting lower guidance values than those of EFSA would have no short term impact on public health.
- The EFSA HRVs were therefore concluded to be adequately protective for short to medium term exposures **as a temporary measure**.
- Food Standards Australia New Zealand is currently undertaking a more comprehensive review of HRVs for PFAS, will have greater scope in terms of time and resources than enHealth, will be able to draw on the deliberations of the workshop, and will have the ability to utilise other expert input to inform their review.

The use by Australian regulatory agencies of risk assessments from international agencies, such as the US EPA or EFSA, as interim measures to support immediate actions or deliberations, is not unusual and is an appropriate mechanism to provide timely responses to emerging issues.

Identified Sources of Variation Between the US EPA and EFSA Assessments

As with all health risk assessments, there are various sources of uncertainties, strengths and weaknesses in both the EFSA and US EPA derivations of their respective HRVs, and some differences in the methodologies applied. The observation that some of the methodologies used by both the US EPA and EFSA deviate from standardised approaches used in Australia and elsewhere does not mean those approaches are wrong. All process in risk assessment is subordinate to the best available science. Equally the latest approaches are not better simply because they are the latest.

Although the US EPA assessment is more recent, the differences between the two assessments and the resultant HRVs are not due to differences in the studies available for assessment by the two agencies and are not due to differences in the interpretations of the available human epidemiology studies. The key sources of variation relate to the use of mathematical modelling of human internal exposures (PFAS levels in blood) by the US EPA and differences in selection of uncertainty factors to derive the final HRVs by the two agencies. Although the mathematical modelling of the US EPA is ostensibly sophisticated it requires the use of a range of assumptions around the behaviour of the chemicals in humans and the respective experimental animals. As a consequence, the modelling approach has potentially replaced one set of uncertainties with another. This type of modelling is not a routine aspect of risk assessment methodologies for major international agencies other than the US EPA (& US ATSDR). Although there may be value in the approach for some aspects of the toxicology of PFAS the approach does not appear to be relevant for some other aspects.

There are indications that, at least for some toxicological effects used as the basis for determination of the HRVs, humans are likely to be less sensitive than animals. Further consideration of this issue is warranted.

Conclusions of the Review

Because of the exceptionally slow build up and decline of PFAS in humans, the systemic (i.e. internal/blood) exposure to PFAS is determined by oral (or other routes of) exposure over very long periods of time (years). As a consequence, even a 10 fold or greater reduction in guidance levels for drinking water and food would take a protracted period of time to significantly impact blood levels (the measure of internal dose). The phasing out of PFAS internationally for most uses, and steps to reduce exposure in areas affected by point sources of contamination, have been shown to result in declining exposures and a progressive decline in serum levels wherever implemented. Consequently, the choice of EFSA HRVs over those of the US EPA has no substantive impact on public health in the short to medium term.

For contaminants of human origin such as PFAS which cannot readily be removed from the environment, the establishment of values that are, with respect to the overall weight of evidence, disproportionately low, has the potential to result in a range of adverse health outcomes which may be greater and more likely than the toxicological risks intended to be avoided. Such outcomes may include prolonged unwarranted stress in exposed populations, the recommendation, or seeking out, of unnecessary medical interventions with their attendant risks, or interventions in pregnancy and avoidance of breast feeding to the detriment of the foetus and neonate. Simplistic selection of the lowest international HRV is therefore not necessarily optimal for the overall protection of public health. Determination of suitable HRVs for PFAS requires a careful consideration of the strengths and weaknesses of the approaches taken by international agencies, and a considered selection of the most appropriate approach/values within the context of the exposure patterns in Australia. A suitably precautionary approach to public health requires a balancing of risk prevention against the potential for risk generation.

The adoption of the EFSA HRVs as **a temporary (i.e. interim)** measure, pending a formal more extensive review by FSANZ, is appropriate and is protective of public health.

Recommendations

Based on the findings of this review, recommendations were made to improve the scientific support provided to enHealth and its working groups and for some key areas requiring attention by FSANZ in its review of PFAS health reference values.