

When it Comes to Quality Assurance, Assume Nothing
by Rick Liva, RPh, ND

An Interesting Twist on Chondroitin Sulfate Testing

In my last column (*IMCJ* 5.6;44-45), I presented assay results from 5 chondroitin sulfate products that came from 5 popular professional-products companies. Each flunked independent potency assays that used a methodology accepted by the United States Pharmacopoeia (USP). Potency results ranged from 14.6% to 85% of label claims. Federal law states that a dietary-supplement product in the marketplace must be 100% true to its label claim at all times throughout its expiration-dating period. If it is not, the product is considered misbranded and illegal and should be recalled by the company.

As soon as that issue of *IMCJ* was out, a supplement-manufacturing company called and wanted to know if their chondroitin sulfate product was one of the brands tested. If one of the subpotent products was theirs, they wanted to know the lot/batch number so they could do a recall. I commend them for their concern and quick response. It is comforting to know that there are companies concerned with quality assurance (QA) that wish to do the right thing to remedy a problem by taking a subpotent product out of the marketplace.

And yet, as appreciated as their efforts are, and with all due respect for their concern, I can't help but ask how any subpotent chondroitin sulfate product (let alone 5) made it to the market in the first place. I also wonder why this particular company did not know for themselves whether or not their product was subpotent. It is a prime example of why every manufacturer needs to have a QA program in place. If this company had been doing batch-to-batch potency testing (not skip-lot testing, which I have warned about before) on the raw materials going into their chondroitin sulfate product, they would have discovered any problems.

As an alternative, a company can skip raw-material testing and simply test the finished product before they move it to market. I never recommend this, however, as finding a problem at this stage in the game gives a company huge financial incentive to look the other way rather than correct the problem. Nonetheless, in the case of the chondroitin sulfate product, either approach would have proved fortuitous—if they'd had a subpotency problem, the company would have detected it in the raw material or finished product and fixed the problem before the product was sold.

And even after this, there is yet another point at which to check product quality. When a company follows current goods-manufacturing procedures (cGMPs), they retain a sample of every lot of product they have made in the past few years. Testing their retained samples of chondroitin sulfate would have quickly and easily revealed a subpotent product. As it stands now, in the case of these 5 subpotent products, some unsuspecting souls may be trying to treat osteoarthritis of the knee with supplements too weak to work.

The only ethical response we could give to the company's question is, "We recommend you do comprehensive QA testing on each lot of your raw materials and finished products to find problems and fix any that exist." Routine testing of each batch of raw material for identity, potency, and purity (testing for an array of contaminants)—as well as finished-product-potency testing—is simply the right thing to do. That said, I suspect and fear that most manufacturers are just not doing this testing. This is why organizations such as Consumer Lab (an independent testing laboratory that evaluates nutrition products) and many others are taking supplements from the marketplace and testing them, only to routinely find subpotent or contaminated products. (See below for more Consumer Lab information.)

Let me be clear. My concern is for the consumer who is getting less-than-acceptable—even hurtful—quality. I am also concerned for the supplement industry, which, within a tightening circle of government scrutiny, risks losing its freedoms. If we don't police ourselves, we may follow in the regulatory footsteps of the European Union (EU), where two pieces of legislation are being hotly debated: the 2002 Food Supplements Directive and an EU regulation on fortified foods that is currently making its way through the rule-making process. As stated in a 2004 issue of *HerbalGram* magazine, "Should the EU impose its various supplement-related directives on its over two-dozen member countries, there is every reason to believe that there is enough critical mass in the US Congress for similar legislation to be passed to ensure that supplements are more stringently regulated, especially related to safety. The impact this would have on the US dietary supplement marketplace would be nothing short of significant..."¹

[sub] Dry Labbing: What is it? Why Should You Care?

In a further effort to track what is happening in the industry, *IMCJ* also sent the chondroitin sulfate samples tested and reported in the last column to a lab that I suspect does "dry labbing." In this scenario, a lab provides a manufacturer with results that are exactly or close to the results it desires, without ever actually performing the analysis. That didn't happen in this case. The results this lab reported on the chondroitin samples were similar to the results we obtained from the first lab—so this time dry labbing wasn't an issue.

How widespread the practice of dry labbing is, I'm not sure; but I have seen it many times. It is easy to spot if you know what you are looking for. Some examples follow. I offer them to help you "learn the ropes" so you are better able to judge for yourself whether the evidence being presented as "scientific" actually supports product-label claims.

The assay data that follow were taken directly from information provided by a professional-products manufacturer. In each case, the testing lab assayed 10 or, in one case, 30 capsules taken randomly from a sealed bottle of the product. While I can't say with certainty that these are "dry labbed" results, they sure look fishy to me. Do the following tables look scientifically valid to you? Read on.

Example #1 Multi-Ingredient Saw Palmetto Product

Ingredient Tested	Assay Result	Label Claim
Saw palmetto extract (calc. as 85% fatty acids)	206.3 mg ± 4.15	160 mg
Pygeum extract (calc. as 13% sterols)	36.15 mg ± 1.45	20 mg
Nettle root (calc. as 5% amino acids)	218.5 mg ± 1.12	200 mg

What is wrong with this picture? First, there are some grave mathematical errors: If you have 160 mg of saw palmetto (*Serenoa repens*) containing 85% fatty acids, you have, at best, 136 mg of fatty acids (160 x .85 = 136). Yet the assay shows 206 mg. How can this be? Equally important, why would a company print such obviously incongruent information? The answer to the last question is that the manufacturer likely suspects that most people won't bother to look, and, if they do, probably won't understand what they are seeing.

The problem with this "assay" goes deeper still. Even if the fatty-acid analysis is correct, there is no way to tell if the 85% fatty acids come from saw palmetto. That is to say, this is not a valid test for saw

palmetto authenticity; a pertinent authenticity test should include, at least, listings for lauric and myristic acids expected from a saw-palmetto extract. Making matters more confusing, the product label lists pumpkin-seed oil as an ingredient. So how do we know if the fatty acids came from the saw palmetto or the pumpkin seed oil? Obviously we don't.

The same math problems exist with the other 2 ingredients in Example #1: 20 mg of pygeum extract containing 13% sterols equals 2.6 mg of sterols, but the assay shows 36.15 mg; 200 mg of nettle root containing 5% amino acids equals 10 mg amino acids, but the assay shows 218.5 mg.

In the long run, when you know what to look for, this kind of faulty information will stand out like a sore thumb when you see incongruent lab results.

Example #2 Multi-Ingredient Blood Pressure Product

Item Tested	Assay Result	Label Claim
<i>Crataegus oxyacantha</i> extract (2% vitexins)	208 mg ± 10	200 mg
<i>Zingiber officinale</i> extract (5% gingerols)	101 mg ± 5	100 mg
<i>Leonurus cardiaca</i> extract 4:1	214 mg ± 11	200 mg

Example #2 demonstrates the same kind of dubious mathematics. In this case, 200 mg of hawthorn (*Crataegus oxyacantha*) extract containing 2% vitexins equals 4 mg, yet the assay shows 208 mg; 100 mg of ginger (*Zingiber officinale*) extract containing 5% gingerols equals 5 mg, yet the assay shows 101 mg. Finally, 200 mg of *Leonurus cardiaca* extract 4:1 is said to assay at 214 mg, but 214 mg of what? The assay itself lists no marker compound. In addition, Chromadex (www.chromadex.com), a supplier of botanical-reference standards, shows that no marker compound exists for this plant. Despite this, the assay reports 214 mg of something. What was found, and how?

Example #3 Multi-Ingredient Herbal Immune Enhancer

Ingredient Tested	Assay Result	Label Claim
Arabinogalactan	516.2 mg ± 4.05	500 mg

Arabinogalactan refers to a kind of polysaccharide derived from the wood of the Western larch (*Larix occidentalis*). As far as I know, this polysaccharide cannot be specified (see www.chromadex.com). At best, some molecular weight determination can be made, but this neither identifies nor quantifies the compound. In addition, there is no standard against which to judge the sample. To make matters even worse, this particular product was mixed with 3 other plant materials that would further skew any ability to specifically identify and quantify arabinogalactan from other compounds.

Example #4 Multi-Ingredient Bioflavonoid Product

Ingredient Tested	Assay Result	Label Claim
Oligomeric proanthocyanidins from grape seed extract (calc. as 92% OPCs)	51.66 mg ± 0.47	46 mg
Silymarins from milk thistle (calc. as 80% silymarins)	83.16 mg	80 mg

According to its label claim, the product in Example #4 contains 50 mg grape-seed extract composed of 92% oligomeric proanthocyanidins (OPCs), which the company says equals 46 mg of OPCs. The

assay claims 51.66 mg of OPCs were detected by high-performance liquid chromatography (HPLC). However, OPCs are nutrients belonging to the flavonoid family, and there is no reference standard against which to quantify that family of compounds (see www.chromadex.com). Thus, a result of 51.66 mg is scientifically impossible.

The label claim also says the product contains 100 mg milk-thistle extract composed of 80% silymarins, which the company says equals 80 mg of silymarins. The assay claims 83.16 mg of silymarins were detected by HPLC. The trouble here is that the term "silymarins" is just too general (for more information, see "*Silybum marianum* and Silymarin" on p.TK of this issue). Some silymarin compounds can be quantified in milk thistle by HPLC: silybin A and B, isosilybin A and B, silydianin, and silychristin. However, each has to be quantified—and should be listed on the assay—separately, and they *never* equal 80% by HPLC in a milk-thistle extract. At best, using an HPLC method, the total percentage of silymarin compounds in milk-thistle extract tops out at 45-55%. (*Editor's note: Most, if not all, milk-thistle labels list 80% silymarins. That is because another assay method, using ultra violet light, is less accurate, and quantifies more compounds under silymarins. The discrepancy in this particular assay is that it claims 80% silymarins using HPLC, which is a more discerning assay. As mentioned, when using the HPCL method, silymarins never exceed 45-55%.*)

All in all, this is a disturbing set of data. How could a testing lab arrive at any of these assay claims other than by sleight of hand or, as the case may be, sleight of pen? The take-home message for clinicians is that you need to become educated in how to read assay results. In a nutshell, you need to learn how to evaluate data to obtain objective, scientifically valid evidence of quality assurance. If you do not, you may be putting yourself and your patients in peril or risk treatment failure.

QA Investments: How Much is Enough?

Consumer Lab assay information over the past several months shows that 70% of herbal sleep supplements fail tests for quality; 50% of ginseng supplements are subpotent or contaminated; 15% of prostate supplements fail testing for a variety of reasons (eg, subpotency, short on specific fatty acids known to be in saw-palmetto extract, etc.); several green-tea products are contaminated with lead or are subpotent; and 1 DHEA product was superpotent, which can lead to overdosing. Consumer Lab tests only a small number of products, so it is likely that numerous subpotent or contaminated products are on the market.

Keeping in mind the extent of the problem, it came to my attention recently that a certain long-established and well-known professional-products company spent approximately \$69,000 on product testing (ie, QA testing) in 2006. Their 2005 product-testing expenditures were much less. This is a manufacturer that has annual sales of about \$16 million, with a product line consisting of more than 160 finished products and a raw-material list of more than 250 different items.

I have made the statement in the past that companies just do not want to spend the money to provide adequate product quality assurance (assaying identification, authenticity, and purity or contamination; as well as verifying label claims for potency). They would rather save money by not testing and put the extra cash into the pockets of the company owner(s) and stockholders. From the financial data provided in this example, let's make a few extrapolations to see if this company's \$69,000 annual expense for product testing is enough to accomplish adequate product QA.

Assumptions

Buy raw materials (250 ingredients) 2x/year.
Make finished products (160 items) 2x/year

Full microbiology profile, with an average cost of \$60/profile (range is \$60-\$100, depending upon the lab)
Potency assay, with an average cost at \$100/assay (range is \$50-\$300, depending upon the test and lab)

Projected Costs

Raw-material microbiology at \$60/profile x 250 products x 2/yr = \$30,000
Finished-product microbiology at \$60/profile x 250 products x 2/yr = \$19,20
Raw-material potency assay at \$100/assay (a low estimate) x 250 products x 2/yr = \$50,000
Total: \$99,200

We have already surpassed their actual spending and have not yet addressed cost for any contamination tests (a formidable amount), botanical-identity testing, finished-product-potency assays, or stability testing. I suspect that with a product line this large, adequate quality-assurance testing would cost somewhere in the range of \$350,000-\$450,000. Are some of their products subpotent, superpotent, or contaminated? Do you know, or do they know? I suspect not.

Marketing Omissions

Recently, I received at my practice promotional literature from 2 professional-products manufacturers—a new catalog and a marketing piece. This is what they had to say about their quality assurance.

According to the catalog, the manufacturer "...creates the best products possible, utilizing research-validated ingredients, purity, and potency...free of preservatives, excipients, or other problem additives...standardized botanical extracts are used whenever possible."

The marketing piece states, "We pride ourselves on our standards: quality products, quality prices, and quality personnel."

Nothing at all is said about quality-assurance verification of raw materials or finished products. Why? I would guess it's because they don't do any.

Obtain Objective Evidence of Quality Assurance

With the examples given above, it is all too obvious that what you see is not necessarily what you get. Whether intentional or not, there are smoke and mirrors here. Lack of quality assurance creates a "buyer-beware" scenario. As a clinician, when you procure supplements to pass along to your clients, you need to be able to judiciously interpret a company's QA information and find the truth. Unfortunately, the truth is not always pretty, and, as we've seen, not always what manufacturers present on product labels. It is discouraging that we are in this predicament, but for the safety of our clients and the future of our industry, the truth must be exposed. We all get a bad name when a company misrepresents its quality-assurance efforts to look like it is selling good products when it really is not. And we are at risk of losing our ability to sell these essential nutrients and medicinals if we don't clean up our act.

The goal of all of my articles on quality assurance is to impress on 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 that clinicians can 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 side bar, then click on "**Manufacturer Certification and Quality Assurance Self-Audit Form.**" Please send this questionnaire to each of your natural-products suppliers and see what comes back. It asks manufacturers 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. It is easy to answer yes to a question on the form; it is more difficult to provide proof. Thus, the questionnaire asks for proof as well as yes-or-no answers.

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.

If you are unfamiliar with quality-assurance issues or need further clarification on how to use the questionnaire tool, I am always available to answer your questions and provide quality-assurance information. Please contact me at rickliva@center4health.com.

In the next issue of *IMCJ*, I will review heavy-metal contamination of dietary supplements. The problem is real, as evidenced by the article written by John Neustadt, ND, in this issue. I will discuss issues related to outdated testing methods, acceptable test methods, acceptable limits of daily consumption of heavy metals, how to calculate the daily load of heavy metals from lab data, and how to interpret lab data correctly and thoroughly.

[bio] Rick Liva, RPh, ND, graduated from Temple University School of Pharmacy in 1975 and National College of Naturopathic Medicine in 1982. He is the managing physician at the Connecticut Center for Health, located in Middletown and West Hartford. Dr Liva is a founding member of the American Association of Naturopathic Physicians and past president of the Connecticut Society of Naturopathic Physicians. He has been involved in dietary-supplements manufacturing since 1985 and is the president, CEO, and director of Quality Control and Quality Assurance at Vital Nutrients, certified by the NSF International and the National Nutritional Food Association (NNFA) for current Good Manufacturing Practices.

References

^{Mark} Schauss, A. A review of the european food supplements and traditional herbal medicines directives. *HerbalGram*. 2004;63:64-69.