STANDARD METHOD REQUIREMENTS FOR HEAVY METALS TESTING IN DIETARY SUPPLEMENTS:

ICP-MS ANALYSIS FOR LEAD, ARSENIC, CADMIUM, MERCURY

Julie Catzalco

PHARMAVITE

Nature Made MegaFood EQUELLE uqora Bonafide

Heavy Metals Method Requirements

Why this matters now

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CORE TAKEAWAY — **A heavy metals specification is only defensible when the test method is scientifically valid, verified for intended use, and understood by regulators, retailers, and states.**

FDA cGMP baseline

21 CFR 111.70 / .75 / .320

1. **Set contaminant specifications**
   Define limits for contamination that may adulterate a dietary supplement.
2. **Use scientifically valid methods**
   Apply an appropriate method for each specification that requires testing.
3. **Verify fit for intended use**
   Confirm examination and testing methods are appropriate for the intended use.

External pressure is rising

Prop 65

State rules | Retailers | Third-Party Standards

- **Q1** Compendial method available?
- **Q2** Validated third-party lab method?
- **Q3** Consensus on performance requirements?

Goal: fewer surprises during retailer review, audits, and state compliance challenges.

METHOD CREDIBILITY ECOSYSTEM

Standards + labs + performance criteria
Compendia and qualified labs help show the method is fit for the specification.

USP Verified | NSF | AOAC International | Canadian Analytical Laboratories | eurofins

Source: 21 CFR 111.70, 111.75, and 111.320. Company confidential and proprietary.

AOAC SMPRs® Application & Importance

What defines SMPRs and why they are critical

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CORE TAKEAWAY — **AOAC SMPRs define the minimum performance requirements needed to ensure a method is scientifically valid, fit-for-purpose, and defensible across regulators, retailers, and labs.**

AOAC SMPRs® Key Characteristics

1. **Defines performance requirements**
   Sets minimum criteria for accuracy, precision, LOD/LOQ, range
2. **Voluntary Consensus Standards**
   Developed by AOAC stakeholders
3. **Enables method flexibility**
   Method agnostic - any technique acceptable if criteria are met
4. **Fit-for-Purpose**
   Ensures the method is appropriate for the intended analyte and matrix

Why SMPRs Are Critical

1. **Used in AOAC Method Approval Programs**
2. **Enables innovation without compromising performance**
3. **Drives consistency and harmonization across labs and regulators**
4. **Improves regulatory and legal defensibility**

PERFORMANCE REQUIREMENTS

- ACCURATE
- REPEATABLE AND REPRODUCIBLE
- SPECIFIC
- LINEAR
- LIMIT OF QUANTITATION (LOQ)

Source: 21 CFR 111.70, 111.75, and 111.320. Company confidential and proprietary.

What Pharmavite has done

Building the foundation to define industry performance standards

CORE TAKEAWAY

Pharmavite has developed and validated a fit-for-purpose heavy metals method that meets rigorous performance criteria, positioning us to help define industry standards through AOAC SMPRs

Method Development & Validation

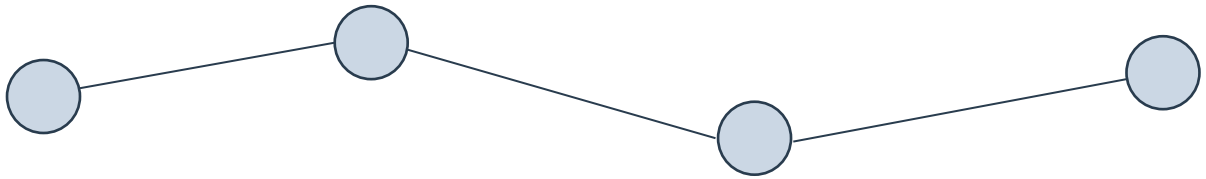
1. **Method Development & Scope**
   - Developed and validated a single ICP-MS method for As, Cd, Hg, Pb across various dosage forms (tablets, gummies softgels, powders, chews)
   - Designed validation to cover complex, interference-prone matrices representative of real products
2. **Scientific Validation**
   - Demonstrated specificity, including evaluation of known interferences (e.g., Zr, Cu, C for As; Mo for Cd)
   - Established linearity across relevant ranges for all analytes ($R^2 \geq 0.999$)
   - Achieved low limits of quantitation (LOQ down to 0.01 ppb; Pb 0.001 ppb)
   - Demonstrated accuracy across multiple matrices and spike levels
   - Achieved precision well within limits (RSD ≤ 20% across repeatability and reproducibility)

What this demonstrates

1. **Defined performance capabilities**
   Established performance limits for accuracy, precision, sensitivity (LOQ), and range
2. **Fit-for-Purpose**
   Demonstrated the method is appropriate for the intended analyte and matrix
3. **External Benchmarking**
   Demonstrated comparability with third-party lab results on same lots

FROM VALIDATED METHOD TO INDUSTRY STANDARD

Pharmavite can partner with AOAC to translate validated method performance into SMPR-defined criteria



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