

Selenium-mercury molar ratio as a basis for relaxing predator-fish MeHg ceilings — the scientific debate

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CORRESPONDENCE

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Abstract

A live methodological debate in seafood toxicology asks whether the selenium-to-mercury molar ratio (Se:Hg) in consumed fish should modulate the regulatory ceiling on methylmercury. The argument: Se and Hg share an extraordinarily high binding affinity (Hg-Se bond ~70 kcal/mol, among the strongest in biochemistry); when molar Se in the consumed fish exceeds molar Hg, the Hg is sequestered as inert HgSe particles in vivo, and net Se remains bioavailable to support selenoprotein synthesis. The toxicological cascade that drives MeHg neurotoxicity (oxidative stress from Se-depleted antioxidant defenses, thyroid disruption from disabled iodothyronine deiodinases) is therefore proposed to depend on Se:Hg balance, not absolute MeHg concentration alone.

1 | Overview

If accepted, this framework would justify relaxing the regulatory MeHg ceiling on Se-rich fish species — notably bluefin tuna, where per Chamorro et al. 2024 Se:Hg is typically >1 despite high absolute Hg. If rejected, the framework is theoretically supported but not yet quantitatively validated, and the absolute MeHg ceiling remains the binding constraint.

This synthesis page lays out the evidence on both sides. The wiki does not take a position; it presents the case for and against. The page exists to provide a citable consolidation of the Se:Hg literature, including the question of whether the evidence currently supports modulating an absolute MeHg ceiling on a selenium basis.

2 | The mechanistic case FOR Se:Hg as a relaxation criterion

Ralston and Raymond 2014 formalized the Selenium Health Benefit Value (HBV) framework. The reasoning:

1. Selenium is required for selenoprotein synthesis (glutathione peroxidase, thioredoxin reductase, iodothyronine deiodinases). Selenoproteins are core antioxidant and thyroid-hormone-metabolism enzymes.
2. Hg-Se binding is extraordinarily strong; when Hg is present in molar excess of Se, dietary Se is sequestered as inert HgSe particles that do not enter the selenoprotein synthesis pool.
3. Se-depleted selenoprotein synthesis is the proximate mechanism of MeHg neurotoxicity (oxidative-stress cascade in developing neural tissue, thyroid disruption affecting maternal-fetal thyroid hormone trafficking).
4. Therefore: MeHg neurotoxicity scales with the Se:Hg deficit, not absolute MeHg concentration.

If this framework is correct, a fish with high MeHg AND high Se (Se:Hg >1) would deliver less neurotoxic risk than a fish with moderate MeHg AND low Se (Se:Hg <1). The Faroe Islands cohort (high MeHg from pilot whale, comparatively low Se from whale matrix) had clear developmental neurotoxicity at maternal-hair Hg ~10 µg/g; the Seychelles cohort (high MeHg from ocean fish, comparatively higher Se from ocean-fish matrix) did not, at similar exposure levels. The Ralston framework offers a mechanistic explanation for this otherwise-puzzling cohort divergence.

Most commercially consumed fish have Se:Hg molar ratios above 1, including bluefin tuna per Chamorro 2024. The notable exceptions where Hg can exceed Se molar are pilot whale, large mako shark, and certain very-large old swordfish individuals. Under the Ralston framework, these are the species where the absolute MeHg ceiling is genuinely binding; for the rest, the Se:Hg ratio modulates risk and a single MeHg-only ceiling under-counts the protective Se co-presence.

3 | The case AGAINST relaxing MeHg ceilings on Se:Hg basis

Three concerns counterweight applying the Ralston framework to threshold-setting:

1. **The quantitative dose-response is not established.** The Ralston framework proposes that Se:Hg modulates MeHg neurotoxicity, but does not yet quantitatively specify HOW MUCH protection a given Se:Hg ratio confers. Without a dose-response curve calibrated against developmental neurotoxicity endpoints, there is no validated basis for translating Se:Hg into a concrete MeHg-ceiling adjustment. EFSA, EPA, JECFA, and FDA all continue to set MeHg PTWIs and RfDs in absolute concentration terms; none has incorporated Se:Hg modulation into the regulatory threshold. Until a regulatory body validates a quantitative Se:Hg-MeHg model, any threshold that relaxed an absolute MeHg ceiling on a selenium basis would be ahead of the regulatory consensus.
2. **The Faroe-vs-Seychelles divergence has alternative explanations.** The Ralston framework is one possible explanation for the divergent neurotoxicity findings in the two cohorts; competing explanations include long-chain polyunsaturated fatty acid (PUFA) co-exposure differences (whale low in EPA/DHA, ocean fish high), genetic-population differences in MeHg metabolism, and exposure-window timing differences. Farina et al. 2011 reviews the mechanistic neurotoxicity literature; the Se-Hg interaction is one of several mechanistic factors, not necessarily the dominant one. Picking Se:Hg as the modulator without ruling out the alternatives risks a confounded basis.
3. **Operational complexity at scale.** Even if Se:Hg modulation is quantitatively correct, requiring per-lot Se AND Hg measurement roughly doubles analytical cost versus Hg-only testing. Any program that adopted Se:Hg modulation would have to weigh the additional analytical burden against the protection-margin gain.

4 | Where the evidence is strongest

The Ralston framework is on firmest ground for the population-level observational explanation (why some high-Hg-fish populations show less neurotoxicity than others) and weakest for translating Se:Hg into a quantitative MeHg-ceiling adjustment. The evidence supports three distinct uses to differing degrees:

- **As an explanatory factor for cohort divergence**, the framework is well-supported by Ralston 2014 plus mechanistic plausibility, and is on solid ground for explaining MeHg risk variation across populations.
- **As a quantitative cap-adjustment factor**, the framework is not yet supported, because no validated dose-response translates Se:Hg into a defined MeHg-ceiling change.
- **As a sub-categorization criterion that identifies low-Se species**, the framework is well-supported: it cleanly flags the species where the absolute MeHg ceiling genuinely binds (pilot whale, large mako shark, very-large swordfish) without requiring per-lot Se testing on every product.

5 | The mercury isotope tracer angle

A separate line of evidence using stable Hg isotope fractionation (Dietz et al. 2025, Li et al. 2022, Motta et al. 2022) can distinguish MeHg from different source pools (atmospheric vs riverine vs marine, photochemical vs microbial methylation). Isotope-based Hg source attribution is a separate technical capability from Se:Hg modulation but bears on the same question: is all "MeHg" the same toxicologically? Different source pools may have different bioavailability and may be associated with different co-nutrient profiles. This is an active research frontier.

Isotope-based source attribution is not yet a routine analytical methodology for routine compliance testing. It remains foundational research that may eventually inform sub-category-level distinctions but is not operational today.

6 | What this synthesis does not yet rest on

- **No regulatory body has validated a quantitative Se:Hg cap-adjustment.** EFSA, JECFA, EPA, FDA all maintain absolute MeHg thresholds. Until at least one regulatory body endorses a Se:Hg-modulated framework, any threshold built on one would sit outside the regulatory consensus.
- **The Faroe-Seychelles cohort divergence has multiple plausible mechanistic explanations.** The Ralston framework is one; PUFA co-exposure is another; genetic-population differences are a third. The wiki's synthesis on the divergence (the Faroe and Seychelles cohort dose-response section in mercury-methyl) treats the explanatory question as open.
- **Quantitative dose-response data for Se:Hg modulation are sparse.** Even within the Ralston framework, the dose-response curve translating Se:Hg into a quantitative neurotoxicity-risk modifier is not established. Lab and animal studies are suggestive; the human-cohort quantitative dose-response that a Se:Hg-modulated threshold would need is not yet in the literature.

7 | What the evidence currently supports

Pending further regulatory consensus and quantitative dose-response evidence, the literature supports the following:

1. **Relaxing an absolute MeHg ceiling on the basis of Se:Hg is not supported by the current evidence.** The Ralston framework is theoretically supported but not yet quantitatively validated, and no regulatory body has incorporated Se:Hg modulation into a MeHg threshold.
2. **Se:Hg cleanly identifies the species where the MeHg burden genuinely binds.** Pilot whale, large mako shark, and very-large swordfish can carry molar Hg in excess of molar Se, so for these species the absolute MeHg burden is the operative constraint and is not offset by co-present selenium.
3. **The framework remains an active research question.** Whether and how Se:Hg should modulate an absolute MeHg threshold turns on regulatory and primary-literature developments; if EFSA, EPA, or JECFA endorses a quantitative Se:Hg framework, the evidence base would change accordingly.

Taken together, the available primary-literature evidence and the regulatory consensus both point in the same direction: absolute MeHg ceilings should not be relaxed on the marginal Se:Hg evidence currently available, and the low-Se species are where the absolute MeHg burden binds most clearly. How any certification program responds to the gap between this literature baseline and a chosen threshold is a policy choice that this wiki does not prescribe.

8 | Downstream pages updated

- mercury-methyl — Selenium-mercury antagonism section presents the Ralston framework with the same caveats this synthesis develops.
- seafood — Levers to reduce contamination section's Formulation lever subsection notes that "co-formulation with selenium-rich ingredients" is a hypothesized lever but not a validated mitigation.
- canned-fish — same as above.
- canned-tuna, shark — Se:Hg-related scientific framing should appear in the contamination_profile narrative where the bivalve-Cd-style pages are built out.

9 | Anchor sources

- ralston2014-selenium-hbv-methylmercury-seafood — Foundational Selenium Health Benefit Value framework.
- chamorro2024-bluefin-tuna-mercury-review — Bluefin tuna Se:Hg evidence supporting the relaxation argument for tuna specifically.
- farina-rocha-aschner-2011-mehg-mechanism — Mechanistic neurotoxicity review providing the alternative--explanations context.
- dietz2025-arctic-mercury-isotopes-greenland, li2022-mercury-isotope-biota-review, motta2022-marine--hg-isotopes — Mercury isotope tracer evidence relevant to the source-attribution sub-question.

10 | How this page was promoted

Established 2026-05-18 from the seafood-axis synthesis work. The Se:Hg framework is one of the contested points in MeHg toxicology bearing on per-species threshold questions; the page exists to provide a citable wiki-side consolidation of the debate rather than re-deriving it each time the question arises. The page is deliberately non-committal between the for-and-against positions; its contribution is the consolidated, evidence-graded assessment of where the framework is and is not on firm ground.

References

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Li M, Huang T, Cheng H, Obrist D, and Yu B · Environmental Science & Technology · 2022 · doi.org/10.1021/acs.est.1c08631
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- [6] Mercury isotopic evidence for the importance of particles as a source of mercury to marine organisms
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REVIEW

STATUS AND LICENCE

Editorially reviewed in-house; no external peer review has been completed on this finding. Published as a preprint with its review state tracked on the article page. Released under CC BY 4.0.

DATA AVAILABILITY

Every source behind this finding is listed with its own extraction record at <https://heavymetalindex.com/synthesis/se-hg-molar-ratio-certification-debate#sources>, each linking to the ingest receipt, the extracted values, and the file hash of the document it was built from.

COMPETING INTERESTS

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