

Facing the Problem of Dietary-Supplement Heavy-Metal Contamination: How to Take Responsible Action

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The last issue of *Integrative Medicine (IMCJ)* 6.2: 38) revealed that dietary supplements are a significant potential source of heavy metal contamination. The problem is real. Now the question remains, what can clinicians do to protect their patients and themselves?

Obviously, all clinicians who prescribe dietary supplements need to know if they are contaminated with toxic metals. Each of us must act responsibly and seek proof from our manufacturers and their suppliers that they are independently testing and evaluating materials for toxic metal load. Please do not—I repeat, do not—accept heavy metal data taken from any supplier’s raw material certificate of analysis (COA). The company manufacturing the product must independently test the material—at least for lead, mercury, cadmium, and arsenic, with the limit of detection at around 10–20 parts per billion (ppb). Clinicians should also know how to perform the necessary calculations to evaluate the toxicity data they receive from manufacturers (see below and also on the IMCJ website for instructions on how to do this).

Acceptable Limits for Daily Consumption of Heavy Metals

Ideally, we should have zero tolerance for nutritional products that contain any amount of toxic metals. Sadly, that is not the world we live in. Toxic metal burden and contamination from food, water, dietary supplements, and other sources are part of what we must cope with. This makes it even more important to be diligent about testing dietary supplements for toxic metals. We cannot depend upon the government or other regulatory bodies to protect us. Incredibly, there is no official authoritative agreement on the safe levels of heavy metal ingestion. The State of California says one thing, the Food and Drug Administration (FDA) says another, the Environmental Protection Agency (EPA) has limits for water only, the United States Pharmacopoeia (USP) has its own standards, and all are different from each other. To the best of our ability we must evaluate the heavy metal toxicity ourselves. We can make this evaluation only by holding our manufacturers accountable for independent testing of the products we purchase from them.

High-Risk Products for Heavy Metal Contamination

The products at greatest risk for toxic metal contamination are botanicals (single herb or herb combinations in extract, powder, capsule, or tablet forms), calcium, magnesium, and products derived from shellfish (eg, glucosamine and chitin). Toxicity is especially problematic when you get into high doses of these products, because the greater the amount ingested, the greater the toxic load—which is the cumulative effect of taking

Toxicity Calculator on IMCJ Website

When you need to determine the daily toxicity load that will result from ingesting a manufacturer’s product—based on their provided raw material assay—make your life simple! Go to www.imjournal.com and click on “Quality Assurance” in the left lower side bar. Then click on “Toxicity Calculator.” You will find a quick and easy answer to your question.

a full dose of the medication over time.

To put this in context, say a manufacturer tests 2 of his supplier’s raw materials for lead—using as examples policosanol (a mixture of very-long-chain aliphatic alcohols purified from sugar cane wax whose main component is octacosanol) and *Schisandra chinensis* extract. Then let’s say each ingredient tests at 4 parts per million (ppm) of lead.

The typical daily dose of policosanol might be 20 mg and of schisandra extract 2,000 mg. With lead at 4 ppm in each raw material, the ingested amount of lead coming from policosanol is 0.08 µg/day, but the amount coming from the schisandra extract is 8 µg/day—a full 100 times more, despite the fact that both raw materials have the same level of contamination at 4 ppm. (The math detailing how to determine this is explained below.) This is why it is so critical to assess the toxic load based on the possible highest daily dose. I would have rejected this particular schisandra extract because of an unacceptably high amount of lead ingestion over time.

The seriousness of this situation highlights why relying on data supplied either by a COA or through skip-lot testing is not enough. Why? COAs can be too easily faked, and skip-lot testing is too random. The problem with skip lot is that each new batch of product is equally at risk for heavy metal contamination—kind of like every time you flip a penny; the odds are always 50:50 for every flip. Raw material suppliers source from all over the world. Lot-to-lot variation can be significant, depending upon from where the material came. Just because a material tested at acceptable limits the last 3 times does not mean it will test in an acceptable range the fourth time. Each batch should be independently tested and evaluated. Unfortunately, most companies do not independently test their raw materials or finished products for heavy metal contamination, or, if they do, their limits of detection are not low enough (see below for an explanation).

Outdated vs Acceptable Testing Methods

There are several ways to test the amount of individual heavy metals in a particular nutritional supplement’s raw

materials. I won't go into an exhaustive explanation of each method. However, based on the experience I have gathered over the past several years, I can summarize the issue with the following. The most important points to appreciate are determining the specific quantification of individual heavy metals and to ascertain the limit of detection (LOD). The lower the LOD, the better. Currently available technology affords LODs in the 10–20 ppb (that is billion) range, which is most desirable. See Tables 1 and 2.

Table 1. Inadequate or Less-Desirable Methods for Individual Toxic Metals

1. **USP Method #231, Heavy Metals as Lead:** This method is very commonly used, but it is seriously outdated as a limit test for determining total heavy metal burden. It has two serious drawbacks: First, it groups all heavy metals together and expresses the result as "lead" because it is compared to a lead standard. Therefore, this methodology does not differentiate one heavy metal from another. Second, its LOD is 5–10 ppm, some 1,000 times too high to be of value. If a manufacturer gives you a test result using USP Method #231, do not accept the information and ask for a more sensitive test.
2. **ICP-OES (Inductively Coupled Plasma-Optical Emission Spectrometry):** This is a better test because it can screen for multiple elements simultaneously at trace levels. But it is still not good enough—the methodology suffers from interferences that can demonstrate positively or negatively on the analysis results. In addition, ICP-OES LOD for heavy metals can range from 10–100 ppb, depending on the sample and element being analyzed. In my opinion, although it is good to be in the desired ppb range, the detection range itself is too wide.

Table 2. Adequate Methods for Individual Toxic Metals

1. **Mercury:** Cold-vapor atomic-absorption method (LOD 5–25 ppb).
2. **Lead:** Graphite-furnace atomic-absorption method (LOD 10–50 ppb).
3. **Arsenic:** Hydride-generation atomic-absorption method (LOD 10–50 ppb).
4. **Cadmium:** Graphite-furnace atomic-absorption method (LOD 5–20 ppb).
5. **Multiple metals:** ICP mass spectrometry. This method can test for several metals at once and has a very low LOD (around 10-20 ppb). This is my preferred methodology and the one on which I generally rely, as it offers a high specificity and the lowest analysis cost when screening for multiple heavy metal elements.

How to Calculate the Daily Load of Heavy Metals from Lab Data

It is extremely important for clinicians to be able to calculate the potential daily loads of toxic metals from the lab data provid-

ed to them. The following steps illustrate how to do this. For simplicity's sake, let's assume this lab data comes from freeze-dried nettle (*Urtica dioica*) leaf powder that went into capsules, with each capsule containing 300 mg of the nettle powder.

1. Determine the typical upper total daily dose. In this case, the product is likely to be prescribed at 2 capsules 3 times per day, a total of 6 caps per day, representing 1,800 mg (or 1.8 g) of powder.
2. Let's assume that test data for the nettle leaf raw material shows it contains lead at 3 ppm.
3. In the math of toxic analysis, 1 ppm translates to 1 mg toxic element/1000 g product (1 mg/1000 g).
4. Converting 1 mg to 1,000 µg, then 1 mg/1000 g = 1,000 µg/1000 g.
5. Converted again, 1,000 µg/1000 g = 1 µg/1 g.
6. Thus, 3 ppm is equivalent to 3 mg lead/ 1,000 g of nettle powder, which equals 3,000 µg for 1,000 g of powder—meaning that, in the end, 3 µg of lead will be ingested for every 1 g of nettle leaf powder ingested.
7. Since the total daily dose of nettle leaf is 1.8 g, multiply 3 µg of lead by 1.8 g of nettle leaf powder ingested daily to arrive at 5.4 µg of lead consumed per day.

If the patient has perennial allergy symptoms and consumes this product daily all year long, they have a total yearly ingested dose of 1,971 µg of lead (5.4 µg/day x 365 days). How do we evaluate whether or not this is acceptable?

California state law says a product cannot contain more than 0.5 µg of lead per daily serving (and, in fact, a warning label on the bottle is required if the lead content is greater than this). Since this product produces 5.4 µg/ day, it is way beyond California standards. The FDA's upper limit for ingestion, however, is a whopping 75 µg/day for an adult—150 times greater. So the product fits well within FDA's range. The USP says up to 10 ppm is acceptable. Since 1 ppm = 1 µg /1 g, if we apply the USP standard to this example, it means that 10 µg of lead can be acceptably ingested for every 1 g of product (10 ppm = 10 µg /1 g). Since the total daily dose of nettle leaf is 1.8 g, this yields an acceptable daily dose of 18 µg of lead per day according to UPS standards. Thus, nettle leaf's 5.4 µg/day makes the limit.

Whom do we believe? I always err on the side of "the lower the better," so I tend to use California's Proposition 65 number of 0.5 µg of lead per daily serving. And, since this is not written in stone, I am OK if the number is slightly above that amount—it is still well below the other standards. If it's significantly above, however, I tend to reject the product. Again, that is why the testing and evaluation are so important. Every company should do an upfront analysis.

To clarify further, if you had a heavy metal result that was in the ppb range, the calculation is done the same way with the conversion factor of 1 ppb = 1 µg/1000 g or 0.001 µg/1 g.

Editor's note: If you are lost by the math, take heart; read the sidebar "Toxicity Calculator on IMCJ Website."

Every company should be using this upfront analysis and

Accepted Standards of Heavy Metal Toxicity for Ingested Products

California Proposition 65 Daily Limits for Heavy Metal Consumption

Lead	0.5 mcg (µg)
Arsenic	10 mcg (µg)
Cadmium	4.1 mcg (µg)

FDA Tolerable Daily Diet Lead Intake

Children <6 yrs old	6 mcg (µg)
Pregnant women	25 mcg (µg)
Adults	75 mcg (µg)

Note: There is a revised FDA ruling: 0.1 ppm of lead in candy likely to be consumed frequently by small children.

United States Pharmacopeia (USP) Limit for Nutritional Supplements

Lead	10 ppm
Arsenic	3 ppm
Cadmium	3 ppm
Mercury	3 ppm

In general, as you can see, the regulatory environment for defining toxic doses of metals is fragmented. It is best to be within range of the lowest limit—in this case, the California standards. If you need more information, contact the California Office of Environmental Health Hazard Assessment (OEHHA, www.oehha.ca.gov) or the Proposition 65 enforcement agency, which is the California Attorney General's Office (<http://ag.ca.gov>). You may also wish to contact the FDA (www.fda.gov) or USP (www.usp.org).

To find specific information relating to toxic contamination, go to:
California OEHHA: <http://www.oehha.ca.gov/prop65/p65faq.html>
California Attorney General's Office: <http://caag.state.ca.us/prop65/index.htm>
FDA: <http://vm.cfsan.fda.gov/~dms/qa-top.html>
USP: <http://www.usp.org/aboutUSP/contactUs.html?h>

evaluation as much as possible before buying raw materials. Here is a situation I encountered recently. I needed to buy green tea extract. The product has a typical upper daily dose of 1650 mg. In order to meet the California lead specification of no more than 0.5 µg of lead per day, the raw material needed to have a lead content of 0.25 ppm or lower. The supplier from whom I wanted to buy could not guarantee that, because they tested for heavy metals using the ICP-OES methodology, and the lowest LOD for lead that they could analyze was 0.34 ppm. This was not low enough to guarantee my need.

This is a good example of a situation in which the test methodology used was inadequate to meet the testing need. To get around the issue, I decided to take a pre-shipment sample from a specified lot of green tea extract raw material and have it independently tested using ICP-MS methodology with a LOD of

0.01 ppm (or 10 ppb). If it passed, I'd buy that lot of material. If not, I'd keep looking. The important point is that I evaluated, I tested, and I made my buying decision based on real data and not on supposition.

How to Evaluate a Company and Its Products

The goal of all of my articles on quality assurance is to impress upon you the urgent need to obtain valid evidence of a product's identity (authenticity), potency, and purity (maximum freedom from contamination).

To help you do this, I developed and wrote a questionnaire for clinicians to use as a supplier quality assurance verification and certification tool. It is available at *IMCJ's* website, www.imjournal.com. When there, click on "Quality Assurance" in the left lower sidebar, then click on "Manufacturer Certification and Quality Assurance Self-Audit Form."

Please send this questionnaire to each of your natural products manufacturers and/or suppliers and see what comes back. It directs them to answer a series of questions, but also asks them for documentation that helps provide verification that they are, in fact, doing what they claim they are doing. The questionnaire asks for proof as well as yes-or-no answers. It is easy to answer yes to a question on a form; it is more difficult to provide proof.

It is also important to note, since I do not list names, that some supplement-manufacturing companies do take most or all the QA measures I have detailed in this and other issues of *IMCJ*. I commend them for their diligence and commitment. It is important for clinicians to know who they are. The only way to find out is to send them the QA form and question them.

Ask, ask, ask, and ask again for proof. Never stop asking for proof of quality assurance testing. If you are not asking for proof, you are burying your head in the sand and risk using contaminated product. The manufacturers that supply you with independent proof are testing, and the manufacturers that give you doublespeak and supply nothing are not testing.

If you are unfamiliar with quality-assurance issues or need further clarification about using either the Questionnaire or Toxicity Calculator, I am available to answer your questions and provide quality assurance information. Please contact me at rickliva@center4health.com.

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