

Clinician Negligence: The Buck Stops Here

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It was just a little over a year ago (*IMCJ* 5.6, Dec 2006/Jan 2007:44-7) that I wrote my first review of product quality testing, at that time reporting on chondroitin sulfate. I began the article with the words, “‘Greed, swindle, con, dupe, fleece, rip off, shortchange, deceive, cheat, careless, negligent.’ These are some of the words that come to mind when I see what does or does not happen with regard to proper quality assurance in the natural products industry.”

In this article I again reveal some recent product quality testing, and, sadly, I again have the same feeling: “Distressing, perplexing, vexing, astounding ...”

Before I begin, I must apologize for being passionate in advocating that people get quality supplements. I also apologize for repeating myself from article to article and carrying a banner about which few seem to care or on which few want to take action. Am I turning into a kvetch? You could see it that way. I’d rather say that I believe in, and speak of, a simple and noble concept.

That noble concept is the exclusive use of authentic (it is what it claims to be), potent (meets label claim), and uncontaminated natural products. Adhering to this concept makes it much more likely that our natural product prescriptions will help our patients. Certainly it seems obvious to all that this is the desired scenario vs using lesser or extremely poor-quality products. Who can refute that? Yet, armed with my experience of having thousands of tests performed on various raw materials for numerous years, I imagine that thousands of times per day clinicians give their patients natural products that are not likely or are much less likely to be clinically effective because the quality is either poor or terrible.

I don’t make up this information or seek it out to point the finger or be vengeful. As I discover it in the course of doing my job, I find and I report it to you. I, myself, am frequently astonished by what does and doesn’t show up in the tests.

[sub1] **The Responsibility Is Ours**

Below, I give specific examples of recent quality assurance (QA) issues and failures I have uncovered. First, I wish to speak about whom I think is responsible and how the perpetual cycle of poor quality can change.

I have always asserted in this column that clinicians who buy from natural product manufacturers have the power to improve the poor quality practices and, hence, reputation of this industry. Clinicians are responsible for either changing the status quo or maintaining it. In other words, we can opt to become devotees of quality, seek proof from manufacturers/suppliers, and then vote with our dollars—spending only with those who can and will prove their QA practices. Basically, what I’m saying is that the buck can stop here—or not. If not, this form of medicine will continue to get black eyes for years to come from the perpetual stories of poor product quality that are sure to be made public.

Clinicians are busy having lives, running practices, and trying to do right by their patients. I know it takes time to act responsibly and do what is needed to hold manufacturers/suppliers accountable for proving quality assurance. Having said this, I must add that if one does not take the time and the actions to assure quality, they just might end up with some of the materials I detail below. Don’t count on the U.S. Food and Drug Administration (FDA) to police this industry. Newly passed current Good Manufacturing Practices (cGMPs) laws are not likely to be enforced, as the FDA does not have the resources to be the watchdog of the dietary

supplement industry. The FDA can't even adequately inspect our food supply¹ (see my earlier article, "New FDA cGMPs for Supplements: Smoke or Substance?" [6.5, Oct/Nov 2007:28-32]). Also, keep in mind that the new cGMP guidelines do not, I repeat do *not* apply to the raw material companies that supply *all* the natural products manufacturers. So, it is up to the manufacturers to comprehensively test raw materials and ensure the authenticity, potency, purity, and composition of the finished product. It is up to us as clinicians to make sure they prove that with valid science.

As I outline and explain the following quality deficiencies, I ask if there are any clinicians out there who would knowingly prescribe any of these products to their patients. I doubt it. However and in reality, some or many clinicians might be prescribing products just like these because they never bother to check for and get proof of quality assurance.

[sub1] Test Results

The following are problems I've found most recently.

[sub2] Toxic Solvent Found in Curcumin Extract

I asked for a sample of curcumin (*Curcuma longa*) extract from a supplier out of India that I wished to verify. The sample was tested for potency and chemical solvent residue. Potency was very good, actually above label claim. Residue testing, however, was a different story altogether. The lab verified the presence and level of the chemical solvent residue 1, 2 Dichloroethane, which showed up at a level of 5 parts per million (ppm). Now 5 ppm may not sound like a lot, but it is; the FDA legal limit for use in pharmaceuticals is 5 ppm. Although this makes it seem acceptable, that is not really the case—1, 2 Dichloroethane is a Class 1 solvent, a category that the FDA has labeled as "solvents to be avoided [because they are] known human carcinogens, strongly suspected human carcinogens, and environmental hazards."² This is what one FDA pharmaceutical guide says about Class 1 solvents (*italics/bold added*):³

*"Class 1 residual solvents should **not** be employed in the manufacture of drug substances, excipients, and drug products because of unacceptable toxicities or deleterious environmental effects of these residual solvents. However, if their use is unavoidable their levels should be restricted. When Class 1 solvents are used, these solvents should be identified and quantified."*

Is the use of 1, 2 Dichloroethane "unavoidable" in creating curcumin extract? Hardly. The most commonly used solvent for a product such as this is acetone. However, using a toxic chemical such as 1, 2 Dichloroethane is more effective than using acetone, so that's the reason why some manufacturers choose it. To give the benefit of the doubt, let's say, to the supplier's mind, 1, 2 Dichloroethane was the only option. Even then, according to the rules cited above, "When Class 1 solvents are used, these solvents should be identified and quantified." The certificate of analysis stated that the solvent used to extract the product was acetone. That's a blatant lie.

[sub 3] *What are the Health Effects of 1, 2 Dichloroethane?*

Short-term Effects: The U.S. Environmental Protection Agency has found the following potential health effects when people are exposed to this toxin at levels above the maximum concentration level (MCL) for relatively short periods of time: central nervous system disorders; and adverse lung, kidney, liver, gastrointestinal, and circulatory effects.⁴

Long-term Effects: This toxin has the potential to cause the following effects from a lifetime exposure at levels above the MCL: cancer.⁵

Needless to say, I did not purchase this supplier's raw material. But I know others have, since this is a popular supplier. Are you prescribing a curcumin extract to some of your patients? Does it have this toxic solvent in it? Would you know? How comfortable can you be when central nervous system disorders, and adverse lung, kidney, liver, gastrointestinal, and circulatory effects, are a distinct possibility? What if you are unaware of the contamination and you prescribed curcumin to a cancer patient at very high levels—say 8–10 g per day or higher. This would end up with a fairly high daily toxic load, taxing an already ill patient. What if you caused that patient harm because the product had 1, 2 Dichloroethane in it? How would that make you feel?

And the real question: How many professional product manufacturers test every batch of raw material for a comprehensive panel of chemical solvents? Do you know?

[sub2] Subpotent and Contaminated Milk Thistle Extract

In June 2007, 7 of 11 tested milk thistle extract products failed ConsumerLab.com testing: 6 for subpotency and 1 for label violations. Testing consisted of a high performance liquid chromatography (HPLC) method for silymarins with retest of failures. The HPLC method used was one standard for the industry, developed by the Institute for Nutraceutical Advancement. The silymarins tested were also the industry standard: silychristin, silydianin, silybin, and isosilybin A & B.

Failed companies with the percentage of label claim for silymarins:

- 1) A retail/professional company—83.8%. It also contained 1.1 mcg of lead per daily serving, exceeding the California state limit.
- 2) A retail company—65.8%
- 3) A retail company—64%
- 4) A retail company—64%
- 5) A popular professional products company—59.2%
- 6) A retail company—19.5%

[sub2] Adulterated *Panax ginseng* Root Extract?

I had to buy *Panax ginseng* root extract recently and had trouble finding a *Panax* root raw material with a high ginsenoside content. I finally found 1 after testing several. The results of the testing made me wonder about the quality of some of the available *P. ginseng* root products on the market, so I looked at numerous products from professional product companies. I decided to test 3. I chose these 3 because they claimed to have very high ginsenoside content. Here are the results:

Professional products company #1 – Label claim was 67.5mg of ginsenosides per capsule; test found 51.3mg, or 76% of label claim.

Professional products company #2 – Label claim was 70mg of ginsenosides per capsule; test found 27.2mg, or 38.8% of label claim.

Professional products company #3 – Label claim was 6.25mg of ginsenosides per tablet; test found 7.31mg, or 117% of label claim.

Company 3 passed and companies 1 and 2 failed for obvious reasons, but there is more mystery to the story. This is the note that came from the lab analyst:

“The tablet sample from company #3 met label claim; the capsule samples from companies 1 and 2 were low. What is of more concern to me, however, is the ginsenoside profile of these latter 2 capsule samples. In *Panax ginseng* root extracts, ginsenoside Rb1 is usually the most or 2nd-most concentrated ginsenoside. This is the case in the tablet sample #3. In both failed capsule samples, however, the Rb1 is the lowest ginsenoside concentration [of all] by far. I believe this may indicate that the extracts from the two failed samples come from arial parts (leaves and/or stems) instead of from the root part of *P. ginseng*. I have asked a colleague of mine at a Canadian academic lab who is very familiar with ginseng analysis to look at the profiles to see if he can determine the source of this material. He agrees that it is not consistent with *P. ginseng* root material, and is looking through files to see if he can match it with other materials.”

Bottom line: These 2 products may not even be ginseng root at all, but, instead, leaf and stem. It appears this is probably the case. The ginsenoside profile is very different for each plant part. If, however, the manufacturer of this product performed a test for plant genus and species identification on the incoming raw material, this kind of adulteration would never happen.

[sub2] Huperzine A for Memory Loss—Snubbed by a Manufacturer

I have a long-standing patient I saw recently. I'll call him WC. He's a pleasant, fit, and younger-looking 70-year-old retired gentleman. He's the kind of person you really want to do your best to help. WC has serious memory loss. To date I have tried many natural medicines to help alleviate this problem, but none have helped. I hunted for another supplement to try and chose huperzine A (a naturally occurring sesquiterpene alkaloid found in the fir moss *Huperzia serrata*). Then I had to find a company that sells a product that has the appropriate dose and also has some reasonable assurance of quality. I found company X. Their website says such things about their quality assurance as, “Trained herbalists evaluate our herbs for quality on the basis of smell, taste and appearance.” “Samples are sent to independent labs to screen for pesticides, sulfites and bacterial contamination.” “Our labs use the latest technology, including Capillary Electrophoresis, High Pressure Liquid Chromatography, Gas Chromatography, and Thin Layer Chromatography, which provide detailed compositional analysis of the molecular level.” During final processing, herbs “are packaged into bottles, inner and outer safety seals are applied, and each bottle is stamped with a lot number and expiration date. A sample of each batch is sent to an outside lab to ensure the accuracy, purity and potency of the finished formula.”

OK, that sounded great. I called the company and asked to speak to the manager of their quality department. I was told they do not have a quality department. That was a bit perplexing—how do you get all that testing done without someone to manage it? I was confused, so I asked for someone to speak with regarding quality practices and was told there is no such person but I could leave a message for the herbalist (also the founder of the company). I left my message.

I then sent the following request to the company asking for some proof of their quality assurance practices as stated on their website.

“Our clinic buys your products through distributor Y. I want to use your product Z with one of my patients. I'd like to know if you did any testing for potency on the huperzine raw material that went into the product and/or if you did any finished product testing to verify the huperzine content per tablet, thus verifying your label claim. I only want to use a product that can prove their label claim with an independent test. I do not want to waste the patient's time or money using a product I ‘assume’ might meet label claim. This is on your website... ‘A sample of each batch is sent to an outside lab to ensure the accuracy, purity and potency of the finished formula.’ Do you have such raw material or finished product test data on hand for this product so that I can see a copy? Please let me know.”

This is the response I got after 3 days of asking via several emails, calls, and 1 fax. A very terse and short “that information is proprietary,” which translates into, “You are not allowed to see whatever we have”—and who knows what that may be. Where is the integrity in that? Do they have something to hide?

I was a quite dismayed because now I have to look around again to find a product I can use with my patient. I felt snubbed in a major way because I felt they did not care about my request or the patient. I plan to test the potency of their product to see how it measures up to their label claim.

[sub2] Feverfew, a Massive Failure—and the Hype and Persuasion of Quality Assurance

Not long ago I had to buy feverfew (*Tanacetum parthenium*, *Chrysanthemum parthenium*) raw material. Supply was short and the availability of quality feverfew was even shorter. I finally found an acceptable supply. In the process of looking around I happened to notice that some available feverfew finished products had high claims for feverfew’s marker compound, parthenolide. I decided to test 1 because I suspected that the company’s parthenolide claim would be very difficult to meet. Before I discuss the results I want to speak about this particular company as an example of how we, as clinicians, are susceptible to being convinced, persuaded, influenced, sold, and, often, easily deceived by the marketing hype that professes quality.

I have tested several of this company’s products over the past few years. The vast majority flunked because they did not meet label claim. The ginseng product outlined above with the 76% of label claim is theirs. I have pointed out their sleight of hand with testing data in this column on more than one occasion. And yet, they routinely profess great quality (as do other companies). To see their marketing material you would think they are top notch. Do I find quality? No. Instead, I find big problems most of the time their products are scrutinized. They often do not pass muster using valid science.

[sub3] *Feverfew Results:*

This product flunked so bad at Lab #1 that I decided to have a second sample tested from the same lot of material at Lab #2. The second lab spent many extra hours testing the sample because they thought it was a high-quality product and they wanted to be sure of the results they were getting.

Label Claim: Feverfew with a parthenolide content of 0.96 mg per capsule.

Lab #1

- A. No parthenolide content was detected via HPLC analysis.
- B. An identity test performed using thin-layer chromatography (TLC) showed that the sample was only minimally characteristic of a dilute feverfew extract.

Lab #2

- A. No parthenolide content was detected using 2 methods: (1) HPLC analysis using a US Pharmacopeia Feverfew Monograph Method and (2) orthogonal analysis with the method of Zhou, et. al.
- B. An identity test performed using TLC showed that the sample profile matches the profile for feverfew as outlined in the *British Herbal Pharmacopeia* (1996 ed).

Even I did not expect these results to be so poor. Just as many of you do, I had harbored a presumption of quality.

There is no question that this product did not meet label claim and is of poor quality. The expiration date on the bottle says, "Best if used by 10-2008." Parthenolide is subject to degradation over time. I know this because our stability testing for a feverfew product reveals that information. However, parthenolide degradation can be adjusted for by adding a manufacturing overage, ie, more product is added to the capsule so the label claim is met throughout the entire expiration date period. This is the sole purpose of doing stability testing. The above company has no apparent stability-testing program. Don't you think they should?

[sub] Conclusion

The take-home message here is that we are all easily swayed by the hype that companies feed us. To distinguish hype from legitimate proof we clinicians must learn the rudiments of scientific validity as it applies to the quality assurance of dietary supplements used as natural medicines. There is no other way around it: We have to step up, ask for proof, evaluate that proof, and vote with our dollars by supporting the companies that meet that criteria. No more being swayed by the hype.

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Editor's Note: When we have run the results of such assays as these in the past we have gotten numerous questions asking why we don't publish the names of companies involved. There are several reasons for this. The first is that this column is not meant to denigrate any particular manufacturer by picking them out. They may have poor products, but so may the next guy. If you eliminate them and use another but don't check to see if the next company is any better than the first, you have accomplished nothing (nor have we). The second and most important reason, as stated at the beginning of this article, is: Clinicians are responsible for changing the status quo or maintaining it. These are *your* patients we are talking about. It is your responsibility to them that is at stake. If we give you the names, it is but a drop in the pond. You need to ask *each and every* one of your manufacturers/suppliers about their quality procedures.

The goal of all of these articles on quality assurance is to impress on you the urgent need for quality standards. To help you do this, Dr Liva developed and wrote a questionnaire for clinicians to question manufacturers and/or suppliers about their quality assurance practices. It is available at *IMCJ's* website, www.imjournal.com. In the menu bar on the left, click on "Quality Assurance" (located near the end), then click on "Manufacturer Quality Assurance Self-Audit Form."

Please send this form 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 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.

When the Self-Audit Form is returned, you also can then use some of the answers to calculate the daily toxicity load (as was calculated for 1, 2 Dichloroethane in the curcumin product, above) that will result from ingesting a manufacturer's product. Again go to the IMCJ website, click on "Quality Assurance," then click on "Toxicity Calculator." Contamination is a serious quality assurance problem and needs to be considered when taking or

prescribing dietary supplements. It is critical to assess the toxic load of various contaminants based on the highest-possible daily dose of a particular manufacturer's product, ie, the amount a person would take as a normal dose in a day. By using the Toxicity Calculator you are able to determine this.

We at the journal agree with Dr Liva. The buck does, indeed, stop with the clinician.

[sidebar] **A Gauge of Reader Interest**

As you can tell by now, *IMCJ* is passionate about quality assurance because we care about the complementary and alternative medicine (CAM) industry and want you, the practitioner, to be able to help your patients by prescribing high-quality supplements. We also want our industry to survive. If poor products continue, the industry is going to have a bad reputation and won't be taken seriously.

We are wondering how important the information presented in this Quality Assurance column is to you.

1. How often do you read this column?

Every issue Most issues Sporadically This is my first time Other
(Please specify what)

2. How much do you care about quality assurance issues?

Very much A little It is interesting, but I remain unmoved Other
(Please specify what)

3. If you do care, are you doing anything about?

Yes No

4. If so, what: _____

5. Have you ever sent a manufacturer or supplier the "Manufacturer Quality Assurance Self-Audit Form"?

Yes No

6. If the answer to #5 is yes:

(a) How many times have you sent it? _____

(b) How many responses have you received? _____

(c) Were you satisfied with the response? Yes No

**Please send your responses to imcjsubmissions@innovisionhm.com. Or you can fax: 303.440.7446.
Or send by mail: *IMCJ*, 2995 Wilderness Place, Ste 205, Boulder, CO 80301.**

Thank you for your participation! Your opinion is valued.

References: [[NOT Final]

1. Timiraos N. Are Chinese export products unsafe? *Wall Street Journal*. July 14, 2007:A5.
2. Guidance for Industry Q3C Impurities: Residual Solvents. <http://www.fda.gov/cber/gdlns/q3cresolvent.htm>

3, US Department of HHS FDA Center for Drug Evaluation and Research Center for Biologics Evaluation and Research
Dec 1997 Guidance for Industry Q3C Impurities: Residual Solvents.

4, Ref TK

5. Ref tk