

The Difference Between Quality Control and Quality Assurance Using an Example of Pomegranate Extract

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In this column, I will distinguish 3 things: first, the distinctive definitions of *quality control* (QC) and *quality assurance* (QA); second, what these terms mean to clinicians; and third, how these terms can be applied to a product such as pomegranate extract. As is the case for any supplement/remedy, by making sure a manufacturer follows some basic quality standards, the clinician can avoid purchasing low-quality products.

I learned about the reported issues with pomegranate extract by conducting testing (the QC portion of this article) on various ingredients available in the marketplace. Pomegranate extract is emerging as a useful clinical tool for the prevention and treatment of health issues such as oxidative stress¹—specifically, it has been shown to exert significant antiatherogenic, antioxidant, antihypertensive, and antiinflammatory effects²—and we will likely be seeing more products containing it.

QC/QA Definitions and FDA's Use of GMPs

The terms *quality control* and *quality assurance* are often used interchangeably to refer to ways of ensuring the quality of a product. In actuality, they have different meanings. Below, I have listed several ways to define both, giving the reader a broad scope of how to reconcile and think about them.

For this to make sense, there first has to be a general consensus on the word *quality*. Within the industry, *quality* means that the dietary supplement under consideration consistently (ie, batch to batch) meets the established specifications for identity, purity, strength, composition, limits on contaminants, and shelf life. It also means that it has been manufactured, packaged, labeled, and held under conditions to prevent adulteration.

To this end, *quality control* means a systematic procedure for ensuring the quality of a dietary supplement (eg, running tests such as thin-layer chromatography, high-performance liquid chromatography, or gas chromatography/mass spectrometry to determine specific amounts of product constituents and/or contaminants). Thus, QC is a company's control over product quality and involves testing, reviews, and (occasionally) simulations and mathematical provings. The end result of QC is the answer as to whether each batch does or does not meet the set product specifications, as mentioned above, for identity, purity, strength, composition, limits on contaminants, and shelf life.

Quality assurance, on the other hand, refers to the processes used to create a product. Examples include process checklists (eg, performance logs) and project audits. Basically, it is the standard by which a company administers its quality measures (versus tests for an individual product), often based on regulations such as the US Food and Drug Administration (FDA) current Good Manufacturing Practices (cGMPs). It involves internal or external audits to ensure compliance with those standards—thus, QA can be ascertained and/or performed by a manager, third-party reviewer, or even a client.

Simply put, QC is conducting “testing” and performing procedures to ensure that established quality specifications for raw material and finished products are met. QA is the strict regulation of all of the processes used to create the final product.

An important point to remember with all of this is that you can have QA while doing very little QC testing. That is to say, a dietary supplements manufacturer can have established raw material and finished product specifications (a part of GMPs) and have all its quality assurance processes in place, but some or all of its products still may not meet standards of acceptable quality control—products may be low potency, contaminated, not last out their shelf life, etc. The FDA cGMPs do not mandate that a manufacturer has to establish high-quality specifications, just that it has to *have* specifications, even if low quality.

This is why I write these columns, so clinicians can understand this important fact. It is also why the recent FDA cGMPs can be used as a cover by disreputable companies to hide behind if, in fact, they have established low-quality specifications.* Comprehensive QC testing is *the* key to producing quality natural products because it covers all the bases for high quality (identity, strength, and a full spectrum of contaminants).

QC and QA as Seen in Pomegranate Extract

Pomegranate juice (PJ) has recently become popular in the United States. It has more potent antioxidant properties than other common fruit juices due to its high content of polyphenols.

Research has been published on the ability of pomegranate polyphenols to be antiproliferative, proapoptotic, antiangiogenic, and capable of inhibiting NF-Kappa Beta activity.³

The most abundant polyphenols in PJ are ellagitannins (ETs), which are not absorbed intact into the blood stream but, instead, are hydrolyzed to ellagic acid and then released into the

*If you find it surprising that the FDA's cGMPs leave open the possibility of inadequate testing and poor-quality products, please read 2 articles in *IMCJ*'s Oct-Nov 2007 issue: “New FDA cGMPs for Supplements: Smoke or Substance?” by Rick Liva, ND, RPh (*IMCJ* 6.5:28-32); and “FDA's Natural Product cGMPs—A Missed Opportunity” by Joe Pizzorno, ND, with Michael D. Levin (*IMCJ* 6.5:8-10).

blood.³ Ellagitannins are also metabolized by gut flora into urolithins, which are conjugated in the liver and then circulated in the blood. These ET metabolites reach many of the target organs where the effects of pomegranate ellagitannins, such as those noted above, are seen.³

PJ's ellagitannins are part of a family of minor tannins that include punicalin and gallagic acid. However, at this time, 2 of these ETs have been found to be unique to pomegranate: punicalagin A & B. Punicalagins have been reported to be responsible for more than half of the juice's potent antioxidant activity.³ They are most abundant in the fruit husk as opposed to the juicy seeds.³

It is by pressing the whole fruit during processing that ellagitannins are extracted into PJ in significant quantities, reaching levels of >2 g/L of juice. PJ also contains other polyphenols such as anthocyanins (cyanidin, delphinidin, and pelargonidin glycosides) and flavonols (quercetin, kaempferol, and luteolin glycosides).³

A significant amount of the published animal and human research has been done using the POM Wonderful brand of juice or the POM Wonderful powdered extract. Why is this significant? It makes sense to me that, since a vast amount of research has been done on this particular juice/extract, any other juices or powdered extracts should have a chemical constituent profile that mimics POM's as closely as possible.

I have had the ellagic acid, ellagic acid hexoside, punicalagin, and anthocyanin content of POM juice analyzed by an independent lab at least twice. In addition, I had other brands' pomegranate products analyzed, including several pomegranate-husk extracts, a concentrated juice product, a freeze-dried, whole-fruit powder, a spray-dried juice powder, and a raw-husk product. I found that no product even came close to the punicalagin, ellagic acid, ellagic acid hexoside, and anthocyanin content of 8 oz of the POM juice. In fact, no pomegranate extract that claimed 40% punicalagins actually tested out at that level; they were all subpotent.

Lastly, and considerably more blatant in their attempt to deceive, some pomegranate extracts that claim 40% ellagic acid are "spiked" with the acid to reach that claim—which is actually not surprising since ellagic acid in naturally occurring pomegranate extract is 2% to 4% on average. Unfortunately, a full discussion of the analytical results are beyond the scope of this article, but I am happy to speak with whomever may want more information on these results.

I mentioned all of the above information because it is relevant to the QC portion of developing a clinically efficacious product. With comprehensive testing (the "bones" of QC) on the starting raw materials, a supplements manufacturer can develop an understanding of the chemical constituents that have proven medical benefit and generally fashion a product that, in the end, will have a high degree of efficacy. Without comprehensive testing, however, this is a gamble. As seen above, if a manufacturer doesn't know—or at least doesn't match—how much ellagic acid and punicalagin is in the researched pomegranate juice, how can it create a product that is equally as effective?

As for the clinician, you need to know if the product you buy matches the specifications of the product that has been researched. It doesn't do anyone any good to buy a pomegranate

extract to be used for clinical benefit if the product being sold doesn't have the same amount of necessary constituents as the researched product. That's what is called borrowed science (and not an equitable borrowing at that).

Beyond whether there is medical benefit to the specified amount of nutrients included in a supplement, the clinician also needs to know if a product actually meets label claim for these amounts (which the ones mentioned above did not). So there is a double whammy. On the latter, consider what I mentioned before about the deficiencies of FDA's cGMPs: current dietary supplement laws allow for a manufacturer to set specifications for its own quality. Unfortunately, some or many manufacturers of dietary supplements will set a "low quality" specification for their raw materials. Hence, it is up to you, the clinician, to find out if that is the case. Ask your vendors what type of comprehensive testing they are routinely performing on their raw materials and finished products. Routine comprehensive testing is the most important key to building high quality into a dietary supplement.

So in this example of pomegranate, QC testing is necessary to verify that the product being sold matches, to some degree, the specifications of the product that has been researched and, also, that the label claim is met. QA is in play throughout because it is the strict regulation of all the processes used to create the final product.

Obtain Objective Evidence of Quality Testing and Then Evaluate the Results

The road to ensuring high quality is successfully traveled when clinicians ask for and obtain valid evidence (test results) of a product's identity (authenticity), purity (maximum freedom from contamination), and shelf-life strength. Then, once you have the test results in hand, they must be evaluated for scientific validity.

To this end, a number of years ago, I developed and wrote a questionnaire entitled "The Manufacturer Quality Assurance Self-Audit Form," which was published in the Aug-Sept 2006 issue (*IMCJ* 5.4:41-44) and has since been available since on the *IMCJ* website. The form is intended to give clinicians a basis upon which to question manufacturers and/or suppliers about their QC and QA practices.

After these several years of use and feedback, I have now renamed the form and developed a more simplified questionnaire (only 20 questions) that clinicians can use as a product-quality testing and verification/certification tool. We have included it in this issue on the pages following this article, and it is also available on the website, www.imjournal.com. On the menu bar, click on "Resources & Content." The second listing on the dropdown menu is "Quality Assurance." On the corresponding web page, you will see "The *IMCJ* Supplement Quality Audit Form."

Take the Time to Verify Quality; Use the Tool

This new questionnaire is considerably shorter than the original and focuses primarily on asking for the test data used to ensure quality. I ask you please, for the sake of your patients' health and safety, to send this form to each of your natural products suppliers and/or manufacturers and see what comes back.

Resources to Help Evaluate QC and QA Data From Suppliers and/or Manufacturers

The academic experience of most clinicians does not educate them on the details of how to ensure quality in dietary supplements. Knowing about and using outside resources is a critical tool in helping you gain some knowledge in this arena. Think of it as part of your continuing education. The following resources are available should you choose to use them (some are consultants who charge for their time and some may be able to briefly help you for no remuneration).

- **Blaze Science Industries LLC:** Technical expertise in scientifically valid testing of dietary supplements. 4547 West 171st St, Lawndale, CA 90260. Phone: 310.920.4517. Contact: Jana Hildreth, CEO and Technical Director. E-mail: janah@socal.rr.com. Website: www.bsillc.org.
- **EAS Consulting Group LLC:** Consultants specializing in FDA regulatory matters. 1940 Duke Street, Suite 200, Alexandria, VA 22314. Phone: 877.327.9808. Contact: Edward A. Steele, President. E-mail: esteele@easconsultinggroup.com. Website: www.easconsultinggroup.com.
- **Flora Research Laboratories:** Resource for evaluation of scientific validity of lab methods used to test dietary supplements. 1000 SE M Street, Unit B, Grants Pass, OR 97526. Phone: 541.472.0980. Contact: James Neal-Kababick, MS, Director, Past Chairman of the Association of Analytical Communities International Dietary Supplement Methods Validation Committee. E-mail: jimk@floraresearch.com. Website: www.flora-research.com.
- **The Natural Products Association Dietary Supplement GMP Certification Program:** 1773 T Street, NW, Washington, DC 20009. Phone: 202.223.0101. Contact: Vicki Whitsitt, Science and QA Assurance Manager. E-mail: vwhitsitt@NaturalProductsAssoc.org. Website: www.naturalproductsassoc.org.
- **QSD Consulting:** A dietary supplement GMP consultant and auditor. 430 Main St, Benton, PA 17814. Phone: 570.925.2880. Contact: Cindy Beehner, Owner. E-mail: cindybqsd@netzero.net. (No website.)
- **QSI: Quality Systems Implementation:** A dietary supplement GMP consultant and auditor. Midvale, UT. Phone: 801.838.9603. Contact: Warren Majerus, MS, Owner. E-mail: majerus@mindspring.com. Website: http://dsgmpdocs.us.
- **Tampa Bay Analytical Research Inc.** Resource for evaluation of scientific validity of lab methods used to test dietary supplements. 10810 72nd St, Unit #206, Largo, FL 33777. Phone: 727.544.8481. Contact: Mark Roman, PhD, Owner, Past Chairman of AOAC International Dietary Supplement Methods Validation Committee. E-mail: mroman@tampabayanalytical.com. Website: www.tampabayanalytical.com

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 to be 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.

I also include a new guidance document that may help you evaluate the responses you receive back (see “Compliance Guide for The *IMCJ* Supplement Quality Audit Form” on page 51, after the questionnaire). Finally, I include a sidebar on this page listing resources in case you need further clarification and education.

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