

Summary
Ingredient Supplier Qualification Workshop

Presented by
The Joint SIDI™ working group
Wednesday, June 24, 2009
CHPA Offices
900 19th Street, NW, Suite 700
Washington, DC

In attendance:

<u>Companies</u>	Nutrilite	NPA
Albion	Pharmavite	NSF
BASF	Perrigo	USP
Bayer	Sabinsa Corp	
Colorcon		<u>Trade Associations</u>
DSM	<u>Government</u>	AHPA
Embria Health Sciences	FDA	CHPA
GNC	ODS, NIH	CRN
Kemin Health		NPA
Kyowa Hakko	<u>Third Party Certifiers</u>	UNPA

The objective of the workshop was several-fold:

- To clarify for the attendees FDA’s expectations for ingredient supplier qualification as it pertains to GMP compliance.
- Provide attendees with the latest information on food safety legislation and how that may impact the dietary supplement industry, specifically by imposing new requirements for supply chain security and traceability.
- To decide whether a proactive approach to establish guidelines and/or an industry sponsored program for ingredient supplier qualification is needed and feasible.

Food safety legislation

The meeting began with guest speaker Amy Muhlberg, Senior Health Policy Advisor to Senator Enzi (Senate Committee on Health, Education, Labor and Pensions) who provided her views of impending food safety legislation. Although she made it clear that such legislation is unlikely to move in the Senate due to other priorities (e.g. healthcare), things could move quickly in the House, and despite not being the target of the legislation, dietary supplements will be affected. She reiterated that Members’ concerns still center on supply chain security, traceability and 3rd party certification, and

explained that many of the proposed provisions in Bills introduced thus far have not been adequately thought out. Amy expects the final food safety bill to resemble that proposed in the House. However there are overlaps between the bills (mandatory recall, parity, traceability). There is, in her opinion, more awareness in the Senate side regarding the differences between dietary supplements and conventional food and existing statutes/regulations that cover dietary supplements, although, consideration of dietary supplement “carve outs” in certain provisions will exact some political cost.

She implored the attendees, as representatives of the dietary supplement industry, to communicate with key food safety legislation sponsors and their staffers early in the stages to help craft legislation that will call for appropriate but not overly burdensome requirements. She expressed that Members such as Sen. Chambliss are very interested in hearing from industry experts. Some specific issues to comment on include those that attendees put forth to Amy: verification of ingredients before entering the US, qualification of 3rd party certifiers, user fees, country of origin labeling (COOL). Regarding COOL, Amy expects that there will not be overwhelming support by analogy with processed foods (most Members area against COOL for processed foods), however, she advised that nothing is a done deal.

Amy’s comments sent a clear message to the attendees: Food safety legislation is coming, it will affect dietary supplements, especially with respect to supply chain, and there is a need for the industry to be proactive in helping Congressional staffers to understand the issues relevant to dietary supplements so that the most appropriate legislation is crafted.

FDA perspective on ingredient supplier qualification

FDA’s Dr. Bill Frankos followed with what attendees indicated was the first in depth look at FDA’s expectations for ingredient supplier qualification. Dietary ingredient suppliers are subject to the food, not supplement GMPs, and the DS GMP makes references to a requirement to qualify ingredient suppliers, but offers little in terms of guidance as to how manufacturers should qualify their suppliers. Dr. Frankos not only reiterated what is stated in the regulation (that manufacturers must verify the information on suppliers’ certificate of analysis before relying on the CofA), but he also maintained that manufacturers must determine that the manufacturing process used by ingredient suppliers is adequate and reliable (i.e. is at least meeting food GMP requirements). It is clear that this would require an onsite audit of a supplier’s facility, but Dr. Frankos would not go so far as to state that onsite audits are “required.” He expressed the Agency’s concern about economically motivated adulteration, and indicated that food GMPs were in the process of being revised to better cope with new threats of EMA and food safety issues.

Dr. Frankos expressed that attention to the preamble of the DS GMPs is critical to understanding FDA's expectations with regard to qualifying suppliers and laid out some key points.

- It is the finished product manufacturer's responsibility to establish proper controls to ensure the quality of products and make documentation available for inspection.
- In lieu of testing for every specification, a supplier's CofA can be relied upon only if that supplier is first qualified; however, dietary ingredient identity testing must still be done by the manufacturer.
- The minimum criteria for qualifying a vendor include:
 - Confirmation of the CofA (manufacturer's own testing or independent lab)
 - CofA must include descriptions of test methods used, limits of detections and actual test results for the lot purchased.
 - Documentation of qualifying supplier (or verification of CofA)
 - Periodic re-qualifying of supplier or reconfirmation of CofA
 - QC personnel confirmation that the documentation has been reviewed and approved
 - Records of audits of the supplier's facility
 - If using a 3rd party auditor, the actual report of the audit (not just the opinion letter) needs be available for inspection; the desire of FDA is to know the deficiencies of the facility and how manufacturers and suppliers will deal with them rather than a simple pass or fail.
 - The audit must encompass not only the manufacturing site, but also the manufacturing process of the ingredient or component that is being sourced.
 - Vendor questionnaires are not sufficient to serve as an audit.

FDA understands that each manufacturer cannot audit every supplier for every ingredient and that qualifying foreign suppliers is difficult, but expects industry to come up with innovative solutions to meet requirements of the regulation and ensure quality. Dr. Frankos advised suppliers and manufactures to communicate to each other to identify and deal with gaps in qualifying the global supply chain, e.g., in the case of herbal ingredients, Good Agricultural Practices should be followed by foreign as well as domestic suppliers. In addition, companies should monitor product complaints and communicate information throughout the supply chain i.e., manufactures should inform a supplier if their ingredient appears in the product that is the subject of an adverse event report. If a supplier becomes aware of product complaints associated with its ingredient through one of its customers, that supplier should let other customers know about those complaints. This way, the quality control unit is able to evaluate and determine what changes in the manufacturing or purchasing is necessary to mitigate concerns regarding a product.

During the Q & A session that followed, some issues were raised:

- Economically motivated adulteration is a major concern for FDA. Although the Agency is not changing requirements of the GMPs (in terms of including dietary ingredients), inspectors are sensitive to the issue and will look for such problems during inspections. FDA is now working on a list of “high risk” products subject to potential economic adulteration.
- With the impending food safety legislation, how far along the supply chain must a manufacturer go in terms of qualifying suppliers?
- With regards to audits, there are potential legal concerns involved in sharing information on audit reports that are bound by supplier-manufacturer confidentiality agreements. Moreover, there are concerns that there will be reluctance on the suppliers’ part to share information with their customers if they know that it may be shared with FDA, perhaps compromising the corrective process that will help improve the quality of suppliers. It was suggested to Dr. Frankos that a summary containing the date of audit, number of observations, major and minor deficiencies, and risk rank could be sufficient. Dr. Frankos encouraged industry to identify potential issues and provide suggestions to FDA on how to address them.
- There is some confusion whether DS GMPs or food GMPs applies to the firm that provides a single ingredient that is put into a capsule. FDA maintains that the manner in which the ingredient is used determines which set of GMPs it is subjected to.
- With regard to inspections, FDA is committed to increasing the number of inspections and the training efforts; it has conducted three major training sessions to prepare for the next round of inspections.

Manufacturer and supplier perspectives on supplier qualification

The second session of the day was dedicated to learning about ingredient supplier qualification from the perspective of an established manufacturer (Perrigo’s Mike Bradley), a large ingredient supplier (DSM’s Anthony Palmieri) and a small ingredient supplier (Embria Health Science’s Kevin Boot). Despite different perspectives on what should be required and/or provided for ingredient supplier qualification, all three companies are committed to quality and all three acknowledged that some kind of industry-sponsored guideline or program for supplier qualification could benefit their respective firms. Standardizing how ingredient suppliers are qualified could help reduce costs for both manufacturers and suppliers and could help to differentiate quality-focused suppliers from their less quality conscious competitors.

Mike Bradley presented an overview of a complex supplier quality management model that involves multiple qualification steps from pre-commercial to commercial phases and is based on risk management principles—establishing high/low risk profiles considering quality risk factors associated with the supply chain, raw material, and

facility. He stressed that onsite audit is only one element of qualification and that communication of manufacturer expectations is critical; further, thorough documentation of supply quality management activities is imperative.

In his opinion, there is a need for an industry sponsored qualification program because currently, there is a lack of understanding by members of the industry of FDA expectations; there is a significant diversity in programs used by industry and also a significant number of redundant qualification activities. All of this could be avoided with an industry wide program that is accepted by both regulators and members of the industry. The key elements needed to be considered for such a program include program cost, standardization (facility audit, documentation), periodic requalification, CofA verification and SIDI verification.

Anthony Palmieri, DSM presented the perspective of a large ingredient supplier. He stressed that a supplier qualification program would benefit industry but needs to be international in scope and must be mandatory instead of voluntary to be effective. He added that a shared third party audit program would consolidate audits, dilute costs, and remove barriers for smaller manufacturers who cannot afford to audit every supplier or even one big supplier (DSM's per audit cost = \$20,000).

Kevin Boot, Embria reiterated some of the issues and needs related to supply chain qualification mentioned by others. He presented some observations as a small supplier, one being that small suppliers develop systems to meet large manufacturers' demands; thus large manufacturers' requirements become the "standard" for smaller manufacturers. Currently, some challenges/concerns that small suppliers have to consider include trade secret disclosure, demands for extra items on the CofA, demands for certification by multiple certification programs, and onsite audits. Suppliers benefit from helping to develop a supplier certification program that can be accredited and coordinated with FDA and has international application.

Benefits and drawbacks of an industry-sponsored supplier qualification program

The third and last session of the day provided the trade associations' perspective on why the dietary supplement industry needs to be proactive and develop guidelines and a supplier qualification program. Daniel Fabricant, NPA, explained that historically, a lack of initiative by industries in the past has cost them and that in the face of some ambiguities in the GMP regulation (suppliers not covered by DS GMPs) and strict new soon-to-be imposed requirements for food safety, the DS industry must act now to address these gaps. Daniel stated that the efficacy of self regulatory initiatives depends on the following factors:

- 1) Complete industry-wide participation
- 2) Uniform standards of ethical conduct

- 3) Holding companies accountable for creating a system of ethical conduct
- 4) Ways of relieving market pressures that drive companies to be unethical.

Some questions Dan posed in going forward with self-regulation include: 1) Are the standards relevant in light of current concerns (Part 110 is not enough, what best practices should be incorporated in new standards?) 2) Does it raise the consciousness of firms and result in better behavior/practices? 3) Does it bring about greater consumer protection and reduce the threat of onerous regulation?

Dave Schoneker (Colorcon/IPEC) provided attendees with IPEC's perspective on what components should be considered for an ingredient supplier qualification program. The excipients industry was faced with a similar set of circumstances at the turn of the century – no excipient-specific GMPs, a series of adulteration scandals that resulted in multiple deaths, and no agreed upon standards for excipient supplier qualification. IPEC has developed guidelines (<http://www.ipecamericas.org>) and a comprehensive excipient supplier qualification program to address all of these gaps – all of which has been lauded by FDA (CDER). Dave surmised that the DS industry should think beyond the need for compliance with existing regulations, since there are gaps that don't ensure supply chain integrity and consumer safety. Good Management Practices (i.e. what is the right thing to do, not just what must be done to be in compliance), not GMPs, should be the driving force.

Some needed industry initiatives might include development of guidelines that cover all aspects of ingredient qualification:

- DS ingredient-specific GMPs (food GMPs are not enough)
- DS ingredient GMP audit guideline
- DS ingredient Good Distribution Practices (GDP) and GDP audit guideline
- DS ingredient C of A guideline
- DS Ingredient manufacturing changes guideline

Dave continued with an explanation of the process of ingredient qualification, beginning with the ingredient manufacturer who must investigate all technical, safety and regulatory aspects of an ingredient and ensure that the manufacturing facility has acceptable GMPs to produce the ingredient to a standard of quality. Those users of the ingredient must have selection criteria that can include SIDI (for dietary ingredients)/EIP (for excipients) availability, supplier GMP compliance (based on qualified audit information), supplier quality/performance assessment information, etc.

Finally, Dave asked the attendees, "How can ingredient users perform audits on all suppliers and how can suppliers host audits from all their customers?" The solution must include third party certification. However, before DS ingredient GMP related guidelines are needed before a 3rd party certification program could be developed to adequately meet the needs of industry.

Pharmavite's Paul Bolar provided the last presentation which analyzed for attendees the benefits and drawbacks of a proactive approach by the dietary supplement industry. He listed improved compliance and cost savings as two of the benefits of developing industry-wide supplier qualification guidelines or a program. Drawbacks included the cost to set up such a program, the lack of participation of a large portion of the industry, and the potential inability for third party certifiers to work together on such an initiative. He presented a pyramid scheme representing the progressive steps towards establishing an industry-wide ingredient supplier qualification program:



Discussion followed during which there was consensus among the attendees that the industry must be proactive in this area of ingredient supplier qualification. There was disagreement as to whether a cautious approach should be taken by initiating smaller, shorter-term projects or whether to aim for a comprehensive program immediately. Specific potential projects discussed included:

- Dietary ingredient-specific GMP guideline
- Dietary ingredient certificate of analysis guideline
- Dietary ingredient supplier audit guideline
- Industry-sponsored ingredient supplier qualification program (including shared audit system)

A session has been planned at the upcoming Expo East show in Boston (Sept 24) to broaden the discussion for the rest of the industry. Also, ingredient supplier qualification could be a component of an ODS session on analytical methods at SupplySide West in November. In advance of September, SIDI working group members agreed to convene at least once (via web meeting) to discuss in more detail how to proceed.