

Development of SRMs for Botanical Dietary Supplements

As part of a multi-year interagency agreement among the National Institute of Standards and Technology (NIST), the National Institutes of Health's Office of Dietary Supplements (NIH/ODS), and the Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition (CFSAN) and the FDA Center for Drug Evaluation and Research (CDER), NIST is developing Standard Reference Materials (SRMs) for botanical dietary supplements. Taxonomically authentic botanical reference materials with assigned values for concentrations of active and/or marker compounds, pesticides, mycotoxins, and heavy metals are being produced to assist in the verification of manufacturers' label claims and for use in quality control during the manufacturing process.

L.C. Sander, K.E. Sharpless, S.A. Wise (Div. 839)

Dietary supplements are products containing vitamins, minerals, herbs or other botanicals, amino acids, etc. that are consumed to increase total daily intake and/or for perceived health benefits. Many people believe that botanical supplements will improve their health and that these "natural" remedies are both effective and free from the side effects that may occur with other medications. There are occasional reports of inaccurate labeling, adulteration, contamination (with pesticides, heavy metals, or toxic botanicals), and drug interactions.

Congress recognized the lack of publicly available, validated analytical methods for dietary supplements – and a lack of reference materials for validation of analytical methods – in 1994 when the Dietary Supplement Health and Education Act (DSHEA) was enacted. As part of DSHEA, NIH/ODS was directed to fund development of analytical methods and reference materials for dietary supplements.

Despite questions about the quality and safety of dietary supplements (including vitamins), about 75% of the US population continues to them. The US consumer spends more than \$20 B on these supplements per year, with expected spending growth of 3% to 5% each year.

A suite of five ephedra SRMs has been developed with assigned values for ephedrine alkaloids and toxic elements (arsenic, cadmium, lead, and mercury): SRM 3240 *Ephedra sinica* Stapf, SRM 3241 *Ephedra sinica* Stapf Native Extract, SRM 3242 *Ephedra sinica* Stapf Commercial Extract, SRM 3243 Ephedra-Containing Solid Oral Dosage Form, and SRM 3244 Ephedra-Containing Protein Powder. SRM 3243 has assigned values for caffeine and synephrine, as well. SRM 3244 has assigned values for

caffeine and for analytes of nutritional interest (fat, protein, vitamins, etc.) Three ginkgo-containing SRMs have been developed with certified values for ginkgolides, bilobalide, flavonoid aglycones, and selected toxic trace elements. The materials in these two suites represent a variety of natural, extracted, and processed sample matrices that provide different analytical challenges; this same model will be used for suites of other botanical materials.

The constituents have been determined by multiple independent methods with measurements performed by NIST and collaborating laboratories. The methods utilized different sample extraction and cleanup steps in addition to different instrumental analytical techniques and approaches to quantification.



The ephedra- and ginkgo-containing suites of SRMs are the first dietary supplement materials offered by NIST with certified values for organic constituents and selected trace elements.

These materials are provided primarily for use in method development and as control materials to support the measurement of these constituents in other similar products. These materials will help manufacturers of dietary supplement products to characterize raw materials to prevent the use of materials that are contaminated or adulterated. In addition, the SRMs will assist self-assessment of consistency and quality in finished products, and to provide a foundation to which label information can be linked. The goal of this ongoing effort is to provide the dietary supplement industry and measurement communities with tools that will lead to improved quality of dietary supplements, and ultimately reduce public health risks that could potentially be associated with these products.

Future Plans: The development of botanical dietary supplement SRMs is an ongoing effort. Materials based on saw palmetto, bitter orange, green tea, St. John's wort, black cohosh, and berries of the genus *Vaccinium* are in progress. Oils extracted from a number of plants (perilla, flaxseed, evening primrose, borage), an extract of carrots, and a mixture of tocopherols are also being prepared as SRMs.