Administrative Report

Review of health-based guideline values for Per- and Polyfluoroalkyl Substances (PFAS) in the *Australian Drinking Water Guidelines*

June 2025

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Administrative Report: Review of health-based guideline values for Per- and Polyfluoroalkyl Substances (PFAS) in the *Australian Drinking Water Guidelines*

Summary

The National Health and Medical Research Council (NHMRC) has updated guidance in the *Australian Drinking Water Guidelines* (the Guidelines) regarding the per- and polyfluoroalkyl substances (PFAS) Fact Sheet, including revised and newly established health-based guideline values.

The PFAS reviewed as part of this update include perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorohexane sulfonic acid (PFHxS), perfluorobutane sulfonic acid (PFBS), hexafluoropropylene oxide dimer acid and its ammonium salt (GenX chemicals).

Based on health concerns, the review has lowered the health-based guideline values for PFOA and PFOS, and established new and separate health-based guideline values for PFHxS and PFBS. A health-based guideline value for GenX chemicals is not currently considered necessary.

This document summarises the development process for updating the guidance on PFAS in Australian drinking water.

Background

NHMRC issues guidelines under section 7(1) of the *National Health and Medical Research Council Act 1992* (the Act). NHMRC is responsible for the *Australian Drinking Water Guidelines* (2011) (the Guidelines), which undergoes a rolling revision to ensure they represent the latest scientific evidence on good quality drinking water. The Guidelines provide guidance to water regulators and suppliers on monitoring and managing drinking water quality. They are intended to provide a framework for the good management of drinking water supplies that if implemented will assure safety at the point of use.

The Guidelines form part of the National Water Quality Management Strategy, an Australian Government initiative in partnership with state and territory governments. The Guidelines are intended as a consistent source of authoritative guidance on drinking water quality management and allows state and territory governments to adapt the guidance to local needs.

Part V of the Guidelines contains fact sheets for chemicals that are typically present in Australian drinking water supplies. The fact sheets contain information on relevant aspects of the chemicals in drinking water, including but not limited to:

- health-related advice (e.g. a health-based guideline value and/or public health advice, health considerations, exposure information and risk summaries)
- supporting information (e.g. guidance on analytical measurements or sampling, water treatment and risk management options).

Since the current version of the Guidelines was published in 2011, updates to specific sections of the Guidelines, including chemical fact sheets, have been undertaken as part of a 'rolling review'

process. Suggestions for potential updates or the development of new advice are considered in response to new evidence, stakeholder needs and available resources. Updates are prioritised and delivered with advice from the Water Quality Advisory Committee (the Committee).

PFAS health-based guideline values

PFAS are a group of over four thousand manufactured chemicals that do not occur naturally in the environment. Humans can be exposed to PFAS present in food, consumer products, dust and drinking water. The major sources of PFAS are expected to be food and consumer products. However, the proportion of exposure from drinking water can increase in individuals living in areas with drinking water containing PFAS.

In August 2018 NHMRC published health-based guideline values for three PFAS (PFOS + PFHxS and PFOA) in Australian drinking water. These guideline values were based on a tolerable daily intake (TDI) developed by Food Standards Australia New Zealand (FSANZ), which refers to the daily amount of a chemical that has been assessed as safe for humans on a long-term basis (FSANZ 2017).

A number of changes to international advice for PFAS have been released since NHMRC published the 2018 PFAS Fact Sheet. For example, in September 2020, the European Food Safety Authority (EFSA) set a new safety threshold for the main PFAS that accumulate in the body (EFSA 2020). In June 2022, the United States Environmental Protection Agency (US EPA) issued interim drinking water health advisories for two types of PFAS (PFOS and PFOA), which were lower than the Australian health-based guideline values for drinking water (US EPA 2022). Two new PFAS drinking water health advisories for PFBS and GenX chemicals were also issued in June 2022. In April 2024, the US EPA issued a Final PFAS National Primary Drinking Water Regulation.

It is not uncommon for guideline values to vary from country to country due to different methodologies and calculations, based on for example, the choice of endpoints and expressions of units used. However, as the United States and European advisory levels were lower than the 2018 Australian values for drinking water, some concern had been raised about whether the 2018 Australian drinking water guideline values for PFAS adequately protected consumers against the health effects of PFAS.

In response to these new advisories and growing community concerns, in late 2022 NHMRC prioritised a review of the Australian health-based guideline values for PFAS (PFOS, PFHxS and PFOA), including consideration of GenX chemicals and PFBS. The review aimed to determine whether a change to NHMRC advice was warranted or not.

This report describes the process undertaken to review the PFAS Fact Sheet and public health advice for PFOA, PFOS, PFHxS, PFBS and GenX chemicals in drinking water.

Development of updated PFAS Fact Sheet

Methodological framework

As part of a broader organisational effort to improve the processes used to develop NHMRC guidelines, NHMRC designed a streamlined methodological framework (the Framework) to guide the rolling revision of chemical fact sheets in the Guidelines.

The Framework is intended to provide greater consistency and alignment with the 2016 *NHMRC Standards for Guidelines* and international best practice in evidence review methods and guideline development. It is also intended to:

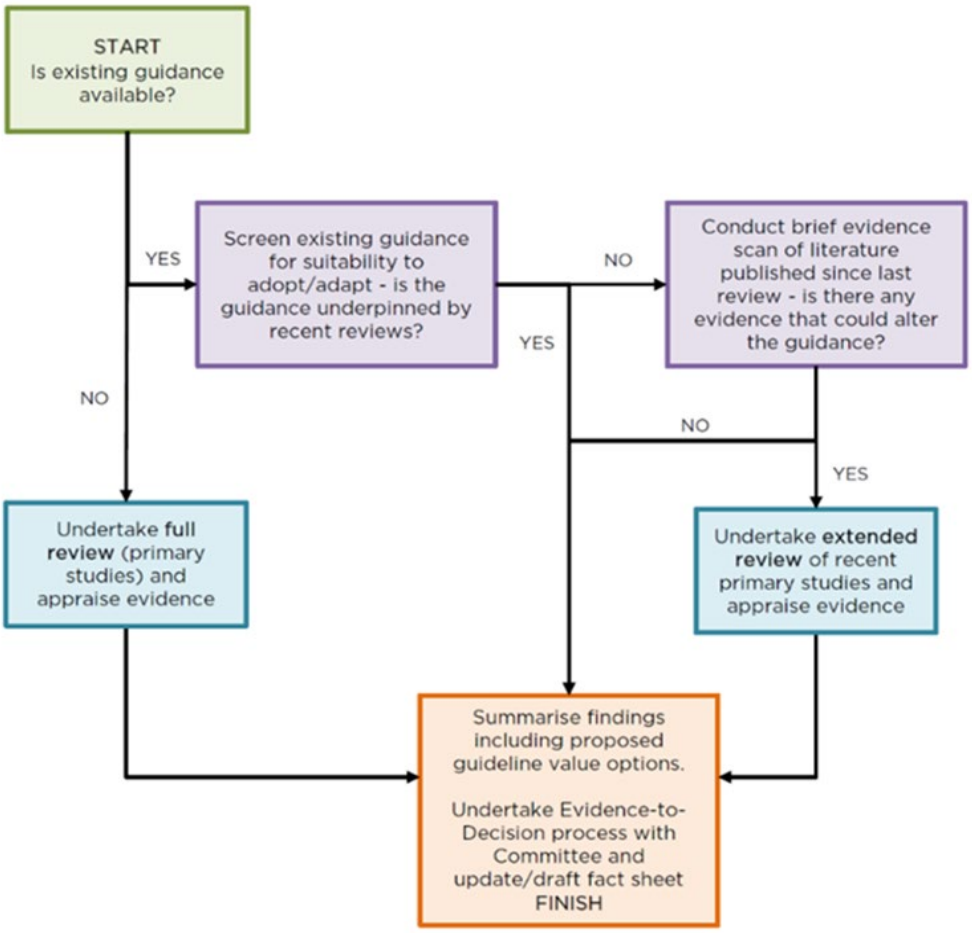
- make efficient use of limited project resources (e.g. funding, team and Committee capacity)
- make greater use of recent reviews undertaken by other jurisdictions and reduce duplication of effort
- minimise the timeframes required to undertake a chemical fact sheet review (depending on whether recent reviews are available)
- allow a more responsive approach to changes in international guidance
- allow more reviews to be undertaken in-house using templates and tools
- help inform future funding bids by identifying chemicals that may require additional funding for contracted evidence reviews.

The Framework provides the option to undertake different levels of review depending on the available evidence (see **Figure 1**). The Framework outlines a staged approach that preferences a transparent adopt/adapt process for evaluating existing health advice (such as international health-based guideline values) in the first instance instead of undertaking a more comprehensive review of primary studies. Other features of the Framework include:

- the option to undertake an evidence scan to check for emerging evidence of concern since the existing guideline was published (if it was not reviewed recently)
- the option to undertake reanalysis of key study findings from existing guidelines if appropriate and advised by the Committee
- the flexibility to customise the review process for each chemical using template research protocols for the different levels of review.

Existing guidance for a chemical may not always be available or appropriate to use for the Australian context. In these cases, a full review of recent primary studies may be required, and additional resources will be needed to undertake the review. Testing of the Framework as part of the rolling revision of the Guidelines has been underway since 2020.

Figure 1: Simplified Decision Tree For Undertaking Evidence Evaluation Reviews Using The Framework



Text alternative of Figure 1

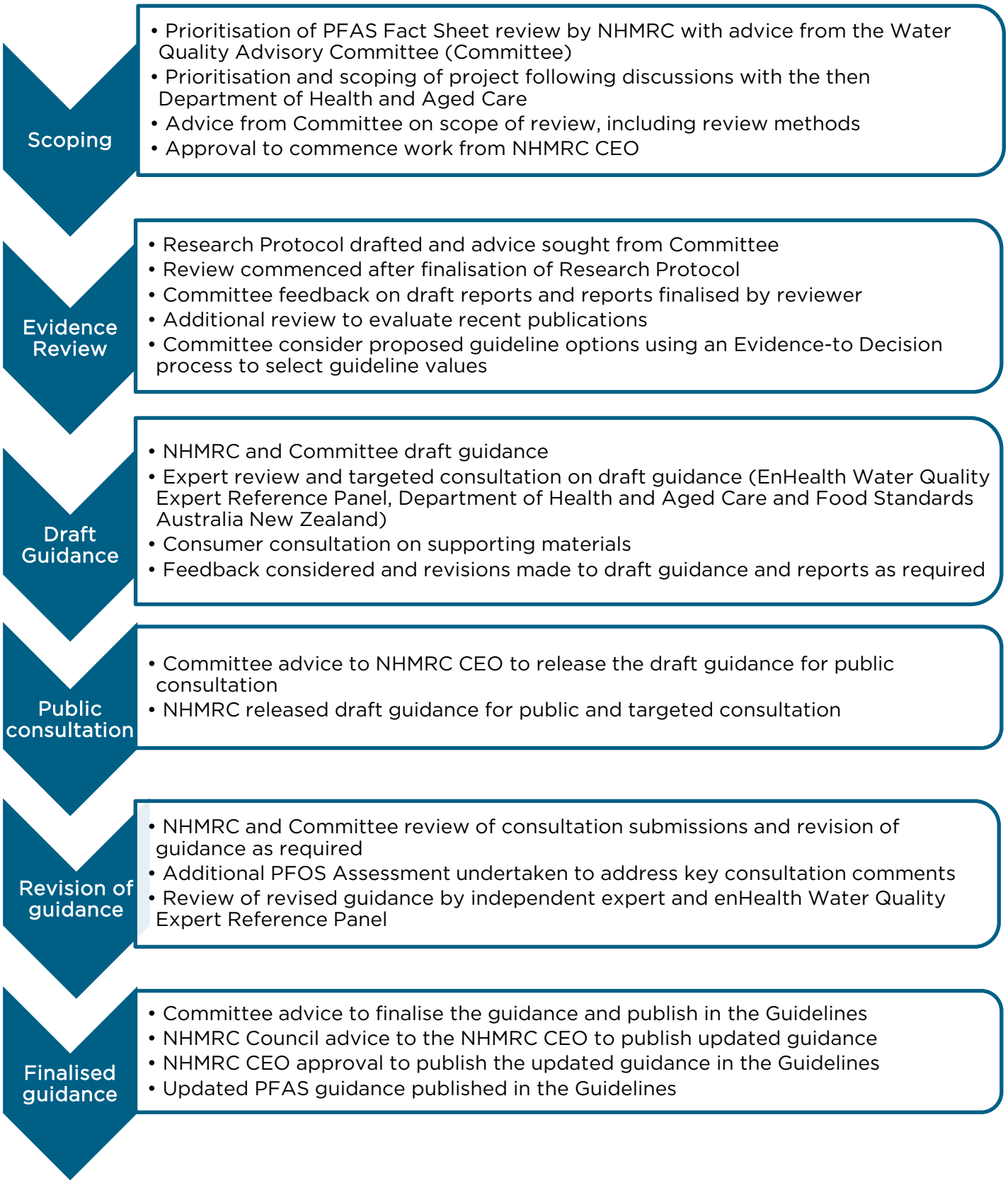
Start – Is existing guidance available?

1) Yes – Screen existing guidance for suitability to adopt/adapt – is the guidance underpinned by recent reviews?
    a) Yes - Summarise findings including proposed guideline value options. Undertake Evidence-to-Decision process with Committee and update/draft fact sheet. FINISH
    b) No – Conduct brief evidence scan of literature published since last review – is there any evidence that could alter the guidance?
        i) Yes – Undertake extended review of recent primary studies and appraise evidence
            (1) Summarise findings including proposed guideline value options. Undertake Evidence-to-Decision process with Committee and update/draft fact sheet. FINISH
    c) No - Summarise findings including proposed guideline value options. Undertake Evidence-to-Decision process with Committee and update/draft fact sheet. FINISH
2) No – Undertake full review (primary studies) and appraise evidence
    a) Summarise findings including proposed guideline value options. Undertake Evidence-to-Decision process with Committee and update/draft fact sheet. FINISH

As existing guidance and guidelines for PFAS underpinned by recent reviews were identified, an adopt/adapt process was considered suitable for the review of the PFAS Fact Sheet.

Key steps undertaken as part of the guidance development process for the PFAS Fact Sheet are summarised in **Figure 2**. This process is consistent with standard processes undertaken for the rolling revision of the Guidelines, NHMRC Standards for Guidelines and NHMRC internal guideline development processes.

Figure 2: Overview of guideline development process



Contracted evidence reviews

In April 2023, NHMRC contracted SLR Consulting Australia (SLR Consulting) to undertake an evidence review to evaluate existing evidence and underpinning studies of guidance and reviews available from selected national and international jurisdictions for five PFAS in drinking water: PFOA, PFOS, PFHxS, PFBS and Gen X Chemicals. The evidence review also included an evidence scan regarding typical PFAS levels detected in Australian drinking water and guidance on PFAS detection, monitoring and treatment. The evidence scan served to inform an update to the supporting information within the existing PFAS Fact Sheet.

The reviewer applied the methodological framework as part of the evidence review by:

- customising a draft research protocol template provided by NHMRC. The research protocol outlines the review scope and parameters for searching, selecting and appraising the evidence.
- confirming any amendments to the draft research protocol with the Committee at a meeting. The Committee confirmed the research questions and other technical details required for the review.
- finalising the research protocol (and any amendments) and seeking approval from NHMRC before commencing the review.
- undertaking a review of evidence for each of the five PFAS chemicals as per the Framework (**Figure 1**), specifically that if recently published guidance/guidelines are available, assessing the methods used by the organisation/agency with an Assessment Tool provided by NHMRC that assesses administrative and technical criteria to determine if they are suitable to adopt/adapt.
- undertaking an evidence scan to support the development or update of supporting information in the chemical fact sheet.
- deriving candidate guideline options for each of the five PFAS in drinking water using Australian assumption values and uncertainty factors.
- presenting the findings of the review in an Evidence Evaluation and Technical Report for Committee consideration.

As part of scoping the review, a literature search of existing health-based guidance/ guidelines was completed based on a predetermined list of source agencies as outlined in the Research Protocol. The volume of information found and needing to be assessed was very large. Due to resource constraints and to deliver the review within a reasonable time, the critical evaluation of studies underpinning existing guidelines values was prioritised, with Committee support, to those studies that had not been previously reviewed and/or considered by an Australian agency for guidance/guideline value development (such as in neither FSANZ 2017, 2021).

Based on Committee advice the scope of the review was also amended to incorporate an additional critical appraisal of the key underpinning study of the current NHMRC health-based guideline value for PFOA (Lau et al. 2006), including how it was assessed and used to derive a guidance value by Burgoon et al. (2023). The Committee also advised that an expert determination of the certainty of this study relative to the other proposed guideline options should be undertaken.

The review did not make recommendations for specific health-based guideline values but provided candidate guideline options for consideration by the Committee. These options were based on existing guidance/guidelines that were found suitable to adopt/adapt to the Australian context, with a critical discussion of the underlying key toxicological studies used by each agency to derive their guidance/guidelines.

The initial evidence review was completed by SLR Consulting in February 2024. Further details on how the evidence review was undertaken is provided in the Research Protocol, Evidence Evaluation and Technical Reports (SLR 2023; 2024a, 2024b). A number of amendments were made to the February Evidence Evaluation Report in October 2024 by the reviewer, following consideration of targeted consultation feedback. Details of accepted amendments made to the report are outlined in the targeted consultation summary table at **Appendix B.**

Addendum to the contracted evidence review

Following the finalisation of the initial contracted evidence review (SLR 2024a, 2024b), the US EPA published their Final PFAS National Primary Drinking Water Regulation in April 2024 for a number of PFAS, including final toxicity assessments for PFOS and PFOA (US EPA 2024a, 2024b). These reports included several key and candidate studies for PFOS and PFOA that had not previously been evaluated in the SLR (2024a, 2024b) review nor by FSANZ (i.e. in neither FSANZ 2017, 2021).

NHMRC contracted SLR Consulting to undertake an additional evidence evaluation and prepare an Addendum Report which considers the key studies in the final US EPA toxicity assessments for PFOS and PFOA (US EPA 2024a, 2024b), as well as another recently published peer-reviewed scientific paper by an international collaboration of scientists deriving guidance values for PFOA (Burgoon et al. 2023). SLR Consulting also undertook an assessment of the available methods, rationales and guidance used by other agencies to derive a total/sum of PFAS guideline value (i.e. a review of approaches for PFAS mixtures assessment in drinking water).

The additional evidence evaluation was undertaken in line with the same methodological framework as used in the initial SLR (2024a, 2024b) review. The resulting options for candidate guideline values for PFOA and PFOS, as well as the findings of a review of approaches for assessing PFAS mixtures, were presented for consideration by the Committee (SLR 2024c). The additional review was completed by SLR Consulting in August 2024.

A number of amendments were made to the August Addendum Report in October 2024 by the reviewer, following consideration of targeted consultation feedback. Details of amendments made to the report where accepted are outlined in the targeted consultation summary table at **Appendix B**.

Additional PFOS assessment following public consultation

Following consideration of comments received during the consultation process, and on advice from the Chemical Subgroup, NHMRC contracted SLR Consulting to undertake an additional assessment of PFOS which was finalised in March 2025 (**Appendix G**). This assessment was intended to help the Committee address a number of comments raised during the consultation process, including concerns about the wording regarding the endpoint of bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) and questioning the US EPA dose-response model used to derive a point of departure for the draft PFOS guideline value for public consultation. This information helped to inform Committee/Chemical Subgroup discussions and additional considerations following consultation (detailed in **Appendix F**). Based on this information, NHMRC, with Committee advice, updated the PFOS Evidence-to-Decision table (**Appendix A**) and revised the health-based guideline value for PFOS.

Evidence-to-Decision process

Evidence reviews provide a comprehensive summary and critical appraisal of the evidence and guideline options but do not include recommendations (e.g. health-based guideline values). The term 'decision' is used to mean the resulting judgement of the evidence made by NHMRC and the Committee.

In March 2024, NHMRC, with advice from the Committee, developed draft Evidence-to-Decision tables for the candidate PFAS guideline values based on the results of the initial Evidence Evaluation Reports (SLR 2024a, 2024b) and relevant criteria from existing Evidence-to-Decision frameworks (e.g. GRADE and WHO-INTEGRATE frameworks as outlined in Alonso-Coello et al. (2016) and Rehfuess et al. (2019)).

The Evidence-to-Decision tables (**Appendix A**) helped to inform Committee discussion and support transparent consideration of the findings from the evidence reviews undertaken by the reviewer (e.g. evidence profiles for candidate guideline values). Public health considerations such as values and preferences, equity, feasibility and resource impacts were noted but not directly considered in decision making when deriving health-based guideline values. NHMRC and the Committee considered the potential impacts of different guideline values, but ultimately the decision about the health-based guideline values is based on what is considered to be the best available health evidence. Public health considerations and cost impacts can be reviewed when jurisdictions are implementing advice from the Guidelines.

Guideline recommendations in the Evidence-to-Decision tables were updated as required on the advice of the Committee based on information received through additional reviews (i.e. Addendum Report (SLR 2024c), the additional assessment for PFOS (**Appendix G**) and feedback from public consultation, targeted consultation and expert review.

The Committee reviewed and considered the Evidence-to-Decision tables when advising on the public consultation draft and subsequent final PFAS guideline values, as summarised in **Table 1** below.

Table 1. Evidence to decision summary

Committee meeting	Members agreed
March 2024 Water Quality Advisory Committee meeting	Members agreed: • that the contracted review and assessment of underlying studies for candidate guideline values (SLR 2024a, 2024b) were of high quality and that they were comfortable with the conclusions drawn by the reviewer. • that the preferred option for PFOA is to maintain the current health-based guideline value of 560 ng/L based on developmental effects observed in mice (Lau et al. 2006) (*note this decision was superseded at the July 2024 Committee meeting*). • to maintain the current health-based guideline value of PFOS + PFHxS of 70 ng/L based on developmental effects observed in rats (Luebker et al. 2005), with PFHxS not exceeding 30 ng/L (rounded from 34 ng/L to 1 significant figure) based on thyroid effects observed in rats (NTP 2022)[1] (*note this decision was superseded at the July 2024 Committee meeting*). • to establish a new health-based guideline value for PFBS of 1000 ng/L, equivalent to 1 µg/L (rounded from 1107 mg/L to 1 significant figure) based on thyroid effects observed in mice (Feng et al. 2017). • to not establish a health-based guideline value for GenX chemicals. Members noted that given the limited evidence available, further toxicological information would be needed before Members would be comfortable setting a health-based guideline value for GenX chemicals.
July 2024 Water Quality Advisory Committee meeting	Members agreed: • that the Addendum (SLR 2024c) was of high-quality and that they were comfortable with the revised conclusions for PFOS and PFOA drawn by the reviewer. • that the derivation of a health-based guideline value for PFOA using a threshold approach was appropriate, given that SLR (2024c) found that the overall weight of evidence is that PFOA is not genotoxic. • to adapt the NTP (2023)[2] study in the guideline derivation for PFOA, based on carcinogenicity in rats (pancreatic acinar adenomas and adenocarcinomas). Thus, a new health-based guideline value of 200 ng/L (rounded from 221 ng/L to 1 significant figure) was advised for PFOA. • to adapt the NTP (2022)[1] study in the guideline derivation for PFOS, based on thyroid effects in rats (i.e. decreased T4 and free T4 hormone levels). Thus, a new health-based guideline value of 4 ng/L (rounded from 4.2 ng/L to 1 significant figure) was advised for PFOS (*note this decision was superseded at the October 2024 Committee meeting*).

[1] Note that NTP (2022) is occasionally cited at NTP (2019) in SLR (2024a, 2024b, 2024c). The NTP (2019) report has been revised since initial publication and updated in 2022 (NTP 2022). Minor revisions were made in NTP (2022) from the 2019 report version, all of which are marked up and identified in Appendix F of the NTP (2022) report.

[2] Note that NTP (2023) is occasionally cited as NTP (2020) in SLR (2024a, 2024b, 2024c). The 2020 NTP report has been revised and updated in 2023 (NTP 2023). Minor revisions were made in NTP (2023) from the 2020 report version, all of which are marked up and identified in the NTP (2023) report.

Committee meeting	Members agreed
August 2024 Water Quality Advisory Committee meeting	Members discussed the updated Evidence to Decision Tables that included information from SLR (2024c) and agreed to review and endorse them in preparation for targeted consultation.
September 2024 Water Quality Advisory Committee meeting	Members discussed targeted consultation feedback received from the Department of Health and Aged Care, Food Standards Australia New Zealand (FSANZ) and the enHealth Water Quality Expert Reference Panel. Details on the key issues raised and how these were addressed are provided in **Appendix B.** Representatives from FSANZ attended the meeting to raise concerns about the key studies used to derive health-based guideline values for PFOS and PFOA. FSANZ considers that: • these studies (NTP 2022[1] and NTP 2023[2]) do not provide sufficient scientific justification for changing the current health-based guideline values. • the critical health effects proposed (thyroid effects) are likely to have limited toxicological relevance to humans, and that the established tolerable daily intakes (TDIs) for PFOS and PFOA, based on reproductive/development effects, remain appropriate. Members discussed the concerns raised around the toxicological basis, the choice of studies and endpoints and uncertainty factors in deriving the health-based guideline values. Members agreed: • the thyroid endpoint in the NTP (2022)[1] study should not be used to derive a health-based guideline value for PFOS due to the lack of clinical relevance of observed effects from rats to humans. • to consider the health-based guideline value for PFOA again after SLR Consulting provides further information about the human relevancy of pancreatic acinar adenomas and adenocarcinomas cited in the NTP (2023)[2] study.

Committee meeting	Members agreed
October 2024 Water Quality Advisory Committee meeting	Members discussed the updated evidence reports and preliminary Committee decisions on potential health-based guideline values for PFOS and PFOA. They also confirmed all health-based guideline values for the public consultation draft PFAS guidance. Members agreed: • to adapt the NTP (2022)[1] study in the guideline derivation for PFOS, based on bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) as the critical health effect (endpoint). • that although there were substantial differences between the modelled benchmark dose approach and measured no observed adverse effect levels (NOAELs) (i.e. 29-fold difference in female rats and 5-fold difference in male rats), Members agreed that the former was a more statistically robust approach to use and results in a lower and more conservative guideline value for PFOS (i.e. 3.4 ng/L instead of 77 ng/L) than the NOAEL approach. Members noted that this is consistent with the US EPA (2024c), which also applied the benchmark dose approach when assessing the data from this study. Thus, a new health-based guideline value of 4 ng/L (rounded up from 3.4 ng/L to 1 significant figure) was advised for **PFOS**. • that although there are uncertainties about the clinical relevance of neoplastic pancreatic tumours in rats to humans, these findings could not be completely dismissed in light of in vitro studies that may support a relevant mode of action in humans. Given the classification of PFOA as a Group 1 carcinogen by IARC and the rating by US EPA (2024b) that the NTP (2023) [2] findings were from a high confidence study, Members agreed the neoplastic pancreatic effects observed in the high-quality NTP (2023) [2] study were an appropriately conservative point of departure to derive a health-based guideline value for PFOA of 200 ng/L (rounded from 227 ng/L to 1 significant figure). Members reconfirmed: • that the health-based guideline value for PFHxS should remain separate (i.e. not combined with PFOS) as there is sufficient toxicological information available to establish a new health-based guideline value for PFHxS of 30 ng/L (rounded from 34 ng/L to 1 significant figure), based on thyroid effects observed in rats (NTP 2022)[1]. • to establish a new health-based guideline value for PFBS of 1000 ng/L, equivalent to 1 µg/L (rounded from 1107 mg/L to 1 significant figure) based on thyroid effects observed in mice (Feng et al. 2017). • to not establish a health-based guideline value for GenX chemicals. At this meeting Members advised the CEO to release the draft guidance for public consultation.

Committee meeting	Members agreed
April 2025 Water Quality Advisory Committee Meeting (out-of-session)	Members reviewed and advised on the revised PFAS Fact Sheet and Evidence-to-decision tables (post-consultation versions) in preparation for Independent Expert Review and consultation with the enHealth Water Quality Expert Reference Panel. Members noted the Additional considerations post-consultation (**Appendix F**) and the draft Public Consultation Summary Report (**Appendix E**). Members confirmed the revised health-based guideline value for PFOS of 8 ng/L (revised from the public consultation draft guideline value of 4 ng/L).
8 May 2025 Water Quality Advisory Committee Meeting	Members discussed and advised on feedback from the enHealth Water Quality Expert Reference Panel and the independent expert reviewer on the draft PFAS Fact Sheet and supporting material. Members reviewed and advised on the updated draft PFAS Fact Sheet and supporting material. At this meeting Members advised NHMRC to publish the updated PFAS Fact Sheet in the *Australian Drinking Water Guidelines* (noting NHMRC would also seek approval through the NHMRC Council to recommend to the CEO to publish the updated guidance in the *Australian Drinking Water Guidelines)*.

Council Meeting June 2024 – delegation for public consultation

At its 232nd Session, the Council of NHMRC noted the increased media interest and community concern in response to the April 2024 US EPA PFAS advice and the delay in releasing updated Australian advice. To prevent further delays in delivering updated advice whilst maintaining rigour and confidence in the guideline review process, Council agreed to the following:

- under section 82(2)(b) of the *NHMRC Act 1992* to delegate, to the Water Quality Advisory Committee, Council's specific powers and functions under section 13 of the *NHMRC Act 1992* to provide guidelines to the CEO in respect of the PFAS guidelines including to prepare a draft of those guidelines, to publish a notice on the NHMRC website for the purpose of public consultation on those guidelines, and to consider submissions made in response.
- to advise the Water Quality Advisory Committee to have regard to the advice of the Chief Medical Officer and Chief Health Officers and consumer advisory group prior to issuing the draft PFAS guidance for public consultation.

Drafting of guidance

The NHMRC Project Team drafted an updated PFAS Fact Sheet based on the February 2024 Evidence Evaluation Report and Technical Report, discussions with the Committee and the outcomes of the evidence-to-decision process at the March 2024 meeting. The Chemical

Subgroup reviewed the draft guidance and provided feedback, before the full Committee reviewed and discussed the updated PFAS Fact Sheet at the May 2024 meeting.

The NHMRC Project Team updated the draft PFAS Fact Sheet based on the findings from the additional review (SLR 2024c), discussions with the Committee and outcomes of the evidence-to-decision process at the July 2024 meeting. The Chemical Subgroup and/or full Committee reviewed the draft guidance and provided feedback out of session or during discussion at committee meetings.

NHMRC, with Committee advice, drafted a NHMRC Statement to accompany the draft PFAS Fact Sheet for release during public consultation to explain some key concepts to stakeholders. The purpose of the public consultation NHMRC Statement was to provide a high-level, plain language summary of the guideline values and focus on potential community concerns such as the critical health effects (particularly carcinogenicity of PFOA), and differences in Australian advice to the US EPA approach. The NHMRC Statement also provided some important context around the management of water quality, which is already provided elsewhere in the *Australian Drinking Water Guidelines*. The draft PFAS Fact Sheet, the NHMRC Statement and supporting information underwent targeted consultation, with feedback sought from the enHealth Water Quality Expert Reference Panel, the Department of Health and Aged Care and FSANZ.

Revisions to the draft PFAS Fact Sheet and supporting documents to address feedback from targeted consultation were made with advice from the Committee. SLR Consulting assisted in drafting responses to technical questions and made edits and corrections to the review reports as required before finalising for public consultation.

In response to feedback on the technical basis of the public consultation draft PFOS guideline value, NHMRC engaged SLR Consulting to undertake an additional PFOS assessment to help provide information to address the key issues raised (**Appendix G**). NHMRC, with Committee/ Chemical Subgroup advice, revised the draft PFAS Fact Sheet, including the proposed health-based guideline value for PFOS. With advice from the Committee and feedback received through an independent expert review and targeted consultation with the enHealth Water Quality Expert Reference Panel, minor revisions were made to the draft PFAS Fact Sheet.

A timeline of the overall guideline development process, including key meetings where the project was discussed, is provided in **Table 2**.

Table 2. Timeline of the PFAS Fact Sheet review

Key guidance development steps	Date
Request from Department of Health and Aged Care for NHMRC to prioritise the review of Australian health-based guideline values for PFAS in drinking water.	October 2022
NHMRC Chief Executive Officer (CEO) approved NHMRC to review the Australian health-based guideline values for PFAS.	November 2022

Key guidance development steps	Date
Memorandum of Understanding with the Department of Health and Aged Care for NHMRC to review Australian health-based guideline values for PFAS in drinking water is signed by both agencies.	February 2023
SLR Consulting contracted to undertake an evidence review of existing PFAS guidance/ guidelines.	April 2023
Finalisation of research protocol by SLR Consulting with Committee consultation.	June 2023
Evidence review undertaken by SLR Consulting with draft reports provided to the Committee for comment.	September 2023
Scope of the evidence review amended with advice from the Committee.	December 2023
Finalisation of evidence review by SLR Consulting with draft reports reviewed by the Committee and comments addressed prior to acceptance by NHMRC.	February 2024
Committee consideration of guideline options and evidence-to-decision process for each PFAS.	March 2024
NHMRC drafted updated PFAS guidance with advice from the Committee Chemical Subgroup.	April 2024
Committee advice to undertake an updated evidence evaluation (Addendum to the SLR (2024a, 2024b) review) to consider the April 2024 US EPA advice for PFOA and PFOS and key studies included in Burgoon et al. 2023 and options for a total/sum of PFAS value.	April 2024
Committee and Chemical Subgroup consideration of scope of additional review; NHMRC drafting of procurement documents and NHMRC Executive approval of additional PFAS review.	May-June 2024
Review of draft guidance by the Committee (draft provided to the Council of NHMRC at its 232nd Session).	June 2024
SLR Consulting contracted to undertake additional evidence review. Draft Addendum Report provided to the Committee for comment. Committee consideration of draft Addendum findings and potential guideline options.	July - August 2024

Key guidance development steps	Date
NHMRC updated PFAS guidance with advice from the Committee.	July – August 2024
Targeted consultation on draft updated guidance with enHealth Water Quality Expert Reference Panel, the Department of Health and Aged Care and FSANZ and independent expert review.	September 2024
Collation of targeted consultation feedback and revision to guidance as required with advice from the Committee.	September - October 2024
Chief Medical Officer/Chief Health Officer and consumer representative consideration of draft guidance and supporting materials.	October 2024
Committee advice to NHMRC CEO to release draft PFAS Fact Sheet for public consultation.	October 2024
Public and targeted consultation period.	October – December 2024
NHMRC and Committee review of consultation submissions and revision to guidance as required.	January -March 2025
SLR Consulting contracted to provide additional information to address key comments from consultation.	February – March 2025
Independent expert review and targeted consultation on final guidance with enHealth Water Quality Expert Reference Panel.	April 2025
Finalisation of guidance with advice from the Committee.	May 2025
Advice from NHMRC Council to publish final guidance in Guidelines.	June 2025
NHMRC CEO final approval to publish guidance in Guidelines.	June 2025
Publication of guidance in the *Australian Drinking Water Guidelines*	**June 2025**

enHealth WQERP – Environmental Health Standing Committee Water Quality Expert Reference Panel
FSANZ – Food Standards Australia New Zealand

Water Quality Advisory Committee advice

The NHMRC Water Quality Advisory Committee (the Committee) provides expert advice to NHMRC on public health issues related to drinking water quality. The primary role of the Committee is the rolling review of the Guidelines.

Following the Framework, the Committee provided advice at several meetings during different stages of the review and guideline development processes, including advice on:

- the draft Research Protocol for the evidence evaluation and scope of the additional evidence review
- the draft Evidence Evaluation and Technical Report and Addendum Report (initially through a subgroup of the Committee (the Chemical Subgroup) and then the full Committee)
- the candidate guideline options presented in the evidence review reports and evidence to decision tables
- the draft updated guidance (initially through the Chemical Subgroup and then full Committee)
- responses to address targeted consultation feedback
- final guideline values for public consultation and advice to the CEO to release the draft guidance for public consultation
- consideration of comments received through public and targeted consultation and proposed responses
- final guideline values for publication and advice to the CEO to publish the guidance in the Guidelines.

Targeted consultation

The Environmental Health Standing Committee (enHealth) Water Quality Expert Reference Panel provided expert feedback on the draft guidance in September 2024 and April 2025 before and after public consultation. Panel membership of the enHealth Water Quality Expert Reference Panel includes jurisdictional representatives working in the field of drinking water quality and public health who can provide feedback on the feasibility and accuracy of NHMRC advice.

The Commonwealth Department of Health and Aged Care and FSANZ were also formally consulted on the draft guidance in September 2024 prior to public consultation. Feedback from other Commonwealth agencies was also sought during November-December 2024.

Some common areas of feedback included:

- concerns around the toxicological basis, the choice of studies and endpoints and uncertainty factors in deriving the health-based guideline values
- comments relating to implementation and feasibility of proposed health-based guideline values, and potential compliance issues in some areas near to contaminated areas

- impacts on other PFAS guidance values (e.g. food, soil and land, recreational water) if any proposed changes to NHMRC advice are accepted and adapted by other Australian guidelines or agencies
- information about typical levels of PFAS detected in drinking water and citing recent data from utilities
- technical questions and clarifications about the evidence review reports.

A number of amendments to the draft guidance were made with advice from the Committee as a result of the feedback provided through targeted consultation. Amendments were also made to the evidence review reports by the contractor, SLR Consulting, as a result of feedback received during targeted consultation. A summary of the key issues raised through targeted consultation before public consultation and how these issues were addressed is provided in **Appendix B**.

Prior to publication, the enHealth Water Quality Expert Reference Panel provided feedback on the draft guidance which resulted in minor revisions to the draft Fact Sheet to improve clarity and consistency. A summary of the key issues raised and how these were addressed is also provided in **Appendix B**. The enHealth Water Quality Expert Reference Panel members were supportive of inclusion of the revised PFAS Fact Sheet in the Guidelines.

NHMRC liaised with Commonwealth agencies and provided the revised guidance prior to final publication.

Public Consultation

From 21 October to 22 November 2024 NHMRC accepted public consultation submissions on the draft PFAS Fact Sheet and the public consultation NHMRC Statement. To support the consultation, supplementary material was provided, which included a CEO message, question-and-answer resource, an Administrative Report and the SLR Consulting evidence review reports.

NHMRC received 86 public consultation submissions from 49 individuals and 37 organisations. NHMRC considered all public consultation submissions with advice from the Committee, particularly the Chemical Subgroup. A public consultation summary is available in **Appendix E**.

Full public consultation submissions, where permission has been given to publish, are available on the NHMRC website.

Independent Expert Review

Independent expert review on the draft PFAS guidance was undertaken before, during and after public consultation. This was to provide an additional quality assurance step as advised by the Water Quality Advisory Committee. The purpose of expert review was to seek feedback on whether the evidence evaluation undertaken was sound and reliable and ensure that the evidence had been appropriately synthesised and interpreted. The post-consultation expert review also sought feedback on whether NHMRC gave due regard to comments received through public consultation. Potential expert reviewers were suggested by members of the Committee or identified by NHMRC for their expertise, particularly in the field of PFAS, water quality, toxicology or environmental health/human health risk assessment. Expert reviewers were required to complete a Disclosure of Interests and a Confidentiality Deed Poll, as per NHMRC standard processes.

- Expert review prior to public consultation was undertaken by Adjunct Professor Brian Priestly from the School of Public Health and Preventive Medicine, Monash University.
- Expert review on the public consultation draft guidance was undertaken by Professor Stuart Khan from the School of Civil Engineering, University of Sydney.
- Expert review on the draft guidance following public consultation was undertaken by Emeritus Professor Jack Ng from the Queensland Alliance for Environmental Health Sciences, University of Queensland.

A summary of expert review comments and how they were addressed is provided in **Appendix C**. Disclosure of Interests of expert reviewers is included in **Appendix D**.

The expert review feedback supported a number of revisions to the review reports during the guideline development process. Expert review reports were provided to the Water Quality Advisory Committee to consider when advising on guideline options for public consultation and publication.

Consumer consultation

The Council of NHMRC advised at its 232nd Session that consumer representatives should be consulted prior to releasing the draft guidance for public consultation. Three members of the NHMRC-MRFF Interim Consumer Advisory Network (Ms Ainslie Cahill, Ms Christine Gunson and Adjunct Professor Darryl O'Donnell) provided feedback on the draft supporting material (CEO Message, NHMRC Statement for public consultation and the Question-and-Answer resource).

Consumer consultation feedback was sought to ensure the materials were understandable by the community and addressed community concerns. The consumer representatives found the material was overall well delivered. It was suggested that more clarification and simple language could be used to assist understanding of certain technical terms. Editorial feedback was also received to improve the structure of the text. Where appropriate, NHMRC updated the draft supporting material to reflect the feedback received from the consumer representatives.

After considering feedback from public consultation, NHMRC revised the web-based PFAS Project Page to include more consumer-friendly information to accompany the updated PFAS Fact Sheet. The added consumer information provides a plain language summary with the aim of helping consumers and those who work with communities understand the health risks from PFAS exposure and other key issues. Consumer consultation feedback was sought to ensure the information would be understandable by the community. Where accepted, NHMRC updated the consumer information to reflect the feedback received from the consumer representatives.

Contributors

The Committee had oversight over the development of the updated guidance during its 2022-2025 committee term. Committee membership for this term is outlined below.

Water Quality Advisory Committee (Term from 29 April 2022 to 31 December 2025)

- Professor Nicholas Ashbolt (Chair), Cooperative Research Centre for Solving Antimicrobial Resistance in Agribusiness, Food and Environments, University of South Australia
- Dr David Cunliffe, South Australian Department for Health and Wellbeing
- Mr Cameron Dalgleish, Tasmanian Department of Health
- Professor Cynthia Joll, Curtin Water Quality Research Centre, Curtin University
- Mr Peter Rogers, Water and Public Health Expert
- Ms Nicola Slavin, Northern Territory Department of Health
- Dr Bala Vigneswaran, Water and Public Health Expert
- Associate Professor Harriet Whiley, College of Science and Engineering, Flinders University
- Professor Frederic Leusch, School of Environment and Science, Griffith University (since 2023)
- Dr Nobheetha Jayasekara (Observer), Australian Industrial Chemicals Introduction Scheme (since 2023)
- Mr Laurence Wilson (Observer), National Indigenous Australians Agency
- Dr Sonia Colville (Observer), Department of Climate Change, Energy, Environment and Water (2022 – 2023)
- Mr Adam Lovell (Observer), Water Services Association of Australia (2022 – 2023)
- Ms Yulia Cuthbertson (Observer), Department of Climate Change, Energy, Environment and Water (since 2024).

Chemical Subgroup

Initial review of draft reports, drafting of updated guidance and subsequent revisions were undertaken by Committee members who were part of the Chemical Subgroup.

The following members of the Water Quality Advisory Committee formed the Chemical Subgroup:

- Professor Cynthia Joll (Subgroup Chair), Curtin Water Quality Research Centre, Curtin University
- Mr Cameron Dalgleish, Tasmanian Department of Health
- Professor Frederich Leusch (since 2023), School of Environment and Science, Griffith University.
- Dr David Cunliffe (since 2025), South Australian Department for Health and Wellbeing.

NHMRC Project Team

Project work by NHMRC was undertaken by the Water Team in the Environmental Health Section of the Research Quality and Advice Branch.

Declarations of Interest

Appointees to committees of NHMRC are required to disclose their interests consistent with Section 42A of the Act, and instructions issued under sections 16A and 16B of the Public Governance, Performance and Accountability Rule 2014 (made under subsection 29(2) of the *Public Governance, Performance and Accountability Act 2013*). Prospective members were specifically asked to identify, to the best of their ability, interests including:

- financial interests: an interest must be declared when benefits or losses either in money or in-kind have occurred or may occur at a level that might reasonably be perceived to affect a person's judgement in relation to fair decisions about evidence and their participation in group decision-making
- other relationships: an interest must be declared when a strong position or prejudice or familial connection or other relationship held by a person could reasonably, or be perceived to, affect a person's judgement in relation to fair decisions about evidence and their participation in group decision-making including making an effort to arrive at a consensus
- affiliations to or associations with any organisations or activities that could reasonably be perceived to be an influence due to a competing interest, either for or against the issues being considered by the committee
- any other influences that might reasonably be considered likely to affect the expert judgement of the individual, or lead to the perception by others that the judgement of the individual is compromised.

Under the Public Governance, Performance and Accountability Act 2013, members have a responsibility to declare any interests to the whole committee, and members have a joint responsibility to decide on the management of any perceived or real conflict. No unmanageable conflicts were identified by the Committee or NHMRC.

Throughout the project, members were reminded of their obligation to consider any interest that may have arisen since the last meeting or with any particular agenda items. All disclosures and determinations about interests were recorded in the minutes of the Committee meetings. Members' relevant expertise and a summary of their disclosed interests were accessible on the NHMRC website throughout the duration of the project.

The relevant expertise of the Committee and a summary of their disclosed interests during the term of their membership is at **Appendix D**. Disclosed interests of the independent evidence reviewer (SLR Consulting Australia) and the three independent expert reviewers are also available at **Appendix D**.

Project funding

This work was funded by NHMRC and the Department of Health, Disability and Ageing.

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Appendix A – Evidence-to-Decision Tables

Evidence-to-decision table – Perfluorooctanoic acid (PFOA) (CAS 335-67-1)

The Evidence-to-Decision (EtD) table below is intended to capture key factors and considerations when comparing and deciding on guideline options. NHMRC and the Water Quality Advisory Committee consider potential impacts of different guideline values, but ultimately the decision about the guideline values is based on what is considered the best available health evidence. This is in alignment with NHMRC Standards for Guidelines. Note this table can be updated or amended to capture additional criteria and factors once stakeholder feedback from targeted/public consultation has been received and considered by NHMRC and the Water Quality Advisory Committee.

Note that guideline options presented below are unrounded, pending advice from the Committee. However, the chosen guideline option presented in the fact sheet is rounded as per the rounding conventions described in Chapter 6 of the *Australian Drinking Water Guidelines*.

Table A1. Evidence-to-decision table for PFOA

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
Draft recommendation	*Based on human health considerations, the concentration of PFOA in drinking water should not exceed 560 ng/L (0.56 µg/L).*	*Based on human health considerations, the concentration of PFOA in drinking water should not exceed [value of 9.5 ng/L to 554 ng/L] [0.0095 to 0.55 µg/L].*
Health evidence profile	A review of existing guidance and guidelines found that the current Australian guideline value of 560 ng/L in drinking water is still considered suitable (SLR 2024a, 2024b).	A review of existing guidance and guidelines (SLR 2024a, 2024b, 2024c) identified several potential guideline values ranging from 9.5 to 554 ng/L that were found suitable to potentially adopt/adapt for the Australian context. These candidate guideline options are based on a range of critical health effects in rats and mice that include skeletal alterations,

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
	The current NHMRC health-based guideline value of 560 ng/L was published in August 2018. It is based on a Tolerable Daily Intake (TDI) of 160 ng/kg bodyweight/day (established by FSANZ (2017)) on the basis of a NOAEL for foetal toxicity in a developmental and reproductive study in mice (Lau et al. 2006). The Lau et al. (2006) study underpinning the current guideline value was assessed as high confidence (SLR 2024a, 2024b). An assessment of the study methodology found that it had been conducted according to OECD Test Guidelines that examined a number of standard endpoints with appropriate sample sizes of treated and control groups. A recent review undertaken by an international panel of scientists (Burgoon et al. 2023) also found Lau et al. (2006) to be one of five studies of sufficient quality to derive a guidance value. While the current NHMRC health-based guideline value for PFOA is one of the highest guideline values for PFOA published, it is	liver toxicity, developmental delays, increased relative liver weight, decreased growth rate and pup survival and non-neoplastic hepatocellular necrosis. The lowest proposed guideline option (9.5 ng/L) is a similar order of magnitude to the drinking water guideline value for PFOA set by the US EPA (2024b) of 4 ng/L, although it is noted that the US EPA value is not health-based but based on a practical quantification limit (ability to measure PFOA accurately). The NHMRC review findings suggested that some of the underpinning studies used to derive the potential recent international guideline values are not of high enough quality to warrant revision of the current Australian guideline value for PFOA (SLR 2024a, 2024b, 2024c). The review found that there was low to very low confidence in some of the key studies used in the included potential guideline candidates based on various issues identified in the respective study methodologies. These included limitations such as uncertainty regarding the clinical relevance of the observed health effects to humans, small sample size and a lack of dose response. However, the review found that some of the candidate studies used by US EPA (2024b) and Burgoon et al. (2023) provide appropriate new information to consider revision of the current Australian health-based guideline value for PFOA (SLR 2024c). The additional review (SLR 2024c) found that there was high to medium confidence in several key studies that examined carcinogenicity and immune effects (Butenhoff et al. 2012; Dewitt et al. 2008; NTP 2023). While Butenhoff et al. (2012) and Dewitt et al. (2008) were found to be of medium confidence (SLR 2024c), the NTP (2023) 2-year carcinogenicity and toxicity study referenced by US EPA (2024b) that observed non-neoplastic hepatic necrosis and neoplastic pancreatic effects was considered to have the highest confidence as it is a high-quality study, was conducted appropriately and assessed effects across all developmental

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOA of 560 ng/L *(based on Lau et al. 2006)*	OPTIONS 2 to 10 Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
	considered to be based on a high-quality study (Lau et al. 2006). The point of departure used by NHMRC from Lau et al. (2006) is much higher than those used by other agencies reviewed (SLR 2024a, 2024b, 2024c) who have based their health advice on different critical health endpoints (e.g. non-threshold cancer effects, immunomodulation effects).	life stages (SLR 2024c). The International Agency for Cancer Research (IARC), who have found that PFOA is a Group 1 carcinogen, also cited NTP (2023) as sufficient evidence of cancer in animals in their evaluation (IARC 2025; Zahm et al. 2024). IARC noted a significant positive incidence of pancreatic acinar cell adenoma or adenocarcinoma in rats associated with PFOA exposure. Although SLR (2024c) noted that the acinar pancreatic neoplastic lesions in rats observed in NTP (2023) are unlikely to be relevant to humans due to their probable formation through the rat-specific peroxisome proliferator-activated receptor alpha (PPARα) pathway (SLR 2024c), it was also noted that the formation of the observed pancreatic effects may occur through modes of action other than the PPARα pathway (currently demonstrated in vitro but not in vivo) and so human relevance could not be discounted (SLR 2024c). In addition, while rats are likely more sensitive to the observed liver effects (hepatocellular necrosis) in NTP (2023) than humans, it was considered there was insufficient information to rule out human relevance of this adverse effect at this time (SLR 2024c). Please refer to **Attachments 1 and 2** (below) for the health evidence profile for these guideline options.
Exposure profile	PFOA has been detected at concentrations ranging from detection limit **to 9.7 ng/L** in Australian raw and/or reticulated drinking water supplies (Hunter Water 2024; Power and Water n,d.; QAEHS 2018a, 2018b; Sydney Water 2024; WCWA 2023), including in a study of 33 Australian drinking water samples (Thompson et al. 2011). This maximum concentration slightly exceeds the lowest candidate guideline option of 9.5 ng/L but will be below the other candidate guideline options under consideration. Due to the uncertainty factors and small relative source contribution (RSC) incorporated into the derivation of the candidate guideline options and the existing Australian health-based guideline value, PFOA is unlikely to present a human health risk from most Australian distributed drinking waters that are not impacted by site contamination. Maximum concentrations of PFOA in contaminated residential and private bores has been detected between 20 to	

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
	10,500 ng/L (AECOM 2017a, 2017b; BSC 2021; GHD 2018). Recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS. Current levels detected in Australian drinking water are available on the websites of many Australian water utilities that publish water monitoring data results (e.g. Sydney Water, TasWater). The main factor to consider for exposure to PFAS in drinking water is whether drinking water infrastructure is located in the vicinity of potentially contaminating activities. However, it is noted that low concentrations of PFAS have been detected in water supplies not impacted by contaminated sites. There are many sites of PFAS contamination in Australia, and if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available) exceedances of PFAS guideline levels may occur (SLR 2024a, 2024b).	
Health benefits vs harms	According to the SLR (2024a, 2024b, 2024c) review, the current candidate guideline value option is considered suitable to maintain for guideline derivation as it is underpinned by a high confidence study. However, there may be concerns as the current guideline value is higher than guideline values in other jurisdictions (e.g. USA and Europe) (see values and preferences). There is also more recently published, high quality evidence that is appropriate to consider for revision of the current Australian health-based guideline value for PFOA.	Lower guideline options are more conservative options compared to higher guideline values. However, the choice of guideline option should balance the need for conservatism against the highest quality evidence and whether the health endpoints under consideration (if using animal studies) are relevant and critical to humans. Lowering the guideline value may result in an increase of exceedances detected in communities, and there may be potential harm for people living in PFAS affected communities (e.g. higher psychological distress), if concentrations are nearing these lower guideline values in their areas. See values and preferences.

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
Values and preferences (consumers, communities)	Human exposure to PFAS is an ongoing concern to consumers and communities, particularly to those who live in communities affected by PFAS. PFAS contamination can have a range of consequences for those affected including impacts on property values, produce, income, reputation and risks to health. Findings from the PFAS Health study showed that people living in PFAS affected communities, irrespective of PFAS blood concentrations, are more likely than those who live in comparison areas to experience psychological distress. It is reasonable to assume that consumers and communities, particularly those experiencing the impacts of contamination, would expect that: • supplied drinking water is safe to drink and that PFAS would not be present in drinking water at levels that might cause harm to public health • new/emerging risks to public health from drinking water are considered by NHMRC and appropriate action is taken depending on the risks to public health • that the selected guideline option will be protective of public health. It is likely that consumers and communities (particularly those affected by PFAS contamination) will continue to be risk-averse to the effects of exposure to PFOA. Some groups will expect Australia to follow the lead of international agencies that have adopted very conservative guideline values or used different critical health endpoints. More than half of the submissions received through public consultation on the draft guidance considered that the proposed guideline values were not low enough and proposed that Australia adopt a zero/no safe limit. Some submissions supported the proposed guideline values and the approach adopted. While the findings of the NHMRC review should reassure the public that the health evidence has been considered and why a particular guideline value was chosen, clear and consistent public health messaging and plain language risk communication will still be required to help explain the differences between international jurisdictions, the uncertainty in the evidence and the NHMRC review process.	

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
Acceptability (other key stakeholders)	The recent public and media interest in the potential carcinogenicity of PFOA (based on overseas advice) will mean that this guideline option might not provide enough certainty to stakeholders such as health regulators and water providers about the level of risk from PFOA at concentrations found in Australian distributed drinking waters. Although the health evidence for recent changes in international guidance/guideline values will have been reviewed and critically assessed by NHMRC using best practice review methods for the Australian context, there might be some concerns that NHMRC is not aligning with other international bodies who have decreased their guideline values for PFOA based on other endpoints and more recently published studies if this guideline option is adopted. However, the review demonstrates that this guideline option is based on a study with higher confidence (Lau et al. 2006) compared to most of the other proposed guideline options identified in the review (SLR 2024a, 2024b, 2024c). However, it is noted	The proposed lowered guideline options for PFOA will be more conservative options. The acceptability of these guideline options to stakeholders who implement the Guidelines will be affected by the certainty of the underpinning evidence. Some of the lower guideline options, while inherently more conservative, were found to be underpinned by key studies that were assessed as having low to very low confidence in their study quality. Stakeholders who have higher resource impacts if these guideline options are implemented may find them less acceptable to implement if the justification for a change in practice is based on low quality evidence that has been found to have low certainty. Guideline options that are underpinned by high confidence studies would be more acceptable to stakeholders. Factors that might impact acceptability of lower guideline options for stakeholders include: • increased regulatory burden for health regulators and/or drinking water authorities as more exceedances in drinking water supplies might be detected as a result of lowering the guideline value • monitoring requirements for water providers may increase, especially in contaminated areas • lack of alignment with other international agencies who have established lower health-based guideline values or used different health endpoints. Whilst some organisations supported the draft guideline values proposed at public consultation, comments received from some key stakeholders outlined potential negative economic, financial, regulatory and social impacts such as: • impacts on other guidance values (e.g. recreational water, soil and land, food, organic products, waste management) if any proposed changes to NHMRC advice are

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
	that there is also a high certainty guideline option based on more recently published evidence with critical health effects (neoplastic pancreatic tumours, non-neoplastic liver effects) observed at a lower concentration than current NHMRC advice (NTP 2023; SLR 2024c). A limited number of submissions from public and targeted consultation supported maintaining the current guideline value for PFOA based on their understanding of the health evidence and the potential impacts on other sectors if the point of departure is lowered.	considered, accepted and adapted by other Australian agencies for their specific purposes. • unintended consequence of public fear/stress and anxiety due to proposed conservative values and current and historical exposure to PFAS • circular economy concerns.

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOA of 560 ng/L *(based on Lau et al. 2006)*	OPTIONS 2 to 10 Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
Feasibility	This guideline option is feasible as no changes to current practice are required.	These lower guideline options are technically feasible. According to the SLR (2024a, 2024b) review, the guideline options would be achievable with existing treatment technologies and readily measurable with current commercial analytical techniques. Several commercial laboratories in Australia have confirmed that it is possible to test for the guideline value options (SLR 2024a). As noted in several consultation comments, sampling of PFAS requires special attention to ensure that contamination of samples with PFAS from external sources (e.g. sunscreen, inks, clothing) does not occur. Although existing conventional water treatment technologies do not appear to be particularly effective at removing PFOA from water, the guideline options are/would be achievable if source waters with concentrations below the guideline value are utilised. However, the guideline options may not be achievable for local drinking water supplies in contaminated areas without addition of a PFAS-removal treatment step or use of an alternative water supply.
Health equity impacts	Some of the guideline values under consideration are more conservative than others, and as a result would be considered more protective of public health. These guideline options would be more protective of the general population, including groups that may be more sensitive (e.g. infants, children and pregnant women). This also includes populations who may be more exposed to PFOA based on their proximity to contaminated sites.	
Resource impacts	None. There would be no change in practice if the current guideline value is retained.	All of the guideline options that result in lowering the current guideline value may have resource impacts on the water sector (e.g. effort and investment in sampling collection and analysis and for some utilities, interventions to meet values). The impact of additional costs and effort is likely to be higher for small water utilities, and particularly those in regional and remote Australia; these communities may require funding and other support from all levels of government.

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
		Public consultation comments note that typical limits of reporting (LOR) for the standard PFAS analysis is 10 ng/L, so guideline values under 10 ng/L may require laboratories to use a trace analysis LOR, which may impact investigation and validation timeframes, and increase costs. A decrease in drinking water guidelines may result in increased regulator expectations, requiring substantial upgrades to existing water treatment plants to be able to comply with the new guidelines. This has implications for industry capacity with high upgrade and operational costs. Water providers may have limited capacity to cover these increased costs amid barriers such as financial sustainability, climate change, lack of alternate water supplies and increasing regulation. Lowering the guideline value may result in an increase of exceedances detected in some communities, noting that recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS. Through various reporting obligations, water utilities may need to report these exceedances publicly. Additional monitoring and treatment programs (including infrastructure) may be required to treat drinking water supplies to meet lowered guideline values. The lower the guideline value, the more treatment will be required. Resulting costs for additional treatment of drinking water supplies, investment in appropriate treatment technologies, operations and maintenance and ongoing sampling costs associated with monitoring and/or removal may be borne by local water providers. In some cases, a new water source may need to be developed to meet guideline values. This may have flow on costs to consumers and communities. Public consultation comments noted that for water supplies that do not meet guideline values, consequential treatment upgrades are likely to involve substantial capital investment and time to implement. Examples of costs can be found in American examples such as the

Criteria	OPTION 1: **Maintain the current health-based guideline value for PFOA of 560 ng/L** *(based on Lau et al. 2006)*	OPTIONS 2 to 10 **Lower health-based guideline value for PFOA in drinking water to a guideline value between 9.5 ng/L and 554 ng/L** *(based on either: Abbott et al. 2007; Butenhoff et al. 2012; DeWitt et al. 2008; Koskela et al. 2016; Li et al. 2017; Loveless et al. 2006; NTP 2023; Onishchenko et al. 2011; Song et al. 2018)* (see Attachments 1 and 2 below for details on guideline options for PFOA)
		US EPA paper 'Technologies and costs for removing PFAS from drinking water' and the document 'Estimating the national cost to remove PFAS from drinking water' (Corona Environmental Consulting and Black & Veatch for the American Water Works Association). Water suppliers will also require time and resources to complete any necessary water quality monitoring and pilot treatment studies. Space constraints for any new treatment processes might also be a limitation.

Table A2. Decisions regarding the guideline options by the Water Quality Advisory Committee for PFOA

Decision	Decisions regarding the following guideline options by the Water Quality Advisory Committee are outlined below:
Option 1	While based on a high-quality study, a guideline value of 560 ng/L was not selected as it was no longer considered appropriate given that high quality, recently published evidence was available to set a new, lower guideline value for PFOA in drinking water.
Options 2-6, 8-10	These guideline values were not selected as they were not considered the best available evidence from which to derive a guideline value. The review considered these studies to be of very low, low or medium confidence based on various study limitations, including uncertainty surrounding the clinical relevance of the observed health effects in humans versus animals, small sample sizes and a lack of clear dose-response relationships or serum PFOA data (SLR 2024a, 2024b, 2024c).
Option 7a	The non-neoplastic critical effect of hepatocellular necrosis was not chosen as the point of departure to derive a health-based guideline value for PFOA of 402 ng/L (based on NTP 2023) as the neoplastic effects in option 7b were considered to be the more critical effect resulting in a lower (more conservative) guideline value.
Option 7b	Members noted that although there are uncertainties about the clinical relevance of neoplastic pancreatic tumours in rats to humans, these findings could not be completely dismissed in light of in vitro studies that may support a relevant mode of action in humans. The IARC Monograph (IARC 2025) cited this NTP study (2023) and noted a significant positive incidence of pancreatic acinar cell adenoma or adenocarcinoma in rats associated with PFOA exposure. The results in female rats were consistent with increased incidence of pancreatic acinar cell lesions reported in male rats. NTP (2023) notes this provides some evidence of carcinogenic activity of PFOA, with NTP (2023) cited by IARC (2025) in supporting its evaluation of PFOA as carcinogenic in humans. Given the classification of PFOA as a Group 1 carcinogen by IARC and the rating by US EPA (2024b) that the NTP (2023) findings were from a high confidence study, Members agreed the neoplastic pancreatic effects observed in the high-quality NTP (2023) study were an appropriately conservative point of departure to derive a health-based guideline value for PFOA of 200 ng/L (rounded from 227 ng/L to 1 significant figure).

Attachment 1: PFOA Evidence Profile (extracted from SLR 2024a, 2024b) – to be read in conjunction with Evidence-to-Decision Table

	Option 1	Option 2	Option 3	Option 4	Option 5
Criteria	**Maintain** the current health-based guideline value for PFOA of **560 ng/L**	**Lower the** health-based guideline value for PFOA in drinking water to **70 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **45 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **16 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **9.5 ng/L**
Health evidence profile					
Source of Drinking Water Guideline (DWG)	NHMRC and NRMMC 2011, FSANZ 2017	NJDEP 2019a New Jersey Department of Environmental Protection	MPART 2019 Michigan's PFAS Action Response Team	OEHHA 2019 California Environmental Protection Agency	ATSDR 2021a US Agency for Toxic Substances and Disease Registry
Health-based guidance value (HBGV)	160 ng/kg/day	20 ng/kg/day	12.9 ng/kg/day	4.5 ng/kg/day	2.7 ng/kg/day
Resulting adaption to a Health-based Drinking Water Guideline (DWG)	560 ng/L	70 ng/L	45 ng/L	16 ng/L	9.5 ng/L
Critical study	**Lau et al. 2006** (developmental toxicity study in pregnant mice)	**Loveless et al. 2006** (rats and mice)	**Onishchenko et al. 2011, Koskela et al. 2016** (pregnant mice)	**Li et al. 2017** (mice)	**Koskela et al. 2016** (pregnant mice)
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[3]	**High** proportion	**High** proportion	**Low** proportion (should have); **High** proportion (must have and may have)	**Low** proportion	**High** proportion
Critical Effect	Decreased pre-weaning growth rate in pups.	Increased relative liver weight in male mice.	Developmental delays (decreased number of inactive periods, altered novelty induced activity and skeletal alteration such as bone morphology and bone cell differentiation in the femurs and tibias) of mice.	Liver toxicity (↑ oxidative DNA damage, changes in mitochondrial membrane potential, and ↑ biomarkers of apoptosis in liver of female mice).	Skeletal alterations (i.e. altered femur and tibial bone morphology, ↓ tibial mineral density) in adult mouse offspring.
Confidence in candidate guideline value	**High**	**Low**	**Very low**	**Low**	**Very low**

[3] Refer to Figure 9-1 Evidence Evaluation Report (p70) for more details (SLR 2024a, 2024b). Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the jurisdiction guidance/guideline is at Appendix D of the Technical Report (SLR 2024a, 2024b).

	Option 1	Option 2	Option 3	Option 4	Option 5
	Study appears to have been conducted using a protocol similar to OECD TG 414 (prenatal developmental toxicity study) and examined a large number of standard endpoints[4] in a sufficiently large number of treatment groups and treated animals. The Lau et al. (2006) study was one of five studies used by an international collaboration of scientists (**Burgoon et al. 2023**) to estimate a PFOA guidance value approximately two times lower than the FSANZ (2017) value. More information on this paper, including the differences in the derivation of guidance values using the Lau et al. (2006) study is on p83 of the Evidence Evaluation Report (SLR 2024a, 2024b).	There is uncertainty with respect to the human relevance of the liver effects observed in this study due to the dearth of mode of action information for these effects and suggested human refractoriness for some of these effects. This aligns with the conclusions in the FSANZ (2017) review.	Koskela et al. (2016) study: small animal numbers (n=6 in treated group), only a single treatment group (one PFOA dose level), inadequate reporting of dietary PFOA levels, lack of measured serum PFOA levels and uncertainty with respect to the clinical relevance of the findings. The use of only one PFOA dose level does not allow for the establishment of dose-response relationships. This study limitation is mitigated by the extensive intermediate-duration oral exposure database, which allows for an overall assessment of dose-response. Onishchenko et al. (2011) study: not conducted in accordance with standardised testing guidelines; apparent small absolute differences in effects observed between the treated and control groups.	Potential that the effects on apoptosis observed in male and female mice may not be relevant to humans. It is arguable whether the effects observed at the lowest dose in this study (0.05 mg/kg/day) in female mice can be considered adverse. FSANZ (2017) indicates that humans may be refractory to the liver effects observed in rodents as a result of PFOA exposure.	Refer to limitations for Koskela et al. (2016) in Option 3. Despite the limitations, the outcome does appear to be compelling and, if relevant to humans, could potentially increase the risk of bone fractures later in life (SLR 2024a).

[4] Endocrine disruptor relevant parameters (i.e. anogenital distance in foetuses and thyroid hormones in dams) were only added to the OECD TG in 2018. These endpoints were not included in the Lau et al. (2006) study, since the OECD TG update superseded the conduct and publication of the Lau et al. (2006) study.

Attachment 2: PFOA Evidence Profile (extracted from SLR 2024c) – to be read in conjunction with Evidence-to-Decision Table

	Option 6	Option 7	Option 8	Option 9	Option 10
Criteria	**Lower the** health-based guideline value for PFOA in drinking water to **554 ng/L**	**Lower the** health-based guideline value for PFOA in drinking water to **227 or 402 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **111 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **75 or 172 ng/L**	**Lower** the health-based guideline value for PFOA in drinking water to **63 ng/L**
Health evidence profile					
Source of Drinking Water Guideline (DWG)	US EPA 2024b	US EPA 2024b	Burgoon et al. 2023	US EPA 2024b	US EPA 2024b
Health-based guidance value (HBGV)	158 ng/kg/day	a) 115 ng/kg/day b) 65 ng/kg/day[5]	32 ng/kg/day	a) 21 ng/kg/day b) b) 49 ng/kg/day[6]	18 ng/kg/day
Resulting adaption to a Health-based Drinking Water Guideline (DWG)	554 ng/L	a) 402 ng/L b) 227 ng/L[5]	111 ng/L	a) 75 ng/L b) 172 ng/L[6]	63 ng/L
Critical study	**Butenhoff et al. 2012** (2-year combined chronic toxicity and carcinogenicity rat study)	**NTP 2023** (2-year carcinogenicity and toxicity study in rats)	**Abbott et al. 2007** (developmental toxicity study in pregnant mice)	**Song et al. 2018** (mice study)	**DeWitt et al. 2008** (mice study)
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[7]	**High** proportion	**High** proportion	**High** proportion	**High** proportion	**High** proportion

[5] US EPA (2024b) used the NTP (2023) study to derive a candidate guidance value based on non-neoplastic effects (i.e. liver cell necrosis), however the agency also present benchmark dose modelling for the neoplastic effects (pancreatic acinar adenomas and adenocarcinomas). The $BMDL_{10RD}$ for neoplastic effects has also been presented in this table and used to derive an additional candidate guideline value using the same uncertainty factors used by US EPA (2024b) for the non-neoplastic effects. However, it is recognised that the acinar pancreatic neoplastic lesions are unlikely to be relevant to humans based on currently available information, although they can't be completely dismissed at this time. Although there is uncertainty with respect to the dose at which non-neoplastic hepatic effects may occur in humans and it is recognised by SLR (2024c) that rats are likely more sensitive to this effect that humans, SLR (2024c) considers there is insufficient information to rule out human relevancy of this effect based on currently available information.

[6] The different values provided (a and b) represent the different clearance values and points of departure (POD) used by the US EPA 2024b. The difference for this result is not clear from SLR's reading of the agency documentation. For this reason, both POD_{HED} values are shown in this table. Refer to Section 6.2.9 in Addendum Report (SLR 2024c) for more information.

7 Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the Burgoon et al. 2023 and US EPA 2024b guidance is in Appendix B of the Addendum Report (SLR 2024c).

	Option 6	Option 7	Option 8	Option 9	Option 10
Critical Effect	Microscopic anatomic pathological evidence of hepatotoxicity & Leydig cell tumours.	a) Non-neoplastic: Hepatocellular necrosis b) Neoplastic: Pancreatic acinar adenomas & adenocarcinomas[5]	Decreased mice pup survival.	Decreased mice pup survival.	Reduction in IgM response to sheep red blood cells (SRBC) (7% cf. controls at LOAEL).
Confidence in candidate guideline value	**Medium** Overall, the resulting adapted guideline value is considered to be of medium confidence, as the underpinning study was well-conducted but lacked serum PFOA measurements reported in the study (it is noted US EPA 2024b provided serum data for the study; it is unclear whether this is modelled or measured data).	**High** The NTP 2023 study is a high-quality study and has been conducted appropriately. The US EPA (2024b) also considered the study to be of high confidence. The candidate guideline value resulting from adaption of the US EPA (2024b) candidate guidance value (and POD for non-neoplastic effects) is considered to be of high confidence. The neoplastic effects observed (acinar pancreatic neoplastic lesions) are unlikely to be relevant to humans based on currently available information, however human relevance cannot be entirely discounted (SLR 2024c). The IARC Monograph cited the NTP study (2023) and noted a significant positive incidence of pancreatic acinar cell adenoma or adenocarcinoma in rats associated with PFOA exposure. NTP (2023) notes this provides some evidence of carcinogenic activity of PFOA, with NTP (2023) cited by IARC (2025) in supporting its evaluation of PFOA as carcinogenic in humans.	**Low** The reliability of the Abbott et al. (2007) study for human health risk assessment purposes is considered to be low due to the high background rate of litter loss in the controls, the high level of litter loss at doses greater than 1 mg/kg bw/day, the lack of clear reporting on maternal mortality, the variable statistical power across the different dose groups, the limited descriptions of the study design and the lack of historical control data for the strain of mouse used.	**Low** Considered to be of low confidence as the Song et al. (2018) study focused on specific endpoints of interest in mice, therefore it did not follow standardised protocols for developmental toxicity experiments screening for a larger suite of endpoints. The reported serum PFOA concentration in the paper is also considered unreliable. Although no statistical difference was reported between litter sizes at PND0, statistical analysis of the various endpoints did not include the litter in the model to guard against an inflated Type I error rate.	**Medium** Study appears to have been conducted appropriately and incorporated a recovery phase; it evaluated a number of parameters including immune system markers. There was a clear dose response observed for reduction in IgM response to SRBC in female mice. Thus, the candidate guideline value resulting from adaption of the US EPA (2024b) candidate guidance value (incorporating the use of a NOAEL instead of a $BMDL_{1SD}$ value) is considered to be of medium confidence. US EPA (2024b) also considered the study to be of medium confidence.

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Evidence-to-Decision table – Perfluorooctane sulfonic acid (PFOS) (CAS 1763-23-1)

The Evidence-to-Decision (EtD) table below is intended to capture key factors and considerations when comparing and deciding on guideline options. NHMRC and the Water Quality Advisory Committee consider potential impacts of different guideline values, but ultimately the decision about the guideline values is based on what is considered the best available health evidence. This is in alignment with NHMRC Standards for Guidelines. Note this table can be updated or amended to capture additional criteria and factors once stakeholder feedback from targeted/public consultation has been received and considered by NHMRC and the Water Quality Advisory Committee.

Note that guideline options presented below are unrounded, pending advice by the Committee. However, the chosen guideline option presented in the fact sheet is rounded as per the rounding conventions described in Chapter 6 of the *Australian Drinking Water Guidelines*.

Table A3. Evidence-to-decision table for PFOS

Criteria	OPTION 1a: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 1b: Establish a health-based guideline value for PFOS of 70 ng/L ***(to consider if establishing separate guideline value for PFHxS)*** *(based on Luebker et al. 2005)*	OPTION 2: Establish a separate health-based guideline value for PFOS of 27 ng/L *(based on Zhong et al. 2016)*	OPTION 3: Establish a separate health-based guideline value for PFOS of 95 ng/L *(based on Zhong et al. 2016)*	OPTION 4: Establish a separate health-based guideline value for PFOS of 3.4 ng/L *(based on NTP 2022)*	OPTION 5: - Establish a separate health-based guideline value for PFOS of 77 ng/L *(based on NTP 2022)*	OPTION 6: - Establish a separate health-based guideline value for PFOS of 8.49 ng/L *(based on NTP 2022)*
Draft recommendation	*Based on human health considerations, the sum of the concentrations of PFOS and PFHxS in drinking water should not exceed 70 ng/L (0.07 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 70 ng/L (0.07 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 27 ng/L (0.027 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 95 ng/L (0.095 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 3.4 ng/L (0.0034 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 77 ng/L (0.077 µg/L).*	*Based on human health considerations, the concentration of PFOS in drinking water should not exceed 8.49 ng/L (0.00849 µg/L).*

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Health evidence profile	A review of existing guidance and guidelines (SLR 2024a, 2024b) found that the current Australian guidance value for PFOS of 20 ng/kg/day and guideline value of 70 ng/L are still considered suitable for guideline derivation. It is also considered reasonable to retain the existing guideline value of 70 ng/L as the sum of PFOS and PFHxS; however, it is noted that the retention of the current health-based guideline value for the sum of PFOS and PFHxS should be considered in the context of the available health evidence for PFHxS. The current NHMRC health-based guideline value for the sum of PFOS and PFHxS (70 ng/L) was published in August 2018. It is based on a tolerable daily intake (TDI) of 20 ng/kg bodyweight/day (established by FSANZ (2017)) on the basis of decreased parental and offspring body weight gains in a multigenerational reproductive toxicity study in rats orally exposed to PFOS (Luebker et al. 2005). At that time, FSANZ	A review (SLR 2024a, 2024b) identified ten existing guidance/guidelines for PFOS that were suitable for potential adoption/ adaption in Australia. Of these, two underpinning studies had not been considered by FSANZ in their 2017 evaluation. These were found unsuitable to derive a tolerable daily intake. These were EFSA (2020) and the US EPA (2022c, 2022e) which used two different studies to underpin their guidance derivations: Abraham et al. (2020) (used by EFSA 2020) and Budtz-Jørgensen and Grandjean (2018) (used by US EPA 2022c, 2022e). Based on a brief critical evaluation of these two studies and consistent with the conclusions made by FSANZ (2021), SLR (2024a, 2024b) concluded that a causal relationship between increased PFAS serum levels and impaired vaccine response cannot be established with reasonable confidence from the available human epidemiological information. The evidence for an association between increasing PFAS serum levels and impaired vaccine response was found to be insufficient for the endpoint to be used for derivation of a PFOS health-based guideline value. Although the reduced antibody response following vaccination has been considered by several jurisdictions as the most robust end point based on epidemiological data, it is unclear whether this correlation results in increased rates of infection and hence the clinical implications are uncertain. An additional review (SLR 2024c) of the key studies considered in reviews by US EPA (2024c) and Burgoon et al. (2023) identified several potential guideline values for PFOS ranging from 3.4 ng/L to 95 ng/L that were considered as being suitable to adopt/adapt for the Australian context. These candidate guideline options are based on critical health effects of decreased plaque forming cell responses of splenic cells in four-week-old male mice and bone marrow effects (i.e. extramedullary haematopoiesis and bone marrow hypocellularity) in rats. The additional review findings suggest two candidate studies					

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	concluded that there was insufficient toxicological and epidemiological evidence to justify establishing a TDI for PFHxS. However, it was decided as a precaution and for the purposes of site investigations, the PFOS TDI should apply to PFHxS. In practice, this means that the level of PFHxS exposure should be added to the level of PFOS exposure; and this combined level be compared to the TDI for PFOS. In the absence of a TDI for PFHxS, FSANZ concluded at the time that it was reasonable to consider that the TDI for PFOS is likely to be conservative and protective of human health as an interim measure. The Luebker et al. (2005) study was assessed as high confidence as it was found to be a comprehensive, high-quality study that had been conducted appropriately and investigated a large number of endpoints (SLR 2024a, 2024b, 2024c).	considered by US EPA (2024c), Zhong et al. (2016) and NTP (2022), provide appropriate new information to consider revision of the current Australian health-based guideline value for PFOS. The Zhong et al. (2016) study was assessed as medium confidence as it appears to have been conducted appropriately, albeit it was of a pilot study nature; it evaluated a large number of immune system markers, as well as hormone levels and clinical parameters. There was a clear dose response for parameters of the immune system to be affected in male mice (SLR 2024c). US EPA (2024c) also considered the Zhong et al. (2016) study to be of medium confidence. The NTP (2022) study was assessed as high confidence as it is a comprehensive, high-quality study, has been conducted appropriately and investigated a large number of endpoints (SLR 2024c). US EPA (2024c) also considered the study to be of high confidence. Several different points of departure from the NTP (2022) study were also proposed based on bone marrow effects and whether a serum NOAEL or modelled benchmark dose were applied (SLR 2024c). There was higher confidence by SLR (2024c) in the application of a point of departure derived from a NOAEL identified from measured serum levels in experimental animals (resulting in a guideline value off 77 ng/L), versus a modelled $BMDL_{10}$ used by the US EPA which did not reconcile with experimental serum data and resulted in a guideline value of 3.4 ng/L. SLR (2024c) noted that there was a large (29-fold) difference between the modelled benchmark dose used by US EPA (2024c) and the measured serum no observed adverse effect level (NOAEL) in female rats (SLR 2024c). There was also a 5-fold difference between the modelled benchmark dose used by the US EPA (2024c) and the NOAEL in male rats (SLR 2024c). Further analysis of benchmark dose models considered by the US EPA (US EPA 2024i) demonstrated that there were potential models that had more scientifically robust dose-response curves than the model considered best fit by US EPA					

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	While the current NHMRC health-based guideline value for PFOS is one of the highest guideline values for PFOS published, it is considered to be based on a high-quality study (Luebker et al. 2005). The point of departure used by NHMRC from Luebker et al. (2005) is much higher than those used by other agencies reviewed (SLR 2024a, 2024b, 2024c) who have based their health advice on different critical health endpoints (e.g. non-threshold cancer effects, immune system, spleen effects). A limited number of submissions from public and targeted consultation supported maintaining the current guideline value for PFOS based on their understanding of the health evidence and the potential impacts on other sectors if the point of departure is lowered.	(2024c), with the best available option (Gamma model) resulting in a candidate guideline value of 8 ng/L (rounded). The choice of benchmark dose model was informed by an analysis by SLR Consulting (SLR 2025). Please refer to **Attachment 1** (below) for the health evidence profile for each guideline option.					

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Exposure profile	PFOS has been detected at concentrations ranging from detection limit to 16.4 ng/L in Australian raw and/or reticulated drinking water supplies (Hunter Water 2024; QAEHS 2018a, 2018b; Sydney Water 2024), including in a study of 33 Australian drinking water samples (Thompson et al. 2011). PFOS+PFHxS concentration was at 90% of the Australian health-based guideline value (i.e. ~60 ng/L) in one bore in a drinking water borefield supplying Esperance, Western Australia (SLR 2024a, 2024b). Once this apparent PFOS/PFHxS contamination was identified, this bore was no longer used. SLR (2024a, b) noted that PFOS is unlikely to present a human health risk from most major Australian distributed drinking waters that are not impacted by site contamination. However, it is noted that low concentrations of PFAS have been detected in water supplies not obviously impacted by contaminated sites. This indicates that compliance with the lower candidate health-based guideline value for PFOS (i.e. 3.4 ng/L) may present an issue in certain circumstances. Nevertheless, based on publicly available monitoring information and due to the large uncertainty factors and small relative source contribution of 10% incorporated into the derivation of the candidate health-based guideline value, PFOS is unlikely to present a human health risk from distributed drinking water from most water supplies. In addition, maximum concentrations of PFOS in contaminated residential and private bores has been detected between 80 to 136,000 ng/L (AECOM 2017, 2017b; Bräunig et al. 2017; BSC 2021; GHD 2018). Recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS. Current levels detected in Australian drinking water are available on the websites of many Australian water utilities that publish water monitoring data results (e.g. Sydney Water, TasWater). The main factor to consider for exposure to PFAS in drinking water is whether drinking water infrastructure is located in the vicinity of potentially contaminating activities. There are many sites of PFAS contamination in Australia, and if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), exceedances of PFAS guideline levels may occur (SLR 2024a, 2024b).						

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Health benefits vs harms	According to the SLR (2024a, 2024b, 2024c) review, these guideline options are still considered suitable for guideline value derivation as they are underpinned by a high confidence study. However, it is noted that if a separate guideline value for PFHxS is established (see PFHxS Evidence to Decision table), and the health-based guideline value for PFOS remains at 70 ng/L, it would potentially raise the allowable amount of PFOS and PFHxS in drinking water to an overall higher concentration of 104 ng/L (i.e. if a guideline value of 34 ng/L for PFHxS is established).		Lower guideline options are more conservative options compared to higher guideline values. However, the choice of guideline option should balance the need for conservatism against the highest quality evidence and whether the health endpoints under consideration (if using animal studies) are most relevant and critical to humans. Lowering the guideline value may result in an increase of exceedances detected in communities, and there may be potential harm for people living in PFAS affected communities (e.g. higher psychological distress), if concentrations are nearing or over the lower guideline values in their areas. See values and preferences.				
Values and preferences	Human exposure to PFAS is an ongoing concern to consumers and communities, particularly to those who live in communities affected by PFAS. PFAS contamination can have a range of consequences for those affected including impacts on property values, produce, income, reputation and risks to						

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(consumers, communities)	health. Findings from the PFAS Health study showed that people living in PFAS affected communities, irrespective of PFAS blood concentrations, are more likely than those who live in comparison areas to experience psychological distress. It is reasonable to assume that consumers and communities, particularly those experiencing the impacts of contamination, would expect that: • supplied drinking water is safe to drink and that PFAS would not be present in drinking water at levels that might cause harm to public health • new/emerging risks to public health from drinking water are considered by NHMRC and appropriate action is taken depending on the risks to public health • that the selected guideline option will be protective of public health. It is likely that consumers and communities (particularly those affected by PFAS contamination) will continue to be risk-averse to the effects of exposure to PFOS. While the findings of the NHMRC review should reassure the public that the health evidence has been considered and why a particular guideline value was chosen, there is likely to be ongoing concern from some groups if Australian advice doesn't completely align with other international agencies that have adopted more conservative guideline values or used different critical health endpoints. More than half of the submissions received through public consultation on the draft guidance considered that the proposed guideline values were not low enough and proposed that Australia adopt a zero/no safe limit. Some submissions supported the proposed guideline values and the approach adopted. Clear and consistent public health messaging and risk communication, including explanations about the differences between international jurisdictions, guideline value derivations and the NHMRC review process, could help explain these issues to consumers and reassure them about Australian processes.						
Acceptability (other key stakeholders)	The recent public and media interest in the potential health effects of PFOS will mean that this guideline option (representing no change in the level of PFOS) might not	The acceptability of these guideline options to stakeholders who implement the Guidelines will be affected by the certainty of the underpinning evidence. Some of the proposed guideline options were found to be underpinned by key studies that were assessed as having medium confidence in their study quality, or low confidence in the methods used to derive a point of departure. Stakeholders who have					

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	provide enough certainty to stakeholders such as health regulators and water providers about the level of risk from PFOS at concentrations found in Australian distributed drinking waters. Although the health evidence for recent changes in international guidance/guideline values will have been reviewed and critically assessed by NHMRC using best practice review methods for the Australian context, there might be some concerns that NHMRC is not aligning with other international bodies who have decreased their guideline values for PFOS based on other endpoints and more recently published studies if this guideline option is adopted. However, the review demonstrates that this guideline option is based on a study with higher confidence (Luebker et al. 2005) compared to most of the other proposed guideline options identified in the review (SLR 2024a, 2024b, 2024c). However, it is noted that there is also a high certainty guideline option based	higher resource impacts if these guideline options are implemented may find them less acceptable to implement if the justification for a change in practice is based on low quality evidence that has been found to have low certainty. Guideline options that are underpinned by high confidence studies would be more acceptable to stakeholders. Factors that might impact acceptability of lower guideline options for stakeholders include: • increased regulatory burden for health regulators and/or drinking water authorities as more exceedances in drinking water supplies might be detected as a result of lowering the guideline value • monitoring requirements for water providers may increase, especially in contaminated areas • lack of alignment with other international agencies who have established lower health-based guideline values or used different health endpoints. Whilst some organisations supported the draft guideline values proposed at public consultation, comments received from some key stakeholders outlined potential negative economic, financial, regulatory and social impacts such as: • impacts on other guidance values (e.g. recreational water, soil and land, food, organic products, waste management) if any proposed changes to NHMRC advice are considered, accepted and adapted by other Australian agencies for their specific purposes. • unintended consequence of public fear/stress and anxiety due to proposed conservative values and current and historical exposure to PFAS. • circular economy concerns.					

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	on more recently published evidence based on bone marrow effects in rats (i.e. extramedullary haematopoiesis and bone marrow hypocellularity) (NTP 2022; SLR 2024c). While establishing a separate guideline value for PFOS is considered appropriate, stakeholders such as consumers and health regulators may find this option less acceptable, as it would potentially raise the overall concentration of PFOS and PFHxS allowable in drinking water from 70 to 104 ng/L based on the sum of their separate health-based guideline values (i.e. 70 ng/L PFOS and 34 ng/L PFHxS = 104 ng/L PFOS+PFHxS).						
Feasibility	These guideline options are feasible as no changes to current practice are required.	These guideline options, including lower guideline options as used by some international jurisdictions, are technically feasible. Several commercial laboratories in Australia have confirmed that it is possible to test for the guideline value options (SLR 2024a). As noted in several consultation comments, sampling of PFAS requires special attention to ensure that contamination of samples with PFAS from external sources (e.g. sunscreen, inks, clothing) does not occur. Although existing conventional water treatment technologies do not appear to be particularly effective at removing PFOS from water, lower guideline options would be achievable if source waters with concentrations below the guideline value are utilised.					

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Health equity impacts	Some of the guideline values under consideration are more conservative than others, and as a result would be considered more protective of public health. These guideline options would be more protective of the general population, including groups that may be more sensitive (e.g. infants, children and pregnant women). This also includes populations who may be more exposed to PFOS based on their proximity to contaminated sites.						
Resource impacts	None. There would be no change in practice if the current guideline value is retained. Setting a separate health-based guideline value for PFOS is unlikely to have resource impacts on the water sector as PFOS and PFHxS are currently measured separately (then reported together).	All of the guideline options that result in lowering the current guideline value may have resource impacts on the water sector (e.g. effort and investment in sample collection and analysis and, for some utilities, interventions to meet guideline values). The impact of additional costs and effort is likely to be higher for small water utilities, and particularly those in regional and remote Australia; these communities may require funding and other support from all levels of government. Public consultation comments note that the standard PFAS analysis is typically 10 ng/L, so guideline values under 10 ng/L may require laboratories to use a trace analysis limit of reporting (LOR), which can impact investigation and validation timeframes, and increase costs. A decrease in drinking water guidelines may result in increased regulator expectations, requiring substantial upgrades to existing water treatment plants to comply with the new guidelines. This has implications for industry capacity, with high upgrade and operational costs. Water providers may have limited capacity to cover increased costs amid barriers such as financial sustainability, climate change, lack of alternate water supplies and increasing regulation. Lowering the guideline value may result in an increase of exceedances detected in some communities, noting that recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS. Through various reporting obligations, water utilities may need to report these exceedances publicly. Additional monitoring and treatment programs (including infrastructure) may be required to treat drinking water supplies to meet lowered guideline values. The lower the guideline value, the more treatment will be required.					

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			Resulting costs for additional treatment of drinking water supplies, investment in appropriate treatment technologies, operations and maintenance and ongoing sampling costs associated with monitoring and/or removal may be borne by local water providers. In some cases, a new water source may need to be developed to meet guideline values. This may have flow on costs to consumers and communities. Public consultation comments noted that for water supplies that do not meet guideline values, consequential treatment upgrades are likely to involve substantial capital investment and time to implement. Examples of costs can be found in American examples such as the US EPA paper 'Technologies and costs for removing PFAS from drinking water' and the document 'Estimating the national cost to remove PFAS from drinking water' (Corona Environmental Consulting and Black & Veatch for the American Water Works Association. Water suppliers will also require time and resources to complete any necessary water quality monitoring and pilot treatment studies. Space constraints for any new treatment processes might also be a limitation.					

Table A4. Decisions regarding the guideline options by the Water Quality Advisory Committee for PFOS

Decision	Decisions regarding the following guideline options by the Water Quality Advisory Committee are outlined below:
Option 1a	A sum of PFOS and PFHxS of 70 ng/L was not selected as it was no longer considered appropriate given that sufficient evidence was available to set separate guideline values for PFOS and PFHxS.
Option 1b	The guideline option of 70 ng/L (based on Luebker et al. *2005)* was not re-selected for guideline derivation, as a guideline option based on a more recently published, high-quality study was available (NTP 2022) to set a more conservative guideline value for PFOS.
Options 2 and 3	The guideline options of 27 and 95 ng/L underpinned by Zhong et al. (2017) were not selected for guideline derivation as guideline options underpinned by higher certainty evidence were available.
Option 4	The guideline option of 3.4 ng/L (rounded to 4 ng/L for public consultation) was not re-selected for guideline derivation for final publication. While Members agreed that the bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) observed in NTP (2022) were the most critical health effects and the best point of departure to derive a guideline value for PFOS, this guideline option was not considered to be the best available guideline option following consideration of feedback from public and targeted consultation and further analysis of available benchmark dose models (SLR 2025). It was considered best practice to prioritise the model with the smallest difference between observed data points and the fitted model values (i.e. lowest scaled residuals). This was determined to be the Gamma model with a $BMDL_{10}$ of 5.688 mg/L (resulting in a guideline value of 8 ng/L – see Option 6 below) (SLR 2025). Although it was noted there were substantial differences between the modelled benchmark dose approach and measured no observed adverse effect levels (NOAELs) (i.e. 29-fold difference in female rats and 5-fold difference in male rats), the former was considered to be a more statistically robust approach than the No Observed Adverse Effect Level (NOAEL) approach. This is consistent with the US EPA (2024c), which also applied the benchmark dose approach when assessing the data from this study.
Option 5	The guideline option of 77 ng/L (based on NTP 2022) was not selected as the health-based guideline value for PFOS as this would raise the current guideline value (to 80 ng/L rounded to 1 significant figure) and a lower, more conservative guideline value for PFOS was available.
Option 6	Members agreed that the bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) observed in NTP (2022) were the most critical health effects and the best point of departure to derive a health-based guideline value for PFOS of 8 ng/L (rounded from 8.49 ng/L to 1 significant figure). The $BMDL_{10}$ of 5.688 mg/L was used to derive the health-based guideline value for PFOS, which was derived from the Gamma dose-response model prioritised in an additional PFOS assessment by SLR Consulting (SLR 2025). Members confirmed using a benchmark dose approach to derive a guideline value for PFOS, noting that it is considered to be a more statistically robust approach to use a benchmark dose rather than a NOAEL to derive a guideline value. Of the two approaches, the use of the modelled $BMDL_{10}$ led to a calculation of a lower guideline value. This is consistent with the US EPA (2024c), which also applied the benchmark dose approach when assessing the data from this study. However, the US EPA chose a different model (the Multistage 1 model rather than the Gamma model chosen by the Water Quality Advisory Committee). As noted in the SLR 2025 Additional PFOS Assessment, the Multistage 1 model chosen by US EPA had the highest scaled residual (which shows the greatest difference between the expected dose and the measured data) and was inconsistent with the US EPA (2012) Technical Guidance on how to select a benchmark dose model.

Attachment 1: PFOS Evidence Profile (extracted from SLR 2024a, 2024b, 2024c) – to be read in conjunction with Evidence-to-Decision Table

	Option 1	Option 2	Option 3	Option 4	Option 5	Option 6
Criteria	**Maintain** the current health-based guideline value for PFOS of **70 ng/L**	**Lower** the health-based guideline value for PFOS in drinking water to 27 **ng/L**	**Raise** the health-based guideline value for PFOS in drinking water to **95 ng/L**	**Lower** the health-based guideline value for PFOS in drinking water to **3.4 ng/L**	**Raise** the health-based guideline value for PFOS in drinking water to **77 ng/L**	**Lower** the health-based guideline value for PFOS in drinking water to **8.49 ng/L**
	Health evidence profile					
Source of Drinking Water Guideline (DWG)	NHMRC and NRMMC 2011, FSANZ 2017	US EPA 2024c	US EPA 2024c	US EPA 2024c	US EPA 2024c	US EPA 2024c
Health-based guidance value (HBGV)	20 ng/kg/day (rounded up from 17)	7.7 ng/kg/day[8] (from $BMDL_{1SD}$)	27 ng/kg/day[8] (from serum NOAEL)	1 ng/kg/day[9] (from $BMDL_{10}$)	22 ng/kg/day[9] (from serum NOAEL)	2.4 ng/kg/day[10] (from $BMDL_{10}$)
Resulting adaption to a Health-based Drinking Water Guideline (DWG)	70 ng/L	27 ng/L	95 ng/L	3.4 ng/L	77 ng/L	8.49 ng/L
Critical study	**Luebker et al. 2005** (developmental toxicity study in pregnant rats)	**Zhong et al. 2016** (mice)		**NTP 2022** (rats)		

[8] Due to the relatively wide range of potential $BMDL_{1\,SD}$ values derived by US EPA (2024c) using different benchmark dose models, it is considered appropriate to use the experimental measured serum NOAEL as the POD for adaption of the US EPA (2024c) values for the Australian context. The value that would result from using the $BMDL_{1\,SD}$ value from US EPA (2024c) is considered to be of lower confidence.

[9] The most sensitive effect from the NTP (2022) study is considered to be extramedullary haematopoiesis and bone marrow hypocellularity, as used by US EPA (2024c). Nevertheless, there are large discrepancies between the US EPA (2024c) estimated $BMDL_{10}$ (2.3 mg/L in female rats, 9.6 mg/L in male rats) and the lowest experimental serum NOAEL achieved in the study (66.97 mg/L in female rats, 51.56 mg/L in male rats), i.e. a 29-fold difference in females, and a 5-fold difference in males. It may therefore be less uncertain to use the measured serum NOAEL from the study as a POD for the critical effects, Thus, higher confidence is placed in the health-based guidance value derived using the experimental NOAEL.

[10] To help address comments received from public/targeted consultation, an analysis of the benchmark dose for the endpoint of increased incidence of decreased extramedullary haematopoiesis in the spleen in female Sprague-Dawley rats was undertaken (SLR 2025), reproducing the methodology in the US EPA Appendix: Human Health Toxicity Assessment for PFOS (US EPA 2024i). This analysis, using US EPA's online BMDS tool, found best practice would be to prioritise the Gamma model with a $BMDL_{10}$ of 5.688 mg/L (SLR 2025).

	Option 1	Option 2	Option 3	Option 4	Option 5	Option 6
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[11]	**High** proportion	**High** proportion		**High** proportion		
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[12]	**High** proportion	**High** proportion		**High** proportion		
Critical Effect	Decreased body weight gain and food consumption in F0 generation (parental toxicity); significant decreased pup weight and weight gain during lactation (offspring toxicity).	15% decreased plaque forming cell responses (i.e. sheep red blood cell-specific IgM production by B-lymphocytes) of splenic cells in 4-week-old male pups (effect seemed to recover at eight weeks of age).		Extramedullary haematopoiesis and bone marrow hypocellularity		
Confidence in candidate guideline value	**High** The study appears to have been conducted appropriately, was designed to examine a sensitive effect (i.e. multigeneration study testing relatively large numbers of dose groups and low dose ranges), reported effects as relative to litter, reported serum PFOS concentrations in adults and pups, and examined a large number of endpoints at multiple time points in multiple dose groups.	**Medium** The study appears to have been conducted appropriately, albeit it was of a pilot study nature; it evaluated a large number of immune system markers, as well as hormone levels and clinical parameters. There was a clear dose response for parameters of the immune system to be affected in male mice. US EPA (2024c) also considered the study to be of medium confidence.		**High** This is a comprehensive, high-quality study, has been conducted appropriately and investigated a large number of endpoints. US EPA (2024c) considered the study to be of high confidence.		

[11] Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the FSANZ 2017/NHMRC guidance/guideline is at Appendix D of the Technical Report, and in Appendix B of the Addendum Report for the US EPA (2024c) guidance.

[12] Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the FSANZ 2017/NHMRC guidance/guideline is at Appendix D of the Technical Report, and in Appendix B of the Addendum Report for the US EPA (2024c) guidance.

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Evidence-to-Decision table – Perfluorohexane sulfonic acid (PFHxS) (CAS 355-46-4)

The Evidence-to-Decision (EtD) table below is intended to capture key factors and considerations when comparing and deciding on guideline options. NHMRC and the Water Quality Advisory Committee consider potential impacts of different guideline values, but ultimately the decision about the guideline values is based on what is considered the best available health evidence. This is in alignment with NHMRC Standards for Guidelines. Note this table can be updated or amended to capture additional criteria and factors once stakeholder feedback from targeted/public consultation has been received and considered by NHMRC and the Water Quality Advisory Committee.

Note that guideline options presented below are unrounded, pending advice from the Committee. However, the chosen guideline option presented in the fact sheet is rounded as per the rounding conventions described in Chapter 6 of the *Australian Drinking Water Guidelines*.

Table A5. Evidence-to-decision table for PFHxS

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
Draft recommendation	*Based on human health considerations, the sum of the concentrations of PFOS and PFHxS in drinking water should not exceed 70 ng/L (0.07 µg/L).*	*Based on human health considerations, the sum of the concentrations of PFOS and PFHxS in drinking water should not exceed 70 ng/L (0.07 µg/L), with the concentration of PFHxS not exceeding 34 ng/L (0.034 µg/L).*	*Based on human health considerations, the concentration of PFHxS in drinking water should not exceed 34 ng/L (0.034 µg/L).*	*Based on human health considerations, the sum of the concentrations of PFOS and PFHxS in drinking water should not exceed 70 ng/L (0.07 µg/L), with the concentration of PFHxS not exceeding 8.5 ng/L (0.0085 µg/L).*

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
Health evidence profile (refer to Attachment 1 below for details on each option)	The SLR (2024a, 2024b) review found that the current Australian guideline value for the sum of PFOS and PFHxS of 70 ng/L in drinking water continues to be considered suitable for guideline derivation. The current NHMRC health-based guideline value of 70 ng/L was published in August 2018. At that time, FSANZ concluded that there was insufficient toxicological and epidemiological evidence to justify establishing a tolerable daily intake (TDI) for PFHxS. However, as a precaution, and for the purposes of site investigations, the PFOS TDI should apply to PFHxS. In practice, this means that the level of PFHxS exposure	The SLR (2024a, 2024b) review found that it is reasonable to retain the existing guideline value of 70 ng/L as the sum of PFOS+PFHxS, with PFHxS not exceeding 34 ng/L. Numerous international jurisdictions have derived drinking water guideline values based on different critical health endpoints (some of which are clearly adverse but others which are not necessarily adverse) in animal studies and human epidemiological studies. Three US State jurisdictions (Minnesota-MDH 2020, Michigan-MPART 2019 and California-OEHHA 2022) all derived a guideline value for PFHxS based on decreased thyroxine (T4) in rats. The critical study underpinning this	The SLR (2024a, b) review found that the value of 34 ng/L for PFHxS is suitable for guideline derivation. The review noted that some jurisdictions (e.g. OEHHA, MPART) have a separate guideline value for PFHxS, whilst other jurisdictions (e.g. US EPA, Massachusetts, EU) use a sum of PFAS where PFHxS is included. This option impacts the guideline value for PFOS. If a separate guideline value for PFHxS is established, and the health-based guideline value for PFOS remains at 70 ng/L, it would potentially raise the current sum of PFOS and PFHxS to an overall higher allowable concentration in drinking water of 104 ng/L	Although this guideline option of 8.5 ng/L has been provided as a potential candidate health-based guideline value to adopt/adapt, it is not considered most relevant to the Australian context in terms of selection of uncertainty factors (UFs) and endpoints. Although based on the same study (NTP 2022), it has used the UF composite of 1000, rather than the UF composite of 300 (considered to be suitable for guideline derivation) used by MDH and MPART to derive a drinking water guideline value of 34 ng/L. More information can be found in the PFHxS Evidence profile at Attachment 1 below.

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
	should be added to the level of PFOS exposure; and this combined level be compared to the TDI for PFOS. In the absence of a TDI for PFHxS, FSANZ concluded at that time that it was reasonable to consider that the TDI for PFOS is likely to be conservative and protective of human health as an interim measure.	derivation is NTP (2022), and according to the SLR (2024a, 2024b) review, provided appropriate new information to potentially adopt/adapt for derivation of candidate guidance/guideline values for PFHxS, as the study evaluated a large number of endpoints, provided serum PFHxS concentrations and was conducted in accordance with relevant standardised testing guidelines. More information can be found in the PFHxS Evidence profile at Attachment 1 below.	(i.e. 70 ng/L PFOS and 34 ng/L PFHxS = 104 ng/L PFOS+PFHxS). It is noted that decreases in thyroid hormones in rodent toxicology studies are generally not considered clinically relevant to humans without a compensatory increase in thyroid-stimulating hormone (TSH) or changes to the pituitary gland observed (SLR 2024a, 2024b). However, evidence of effects of thyroid histopathology in rats was observed by Butenhoff et al. (2009) at higher serum PFHxS concentrations. Associations between PFAS exposure and thyroid hormone status were also observed in some human epidemiological studies (e.g. Ballesteros et al. 2017; Boesen	

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
			et al. 2020; Coperchini et al. 2021). On this basis it is concluded that consideration of the potential human relevancy of the thyroid hormone changes observed in the 28-day NTP (2022) study with PFHxS is appropriate.	
Exposure profile	PFHxS has been detected at concentrations ranging from detection limit to 19.1 ng/L in Australian raw and/or reticulated drinking water supplies (QAEHS 2018a, 2018b; Sydney Water 2024; WCWA 2023), including in a study of 33 Australian drinking water samples (Thompson et al. 2011). This range of concentrations are below all the candidate health-based guideline values, except option 4. However, PFOS+PFHxS concentration was at 90% of the current Australian health-based guideline value (i.e. ~60 ng/L) in one bore in a drinking water borefield supplying Esperance, Western Australia (SLR 2024a, 2024b). Once this apparent PFOS/PFHxS contamination was identified, this bore was no longer used. This indicates that compliance with the candidate health-based guideline values for PFHxS may present an issue in certain circumstances. Nevertheless, due to the large uncertainty factors and small relative source contribution of 10% incorporated into the derivation of the candidate health-based guideline value, PFHxS is unlikely to present a human health risk from distributed drinking water in most regions of Australia. However, there are many sites of PFAS contamination in Australia, and, if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), PFHxS may be present at concentrations greater than the candidate health-based guideline value and the existing Australian health-based guideline value in these cases (SLR 2024a, 2024b). Maximum concentrations of PFHxS in contaminated residential and private bores have been detected between 130 to 54,300 ng/L (AECOM 2017a, 2017b; Bräunig et al. 2017; BSC 2021; GHD 2018). Recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS.			

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
	Current levels detected in Australian drinking water is available on the website of many Australian water utilities that publish water monitoring data results (e.g. Sydney Water, TasWater). The main factor to consider for exposure to PFAS in drinking water is whether drinking water infrastructure is located in the vicinity of potentially contaminating activities. There are many sites of PFAS contamination in Australia, and if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), exceedances of PFAS guideline levels may occur (SLR 2024a, 2024b).			
Health benefits vs harms	According to the SLR (2024a, 2024b) review, this guideline option is considered suitable for guideline value derivation; however, it is noted that a high quality, recently published study is available for consideration to set a separate guideline value for PFHxS.	According to the SLR (2024a, 2024b) review, this guideline option is considered suitable for guideline derivation as it is underpinned by a high confidence study. Including a separate guideline value for PFHxS may help build awareness and drive health research in this area for this chemical.	This option is considered suitable for guideline derivation, however, may have impacts on the guideline value for PFOS and the total sum of both chemicals.	This guideline option is more conservative and protective of health; however, the derivation for this option is not considered most relevant to the Australian context (see evidence profile at **Attachment 1**).
Values and preferences (consumers, communities)	Human exposure to PFAS is an ongoing concern to consumers and communities, particularly to those who live in communities affected by PFAS. PFAS contamination can have a range of consequences for those affected including impacts on property values, produce, income, reputation and risks to health. Findings from the PFAS Health study showed that people living in PFAS affected communities, irrespective of PFAS blood concentrations, are more likely than those who live in comparison areas to experience psychological distress.			

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
	It is reasonable to assume that consumers and communities, particularly those experiencing the impacts of contamination, would expect that: • supplied drinking water is safe to drink and that PFAS would not be present in drinking water at levels that might cause harm to public health • new/emerging risks to public health from drinking water are considered by NHMRC and appropriate action is taken depending on the risks to public health • that the selected guideline option will be protective of public health. It is likely that consumers and communities (particularly those affected by PFAS contamination) will continue to be risk-averse to the effects of exposure to PFHxS. Some groups will expect Australia to follow the lead of international agencies that have adopted more conservative guideline values or used different critical health endpoints. More than half of the submissions received through public consultation on the draft guidance considered that the proposed guideline values were not low enough and proposed that Australia adopt a zero/no safe limit. Some submissions supported the proposed guideline values and the approach adopted. While the findings of the NHMRC review should reassure the public that the health evidence has been considered and why a particular guideline value was chosen, clear and consistent public health messaging and plain language risk communication will be required to help explain the differences between international jurisdictions, the difference in guideline value derivation calculations and the NHMRC review process.			
Acceptability (other key stakeholders)	The recent public and media interest in the potential health effects of PFAS will mean that this guideline option might not provide enough certainty to stakeholders such as health	Establishing a separate guideline value for PFHxS will provide some confidence to stakeholders about safe levels of PFHxS in drinking water given that new information is now	While establishing a separate guideline value for PFHxS (34 ng/L) is considered suitable, stakeholders such as health regulators may find this option less acceptable if the	See Option 2. This is the more conservative option. However, as the review (SLR 2024a, 2024b) found the derivation of this candidate

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
	regulators and water providers about the level of risk from PFHxS at concentrations found in Australian distributed drinking waters. Although the health evidence for recent changes in international guidance/ guideline values will have been reviewed and critically assessed by NHMRC using best practice review methods for the Australian context, there might be some concerns that NHMRC is not aligning with other international bodies who have decreased their guideline values for PFHxS based on other endpoints if this guideline option is adopted. However, it is noted that there is a high-quality guideline option based on more recently published	available to derive a guideline value. Factors that might impact acceptability for stakeholders if a separate guideline value for PFHxS is established include: • Potential increased monitoring requirements (especially in contaminated areas) may be less acceptable to water providers given that levels of PFHxS in typical drinking water supplies in Australia have not previously presented health risks (noting that there is limited data available) • potential increased regulatory burden for health regulators and/or drinking water authorities as a result of increasing monitoring requirements.	guideline value for PFOS remained at 70 ng/L, as it would potentially raise the overall concentration of PFOS and PFHxS allowable in drinking water from 70 to 104 ng/L based on the sum of their separate health-based guideline values. Refer to Option 2 for factors that might impact acceptability for stakeholders if a guideline value is established for PHFxS.	guideline value as not as relevant in the Australian context, stakeholders who implement the Guidelines will likely find this option less acceptable. Guideline options that are underpinned by high confidence studies would be more acceptable to stakeholders.

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
	evidence for thyroid effects (NTP 2022; SLR 2024a, 2024b).	Given that the health evidence for recent changes in international guidance/guideline values will have been reviewed and critically assessed by NHMRC using best practice review methods for the Australian context, this guideline option should provide certainty to stakeholders such as health regulators and water providers that PFHxS at concentrations found in Australian distributed drinking waters is unlikely to present a human health risk.		
Feasibility	This guideline option is feasible as no changes to current practice are required.	Establishing a guideline value for PFHxS is technically feasible. According to the SLR (2024a, 2024b) review, the candidate guideline options would be achievable with existing treatment technologies and readily measurable with current commercial analytical techniques. Several commercial laboratories in Australia have confirmed that it is possible to test for the guideline value options (SLR 2024a). As noted in several consultation comments, sampling of PFAS requires special attention to ensure that contamination of samples with PFAS from external sources (e.g. sunscreen, inks, clothing) does not occur. Although existing conventional water treatment technologies do not appear to be particularly effective at removing PFAS from water, the guideline options are/would be achievable if source		

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
		waters with concentrations below the guideline value are utilised. However, the guideline options may not be achievable for local drinking water supplies in contaminated areas without addition of a PFAS-removal treatment step or use of an alternative water supply.		
Health equity impacts	Some of the guideline values under consideration are more conservative than others, and as a result would be considered more protective of public health. These guideline options would be more protective of the general population, including groups that may be more sensitive (e.g. infants, children and pregnant women). This also includes populations who may be more exposed to PFHxS based on their proximity to contaminated sites.			
Resource impacts	None. There would be no change in practice if the current guideline value is retained.	Establishing a separate guideline value for PFHxS may have resource impacts on the water sector (e.g. effort and investment in sampling collection and analysis and for some utilities, interventions to meet values)., however this is unlikely as PFHxS and PFOS are currently measured individually. The impact of additional costs and effort is likely to be higher for small water utilities, and particularly those in regional and remote Australia; these communities may require funding and other support from all levels of government. Public consultation comments note that the standard PFAS analysis is typically 10 ng/L, so guideline values under 10 ng/L may require laboratories to use a trace analysis limit of reporting (LOR), which can impact investigation and validation timeframes, and increase costs. A decrease in drinking water guidelines may result in increased regulator expectations, requiring substantial upgrades to existing water treatment plants to comply with the new guidelines. This has implications for industry capacity, with high upgrade and operational costs. Water providers may have limited capacity to cover increased costs amid barriers such as financial sustainability, climate change, lack of alternate water supplies and increasing regulation. Establishing a guideline value may result in an increase of exceedances detected in some communities, noting that recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS.		

Criteria	OPTION 1: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L *(based on Luebker et al. 2005)*	OPTION 2: Maintain the current health-based guideline value for PFOS + PFHxS of 70 ng/L, with PFHxS not exceeding 34 ng/L *(based on Luebker et al. 2005; NTP 2022)*	OPTION 3: Establish a new health-based guideline value for PFHxS of 34 ng/L *(based on NTP 2022)*	OPTION 4: Establish a new health-based guideline value for PFHxS of 8.5 ng/L *(based on NTP 2022)*
		Through various reporting obligations, water utilities may need to report these exceedances publicly. Additional monitoring and treatment programs (including infrastructure) may be required to treat drinking water supplies to meet guideline values. However, this may only be an issue if using contaminated water supplies, which are not advised to be used. The lower the guideline value, the more treatment will be required. Resulting costs for additional treatment of drinking water supplies, investment in appropriate treatment technologies, operations and maintenance and ongoing sampling costs associated with monitoring and/or removal may be borne by local water providers. In some cases, a new water source may need to be developed to meet guideline values. This may have flow on costs to consumers and communities. Public consultation comments noted that for water supplies that do not meet guideline values, consequential treatment upgrades are likely to involve substantial capital investment and time to implement. Examples of costs can be found in American examples such as the US EPA paper 'Technologies and costs for removing PFAS from drinking water' and the document 'Estimating the national cost to remove PFAS from drinking water' (Corona Environmental Consulting and Black & Veatch for the American Water Works Association. Water suppliers will also require time and resources to complete any necessary water quality monitoring and pilot treatment studies. Space constraints for any new treatment processes might also be a limitation.		

Table A6. Decisions regarding the guideline options by the Water Quality Advisory Committee for PFHxS

Decision	Decisions regarding the following guideline options by the Water Quality Advisory Committee are outlined below:
Option 1	A sum of PFOS and PFHxS of 70 ng/L was not selected as it was no longer considered appropriate given that sufficient evidence was available to set a separate guideline value for PFHxS.
Option 2	A sum of PFOS and PFHxS of 70 ng/L with PFHxS not exceeding 34 ng/L was not selected as it was no longer considered appropriate given that sufficient evidence was available to set a separate guideline value for PFHxS.
Option 3	Members agreed that there was sufficient toxicological information available to establish a health-based guideline value for PFHxS of 30 ng/L (rounded from 34 ng/L to 1 significant figure) based on thyroid effects observed in rats (NTP 2022). It is noted that whilst it would be ideal to use chronic studies to derive the guideline value for PFHxS, in lieu of available chronic studies, the 28-day NTP (2022) study used to underpin the guideline value for PFHxS is the best available evidence at this time.
Option 4	The guideline option of 8.5 ng/L (based on NTP 2022) was not selected for guideline derivation as it was not considered to be the most relevant option for the Australian context in terms of selection of uncertainty factors and endpoints.

Attachment 1: PFHxS Evidence Profile (extracted from SLR 2024a, 2024b) – to be read in conjunction with Evidence-to-Decision Table

	Option 1	Option 2		Option 3	Option 4
Criteria	**Maintain** the current health-based guideline value for PFOS + PFHxS of **70 ng/L**	**Maintain** the current health-based guideline value for PFOS + PFHxS of **70 ng/L,** with PFHxS not exceeding **34 ng/L**		**Establish a new** health-based guideline value for PFHxS of **34 ng/L**	**Establish a new** guideline value for PFHxS of **8.5 ng/L**
Source of Drinking Water Guideline (DWG)	NHMRC and NRMMC 2011, FSANZ 2017	MDH 2020b Minnesota Department of Health	MPART 2019 Michigan's PFAS Action Response Team	MDH 2020b MPART 2019	OEHHA 2022 California Environmental Protection Agency
Health-based guidance value (HBGV)	20 ng/kg/day (rounded up from 17)	9.7 ng/kg/day	9.7 ng/kg/day	9.7 ng/kg/day	2.4 ng/kg/day
Resulting adaption to a Health-based Drinking Water Guideline (DWG)	70 ng/L (sum of PFOS+PFHxS)	34 ng/L	34 ng/L	34 ng/L	8.5 ng/L[13]
Critical study	**Luebker et al. 2005** (rats)	**NTP 2022** (toxicity study in rats)			
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[14]	**High** proportion	**Low** proportion	**Low** proportion (should have); **High** proportion (must have and may have)		**High** proportion
Critical Effect	Decreased bodyweight gain & food consumption in parental generation; decreased pup weight & weight gain during lactation (offspring toxicity).	Decreased T4 (thyroxine) in male rats			

[13] Although based on same study (NTP 2022), the difference in value (8.5 to 34) is due to the application of an additional uncertainty factor (UF) - overall composite UF of 1,000 vs 300. However, UF of 300 is considered health protective (refer to p59 of the Evidence Evaluation Report (SLR 2024a, 2024b) for more details).

[14] Refer to Figure 7-1 Evidence Evaluation Report (p55) for more details (SLR 2024a, 2024b). Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the jurisdiction guidance/guideline is at Appendix D of the Technical Report (SLR 2024a, 2024b).

	Option 1	Option 2	Option 3	Option 4
Other comments/ information		The SLR (2024a, 2024b) review noted that in general, the effects in male and female rats administered PFHxS were of lower magnitude (e.g. liver or clinical pathology findings) or not apparent compared to the effects in rats exposed to PFBS and PFOS. Some effects were observed in the liver, however noted to potentially not be relevant to humans. However, the relevance of effects in other organ systems can't be discounted. SLR (2024a, 2024b) noted the uncertainty with respect to human relevancy of the observed thyroid effects based on currently available information and the potential conservatism in any resulting guidance value. It was concluded that potential human relevancy of the thyroid hormone changes observed in the 28-day NTP (2022) study with PFHxS cannot be discounted based on currently available information and in the absence of chronic studies. According to the SLR (2024a, 2024b) review, because the NTP (2022) study was conducted in accordance with relevant standardised testing guidelines, evaluated a large number of endpoints, and provided serum PFHxS concentrations, it is concluded to be appropriate new information to potentially adopt/adapt for derivation of candidate guidance/guideline values for PFHxS.		Although this DWG value of 8.5 ng/L has been provided as a potential candidate option to adapt/adopt, it is not considered most relevant to the Australian context in terms of selection of uncertainty factors (UFs) and endpoints. Although based on same study (NTP 2022), it has used the UF composite of 1000, rather than the UF composite of 300 (considered to be health protective) used by MDH and MPART to derive DWG of 34 ng/L.

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Evidence-to-Decision table – Perfluorobutane sulfonic acid (PFBS) (CAS 375-73-5)

The Evidence-to-Decision (EtD) table below is intended to capture key factors and considerations when comparing and deciding on guideline options. NHMRC and the Water Quality Advisory Committee consider potential impacts of different guideline values, but ultimately the decision about the guideline values is based on what is considered the best available health evidence. This is in alignment with NHMRC Standards for Guidelines. Note this table can be updated or amended to capture additional criteria and factors once stakeholder feedback from targeted/public consultation has been received and considered by NHMRC and the Water Quality Advisory Committee.

Note that guideline options presented below are unrounded, pending advice by the Committee. However, the chosen guideline option presented in the fact sheet is rounded as per the rounding conventions described in Chapter 6 of the *Australian Drinking Water Guidelines.*

Table A7. Evidence-to-decision table for PFBS

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
Draft recommendation	*No health-based guideline value is proposed for PFBS.* *PFBS in drinking water would not be a health concern unless concentrations exceeded 1,041 ng/L.*	*Based on human health considerations, the concentration of PFBS in drinking water should not exceed [value of 1,041 ng/L to 2,939 ng/L] [1.04 to 2.94 µg/L].*
Health evidence profile	A review was conducted to identify existing sources of national/international guidance or guidelines on the impact of exposure to PFBS in drinking water on human health outcomes (SLR 2024a, 2024b). The SLR (2024a, 2024b) review found that overt adverse health effects from drinking water exposure to PFBS in humans have not been explicitly recorded in any of the existing guidance/guidelines found suitable to adopt/adapt. However, numerous jurisdictions have derived drinking water guideline values based on different critical health endpoints from animal studies. Where drinking water guideline values have been derived for PFBS, the jurisdictions have agreed that the most sensitive health endpoint is decreased total thyroxine (T4) hormone levels in animal studies (rats). The SLR (2024a, 2024b) review identified reliable toxicological evidence to derive health-based guideline values ranging from **1,041 to 2,939 ng/L**. These potential guideline options were considered as being suitable to adopt/adapt for the Australian context. These candidate guideline options are based on the critical health effect in mice of decreased total thyroxine (T4) hormone levels in female rat	

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
	offspring on postnatal day 1 (Feng et al. 2017; NTP 2022). These values are also likely conservative due to time of serum collection after the last administered dose; due to the short half-life of PFBS, serum concentrations in dams in both studies may have been 2-3x higher directly after administration of the last dose. Using higher serum concentrations to derive guidance values would also result in higher (i.e. less stringent) guideline values. While the NTP (2022) study was conducted in accordance with relevant standardised testing guidelines and evaluated a large number of endpoints, Feng et al. (2017) was considered to be the best available study as it was considered to have been conducted appropriately and evaluated more sensitive endpoints of interest (i.e. female reproductive performance and developmental effects) (SLR 2024a, 2024b). There is some uncertainty with respect to the human relevancy of the observed thyroid effects in the key studies based on currently available information. The decreased T4 and T3 observed in the NTP (2022) study in rats administered PFBS was not accompanied by increased TSH or thyroid histopathological findings. However, it was noted that a developmental/reproductive toxicity study in mice by Feng et al. (2017) also found decreased T3 and T4 levels at postnatal day 30 which were accompanied by slight but statistically increased serum TSH. As there is a lack of chronic toxicity studies with PFBS, and the Feng et al. (2017) study found increased TSH accompanied the decreased T3 and T4 levels, it is concluded that the potential human relevancy of this effect for PFBS cannot be discounted based on currently available information. Please refer to **Attachment 1** below for the health evidence profile for more details on these guideline options.	
Exposure profile	PFBS concentrations of up to **2.2 ng/L** have been found in Queensland drinking water source waters (QAEHS 2018a, 2018b). There are few PFBS data in drinking water elsewhere in Australia. From the limited amount of literature identified in the public domain from the SLR review (2024a, 2024b), the levels of PFBS in Australian distributed drinking water concentrations are at the low end of concentrations observed in various international jurisdictions (including the US and parts of Europe). Maximum concentrations of PFBS in contaminated residential and private bores has been detected between 40 to 6,520 ng/L (AECOM 2017a, 2017b; GHD 2018). Recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of	

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
	PFAS. Current levels detected in Australian drinking water is available on the website of many Australian water utilities that publish water monitoring data results (e.g. Sydney Water, TasWater). Based on the limited data available, provided drinking water catchments are protected from PFBS contamination and alternative water supplies are available if PFBS contamination is identified, it appears that PFBS concentrations in distributed drinking water in Australia are markedly lower than any of the candidate health-based guideline values, suggesting PFBS is unlikely to present a human health risk from distributed drinking water in Australia. However, there are many sites of PFAS contamination in Australia, and, if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), PFBS may be present at concentrations above the candidate health-based guideline values in these cases. The main factor to consider for exposure to PFAS in drinking water is whether drinking water infrastructure is located in the vicinity of potentially contaminating activities. There are many sites of PFAS contamination in Australia, and if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), exceedances of PFAS guideline levels may occur (SLR 2024a, 2024b).	
Health benefits vs harms	Given the limited data/information regarding levels of PFBS in Australian distributed drinking water, it is uncertain whether this guideline option will be protective of public health or not given that there is high quality evidence available demonstrating potential health effects. Information in the PFAS Fact Sheet including uncertainties around actual risks may help build awareness and drive health research in this area. Providing information on a level where health effects might be expected to occur for PFBS may help protect public health in the absence of data/information regarding PFBS chemical levels in Australian distributed drinking water. It may also allow	Establishing a health-based guideline value for PFBS may allow for the generation of datasets to help clarify the level of risk to consumers.

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
	the generation of datasets to help clarify the level of risk to consumers as the health-based target can be used in site investigations and monitoring of water supplies where needed.	
Values and preferences (consumers, communities)	Human exposure to PFAS is an ongoing concern to consumers and communities, particularly to those who live in communities affected by PFAS. For some, knowing that their community is affected by PFAS may increase stress and worry. PFAS contamination can have a range of consequences for those affected including impacts on property values, produce, income, reputation and risks to health. Findings from the PFAS Health study showed that people living in PFAS affected communities, irrespective of PFAS blood concentrations, are more likely than those who live in comparison areas to experience psychological distress. It is reasonable to assume that consumers and communities, particularly those experiencing the impacts of contamination, would expect that: • supplied drinking water is safe to drink and that PFAS would not be present in drinking water at levels that might cause harm to public health • new/emerging risks to public health from drinking water are considered by NHMRC and appropriate action is taken depending on the risks to public health • that the selected guideline option will be protective of public health. It is likely that consumers and communities (particularly those affected by PFAS contamination) will continue to be risk-averse to the effects of exposure to PFAS, including PFBS. To NHMRC's knowledge, consumers have not previously raised concerns specifically about PFBS in drinking water supplies. While the findings of the recent NHMRC evidence review should reassure the public that the health evidence has been considered and why a particular guideline value was chosen, there is likely to be ongoing concern from some groups that Australian advice doesn't align with other international jurisdictions such as the US EPA if a guideline value for PFBS isn't adopted. In addition, there might be an expectation from communities that all PFAS are equally toxic and that guideline values will be derived for all PFAS that are found in Australia.	

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
	More than half of the submissions received through public consultation on the draft guidance considered that the proposed guideline values were not low enough and proposed that Australia adopt a zero/no safe limit. Some submissions supported the proposed guideline values and the approach adopted. Clear and consistent public health messaging and risk communication, including explanations about the differences between international jurisdictions, guideline value derivations and the review process, could help explain these issues to consumers and reassure them about Australian processes.	
Acceptability (other key stakeholders)	Given that the health evidence has been reviewed and potential candidate guideline options proposed, if this guideline option is adopted, there might be some concerns that NHMRC is not following other international agencies (e.g. Health Canada, EFSA, US EPA, some US States) that have established similar drinking water guideline values for PFBS. Inclusion of information on the level at which health effects might be expected to occur for PFBS chemicals in drinking water might be a more acceptable guideline option to water providers as it provides a health-based target for PFBS chemicals for use in site investigations if needed.	Options to establish a health-based guideline value for PFBS will provide some confidence to stakeholders about safe levels of PFBS in drinking water given that new information is available from which to derive a guideline value, so might be more acceptable from the health protection perspective. Factors that might impact acceptability for stakeholders if a guideline value is established include: • increased testing requirements as a new health-based guideline value may be embedded in the testing requirements for ISO 21675:2019. • increased monitoring requirements may be less acceptable to water providers given that levels of PFBS in typical drinking water supplies in Australia have not previously presented health risks (noting that there is limited data available) • increased regulatory burden for health regulators and/or drinking water authorities as a result of increasing monitoring requirements.

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
Feasibility	This guideline option is feasible as no changes to current practice are required.	Establishing a guideline value for PFBS is technically feasible. As noted in 'Exposure Profile' above, PFBS concentrations in distributed drinking water in Australia are markedly lower than any of the candidate health-based guideline values. However, the guideline options may not be achievable for local drinking water supplies in contaminated areas without addition of a PFAS-removal treatment step or use of an alternative water supply. According to the SLR (2024a, 2024b) review, the proposed guideline options would be achievable with existing treatment technologies and readily measurable with current commercial analytical techniques. Several commercial laboratories in Australia have confirmed that it is possible to test for the guideline value options (SLR 2024a). As noted in several consultation comments, sampling of PFAS requires special attention to ensure that contamination of samples with PFAS from external sources (e.g. sunscreen, inks, clothing) does not occur.
Health equity impacts	Some of the guideline values under consideration are more conservative than others, and as a result would be considered more protective of public health. These guideline options would be more protective of the general population, including groups that may be more sensitive (e.g. infants, children and pregnant women). This also includes populations who may be more exposed to PFBS based on their proximity to contaminated sites.	
Resource impacts	Providing information about a potential level of concern or a health-based target instead of a guideline value for PFBS	Establishing a guideline value for PFBS may have resource impacts on the water sector (e.g. effort and investment in sampling collection and

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
	chemicals may have potential resource impacts if routine monitoring is introduced at specific sites based on the level of risk. This guideline option will likely have less overall resource impacts than establishing a health-based guideline value which will be more broadly implemented. The use of a health-based target will allow for site-specific monitoring of water supplies that might pose the highest risk.	analysis and for some utilities, interventions to meet a new value). Resources may be required to monitor and test for PFBS in water supplies if a new guideline value for PFBS is introduced in the Guidelines. The impact of additional costs and effort is likely to be higher for small water utilities, and particularly those in regional and remote Australia; these communities may require funding and other support from all levels of government. Water providers may have limited capacity to cover increased operational costs amid barriers such as financial sustainability, climate change, lack of alternate water supplies and increasing regulation Establishing a guideline value may result in an increase of exceedances detected in some communities, noting that recent monitoring activities across Australia have demonstrated that most Australian distributed drinking water supplies contain low or negligible concentrations of PFAS. Through various reporting obligations water utilities may need to report these exceedances publicly. Additional monitoring and treatment programs (including infrastructure) may be required to treat drinking water supplies to meet guideline values. However, this may only be an issue if using contaminated water supplies, which are not advised to be used. The lower the guideline value, the more treatment will be required. Resulting costs for additional treatment of drinking water supplies, investment in appropriate treatment technologies, operations and maintenance and ongoing sampling costs associated with monitoring and/or removal may be borne by local water providers. In some cases, a new water source may need to be developed to meet guideline values. This may have flow on costs to consumers and communities.

Criteria	OPTION 1: - Maintain status quo (no health-based guideline value for PFBS)	OPTIONS 2, 3, 4, 5 - Establish health-based guideline value for PFBS in drinking water to a guideline value between 1,041 ng/L and 2,939 ng/L *(based on either: Feng et al. 2017; NTP 2022)* (see Attachment 1 below for more information on guideline options for PFBS)
		Public consultation comments noted that for water supplies that do not meet guideline values, consequential treatment upgrades are likely to involve substantial capital investment and time to implement. Examples of costs can be found in American examples such as the US EPA paper 'Technologies and costs for removing PFAS from drinking water' and the document 'Estimating the national cost to remove PFAS from drinking water' (Corona Environmental Consulting and Black & Veatch for the American Water Works Association. Water suppliers will also require time and resources to complete any necessary water quality monitoring and pilot treatment studies. Space constraints for any new treatment processes might also be a limitation.

Table A8. Decisions regarding the guideline options by the Water Quality Advisory Committee for PFBS

Decision	Decisions regarding the following guideline options by the Water Quality Advisory Committee are outlined below:
Option 1	Not setting a guideline value for PFBS was not considered appropriate given that sufficient evidence was available to set a separate guideline value for PFBS.
Option 2	This option was not considered appropriate as the decreased T4 and T3 observed in the NTP (2022) study in rats administered PFBS was not accompanied by increased TSH or thyroid histopathological findings (as observed in Feng et al. 2017). This indicates there is uncertainty with respect to the human relevancy of the effect based on currently available information from this study.
Option 3	Members were less comfortable with a guideline value of 2000 ng/L compared to 1000 ng/L as this option incorporated a smaller uncertainty factor and therefore a more conservative guideline value of 1000 ng/L also had a higher margin of safety.
Option 4	Members agreed to establish a new health-based guideline value for PFBS of 1000 ng/L, equivalent to 1 µg/L (rounded from 1107 mg/L to 1 significant figure) based on thyroid effects observed in mice (Feng et al. 2017). The clinical relevance of the observed decreases in thyroid hormones to humans were supported by these effects being accompanied by a small but statistically significant increase in TSH in mice exposed to PFBS in Feng et al. (2017) (SLR 2024a, 2024b). It is noted that whilst it would be ideal to use chronic studies to derive a guideline value for PFBS, in lieu of available chronic studies, the 60-day toxicity study in mice by Feng et al. (2017) used to underpin the guideline value for PFBS is the best available evidence at this time.
Option 5	Members agreed that this particular endpoint is similar to Option 4 and would end up at the same value of 1000 ng/L with rounding.

Attachment 1: PFBS Evidence Profile (extracted from SLR 2024a, 2024b) – to be read in conjunction with Evidence-to-Decision Table

	Option 1	Option 2	Option 3	Option 4	Option 5
Criteria	**Maintain** status quo (no health-based guideline value for PFBS)	**Establish new** health-based guideline value for PFBS in drinking water of **2,939 ng/L**	**Establish new** health-based guideline value for PFBS in drinking water of **2,252 ng/L**	**Establish new** health-based guideline value for PFBS in drinking water of **1,107 ng/L**	**Establish new** health-based guideline value for PFBS in drinking water of **1,041 ng/L**
Health evidence profile					
Source of Drinking Water Guideline (DWG)	N/A – PFBS not considered by FSANZ 2017	MDH 2022e, g Minnesota Department of Health	OEHHA 2021 Office of Environmental Health Hazard Assessment (OEHHA). California Environmental Protection Agency.	US EPA 2022c, 2022k United States Environmental Protection Agency	MPART 2019 Michigan's PFAS Action Response Team WSDH 2019a, 2022b, 2023a Washington State Department of Health
Health-based guidance value (HBGV)	n/a	86 ng/kg/day (840)[15] ng/kg/day	643 ng/kg/day	316 ng/kg/day	297 ng/kg/day
Resulting adaption to a Health-based Drinking Water Guideline (DWG)	n/a	302 (2,939) ng/L	2,252 ng/L	1,107 ng/L	1,041 ng/L
Critical study	n/a	**NTP (2022)** (rats-toxicology study)	**Feng et al. (2017)** (mice – toxicology study)		
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[16]	n/a	**Low** proportion (must and should have) **High** proportion (may have) MDH 2022g	**High** proportion (must and may have) **Low** proportion (should have)	**High** proportion US EPA 2021c	**Low** proportion (should have); **High** proportion (must and may have) MPART 2019
Critical Effect	n/a	Decreased thyroxine (T4) hormone levels in female rats	Decreased total T4 in female rat offspring on postnatal day (PND) PND1		

[15] Two values are provided to indicate the different half-life assumptions used by MDH 2022 compared to NTP (2022) in the derivation. If the half-lives cited in the NTP (2022) study were used, the toxicokinetic adjustment factor, which is very sensitive to the input half-lives assumed for female rats and humans, would change (an order of magnitude difference). The values in brackets are those that would result from using the half-lives cited by NTP (2022). See Section 8.2.1, p63 and Table 8-1, p68-69 of the Evidence Evaluation Report for details (SLR 2024a, 2024b).

[16] Refer to Figure 8-1 Evidence Evaluation Report (p62) for more details (SLR 2024a, 2024b). Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the jurisdiction guidance/guideline is at Appendix D of the Technical Report (SLR 2024a, 2024b).

	Option 1	Option 2	Option 3	Option 4	Option 5
Confidence in candidate guideline value	n/a	As the study was conducted in accordance with relevant standardised testing guidelines and evaluated a large number of endpoints, it is concluded to be appropriate information to potentially adopt/adapt for derivation of candidate guidance/ guideline values for PFBS. It is noted that OEHHA (2021d) considered both the NTP (2022) and Feng et al. (2017) studies for deriving a TRV but **decided against using the NTP (2022) study** because of the large toxicokinetic differences between female rats and humans, and uncertainty around the utility of the rat model for effects in humans of maternal thyroid hormone disruption on foetal development.	As the study was peer reviewed, appears to have been conducted appropriately and evaluated relatively sensitive endpoints of interest (female reproductive performance and developmental effects); it is concluded to be appropriate information to potentially adopt/adapt for derivation of candidate guidance/guideline values for PFBS. The decreased T4 and T3 observed in the NTP (2022) study in rats administered PFBS was not accompanied by increased TSH or thyroid histopathological findings. This indicates there is uncertainty with respect to the human relevancy of the effect based on currently available information. Nevertheless, it is noted that a developmental/ reproductive toxicity study in mice by Feng et al. (2017) also found decreased T3 and T4 levels at postnatal day 30 which were accompanied by slight but statistically increased serum TSH. As there is a lack of chronic toxicity studies with PFBS, and the Feng et al. (2017) study found increased TSH accompanied the decreased T3 and T4 levels, it is concluded that the potential human relevancy of this effect for PFBS cannot be discounted based on currently available information.		

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Evidence-to-Decision table – GenX chemicals - hexafluoropropylene oxide ammonium salt (CAS No 62037-80-3) plus hexafluoropropylene oxide dimer acid (CAS No 13252-13-6)

The Evidence-to-Decision (EtD) table below is intended to capture key factors and considerations when comparing and deciding on guideline options. NHMRC and the Water Quality Advisory Committee consider potential impacts of different guideline values, but ultimately the decision about the guideline values is based on what is considered the best available health evidence. This is in alignment with NHMRC Standards for Guidelines. Note this table can be updated or amended to capture additional criteria and factors once stakeholder feedback from targeted/public consultation has been received and considered by NHMRC and the Water Quality Advisory Committee.

Note that guideline options presented below are unrounded, pending advice from the Committee. However, the chosen guideline option presented in the fact sheet is rounded as per the rounding conventions described in Chapter 6 of the *Australian Drinking Water Guidelines*.

Table A9. Evidence-to-decision table for GenX chemicals

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Draft recommendation	*No health-based guideline value is proposed for GenX chemicals.*	*No health-based guideline value is proposed for GenX chemicals.* *GenX chemicals in drinking water would not be a health concern unless concentrations exceeded [12 or 263 ng/L].*	*Based on human health considerations, the concentration of Gen X chemicals in drinking water should not exceed [12 or 263 ng/L] [0.012 or 0.26 µg/L].*

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Health evidence profile	A review of existing sources of national/ international guidance or guidelines found that there is currently insufficient health evidence to derive a health-based guideline value for GenX chemicals in drinking water (SLR 2024a, 2024b). Most jurisdictions that were reviewed have not set a guideline value for GenX chemicals in drinking water. Several guidance/guidelines set by agencies in the United States were found suitable to adopt/adapt based on administrative and technical processes assessed in the review. However, these were found to be informed by a single industry-funded study (Dupont 2010), which may affect the quality of the study due to conflict of interest and risk of bias. It is uncertain if this option will be protective of health given that no information on levels of GenX chemicals in Australian water supplies were identified in the review.	Although the SLR (2024a, 2024b) review found insufficient evidence to derive a health-based guideline value for GenX chemicals, a concentration of potential concern (12 or 263 ng/L) can be derived based on the limited toxicity data available. According to the review, overt adverse health effects from drinking water exposure to GenX chemicals in humans were not explicitly recorded in any of the existing guidance/guidelines found suitable to adopt/adapt. However, where drinking water guideline values have been derived for GenX chemicals in the United States, the relevant agencies agreed that the most sensitive health endpoint is liver effects (increased absolute and relative liver weight and histopathological changes in the liver) from a single unpublished reproductive/ developmental toxicity study in mice (DuPont 2010). The difference in the different levels of concern under consideration (12 vs 263 ng/L) is a result of adopting uncertainty	See health evidence profile for guideline option 2. It is uncertain if this guideline option will be protective of health as there is only one unpublished toxicological study available on which to base a candidate health-based guideline value. While the US EPA and other agencies in the United States have found the study suitable to use for deriving drinking water guideline values, there are some methodological issues, including potential risk of bias and the need for the source evidence to be publicly available.

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
		factors used by MPART (2019) or the US EPA (2021, 2022). The US EPA applies higher uncertainty factors for study timeframe and limited database (i.e. a UF of 10 instead of 3 applied by MPART (2019)), resulting in a much lower guideline value of 12 ng/L. According to the findings of the review, using higher uncertainty factors for both study timeframes and databases is not considered warranted. As a result, the lower guideline option (12 ng/L) was found to be less relevant to the Australian context. While the US EPA (2021e, 2022c) and other agencies found that the Dupont (2010) study was well conducted, there are some concerns about the study methods, such as a lack of transparency regarding the source evidence and potential risk of bias (e.g. confounding issues with the purity of the chemical tested, industry funding).	

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Exposure profile	The SLR (2024a, 2024b) review found that concentrations of GenX chemicals in overseas distributed drinking waters (<5 ng/L) are much lower than the concentrations of potential concern. No information regarding GenX chemical levels in Australian distributed drinking water was identified from the literature retrieved. While the import and industrial use of GenX chemicals in Australia has not been approved through the Australian Industrial Chemicals Introduction Scheme, it is possible that these chemicals may be present in Australia as trace residues in/on products that may end up in landfill and leach into water supplies at low levels. It is unknown whether GenX chemicals are present in Australia at concentrations lower or higher than the candidate health-based guideline values. It is suggested additional research is needed to determine whether GenX chemicals are found in any Australian source waters or drinking waters, which would also inform whether a health-based guideline value is required.		
Health benefits vs harms	Given the lack of data/information regarding GenX chemical levels in Australian distributed drinking water, it is uncertain whether this guideline option will be protective of public health or not. Information in the PFAS Fact Sheet including uncertainties around actual risks may help build awareness and drive health research in this area.	Providing information about levels where health effects might be expected to occur for GenX chemicals may help protect public health in the absence of data/ information regarding GenX chemical levels in Australian distributed drinking water. It may also allow the generation of datasets to help clarify the level of risk to consumers as the health-based target can be used in site investigations and monitoring of water supplies. Using a health-based target of 10 ng/L would be a more conservative option. However, the derivation for this option is not considered most relevant to the Australian context (see evidence profile).	Establishing a health-based guideline value for GenX chemicals will be protective of public health in the absence of data/ information regarding GenX chemical levels in Australian distributed drinking water. It may also allow the generation of datasets to help clarify the level of risk to consumers.

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Values and preferences (consumers, communities)	Human exposure to PFAS is an ongoing concern to consumers and communities, particularly to those who live in communities affected by PFAS. For some, knowing that their community is affected by PFAS may increase stress and worry. Findings from the PFAS Health study showed that people living in PFAS affected communities, irrespective of PFAS blood concentrations, are more likely than those who live in comparison areas to experience psychological distress. PFAS contamination can have a range of consequences for those affected including impacts on property values, produce, income, reputation and risks to health. It is reasonable to assume that consumers and communities, particularly those experiencing the impacts of contamination, would expect that: • supplied drinking water is safe to drink and that PFAS would not be present in drinking water at levels that might cause harm to public health • new/emerging risks to public health from drinking water are considered by NHMRC and appropriate action is taken depending on the risks to public health • that the selected guideline option will be protective of public health. It is likely that consumers and communities will be very risk adverse to the effects of exposure to GenX chemicals. While the findings of the NHMRC review should reassure the public that the health evidence has been considered any why a particular guideline value was chosen (or not), there is likely to be ongoing concern from some groups that Australian advice doesn't align with other international agencies such as the US EPA if a guideline value isn't adopted. The uncertainty around the presence of GenX chemicals in Australian water supplies and the evidence base may increase concerns. In addition, there might be an expectation from communities that all PFAS are equally toxic and that guideline values will be derived for all PFAS that are found in Australia, including newer substances such as GenX chemicals. Clear and consistent public health messaging and risk communication, including explanations about the differences between international jurisdictions, guideline value derivations and the review process, could help explain these issues to consumers and reassure them about Australian processes.		

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Acceptability (other key stakeholders)	Given that the SLR (2024a, 2024b) review found that there is currently insufficient evidence to derive a health-based guideline value for GenX chemicals, this option would likely be acceptable to stakeholders. Setting a health-based guideline value that would result in a change in practice without a clear body of evidence would not be readily supported by health regulators or water providers.	Inclusion of information on the level at which health effects might be expected to occur for GenX chemicals in drinking water could provide some confidence to stakeholders who implement the Guidelines from a health protection perspective, as it will provide a health-based target for GenX chemicals for use in site investigations if needed. However, ready access to testing for GenX chemicals may take some time, as according to the SLR (2024a, 2024b) review, GenX chemicals are not routinely measured by Australian laboratories and have only recently been added to analytical schedules offered by some commercial laboratories. Factors that might impact acceptability of a health-based target of potential concern for GenX chemicals include: • increased testing requirements as GenX chemicals are currently not routinely measured by Australian laboratories • increased regulatory burden for health regulators and/or drinking water authorities as a result of increasing monitoring/measuring requirements.	Establishment of a health-based guideline value for GenX chemicals could provide some confidence to stakeholders from a health protection perspective. However, the routine monitoring of GenX chemicals would take some time to implement, as according to the SLR (2024a, 2024b) review, GenX chemicals are not routinely measured by Australian laboratories and have only recently been added to analytical schedules offered by some commercial laboratories. Factors that might impact acceptability of a health-based guideline value for stakeholders include: • increased testing requirements as GenX chemicals are currently not routinely measured by Australian laboratories • increased monitoring requirements may be less acceptable to water providers, particularly if the review found limited evidence for establishing the health-based guideline value • increased regulatory burden for health regulators and/or drinking water authorities as a result of increasing monitoring/measuring requirements.

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
Feasibility	This guideline option is feasible as no changes to current practice are required.	Including a health-based target or establishing a health-based guideline value may be feasible as these levels would be readily measurable with current commercial analytical techniques. However, as GenX chemicals are not routinely measured by Australian laboratories and have only recently been added to analytical schedules offered by some commercial laboratories, it is likely to be resource-intensive to commence measurement and may take time to implement routine monitoring if required.	
Health equity impacts	Some of the guideline values under consideration are more conservative than others, and as a result would be considered more protective of public health. These guideline options would be more protective of the general population, including groups that may be more sensitive (e.g. infants, children and pregnant women). This also includes populations who may be more exposed to PFAS based on their proximity to contaminated sites.		
Resource impacts	None. There would be no change in current practice if no guideline value is established.	This guideline option will likely have less overall resource impacts than establishing a health-based guideline value which will be more broadly implemented. The use of a health-based target will allow for site-specific monitoring of water supplies that might pose the highest risk. Providing information about a potential level of concern or a health-based target instead of a guideline value for GenX chemicals may have potential resource impacts if routine monitoring is introduced at specific sites based on the level of risk.	Establishing a health-based guideline value for GenX chemicals will have resource impacts on the water sector (e.g. effort and investment in sampling collection and analysis and for some utilities, interventions to meet a new value). Additional testing services would be required as GenX chemicals are not routinely measured by Australian laboratories and have only recently been added to analytical schedules offered by some commercial laboratories. The impact of additional costs and effort is likely to be higher for small water utilities,

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
			and particularly those in regional and remote Australia; these communities may require funding and other support from all levels of government. Water providers may have limited capacity to cover increased operational costs amid barriers such as financial sustainability, climate change, lack of alternate water supplies and increasing regulation Additional widespread monitoring and potentially treatment programs (including infrastructure) may be required to meet the candidate guideline value if exceedances are detected. Through various reporting obligations water utilities may need to report these exceedances publicly. Resulting costs for additional treatment of drinking water supplies, investment in appropriate treatment technologies, operations and maintenance and ongoing sampling costs associated with monitoring and/or removal may be borne by local water providers. In some cases, a new water source may need

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
			to be developed to meet guideline values. This may have flow on costs to consumers and communities. However, this may only be an issue if using contaminated water supplies, which are not advised to be used. Public consultation comments noted that for water supplies that do not meet guideline values, consequential treatment upgrades are likely to involve substantial capital investment and time to implement. Examples of costs can be found in American examples such as the US EPA paper 'Technologies and costs for removing PFAS from drinking water' and the document 'Estimating the national cost to remove PFAS from drinking water' (Corona Environmental Consulting and Black & Veatch for the American Water Works Association.

Criteria	OPTION 1: Maintain status quo (no health-based guideline value for GenX chemicals)	OPTION 2: - No health-based guideline value for GenX chemicals - Provide information on health effects that might occur > [*12 or 263 ng/L*] (including derivation of a potential health-based target)	OPTION 3: Establish health-based guideline value for GenX chemicals [*12 or 263 ng/L*] *(based on Dupont 2010)*
			Water suppliers will also require time and resources to complete any necessary water quality monitoring and pilot treatment studies. Space constraints for any new treatment processes might also be a limitation.

Table A10. Decisions regarding the guideline options by the Water Quality Advisory Committee for GenX chemicals

Decision	Decisions regarding the following guideline options by the Water Quality Advisory Committee are outlined below:
Option 1	Members agreed to not establish a health-based guideline value for GenX chemicals. Members noted that given the limited evidence available, further toxicological information would be needed before Members would be comfortable setting a health-based guideline value for GenX chemicals.
Option 2	This option was not considered appropriate as further toxicological information would be needed before Members would be comfortable providing information on a health-based guideline value for GenX chemicals.
Option 3	This option of establishing a health-based guideline value (of *12 or 263 ng/L)* was not considered appropriate given the limited evidence available and concerns about conflicts of interest of the underpinning study.

Attachment 1: GenX Chemicals Evidence Profile (extracted from SLR 2024a, 2024b) – to be read in conjunction with Evidence-to-Decision Table

	Option 1	Option 2	Option 3	
Criteria	**Maintain** status quo (no health-based guideline value for GenX chemicals)	**Maintain** status quo (no health-based guideline value for GenX chemicals) Provide information on health effects that might occur >[12 or 263 ng/L]	**Establish new** health-based guideline value for GenX chemicals in drinking water of **263 ng/L**	**Establish new** health-based guideline value for GenX chemicals in drinking water of **12 ng/L**
Health evidence profile				
Source of Drinking Water Guideline (DWG)	N/A – GenX chemicals not considered by FSANZ 2017	N/A – GenX chemicals not considered by FSANZ 2017	MPART 2019 Michigan's PFAS Action Response Team	US EPA 2021e, 2022c, 2022j; WSDH 2022, 2023a; NJDEP 2023a United States Environmental Protection Agency; Washington State Department of Health
Health-based guidance value (HBGV)			75 ng/kg/day	3.3 ng/kg/day
Resulting adaption to a Health-based Drinking Water Guideline (DWG)			263 ng/L	12 ng/L
Critical study			**Dupont (2010)** (mice study)	
Proportion of technical/ administrative criteria for potential adoption/ adaption into Guidelines[17]			**High** proportion	**High** proportion (US EPA 2021e)
Other comments/ information			SLR (2024a, 2024b) noted that there is only one toxicological study available on which to base a candidate DWG. There is also concern with respect to the reported purity (i.e. 84%) of GenX in the DuPont (2010) study.	

[17] Refer to Figure 10-1 Evidence Evaluation Report (p87) for more details (SLR 2024a, 2024b). Jurisdiction guidance/guideline met a high (i.e. ~>60%) proportion of 'must-have' and 'should-have' criteria; lower proportions of criteria indicate these guidance documents potentially do not conform with modern methods of undertaking systematic reviews. Full details of the assessment of the jurisdiction guidance/guideline is at Appendix D of the Technical Report (SLR 2024a, 2024b).

References for GenX Chemicals Evidence-to-Decision Table:

Dupont (2010). Oral (gavage) reproduction/developmental toxicity study in mice (OECD TG 421; modified according to the Consent Order) DuPont-18405-1037. Unpublished. As cited in MPART 2019a.

FSANZ (2017). Hazard Assessment Report: Perfluorooctane sulfonate (PFOS), Perfluorooctanoic acid (PFOA) and Perfluorohexane sulfonate (PFHxS). Food Standards Australia New Zealand. Australian Government.

MPART (2019). Health-Based Drinking Water Value Recommendations for PFAS in Michigan. June 27, 2019. Michigan Science Advisory Workgroup. Michigan's PFAS Action Response Team (MPART).

SLR (2024a). Evidence Evaluations for Australian Drinking Water Guidelines Chemical Fact Sheets – PFOS, PFHxS, PFOA, PFBS, and GenX Chemicals. Evaluation and Technical Reports prepared for the National Health and Medical Research Council. SLR Consulting Australia. 1 February 2024.

SLR (2024b). Evidence Evaluations for Australian Drinking Water Guidelines Chemical Fact Sheets – PFOS, PFHxS, PFOA, PFBS, and GenX Chemicals. Technical Report prepared for the National Health and Medical Research Council. SLR Consulting Australia. 1 February 2024.

US EPA (2021e). Human Health Toxicity Values for Hexafluoropropylene Oxide (HFPO) Dimer Acid and Its Ammonium Salt (CASRN 13252-13-6 and CASRN 62037-80-3). Also Known as "GenX Chemicals". EPA-Final. EPA Document Number: 822R-21-010. October 2021. United States Environmental Protection Agency (US EPA).

US EPA (2022c). Technical Fact Sheet: Drinking Water Health Advisories for Four PFAS (PFOA, PFOS, GenX chemicals, and PFBS). EPA Document No. EPA 822-F-22-002. June 2022. United States Environmental Protection Agency (US EPA).

WSDH (2022). Per- and Polyfluoroalkyl Substances Chemical Action Plan. Publication 21-04-048. Revised September 2022. Washington State Department of Ecology. Washington State Department of Health (WSDH).

WSDH (2023). 2023 EPA Proposal to Regulate PFAS in Drinking Water. 331-718. 3/15/2023. Washington State Department of Health (WSDH).

Appendix B – Targeted consultation summary

Targeted consultation on the draft PFAS Fact Sheet was undertaken several times during the guideline development process: prior to public consultation; during public consultation; and prior to final publication in the *Australian Drinking Water Guidelines*.

Targeted consultation prior to public consultation

The enHealth Water Quality Expert Reference Panel, the Department of Health and Aged Care and Food Standards Australia New Zealand (FSANZ) were formally consulted in September 2024 on the draft PFAS Fact Sheet and supporting documents. As part of the consultation, NHMRC sought feedback on the following questions:

1. Is the draft guidance relevant, accurate and easy to understand?
2. Do you support the approaches taken to review the evidence and develop the guidance?
3. Do you have any other comments about implementation or feasibility of the proposed health-based guideline values?

The opportunity to provide specific comments and/or tracked changes in the documents was also provided.

Feedback received suggested a number of proposed revisions to the draft PFAS Fact Sheet, the review reports, the evidence to decision tables, the NHMRC Statement for public consultation and the Question and Answer (Q&A) resource. In some instances, specific edits were made to clarify or simplify the language used as well as include additional references within the draft PFAS Fact Sheet. Some common areas of feedback included:

- concerns around the toxicological basis, the choice of studies and endpoints and uncertainty factors in deriving the health-based guideline values
- the approach of considering different candidate values (‘guideline options’) for the same chemical and presenting them as equally health protective (in the evidence review reports and evidence-to-decision tables), stating that this apparent flexibility in the guideline value derivation process may be confusing for end users
- comments relating to implementation and feasibility within jurisdictions of proposed new health-based guideline values, and potential compliance issues in some areas near to contaminated areas
- raising the likelihood of impacts on other PFAS guidance values (e.g. FSANZ tolerable daily intake values that are the basis for food trigger points and soil guidelines) if any proposed changes to NHMRC advice are accepted and adapted by other Australian guidelines or agencies
- the various PFAS exposure pathways and relative contribution of drinking water, commenting that drinking water is just one of many significant sources represented by personal care products, food, food packaging, many consumer goods, clothing, air and dust
- information about typical levels of PFAS detected in drinking water and citing recent data from utilities
- concerns that the level of detail included in the draft PFAS Fact Sheet, particularly in the health considerations section, and the potential for it to be considered too technical and lengthy for the average reader of the Guidelines
- technical questions and clarifications about the evidence review reports.

Summary of targeted consultation feedback prior to public consultation

A summary of key issues raised during the targeted consultation process is captured in the tables below.

Question 1: Is the draft guidance relevant, accurate and easy to understand?

Table A11. Summary of targeted consultation feedback on Question 1 (prior to public consultation)

Feedback received	Response
Comments that the draft PFAS Fact Sheet is relevant and accurate but may be difficult to understand for those without a background in toxicology or NHMRC's guideline development processes. However, simplifying it for average readers would require extensive explanatory material. It is suggested that NHMRC make a public statement addressing the implications of potential changes in guideline values.	Noted. The draft Fact Sheet and the supporting review reports provide more technical information about the complex review process used to review the PFAS Fact Sheet. It is intended that supporting information such as the Q&A resource, the public consultation NHMRC Statement and other comms materials will provide some clarification on the process for lay readers. These documents can be readily updated, if necessary, as more questions arise.

Question 2: Do you support the approaches taken to review the evidence and develop the guidance?

Table A12. Summary of targeted consultation feedback on Question 2 (prior to public consultation)

Feedback received	Response
Support for the approach taken and confidence in the proposed draft guideline values being underpinned by high-quality studies. However, the presentation of multiple candidate values for the same PFAS chemical may be confusing for general readers.	Noted. NHMRC has developed a more streamlined approach for considering guideline values that have recently been reviewed by other agencies. Those guidelines found suitable to adopt/adapt based on their administrative and technical guideline development processes are collated in the review reports and presented for consideration by NHMRC and the Water Quality Advisory Committee (the Committee). While it may be confusing to see a range of guideline options in the review reports and evidence to decision tables, they are intended to demonstrate how the Committee have made their decisions and what they have considered alongside the health evidence to determine why/why not certain guideline options were accepted or not. This is based on an understanding of the certainty in the underpinning toxicological studies, whether the chosen endpoints are clinically relevant, and which end points are considered the most critical and protective of health. This has been clarified in the Q&A resource.

Question 3: Do you have any other comments about implementation or feasibility of the proposed health-based guideline values?

Table A13. Summary of targeted consultation feedback on Question 3 (prior to public consultation)

Feedback received	Response
As drinking water is a minor source of PFAS exposure, it may be difficult to justify expensive action to reduce levels when it appears little action is happening for other, more significant sources (e.g. personal care products, food and food packaging, clothing etc.). Suggest that jurisdictions phase-in any updated guidance, using a risk-based approach to ensure resources are not diverted away from more salient harms.	Noted. PFAS exposure occurs through many different pathways, and this has been mentioned in the PFAS Fact Sheet and supporting information. Information on how the Guidelines are implemented by the states/territories is already within the Guidelines and also noted within the supporting documentation for public consultation (e.g. public consultation NHMRC Statement, Q&A resource), where it may be more appropriate to discuss than the draft PFAS Fact Sheet.
Regulator discussion is needed on the monitoring approach and where it fits in under the risk assessment framework of the Guidelines.	Noted. Monitoring approaches are likely to be jurisdiction-based and site-specific. Further discussion may be required to determine whether any additional monitoring advice on approaches will be useful or appropriate in the Guidelines. Any proposed changes supported by jurisdictions can be considered by NHMRC with advice from the Committee. Monitoring and implementation are addressed in the public consultation NHMRC Statement.
Suggestions on messaging comparing US EPA and the Guidelines – why the values are different, acknowledging the different implementation/ regulatory landscape (e.g. US EPA not enforcing PFAS limits until 2029).	Noted. Differences between guideline values and approaches are acknowledged in the public consultation NHMRC Statement and Q&A resource.

Feedback received	Response
Impact of updated health-based guideline values on other guidance values (e.g. tolerable daily intake used as a trigger point for food; recreational water quality guidelines that are based on values in the Guidelines, which may result in waterways in urban areas being unsuitable for swimming).	Noted. The tolerable daily intake used by other agencies might not change as a result of the NHMRC review – this is up to the relevant agencies. The scope of the NHMRC review was to determine whether changes in NHMRC advice in the Guidelines were warranted. Further review of guidance values other than drinking water is outside the scope of this review; however, it is noted that there will be impacts on other PFAS guidance values if any proposed changes to NHMRC advice are considered, accepted and adapted by other Australian agencies for their specific purposes. Review reports and draft PFAS Fact Sheet have been revised to reflect final advice from the Committee. It is also noted that the proposed changes to guideline values are out for public consultation and may change pending public submissions, further expert review and publication of further evidence (such as the International Agency for Research on Cancer (IARC) monograph) before the guideline values are finalised. Recreational water quality guidelines for PFAS will be reviewed as part of the general update to those guidelines and pending finalisation of advice for drinking water.

General comments (draft PFAS Fact Sheet and Review Reports):

General description

Table A14. Summary of targeted consultation feedback on draft PFAS Fact Sheet (General description)

Feedback received	Response
Reiterate principle in the *Australian Drinking Water Guidelines* that PFAS guideline values define water that is safe to drink over a lifetime; amend text to state that only some PFAS are persistent in the environment.	Noted and accepted. Text amended. Safety over a lifetime is included in the public consultation NHMRC Statement and Q&A resource and already defined in the Guidelines.
Explain the term "GenX", highlighting that it refers to the next generation of fluoropolymer manufacturing processes that aim to be safer and more sustainable.	Noted and accepted. Suggested wording added to information for GenX under 'Levels detected in Australian drinking water' section.

Feedback received	Response
Include additional references for: • biomagnification • PFAS in landfill leachates and sewage effluent from Australian studies • PFAS ban/restriction under DCCEEW's Industrial Chemicals Environmental Management Standard (IChEMS) - to commence on 1 July 2025 • attribution to indicate that estimates of exposure via drinking water for a non-exposed community are ~3% (Thompson et al. 2011)	Noted and accepted. Text amended and references added for: • biomagnification • PFAS in landfill leachates (Australian studies provided) • IChEMS • Thompson et al. 2011

Levels detected in Australian drinking water

Table A15. Summary of targeted consultation feedback on draft PFAS Fact Sheet (Levels detected in Australian drinking water)

Feedback received	Response
Questioning whether information about the levels of PFAS detected in Australian drinking water is required, as it seems historical	Noted. Text retained, as this is a standard section in chemical fact sheets and provides some indication of levels in drinking water that provide information on potential exposure for the risk assessment.
Comments about the biomonitoring program and questioning the relevancy of the reference in this section.	Noted and accepted. Text amended and reference to biomonitoring removed due to lack of relevance for this section of the PFAS Fact Sheet.
Suggestions to include references and/or recent monitoring results from water utilities	Noted and accepted. Text amended to include more recent examples. Reference added for levels for PFOS and PFHxS in relevant sections.
Suggestions for rewording and/or restructuring sentences to improve clarity and accuracy of text.	Noted and accepted. Text amended to improve clarity of the text.

Treatment of drinking water

Table A16. Summary of targeted consultation feedback on draft PFAS Fact Sheet (Treatment of drinking water)

Feedback received	Response
Re. home water treatment, this could remove/reduce fluoride and lead to increased tooth decay	Noted and accepted. Text added to note potential removal of beneficial chemicals.

Health consideration

Table A17. Summary of targeted consultation feedback on draft PFAS Fact Sheet (Health considerations)

Feedback received	Response
While some detailed discussion is necessary (e.g. PFOA carcinogenicity), the current text is too technical and lengthy for the audience of the Guidelines. Suggest making it more concise by only including key details, reducing the number of studies and statements mentioned (e.g. remove limitations of epidemiological studies) and condensing some paragraphs (e.g. IARC classifications).	Not accepted. The Committee advised to present this information differently than typical fact sheets given the interest in overseas advice and public expectations. The information is intended to help provide the rationale leading to the choices in endpoints and studies for guideline derivations. Overall IARC classifications provided here for context and comparison with ANU study before discussing in more detail for individual chemicals. Providing the limitations of epidemiological studies are important to justify why they haven't been used to derive a guideline value.
Review IARC monograph once it is available and clarify whether IARC considered community level exposures of PFAS and their association with cancers.	Noted. The IARC monograph will be reviewed when published and any changes to the PFAS Fact Sheet made as required as advised by the Committee. From limited information in the IARC summary (Zahm et al. 2024), there were inconsistent findings re: cancer associations from studies examining community level exposures of PFOA and PFOS (hence 'limited' or 'inadequate' evidence for cancer in humans for PFOA and PFOS respectively).
Rephrase sentences to improve clarity and accuracy of statements (e.g. the ANU study data are from heavily contaminated communities and are not typical levels found in Australia).	Accepted. Text amended to improve clarity and accuracy.
PFOA section: The NTP study on PFOA was questioned for its peer review status and control of potential confounders, such as background cancer incidence in animals.	The NTP (2023) study was peer reviewed before publication, with reviewers evaluating study quality, including against confounders and controls/background incidence. It was found that for both male and female rats, the incidence of acinar findings (for which historical control data were provided) in experimental controls were similar to historical controls. A footnote on study quality has been added to the 'Health considerations' section to clarify the meaning of a high-quality study and how it was assessed by the reviewers.

Feedback received	Response
PFOA section: Concerns raised about the human relevancy of the neoplastic acinar pancreatic lesions and the liver effects observed in rats exposed to PFOA in the NTP (2023) study and the subsequent use of these endpoints in deriving a candidate guidance value for PFOA.	Partially accepted. Text amended to reflect final choice of guideline option for PFOA after feedback from targeted consultation and advice from the Committee and reviewer. Amendments made to review reports to provide more information/ references to clarify clinical relevance of neoplastic pancreatic effects observed with PFOA in the NTP (2023) study. There is high confidence that the hepatic neoplastic lesions are unlikely to be relevant to humans, as this is supported by the human relevancy mode of action analysis conducted by Klaunig et al. (2012). However, with respect to hepatic necrosis (a non-neoplastic effect of PFOA in animal studies), the external independent scientific reviewer of the Addendum report supported the use of non-neoplastic hepatic effects as an appropriate endpoint on which to base a point of departure for PFOA. Although there is uncertainty with respect to the dose at which non-neoplastic hepatic effects may occur in humans and it is recognised by the reviewer that rats are likely more sensitive to this effect than humans, they consider there is insufficient information to rule out human relevancy of this effect at this time.
PFOS section: Concerns raised with clinical relevance of thyroid effects observed in NTP (2022) to humans. A number of comments were made regarding endpoint selection with respect to the decreases in thyroid hormone levels, its relevancy to humans, thyroid hormone analysis and the benchmark dose analysis undertaken by the reviewers for thyroid hormone effects.	Accepted. Text amended to reflect final choice of guideline option for PFOS after feedback from targeted consultation and advice from the Water Quality Advisory Committee and reviewer. Review reports amended to clarify clinical relevance of thyroid effects observed in NTP (2022).

Feedback received	Response
PFOS section/mice developmental study (Zhong et al. 2016): Immunomodulation has previously been determined as unsuitable as a critical endpoint for quantitative risk assessment for PFAS. While PFOS can adversely modulate immune system responsiveness (Drew and Hagan 2016), there are significant uncertainties regarding species sensitivity, strain sensitivity and the influence of route of administration on immune system modulation by PFOS that are yet to be resolved. As a result, it has not been possible to determine a reliable NOAEL or LOAEL for adverse effects on immune function for use in a quantitative risk assessment of PFOS.	Noted. No changes made. While previous reviews have determined that immunomodulation is unsuitable, the current review is tasked with determining if this may be different now in light of more recent studies. In 2016, the opinion was that immunomodulation can be used for hazard identification, but not really dose response, assessment, at the time. It is a standard expectation that as more data become available, this conclusion may need to be revisited. It is also noted the Zhong et al. (2016) study was not reviewed / included in the Drew and Hagen (2016) review.
PFOS section: Concerns raised about selecting a 28-day toxicity study in rats (NTP 2022) to establish a tolerable daily intake for PFOS. Comments included: • that it is unusual in chemical risk assessment and has not been justified by SLR Consulting. • typically, short-term studies should be at least 3 months to be suitable for establishing a TDI (IPCS, 2020). • long-term and reproductive/developmental studies are available for PFOS and considered more appropriate for establishing a TDI.	Partially accepted. It is not unusual for this to occur if the study is considered to be a high-quality study. However, it can be more unusual where chronic studies are available. Amendments made to the Addendum Report to refer to the effects on thyroid hormone (or lack thereof) in other chronic studies with PFOS.

Feedback received	Response
PFBS section: Comments questioning the limitations of the NTP (2022) study and considerations that Feng et al. (2017) was considered the best available study to underpin the health-based guideline value for PFBS, rather than NTP (2022), despite NTP studies underpinning other PFAS guideline values.	Accepted. Text amended in Health Considerations and Guideline Derivation sections to highlight concerns about observed effects in the NTP (2022) study for PFBS and rationale for choice of Feng et al. (2017) as the key study for deriving a health-based guideline value. The Evidence Evaluation Report concluded that any of the values in the range of 1,050 to 2,100 ng/L would be sufficiently health protective for PFBS, noting that 2,940 ng/L was derived using the rat toxicology study from NTP (2022) and values ranging from 1,050 to 2,100 ng/L were derived using the mouse toxicology study by Feng et al. (2017). It did not conclude that either study was more appropriate for derivation. The reviewers evaluated the NTP (2022) study for study quality including against confounders and controls/ background incidence and found that the NTP (2022) study was high quality. The NTP (2022) study was peer reviewed (details of peer reviewers provided in the report). Both studies (NTP (2022) and Feng et al. (2017) were considered high quality by the reviewers.

Guideline derivations sections

Table A18. Summary of targeted consultation feedback on draft PFAS Fact Sheet (Guideline derivation sections)

Feedback received	Response
Suggestion to include the relative contribution of drinking water to daily intake in Fact Sheet and Q&A resource.	Accepted. Information on estimates for relative contribution added to general description section and included in Q&A resource.
For consistency with other fact sheets in the Guidelines, and to avoid confusion about what a mathematically "correct" guideline value should be, the dot points detailing the rounding of each guideline value and the reference to chapter 6 should be removed.	Noted but no changes made. Committee advised to include information on rounding convention to show where the final number came from, consistent with more recent fact sheets.

Feedback received	Response
Question about the consideration of guideline options for PFOS that are all considered 'health protective' as described in SLR reports (e.g. 70 ng/L versus 4 ng/L) and unclear explanation of why one is picked over the other.	Noted. Text amended to reflect choice in final guideline options following feedback from targeted consultation and advice from the reviewers and the Water Quality Advisory Committee. Reports amended to clarify the different guideline options that were suitable for adopting/adapting for consideration by the Committee.
PFOS: The report also suggests that existing PFOS levels comply with the 4 ng/L guideline due to the relative source contribution, and so slight exceedances will not cause health effects. However, this is not how Drinking Water Guidelines are applied, as water utilities must provide water that meets the guidelines, and failing to do so can have health impacts. Additionally, the report notes that areas near heavily contaminated sites are likely to struggle with meeting this guideline.	Noted. The review reports presented different guideline options that were suitable for adopting/adapting for consideration by the Committee. The Committee have considered the options for deriving a guideline value based on what they consider the most critical health effect from the best available evidence.
PFOS: Suggestion for the Fact Sheet to reference the evidence evaluation (SLR a, b) regarding the current guideline value of PFOS of 70 ng/L considered to be health protective.	Partially accepted. Text amended to reflect final choice of guideline option for PFOS following feedback from targeted consultation and advice from the reviewers and the Water Quality Advisory Committee. Reports amended to clarify the different guideline options that were suitable for adopting/adapting for consideration by the Committee.
PFOS: Comments questioning the rationale behind the choice of thyroid effects as the critical effect and seeking clarification on what a reduction in T4 and free T4 mean without changes in serum thyroid stimulating hormone (TSH) levels and histopathology of the clinical relevance for humans.	Accepted. Text amended to reflect final choice of guideline option for PFOS after feedback from targeted consultation and advice from the Water Quality Advisory Committee and reviewer. Review reports amended to clarify clinical relevance of thyroid effects observed in NTP (2022).

Feedback received	Response
PFOS: Comments questioning the rationale for undertaking an additional review subsequent to US EPA updating its Drinking Water Guidelines (April 2024) (i.e. Addendum Report by SLR Consulting) and seeking clarity on dates of NTP study versions (2019 and 2022).	Noted. The reviewers undertook an initial review of existing guidance/guidelines that was finalised in February 2024 (SLR 2024a, 2024b). The NTP (2022) report was not discussed in these review reports because it was not used as a key study by other international assessments to derive a guideline value for PFOS at that time and was therefore not included for discussion. When the US EPA published their final advice for PFOS in April 2024, the final assessment report included a new basis for their drinking water guideline value and the Water Quality Advisory Committee advised that this should be considered as part of the PFAS Fact Sheet review. This included a review of several human and animal studies that had been considered by the US EPA in their final PFOS assessment. This time, the NTP (2022) study had been considered by the US EPA as a candidate study in deriving a reference dose for PFOS and was therefore included and discussed in the Addendum report. It was presented as a potential guideline option as it was considered a high-quality study and suitable to adopt/adapt (SLR 2024c). Review reports updated to make citations consistent, and footnote added to section 5.2 of Addendum Report. NTP (2019) and NTP (2022) are the same study, and both citations have been used in SLR (2024 a, 2024b, 2024c) depending on each guidance/guideline document under review. The NTP (2019) report has been revised since initial publication and updated in 2022 (NTP 2022). The most current version of the report (NTP 2022) was the only version considered by the reviewers during the review process, regardless of how it was cited in the reports.
PFOS: The fact sheet references the NTP 2022 report for the Point of Departure (POD) and uses an uncertainty factor of 300. The toxicokinetics was assessed using PBPK modelling to convert serum concentration from rats to a human equivalent dose, but there is not enough information to confirm is this was done correctly.	Noted. Details provided in the review reports. Toxicokinetic adjustment was undertaken by applying a PFOS clearance factor of 0.000128 L/kg-day and a PFHxS clearance factor of 0.00009 L/kg-day to the PFOS and PFHxS, respectively, serum points of departure to derive a human equivalent dose point of departure.

Feedback received	Response
Concerns that the uncertainty factors applied for the PFOS and PFHxS guideline values are based on a short-term study when long-term and reproductive/ development studies are available. Additionally, is there a standard reference for the uncertainty factors used? It is also inconsistent to apply a 10-fold uncertainty factor for short-term issues to one chemical and not the other as both PFOS and PFHxS are similar chemicals.	Noted but no changes made. Although some information on the choice of uncertainty factor is provided by enHealth (2012, pg. 71), professional judgement is required. The reviewers considered the uncertainties and concluded a similar total uncertainty factor of 300 would be warranted for PFOS (and PFHxS) for use of an endpoint from the 28-day NTP study. SLR (2024a, 2024b) justified the omission of an uncertainty factor (UF) for a sub-chronic study in the guideline derivation for PFHxS as it was considered suitably covered by the UF of 10 for a limited database (including lack of chronic studies). This decision was also considered against the balance of having an unnecessarily high UF of 3000 and the conclusion by the reviewers that 300 would be suitably health protective for PFHxS.

General comments (Review Summary/public consultation NHMRC Statement)

Table A19. Summary of targeted consultation feedback on the review summary/ public consultation NHMRC Statement

Feedback received	Response
Amend text to clarify the following points: • sentence about defined scope and limited resources unnecessary, as following sentences clarify the focus on the selected PFAS. • include more text about why other PFAS have not been included • noting about resources for the rolling revision of guidelines may not be suitable for a public statement • be clear that exposure from drinking water for a non-exposed community estimated to be ~3% of total PFAS exposure (Thompson et al, 2011) • elaborate on why NHMRC found the available human studies to be unreliable/inappropriate for deriving guideline values • point to monitoring responsibilities (state/territory vs commonwealth)	Accepted. Text amended to clarify.

Feedback received	Response
Re: estimation of approximately 2-3% of total PFAS exposure. Is this used for the derivation or 10%? Need to clarify for the Q&A as it says 10% is more conservative than 20%, but also mentions 2%.	Accepted. Q&A amended to clarify relative source contribution used in guideline derivation.
'It is expected that it will take time and resources to implement the new PFAS health-based guideline values in Australia…' Can this be acknowledged in the Q&As/guidelines also?	Accepted. Has been acknowledged in Q&As.
Consider emphasising *it is not uncommon for international agencies to differ in the way that they calculate guideline levels and manage risks from chemicals*	Noted but no changes made. This point is also addressed in the FAQs, can consider other methods of emphasis if available to NHMRC at final publication.
Can the Fact Sheet include reference to the SLR assessment that 'the existing 70 ng/L guideline value for PFOS+PFHxS are considered to be sufficiently health protective'? Could this summary, the Fact Sheet and Q+A acknowledge this?	Noted. Text amended to reflect choice in final guideline options following feedback from targeted consultation and advice from the reviewers and the Water Quality Advisory Committee. Review reports amended to clarify the different guideline options that were suitable for adopting/adapting for consideration by the Committee.
Suggested edit to add, based on communication from the US EPA, '…providing 3 years for monitoring requirements and 5 years…' to take action to reduce elevated levels of PFAS	Accepted. Text amended. Additional information included in Q&As.

General comments (Evidence to Decision tables)

Table A20. Summary of targeted consultation feedback on draft evidence to decision tables

Feedback received	Response
PFOA: Note that current sampling has detected PFAS in water sources even without high-risk sources, highlighting its widespread presence. Additionally, low concentrations of PFAS have been found in water supplies not affected by contaminated sites. Some localities may have no other option than to use a source water with levels below the guideline value, or a shandy of water sources to ensure the guideline values are met. Suggested edits made to text. Add "*Through various reporting obligations water utilities may need to report these exceedances publicly. In some cases, a new water source may need to be developed to meet guideline values.*"	Accepted. Text amended and actioned across other EtD tables where relevant.
PFOS: It is not relevant to note that *communities are likely to remain cautious about PFOS exposure, despite the NHMRC review aiming to reassure the public, by explaining the chosen guideline value, because the guidelines do not align with more conservative international standards*, as the preferred PFOA guideline value is 4 ng/L, which does align with the US EPA.	Partially accepted. Amended paragraph, as some of this information is still relevant as the Values and Preferences section covers guideline value options from 70 to 4 ng/L (not just the lowest option) to demonstrate why some of these options might not be acceptable to consumers.
'Values and preferences' section in Evidence to Decision tables needs refinement for clarification: "Clear and consistent public health messaging and risk communication, including explanations about the differences between international jurisdictions, guideline value derivations and the NHMRC review process, could help."	Accepted. Text added to clarify.

Feedback received	Response
PFHxS – Health evidence profile: Could the Fact Sheet include reference to the SLR assessment that 'the existing 70 ng/L guideline value for PFOS+PFHxS are considered to be sufficiently health protective'? It is uncertain whether/how this should be qualified by statement in the 'evidence to decision' document 'It is uncertain that this value will continue to be protective of health for PFHxS in light of the NTP (2022) study which was not available to FSANZ when considering the derivation of a guideline value for PFHxS.'	Noted. Text amended to reflect changes to Review Reports to clarify the different guideline options that were suitable for adopting/adapting for consideration by the Committee.
PFHxS – Exposure profile: 'However, there are many sites of PFAS contamination in Australia, and, if water from these contaminated sites is used as a local source of drinking water (e.g. backyard bore in rural location where distributed water is not available), PFHxS may be present at concentrations greater than the candidate health-based guideline value and the existing Australian health-based guideline value in these cases'. Is this statement specific to PFHxS?	Noted. Statement specific to PFHxS and reference added to review report.
PFBS – Feasibility: Feasibility concerns for options 2-5 seem to be inconsistent with the exposure profile information earlier on in the table, page 2. Certainly, in Queensland, detections of PFBS in drinking water sources and drinking water is rare and levels are in the low ng/L range at most.	Accepted. Text amended.

Targeted consultation on public consultation drafts

In parallel with public consultation, NHMRC sought feedback from members of the Regulatory Science Network as well as the following Commonwealth agencies on the public consultation draft PFAS Fact Sheet:

- The then-Department of Health and Aged Care
- Food Standards Australia New Zealand
- Department of Defence
- Department of Climate Change, Energy, the Environment and Water
- Department of Agriculture, Fisheries and Forestry
- The then-Department of Infrastructure, Transport, Regional Development, Communications and the Arts
- Australian Industrial Chemicals Introduction Scheme (AICIS).

A summary of the key issues raised during this targeted consultation process is captured in the table below. NHMRC considered all feedback received with advice from the Committee, particularly the Chemical Subgroup.

Summary of targeted consultation feedback received on public consultation draft guidance:

Table A21. Summary of targeted consultation feedback on public consultation draft guidance

Feedback received	Response
Consider impacts to other industries/ stakeholders, including implications for risk assessment and management of PFAS contaminated sites.	Noted. While practical implications around implementation such as feasibility, treatment, compliance and cost impacts were noted by NHMRC and the Water Quality Advisory Committee when considering the different guideline options to adopt/adapt in Australia, the ultimate decisions were based on what was considered to be the highest certainty health evidence for the most critical health effects that are achievable and protective of public health. Further review of guidance values other than drinking water is outside the scope of this review; however, it is noted that there can potentially be impacts on other PFAS guidance values (e.g. for food, recreational water quality) if any proposed changes to NHMRC advice are considered, accepted and adapted by other Australian agencies for their specific purposes. Evidence-to-Decision tables in the Administrative Report have been updated to include additional information on impacts after considering feedback from consultation.

Feedback received	Response
The approach taken to develop the draft guidance could have been improved by ensuring early engagement with relevant regulatory authorities and Commonwealth agencies currently delivering PFAS investigations and managing PFAS projects and liabilities. This consultation would have resulted in consideration of the potential practical implications of the proposed changes prior to their public release.	Noted. NHMRC undertook targeted consultation with the enHealth Water Quality Expert Reference Panel, FSANZ and the then-Department of Health and Aged Care prior to public consultation. Broader consultation with other agencies was taken in parallel to public consultation due to time constraints. Implementation of the revised guidance is outside the remit of NHMRC. While practical implications around implementation such as feasibility, treatment, compliance and cost impacts were noted by NHMRC and the Water Quality Advisory Committee when considering the different guideline options to adopt/adapt in Australia, the ultimate decisions were based on what was considered to be the highest certainty health evidence for the most critical health effects that are achievable and protective of public health.
Concerns around implementation and capacity for some stakeholders to adopt/meet the proposed guideline values, suggesting that NHMRC outline implementation expectations including transition timeframes to implement any new PFAS guideline values.	Noted. NHMRC issues drinking water guidelines as per the NHMRC Act. NHMRC guidelines are recommendations only. Responsibility for the implementation of the *Australian Drinking Water Guidelines*, including timeframes, is outside the remit of NHMRC. Clarification on timeframes is provided in the Question-and-Answer resource.
Concerns around unintended consequences of revised health-based guideline values, including on other PFAS guidance values (e.g. food, recreational water, soil and land etc.)	Noted. The scope of the NHMRC PFAS fact sheet review was to determine whether the current advice in the *Australian Drinking Water Guidelines* remains appropriate. Review of guidance values other than drinking water is outside the scope of this review; however, it is noted that there can potentially be impacts on other PFAS guidance values (e.g. for food, soil and land, waste management) if any proposed changes to NHMRC advice are considered, accepted and adapted by other Australian agencies for their specific purposes.

Feedback received	Response
In the context of potential application of the draft guidance for PFAS management activities, it will be important that future iterations of the PFAS National Environmental Management Plan (NEMP) continue to reinforce that an exceedance of a national guidance value does not necessarily constitute a risk to health and instead requires that site-specific risk assessment is undertaken.	Noted. The NEMP is referenced in the PFAS Fact Sheet and supporting information; however, alignment of NHMRC advice with the NEMP is outside the remit of NHMRC.
Concerns about the technical basis for the proposed PFOS health-based guideline value (e.g. concerns about the endpoint, transcribed results of underpinning study, choice of study, application of the modelled benchmark dose instead of the measured no observed adverse effect level (NOAEL))	Noted. NHMRC and the Water Quality Advisory Committee considered the feedback provided by expert review and key stakeholders alongside the information provided in the review reports when deciding on what was considered to be the most appropriate, highest confidence health-based guideline value for PFOS. The guideline value for PFOS has been revised using a more robust benchmark dose following consideration of consultation feedback. The choice of benchmark dose model was informed by an analysis by SLR Consulting Australia. Further information is provided in the PFAS Fact Sheet and Appendix F and G of this Administrative Report.
Concerns about the human relevancy of the endpoint/critical health effect selected for PFOA (neoplastic pancreatic acinar adenomas and adenocarcinomas) health-based guideline value.	Noted. NHMRC and the Water Quality Advisory Committee have determined that the NTP (2023) study is the best available evidence to derive a health-based guideline value for PFOA. Although uncertainties about the clinical relevance of neoplastic pancreatic acinar adenomas and adenocarcinomas after PFOA exposure in rats were noted by the reviewer, it was also noted by the reviewer that these observed pancreatic effects may occur through modes of action other than the PPARα pathway (currently demonstrated in vitro but not in vivo) and so human relevance could not be discounted. This was also supported by the International Agency for Research on Cancer (IARC), which cited the carcinogenic effects observed in animals in the NTP (2023) study as supporting its evaluation of PFOA as carcinogenic in humans.

Feedback received	Response
Concerns around use of thyroid effects as an endpoint for deriving health-based guideline values for PFBS and PFHxS but deeming thyroid effects unsuitable for PFOS.	Noted. Thyroid endpoints have been selected as the point of departure for the PFHxS and PFBS health-based guideline values. NHMRC and the Water Quality Advisory Committee note that it is critical to evaluate each PFAS based on the best available evidence for that particular chemical, so as a consequence endpoints may differ between PFAS. The choice of thyroid endpoints were considered separately for each chemical. The rationale supporting each decision regarding relevancy of the thyroid endpoint are provided in the review reports and in the guideline derivation sections.
Suggestions that NHMRC should develop a Regulatory Impact Statement to ensure impacts/implications are thoroughly considered.	Noted. NHMRC does not provide a regulatory impact statement (RIS) when reviewing the *Australian Drinking Water Guidelines*. The Productivity Commission has determined that NHMRC is not required to undertake a RIS as the Australian Drinking Water Guidelines do not have a regulatory status. A Q&A was added to the resource to address this feedback. The Evidence-to-Decision tables were used as a framework to structure discussions with the Water Quality Advisory Committee. While impacts and implications were noted during the evidence-to-decision process, they were not included in the final decision making which are based on the certainty in the health evidence. This has been clarified in the updated Evidence-to-Decision tables where minor edits were made to include additional information on impacts received from stakeholders through consultation.

Targeted consultation on revised drafts prior to publication

NHMRC liaised with Commonwealth agencies and provided the revised guidance prior to final publication. The enHealth Water Quality Expert Reference Panel was formally consulted in April 2025 on the revised draft PFAS Fact Sheet as part of the rolling revision of the *Australian Drinking Water Guidelines*.

Summary of targeted consultation feedback received on revised drafts prior to publication

Table A22. Summary of targeted consultation feedback on drafts prior to publication

Feedback received	Response
Suggestion to improve clarity around the definition of short and long-chain PFAS	Noted and accepted. Amendments made to PFAS Fact Sheet in the 'Treatment of Drinking Water' section.
Suggestion to change TOPA (Total Oxidizable Precursor Assay) to TOP Assay, as per terminology by Sedlak.	Noted and accepted. Amendments made to PFAS Fact Sheet to replace TOPA with TOP Assay in the 'Measurement' section.
Consistency of terminology of use of tolerable daily intake vs acceptable daily intake, with the suggestion to not use these terms interchangeably.	Noted and accepted. Amendments made to all references in the PFAS Fact Sheet of 'acceptable daily intake' to 'tolerable daily intake', as per the enHealth Environmental Health Risk Assessment Guidelines for assessing human health risks from environmental hazards that defines tolerable daily intake as: '*An estimate of the intake of a substance that can occur over a lifetime without appreciable health risk (WHO 1994a). This is conceptually the same as the 'acceptable daily intake' and 'reference dose' but used when the substance is an unintended contaminant in food or an environmental medium such as air, water or soil. This terminology avoids the implication that the contaminant is 'accepted'*.
Suggested amendments regarding routine monitoring not being ad hoc or as needed, as routine monitoring is now occurring around Australia.	Noted and accepted. Amendments made to PFAS Fact Sheet in the 'Levels detected in Australian Drinking Water' section.
Suggestion to delete the sentence about the guideline values applying to Australian drinking water delivered to customers, not raw water sources, noting that any reference to customers should be avoided.	Noted and partially accepted. The Water Quality Advisory Committee advised that although this is implicit in the *Australian Drinking Water Guidelines*, given the ongoing confusion by media/public when comparing levels in raw waters, it is worth in this instance reiterating it in the Fact Sheet. Further, including this point explicitly was raised several times through public consultation. The sentence was retained in the PFAS Fact Sheet and 'customers' was changed to 'consumers'.

Appendix C – Expert Review summary

Expert review was undertaken on the draft guidance before, during and after public consultation between the following dates:

- Prior to public consultation: 13 September to 9 October 2024
- Public consultation: 21 October to 22 November 2024
- Post-public consultation: 10 to 23 April 2025

As part of the consultation, NHMRC sought specific feedback on the following:

1. **Please comment on the appropriateness of the guidance (Fact Sheet) in regard to its readability and usefulness, given the target audience of the *Australian Drinking Water Guidelines*, e.g. is the draft Fact Sheet relevant, accurate and easy to understand?**
2. **Do you support the approaches taken to review the evidence and derive the health-based guideline values? e.g.**
    - whether appropriate evidence has been identified and reviewed, and if any evidence has been missed, given the scope and review approach of this fact sheet update (as outlined in the Research Protocol)
    - whether the evidence has been appropriately considered, interpreted and translated, using the Evidence-to-Decision Framework for each PFAS chemical to derive the health-based guideline values in the draft Fact Sheet?
3. **General/overall comments on the draft Fact Sheet and supporting information**

In addition to the above, the post-public consultation expert review also sought specific feedback on the following:

4. **Do you consider that NHMRC has given due regard to comments received through public consultation? e.g.**
    - whether the key issues relating to the evidence base raised during consultation have been considered appropriately
    - whether due consideration has been given to submissions.

To be eligible for undertaking expert review, reviewers were required to complete a Disclosure of Interest prior to receiving any documents. Disclosed interests of independent expert reviewers are listed in **Appendix D**. A summary of key issues raised by the expert reviewers and how they were addressed is provided in the table below.

Summary of expert review feedback and responses

Question 1: Please comment on the appropriateness of the guidance (Fact Sheet) in regard to its readability and usefulness, given the target audience of the *Australian Drinking Water Guidelines*, e.g. is the draft Fact Sheet relevant, accurate and easy to understand?

Table A23. Summary of expert review feedback and response to Question 1

Feedback	Response
Expert reviewers found the draft PFAS Fact Sheet well-researched, well-referenced, with adequate supporting data, making it useful for the target audience. The Fact Sheet is accurate, which ensures the guidance is scientifically sound and reliable. The Fact Sheet also emphasises evaluating the quality of studies, with those selected for guideline derivation generally rated as 'high confidence'.	Noted.
While it is information-dense, which might affect general public readability, this is justified due to the expected high level of scrutiny. However, some sections, particularly those detailing the derivation of guideline values, could benefit from simplified language/ visual aids for non-expert readers.	Noted. The PFAS Fact Sheet within the *Australian Drinking Water Guidelines* is a technical document intended for water regulators, water managers and water professionals. Recognising that there is significant public interest in this issue, NHMRC also developed other communication materials for public consultation to assist with communications. After considering consultation feedback, NHMRC has also developed more consumer-friendly information for the NHMRC website to help the general public/consumers and those who work with communities explain the health risks and other key issues.
Specify that $BMDL_{10}$ (not just BMDL) was used to derive the guideline values using benchmark doses.	Accepted and actioned.

Question 2: Do you support the approaches taken to review the evidence and derive the health-based guideline values?

Table A24. Summary of expert review feedback and response to Question 2

Feedback	Response
The evidence reviewed is thorough and appropriate, with no glaring omissions of essential evidence. The transparent process effectively captures the most important and reliable evidence. No further information is needed to support the derivation of the health-based guideline values. The evidence has been appropriately considered, interpreted, and translated using the Evidence-to-Decision Framework, ensuring the guideline values are based on robust and reliable evidence. The Evidence-to-Decision Framework is robustly applied and well-documented, allowing readers to understand and revisit key steps. This transparency is exemplary and provides strong defensibility to the conclusions. The proposed guideline values for PFOA, PFOS, PFHxS, and PFBS are well-supported, conservative, and provide adequate health protection for Australian consumers of potable water.	Noted. No edits required.
Although supporting the use of a threshold approach for PFOA from a cancer endpoint, there was some reservation about using a carcinogenicity endpoint (pancreatic acinar adenomas and adenocarcinomas) for PFOA rather than a non-neoplastic endpoint. However, the reviewer notes that a benchmark dose calculated from a non-neoplastic endpoint would not be materially different from that calculated for cancer incidence, so it likely makes little difference whether the neoplastic or non-neoplastic effects are used to derive the health-based guideline value for PFOA.	Noted. NHMRC and the Water Quality Advisory Committee determined that the NTP (2023) study is the best available evidence to derive a health-based guideline value for PFOA. Although uncertainties about the clinical relevance of neoplastic pancreatic acinar adenomas and adenocarcinomas after PFOA exposure in rats were noted by the independent evidence reviewer, it was also noted by the reviewer that these observed pancreatic effects may occur through modes of action other than the PPARα pathway (currently demonstrated in vitro but not in vivo) and so human relevance could not be discounted. This was also supported by the International Agency for Research on Cancer (IARC), which cited the carcinogenic effects observed in animals in the NTP (2023) study as supporting its evaluation of PFOA as carcinogenic in humans.

Feedback	Response
The PFAS Fact Sheet is complex in identifying appropriate toxicological models and endpoints, and so it is suggested a clearer explanation should be included on why certain (possible) human carcinogen endpoints are not calculated using a cancer slope factor. Have other cancer slope factors been derived for these chemicals (beyond the one quoted above) and have these been reviewed? How would their application impact final health-based guideline values?	Noted. Discussion on why cancer slope factors have been used to derive health-based guideline values for some carcinogenic chemicals and not others is provided in Section 6.3.3 of the *Australian Drinking Water Guidelines*. A question-and-answer has also been developed to address this issue. Cancer slope factors used by other agencies to derive PFAS guideline values were reviewed and discussed in the SLR review reports but were determined by the reviewer to be the best available evidence for consideration as guideline options.
Due to the application of the large uncertainty factors, the health-based guideline values are possibly overly conservative, although it does provide an additional margin of safety for expected exposures to PFAS from most potable water sources in Australia. For slightly improved transparency, individual uncertainty factors could be presented in each of the guideline value calculations, instead of a combined uncertainty factor.	Noted and accepted. Individual uncertainty factors have been described in the PFAS Fact Sheet in dot points following the guideline value calculations.
It is questionable why the PFOS guideline value was rounded from 3.4 ng/L to 4 ng/L. It might be more appropriate to round it to 3 ng/L. There may be some carry-over error in the calculation.	Noted. The PFOS guideline value has been revised following consideration of consultation feedback and rounded as per the convention outlined in Section 6.3.3 of the *Australian Drinking Water Guidelines*.
The guidance needs to specify what "lifetime" means in years in Australia, as different jurisdictions may define it differently.	Noted. A definition of “lifetime” is not currently provided in the *Australian Drinking Water Guidelines* or guidance provided by enHealth – it would also require a more holistic consideration of exposure within the *Australian Drinking Water Guidelines*, which is beyond the scope of this current review but may be considered in the future as part of the rolling review process.

Feedback	Response
The SLR Consulting responses and corresponding document edits were thorough and well-supported by extensive detail. Significant changes by SLR Consulting consisted of the inclusion of discussions on the human relevance of thyroid changes and pancreatic lesions in rat studies, and consequential changes to the guideline options for PFOS and PFOA.	Noted. No edits required.
The variability in health-based guidance values across jurisdictions is noted, with a suggestion to clarify that differences are due to study selection and conservatism in calculations, not necessarily implying different levels of health protection.	No edits required. This is covered in the Question-and-Answer resource (e.g. Why are some of the Australian drinking water guideline values for PFAS higher than levels in other countries?).

Question 3: General/overall comments on the draft Fact sheet and supporting information

Table A25. Summary of expert review feedback and response to Question 4

Feedback	Response
The revised PFAS Fact Sheet and supporting information are well-constructed and provide a solid foundation for managing PFAS contamination in drinking water. NHMRC's approach is thorough, transparent, and responsive to stakeholder feedback, ensuring that the guidelines are both scientifically sound and practical.	Noted.
The derivation of water quality guidelines follows a four-stage process, which has been well described and applied in the evidence review; (1) deriving a Toxicity Reference Value (TRV); (2) determining a point of departure (POD); (3) adjusting for a human equivalent dose; (4) developing a health-based guideline value.	Noted. No edits required.
The justification for rejecting immunomodulation as a critical endpoint was valid. Several studies were referenced that criticised agencies that selected immunomodulation as an endpoint and showed inconsistencies in PFAS-related immune responses. The mechanisms of interaction between PFAS and the immune system, and the relevance to human populations are not yet fully understood.	Noted. No edits required.

Feedback	Response
Adjusting NOAEL or benchmark doses from animal studies to determine a Human Equivalent Dose (HED) relies on accurate toxicokinetic parameters and models, which has been applied appropriately by SLR Consulting Australia in their evidence evaluation.	Noted. No edits required.
Suggestion that the guideline values should be presented in units of micrograms per litre (mg/L) without the accompanying translation to nanograms per litre (ng/L).	Not accepted. The Water Quality Advisory Committee advised that guideline values for PFAS should be presented as ng/L in-text, and as both ng/L and µg/L in headlines, noting examples of other chemicals within the Guidelines that present headline values in multiple units.
It is excellent and appropriate that NHMRC maintained health-based, evidence-based guideline values without adopting more arbitrary values by following the lead of the US EPA and other agencies.	Noted. No edits required.
Simplifying technical language and adding visual aids could enhance readability and accessibility.	Noted and accepted. NHMRC has developed more consumer-friendly information with simplified language and visual aids for the NHMRC website to help the general public/consumers and those who work with communities explain the health risks and other key issues.

Question 4: Do you consider that NHMRC has given due regard to comments received through public consultation?

Table A26. Summary of expert review feedback and response to Question 4

Feedback	Response
NHMRC has carefully considered comments from public consultation. Key issues related to the evidence base have been addressed. Submissions have been given due consideration, with comprehensive and transparent responses. The revisions to the draft guidance reflect a thorough and responsive approach to stakeholder feedback.	Noted.

Appendix D – Declarations of interest

The declarations of interest of Committee and Chemical Subgroup members at the time of their involvement in the development of the guidance are listed in the table below. Consideration of the declarations of interests of members of the Water Quality Advisory Committee during the period 2022-2025 were undertaken according to NHMRC committee policy at the time.

2022-2025 Water Quality Advisory Committee

Table A27. Declarations of interests for Members of the Water Quality Advisory Committee

Name/Position	Area of Expertise	Declaration of Interests
Professor Nicholas J. Ashbolt (Chair) Cooperative Research Centre for Solving Antimicrobial Resistance in Agribusiness, Food and Environments, University of South Australia	Extensive experience in health-related water microbiology as a researcher/ academic, mostly in the field of environmental pathogen detection, fate and transport interpretation (via Quantitative Microbial Risk Assessment)	• Executive Dean, Faculty of Science and Environment, Southern Cross University (2019-2023). • WHO Technical Advisory Group on Water Quality and Health (since 2015-current), for input into drinking, recreational and reuse guidance documents and microbial pathogen performance of on-site drinking water treatment devices. • Water Research Foundation (WRF) Academic Advisory Committee (2016-2019) and Project Advisor Committee (PAC, 2019-2022) for WRF 5040, Successful Implementation of Decentralized Reuse and Treatment Systems. • National Water Research Institute (NWRI) expert panel member (2015-2021) on various non-potable water risk management and regulation projects. • Editor in Chief voluntary role as part of his professional contributions as a Fellow of the International Water Association. • Led water microbiology research into premise plumbing pathogens (e.g. Legionella pneumophila, Pseudomonas aeruginosa, non-tuberculous mycobacteria) and the role of free-living amoeba hosts that also supported viable human enteric viruses through treatment processes and environmental dissemination. • Numerous national and international research grants and collaborations • Has consulted on wastewater reuse • Royalties from patents managed by Macquarie University, Australia • Partner works for company Water^3 • Senior editor for HealthStream, a quarterly newsletter from Water Research Australia (WaterRA) that summarizes international literature relevant to the drinking water industry and notes recent outbreaks or investigations • Travel, accommodation and workshop paid by SUEZ CIRSEE (Paris) for role as a mentor for their Health and Environment postgraduate conference, Cannes, France June 26-28, 2023 and technical advisory team with four other invited senior academics across England, France and Australia. • Involvement in risk assessment projects with the Cooperative Research Centre for Solving Antimicrobial Resistance in Agribusiness, Food and Environments (CRC SAAFE) with Water RA and the South Australia Environment Protection Authority.

Name/Position	Area of Expertise	Declaration of Interests
Professor Cynthia Joll Deputy Director, Curtin Water Quality Research Centre, Curtin University	Expertise in analytical chemistry with a focus on disinfection by-products, both in terms of formation, detection and analysis of the chemicals.	• Previously Deputy Director, Curtin Water Quality Research Centre, Curtin University. The Curtin Water Quality Research Centre was a Strategic Research Alliance with the Water Corporation of WA. Member representative for Curtin University to Water Research Australia. Currently, Professor and Leader of the Curtin Water Quality Research Group. • Chief Investigator on past ARC Linkage projects on disinfection by-products in drinking water systems, and other drinking water and wastewater projects, with partner organisations Water Corporation of WA and Water Research Australia. • Current, past and future projects funded by water utilities on wastewater treatment, water recycling, and drinking water treatment and distribution, including formation of disinfection by-products and analysis of their concentrations in drinking water distribution systems. • Published numerous research papers, conference publications, reports, books and book chapters on wastewater treatment, water recycling, source water quality and drinking water treatment and distribution, including disinfection by-products. • Participation in national and international academic and industry conferences • Current, past and future projects funded by industry partners, government (e.g. NESP) and CSIRO on PFAS in drinking waters, wastewaters, water recycling and manufactured and waste products (e.g. for recycling purposes). • Lectures at Curtin University on environmental chemistry, water chemistry and analytical chemistry. • Travel support to attend research meetings of Water Research Australia where topics such as drinking water treatment and disinfection by-products have been discussed. • Current, past and future projects funded by the water industry relating to corrosion and metal concentrations in drinking water distribution systems

Name/Position	Area of Expertise	Declaration of Interests
Dr David Cunliffe Principal Water Quality Adviser Health Regulation and Protection SA Health	Expertise in water regulation, microbiology and risk assessment.	• Provide specialist advice and policy on public health aspects of water quality including management and provision of drinking water, management and use of recycled water and use of recreational waters. • Contribution to WHO Drinking Water Guidelines leading to publication of background documents (e.g. on toxic cyanobacteria in 2021), specialist texts and two addenda to the 4th edition of the guidelines. • Occasional invitations to provide keynote presentations at international meetings. • Published a number of scientific research journal articles • Contributed to: WHO (2021) Water, sanitation, hygiene, and waste management for SARS-CoV-2, the virus that causes COVID-19, NRMMC/EPHC/NHMRC (2008) Australian Guidelines for Water Recycling: Managing Health and Environmental Risks (Phase 2). Augmentation of Drinking Water Supplies, enHealth Guidance on the Use of Rainwater Tanks and Numerous fact sheets and guidance documents for the SA Department for Health and Wellbeing on drinking water and recreational waters • Membership of the program committees including for the Singapore International Water Week and Australian Water Association Annual Conference OzWater. • Membership of the International Water Association and Australian Water Association. • Membership of the Hong Kong Drinking Water Safety Advisory Committee from 2018. • Chair of the enHealth Water Quality Expert Reference Panel since 2017. • Chair of the External Audit Panel Singapore Public Utilities Board since 2020. • Chair of the WHO Drinking Water Guideline Coordinating Committee. • Has published papers on water quality related issues. • Involvement in risk assessment projects with the Cooperative Research Centre for Solving Antimicrobial Resistance in Agribusiness, Food and Environments (CRC SAAFE) with Water RA and the South Australia Environment Protection Authority.

Name/Position	Area of Expertise	Declaration of Interests
Mr Cameron Dalgleish State Water Officer Tasmanian Department of Health	Expertise in environmental science, water quality and risk management, auditing, public health.	• Health regulator for drinking water safety in Tasmania; administering legislation, policy and guidelines for both drinking water quality and fluoridation. A working understanding of the implementation of the ADWG framework • An environmental scientist specialising in water chemistry with over 20 years' experience in the water industry. Previously worked across construction, natural resource conservation, environmental management and as a health regulator. • Appointments: Member of the enHealth Water Quality Expert Reference Panel, the National Recycled Water Regulators Forum and the Australian Water Association. Secretariat of the Tasmanian Fluoridation Committee. • Department of Health Tasmania Member Representative to Water Research Australia. • Has published journal articles, reports, fact sheets, guidelines and presentations at national conferences, seminars and workshops. • Public Servant: State Water Officer, Department of Health Tasmania. • Project contributor for the development of Operator Competencies in the water industry and development of a WaterVal granular media filter validation protocol, both coordinated by Water Research Australia. • Areas of expertise: Environmental science, water quality and chemistry, risk management, auditing, public health. • Holds stock market investments, and partner is a joint investor in managed fund investments. Neither have influence in the selection of shares purchased on their behalf.
Professor Frederic Leusch School of Environment and Science, Griffith University	Expertise in environmental toxicology, chemical pollutants in the environment, endocrine disruption, bioanalytical tools in water quality assessment, chemical risk assessment and guideline development.	• Several consultancies funded by water industry, specifically on contaminants of emerging concern. • ARC Linkage grants include many water utilities in Australia (including Water Research Australia). • Previous member of the Project Review Team for Water Research Australia, which reviews research projects submitted for Water RA funding and provide advice on suitability to Water RA's research agenda. • Received travel support from Water Research Australia to present on research supported by Water RA at their annual research conference. • Teaches on water quality issues at Griffith University and has given lectures at various institutions on water quality issues and various drinking water guidelines. • Previously involved on the Commonwealth Games Independent Expert Panel on water quality, providing advice on water quality and monitoring programme for the 2018 Commonwealth Games. • Many publications on water quality, all published in peer-reviewed journals. • Independent Advisory Panel Member in the Faure New Water Scheme, Cape Town, South Africa. • Member of the Advisory Committee on the Environmental Management of Industrial Chemicals (IChEMS Advisory Committee).

Name/Position	Area of Expertise	Declaration of Interests
Dr Harriet Whiley Associate Professor in Environmental Health, Flinders University	Leads the Flinders Water Quality and Health Research Consortium and is the Water and Health theme leaders for the Biofilm Research and Innovation Consortium	• Holds an indirect, non-pecuniary interest through my role as SA Branch Committee Member for the Australian Water Association (2021-2022). • Holds an indirect financial interest through my ongoing research collaborations with Enware, a manufacturer and distributer of commercial and industrial plumbing products. • Flinders University representative for Water Research Australia. • Numerous past, present and current research projects on water quality which have received both grant and industry funding. This includes research on biofilms, opportunistic pathogens, rainwater, plumbing materials and risk management approaches. • Has published in academic journals and industry magazines on topics such as lead and water quality risks. • Has presented at academic and industry conferences and workshops. • Holds an indirect, non-pecuniary interest through her role on the Legionella Management Advisory Group. • Deputy Director of the ARC ITTC for Biofilm Research & Innovation • Holds an indirect, non-pecuniary interest through her role on the Legionella Management Advisory Group.
Dr Bala Vigneswaran NSW Department of Climate Change, Energy, the Environment and Water	Experience in water-related public health, water microbiology, water chemistry, water recycling, hydrology, water quality risk assessment and risk management	• Previously served in New South Wales regional councils for over five years in positions concerning water resources, water treatment processes and system compliance.
Mr Peter Rogers Water and public health expert	Expertise in critically analysing scientific evidence in public health including the areas of drinking water quality, wastewater management, beach water quality, asbestos management and disaster management.	• Former Principal Policy Development Officer – Water and Wastewater portfolio, Northern Territory Department of Health

Name/Position	Area of Expertise	Declaration of Interests
Ms Nicola Slavin Principal Policy Officer, Northern Territory Department of Health	Expertise in Indigenous Environmental Health and Public Health policies, strategies and legislation.	• Northern Territory representative on enHealth Water Quality Expert Reference Panel and the National Recycled Water Regulators Subgroup • Northern Territory representative on enHealth Expert Reference Panel on Aboriginal and Torres Strait Islander Environmental Health
Mr Laurence Wilson (Observer) National Indigenous Australians Agency		• No interests declared
Mr Adam Lovell (Observer 2022-2023) Water Services Association of Australia (WSAA)	Peak industry body representing the urban water industry.	• Water Services Association of Australia (WSAA) - Executive Director • Global Water Research Coalition (GWRC) – Board Chair • The GWRC is a non-profit organisation that serves as a focal point for the global collaboration for research planning and execution on water and wastewater related issues.
Dr Nobheetha Jayasekara (Observer, since May 2023) Australian Industrial Chemicals Introduction Scheme	Expertise and knowledge of toxicology, chemical regulation and risk assessment.	• No interests declared
Ms Yulia Cuthbertson (Observer, since 2024) Department of Climate Change, Energy, the Environment and Water	Represents interests of the Department of Climate Change, Energy, the Environment and Water and the Water Quality team from the National Strategies and Assessments section of the Water Policy Division in particular	• No interests declared

The declarations of interest of the independent evidence reviewers at SLR Consulting Australia are listed in the table below:

Table A28. Declarations of interests of the independent evidence reviewers at SLR Consulting Australia

Name/Position	Declaration of Interests
Tarah Hagen Technical Director, Toxicologist & Risk Assessor – Asia Pacific	• Various paid consultancy work (e.g. conducting numerous health risk assessments for clients where PFAS were the chemicals of potential concern requiring assessment; preparation and/or review of draft technical and evaluation reports for previous consultancies with NHMRC (evidence evaluations for 11 inorganic chemicals, full reviews for 4 inorganic chemicals, evidence evaluation & addendum for PFAS review, plus addressing comments on these reports). • Previous Director/staff member of ToxConsult Pty Ltd and as part of day-to-day-consulting activities, provided the report "Assessment of International and National Agency Processes for Deriving Health Based Guideline Values and Drinking Water Guidelines" to NHMRC.
Giorgio De Nola Principal – Toxicology & Risk Assessment	• Various paid consultancy work (e.g. involved in numerous health risk assessments as part of contaminated land audits as well as for other clients where PFAS were chemicals of potential concern requiring assessment; involved in preparation and/or review of draft technical and evaluation reports for previous and/or current consultancies with NHMRC (evidence evaluations for 11 inorganic chemicals, full reviews for 4 inorganic chemicals).
Dr Rhian Cope Technical Director, Toxicologist & Risk Assessor – Asia Pacific	• As part of day-to-day consulting activities at SLR Consulting, involved in assisting with undertaking study evaluations for a previous consultancy with NHMRC (Addendum to evidence evaluation for PFAS).
Maria Consuelo Reyes Campos	• As part of day-to-day consulting activities at SLR Consulting, involved in literature searching for the NHMRC's PFAS review.

The declarations of interest of the independent expert reviewers are listed in the table below:

Table A29. Declarations of interests of the independent expert reviewers

Name/Position	Declaration of Interests
Adjunct Professor Brian Priestly School of Public Health & Preventive Medicine, Monash University	• Literature review and briefing on PFAS health effects for Air Services Australia and the Victorian Department of Human Services • Appeared as an expert witness to the Victorian Parliamentary inquiry into Fiskville 2015 • Provided advice to FSANZ on the development of Health-based Guidance values for PFOS & PFOA, 2017 • Provided briefings on health effects of PFAS and review of documents for legal firms acting for the Department of Defence, 2017-2022 • Visited local fire stations to brief staff on PFAS health effects (NSW Fire Service 2019 • Literature review and contribution to CSIRO report on the health effects of short-chain PFAS, 2021 • Literature review of the occurrence of PFAS in food for the Office of the NSW Chief Scientist & Engineer, 2016 • Participated in an expert panel on grouping of PFAS for risk assessment; co—author of manuscript published in Reg Tox Pharmacol 2022 (SciPinion – a U.S. consortium, 2021-2022) • Participated in workshops to discuss development of guidance for PFAS risk assessment (enHealth Council 2015) • Panel member NHMRC PFAS Targeted Call for Research Reference Group (2018) • Peer review and comment on several reports prepared by ToxConsult Pty Ltd on PFAS contamination at the Fiskville training college, including comment on the development of site-specific PFOS/PFOA Toxicity Reference Values for the Country Fire Authority Victoria 2013-2015
Professor Stuart Khan School of Civil Engineering, University of Sydney	• Chair of NHMRC's Recreational Water Quality Advisory Committee, which is currently working on revising Australian guidelines for recreational water quality and where PFAS are a specific group of contaminants of interest. • Member of Water Research Australia where bids for funded research projects on a range of water quality and treatment topics where PFAS is highly topical. • Publication of journal articles, some recent papers have addressed issues relating to PFAS. • Member of the NSW Government Independent Water Advisory Committee, providing advice to the Department of Climate Change, Energy, the Environment and Water on statewide urban water management issues to support the achievement of outcomes sought by water strategies and help them understand emerging risks and challenges. • Research funded by a wide variety of water utilities, which at times have included Sydney water, WaterNSW, SEQWater, Melbourne Water, Water Corporation and many others. • Active member of the Fellowship and the Academy of Technological Sciences and Engineering (ATSE) • Member of the Australian Water Association (AWA) • International Water Association (IWA) Fellow. • Regular public commentator regarding water quality issues (e.g. the Guardian Australia newspaper)

Name/Position	Declaration of Interests
Emeritus Professor Jack Ng Queensland Alliance for Environmental Health Sciences The University of Queensland	• Principal supervisor for various PhD studies/projects on mixture toxicity of PFAS (e.g. Genotoxicity assessment of per- and polyfluoroalkyl substances mixtures in human liver cells, 2022; Toxicity assessment of historical aqueous film-forming foams (AFFFs) using cell-based assays, 2022; Combined effects of mixed per- and polyfluoroalkyl substances on the Nrf2-ARE pathway in ARE reporter-HepG2 cells, 2022; Assessing the human health risks of per- and polyfluoroalkyl substances: a need for greater focus on their interactions as mixtures, 2021. • Member of the IARC Monographs Working Group and co-author of Volume 135, Perfluorooctanoic acid (PFOA) and Perfluorooctanesulfonic acid (PFOS) published by IARC in 2025 and co-author of the IARC News Release in the Lancet Oncology journal,

Appendix E – Public consultation summary report

Background

The *Australian Drinking Water Guidelines* (the Guidelines) are intended to provide a framework for the good management of drinking water supplies. The Guidelines are designed to provide an authoritative reference on what defines safe, good quality water, how it can be achieved and how it can be assured. The National Health and Medical Research Council (NHMRC) maintains the Guidelines through a rolling revision process to ensure they represent the latest scientific evidence on good quality drinking water.

NHMRC has updated guidance in the Guidelines regarding the per- and polyfluoroalkyl substances (PFAS) Fact Sheet, including revised and newly established health-based guideline values. The draft guidance material and supporting information for public consultation included:

- a revised draft PFAS Fact Sheet
- an NHMRC Statement: Public consultation on PFAS in drinking water
- an Administrative Report outlining the guidance development process including the evidence-to-decision process
- the evidence review reports: Research Protocol, Evidence Evaluation Report, Technical Report and Addendum to the Evidence Review.

NHMRC sought public comment on the draft guidance between 21 October to 22 November 2024. Stakeholders were invited under paragraph 13(d) of the NHMRC Act 1992 to make submissions to NHMRC about the draft guidance. Extensions were granted upon request.

Consultation questions

The questions asked during public consultation were as follows:

1. Do you have any comments on the overall approach taken to develop the draft guidance?
2. Do you have any comments about the implementation or application of the draft guidance?
3. Do you have any specific comments on the draft PFAS Fact Sheet?
4. Do you have any specific comments on the draft NHMRC Statement: Public consultation on PFAS in drinking water?

Public submissions

NHMRC received 86 public consultation submissions from 49 individuals and 37 organisations. High level details of respondents are listed below, with organisations named where permission has been given to do so.

- Australasian Land and Groundwater Association
- Australian Academy of Technical Sciences and Engineering
- Australian Beverages Council Limited
- Australian Institute of Petroleum
- Australian Medical Association
- Australian Sustainable Business Group
- Banana Shire Council
- Cancer Council Australia
- Chemistry Australia
- Department of Health WA
- Dungog branch of Country Women's Association
- Envirolab

- Environmental Risk Sciences
- Epic Environmental Pty Ltd
- Friends of the Earth Australia
- Geosyntec Consultants and ExxonMobil Australia
- GHD
- Guam Water Authority
- Hunter Water Corporation
- Local Government Association of Queensland
- MidCoast Council
- National Centre for Epidemiology and Population Health (NCEPH)
- Public Health Association Australia
- Queensland Water
- Rainforest Reserves Australia
- Save Our Surroundings Riverina
- Senversa
- Shellharbour City Council
- Stop PFAS
- Sydney Knitting Nannas
- TasWater
- Veolia ANZ
- VicWater
- Water Services Association of Australia
- 49 individuals
- 2 organisations
- 1 commercial business

Responses to public submissions

The public consultation submissions raised a number of key issues for consideration by NHMRC with advice from the Committee. A high-level summary of these issues is provided in **Table 1** below, along with the response from NHMRC and the Water Quality Advisory Committee (Committee). Minor edits and clarifications were actioned where accepted. SLR Consulting Australia (SLR) was also contracted to assist in providing further information to address selected consultation comments as advised by the Committee (see **Appendix F and G**). Note that comments on issues unrelated to the PFAS review were not considered as part of this process and are not included in the table below.

Scope of the PFAS review

Table A30. Key issues raised during public consultation relating to the scope of the PFAS review

Key Issue/ Comment	Response
Concerns that only five PFAS have been reviewed.	Noted. While the scope of the revised guidance considers five select PFAS, additional PFAS may be reviewed by NHMRC in future as part of the rolling revision of the *Australian Drinking Water Guidelines*.
Concerns that a total/sum of PFAS guideline value has not been developed.	Noted. NHMRC reviewed the different approaches that international jurisdictions (including the US EPA and Europe) used to derive a single total/sum guideline value for a PFAS mixture in drinking water. Based on the findings from the review (available in the Addendum Report), NHMRC and the Water Quality Advisory Committee had concerns about the feasibility of implementing a guideline value for a PFAS sum/mixture with the current options available, given the limited health evidence available for other PFAS. Therefore, no single total/sum guideline value for a PFAS mixture has been proposed at this time but it may be reconsidered should further evidence and methods become available.
Concerns that NHMRC did not review exposures of PFAS from sources other than drinking water.	Noted. Sources of exposure to PFAS other than drinking water are outside the scope of the current review. The *Australian Drinking Water Guidelines* note that intake from food, pharmaceuticals and other products can be significant sources of chemical exposure.
Concerns that NHMRC did not include up to date information on typical levels of PFAS in Australian drinking water supplies	Noted and partially accepted. NHMRC is aware that there are monitoring activities underway to understand the level of PFAS contamination around Australia. Amendments have been made to the PFAS Fact Sheet to refer to published water monitoring data results on water supplier websites as additional examples.

NHMRC PFAS review and proposed health-based guideline values

Table A31. Key issues raised during public consultation relating to the **NHMRC PFAS review and proposed health-based guideline values**

Key Issue/ Comment	Response
Concerns that there is no safe level or threshold of PFAS in drinking water, hence the PFAS guideline values should be set at zero.	Noted. NHMRC, with advice from the Water Quality Advisory Committee, undertook a comprehensive review and selected the key studies considered to have the highest certainty in terms of study quality and methods to derive the health-based guideline values in Australian drinking water. These values indicate the amount of PFAS in drinking water that a person can consume on a daily basis over a lifetime without any appreciable risk to health. They are protective of human health, are very conservative and take into account Australia's conditions and context. The threshold approach was determined to be appropriate to derive the PFAS guideline values, which assumes there is a dose of PFAS below which no adverse health effects are expected to occur. The draft PFAS guideline values also include wide safety margins and so are expected to be well below the level at which any negative effects could occur.
Concerns raised that the draft PFAS guideline values do not align with those set by the United States Environmental Protection Agency (US EPA), the World Health Organization (WHO) or the European Union, which are seen as best practice.	Noted. NHMRC does not automatically adopt overseas values without thorough review. NHMRC carefully considered international guidance, including those from the US EPA, European Union, and WHO, and derived guideline values based on what is considered to be the highest certainty health evidence for the most critical health effects that are achievable and protective of public health.
Concerns about why NHMRC reached a different conclusion for health-based guideline values than the findings suggested by the reviewer, expert review and other stakeholders.	Noted. The evidence review completed by SLR Consulting Australia presented a range of guideline values suitable to be adopted/adapted in the updated PFAS guidance. The Committee considered the range of suitable guideline values in regard to the Australian context and selected draft PFAS guideline values based on their analysis of the certainty in the underpinning studies, whether the chosen endpoints are clinically relevant and which endpoints are considered the most critical and protective of health. NHMRC and the Water Quality Advisory Committee considered the feedback provided by expert review and key stakeholders alongside the information provided in the review reports when deciding on what was considered to be the most appropriate, highest confidence health-based guideline values for the selected PFAS. This includes choice of safety factors to give an appropriate margin of safety. Further information is provided in the Administrative Report.

Key Issue/ Comment	Response
Concerns about the technical basis for the proposed PFOS health-based guideline value (e.g. concerns about the endpoint, choice of study, application of the modelled benchmark dose instead of the measured no observed adverse effect level (NOAEL))	Noted. NHMRC and the Water Quality Advisory Committee considered the feedback provided by expert review and key stakeholders alongside the information provided in the review reports when deciding on what was considered to be the most appropriate, highest confidence health-based guideline value for PFOS. NHMRC and the Water Quality Advisory Committee have determined that the NTP (2022) study is the best available evidence to derive a health-based guideline value for PFOS. Incorrect wording regarding the extramedullary hematopoiesis effects observed in the NTP (2022) study has been noted (see Administrative Report). NHMRC and the Water Quality Advisory Committee note that while the SLR Consulting evidence review report addressed the limitations with the use of a 28-day study, the NTP (2022) study is a more recent, high-quality study that shows adverse health effects occurring at a lower level than those observed in chronic studies, so should not be discounted. The short-term study limitations are accounted for by using an additional uncertainty factor in the guideline derivation. NHMRC and the Water Quality Advisory Committee consider that it is a more statistically robust approach to use a benchmark dose rather than a NOAEL to derive a health-based guideline value for PFOS. US EPA also applied the benchmark dose approach rather than using NOAELs when assessing the data from the same study selected by NHMRC. The guideline value for PFOS has been revised using a more robust benchmark dose following consideration of consultation feedback. The choice of benchmark dose model was informed by an analysis by SLR Consulting Australia. Further information is provided in the PFAS Fact Sheet and Administrative Report.
Concerns about the human relevancy of the endpoint/critical health effect selected for PFOA (neoplastic pancreatic acinar adenomas and adenocarcinomas).	Noted. NHMRC and the Water Quality Advisory Committee have determined that the NTP (2023) study is the best available evidence to derive a health-based guideline value for PFOA. Although uncertainties about the clinical relevance of neoplastic pancreatic acinar adenomas and adenocarcinomas after PFOA exposure in rats were noted by the reviewer, it was also noted by the reviewer that these observed pancreatic effects may occur through modes of action other than the PPARα pathway (currently demonstrated in vitro but not in vivo) and so human relevance could not be discounted. This was also supported by the International Agency for Research on Cancer (IARC), which cited the carcinogenic effects observed in animals in the NTP (2023) study as supporting its evaluation of PFOA as carcinogenic in humans.

Key Issue/ Comment	Response
Concerns about the selected studies underpinning the PFBS and PFHxS health-based guideline values, including queries about the endpoint/critical health effect of thyroid hormone disruption and the relevance of this endpoint to human health, and also the application of the dose-response model to generate a benchmark dose for PFBS.	Noted. In light of consultation comments, the Committee's Chemical Subgroup discussed the 28-day study by NTP (2022) for PFHxS and the 60-day study by Feng (2017) for PFBS. While noting it would be ideal to use chronic studies to derive guideline values, in lieu of available chronic studies, the Subgroup agreed that these studies are the best available evidence at this time. Minor edits have been made to the Evidence-to-Decision tables for PFHxS and PFBS to clarify this issue (see **Appendix A** of the Administrative Report). Thyroid endpoints were selected as the point of departure for the PFHxS and PFBS health-based guideline values and were considered separately for each chemical. The rationale supporting each decision regarding relevancy of the thyroid endpoint are provided in the evidence review reports and in the guideline derivation sections of the revised PFAS Fact Sheet. NHMRC and the Water Quality Advisory Committee consider that it is a more statistically robust approach to use a benchmark dose rather than a no observed adverse effect level to derive a health-based guideline value. This approach has been taken to derive the guideline value for PFHxS and PFBS. Other agencies also applied the benchmark dose approach rather than using NOAELs when assessing the data from the same studies selected for PFHxS and PFBS by NHMRC. Further information is provided in the Administrative Report and evidence review reports.
Concerns about uncertainty factors used	Noted. Information regarding the choice of safety factors and benchmark doses used in guideline derivations are provided in the review reports for each proposed guideline option, the guideline derivation section of the draft PFAS Fact Sheet and in the Administrative Report. The safety factors used in the calculations for each chemical under review are determined using professional judgement of the reviewer on a case-by-case basis depending on the nature of the underpinning study and available toxicological database for the chemical. This aligns with approaches outlined in Section 6.3.3 in the *Australian Drinking Water Guidelines*, and guidance on risk assessment from the Environmental Health Standing Committee (enHealth). The safety factors proposed by the reviewer were reviewed by and agreed to by the Water Quality Advisory Committee.

Key Issue/ Comment	Response
Concerns about the method of review, such as using an adopt/adapt review approach versus a traditional chemical risk assessment or full systematic review of primary studies	Noted. NHMRC used an adopt/adapt approach to review the PFAS Fact Sheet, using recently published guidance/guidelines from other jurisdictions that were critically appraised and found to have suitable guideline development approaches and methodologies to NHMRC processes, and have recently undertaken comprehensive reviews of the evidence base. This is an internationally accepted best practice approach for guideline development and significantly reduces duplication of effort and resources. The methodology for this approach, including how the included evidence was searched, selected and considered, was outlined in the Research Protocol, with more technical details provided in the evidence review reports. Noted. NHMRC used an adopt/adapt approach to review the PFAS Fact Sheet, using recently published guidance/guidelines from other jurisdictions that were critically appraised and found to have suitable guideline development approaches and methodologies to NHMRC processes, and have recently undertaken comprehensive reviews of the evidence base. This is an internationally accepted best practice approach for guideline development and significantly reduces duplication of effort and resources. The methodology for this approach, including how the included evidence was searched, selected and considered, was outlined in the Research Protocol, with more technical details provided in the evidence review reports.
Concerns about assumption values used by NHMRC to attribute proportion of PFAS exposure from drinking water	Noted. The Guidelines note that intake from food, pharmaceuticals and other products can be significant sources of chemical exposure. Acceptable intake values derived from animal dose data are assumed to encompass all sources of exposure, as outlined in Section 6.3.3 in the Guidelines, which would include background intake from other sources. In deriving Australian health-based guideline values, the Guidelines assume that for chemicals that are used commercially or industrially, water contributes 10 per cent of intake. This is the approach that has been taken to derive the PFAS guideline values in this update. Further clarification on this issue is provided in the Question-and-Answer resource.
Concerns that decisions about the health-based guideline values were based on other factors such as public preferences or politics.	Not accepted. Factors such as consumer preferences, stakeholder acceptability, feasibility, treatment, compliance and cost impacts were noted during the evidence-to-decision process by NHMRC and the Water Quality Advisory Committee when considering the different guideline options to adopt/adapt in Australia. However, the decisions about the guideline values were based on what was considered to be the highest certainty health evidence for the most critical health effects that are achievable and protective of public health. Further information is available in the Administrative Report.

Impacts of implementing the revised guidelines

Table A32. Key issues raised during public consultation relating to the **impacts of implementing the revised guidelines**

Key Issue/ Comment	Response
Requests for NHMRC to develop additional guidance on: • transition timeframes to implement any new PFAS guideline values • the actions required if PFAS levels exceed the revised guideline values.	Not accepted. Implementation of the Guidelines is outside the remit of NHMRC. In addition, detailed technical or operational guidance is outside the scope of the Guidelines. General guidance on managing water quality including managing exceedances is provided elsewhere in the Guidelines. The Guidelines are not mandatory standards, but the states and territories do reference or adopt the Guidelines, and the relevant health authorities and/or drinking water regulators have the responsibility to implement and monitor these policies. Information on this issue including timeframes has been provided in the Question-and-Answer resource.
Requests for NHMRC to emphasise that any detections of exceedances should not be seen as a pass/fail	Noted. As outlined in the Guidelines (which the PFAS Fact Sheet will be inserted into when finalised), all chemical guideline values, including any detections of PFAS higher than the guideline values, should trigger an investigation of potential sources of contamination in case these can be managed to bring the water supply back under guideline values. However, implementation of the Guidelines in different regulatory settings is outside the remit of NHMRC.
Requests for NHMRC to mandate or implement regular and transparent monitoring of PFAS in drinking water sources.	Not accepted. It is outside the remit of NHMRC to mandate or implement monitoring requirements for PFAS, or any chemicals, in drinking water sources. The Guidelines recommend a site-specific, risk-based approach to monitoring chemicals of concern (which includes PFAS) as outlined in the Guidelines risk management framework. The role of NHMRC, as set out in Section 7 of the National Health and Medical Research Council Act 1992, is to inquire into, issue guidelines on, and advise and make recommendations to the Commonwealth, as well as the states and territories, on matters such as public health and matters relating to the improvement of health. This includes developing nationally consistent, evidence-based advice such as the Guidelines that can be applied by jurisdictions throughout Australia in the context of their own administrative and legislative frameworks. Management of drinking water, including monitoring requirements, depends on the legislated arrangements for water supply within each jurisdiction. The relevant state/territory health and/or drinking water regulator is responsible for regulating supply and establishing monitoring requirements. Given the public interest in PFAS and the need for a broader understanding of the risks from PFAS in drinking water, it is also suggested in the Guidelines that water providers regularly share information with the community on the current risks in their catchment and the findings from background testing.

Key Issue/ Comment	Response
Concerns that there should be an importation ban on any products entering Australia that contain PFAS.	Noted. The importation and regulation of PFAS, including placing an importation ban on products entering Australia, is outside the remit of NHMRC.
Concerns that the draft guideline values will have negative economic, financial, regulatory and/ or social impacts, including but not limited to: • limited capacity or funds available to analyse and treat drinking water to meet the updated guideline values, which may lead to an increase in the cost of drinking water for consumers. • revisions to other guideline values such as recreational water, soil and food, which may result in waterways unsuitable for recreational use, soil unsuitable for residential purposes, food no longer safe for consumption or export and organic products (such as biosolids, compost etc.) not able to be used for other purposes, impacting the circular economy. • high degree of public fear/ stress and anxiety around current and historical exposure to PFAS	Noted. The scope of the NHMRC PFAS review was to determine whether the current advice in the Guidelines remains appropriate. NHMRC and the Water Quality Advisory Committee noted potential impacts of different guideline values (including potential economic, regulatory, social and cost impacts) during the evidence-to-decision process (see Evidence-to-Decision tables in **Appendix A** of the Administrative Report), but decisions about the guideline values were based on what was considered the best available health evidence. The Evidence-to-Decision tables have been updated with relevant impacts raised through consultation. Further information is provided in the Administrative Report. It is noted that there may be significant cost implications for some communities which have drinking waters that exceed the guideline values. Implementation of the Guidelines by the states and territories is at the discretion of each state and territory health authority and/or drinking water regulator, usually in consultation with water suppliers, and should include an appropriate economic analysis such as a cost-benefit evaluation of regulatory alternatives, prior to implementation. Review of guidance values other than drinking water is outside the scope of this review; however, it is noted that there can potentially be impacts on other PFAS guidance values (e.g. for food, soil and land, waste management) if any proposed changes to NHMRC advice are considered, accepted and adapted by other Australian agencies for their specific purposes. NHMRC has developed more consumer-friendly information for the NHMRC website after considering feedback from consultation. This aims to provide a plain language summary and to help consumers and those who work with communities explain the health risks and other key issues.

Accessibility of the guidance to the public

Table A33. Key issues raised during public consultation relating to **accessibility of the guidance to the public**

Key Issue/ Comment	Response
Request for NHMRC to improve the PFAS guidance material or develop more supporting material that is concise, clear and accessible for the public.	Noted. Recognising the importance of providing additional context to stakeholders during public consultation, NHMRC developed a number of resources to assist in key messaging (e.g. the public consultation NHMRC Statement, CEO message and Question-and-Answer resource). The supplementary material was produced to improve accessibility of the PFAS Fact Sheet and address key concerns in a more concise and clear manner. Prior to release for public consultation, consumer representatives reviewed the supporting information to ensure the supporting material was understandable by the community and addressed community concerns. NHMRC has developed more consumer-friendly information for the NHMRC website after considering feedback from consultation. This aims to provide a plain language summary and to help consumers and those who work with communities to explain the health risks and other key issues.

NHMRC public consultation process

Table A34. Key issues raised during public consultation relating to **accessibility of the NHMRC public consultation process**

Key Issue/ Comment	Response
Concerns with the NHMRC public consultation portal (e.g. restricting comments to boxes without option for uploading detailed comments/ documents).	Noted. There are currently restrictions due to security reasons preventing the upload of attachments to the public consultation portal for NHMRC consultations. Contact details for the NHMRC Water Team were provided and all requests for material to be sent via email, including additional attachments, were accepted and were considered.
Concerns about how NHMRC has consulted with stakeholders: • not providing enough time • not consulting enough key agencies prior to public consultation	Noted. Given the public interest in this issue, NHMRC has tight timeframes to undertake this review and to publish in the *Australian Drinking Water Guidelines*. The public consultation period for the draft guidance was in alignment with NHMRC's legislated requirement for public consultation (30 days). Extensions were offered and granted by request. NHMRC undertook targeted consultation with consumers, the enHealth Water Quality Expert Reference Panel, FSANZ and the then-Department of Health and Aged Care prior to public consultation. Broader consultation with other agencies was taken in parallel to public consultation due to time constraints.

Appendix F – Additional considerations following consultation

This document is intended to summarise key considerations undertaken by NHMRC and the Water Quality Advisory Committee (the Committee) in January – March 2025 to address key issues raised in feedback received through the consultation process.

Key issues under consideration following consultation

A number of issues were raised during public and targeted consultation on the draft guidance. NHMRC and the Committee gave due regard to each submission and edits were made to the guidance where accepted. A summary of the key issues and responses has been provided in the Public Consultation Summary report at **Appendix E**.

Several specific issues relating to the technical basis for the PFOS and PFOA health-based guideline values were flagged for further consideration by members of the Chemical Subgroup, including:

PFOS:

- concerns about selecting the endpoint of bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) to derive the health-based guideline value for PFOS
- issues with either the use of a 28-day study versus a 2-year study and/or application of an uncertainty factor for the use of a short-term study in the guideline derivation
- concerns that there is incorrect wording to describe the adverse health effect for extramedullary hematopoiesis observed in the NTP (2022) study that appears to have originated from the US EPA risk assessment[18] (US EPA 2024c) and been carried through into the NHMRC review process
- disagreement with the application of the modelled benchmark dose selected by the US EPA in their assessment of the NTP (2022) study instead of the measured no observed adverse effect level (NOAEL)
- questions about the US EPA dose-response models[19] that were used to derive a benchmark dose to underpin the draft PFOS guideline value (US EPA 2024i).

PFOA:

- concerns that the non-neoplastic hepatocellular necrosis may be a more appropriate endpoint to derive a health-based guideline value for PFOA, instead of neoplastic pancreatic acinar adenomas and adenocarcinomas.

The Chemical Subgroup advised NHMRC to seek further information from SLR Consulting Australia (SLR) to address the following questions:

1. Several consultation submissions noted that there is incorrect wording around the adverse health effect for extramedullary hematopoiesis that appears to have originated from the US EPA risk assessment. Does the incorrect wording from the US EPA on the splenic extramedullary haematopoiesis (quoted below), impact the confidence rating provided in

[18] Wording within the US EPA Human Health Toxicity Assessment for PFOS and Related Salts (April 2024) (US EPA 2024c)

[19] Models shown in Figure E-17 and Figure E-18 in *US EPA Appendix: Human Health Toxicity Assessment for PFOS (April 2024).*

the SLR Consulting Addendum Report (i.e. high confidence)? '*...increased bone marrow hypocellularity in conjunction with extramedullary hematopoiesis were observed. Extramedullary hematopoiesis, blood cell production outside of the bone marrow, occurs when normal cell production is impaired. Bone marrow hypocellularity in parallel with extramedullary hematopoiesis suggest that PFOS impedes hematopoiesis in the bone marrow*.' (US EPA 2024c)

2. The last sentence in section 4.1.1.2 (quoted below; p359 of 514) refers to the endpoint of extramedullary haematopoiesis being consistent with other studies; is this still relevant considering the incorrect wording from the US EPA as mentioned above? '*The endpoint of splenic extramedullary hematopoiesis was observed in both sexes and was consistent with other high and medium confidence studies that reported alterations in circulating immune cells, splenic cellularity, and thymic cellularity, both of which increase the confidence in this endpoint (Table 4-1)*.'(US EPA 2024c)
3. The SLR Consulting Addendum Report notes the limitations of the Multistage Degree 1 dose-response model (Figure E-18) used by the US EPA to derive the lowest $BDML_{10}$ in US EPA Appendix: Human Health Toxicity Assessment for PFOS (April 2024). The NHMRC Chemical Subgroup has looked into this further and found that amongst the range of dose-response models provided in Table E-64, the benchmark dose with the lowest p value and highest AIC value was chosen. If you were going to apply the benchmark dose approach to derive a Point of Departure (POD) for PFOS from Table E-64 (or Table E-62 if that dataset is suitable), is there a case for using Weibull model or any of the other models reported in Table E-64 as a better choice for the dose-response curve based on probability and AIC?

The Chemical Subgroup also noted that questions regarding the relevancy of the PFOA guideline endpoint could be addressed pending review of the International Agency for Research on Cancer (IARC) Monograph (IARC 2025).

Additional independent PFOS assessment

On advice from the Committee via its Chemical Subgroup, NHMRC engaged SLR Consulting Australia (SLR) to provide an additional PFOS assessment to help address issues raised through public and targeted consultation (see **Appendix G**). Key conclusions from the PFOS additional assessment by SLR are as follows:

- confirmation by SLR that the US EPA (2024c) report indeed transcribed the incorrect wording of the splenic extramedullary haematopoiesis effect in rats found in the NTP (2022) study: Instead of an *increased bone marrow hypocellularity in conjunction with extramedullary hematopoiesis* observed; *an increased incidence of decreased splenic extramedullary haematopoiesis accompanied by increased bone marrow hypocellularity* was actually observed.
- the incorrect wording by the US EPA of the splenic extramedullary haematopoiesis effect in rats found within the NTP (2022) study did not impact the confidence rating of the study or the confidence of the endpoint selection. The increased incidence of decreased splenic extramedullary haematopoiesis accompanied by increased bone marrow hypocellularity was deemed to be real and adverse, and unlikely to be a direct effect of stress of treatment.

- the reproduced US EPA benchmark dose modelling results by SLR were similar to US EPA results with slightly different p-values and AIC values. Given the viability of a large number of models all with similar AIC values, best practice would be to prioritise the model that has the smallest difference between observed data points and the fitted model values (i.e. lowest scaled residuals). From the SLR assessment, this was determined to be the Gamma model with a $BMDL_{10}$ of 5.688 mg/L (SLR 2025).
- SLR also determined that as all of the evaluated models are viable and have similar AIC values (48.574 to 52.979), it is possible, based on current US EPA (2012) guidance for using benchmark doses, to use the simple average or geometric mean of the benchmark doses with the lowest AIC values. If this approach is taken, the arithmetic mean across the models with AIC values < 50 (Multistage 2, 4 and 5, logistic and probit) is (3.608 + 3.415 + 3.387 + 5.143 + 5.025)/5 = 4.12 mg/L.

The SLR Additional PFOS Assessment (SLR 2025) is at **Appendix G** of this report.

Conclusions

The Chemical Subgroup considered the additional PFOS assessment (**Appendix G**) and the IARC monograph (IARC 2025) and reached the following conclusions:

- Interpretation of NTP (2022) results and critical health endpoint: Members agreed that the NTP (2022) 28-day study remains the best available evidence to establish a health-based guideline value for PFOS in Australian drinking water, with the increased incidence of decreased splenic extramedullary haematopoiesis accompanied by increased bone marrow hypocellularity remaining the most critical adverse health effect.
- Use of 28-day study vs. 2-year study: Whilst the SLR Consulting evidence review report addressed the limitations with the use of a 28-day study, Members considered that the NTP (2022) study is a recent, high-quality study that shows adverse health effects occurring at a lower level than those observed in chronic studies, so should not be discounted. The short-term study limitations are accounted for by using an additional uncertainty factor in the guideline derivation. The lack of replication in the longer duration studies cannot be adequately assessed because of the differences in systemic exposure at the critical time point of 28 days (SLR 2025). SLR further commented that it is difficult to determine consistency due to methodological differences between studies, however, more consistencies may emerge once the NTP publishes their 2-year findings.
- Using a benchmark dose versus NOAEL approach for NTP (2022): While noting the concerns raised about the large difference between the measured serum NOAEL and the benchmark dose used by the US EPA (and adapted by NHMRC), Members reconfirmed using the benchmark dose to derive a guideline value for PFOS, noting that it is considered to be a more statistically robust approach to use a benchmark dose rather than a NOAEL to derive a guideline value. Of the two approaches, the use of the modelled $BMDL_{10}$ led to calculation of a lower guideline value. This is supported by the US EPA, who also selected the benchmark dose approach over the NOAEL when assessing the NTP (2022) study (US EPA 2024c).

- Selection of benchmark dose models to determine best point of departure: Members agreed that the Gamma model from US EPA (2024i) is the preferred benchmark dose model to use to determine a point of departure (as a $BMDL_{10}$) for deriving a health-based guideline value for PFOS. Members noted that the US EPA chose the Multistage 1 model, which gave the lowest benchmark dose however was inconsistent with the US EPA (2012) Benchmark Dose Technical Guidance (the Multistage 1 model had a higher AIC value than other models). Members noted that the ideal model has the smallest difference between observed data points and the fitted model values (i.e. lowest scaled residuals). From the SLR assessment (SLR 2025), this was determined to be the Gamma model with a $BMDL_{10}$ of 5.688 mg/L, which produces a health-based guideline value of 8.49 ng/L (rounded to 8 ng/L). Members noted that although the Gamma model minimised the difference between the observed data points and scaled residuals, the distribution of the Gamma model included a large difference between the benchmark dose lower confidence levels (BMDL) and benchmark dose (BMD) values (wide confidence interval). Members also explored several other modelled options which supported a guideline value for PFOS of 8 ng/L.
- Choice of critical health endpoint for PFOA: Members of the Chemical Subgroup reviewed the IARC Monograph (published in February 2025) and concluded that the Monograph supported the neoplastic pancreatic acinar adenomas and adenocarcinomas endpoint for PFOA. Members also noted that SLR could not dismiss the relevancy of the neoplastic pancreatic acinar adenomas and adenocarcinomas endpoint for PFOA (SLR 2024c). It was concluded that no changes were required for the PFOA health-based guideline value.

Revised guideline derivation for PFOS

The extrapolation of the selected point of departure for PFOS using the Gamma benchmark dose model in female rats to a human health-based guideline value for drinking water is outlined below. This uses the same clearance factors and uncertainty values used for NTP (2022) used in Table 5-2 in SLR (2024c).

Parameter		NTP (2022) – candidate study in US EPA (2024c)
Critical study		NTP (2022)
Study population		Rats
Form of PFOS studied		PFOS (>96% pure)
Exposure route		Oral (gavage)
Study timeframe		28 days
Critical Effect		Extramedullary haematopoiesis and bone marrow hypocellularity
Serum Point of Departure (mg/L)		$BMDL_{10}$ = 5.688 in female rats [(1)]
Clearance Factor (L/kg-day)		0.000128
Point of Departure HED (mg/kg bw/day)		0.000728
Uncertainty factors	UF_A	3
	UF_H	10

Parameter		NTP (2022) – candidate study in US EPA (2024c)
	$UF_{subchronic}$	10
	$UF_{database}$	1
	$UF_{composite}$	300
Health-based guidance value (ng/kg/day)		2.43
Relative source contribution (RSC) to drinking water		0.1
Resulting adaption to a Health-based DWG (2) (ng/L)		8.49

DWG = Drinking Water Guideline; BMDL = Lower Benchmark Dose; HED = Human Equivalent Dose; UF_A = Uncertainty factor for extrapolation from animals to humans; UF_H = Uncertainty factor for human variability; $UF_{subchronic}$ = Uncertainty factor for extrapolation from a subchronic to a chronic study; $UF_{composite}$ = Composite (i.e. total) uncertainty factor; $UF_{database}$ = Uncertainty factor to account for the limited database of toxicological studies.

(1) Modelled serum point of departure as a $BMDL_{10}$ from the Gamma benchmark dose model for female rats as outlined by US EPA (2024i). To help address comments received from public/targeted consultation, an analysis of the benchmark dose for the endpoint of increased incidence of decreased extramedullary haematopoiesis in the spleen in female Sprague-Dawley rats was undertaken (SLR 2025), reproducing the methodology in the US EPA Appendix: Human Health Toxicity Assessment for PFOS (US EPA 2024i). This analysis, using US EPA's online BMDS tool, found best practice would be to prioritise the Gamma model with a $BMDL_{10}$ of 5.688 mg/L (SLR 2025).

(2) Adaption of guidance value has been undertaken using the default assumptions for derivation of DWGs in Australia using the default equation described in Chapter 6.3.3 of the *Australian Drinking Water Guidelines*.

DWG (ng/L) = [Guidance value (ng/kg bw/day) x 70kg (adult) x 0.1 for adult] ÷ 2 L/day for adult

Using the Gamma model $BMDL_{10}$ from US EPA (2024i) results in a revised health-based guideline value of 8 ng/L (rounded), which was derived as follows:

$$8 \text{ ng/L (equivalent to 0.008 µg/L)} = \frac{728 \text{ ng/kg bw/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 300}$$

where:

- 728 ng/kg bw/day (0.000728 mg/kg bw/day) was the acceptable daily intake of PFOS in humans determined from a benchmark dose derived on the basis of bone marrow effects (extramedullary haematopoiesis and bone marrow hypocellularity) from a sub-chronic (28-day) toxicity study in female rats (NTP 2022; SLR 2024c; SLR 2025).
- Although there were substantial differences between the modelled benchmark doses and measured no observed adverse effect levels (NOAELs) in the NTP (2022) study (i.e. 29-fold difference in female rats and 5-fold difference in male rats), the former was considered to be a more statistically robust approach and was adopted in the guideline derivation for PFOS. Although this was consistent with the US EPA (2024c), which also applied the benchmark dose approach when assessing the data from this study, the benchmark dose used for this

derivation is based on the best practice benchmark dose model as per the additional PFOS assessment (SLR 2025).

- Because of the large differences observed in the half-lives of PFOS in humans compared to animals, pharmacokinetic modelling was applied to the serum PFOS concentrations measured in experimental animals at the benchmark dose for the observed effects to calculate the human equivalent dose (a dose in humans anticipated to provide the same degree of effect as that observed in animals at a given dose) (SLR 2024c).
- 300 was the uncertainty factor applied to the human equivalent dose derived from an animal study. The uncertainty factor incorporated a factor of 3 to account for the uncertainty of extrapolating from animals to humans, a factor of 10 to account for human variability and a factor of 10 for use of a short-term study (SLR 2024c).
- 70 kg was taken as the average weight of an adult.
- 0.1 was a proportionality factor based on the conservative assumption that drinking water accounts for 10% of the acceptable daily intake.
- 2 L/day was the reference value of water consumed by an adult.
- The calculated value of 8.49 ng/L was rounded to a health-based guideline value of 8 ng/L as per the rounding conventions described in Chapter 6.

Edits were made to the PFAS Fact Sheet to align with the conclusions reached by NHMRC and the Committee regarding the PFOS point of departure and subsequent change to the health-based guideline value. The Evidence to Decision table for PFOS was also updated as a result of the revision of the PFOS health-based guideline value (see **Appendix A**).

References

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Appendix G – PFOS Additional assessment by SLR Consulting Australia

Revision Record

Revision	Date	Prepared By	Checked By	Authorised By
1.0	10 February 2025	Tarah Hagen, MSc, DABT, FACTRA	Rhian Cope, PhD, DABT, DABVT, FACTRA	Tarah Hagen
2.0	3 March 2025	Tarah Hagen, MSc, DABT, FACTRA	Rhian Cope, PhD, DABT, DABVT, FACTRA	Tarah Hagen

Basis of Report

This report has been prepared by SLR Consulting Australia (SLR) with all reasonable skill, care and diligence, and taking account of the timescale and resources allocated to it by agreement with the National Health and Medical Research Council (the Client). Information reported herein is based on the interpretation of data collected, which has been accepted in good faith as being accurate and valid.

This report is for the exclusive use of the Client. No warranties or guarantees are expressed or should be inferred by any third parties. This report may not be relied upon by other parties without written consent from SLR.

SLR disclaims any responsibility to the Client and others in respect of any matters outside the agreed scope of the work.

1.0 Introduction and Background

The National Health and Medical Research Council (NHMRC) has requested SLR Consulting Australia Pty Ltd (SLR) to undertake additional review work as part of the 2024 *NHMRC Review of Australian Health-based Guideline Values for Per- and Polyfluoroalkyl Substances (PFAS) in Drinking Water.*

The additional work is seeking answers to several questions/issues raised during public and targeted consultation regarding the assessment of perfluorooctane sulfonic acid (PFOS) from the *US EPA Human Health PFOS Toxicity Assessment* (April 2024).

Three issues/questions were requested to be addressed. The first two are reiterated and addressed in **Section 2.0**, and the third in **Section 3.0**.

2.0 Questions 1 and 2

2.1 Question 1

Issue/Question 1 is reiterated below.

Several consultation submissions noted that there is incorrect wording around the adverse health effect for extramedullary hematopoiesis that appears to have originated from the United States Environmental Protection Agency (US EPA) risk assessment.

Does the incorrect wording from the US EPA on the splenic extramedullary haematopoiesis (quoted below), impact the confidence rating provided in the SLR Consulting Addendum Report (i.e. high confidence)?

'…increased bone marrow hypocellularity in conjunction with extramedullary hematopoiesis were observed. Extramedullary hematopoiesis, blood cell production outside of the bone marrow, occurs when normal cell production is impaired. Bone marrow hypocellularity in parallel with extramedullary hematopoiesis suggest that PFOS impedes hematopoiesis in the bone marrow.' (US EPA 2024)

The US EPA (2024b) report indeed transcribed the incorrect wording of the splenic extramedullary haematopoiesis effect in rats found in the NTP (2022) study. The NTP (2022) study found an increased incidence ($p < 0.05$; ≥ 70% in males and ≥ 80% in females *cf*. control) of decreased splenic extramedullary haematopoiesis accompanied by a significantly ($p < 0.05$) increased incidence (≥ 40% in males and ≥ 50% in females *cf*. control) of bone marrow hypocellularity at ≥ 2.5 mg/kg bw/day.

Extramedullary haematopoiesis is a normal occurrence in the spleen of rodents. The finding of decreased extramedullary haematopoiesis in rats was characterised by the absence of or presence of very rare erythroid elements as compared to the presence of normal, minimal to moderate extramedullary haematopoiesis seen in vehicle controls (NTP 2022). The combination of the finding of decreased extramedullary haematopoiesis together with increased incidence of bone marrow hypocellularity in rats dosed with PFOS suggests a suppression in erythropoiesis.

According to NTP (2022) the suppression may be a direct effect or may be secondary to the stress of treatment (i.e. anaemia of chronic stress/disease). In studies in which rats exhibit decreased reticulocyte counts and/or bone marrow hypocellularity along with decreased dietary intake and/or body weight gain, decreased haematopoiesis is likely secondary to the inanition, rather than a primary test article related change (Everds et al. 2013).

However, in the 28-day NTP (2022) study with PFOS, haematology parameters do not show evidence of the typical stress leukogram and there were no effects on body weights or food consumption, which suggests that stress was an unlikely factor for the effects observed. Given that inanition can also include effects secondary to altered nutrition it is notable that there was no evidence of typical nutrition-associated effects on the erythron in the NTP (2022) study (i.e. no changes in erythrocyte size or volume, no changes in erythrocyte staining and no changes in erythrocyte haemoglobin parameters). The magnitude of the observed effects (both the increased incidence of bone marrow hypocellularity and the increased incidence of decreased extramedullary haematopoiesis) is also marked at the top three doses of the study. This indicates the effect should be regarded as adverse.

The incorrect wording does not impact the confidence rating of the NTP (2022) study, nor does it impact the confidence rating of the endpoint selected by US EPA (2024b).

2.2 Question 2

Issue/Question 2 is reiterated below.

The last sentence in section 4.1.1.2 (quoted below; p359 of 514) refers to the endpoint of extramedullary haematopoiesis being consistent with other studies; is this still relevant considering the incorrect wording from the US EPA as mentioned above?

'The endpoint of splenic extramedullary hematopoiesis was observed in both sexes and was consistent with other high and medium confidence studies that reported alterations in circulating immune cells, splenic cellularity, and thymic cellularity, both of which increase the confidence in this endpoint (Table 4-1).'(US EPA 2024).

In terms of consistency of the effects observed in the 28-day NTP (2022) study with other studies, the following observations are made:

- It is noted that no clear treatment-related effect on splenic (or liver) extramedullary haematopoiesis or bone marrow was observed in a 2-year chronic toxicity study conducted with PFOS in the same breed of rats (i.e. Sprague-Dawley) (Butenhoff et al. 2012b). The doses administered in the Butenhoff et al. (2012b) study resulted in overall lower serum PFOS concentrations at 4 weeks compared with the plasma PFOS concentrations achieved in the NTP (2022) study and the plasma PFOS concentrations at which the effects in question were observed[20]. This may indicate the following:
    - The lowest plasma PFOS concentrations in the NTP (2022) study at which the effects of interest were observed to be significantly different from controls were approximately 4x higher than the highest serum PFOS concentrations achieved at a comparable time point (i.e. 4 weeks) in the Butenhoff et al. (2012b) study. This may indicate that PFOS exposures were not high enough in the first 4 weeks of the Butenhoff et al. (2012b) study to affect erythropoiesis. Nevertheless, it is noted that serum PFOS concentrations in the Butenhoff et al. (2012b) study at week 53 for males and at week 14 for females were similar to the plasma PFOS concentrations in the NTP (2022) study which resulted in effects on erythropoiesis. The above suggests that the effects on erythropoiesis may recover with longer term exposure, however this cannot be stated with absolute certainty.
    - The Butenhoff et al. (2012b) study noted no effects on extramedullary haematopoiesis in the liver of rodents, which is consistent with the findings in the NTP (2022) study which only found decreased extramedullary haematopoiesis (compared with controls) in the spleen.

[20] In Butenhoff et al. (2012b), serum concentrations (mean ± standard deviation) at week 4 were <limit of quantitation, 910 ± 620, 4330 ± 1160, 7570 ± 2170 and 41800 ± 7920 ng/mL in males administered 0, 0.5, 2, 5, or 20 µg K+PFOS/g, respectively, in the diet. In females, week 4 serum PFOS concentrations were 26 ± 7, 1610 ± 210, 6620 ± 500, 12600 ± 1730, and 54000 ± 7340 ng/mL, respectively. These concentrations increased over time to 146000 ± 33500 ng/mL in males at week 53 and 69300 ± 57900 in males at terminal sacrifice. In females, PFOS serum concentrations at week 14 (week 53 were not available) were 223000 ± 22400 ng/mL and 233000 ± 124000 ng/mL at terminal sacrifice.

In the NTP (2022) gavage study, plasma PFOS concentrations at the end of the 4-week study were <limit of detection, 23730 ± 1114, 51560 ± 3221, 94260 ± 3144, **173700 ± 9036**, and **318200 ± 8868 ng/mL** in males administered 0, 0.312, 0.625, 1.25, 2.5 or 5 mg PFOS/kg bw/day. In female rats in the NTP (2022) study, PFOS plasma concentrations were 54 ± 4, 30530 ± 918, 66970 ± 1629, 135100 ± 3877, **237500 ± 5218**, and **413556 ± 8071 ng/mL**, respectively. The effects of interest for this discussion (i.e. increased incidence of bone marrow hypocellularity and increased incidence of decreased splenic extramedullary hematopoiesis) were observed at the NTP (2022) plasma concentrations which are bolded above.

    - The effect (being a histopathological finding) may have occurred 4 weeks into the Butenhoff et al. (2012a) study and then recovered but there was no interim sacrifice at this time point to enable its observation.

- Critically, alterations in circulating immune cells, splenic cellularity, and thymic cellularity (as cited by US EPA 2024b) are not confirmatory evidence of effects on erythroid cell lineage progression during haematopoiesis (e.g. some sort of "bleed over" from effects on the bone marrow and splenic erythroid lineage to the leukocyte lineages) since the generation of the leukon occurs via several different immune system pathways, via different circulatory patterns in the body, via different cell proliferative stimuli and at multiple other locations that are not involved in haematopoiesis. Essentially, just because a stimulus that may inhibit haematopoiesis is present does not mean that this stimulus will automatically result in suppression of leukogenesis and immune system development/function (and vice versa). There is insufficient information to determine if the two separate effects are mechanistically related.

Overall, the incorrect wording in the US EPA (2024b) evaluation does not impact the confidence rating of the endpoint selected by US EPA (2024b). The endpoint selected was detected and was adverse. The lack of replication in the longer duration studies cannot be adequately assessed because of the differences in systemic exposure at the critical time point of 28 days.

3.0 Question 3

Issue/Question 3 is reiterated below.

The SLR Consulting Addendum Report notes the limitations of the Multistage Degree 1 dose-response model (Figure E-18) used by the US EPA to derive the lowest $BDML_{10}$ in US EPA Appendix: Human Health Toxicity Assessment for PFOS (April 2024). The NHMRC Chemical Subgroup has looked into this further and found that amongst the range of dose-response models provided in Table E-64, the BMDL with the lowest p value and highest AIC value was chosen.

If you were going to apply the BMDL approach to derive a Point of Departure (POD) for PFOS from Table E-64 (or Table E-62 if that dataset is suitable), is there a case for using Weibull model or any of the other models reported in Table E-64 as a better choice for the dose-response curve based on probability and AIC?

SLR has reanalysed the benchmark dose (BMD) for the increased incidence of decreased extramedullary haematopoiesis in the spleen in female Sprague-Dawley rats, reproducing the methodology in the US EPA Appendix: Human Health Toxicity Assessment for PFOS (US EPA 2024b) (**Figure 3-1**). We used dichotomous models to fit the dose-response data from Table E-63 and applied a benchmark response (BMR) of 10% extra risk, following US EPA's benchmark Dose Technical Guidance (US EPA 2012). A 10% extra risk is the standard reporting level for quantal (dichotomous) data, as it allows for consistent comparisons across chemicals and endpoints. This level is typically chosen because it is at or near the limit of statistical power for most endpoints in most standard chronic toxicology studies.

SLR was able to reproduce the analysis from US EPA using US EPA's online BMDS tool[21]; there were slight differences between some of the p- and AIC values (**Figure 3-1**).

Figure 3-1: BMDS Online Tool Analysis Results

Dataset Name: Dataset #1

Dose	N	Incidence
0	10	2
10	10	3
20	10	3
40	10	8
80	10	10
159.6	10	10

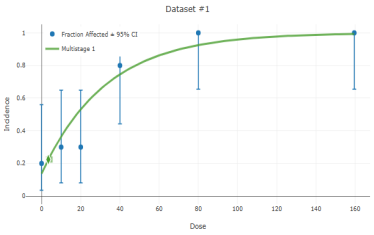
Option Set: #1

BMR Type	Extra Risk
BMR	0.1
Confidence Level (one sided)	0.95
Maximum Multistage Degree	5

Maximum Likelihood Approach Model Results

Model	BMDL	BMD	BMDU	P-Value	AIC	Scaled Residual at Control	Scaled Residual near BMD	Recommendation and Notes
Restricted Models								
Hill	9.029	26.188	35.306	0.955	50.8	-0.45	0.191	Viable
Gamma	5.688	21.762	31.254	0.966	50.723	-0.366	0.01	Viable
LogLogistic	9.029	26.188	35.306	0.955	50.8	-0.45	0.191	Viable
Multistage 1°†	2.273	3.453	5.625	0.449	52.979	0.571	0.571	Recommended - Lowest BMDL
Multistage 2	3.608	11.53	16.515	0.948	49.243	0.068	0.341	Viable
Multistage 3	3.518	16.495	23.64	0.959	50.753	-0.167	-0.325	Viable
Multistage 4	3.415	16.524	27.241	0.996	48.627	-0.139	-0.224	Viable
Multistage 5	3.387	16.073	29.369	0.998	48.574	-0.121	-0.175	Viable
Weibull	5.025	17.972	27	0.962	50.737	-0.233	-0.244	Viable
Unrestricted Models								
Logistic	5.143	7.583	11.196	0.878	49.807	0.487	0.252	Viable
LogProbit	8.797	22.476	37.166	0.963	50.751	-0.392	0.074	Viable
Probit	5.025	7.168	10.323	0.889	49.662	0.457	0.187	Viable

° BMDS recommended best fitting model
† User selected best fitting model



Results from US EPA (2024) Appendix reproduced below.

Table E-64. Summary of Benchmark Dose Modeling Results for Extramedullary Hematopoiesis in the Spleen in Female Sprague-Dawley Rats Following Exposure to PFOS (NTP, 2019)

Model[a]	Goodness of Fit		Scaled Residual		BMD_{10} (mg/L)	$BMDL_{10}$ (mg/L)	Basis for Model Selection
	p-value	AIC	Dose Group Near BMD	Control Dose Group			
Dichotomous Hill	0.849	52.8	0.2	−0.5	26.4	9.1	EPA selected the Multistage Degree 1 model. All models had adequate fit (p-values greater than 0.1), the BMDLs were sufficiently close (less than threefold difference), and the Multistage Degree 1 model had the lowest BMDL.
Gamma	0.966	50.7	0.0	−0.4	21.8	5.7	
Log-Logistic	0.956	50.8	0.2	−0.4	25.7	9.1	
Multistage Degree 5	0.989	50.6	−0.2	−0.1	16.1	3.4	
Multistage Degree 4	0.981	50.6	−0.2	−0.1	16.5	3.4	
Multistage Degree 3	0.959	50.8	−0.3	−0.2	16.5	3.5	
Multistage Degree 2	0.948	49.2	0.3	0.1	11.5	3.6	
Multistage Degree 1	**0.448**	**53.0**	**0.6**	**0.6**	**3.5**	**2.3**	
Weibull	0.990	48.7	−0.2	−0.2	18.0	5.0	
Logistic	0.877	49.8	0.3	0.5	7.6	5.1	
Log-Probit	0.963	50.8	0.1	−0.4	22.5	8.8	
Probit	0.888	49.7	0.2	0.5	7.2	5.0	

Notes: AIC = Akaike information criterion; BMD = benchmark dose; BMDL = benchmark dose lower limit; BMD_{10} = dose level corresponding to a 10% response level; $BMDL_{10}$ = lower bound on the dose level corresponding to the 95% lower confidence limit for a 10% response level.
[a] Selected model in bold.

Using the output from SLR's reanalysis produced with the US EPA BMD model, the models were assessed by SLR (**Table 3-2)** based on goodness-of-fit parameters, as outlined in US EPA's

[21] Available at: https://bmdsonline.epa.gov/

Benchmark Dose Technical Guidance Document (US EPA 2012). The key parameters for each of the models from the reproduced analysis are presented in **Table 3-1**.

Table 3-1: Goodness-of-fit-parameters

Model	BMDL	BMD	p-value	AIC	Scaled Residual near BMD
Restricted Models					
Hill	9.029	26.188	0.955	50.8	0.191
Gamma	5.688	21.762	0.966	50.723	0.01
LogLogistic	9.029	26.188	0.955	50.8	0.191
Multistage 1	2.273	3.453	0.449	52.979	0.571
Multistage 2	3.608	11.53	0.948	49.243	0.341
Multistage 3	3.518	16.495	0.959	50.753	-0.325
Multistage 4	3.415	16.524	0.996	48.627	-0.224
Multistage 5	3.387	16.073	0.998	48.574	-0.175
Weibull	5.025	17.972	0.962	50.737	-0.244
Unrestricted Models					
Logistic	5.143	7.583	0.878	49.807	0.252
LogProbit	8.797	22.476	0.963	50.751	0.074
Probit	5.025	7.168	0.889	49.662	0.187

Table 3-2: BMDL Selection Approach

No.	US EPA (2012) Technical Guidance on BMDL selection	SLR's Comment
1	Assess goodness-of-fit, using a value of p = 0.1 to determine a critical value.	All the models presented in **Table 3-1** have p-values greater than 0.1, indicating a good fit.

No.	US EPA (2012) Technical Guidance on BMDL selection	SLR's Comment
2	Further reject models that apparently do not adequately describe the relevant low-dose portion of the dose-response relationship, examining residuals and graphs of models and data. It measures the deviation of the response predicted by the model from the actual data. If the residuals are scaled by their estimated variability (SE), then such scaled, or standardized, residuals that exceed 2 in absolute value warrant further examination of the model fit.	Evaluate Residuals & Model Behaviour at Low Doses: ○ All scaled residuals are below 2 (in absolute value), confirming that all models fit the data adequately. ○ The highest scaled residual (which shows the greatest difference to the expected dose) corresponds to the Multistage Degree 1 model selected by the US EPA. ○ The Gamma model has the lowest scaled residual, indicating minimal deviation from expected values.
3	As the remaining models have met the recommended default statistical criteria for adequacy and visually fit the data, any of them theoretically could be used for determining the BMDL. The remaining criteria for selecting BMDL are necessarily somewhat arbitrary and are suggested as defaults.	Identify Suitable Models: Based on this statement, any of the BMDL values presented in **Table 3-1** (similar to the values presented in Table E-64 of the US EPA PFOS Appendix) could theoretically be used to determine the BMDL.
The following step is identified as an arbitrary step in US EPA (2012)		

No.	US EPA (2012) Technical Guidance on BMDL selection	SLR's Comment
4	If the BMDL estimates from the remaining models are sufficiently close (given the needs of the assessment), reflecting no particular influence of the individual models, then the model with the lowest AIC may be used to calculate the BMDL for the POD. This criterion is intended to help arrive at a single BMDL value in an objective, reproducible manner. If two or more models share the lowest AIC, the simple average or geometric mean of the BMDLs with the lowest AIC may be used.	In the US EPA Appendix: Human Health Toxicity Assessment for PFOS (US EPA 2024b) document (Section E.2.4.2), it has been stated: "*…the BMDLs were sufficiently close (less than threefold difference) among adequately fitted models, and the Multistage Degree 1 model had the lowest BMDL.*" To follow the approach provided in US EPA's benchmark dose technical guidance document (US EPA 2012), in this case, the Multistage Degree 5 model has the lowest AIC and could be selected as the preferred model (with the serum $BMDL_{10}$ of 3.387 mg/L). It is of note that the Multistage Degree 1 model, which was selected by the US EPA (2024b) as the preferred model, has the highest AIC. This seems to be at odds with the advice provided in US EPA (2012). US EPA (2024b) appears to have followed internal scientific policy (US EPA 2012, Appendix A.1) and has simply selected the lowest BMDL without providing a scientific justification for doing so.

Conclusion:

Based on guidance provided by US EPA (2012), the following conclusions can be drawn with respect to the reanalysis of the BMD modelling results for decreased splenic extramedullary haematopoiesis in female rats (in NTP 2022 study):

- All models in **Table 3-1** are statistically "Viable" and a good fit to the data from the NTP (2022) study.
- If the priority is to minimise the difference between observed data points and the fitted model values (scaled residuals) close to the BMD (i.e. the goodness of curve fit at the relevant low dose portion of the dose-response relationship), the Gamma model ($BMDL_{10}$ = 5.688 mg/L) is likely to be preferable (US EPA 2012).
- If prioritising model selection based on the lowest AIC, the Multistage Degree 5 model ($BMDL_{10}$ = 3.387 mg/L) should be chosen. Notably, the US EPA (2024b) selected the Multistage Degree 1 model, despite its higher AIC. Critically, the primary purpose of selecting the model with the lowest AIC is "*intended to help arrive at a single BMDL value in an objective, reproducible manner*" (US EPA 2012). As noted in the US EPA (2012) BMD

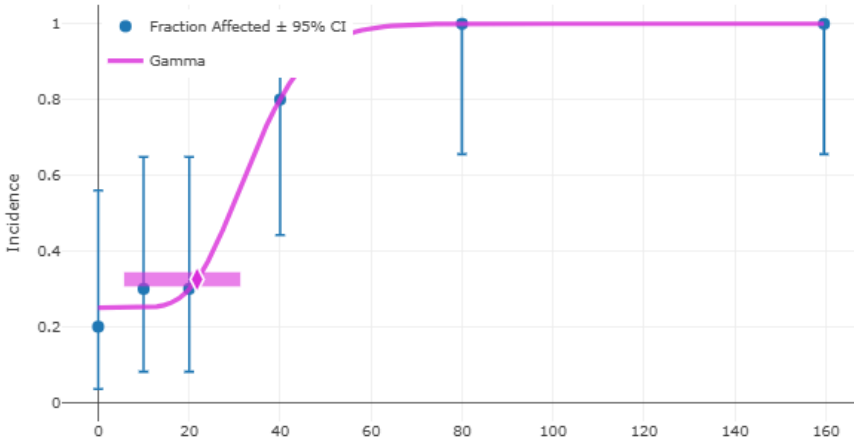
guidance, use of such a criterion is "*necessarily somewhat arbitrary and are suggested as defaults*."

- Given that all of the evaluated models are viable and have similar AIC values (48.574 to 52.979), it is possible, based on current US EPA (2012) guidance, to use the simple average or geometric mean of the BMDLs with the lowest AIC values (US EPA 2012). If this approach is taken the arithmetic mean across the models with AIC values < 50 (Multistage 2, 4 and 5; logistic, and probit) is (3.608 + 3.415 + 3.387 + 5.143 + 5.025)/5 = 4.12 mg/L. Again, this approach is somewhat arbitrary.

Overall, based on the US EPA (2012) BMD guidance and given the viability of a large number of models all with similar AIC values, the best practice would be to prioritise the model that has the smallest difference between observed data points and the fitted model values (i.e. lowest scaled residuals) in the low dose portion of the dose-response relationship near the BMD. This is the Gamma model with a $BMDL_{10}$ of 5.688 mg/L (Figure 3 2).

Figure 3-2: Dose Response Curve Gamma Model

Modeling Summary	
BMD	21.762
BMDL	5.688
BMDU	31.254
AIC	50.723
P-value	0.966
Model d.f.	3
Log-Likelihood	-22.361
Chi^2	0.267



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