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SPECIAL REPORT

Natural Products INSIDER's 100% Ingredient Identification Forum

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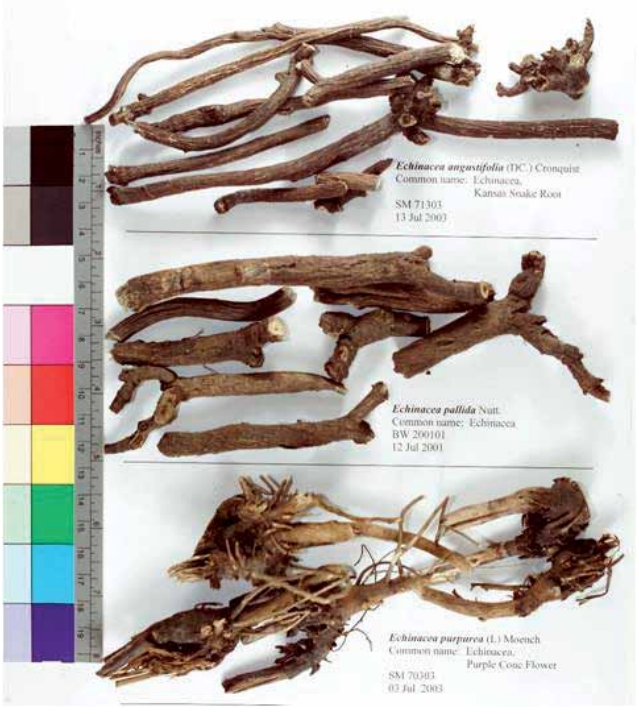
While federal law mandates 100 percent testing to ensure identity of incoming dietary ingredients, a host of challenges can compromise the process. At SupplySide MarketPlace, **Natural Products INSIDER** hosted a forum, sponsored by Grace Davison, that delved into a range of issues related to 100-percent ingredient identification testing. From testing methodologies to case studies, industry experts shared insights to help guide attendees toward full regulatory compliance. Among the key issues addressed in this forum were the acquisition and use of verified botanical references, application of different types of botanical identification tools, and case studies on adulteration.

Trish Flaster, executive director of Botanical Liaisons, kicked things off by discussing how to acquire and use authentic, verified references for botanicals from field to manufacturing to document the identity of ingredients in any test—sensory, macroscopic, FTIR, NIR—and in a court of law. Voucher specimens, she explained, have been verified by a botanical expert and authenticated to ensure they can be used to confirm identity of botanicals.

She walked through the variety of data that should be collected, starting with the botanical name and details about the collector, into the specifics about the plant such as leaves—not only how the leaf looks, but the type of hairs, or the variegates in the leaves. Flaster next offered case studies to demonstrate why authenticated references are critical. She started with Echinacea, noting that the roots of the various species are very different in appearance (shown at right). E. angustifolia and E. pallida root look similar, while E. purpurea is very different; however, there are very different anatomical features in the roots that can help with identification.



Other examples Flaster discussed were arnica and cohosh. But, she added, "Without the first voucher, you don't have anything to refer to and ensure that you have the right botanical."

The next speaker, Clare Dus, vice president, Sensory Spectrum, discussed the use of sensory evaluation methods to help in developing sensory identity qualifications, including outlining the

process for developing accurate lexicons to describe products and establishing rating scales to describe impact. First, she explained the concept of sensory integrity, noting, "It's the order of how things present themselves, added to the idea of harmony and whether attributes are in balance as you experience them."

Next, Dus discussed sensory evaluation, which is a scientific discipline that deals with methods to evoke, measure, analyze and interpret human responses to the properties of foods and other materials as perceived through the five senses. As she explained, the stimulus is detected by one of the senses, which perceives or experiences a sensation, leading to a description formed in the brain for ultimate response. The challenges come from understanding sensory properties are the characteristics perceived through the senses, not the liking or preference. That is then filtered through a screen of expectations to lead to a consumer response, which relates to quality perception, brand identity and more. As she proceeded through her discussion, Dus focused on product understanding, explaining that companies that know sensory attributes can then understand and describe the sensory experience for selected ingredients, optimize the ingredients' sensory experience, track the sensory experience through use, distribution and shelf life, and even track the sensory experience of competitors' ingredients.

One of the key considerations is building a lexicon that allows sensory testers to identify pertinent attributes.

Building the Lexicon

Frame of Reference
Large array of samples by category
Broad representation of modality characteristics
6-12 samples: commercial and prototypes
Term Development
Evaluate
List characteristics
Group according to categories
Use of References
Represent one or more terms from each grouping
Clear demonstration of the term or characteristic
Develop List of Descriptors
Refine list of all terms
Describe all relevant characteristics without being redundant

She then put the lexicon idea into use. For example, looking at the lemon focus in lemonade, the testers could start with a draft lexicon of aromatics, such as cooked lemon, lemon drops or bathroom cleaner. References can then be used to offer examples of flavor, such as lemon rind or lemon pie filling. Then the panelists would move into the next phase to be able to describe the total lemon impression. Dus put this idea into practice by offering attendees comparative tastings of pomegranate arils and of candied ginger. Ultimately, sensory comparisons could impact product development, particularly from a cost perspective, to see whether an ingredient could still meet consumer expectations from a sensory perspective.

Gay Timmons, president, Oh, Oh Organics, was next on the agenda, focusing on "process certification," answering the questions *what does process certification do* and *how does process certification work*? Timmons broke out the issue of what process certification does into five distinct areas. First is supply chain verification, whereby process certification allows a supply chain to be linked from site to site through written plans that verify source inputs, process outcome, a written management plan, the documented implementation of the plan, and an audit trail. "The integrity of the process is going to tell me how valid the label is," she said. "The big benefit of this is in terms of the whole concept of quality assurance and quality control. Having process certification as a codified process in your business and through the supply chain is similar to GMPs [good manufacturing practices] where you have the audit trail."

Next is the ability to verify label claims, as many process certification programs are implemented to verify label claims are truthful, such as the USDA Organic Program, the Sustainable Forestry Initiative or even the Good Housekeeping seal. Connected to that is the issue of consumer assurance, in which the use of seals—like those available from those programs listed previously—is a marketing tool to provide legitimacy. Such a program also has the benefit of saving money, as group participants can share costs and centralize records. Finally, process certification provides transparency, as the third-party verification is a recorded process, and accreditation is often used to vet the certifiers.

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Timmons offered three case studies to illustrate how process certification programs can assist in supply chain support. For example, in the case of organic tulsi, an annual botanical, many hundreds of growers may contribute organic tulsi to a single processor. The assigned person at the processor keeps records including verifying the source of the original seed and the yield of each specific harvest. "The quality can be integrated into

this system," Timmons said. The processor also holds responsibility to record the sub-lots in the master lot, sales to the exporter—who is also certified in the supply chain, and verifying the seed source.

In conclusion, Timmons offered two critical parts to process verification. First is the mass audit, which is similar to forensic accounting, in which all the numbers are reviewed. "Each member of the supply chain must demonstrate the ability to maintain records that can be made available on request to the certifier," she said. Then it is a review of the numbers such as inputs, shrink and loss in filling, which is all incorporated into the management plan. That written plan is the second part, in which companies must write down what they will do, how they will prove it was done, where the plan and records will be maintained, and planning to change the plan when practices change.

Testing methodologies were the focus of the talk by James Neal-Kababick, director, Flora Research Laboratories, specifically discussing the merits of techniques including microscopy, High Performance Thin-Layer Chromatography (HPTLC), FTIR and NIR (two vibrational spectroscopy methods), as well as when and how they can be applied to meet cGMP identity requirements. He kicked things off by noting 100-percent identity testing is not just a good idea, "it's the law. You must establish an identity specification." The identity specifications that can be used include microscopic or macroscopic analysis, or other scientifically valid methods that have been demonstrated to be fit for purpose. Neal-Kababick cited several concerns with identity methods:

- Most identity methods are focused on the identity of the plant or dietary ingredient as itself
- This does not necessarily detect adulteration with non-botanical or dissimilar methods
- Utilization of a suite of identity methods is critical to ensure that dietary ingredients are properly identified
- Complementary techniques provide a greater chance that adulterated materials will be detected before they are incorporated into products

Another major area of concern is ensuring testing is conducted on a representative sample that accurately portrays the material being sampled. "This is the 10-ton elephant in the room," he said. He suggested developing an appropriate sampling plan and working with a reputable lab that can accurately composite the sample you submit, as "everything starts falling apart when it comes to analytical testing if you don't have appropriate samples."

Neal-Kababick then moved into a review of different testing methodologies, noting there are myriad considerations as labs look for easy-to-use methods that have data rich features with a fast run time and offer high throughput. HPTLC, for example, is an excellent fundamental technique to examine botanical materials, which offers multi-dimensional features that allow comparison of test samples

against reference materials. He particularly cited the ability to use scanning densitometry, a quantitative technique that is underutilized in connection with HPTLC testing, calling out the ability to see the UV imaging.

Microscopy, in contrast, allows the lab tech to study very small samples, but that is also its drawback. "You must make multiple mounts," he said, "because you'll likely see foreign organic matter and have a greater opportunity of getting just the good or the bad sample." Another testing method he discussed was vibrational spectroscopy, addressing both FTIR and NIR methods, which have very different applications. FTIR, he said, is fast and easy to run, and is great for singles and several botanicals, but requires appropriate sampling techniques and isn't ideal for detecting adulteration. NIR, in contrast, is "probably the most misunderstood and problematic tool for identity in our industry," Neal-Kababick said. "It is powerful and extremely fast if you know what you're doing, but it is a disaster if you don't know what you're doing." The key is developing a chemometric model for botanical identity, and then finding the "sweet spot" where the differentiation happens among samples.

Next up were two talks about supply chain traceability and adulteration, focusing on pomegranate. First, Dana Krueger, president of Krueger Food Laboratories Inc., and Stefan Wypyszyk, senior business development manager of Stiebs LLC's Nutraceutical Division looked at methodology used on pomegranate juice concentrate and extract as it relates to GMPs, as well as the commercial challenges in the industrial pomegranate extract market. Wypyszyk, started by laying out the challenges of identity, offering questions to ask suppliers (see chart 2).

Challenges of Identity — Questions to Ask Your Supplier

Identity of What?
Methods and results can change depending on the form and process used

- **Plant Part(s)**
  - Whole Fruit
  - Arils (Juice)
  - Peel
  - Leaves
  - Flowers
- **Form of Biomass**
  - Fresh
  - Dried
- **Manufacturing Process**
  - Solvent System
  - Extraction
  - Fractionation/Isolation
- **What's reference standard based on**
- **Traceability**

As more processing is applied to a product GMPs ↑ while Identity ↓

Fresh Whole Pomegranate Fruit

↓

Pomegranate Juice

↓

Pomegranate Fruit Pomace

↓

Pomegranate Extract

↓

Pomegranate Extraction + Isolation/Separation

↓

Blends

He next used pomegranate as an example of how to look at traceability and identity, noting that while the identity of pomegranate juice and fruit is well established, there is no industry standard for identification of an extract. "Marker compounds are often inappropriately used as a standard of identification, while they are often indications of a standardized manufacturing process," Wypyszyk said, turning the presentation over to Kruger.

Kruger first laid out some of the key identity indicators of pomegranate juice, particularly the composition such as anthocyanins, phenolics, isotope ratio and organic acids; however, total phenolics and ellagic acid are not good indicators of pomegranate identity, as the phenolics are not pomegranate specific and ellagic acid is easily obtained from non-pomegranate sources. He suggested better indicators of identity would be a specific pomegranate anthocyanin profile, or the punicalagins that are specific to pomegranate and have a common ratio seen in relation to ellagic acid. Kruger then offered several HPLC analyses showing comparisons based on anthocyanins, phenolics and ellagic acid to illustrate the differences that can be seen.

The second discussion of pomegranate was led by Blake Ebersole, technical director, Verdure Sciences, who focused on various methods and controls that can be used by manufacturers to answer basic quality and method validity questions. He started by harkening back to Flaster's presentation, emphasizing the importance of having valid, authenticated reference materials, and then citing the challenges inherent in many identity tests when used on botanical powders. For example, HPTLC has issues with the natural variation inherent in the source material, while organolepsis may lack the specificity and sensitivity necessary. Ebersole then emphasized the importance of developing an ID program specific to each ingredient, taking into account variables such as the supply chain, varieties/chemotypes, substitutes/adulterants, processing differences, available methodologies and methodology limitations. As an example, he broke down an orthogonal identification of pomegranate extract, running from supply chain documentation into organolepsis, qualitative and quantitative chemical testing, as well as microscopy. When it comes to reference materials, Ebersole added, "We see lots of opportunities particularly for documentation of where the materials come from. For example, the pomegranate fruit has many different parts; the seeds have different properties than the peel and the fruit. ... Harvest protocol is affected by climate conditions and season, and processing is key to impacting the chemical composition of the material."

The final speaker of the forum was Maged H. Sharaf, Ph.D., the principal scientific liaison for dietary supplements at the U.S. Pharmacopeia (USP), who focused on the

USP standard monographs, including the process and application of USP standards to ensure identity of various dietary ingredients. Sharaf again emphasized the regulatory requirement for 100 percent identity testing of dietary ingredients, but acknowledged it is not as easy as it may appear. He noted it often takes more than one valid method/test to unequivocally identify an ingredient; that the process becomes more involved as the complexity of the ingredient increases; and that it goes beyond just selecting the appropriate test but also to understand the characteristics of the article and its relation to related articles that could be present for some reason. Sharaf offered a comparison among identification of alpha-lipoic acid, chondroitin sulfate and omega-3 fatty acids to illustrate the changing complexity of molecules and the various sourcing issues and adulterant concerns that could impact the necessary testing. He noted botanical ingredients are even more complex, using black pepper—a single botanical—to call out concerns related to testing methods and identifying appropriate source.

Flaster closed out the forum by encouraging industry members to get more involved in the conversation. "FDA is really saying it's up to us," she said, noting industry is looking at a grey area but not getting direct oversight. "By creating forums to discuss these issues and technologies, hopefully we could develop guidelines for use by industry that could be adopted by FDA rather than the agency putting something singular in place that would be economically burdensome." ❑