

Quality Assurance Recap. Salient Points for the Clinician: What We Should Know and Follow

By Rick Liva RPh, ND

Ascertaining dietary-supplement quality is of paramount importance to help clinicians ensure efficacy, reduce adverse reactions, and protect the patient or end user from contamination. This is an issue that demands the attention of every practicing clinician.

I have covered a lot of ground in the last 6 articles [starting in *IMCJ* 4(3)]. The information I have presented is comprehensive, and, as such, can be confusing. In this issue of the journal I intend to summarize much of the previous information so it is short and to the point. My goal is to have each clinician achieve a working knowledge on how to evaluate quality in natural products.

I must admit to being baffled and a bit disappointed regarding the whole issue of natural products' quality assurance. It has been my experience over the past several years that many clinicians don't seem to care about quality—they don't bother to take into account the myriad essential factors necessary to evaluate it, nor spend the time trying to assess their suppliers to see if they adhere to any quality assurance (QA) standards. Also, I continually see suppliers with low integrity.

About a month ago I started an investigation to gather some information on supplier conformance with quality-assurance testing. I asked 3 dietary supplement manufacturers for information on 2 formulas, requesting them to answer questions about their raw-material and finished-product quality-assurance testing practices. These companies are well known and NSF- cGMP certified, so I assumed they would perform at a high level of quality-assurance testing as outlined in this article. As of the time of printing, I have only heard back from 2 of the 3. Company #1 does a small amount of testing on raw materials (identification and potency—but only if there is a marker compound—and microbiology) and less on finished-product testing (microbiology and label-claim testing only if the customer requires it). Company #2 does close to nothing. Following is the response from company #2. I thought it was important to show how flagrant is its disregard for providing a product that is quality assured.

In response to the testing of their raw materials: "We purchase raw materials from reputable vendors, many of which we have been to audit [visited on site]. Each lot is required to have a Certificate of Analysis, which is reviewed. Organoleptics [sight, smell and taste] are also checked. We do random skip-lot testing on raw materials to verify vendor Certificates of Analysis." Even if a supplier (vendor) is doing all the QA/QC they are supposed to be doing, accepting their material without independent verification is inappropriate. The receiver of the material has to test the product for a statistically significant number of batches (usually 6-9) and each batch has to pass successfully. This level of testing needs to be accomplished *before* they can consider any skip lot testing. Even then an identification test and a microbiological examination needs to be

performed and can never be skipped when doing skip lot testing (other things can be skipped like solvent residue testing).

In response to the testing of their finished products: “Approximately every 15th product manufactured is sent to an outside laboratory for microbiology analysis (bacteria, yeast and mold)”. What about testing the other 14 batches that got made? They don’t deserve to be tested for bacteria, yeast or mold contamination? Every batch of finished product should always be tested to make sure it is not contaminated with bacteria, yeast or mold.

“We do a post-batch review for accuracy.” What does this mean? Accuracy of what? This does not give the clinician or consumer any information to use to assess this company’s thoroughness of post batch review. It should include a comprehensive review of the manufacturing batch production record, weight recordings during the run, a quality check for minor, major and critical defects in capsules or tablets and it should include a sign off by the quality department.

This very poor and inadequate level of quality assurance should be of great concern to all clinicians. Unfortunately, it seems to be the more the norm than the exception. Are you using some of this company’s products? You might be.

If clinicians think even for a moment that they are not prescribing products with solvent residue or other significant QA issues, they are sorely mistaken. In my experience, these kinds of problems are all too common. However. You’d have no idea unless you had taken the time to find out and get proof of a company’s QA claims.

There are huge holes in natural product manufacturing. The above example is just one. In my last column I said, “if you are providing dietary supplements to your patients from manufacturers that do not test their raw materials or finished products, you are putting your patients at risk. The risk comes from selling products that are inauthentic, sub-potent or super-potent, or contaminated. If supplements are untested, quality deficiencies *will* get through to your patients—it’s like playing a game of Russian roulette: the bullet (a poor-quality product) is in the gun (your pharmacy) somewhere, and it is just a matter of time before the gun erupts (and woe to the patient, and perhaps your legal budget, when it does)”.

Definition of “High Quality”

From the outset it is crucial to define a “high-quality” supplement. High quality describes a product that has had its authenticity verified, meets its potency claims, and is not contaminated or contains only a minimal, acceptable amount of contaminant(s).

The Buying Decision—A Clinician’s Responsibility and a Critical Factor

I assert that most clinicians do little or nothing to assess and verify product quality before they chose a supplier. We often base our buying decisions on what other

clinicians, educators, and mentors have told us. We may like the salesperson, believe the company's quality story, be influenced by their marketing claims, or recognize that the company has good clinical education that ties their products to our own need for information. In essence, usually everything *but* evidence of quality verification drives our decision. I have said every time before and I say again, it is critical to verify quality claims. To verify is to prove the truth of something by the presentation of evidence.

Why don't clinicians generally ask for evidence to verify that a manufacturer is providing high-quality products? We are too busy, we assume companies are providing the quality we seek, we don't know how to separate the marketing hype from the real evidence, and, lastly, we fall back on a refrain I have heard many times: "I get good clinical results." While this may be true, it does not address the issue of contaminated products. It is possible to get a good clinical result with a product that has high or unacceptable levels of heavy metals, solvent residue, aflatoxins, or herbicides and pesticides. If this occurs, the issue of Russian roulette becomes one of the smoking gun—the finger will be pointed directly back to you, the clinician.

This is a huge missing piece, and to avoid it is a great dishonor to the wonderful practice of natural medicine. Clinicians have a charge and responsibility to fill the gap. Quality assurance evaluation is not difficult, but it does take some time and, yes, money. Still. Consider, we prescribe these products to help our patients, friends, and loved ones. Do they deserve any less?

The Power You Hold As a Buyer

If clinicians find that one or more of their favorite companies are not performing adequate quality-assurance testing, you can certainly ask them to start to do so or risk losing your business.

Why Are cGMPs Needed?

The proposed US Food and Drug administration (FDA) current good manufacturing practices (cGMP) regulations for dietary ingredients and dietary supplements are necessary to promote and protect public health and safety. Unlike other major product areas, however, there are no finalized FDA regulations specific to dietary ingredients and dietary supplements that establish a minimum standard of practice for manufacturing, packaging, or holding. The absence of minimum standards has contributed to the adulteration and misbranding of dietary ingredients and dietary supplements by contaminants. Contributing to this is that manufacturers do not set and meet specifications for their products, including specifications for identity, purity, quality, strength, and composition.

Mandatory Quality Assurance Testing. Why Is It So Important?

Every end user of dietary supplements deserves to know that the product was manufactured and tested in a way that assures authenticity, lack of adulteration, claimed potency and maximum freedom from contamination. The cGMPs would require that appropriate testing determine whether quality-assurance specifications are met for a particular final product.

SEPARATING MARKETING HYPE FROM VERIFIABLE QUALITY

The Seven Golden Questions for Quality Assurance

The following are quality questions to ask a manufacturer to verify QA procedures (sometimes called quality control, QC) and what proof they should supply to substantiate the claim. (Please note that a supplier's certificate of analysis is *never* acceptable as verification of quality assurance.)

1. Has the manufacturer been independently audited and certified for cGMP compliance by one of the following:
 - a) The National Nutritional Foods Association (NNFA, an industry trade group)
 - b) NSF International (a non-profit, non-governmental organization tagged as The Public Health and Safety Company™)
 - c) The United States Pharmacopeia (USP, the official public-standards-setting authority for all prescription and over-the-counter medicines, dietary supplements, and other healthcare products manufactured and sold in the United States), or
 - d) The Therapeutic Goods Administration (TGA, Australia's regulatory agency for medical drugs and devices)?

For verification, ask for a copy of their most recent cGMP audit report.

2. Does the manufacturer test each material (*not* random lots) for a profile, potency assay, identification individual heavy metals, chemical (s), herbicides/pesticides, and
 6. Does the manufacturer have potency test data and every raw for label-claim verification through their microbiology expiration dating period, ie, Stability Testing or authenticity, Program. solvent residue aflatoxins?

For verification, ask for copies of stability potency assays on 3 different finished product batches that were tested to verify the expiration date claim. For example, if a 24-month expiration date is claimed, the product would have had potency assays done at 12 and 24 months after the finished product assays were completed.

For verification, ask for the following:

Quality assurance test data on 2 botanical raw materials. The results

- a) identification or authenticity of the and species;
 - b) a potency assay (if a potency claim is made);
 - c) a bacteria/yeast and mold microbiology profile;
 - d) individual test results for lead, mercury, arsenic, cadmium, aluminum, or chromium;
 - e) chemical solvent residue profile used solvents;
 - f) herbicide/pesticide profile; and

For verification, ask for a copy of their supplier or lab-quality practices questionnaire or audit procedure.

When you ask for this information, the reply might be, "This is proprietary information that we can't divulge." That may be a smoke screen or a genuine concern to protect intellectual property. If you get that response, ask the manufacturer to at least answer questions 2, 5, and 6, as they are only supplying results and should not divulge anything of consequence. If they won't give you anything, be Of commonly

g) aflatoxins profile.

(Botanicals require greater quality assurance verification than vitamins, minerals, etc.)

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Quality assurance test data on 1 vitamin, 1 mineral and 1 amino acid raw material. The results should include:

- a) identification or authenticity data,
- b) a potency assay,
- c) a bacteria/yeast & mold microbiology profile, and
- d) a chemical solvent residue profile of commonly used solvents.

3. Does the manufacturer have written standard operating procedures (SOPs) that govern all of its manufacturing practices?

For verification, ask them to send you the table of contents from their SOPs and the table of contents of the forms that are _____ associated with those SOPs.

4. Does the manufacturer have written raw-material and finished-product specifications that it must meet to use a raw material and release a finished product for sale?

For verification, ask for 2 examples of their QA/QC department-approved raw- material and finished-product specifications.

5. Does the manufacturer perform full-profile finished-product assays on all batches to verify label claims?

For verification, ask for copies of potency assays on 3 different finished product batches. Request the data on a multi-ingredient product such as a multivitamin/mineral product or a B -complex product, and ask for examples of finished product potency assays for 2 single-item finished products, such as green tea extract or a vitamin or mineral product.

6. Does the manufacturer have potency test data for label-claim verification through their expiration dating period, ie, a stability testing program.

For verification, ask for copies of stability potency assays on 3 different finished product batches that were tested to verify the expiration date claim. For example, if a 24-month expiration date is claimed, the product would have had potency assays done at 12 and 24 months after the finished product assays were completed.

7. Does the manufacturer put suppliers and labs through any kind of certification process to evaluate *their* QA/QC practices?

For verification, ask for a copy of their supplier or lab-quality practices questionnaire or audit procedure.

When you ask for the information in these 7 questions, the reply might be, "This is proprietary information that we can't divulge." That may be a smoke screen or a genuine concern to protect intellectual property. If you get that response, tell the manufacturer you will sign a confidentiality agreement to keep the information private or, if they still balk, ask them to at least answer questions 2, 5, and 6, as they are only supplying results and should not divulge anything of consequence. If they won't give you anything, buy from someone else.

Be proactive, take the time to get comprehensive proof of quality assurance from your suppliers. It's only then that you can legitimately offer your clients supplements you know to be top quality.