Tab 2

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Dietary Supplements Standards Update

Sarah Kozanecki, NSF International
May 20, 2008

NSF/ANSI 173-2008

- Included:
  - Issue 14
  - Issue 22
  - Issue 27 (superceded other two issues)
- Removed Annex D (informational)
- Published April 2008

173i27 – GMP

- Replaces Section 8 with 21 CFR § 111.
- Additional requirements, including Recall procedures, compliance with the 2002 Bioterrorism Act, and AER reporting system, which are not covered in 21 CFR § 111, remain.
- Passed in March 2008.
- Incorporated into 173-2008.

173i22 – AER requirements

- Requirement that manufacturers comply with new federal legislation on the reporting of adverse events from dietary supplements to the US FDA.
- Passed in October 2007.
- Superceded by Issue 27.

173i14 –

- Revised Section 8 (8.6.3) to require both identity testing and other testing of raw materials, including purity, quality, strength, and composition as applicable.
- Passed in August 2007.
- Superceded by Issue 27.

Unresolved Issues

173i18 – Allergen and “free” claims

- Establish testing requirements for allergen-free claims and state typical methods and detection limits in terms of ppm.
- Discussed at November 2007 JC meeting
- Revision 2: Balloted to JC/TC in April 2008
- Two negatives to resolve:
  - request for reduced testing and alternative methods of compliance.

173i20 – Fish Oil Contamination

- Incorporates testing requirements for potential contaminants in fish oil
- Negatives received at JC were considered and incorporated into second revision
- Balloted to JC/TC in 2007
- One negative on non-germane issue.
- Ballot will proceed to CPHC.

173i24 – Tables 5 and 6A and B

- Include revised definition of “botanical ingredient” and add definition of “botanical ingredient extract” and “botanical ingredient non-extract.”
- Included language for footnotes in Tables 5 and 6 A and B related to microbial limits.
- Balloted in October 2007: negative received at TC
- Revision has been made, for JC approval.

173i26 – Regulated Metals

- Proposal to update regulated metal allowable levels in accordance with North American standards.
- First revision balloted 7/2007
- Discussed at November 2007 JC meeting

  LEAD:
  - Decision made to ballot all metals except lead
  - Lead would be addressed in separate ballot
  - Further data review on lead levels warranted

  MERCURY:
  - JC moved to set criteria for total mercury and inorganic mercury levels separately
- Clif McLellan will discuss in further detail.

173i28 – Tables 3 and 4 Test Methods

- Test methods had not been reviewed since 2001
- Discussed at 2007 JC meeting
- Agreed to review – revisions made are up for JC approval for 2nd revision.
- Kerri LeVanseler will lead discussion of new proposed language.

173i29 – QC

- Revisions proposed to 6.2.5, Quality Assurance for quantitative test methods
- Many negatives received, some of which went beyond the scope of the ballot.
- Further discussion will be led by Kerri LeVanseler.

Issue Papers

- Changes or additions
- Forms obtained by request
- Tracking number
    - Ex. DWA-2006-3
- JC Chair:
    - Open forum
    - Balloted
- JC Meeting Agenda

Information Papers

- Updates
- Obtained by request
- Tracking number
    - Ex. DWA-2006-3
- Usually discussed at Joint Committee meetings
- JC Meeting Agenda

Thank you!

Questions/Comments?

Sarah Kozanecki
kozanecki@nsf.org

MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE: April 2, 2008

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i18r2)

Enclosed is the ballot for Draft 2of NSF/ANSI 173 issue 18. Please review the proposal and return your ballot **by the ballot due date of April 23, 2008.**

Purpose

To incorporate language for assessment of allergen-free claims and describe methods to be employed and detection limits in terms of ppm present in the product.

Background

This issue was brought forward because label verification is an integral feature of Standard 173. Multiple products possess claims relating to the absence of certain analytes, such as allergens. Currently, in respect to dietary supplement products, there is no defined concentration threshold as to what constitutes "free" in terms of allergens. For gluten, the FDA has established a limit in foods that claim to be gluten free. However, for other major food allergens, such as dairy, egg, soy, nuts and corn, there is no definition in terms of the parameter which should be monitored nor the acceptance level which would be appropriate to verify "free" and "non" claims.

This was balloted to the Joint Committee in February 2006 and to the Council of Public Health Consultants (CPHC) in June 2006. A negative was received at the CPHC that expressed concern that there was a lack of health based pass/fail criteria, lack of valid test methods, and lack of clarity as to what "allergic responses" are covered. After several additional opportunities to comment on inclusion of language for label verification for allergens, including discussion at the March and November 2007 JC meetings and a straw ballot sent to all JC members. It was agreed that although the statements made during the CPHC balloting had merit, allergens *should* be addressed in NSF/ANSI 173 and the Standard should be revised to reference the FDA rule for gluten-free claims. For other claims, it was agreed that the Standard should reference the current best practice. The Joint Committee motioned this language to ballot at the November 2007 JC meeting.

Public Health Impact

The proposed revision ties into the general concept of verifying label claims.

If you have any questions about the technical content of the ballot, you may contact me in care of:

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E-mail: kozanecki@nsf.org

NSF International Standard for Dietary Supplements — Dietary supplements

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5.3.4 Natural toxins

Botanicals listed in annex A shall not contain aristolochic acid (limit of detection = 0.5 μg/gm).

5.3.5 Known adulterants

Products shall be evaluated to ensure they do not contain known adulterants including, but not limited to, the following:

- *Eleutherococcus senticosus* shall not contain *Periploca sepium* root.
- *Plantago lanceolata* shall not contain *Digitalis lanata* leaf.
- *Scutellaria lateriflora* shall not contain *Teucrium chamaedrys*.
- Stephania tetranda shall not contain Aristolochia fangchi.

5.3.6. Food Allergen Claims

Raw materials and finished products which claim the absence of specific allergens shall be evaluated in accordance with 7.5 and/or 8. Raw materials and finished products shall not contain specific proteins or other analyte(s) associated with the allergen at levels above the method detection limits.

5.3.7 Genetically Modified Organism (non-GMO) Claims

Claims that the product contains no genetically modified organisms (no GMO) shall be verified in accordance with 7.5 and/or 8.

5.3.~~6~~8 Other product claims

Claims that the product is free of a particular contaminant or substance shall be verified in accordance with 7.4 and/or 8.

5.4 Disintegration

Supplements shall be verified as meeting the requirements for disintegration when tested using the methods described in USP 25-NF 20. The minimum exposure time to immersion fluids shall not be less than 60 min. Chewables and liquid extracts are exempt from disintegration testing requirements.

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7.4 Test methods for chemical contaminants

Testing shall be performed based on USFDA's Method for Determination of Aristolochic Acid in Traditional Chinese Medicines and Dietary Supplements.

The most appropriate method shall be used to confirm claims for the product under evaluation. The source of these methods may include AOAC International, USP, EPA, FDA, AHP, European, German, Japanese monographs, INA, industry standards, etc. The use of any new method shall require that a validation be performed which includes an evaluation of specificity, linearity, reproducibility, spike recovery and method detection limit. More rigorous validation could follow according to the guidelines of ICH, FDA, CEN, GLP, AOAC, as appropriate.

Unless manufacturers have controls in place to assess the rancidity of oil ingredients, the following testing shall be performed. The Peroxide Value of the oil shall be tested according to AOAC Method 965.33 (which is equivalent to AOCS

8-53). The p-Anisidine Value of the oil shall be tested by AOCS Cd 18-90.[7] The Totox Number will be calculated as the sum of the p-Anisidine Value and two times the Peroxide Value.

7.5 Test methods for food allergens

7.5.1 Gluten

Testing shall be performed based on the RIDASCREEN Gliadin Enzyme Immunoassay for the quantitative analysis of gliadins and corresponding prolamines (Manufactured by r-Biopharm). The typical detection level for the testing of raw ingredients and finished products is 20 ppm or less.

7.5.2 Soy

Testing shall be performed based on the End-Point Polymerase Chain Reaction (PCR) method (licensed technology by Genetic ID) or equivalent. The typical detection level for testing, using this semi-quantitative method for raw ingredients and finished products, is 1.5 ng/g of DNA.

7.5.3 Milk

Testing shall be performed based on the Veratox Total Milk Allergen Immunoassay for the quantitative analysis of milk proteins (Manufactured by Neogen). The typical detection level for the testing of raw ingredients and finished products is 2.5 ppm.

7.5.4 Other food allergens

The most appropriate method shall be used to confirm claims for the product under evaluation. The source of these methods may include AOAC International, USP, EPA, FDA, AHP, European, German, Japanese pharmacopoeial monographs, INA, industry standards, etc. The use of any new method shall require that a validation be performed which includes an evaluation of specificity, linearity, reproducibility, spike recovery and method detection limit. More rigorous validation could follow according to the guidelines of ICH, FDA, CEN, GLP, AOAC, as appropriate.

7.6 Test method for genetically modified organisms

Testing shall be performed based on the End-Point Polymerase Chain Reaction (PCR) method (licensed technology by Genetic ID) or equivalent. The typical detection level for testing, using this semi-quantitative method for raw ingredients and finished products, is 0.01% GMO DNA.

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Voting Details – 173i18r2

Voter Name	Company	Category	Vote
Arnold, Heather	Access Business Group LLC	Industry	--
Bradley, Michael	Perrigo of South Carolina	Industry	Negative w/Comment
Brown, Paula	British Columbia Institute of Technology	Public Health / Regulatory	--
Clemens, Roger	University of Southern Calif.-School of Ph...	Public Health / Regulatory	--
Eisner, Staci	BBS/Pluspharma	Industry	--
Fitzloff, John	University of Illinois at Chicago	Public Health / Regulatory	--
Hussien, Helmi	Health Canada	Public Health / Regulatory	--
Jaksch, Frank	Chromadex	User	Affirmative
LeVanseler, Kerri	NSF International	User	Affirmative
Lilly, Jason	Neogen	User	Affirmative
McGuffin, Michael	American Herbal Products Assoc.	Industry	--
Mishra, Anita	AOAC INTERNATIONAL	User	--
Peterson, Jo Ann	National Enzyme Company	Industry	--
Rocco, Vincent	Schiff Nutrition International	Industry	--
Shao, Andrew	Council for Responsible Nutrition	User	Affirmative
Sharpless, Katherine	NIST	Public Health / Regulatory	--
Sudberg, Sidney	Alkemists Pharmaceuticals Inc.	User	--
Sullivan, Darryl	Covance Inc.	Industry	Affirmative
Upton, Roy	American Herbal Pharmacopoeia	User	--
Varaiya, Chirag	Jarrow Industries	Industry	--
Whitsitt, Victoria	Natural Products Association	Industry	--
Windust, Anthony	National Research Council Canada	Public Health / Regulatory	--

Michael Bradley Comment

We believe that the section as rewritten is strong, but should have provisions to allow for reduced testing after a history of compliance and through verification of the formula by the NSF review process. For example, if a product makes a "Gluten Free" claim, the product should be tested to verify that it does not contain any Gluten; however, once a testing history has been established and the formula clearly does not contain any raw materials that would likely be known sources of Wheat, Rye, Barley, etc., then reduced testing is a practical solution.

Section 7.5.4 Other Food Allergens: If a Food Allergen claim is made and there is no test method known, is it possible to substantiate a claim based on a formula review and a process inspection? The formula review could confirm the absence of the ingredient or by-products of the ingredient that is the subject of the claim and the process inspection can confirm that there is no potential for cross-contamination such as would be the case if the ingredient that is the subject of the allergen claim were not used in the facility.

Michael Bradley Proposed Solution

Modify the wording to allow NSF to apply reduced testing principles and also to allow for alternative means of compliance where no method exists.

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MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE: March 26, 2008

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i20r2)

Enclosed is the ballot for Draft 2 of NSF/ANSI 173 issue 20. Please review the proposal and return your ballot **by the ballot due date of April 16, 2008** via the e-balloting system.

Purpose

To incorporate testing requirements for potential contaminants in fish oil.

Background

Special concerns exist for contaminants in fish oil. In the fish oil industry, there are recommended quality criteria published for maximum levels of PCBs (within the Council for Responsible Nutrition Voluntary monograph on Omega 3 products), and dioxin and furan (by WHO). Since Standard 173 does not discuss these contaminants, a policy regarding these contaminants needs to be defined and incorporated into the standard.

This issue was brought to the attention of the Dietary Supplement Joint Committee during their meeting in March 2007 where it was motioned to ballot. A negative was received, indicating a need for further clarification in the draft language. These comments were incorporated where appropriate and are reflected in this version of the language for your review.

Public Health Impact

Fish oil contaminants may contribute to harmful levels of PCBs and/or dioxins and furans. The proposed revision provides minimum testing requirements to identify the presence of these contaminants.

If you have any questions about the technical content of the ballot, you may contact me in care of:

Sarah Kozanecki, Joint Committee Secretariat
Standards Specialist, Standards
NSF International
Tel: (734) 827-6867
Fax: (734) 827-3886
E-mail: kozanecki@nsf.org

NSF International Standard for Dietary Supplements — Dietary supplements

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5.3 Contaminants

5.3.1 Metals

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5.3.3 Microbiological contaminants

Raw materials shall not contain aflatoxins at levels greater than 20 ppb and shall not contain microorganisms in quantities greater than permitted in tables 5A and 5B.

Finished products shall not contain aflatoxins at levels greater than 20 ppb and shall not contain microorganisms in quantities greater than permitted in tables 6A and 6B.

Finished products in a liquid form with an alcohol content less than or equal to 50% shall not contain *Pseudomonas aeruginosa*.

Finished products with an alcohol content greater than or equal to 50% are exempt from microbial testing.

5.3.4 Natural toxins

Botanicals listed in annex A shall not contain aristolochic acid (limit of detection is 0.5 μg/gm).

5.3.5 Known adulterants

Products shall be evaluated to ensure that they do not contain known adulterants including, but not limited to, the following:

- *Eleutherococcus senticosus* shall not contain *Periploca sepium* root.
- *Plantago lanceolata* shall not contain *Digitalis lanata* leaf.
- *Scutellaria lateriflora* shall not contain *Teucrium chamaedrys*.
- *Stephania tetranda* shall not contain *Aristolochia fangchi*.

5.3.6 Industrial Contaminants

For ingredients and products containing natural fish oil, manufacturers shall have controls in place to screen for polychlorinated biphenyls (PCBs), polychlorinated dibenzo-para-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like PCBs in the oil ingredient.

The content of dioxins and furans expressed as the sum of PCDDs and PCDFs shall not exceed 2 pg WHO-TEQ per gram of oil, dioxin-like PCBs shall not exceed 3 pg WHO-TEQ per gram of oil, and total PCBs shall not exceed 0.09 mg/kg of oil (w/w).[1] Total PCBs shall, at a minimum, include IUPAC congeners 28, 52, 101, 118, 138, 153, and 180.

[1] Council for Responsible Nutrition, Omega 3 Fatty Acids Voluntary Monograph, March 2006. Dioxin limits include the sum of polychlorinated dibenzo-*para*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) and are expressed in World Health Organization (WHO) toxic equivalents using WHO-toxic equivalent factors (TEFs). This means that analytical results relating to 17 individual dioxin congeners of toxicological concern are expressed in a single quantifiable unit: TCDD toxic equivalent concentration or TEQ.

5.3.~~6~~7 Other product claims

Claims that a product is free of a particular contaminant or substance shall be verified in accordance with 7.4 and/or 8.

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7.4 Test methods for chemical contaminants

Testing shall be performed based on USFDA's Method for Determination of Aristolochic Acid in Traditional Chinese Medicines and Dietary Supplements.

The most appropriate method shall be used to confirm claims for the product under evaluation. The source of these methods may include AOAC International, USP, EPA, FDA, AHP, European, German, Japanese monographs, INA, industry standards, etc. The use of any new method shall require that a validation be performed which includes an evaluation of specificity, linearity, reproducibility, spike recovery, and method detection limit. More rigorous validation could follow according to the guidelines of ICH, FDA, CEN, GLP, and/or AOAC, as appropriate.

Unless a manufacturer has controls in place to assess the rancidity of oil ingredients, the following testing shall be performed. The Peroxide Value of the oil shall be tested according to AOAC Method 965.33 (which is equivalent to AOCS 8-53). The p-Anisidine Value of the oil shall be tested by AOCS Cd 18-90.[7] The Totox Number shall be calculated as the sum of the p-Anisidine Value and two times the Peroxide Value.

7.5 Test methods for industrial contaminants

Testing of fish oil samples for PCBs and dioxin-like PCBs shall be performed utilizing a high resolution gas chromatography-high resolution mass spectrometry (HRGC-HRMS) method, EPA Method 1668, Revision A: Chlorinated Biphenyl Congeners in Water, Soil Sediment and Tissue by HRGC-HRMS. Testing of fish oil samples for dioxins and furans shall be performed utilizing a high resolution gas chromatography-high resolution mass spectrometry (HRGC-HRMS) method, EPA Method 1613, Revision B: Tetra- through Octa-Chlorinated Dioxins and Furans by Isotope Dilution HRGC-HRMS. The preparation steps for these methods are applicable to water, soil, fish tissue and other environmental samples. For the analysis of fish oil, for both methods, the preparation of the sample involves dissolution in hexane followed by column based sample clean-up steps prior to the described instrumental analysis.

Manufacturers shall meet this testing requirement by one of the following routes;

- through the use of compliant ingredients as demonstrated by third party testing; or
- performing testing utilizing a laboratory accredited for PCBs, Dioxin and Furans under ISO 17025 and providing the sample results, data, and quality control results, for review to support compliance

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May 8, 2008

Darryl Sullivan
Senior Manager
Covance Inc.
3301 Kinsman Blvd.
Madison, WI 53704

Dear Mr. Sullivan:

Thank you for your comments on the Joint Committee ballot of Standard 173 (173i20r2) regarding the assessment of Fish oil contaminant testing. Attached are your comments on this issue and the response of the issue proponent, Kerri LeVanseler of NSF International.

Name: Darryl Sullivan **Vote:** No

Comment: This section recommends testing for Aristolochic Acid using the US FDA Method. This method was modified, optimized and fully validated. This is now an AOAC Official Method; method 2007.05.

I recommend that this method be referenced.

Kerri LeVanseler's response follows:

> Thank you for your comment; however, the language pertaining to the aristolochic acid test method is not up for ballot at this time. Therefore, your comment has been determined to be non-germane to the fish oil issue. We do appreciate your input, and based on your recommendation of this change, I will prepare a new issue paper related to updating the reference for the Aristolochic Acid method.

I hope the above addresses your concerns. If you would like to change your vote in light of these comments, please contact Sarah Kozanecki at kozanecki@nsf.org to do so. If you have additional comments, or wish to discuss these points further, please contact me directly.

Thank you again for your thorough review.

Mary Hardy
Chair, Joint Committee for Dietary Supplements
c/o Joint Committee Secretariat, Sarah Kozanecki
Standards Specialist, Standards
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MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE: October 31, 2007

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i24r1)

Enclosed is the ballot for Draft 1 of NSF/ANSI 173 issue 24. Please review the proposal and return your ballot **by the ballot due date of November 21, 2007** via the e-balloting system or by e-mail to Ms. Pippa Durbin at durbin@nsf.org.

Purpose

Add modifications to the standard language to define the types of ingredients that are associated with the acceptable limits categories in tables 6A and 6B.

Background

Tables 6A and 6B establish acceptable limits for microbiological contaminants in dietary supplement finished products. They currently do not specify whether the product categories are based on dietary ingredients listed in the supplemental facts panel or ingredients listed elsewhere on the label. The proposed practice would be to base the category on the ingredients as provided in the full product formulation.

The proposed change to the definition of 3.4 “botanical ingredient” is from “an ingredient of plant species or form” to a more industry recognized definition of “botanical ingredient” (NHI-ODS). In addition, definitions for “botanical ingredient – extract” (NHI-ODS) and “botanical ingredient - non-extract” (ABC) are proposed. The addition of these definitions will help clarify language in tables 6A and 6B.

Public Health Impact

Changing the definition of “botanical ingredient” and adding the definitions of “botanical ingredient – extract” and “botanical ingredient - non-extract” will help clarify the categories of dietary supplement products outlined in tables 6A and 6B. The proposed revision will only have positive public health impacts.

If you have any questions about the technical content of the ballot, you may contact me in care of:

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NSF International Standard for Dietary Supplements — Dietary supplements

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3 Definitions

Terms used in this Standard that have special technical meaning are defined here.

3.1 active ingredient: The principal ingredient identified in a product's name or on its principal display panel.

3.2 adulteration: As defined by the Federal Food and Cosmetic Act, §402, adulterated food is defined in Title 21, USC §342.

3.3 batch or lot: A specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and/or is produced according to a single manufacturing order during the same cycle of manufacture.

3.4 botanical ingredient (botanical): ~~An ingredient of plant species or form.~~ An ingredient consisting of, or derived from a plant or microorganism (i.e. fungi or cyanobacteria).

3.4.1 botanical ingredient - extract: The complex, multicomponent mixture obtained after using a solvent to dissolve components of the biomass. Extracts may be in dry, liquid, or semi-solid form. Excipients may be added to extracts to adjust the concentration, enhance stability, limit microbial growth, and to improve drying, flow, or other manufacturing characteristics. Extracts are not the same as expressed juices, pure chemicals isolated from an herb, or synthetically modified plant constituents.

3.4.2 botanical ingredient - non-extract: Crude botanical material (whole, cut or powdered herb)

3.5 chewable: Intended to be reduced through mastication.

3.~~8~~6 dietary ingredient: An ingredient intended for use or used in a dietary supplement that is a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, or extract.

3.6.1 Class I (dietary ingredient): An added nutrient.

3.6.2 Class II (dietary ingredient): A naturally occurring (indigenous) nutrient.

3.~~9~~7 dietary supplement: A product (other than tobacco) that:

– is intended to supplement the diet and bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients;

– is intended for ingestion in pill, capsule, tablet, powder, or liquid form;

– is not represented for use as a conventional food or as the sole item of a meal or diet;

– is labeled as a "dietary supplement" or has the word "dietary" deleted and replaced by the name of the dietary ingredient/s in the product (e. g.; calcium supplement) or an appropriately descriptive term indicating the type of dietary ingredients that are in the product (e. g., herbal supplement with vitamins); and

– includes an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351, of the Public Health Service Act (42 U. S. C. 262), and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary [(U. S. Department of Health and Human Services, USFDAP)] has issued a regulation, after notice, and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 402(f), and does not include an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351 of the Public Health Service Act (42 U. S. C. 262) or an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful.

3.~~10~~8 finished product: A product requiring no further processing prior to sale to the consumer.

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Table 5A – Acceptable limits for microbiological contaminants in raw materials

Ingredient	Aerobic	Yeast/Mold	Enterobacteriaceae
Vitamin and/or mineral ingredient	1×10^3 CFU/g	1×10^2 CFU/g	1×10^2 CFU/g
Botanical ingredient – non-extract	1×10^7 CFU/g	1×10^5 CFU/g	1×10^4 CFU/g
Botanical ingredient – extract / Other dietary supplement ingredient	1×10^4 CFU/g	1×10^3 CFU/g	1×10^2 CFU/g

Table 5B – Acceptable limits for pathogenic microbiological contaminants in raw materials

Ingredient	Salmonella sp.	Escherichia coli[1]	Staphylococcus aureus
Vitamin and/or mineral ingredient	ND[2]	ND[2]	ND[2]
Botanical ingredient – non-extract[1]	ND[2]	1×10^2 CFU/g	ND[2]
Botanical ingredient – extract / Other dietary supplement ingredient	ND[2]	ND[2]	ND[2]

[1] Upon the presence of *Escherichia coli*, 7.3.6.2 is to be followed to determine whether the colonies are enterovirulent. There is a zero tolerance for the presence of enterovirulent *Escherichia coli.*

[2] ND = Not Detected. Not Detected requires that no colonies shall be present in 10 g of sample when tested under the conditions of the USP method cited in 7.3. The detection level for this testing is 10 CFU/g for the period of time tested.

Table 6A – Acceptable limits for microbiological contaminants in finished products[1]

Finished Products		Aerobic	Yeast/Mold	Enterobacteriaceae
Category 1	Finished products containing only vitamin and minerals	1×10^3 CFU/g	1×10^2 CFU/g	1×10^2 CFU/g
Category 2	Finished products containing botanical ingredients – non-extract	1×10^7 CFU/g	1×10^5 CFU/g	1×10^4 CFU/g
Category 3	Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient	1×10^4 CFU/g	1×10^3 CFU/g	1×10^2 CFU/g

[1] The category designation shall be based on the ingredients as provided in the full product formulation. For a product containing ingredients from more than one category, the category with the least restrictive pass/fail levels shall be used.

Table 6B – Acceptable limits for pathogenic microbiological contaminants in finished products[1]

Finished Products		Salmonella sp.	Escherichia Coli[~~1~~2]	Staphylococcus aureus
Category 1	Finished products containing only vitamin and minerals	ND[~~2~~3]	ND[~~2~~3]	ND[~~2~~3]
Category 2	Finished products containing botanical ingredients – non-extract	ND[~~2~~3]	1×10^2 CFU/g	ND[~~2~~3]
Category 3	Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient	ND[~~2~~3]	ND[~~2~~3]	ND[~~2~~3]

[1] The category designation shall be based on the ingredients as provided in the full product formulation. For a product containing ingredients from more than one category, the category with the least restrictive pass/fail levels shall be used.

Examples:

a) A product containing only Vitamin C and Zinc shall be in category 1.
b) A product containing Vitamin C, Zinc and Echinacea shall be in category 2.
c) A product containing Vitamin C, Zinc, and Green Tea Extract shall be in category 3.

[~~1~~2] Upon the presence of *Escherichia coli*, 7.3.6.2 is to be followed to determine whether the colonies are enterovirulent. There is a zero tolerance for the presence of enterovirulent *Escherichia coli.*

[~~2~~3] ND = Not detected. Not Detected requires that no colonies shall be present in 10 g of sample when tested under the conditions of the USP method cited in 7.3. The detection level for this testing is 10 CFU/g for the period of time tested.

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Technical Committee Comments Summary for Standard 173 i24 r1

Date of Vote: 10/31/2007 - 12/21/2007

Name: Ernest Julian **Vote:** No

Comments: I am concerned about the least restrictive pass/fail level being used in Tables 6A and 6B. If a product had high aerobic, yeast/mold, enterobacter, or E. coli and it was a Category 1 or 3 product, the company could resubmit and add a trace amount of botanical ingredients to get the product approved with a lower standard even though there were poor processing practices at the facility.

Name: Joseph Smucker **Vote:** Yes

Comments: Added vote per phone call. JP/pd

NSF International Standard for Dietary Supplements — Dietary supplements

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3 Definitions

Terms used in this Standard that have special technical meaning are defined here.

3.1 active ingredient: The principal ingredient identified in a product's name or on its principal display panel.

3.2 adulteration: As defined by the Federal Food and Cosmetic Act, §402, adulterated food is defined in Title 21, USC §342.

3.3 batch or lot: A specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and/or is produced according to a single manufacturing order during the same cycle of manufacture.

3.4 botanical ingredient (botanical): ~~An ingredient of plant species or form.~~ An ingredient consisting of, or derived from a plant or microorganism (i.e. fungi or cyanobacteria).

3.4.1 botanical ingredient - extract: The complex, multicomponent mixture obtained after using a solvent to dissolve components of the biomass. Extracts may be in dry, liquid, or semi-solid form. Excipients may be added to extracts to adjust the concentration, enhance stability, limit microbial growth, and to improve drying, flow, or other manufacturing characteristics. Extracts are not the same as expressed juices, pure chemicals isolated from an herb, or synthetically modified plant constituents.

3.4.2 botanical ingredient - non-extract: Crude botanical material (whole, cut or powdered herb)

3.5 chewable: Intended to be reduced through mastication.

3.~~8~~6 dietary ingredient: An ingredient intended for use or used in a dietary supplement that is a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, or extract.

3.6.1 Class I (dietary ingredient): An added nutrient.

3.6.2 Class II (dietary ingredient): A naturally occurring (indigenous) nutrient.

3.~~9~~7 dietary supplement: A product (other than tobacco) that:

– is intended to supplement the diet and bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients;

– is intended for ingestion in pill, capsule, tablet, powder, or liquid form;

– is not represented for use as a conventional food or as the sole item of a meal or diet;

– is labeled as a "dietary supplement" or has the word "dietary" deleted and replaced by the name of the dietary ingredient/s in the product (e. g.; calcium supplement) or an appropriately descriptive term indicating the type of dietary ingredients that are in the product (e. g., herbal supplement with vitamins); and

– includes an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351, of the Public Health Service Act (42 U. S. C. 262), and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary [(U. S. Department of Health and Human Services, USFDAP)] has issued a regulation, after notice, and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 402(f), and does not include an article that is approved as a new drug under section 505, certified as an antibiotic under section 507, or licensed as a biologic under section 351 of the Public Health Service Act (42 U. S. C. 262) or an article authorized for investigation as a new drug, antibiotic, or biological for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, which was not before such approval, certification, licensing, or authorization marketed as a dietary supplement or as a food unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, finding that the article would be lawful.

3.~~10~~8 finished product: A product requiring no further processing prior to sale to the consumer.

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Table 5A – Acceptable limits for microbiological contaminants in raw materials

Ingredient	Aerobic	Yeast/Mold	Enterobacteriaceae
Vitamin and/or mineral ingredient	1×10^3 CFU/g	1×10^2 CFU/g	1×10^2 CFU/g
Botanical ingredient – non-extract	1×10^7 CFU/g	1×10^5 CFU/g	1×10^4 CFU/g
Botanical ingredient – extract / Other dietary supplement ingredient	1×10^4 CFU/g	1×10^3 CFU/g	1×10^2 CFU/g

Table 5B – Acceptable limits for pathogenic microbiological contaminants in raw materials

Ingredient	Salmonella sp.	Escherichia coli[1]	Staphylococcus aureus
Vitamin and/or mineral ingredient	ND(2)	ND(2)	ND(2)
Botanical ingredient – non-extract(1)	ND(2)	1×10^2 CFU/g	ND(2)
Botanical ingredient – extract / Other dietary supplement ingredient	ND(2)	ND(2)	ND(2)

(1) Upon the presence of *Escherichia coli*, 7.3.6.2 is to be followed to determine whether the colonies are enterovirulent. There is a zero tolerance for the presence of enterovirulent *Escherichia coli.*

(2) ND = Not Detected. Not Detected requires that no colonies shall be present in 10 g of sample when tested under the conditions of the USP method cited in 7.3. The detection level for this testing is 10 CFU/g for the period of time tested.

Table 6A – Acceptable limits for microbiological contaminants in finished products(1)

Finished Products		Aerobic	Yeast/Mold	Enterobacteriaceae
Category 1	Finished products containing only vitamin and minerals	1 x 10^3 CFU/g	1 x 10^2 CFU/g	1 x 10^2 CFU/g
Category 2	~~Finished products containing botanical ingredients – non-extract~~ Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient	1 x ~~10^7~~ 10^4 CFU/g	1 x ~~10^5~~ 10^3 CFU/g	1 x ~~10^4~~ 10^2 CFU/g
Category 3	~~Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient~~Finished products containing botanical ingredients – non-extract	1 x ~~10^4~~ 10^7 CFU/g	1 x ~~10^3~~ 10^5 CFU/g	1 x ~~10^2~~ 10^4 CFU/g

(1) The category designation shall be based on ~~the~~ ingredients present at 1% or more by weight in the formula as provided in the full product formulation. For a product containing ingredients from more than one category, the finished product category ~~with the least restrictive pass/fail levels shall be used~~will be assigned based on the ingredient with the highest category number.

Table 6B – Acceptable limits for pathogenic microbiological contaminants in finished products(1)

Finished Products		Salmonella sp.	Escherichia Coli~~(1)~~(2)	Staphylococcus aureus
Category 1	Finished products containing only vitamin and minerals	ND~~(2)~~(3)	ND~~(2)~~(3)	ND~~(2)~~(3)
Category 2	~~Finished products containing botanical ingredients – non-extract~~Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient	ND~~(2)~~(3)	~~1 x 10^2 CFU/g~~ ND~~(2)~~(3)	ND~~(2)~~(3)
Category 3	~~Finished products containing Botanical ingredient – extract / Other dietary supplement ingredient~~ Finished products containing botanical ingredients – non-extract	ND~~(2)~~(3)	~~ND(2)~~1 x 10^2 CFU/g	ND~~(2)~~(3)

(1) The category designation shall be based on ~~the~~ ingredients present at 1% or more by weight in the formula as provided in the full product formulation. For a product containing ingredients from more than one category, the finished product category ~~with the least restrictive pass/fail levels shall be used.~~will be assigned based on the ingredient with the highest category number.

Examples:

a) A product containing only Vitamin C and Zinc shall be in category 1.

b) A product containing Vitamin C, Zinc, and Green Tea Extract shall be~~A product containing Vitamin C, Zinc and Echinacea shall be~~ in category 2.

c) A product containing Vitamin C, Zinc and Echinacea shall be ~~A product containing Vitamin C, Zinc, and Green Tea Extract shall be~~ in category 3.

~~1~~(2) Upon the presence of *Escherichia coli*, 7.3.6.2 is to be followed to determine whether the colonies are enterovirulent. There is a zero tolerance for the presence of enterovirulent *Escherichia coli.*

~~2~~(3) ND = Not detected. Not Detected requires that no colonies shall be present in 10 g of sample when tested under the conditions of the USP method cited in 7.3. The detection level for this testing is 10 CFU/g for the period of time tested.

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MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE: July 24, 2007

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i26r1)

Enclosed is the ballot for Draft 1 of NSF/ANSI 173 issue 26. Please review the proposal and return your ballot **by the ballot due date of August 14, 2007** via the e-balloting system or by e-mail to Ms. Pippa Durbin at durbin@nsf.org.

Purpose

To update the current allowable levels for metal contaminants to be more reflective of North American Standards.

Background

The current levels were originally established in 2003 with an emphasis on international criteria including that found in British Pharmacopoeia etc. It is proposed that the criteria should be more strictly based on the most current North American health effects evaluations. An impact analysis of all NSF certified raw materials and finished products concluded that all currently certified products would still meet the proposed criteria.

Public Health Impact

This would bring the standard in compliance with other health effect evaluation standards resulting in a reduction of nearly all of the criteria and creating a more protective standard.

If you have any questions about the technical content of the ballot, you may contact me in care of:

Jaclyn Bowen, Joint Committee Secretariat
Standards Specialist, Standards
NSF International
Tel: (734) 769-5139
Fax: (734) 827-6162
E-mail: bowen@nsf.org

NSF International Standard for Dietary Supplements — Dietary supplements

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5.3 Contaminants

5.3.1 Metals

~~**5.3.1.1 Raw materials**~~

~~Raw materials shall not contain undeclared metals in amounts greater than the following:~~

- ~~arsenic content shall not exceed 5 parts per million (ppm);~~
- ~~cadmium content shall not exceed 0.3 ppm;~~
- ~~chromium (VI) content shall not exceed 2 ppm;~~
- ~~lead content shall not exceed 10 ppm; and~~
- ~~mercury content shall not exceed 0.2 ppm.~~

~~**5.3.1.2 Finished products**~~

~~Finished products shall not contain undeclared metals at rates of intake greater than the following:~~

- ~~arsenic content shall not exceed 0.01 milligrams per daily dose (mg/d);~~
- ~~cadmium content shall not exceed 0.006 mg/d;~~
- ~~chromium (VI) content shall not exceed 0.02 mg/d;~~
- ~~lead content shall not exceed 0.02 mg/d; and~~
- ~~mercury content shall not exceed 0.02 mg/d.~~

5.3.1.1 Raw materials

Raw materials shall not contain undeclared metals in amounts greater than the following:

- arsenic content shall not exceed 5 parts per million (ppm);
- cadmium content shall not exceed 6 ppm;
- chromium (VI) content shall not exceed 2 ppm;
- lead content shall not exceed 0.6 ppm; and
- mercury content shall not exceed 2 ppm.

5.3.1.2 Finished products

Finished products shall not contain undeclared metals at rates of intake greater than the following:

- arsenic content shall not exceed 0.01 milligrams per daily dose (mg/d);
- cadmium content shall not exceed 0.006 mg/d;
- chromium (VI) content shall not exceed 0.02 mg/d;
- lead content in products claimed for children shall not exceed 0.0006 mg/d;
- lead content in products claimed for women shall not exceed 0.0025 mg/d;
- lead content in all other products shall not exceed 0.0075 mg/d; and
- mercury content shall not exceed 0.002 mg/d.

Annex B
(informative)

Reference information for contaminant level acceptance criteria

This annex contains reference information regarding the sources of information used to establish acceptance criteria for contaminant levels.

~~B.1 Metals~~

~~Acceptance limits for cadmium and lead were obtained from the Joint FAO/WHO Expert Committee on Food Additives, World Health Organization,[1] International Programme on Chemical Safety, Safety Evaluation of Certain Food Additives and Contaminants.~~

~~The acceptance limit for chromium was obtained from the U. S. Environmental Protection Agency[2] (1998), Integrated Risk Information System (IRIS): Hexavalent Chromium.~~

~~The acceptance limit for mercury was obtained from the U. S. Environmental Protection Agency[19] (1989), Integrated Risk Information System (IRIS): Mercury (inorganic).~~

~~The acceptance limit for arsenic was obtained from the British Herbal Pharmacopoeia.[3]~~

B.1 Metals

The acceptance limit for arsenic was obtained from the British Herbal Medicine Association, British Herbal Pharmacopoeia, 1996.

The acceptance limit for cadmium was obtained from the U. S. Environmental Protection Agency (1985), Integrated Risk Information System (IRIS): Cadmium.

The acceptance limit for chromium was obtained from the U. S. Environmental Protection Agency (1998), Integrated Risk Information System (IRIS): Hexavalent Chromium.

The acceptance limit for lead was obtained from the US Food and Drug Administration (FDA). 1993. Guidance Document for Lead in Shellfish. Center for Food Safety and Applied Nutrition. August 1993.

The acceptance limit for mercury was obtained from the U. S. Environmental Protection Agency[19] (1989), Integrated Risk Information System (IRIS): Mercury (inorganic).

B.2 Microbiological contaminants

The acceptance limits contained in tables 5A, 5B, 6A, and 6B for microbiological contaminants were established with consideration of limits allowed by WHO and USP and were agreed to by the Joint Committee on Dietary Supplements.

[1] World Health Organization, 1211 Geneva 27, Switzerland

[2] U. S. Environmental Protection Agency, Environmental Criteria and Assessment Office, Cincinnati, Ohio

[3] British Herbal Medicine Association, British Herbal Pharmacopoeia, 1996

Joint Committee Comments Summary for Standard 173 i26 r1
Date of Vote: 7/24/2007 - 8/17/2007

Name: Michael Bradley **Vote:** No

Comments: The Perrigo Company objects to the proposal to set universal standard limits that would apply to all raw materials and finished products because we believe that the proposed limits are overly restricted and not consistent with current manufacturing process capabilities.

For example, setting a standard of 0.6 ppm limit for lead in all raw materials is not consistent with the limits set forth in the Food Chemical Codex. Typical limits for lead in the Food Chemical Codex branch between 1 and 5 ppm. We believe that the 0.6 ppm limit would be overly restrictive and cause many companies to product in violation of the new proposed standard. In addition, a universal limit of 0.6 ppm does not take into account the use level of the raw material in the finished dosage form. Raw materials that are used in small quantities do not need to have limits set at extremely low values because their contribution of heavy metals in the finished dosage form is usually insignificant.

The same type of logic applies to finished dosage forms. Many manufacturers apply criteria from the Codex and other compendial references for their finished dosage forms. In addition, many manufacturers must also apply correction factors for naturally occuring lead as allowed under the Proposition 65 statute.

We recommend that heavy metals limits be applied to raw materials as documented in the current edition of the Food Chemicals Codex or other compendial reference.

For finished dosage forms, we recommend that the limit be established based on the heavy metals specifications set for the raw materials that are utilized in the product taking into account the percent by weight of the individual raw materials and the uncertainty associated with the assays for trace metals.

Mike Bradley
August 16, 2007

Name: Roger Clemens **Vote:** Yes

Comments: I assume that the proposed standards do not compromise Prop 65 guidelines (California) and WHO recommendations.

Do we need to specify analytical methodology for each component, such as EPA protocols?

Roger

Name: Staci Eisner **Vote:** No

Comments: 1) The revised lead standard for raw materials is completely untenable.

2) I don't have a lot of data on finished products but I believe the lowered standards for finished products are also untenable. I would need to hear from people who actually make finished products (including specifically botanical products), that these new requirements are ok for them, before I would vote yes on this.

3) This kind of important change SHOULD NOT simply be thrown at us by staff! There should be a thorough discussion by all members of the task force before it comes to a vote. I cannot possibly vote yes for this without hearing from a broad cross-section of industry that any of this is feasible.

Name: Michael McGuffin **Vote:** No

Comments: These levels are not realistic; appear to be arbitrary. We need to discuss this in the forum of a meeting of the committee.

Name: Jo Ann Peterson **Vote:** No

Comments: I feel more input is needed before changing the standards so dramatically. I have doubts, especially with the revised lead standards,that compliance is possible, at least in the near future. Take for example, enzyme raw materials. The majority of these are from foreign sources, as with many other DS raw materials. The current observed International Standard for lead levels for enzyme raw mateials is <5 ppm. This is also the Standard adopted in Australia. It would not be in our power as a customer to be able to affect these established standards in order to be compliant with US standards.
I have no other proposed solution at this time other than my original statement of more input is needed.

Name: Katherine Sharpless **Vote:** Abstain

Comments: I don't care for the idea of making some of the limits less restrictive. When were the WHO/FAO guidelines put into place? The EPA limits seem fairly old and I'm wondering why they were not considered originally. If you take the lower limit in all cases, would approved products no longer be in compliance? I'm abstaining because I don't know whether there's truly a difference in health risks between the two levels.

Name: Heather Snider **Vote:** Yes

Comments: I am voting yes under the condition that lead shall not exceed 0.5 ppm (5.3.1.1) to comply with California Prop 65 requirements.

Name: Darryl Sullivan **Vote:** No

Comments: This proposed standard seems to contain limits that are far too high. I cannot accept allowing 2 ppm pf mercury, for example, in a raw material.

Name: Roy Upton **Vote:** No

Comments: While this is not an area of expertise of mine, I feel that the proposed limit established for lead is completely inappropriate. I understand the rationale for this. However, this is close to California Prop 65 limits (0.5 ppm for reproductive warnings) which wre based on 1000 times less than the NOEL based on a life-long daily consumption pattern. Most botanicals are not usd in this way and so should not necessarily be basd on the same parameters. Also, I am not sure consumption of shellf fish should be used as a guiding post for herbal consumption. I am also not sure that the 1993 FDA guidelines represent their latest. Last year they opposed the State of Californias requirement to label seafood with reproductive and carcinogenicity warnings so they must have a position that is different than the 0.5 ppm. Lastly, the lead values particularly are inconsistent with natonal and international standards. Example: for lead in licorice root the NSF proposal would limit this to the 0.6 ppm with a total of 15.6 ppm (sum of metals included in NSF proposal). A monograph in the CFR allows for 40 ppm total heavy metals including lead without differentiation. The USP monograph alllows for 30 ppm in total metals including lead without differentiation; the Chinese pharmacopoeia 27.5 total metals and 5 ppm lead; in Germany 10 and 5 ppm lead in spices and medcines, respectively; in India, 10 ppm (proposed); for WHO 10 ppm. This is only an example of a single botanical for which the NSF proposal is completely inconsistent with Federal (CFR), national (USP), and Iinternational (Germany, India, WHO) standards. ALso, THe British Herbal Pharmacopoeia is superceded by the British Pharmacopoeia and European Pharmacopoeia so should not be usd as a guiding post.

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173i26 – Regulated Metals

Clif McLellan presented the ballot history for this issue, including the reason for balloting this change. He explained that the current requirements were established in 2003 based on international criteria and without any data indicating what levels to expect in the products. He stressed that the reduction that is proposed would have no impact on products already certified. As he walked through the proposed changes, he explained how the criteria were calculated, including the factor of the relative source contribution. C. McLellan also addressed the negative comments that were received during the ballot period.

M. McGuffin stated that California "Prop 65" levels are in terms of µg/day, as are Health Canada's and FDA's. He suggested that NSF/ANSI 173 also use µg/day for consistency. C. McLellan agreed that this was reasonable. He also added that clarification was needed to the term "per daily dose". M. McGuffin also pointed out that most other standards specifically reference methyl mercury when addressing mercury levels. He suggested that NSF/ANSI 173 do the same. C. McLellan agreed that it was appropriate to differentiate organic and inorganic. K. Levanseler suggested testing for total and leaving the option for speciating if the total mercury level was above the allowed.

M. McGuffin asked why there are levels for ingredients rather than raw materials. K. Levanseler stated that the concern is that a manufacturer will fail after encapsulating a raw material. On finished products, limits can be set in terms of daily dose. With raw materials though, some assumptions must be made in order to have a correlation to daily dose. She also clarified that the raw material limits are for the materials themselves, they do not take into account the amount of materials that a manufacturer of finished product could potentially use.

S. Dentali and C. McLellan discussed putting use limits on raw materials. Kristen Holt clarified that if a raw material meets the Standard, the manufacturer should be able to calculate how much can be used in the finished product in order to meet the finished product requirements. V. Frankos stated that daily servings vary greatly, however, and that puts the burden on the manufacturer to determine what the appropriate level is for each supplier. R. Upton stated that this can be complicated. M. McGuffin suggested that since the scope of the Standard does not include raw materials, these limits be removed. However, K. Levanseler countered that the scope of the standard does include raw materials and in some finished products, the allowable level of the contaminant would be below the detection limit (e.g., PCBs and dioxins in fish oil). These cannot be tested at the finished product level. Therefore, she maintained that having levels for raw materials does add value.

Lead

S. Eisner questioned why the proposed lead level was below that allowable for bottled water. She added that since the contribution from supplements to daily lead intake is so minute, the lower level proposed is not beneficial and would only preclude otherwise good products from being certified. K. Levanseler stated that this issue was brought forward because many companies have been involved in the California "Prop 65" issue. R. Upton argued that the limit should not be set based on one state's requirements. In California, he argued, this is a labeling issue only. M. McGuffin disagreed and argued that when possible, levels should be lowered (he cited cadmium as an example). C. McLellan clarified that it was not the

intent to base the level on that in "Prop 65". When achievable, he argued, the levels should be reduced. R. Upton reiterated that there are many products that are not "good" from the herbal ingredient perspective that are able to meet the level because of fillers. He suggested making sure that the levels are based on what is attainable by sampling a broad sample of good quality products to support this change. C. McLellan argued that the toxicological data could not be considered in this case because there is no safe level of lead. Instead, the level is based upon a trigger point designated by the WHO.

C. McLellan explained that the changes were balloted, and there are negatives to address. S. Eisner suggested a tiered approach for products and a differentiation between synthetic versus animal- or mineral-derived products. M. McGuffin stated that he had data on botanicals for consideration in the new revision. C. McLellan stated that it would be helpful to see that data.

> **Motion:** K. Levanseler moved to address lead in a separate ballot, and reballot this proposal for requirements for the other metals. Meanwhile, the data for lead should be reviewed. M. McGuffin seconded.
>
> **Vote:** All in favor.
>
> ***Motion passes.***

Mercury

M. McGuffin stated that for mercury, there are 4-5 Prop 65 settlements that specify amounts permitted in products without labeling. There is also another reference to review that sets the limit for inorganic mercury at 3 µg/day and all other types at 0.3 µg/day. K. Levanseler responded that the proposal was simply to drop the limit 10-fold. It was suggested that the ballot be changed to include a limit for total mercury and a limit for inorganic mercury.

> **Motion:** M. McGuffin moved to change the ballot on mercury to be a limit for total mercury and a separate limit for inorganic mercury. R. Upton seconded.
>
> **Vote:** All in favor.
>
> ***Motion passed. C. McLellan was charged with developing language to be balloted.***

It was suggested that levels be specified that the are based on an assumed number of grams of consumption for ingredients.

Cadmium

M. McGuffin posed the question of whether the cadmium level should stay at 6 µg/day or be lowered to 4.1 µg/day. C. McLellan responded that one's opinion on that matter would depend on their opinion of political reasons for the limit. Every other limit is health-based, which is why 6 µg/day was used here. M. McGuffin agreed that the limit should be left at 6 µg/day for that reason.

The group discussed whether the limit should consider the source of the product and what should be the basis. V. Frankos stated that if herbal products have naturally high levels, the limit on use should reflect that and final product should use less to keep lead levels down. S. Eisner stated that the industry does not make the assumption that herbal products do not have an added benefit. V. Frankos maintained that the level should be health-based. R. Upton emphasized that efficacy must also be considered. M. McGuffin pointed out that the GMP mandates that a Standard must be set for contaminants that cause a product to be "adulterated" – or to contain poisonous or deleterious levels of contaminants that render it injurious.

Exceptions to the Standard

Katherine Sharpless asked about exceptions. K. Levanseler stated that exceptions are precluded by the Standard. Sonya Agbessi asked if exceptions should be allowed if based on sound scientific evidence.

Motion: Allison McCutcheon moved to incorporate language into 173, which would allow exceptions to the standard if supported by sound scientific evidence. M. McGuffin seconded.

Discussion: C. McLellan stated that this would be difficult to implement. K. Holt stated that her preference is that the JC specify when exemptions are allowed so that NSF does not have the burden of determining what level of evidence is sufficient.

K. Levanseler suggested submitting an issue paper to address this. C. McLellan clarified that it should address the Standard and stay away from certification issues.

Amendment: S. Eisner suggested that the motion be revised to recommend further development of the exemptions. A. McCutcheon and M. McGuffin accepted the amendment.

Vote: All in favor.

Motion passes. A. McCutcheon was charged with bringing this forward as an issue paper.

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Joint Committee Issue Document

NOTE: An issue document may be submitted at any time – it comprises two parts: the cover sheet (this page) and a description of the issue to be submitted to the Joint Committee (following page). A separate issue form is required for each issue submitted. Issue papers include proposals for modification of a standard, information reports (of current research, etc.) and reports of Task Forces. An issue paper shall be categorized as being for ACTION or for INFORMATION. Submitters should limit the Issue Paper to 1 or 2 pages – attachments detailing full recommendations or background information may be attached with supplementary information. The Chairperson of the appropriate Joint Committee will respond within 30 days of receipt of the issue document advising what steps will be taken. Any issue document intended for discussion at a Joint Committee meeting must be received at least 21 days prior to the meeting to ensure inclusion in the agenda.

Submit to:

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Attn: Standards Department
789 Dixboro Rd.
Ann Arbor, Michigan 48105

Fax: 734-827-6831
e-mail: standards@nsf.org

Submitter's contact information:

Name: Kerri LeVanseler

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Signature of Submitter * Kerri L. Levanseler Date 2/22/07

**Type written name will suffice as signature*

Please insert a check (X) in the appropriate place to indicate if you wish the item to be considered as an action item or as an information item.

Action _____X_____ Information _____ _____

NSF Standard(s) Impacted**: 173**

Issue Statement:
Provide a concise statement of the issue, which reference as appropriate any specific section(s) of the standard(s) that are related to the issue.

Within the Dietary Supplement Standard NSF/ANSI 173 there are tables that indicate the "Test methods for dietary ingredients" (Table 3) and "Test methods for marker constituent compounds" (Table 4). The content of these tables has not been reviewed or evaluated since the release of the first version of the standard in 2001.

Background:
Provide a brief background statement indicating the cause and nature of concern, the impacts identified relevant to public health, public understanding, etc, and any other reason why the issue should be considered by the Committee.

Tables 3 & 4 need to be expanded and updated to more accurately reflect the test methods currently in use for products and ingredients being evaluated in the NSF certification program.

Recommendation:
If action by the Joint Committee is being requested, clearly state what action is needed: e.g., recommended changes to the standard(s) including the current text of the relevant section(s) indicating deletions by use of ~~strike-out~~ and additions by highlighting or underlining; e.g., reference of the issue to a Task Force for detailed consideration; etc. If recommended text changes are more than a half page, please attach a separate document.

Revised tables are attached.

Supplementary Materials (photographs, diagrams, reports, etc.):
If not provided electronically, the submitter will be responsible to have sufficient copies to distribute to committee members.

Submitter _Kerri L. Levanseler Date __2-22-07

Table 3 – Test methods for dietary ingredients

Dietary ingredient Latin binomial (standardized common name)	Plant part	Chemical identification method	Source of methods	Validation of method[1]
Actaea racemosa (Black Cohosh)	root/rhizome	TLC[2]	BHP	mutual recognition
Aesculus hippocastanum (Horse Chestnut)	fruit	TLC[2]	BHP	mutual recognition
Allium sativum (Garlic)	cloves	TLC[2]	USP	mutual recognition
Astragalus membranaceus (Astragalus Root)	root	TLC[2]	AHP	mutual recognition
Capsicum annuum (Cayenne)	fruit	TLC[2]	BHP	mutual recognition
Crataegus monogyna, Crataegus laevigata (Hawthorn)	berry/leaf/flower	TLC[2]	AHP	mutual recognition
Echinacea angustifolia, *Echinacea pallida* *Echinacea purpurea*, (Echinacea)	root/aerial parts	TLC[2]	BHP	mutual recognition
Eleutherococcus senticosus (Eleuthero)	root/rhizomes	TLC[2]	BHP	mutual recognition
Ganoderma lucidum (Reishi Mushroom)	whole	TLC[2]	AHP	mutual recognition
Ginkgo biloba (Ginkgo)	leaf	TLC[2]	USP	mutual recognition
Hydrastis Canadensis L. (Goldenseal)	root	TLC[2]	BHP	mutual recognition
Hypericum perforatum (St. John's Wort)	aerial parts	TLC[2]	AHP	mutual recognition
Matricaria recutita (Chamomile)	aerial parts	TLC[2]	USP	mutual recognition
Panax ginseng (Asian Ginseng) (Chinese Ginseng) (Korean Ginseng)	Root	TLC[2]	USP	mutual recognition
Piper methysticum (Kava)	rhizome	TLC[2]	BHP	mutual recognition
Serenoa repens (Saw Palmetto)	berry	TLC[2]	USP	mutual recognition
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (Willow Bark)	Bark	TLC[2]	AHP	mutual recognition
Silybum marianum (Milk Thistle)	seed	TLC[2]	USP	mutual recognition
Schisandra chinensis (Schisandra Berry)	berry	TLC[2]	AHP	mutual recognition
Tanacetum parthenium (Feverfew)	aerial parts	TLC[2]	USP	mutual recognition
Uncaria tomentosa (Cat's Claw)	bark	TLC[2]	BHP	mutual recognition
Vaccinium macrocarpoon, Vaccinium oxycoccos (Cranberry Fruit)	fruit	HPLC[3]	USP	mutual recognition
Valeriana officinalis (valerian)	root	TLC[2]	AHP	mutual recognition
Viburnum opulus (Cramp Bark)	stem/root	TLC[2]	AHP	mutual recognition
Viburnum prunifolium (Black Haw Bark)	stem/root	TLC[2]	AHP	mutual recognition
Vitex agnus-castus (Chaste tree)	fruit	HPTLC[4]	AHP	mutual recognition
Withania somnifera (Ashwagandha Root)	root	TLC[2]	AHP	mutual recognition
Zingiber officinale (Ginger)	root/rhizome	TLC[2]	USP	mutual recognition

Table 3 – Test methods for dietary ingredients

[1] Methods Validation Levels (AOAC draft document dated 12/13/00)	
1. Collaborative Method Validation	8-10 laboratory validation study
2. Mutual Recognition Method Validation	3-4 laboratory validation study
3. Peer-Verified Method Validation	Single independent laboratory validation study in addition to in-house validation
4. In-House Method Validation	In-house validation study with but not limited to accuracy, precision, linearity, ruggedness, robustness, specificity, sensitivity, limit of detection, and limit of quantitation.
5. Emergency Method Validation	Validation study with two different positive and negative controls.

[2] TLC = thin layer chromatography

[3] HPLC = high-performance liquid chromatography

[4] HPTLC = high-performance thin layer chromatography

– concluded –

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test method	Validation of method
Actaea racemosa (Black cohosh)	Actein, 26-deoxycimifigoside, Cimiracemoside A, 27-deoxyactein, Acetyl shengmanol xyloside, Cimicifugoside, Cimiracemoside F, Cimiracemoside C, and Cimiracemoside E.	INA, Black Cohosh Assay by ELSD	mutual recognition method
Allium sativum (Garlic)	Allicin	INA, Allicin by High-Performance Liquid Chromatography	in-house method
Astragalus membranaceus (Astragalus Root)	Calycosin, Formononetin, Ononin	AHP, Astragalus Flavonoids by HPLC	mutual recognition method
Camellia sinensis (Green tea)	Epigallocatechin, catechin, Epicatechin, Epigallocatechin gallate, Catechin Gallate, Gallocatechin gallate, Epicatechin Gallate and Gallic acid	INA, Catechins and Gallic Acid in Green Tea by HPLC	in-house method
Crataegus monogyna, Crataegus laevigata (Hawthorn Leaf and Flower)	Vitexin	AHP, Flavonoids in Hawthorn Leaf and Flower by HPLC	mutual recognition method
Echinacea angustifolia Echinacea pallida Echinacea purpurea (Echinacea)	Caftaric acid, Cichoric acid, Chlorogenic acid, Echinacoside	INA, Phenolics in Echinacea by HPLC	in-house method
Ginkgo biloba (Ginkgo)	Ginkgolide A, Ginkgolide B, Bilobalide	INA, Ginkoterpenoid Assay by HPLC	in-house method
Ginkgo biloba (Ginkgo)	Kaempferol, Quercetin, Isorhamnetin	INA, Ginkgo Flavonol Glycoside Assay by HPLC	in-house method
Hypericum perforatum (St. John's Wort)	Rutin trihydrate, Hyperoside, Hypericin, Quercitrin, Chlorogenic Acid, Hyperforin, Isoquercitrin, Quercetin, Pseudohypericin	INA, St. John's Wort Assay by HPLC	in-house method
Piper methysticum (Kava)	Desmethoxyyangonin, Dihydromethysticin, Dihydrokavain, Methysticin, Yangonin, Kavain	INA, Kavalactone Assay by HPLC	in-house method
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (Willow Bark)	Salicin, L-Picein	AHP, Willow Bark Assay by HPLC	in-house method
Schisandra	Schisandrin A, Schisandrin B	AHP, Schisandra	mutual

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test method	Validation of method
chinensis (Schisandra Berry)		berry Assay by HPLC	recognition method
Serenoa repens (Saw palmetto)	Hexanoic, Hexanoic, Nonanoic Decanoic, Dodecanoic, Tetradecanoic, Hexadecanoic, Heptadecanoic, Octadecanoic, 9-Octadecenoic, 9,12-Octadecadienoic, 9,12,15-Octadecatrienoic acids	INA, Fatty Acid Content in Saw Palmetto by Gas Chromatography	in-house method
Serenoa repens (Saw palmetto)	Stigmasterol, campesterol, brassicasterol, and ß-sitosterol	INA, Sterols Content in Saw Palmetto by Gas Chromatography	in-house method
Valeriana officinalis (Valerian)	Valerenic acid, acetoxyvalerenic acid, hydroxyvalerenic acid	AHP, Valerenic Acids in Valerian by HPLC	mutual recognition method
Vitex agnus-castus (Chaste tree)	Casticin	AHP, Casticin Assay in Chaste Tree Fruits by HPLC	mutual recognition method

– concluded –

Table 3 – Test methods for dietary ingredients

Dietary ingredient Latin binomial (standardized common name)	Typical Plant part	Monograph Reference	Chemical identification method	Source of Chemical identification method
Actaea racemosa (Black Cohosh)	root/rhizome	BHP	TLC	NSF International
Aesculus hippocastanum (Horse Chestnut)	fruit	BHP	TLC	Alkemists Pharmaceutical
Allium sativum (Garlic)	cloves	USP	TLC	CAMAG
Alpinia officindrum (Galangal)	root	-	TLC	NSF International
Angelica (Dong Quai)	root	AHP	HPLC	NSF International
Asteraceae stevia (Sweet leaf)	leaf	-	TLC	NSF International
Astragalus membranaceus (Astragalus Root)	root	AHP	TLC	Alkemists Pharmaceutical
Brassica oleracea (Broccoli)	head	-	TLC	NSF International
Camellia thea (Green tea)	leaf	-	TLC	CAMAG
Capsicum annuum (Cayenne)	fruit	BHP	TLC	NSF International
Centella asiatica (Gotu Kola)	leaf	-	TLC	NSF International
Cinnamomum verum (Cinnamon)	bark	-	TLC	NSF International
Citrus bioflavonoids	NA	-	HPLC	NSF International
Crataegus monogyna, Crataegus laevigata (Hawthorn)	berry/leaf/flower	AHP	TLC	NSF International
Curcumea longa (Turmeric)	root	-	TLC	NSF International
Echinacea angustifolia, *Echinacea pallida* *Echinacea purpurea*, (Echinacea)	root/aerial parts	BHP	HPLC	NSF International
Eleutherococcus senticosus (Eleuthero)	root/rhizomes	BHP	TLC	NSF International
Ganoderma lucidum (Reishi Mushroom)	whole	AHP	TLC	AHP
Ginkgo biloba (Ginkgo)	leaf	USP	TLC	NSF International
Grape Seed	seed	-	HPLC	NSF International
Grape Skin	skin	-	TLC	NSF International
Gymnema sylvestra	leaf	-	TLC	NSF International
Hydrastis Canadensis L. (Goldenseal)	root	BHP	HPLC	NSF International
Hypericum perforatum (St. John's Wort)	aerial parts	AHP	HPLC	NSF International
Hyssopus officinalis (Rosemary)	leaf	-	TLC	NSF International
Lepidium meyenii (Maca root)	root	-	TLC	NSF International
Licorice	root	EP	TLC	EP
Matricaria recutita (Chamomile)	aerial parts	USP	TLC	NSF International
Olea Europaea (Olive)	fruit	-	TLC	NSF International
Panax ginseng (Asian Ginseng) (Chinese Ginseng) (Korean Ginseng)	root	USP	TLC	CAMAG
Paullinia cupana (Guarana)	seed	-	TLC	NSF International
Pfaffia paniculata (Suma)	root	-	TLC	NSF International
Pygeum africanum (Pygeum)	bark	-	TLC	NSF International
Serenoa repens (Saw Palmetto)	berry	USP	GC	NSF International
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (Willow Bark)	Bark	AHP	TLC	NSF International
Silybum marianum (Milk Thistle)	seed	USP	TLC	NSF International
Schisandra chinensis (Schisandra Berry)	berry	AHP	TLC	NSF International
Spinacia oleracea (Spinach)	leaf	-	TLC	NSF International
Spirulina	whole	-	TLC	NSF International
Tanacetum parthenium (Feverfew)	aerial parts	USP	TLC	NSF International
Uncaria tomentosa (Cat's Claw)	bark	BHP	TLC	BHP
Urtica dioica (Nettle Leaf)	leaf	EP	TLC	NSF International
Vaccinium macrocarpoon, Vaccinium oxycoccos (Cranberry Fruit)	fruit	USP	HPLC	NSF International
Vaccinium myrtillus (Bilberry)	fruit	-	TLC	NSF International
Vaccinium spp. (Blueberry)	fruit	-	TLC	NSF International
Valeriana officinalis (Valerian)	root	AHP	TLC	NSF International
Viburnum opulus (Cramp Bark)	bark	AHP	TLC	NSF International
Viburnum prunifolium (Black Haw Bark)	bark	AHP	TLC	AHP
Vitex agnus-castus (Chaste tree)	fruit	AHP	TLC	NSF International
Withania somnifera (Ashwagandha Root)	root	AHP	TLC	NSF International
Zingiber officinale (Ginger)	root/rhizome	USP	TLC	NSF International

BHP = British Herbal Pharmacopeia
USP = United States Pharmacopeia
AHP = American Herbal Pharmacopeia
EP = European Pharmacopeia
TLC = High Performance Thin Layer Chromatography
HPLC = High-Performance Liquid Chromatography
GC = Gas Chromatography

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test Method	Validation of method[1]
Actaea racemosa (Black cohosh)	Triterpene glycosides: Actein, 26-deoxycimifigoside, Cimiracemoside A, 27-deoxyactein, Acetyl shengmanol xyloside, Cimicifugoside, Cimiracemoside F, Cimiracemoside C, and Cimiracemoside E.	INA, HPLC	Peer-verified
Aesculus hippocastanum (Horse Chestnut)	Escin	NSF, HPLC	In-house
Allium sativum (Garlic)	Allicin	INA, HPLC	Peer-verified
Angelica (Dong Quai)	Ligustilide	NSF, HPLC	In-house
Astragalus membranaceus (Astragalus Root)	Calycosin, Formononetin, Ononin	AHP, HPLC	Peer-verified
Camellia sinensis (Green tea)	Epigallocatechin (EGC), Catechin, Epicatechin, Epigallocatechin gallate (EGCG), Catechin Gallate, Gallocatechin gallate (GCG), Epicatechin Gallate (ECG) and Gallic acid	INA, HPLC	Peer-verified
Coleus	Forskolin	NSF, HPLC	In-house
Crataegus monogyna, Crataegus laevigata (Hawthorn Leaf and Flower)	Vitexin	AHP, HPLC	Mutual recognition
Curcumea longa (Turmeric)	Curcuminoids: Curcumin, Demethoxycurcumin, Bis-demethoxycurcumin	NSF, HPLC	In-house
Echinacea angustifolia Echinacea pallida Echinacea purpurea (Echinacea)	Total Phenolics: Caftaric acid, Cichoric acid, Chlorogenic acid, Echinacoside	AHP, HPLC	Mutual recognition
Eleutherococcus senticosus (Eleuthero)	Eleutherosides	INA, HPLC	Peer-verified
Fenugreek	4-hydroxyisoleucine	NSF, HPLC	In-house
Feverfew	Parthenolide	AHP, HPLC	Peer-verified
Ginkgo biloba (Ginkgo)	Ginkgo Terpene Lactones (Ginkgolide A, Ginkgolide B, Bilobalide)	INA, HPLC	Peer-verified
Ginkgo biloba	Ginkgo Flavonglycosides	AOAC, HPLC	Collaborative

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test Method	Validation of method[1]
(Ginkgo)	(Kaempferol, Quercetin, Isorhamnetin)		
Gymnema sylvestra	Gymnemic acids	NSF, HPLC	In-house
Hypericum perforatum (St. John's Wort)	Rutin trihydrate, Hyperoside, Hypericin, Quercitrin, Chlorogenic Acid, Hyperforin, Isoquercitrin, Quercetin, Pseudohypericin	INA, HPLC	Peer-verified
Panax ginseng (Asian Ginseng) (Chinese Ginseng) (Korean	Ginsenosides	INA, HPLC	Peer-verified
Picrorhiza kurroa	Picrosides	NSF, HPLC	In-house
Pueraria lobata (Kudzu)	Kudzu Isoflavones	NSF, HPLC	In-house
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (Willow Bark)	Salicin	AHP, HPLC	Peer-verified
Schisandra chinensis (Schisandra Berry)	Schisandrin A, Schisandrin B	AHP, HPLC	Peer-verified
Serenoa repens (Saw palmetto)	Fatty Acids: Hexanoic, Hexanoic, Nonanoic Decanoic, Dodecanoic, Tetradecanoic, Hexadecanoic, Heptadecanoic, Octadecanoic, 9-Octadecenoic, 9,12-Octadecadienoic, 9,12,15-Octadecatrienoic acids	AOAC, Gas Chromatography	Collaborative
Serenoa repens (Saw palmetto)	Phytosterols: Stigmasterol, campesterol, brassicasterol, and ß-sitosterol	AOAC, Gas Chromatography	Collaborative
Silybum marianum (Milk Thistle)	Silymarins	INA, HPLC	Peer-verified
Soy	Soy Isoflavones	NSF, HPLC	In-house
Tribulus terrestris (Steroidal saponins)	Saponins	Gravimetric Method	Emergency
Trifolium pratense (Red Clover)	Clover Isoflavones	NSF, HPLC	In-house
Valeriana officinalis (Valerian)	Valerenic Acids: Valerenic acid, acetoxyvalerenic acid, hydroxyvalerenic acid	AHP, HPLC	Mutual recognition
Vitex agnus-castus (Chaste tree)	Casticin (flavonoid)	AHP, HPLC	Mutual recognition

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test Method	Validation of method[1]

[1] Methods Validation Levels (AOAC draft document dated 12/13/00)

1. Collaborative Method Validation	8-12 laboratory validation study
2. Mutual Recognition Method Validation	3-4 laboratory validation study
3. Peer-Verified Method Validation	Single independent laboratory validation study in addition to in-house validation
4. In-House Method Validation	In-house validation study with but not limited to accuracy, precision, linearity, ruggedness, robustness, specificity, sensitivity, limit of detection, and limit of quantitation.
5. Emergency Method Validation	Validation study with two different positive and negative controls.

INA = Institute for Nutraceutical Advancement
AHP = American Herbal Pharmacopeia
NSF = NSF International
AOAC = AOAC International
HPLC = High-Performance Liquid Chromatography

– concluded –

MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE:

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i28r1)

Enclosed is the ballot for Draft 1 of NSF/ANSI 173 issue 28. Please review the proposal and return your ballot **by the ballot due date of .**

Purpose

To update Tables 3 and 4.

Background

The current tables of test methods were originally established in 2001 when the standard was first written and have not been reviewed since that time. In order to ensure that these test methods are up-to-date, the Joint Committee has been asked to review the content. Additional table format/title changes have been recommended to clarify the information being presented.

Public Health Impact

This would update the standard in accordance with the latest test methods to ensure that NSF/ANSI 173 describes the product testing as accurately as possible.

If you have any questions about the technical content of the ballot, you may contact me in care of:

Sarah Kozanecki, Joint Committee Secretariat
Standards Specialist
NSF International
Tel: (734) 827-6867
Fax: (734) 827-3886
E-mail: kozanecki@nsf.org

NSF International Standard for Dietary Supplements —
Dietary supplements

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Table 3 – Test methods for ~~dietary ingredients~~ conformity with botanical ingredient identity

Dietary ingredient Latin binomial (standardized common name)	Typical Plant part	~~Source of methods~~ Monograph Reference[(1)]	Chemical identification method	~~Validation of Method~~[(1)]	Source of Chemical identification method
Actaea racemosa (Black Cohosh)	root/rhizome	BHP	TLC[(2)]	~~mutual recognition~~	NSF International
Aesculus hippocastanum (Horse Chestnut)	fruit	BHP	TLC[(2)]	~~mutual recognition~~	Alkemists Pharmaceutical
Allium sativum (Garlic)	cloves	USP	TLC[(2)]	~~mutual recognition~~	CAMAG
Alpinia officinarum (Galangal)	root	-	TLC[(2)]		NSF International
Angelica sinensis (Dong Quai)	root	AHP	HPLC[(3)]		NSF International
Arthrospira platensis (Spirulina)	whole	-	TLC[(2)]		NSF International
Astragalus membranaceus (Astragalus ~~Root~~)	root	AHP	TLC[(2)]	~~mutual recognition~~	Alkemists Pharmaceutical
Brassica oleracea L. var italica (Broccoli)	head	-	TLC[(2)]		NSF International
Camellia sinensis (Tea)	leaf	-	TLC[(2)]		CAMAG
Capsicum annuum (Cayenne)	fruit	BHP	TLC[(2)]		NSF International
Centella asiatica (Gotu Kola)	leaf	-	TLC[(2)]		NSF International
Cinnamomum verum (Cinnamon)	bark	-	TLC[(2)]		NSF International
Citrus bioflavonoids	NA	-	HPLC[(3)]		NSF International
Crataegus monogyna, Crataegus laevigata (Hawthorn)	berry/leaf/flower	AHP	TLC[(2)]	~~mutual recognition~~	NSF International
Curcuma longa (Turmeric)	root	-	TLC[(2)]		NSF International
Echinacea angustifolia, *Echinacea pallida* *Echinacea purpurea*, (Echinacea angustifolia Echinacea pallida Echinacea purpurea)	root/aerial parts	BHP	HPLC[(3)]	~~mutual recognition~~	NSF International
Eleutherococcus senticosus (Eleuthero)	root/rhizomes	BHP	TLC[(2)]	~~mutual recognition~~	NSF International

Table 3 – Test methods for ~~dietary ingredients~~ conformity with botanical ingredient identity

Ganoderma lucidum (Reishi ~~Mushroom~~)	whole	AHP	TLC[2]	~~mutual recognition~~	AHP
Ginkgo biloba (Ginkgo)	leaf	USP	TLC[2]	~~mutual recognition~~	NSF International
Gymnema sylvestre (Gymnema)	leaf	-	TLC[2]		NSF International
Hydrastis canadensis L. (Goldenseal)	root	BHP	HPLC	~~mutual recognition~~	NSF International
Hypericum perforatum (St. John's Wort)	aerial parts	AHP	HPLC	~~mutual recognition~~	NSF International
Hyssopus officinalis (Hyssop)	leaf	-	TLC[2]		NSF International
Lepidium meyenii (Maca)	root	-	TLC[2]		NSF International
Glycyrrhiza glabra (Licorice)	root	EP	TLC[2]		EP
Matricaria recutita (Chamomile)	aerial parts	USP	TLC[2]	~~mutual recognition~~	NSF International
Olea Europaea (Olive)	fruit	-	TLC[2]		NSF International
Panax ginseng (Asian Ginseng) (Chinese Gingseng) (Korean Ginseng)	root	USP	TLC[2]	~~mutual recognition~~	CAMAG
Paullinia cupana (Guaraná)	seed	-	TLC[2]		NSF International
Pfaffia paniculata (Suma)	root	-	TLC[2]		NSF International
~~*Piper methyscticum* (Kava)~~	~~rhizome~~	~~BHP~~	~~TLC[2]~~	~~mutual recognition~~	
Prunus africana (Pygeum)	bark	-	TLC[2]		NSF International
Serenoa repens (Saw Palmetto)	berry	USP	GC[4]	~~mutual recognition~~	NSF International
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (~~Willow Bark~~ Violet Willow, Brittle Willow, Laurel Willow, Purple Willow)	Bark	AHP	TLC[2]	~~mutual recognition~~	NSF International
Silybum marianum (Milk Thistle)	seed	USP	TLC[2]	~~mutual recognition~~	NSF International
Schisandra chinensis (Schisandra)	berry	AHP	TLC[2]	~~mutual recognition~~	NSF International
Spinacia oleracea (Spinach)	leaf	-	TLC[2]		NSF International
Stevia rebaudiana (stevia)	leaf	-	TLC[2]		NSF International
Tanacetum parthenium (Feverfew)	aerial parts	USP	TLC[2]	~~mutual recognition~~	NSF International
Uncaria tomentosa (Cat's Claw)	bark	BHP	TLC[2]	~~mutual recognition~~	BHP
Urtica dioica (Stinging Nettle)	leaf	EP	TLC[2]		NSF International

Table 3 – Test methods for ~~dietary ingredients~~ conformity with botanical ingredient identity

Vaccinium macrocarpoon, Vaccinium oxycoccos (Cranberry ~~fruit~~)	fruit	USP	HPLC[3]	~~mutual recognition~~	NSF International
Vaccinium myrtillus (Bilberry)	fruit	-	TLC[2]		NSF International
Vaccinium pallidum. (Blueberry)	fruit	-	TLC[2]		NSF International
Valeriana officinalis (Valerian)	root	AHP	TLC[2]	~~mutual recognition~~	NSF International
Viburnum opulus (Cramp Bark)	bark	AHP	TLC[2]	~~mutual recognition~~	NSF International
Viburnum prunifolium (Black Haw ~~Bark~~)	bark	AHP	TLC[2]	~~mutual recognition~~	AHP
Vitis vinifera (Grape)	seed	-	HPLC[3]		NSF International
Vitis vinifera (Grape)	skin	-	TLC[2]		NSF International
Vitex agnus-castus (Chaste tree)	fruit	AHP	TLC[2]	~~mutual recognition~~	NSF International
Withania somnifera (Ashwagandha)	root	AHP	TLC[2]	~~mutual recognition~~	NSF International
Zingiber officinale (Ginger)	root/rhizome	USP	TLC[2]	~~mutual recognition~~	NSF International

[1] Monograph references:
BHP = British Herbal Pharmacopeia
USP = United States Pharmacopeia
AHP = American Herbal Pharmacopeia
EP = European Pharmacopeia
[2] TLC = High Performance Thin Layer Chromatography
[3] HPLC = High-Performance Liquid Chromatography
[4] GC = Gas Chromatography

– concluded –

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test method[1]	Validation of method[2]
Actaea racemosa (Black cohosh)	Triterpene glycosides: Actein, 26-deoxycimifigoside, Cimiracemoside A, 27-deoxyactein, Acetyl shengmanol xyloside, Cimicifugoside, Cimiracemoside F, Cimiracemoside C, and Cimiracemoside E.	INA, ~~Black Cohosh Assay by ELSD~~ HPLC	~~Mutual recognition method~~ Peer-verified
Aesculus hippocastanum (Horse Chestnut)	Escin	NSF, HPLC	Single Lab
Allium sativum (Garlic)	Allicin	INA, ~~Allicin by High-Performance Liquid Chromatography~~ HPLC	~~In-house method~~ Peer-verified
Angelica sinensis (Dong Quai)	Ligustilide	NSF, HPLC	Single Lab
Astragalus membranaceus (Astragalus ~~Root~~)	Calycosin, Formononetin, Ononin	AHP, ~~Astralagus Flavonoids by~~ HPLC	~~Mutual recognition method~~ Peer-verified
Camellia sinensis (~~Green~~ Tea)	Epigallocatechin (EGC), Catechin, Epicatechin, Epigallocatechin gallate (EGCG), Catechin Gallate, Gallocatechin gallate (GCG), Epicatechin Gallate (ECG) and Gallic acid	INA, ~~Catechins and Gallic Acid in Green Tea by~~ HPLC	~~In-house method~~ Peer-verified
Crataegus monogyna, Crataegus laevigata (Hawthorn ~~Leaf and Flower~~)	Vitexin	AHP, ~~Flavenoids in Hawthorn Leaf and Flower by~~ HPLC	~~Mutual recognition method~~ Peer-verified
Curcuma longa (Turmeric)	Curcuminoids: Curcumin, Demethoxycurcumin, Bis-demethoxycurcumin	NSF, HPLC	Single Lab
Echinacea angustifolia, Echinacea pallida, Echinacea purpurea (Echinacea angustifolia, Echinacea pallida, Echinacea purpurea)	Total Phenolics: Caftaric acid, Cichoric acid, Chlorogenic acid, Echinacoside	AHP, ~~Phenolics in Echinacea by~~ HPLC	~~In-house method~~ Peer-verified
Eleutherococcus senticosus (Eleuthero)	Eleutherosides	INA, HPLC	Peer-verified
Trigonella foenum-graecum	4-hydroxyisoleucine	NSF, HPLC	Single Lab

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test method[(1)]	Validation of method[(2)]
(Fenugreek)			
Tanacetum parthenium (Feverfew)	Parthenolide	AHP, HPLC	Peer-verified
Ginkgo biloba (Ginkgo)	Ginkgo Terpene Lactones (Ginkgolide A, Ginkgolide B, Bilobalide)	INA, ~~Ginkoterpenoid Assay by~~ HPLC	~~In-house method~~ Peer-verified
Ginkgo biloba (Ginkgo)	Ginkgo Flavonglycosides (Kaempferol, Quercetin, Isorhamnetin)	~~INA,~~ AOAC, ~~Ginkgo Flavonol Glycoside Assay by~~ HPLC	~~In-house method~~ Collaborative
Gymnema sylvestra	Gymnemic acids	NSF, HPLC	Single Lab
Hypericum perforatum (St. John's Wort)	~~Rutin trihydrate, Hyperoside,~~ Hypericin, ~~Quercetin, Chlorogenic acid, Hyperforin, Isoquercetin, Quercetin,~~ and Pseudohypericin or Hyperforin	INA, ~~St. John's Wort Assay by~~ HPLC	~~In-house method~~ Peer-verified
~~*Piper methysticum* (Kava)~~	~~Desmethoxyyangonin, Dihydromethysticin, Dihydrokavain, Methysticin, Yangonin, Kavain~~	~~INA, Kavalactone Assay by HPLC~~	~~In-house method~~
Panax ginseng (Asian Ginseng)	Ginsenosides	INA, HPLC	Peer-verified
Picrorhiza kurrooa (Picrorhiza)	Picrosides	NSF, HPLC	Single Lab
Pueraria montana (Kudzu)	Kudzu Isoflavones	NSF, HPLC	Single Lab
Plectranthus amboinicus, Plectranthus barbatus (Indian borage, forskohii)	Forskolin	NSF, HPLC	Single Lab
Salix daphnoides, Salix fragilis, Salix pentandra, Salix purpurea (~~Willow Bark~~ Violet Willow, Brittle Willow, Laurel Willow, Purple Willow)	Salicin~~, L Picein~~	AHP, ~~Willow bark Assay by~~ HPLC	~~In-house method~~ Peer-verified
Schisandra chinensis (Schisandra ~~Berry~~)	Schisandrin A, Schisandrin B	AHP, ~~Schisandra berry Assay by~~ HPLC	~~Mutual recognition method~~ Peer-verified

Table 4 – Test methods for marker constituent compounds

Dietary ingredient Latin binomial (Standardized common name)	Marker constituent compound	Test method[(1)]	Validation of method[(2)]
Serenoa repens (Saw palmetto)	Fatty Acids: Hexanoic, ~~Hexanoic,~~ Nonanoic, Decanoic, Dodecanoic, Tetradecanoic, Hexadecanoic, Heptadecanoic, Octadecanoic, 9-Octadecenoic, 9,12-Octadecadienoic, 9,12,15-Octadecatrienoic acids	~~INA,~~ AOAC, ~~Fatty Acid Content in Saw Palmetto by Gas Chromatography~~GC	~~In-house method~~ Collaborative
Serenoa repens (Saw palmetto)	Phytosterols: Stigmasterol, campesterol, brassicasterol, and ß-sitosterol	~~INA,~~ AOAC, ~~Sterols Content in Saw Palmetto by Gas Chromatography~~GC	~~In-house method~~ Collaborative
Silybum marianum (Milk Thistle)	Silymarins	INA, HPLC	Peer-verified
Glycine max (Soy Bean)	Soy Isoflavones	NSF, HPLC	In-house
Tribulus terrestris (Tribulus)	Saponins	Gravimetric Method	Research
Trifolium pratense (Red Clover)	Clover Isoflavones	NSF, HPLC	Single Lab
Valeriana officinalis (Valerian)	Valerenic Acids: Valerenic acid, acetoxyvalerenic acid, hydroxyvalerenic acid	AHP, ~~Valerenic Acids in Valerian by~~ HPLC	~~Mutual recognition method~~ Peer-verified
Vitex agnus-castus (Chaste tree)	Casticin (flavonoid)	AHP, ~~Casticin Assay in Chaste Tree Fruits by~~ HPLC	~~Mutual recognition method~~ Peer-verified

[(1)] Test methods

INA = Institute for Nutraceutical Advancement
AHP = American Herbal Pharmacopeia
NSF = NSF International
AOAC = AOAC International
HPLC = High-Performance Liquid Chromatography
GC = Gas Chromatography

[(2)] Methods Validation Levels

1. Collaborative Method Validation	Validation study involving 8 or more laboratories.
2. Peer-Verified Method Validation	Single independent laboratory validation study with one or more independent laboratories confirming method (includes intermediate precision).
3. Single Laboratory Method Validation	In-house validation study with, but not limited to, accuracy, precision (repeatability), linearity, robustness, specificity, limit of detection, and limit of quantitation.
4. Research Method	Method developed without executing a formal validation. (ex. in-house quality control methods used for specific sample matrices)

– concluded –

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MEMORANDUM

TO: Joint Committee on Dietary Supplements

FROM: Mary Hardy, Joint Committee Chairperson on Dietary Supplements

DATE: February 1, 2008

SUBJECT: Revisions to NSF/ANSI 173 – Dietary Supplements (173i29r1)

Enclosed is the ballot for Draft 1 of NSF/ANSI 173 issue 29. Please review the proposal and return your ballot **by the ballot due date of February 22, 2008** via the e-balloting system.

Purpose

To revise 6.2.5 "Quality assurance for quantitative test methods"

Background

Originally, a QC section was added to the standard to provide information regarding the typical practices and quality checks involved for the analysis of supplements as performed by the NSF International Chemistry Laboratories. The section was not written to provide the flexibility needed based on the range of techniques that might need to be employed. Also, it is important that the language of this section is consistent with the method specific standard operating procedures currently in use at NSF International.

Public Health Impact

This will have no negative impact on public health.

If you have any questions about the technical content of the ballot, you may contact me in care of:

Sarah Kozanecki, Joint Committee Secretariat
Standards Specialist, Standards
NSF International
Tel: (734) 827-6867
Fax: (734) 827-3886
E-mail: kozanecki@nsf.org

NSF International Standard for Dietary Supplements —
Dietary supplements

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6 Test methods used by testing laboratories for identification and quantification of ingredients – raw materials and finished products

6.1 Identification test methods

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6.2 Quantification test methods

6.2.1 Botanicals

If declared on the label, the identity of marker constituents shall be evaluated in accordance with the methods in table 4. If no method exists or if improved technology allows for a more accurate and precise method to be developed, one may be developed. The use of any new method shall require that a validation be performed, following the principles of the AOAC Single Lab Validation Guideline as a minimum, which includes an evaluation of specificity, linearity, reproducibility, accuracy, spike recovery, and method detection limit (if applicable). More rigorous validation could follow according to the guidelines of ICH, FDA, GLP, CEN, and/or AOAC, as appropriate.

6.2.2 Vitamins

The quantity of vitamins shall be evaluated in accordance with the methods listed in the USP-NF. If no method exists or if improved technology allows for a more accurate and precise method to be developed, one may be developed. The use of any new method shall require that a validation be performed, following the principles of the AOAC Single Lab Validation Guideline as a minimum, which includes an evaluation of specificity, linearity, reproducibility, accuracy, spike recovery, and method detection limit (if applicable). More rigorous validation could follow according to the guidelines of ICH, FDA, GLP, CEN, and/or AOAC, as appropriate.

6.2.3 Minerals

The quantity of minerals shall be evaluated in accordance with the methods listed in the USP-NF. If no method exists or if improved technology allows for a more accurate and precise method to be developed, one may be developed. The use of any new method shall require that a validation be performed, following the principles of the AOAC Single Lab Validation Guideline as a minimum, which includes an evaluation of specificity, linearity, reproducibility, accuracy, spike recovery, and method detection limit (if applicable). More rigorous validation could follow according to the guidelines of ICH, FDA, GLP, CEN, and/or AOAC, as appropriate.

6.2.4 Other dietary supplement ingredients

An effort shall be made to seek out the most appropriate method to confirm claims for the product under evaluation. The source of these methods may include AOAC International, USP-NF, AHP, European, German, Japanese monographs, INA, etc. The use of any new method shall require that a validation be performed, following the principles of the AOAC Single Lab Validation Guideline as a minimum, which includes an evaluation of specificity, linearity, reproducibility, accuracy, spike recovery, and method detection limit (if applicable). More rigorous validation could follow according to the guidelines of ICH, FDA, GLP, CEN, and/or AOAC, as appropriate.

6.2.5 Quality assurance for quantitative test methods

Many of the quantitative test methods for dietary supplement samples are performed utilizing chromatographic procedures. The typical quality assurance criteria that are applied are described in the following sections, however, some methods may have unique criteria which would be defined within the laboratory standard operating procedures or other reference method. For example, non-chromatographic test methods (such as titration and potentiometric techniques, uv-visible and gravimetric procedures, micro-assays, etc.) would employ quality assurance steps as applicable to the situation.

6.2.5.1 Calibration

Quantification test methods shall be performed using certified reference standards as calibration standards. The standards are typically purchased as single chemicals with greater than 95% purity. If a high-purity standard is not available, a lower-purity material shall be used if there is a means by which the actual purity can be measured (e. g., uv absorbance).

6.2.5.1.1 Multi-level calibration curves

Multi-level calibration curves shall be prepared with a minimum of three concentration levels such that any sample preparations under evaluation would be bracketed by a calibration standard. Curves shall give a correlation ~~coefficient~~ coefficient (r) of 0.995 or higher.

6.2.5.1.2 Single-level calibrations ~~curves~~

If a single level calibration is employed, the standard shall be run in triplicate and the relative standard deviation between these runs shall not exceed 2%. The detector response of the prepared sample shall be within 90% -%110 of that of the standard.

6.2.5.1.3 Blanks

A method/reagent blank shall be included in each analytical run. The blank response for the analyte of interest shall not be greater than one half the response of the lowest calibration standard for multi-level calibration curves. For single-level calibrations, the blank response for the analyte of interest shall not exceed 5% of the sample response.

6.2.5.1.4 Reproducibility/accuracy

All unfamiliar matrices shall be prepared in triplicate.

Whenever possible, two additional preparations shall be spiked with the reference standard(s) to assess recovery/accuracy. The recovery in the range of 70-130% of the theoretical spike value is considered acceptable.

The reproducibility between the two spiked samples as measured by ~~percent~~ relative percent difference (RPD) shall be no greater than 20%. The reproducibility of the method is also evaluated by the percent relative standard deviation (%RSD) of the triplicate sample preparations, which should not exceed 25%,

NOTE – When spiking with the reference standard is price prohibitive, a control sample with a known result shall be tested as part of the analysis run; this shall include a certified reference material or a sample that has been analyzed in the past.

6.2.5.1.5 Continuing Calibration Verification (CCV)

In order to assess instrument stability, a Continuing Calibration Verification (CCV) or bracketing standard~~s~~ shall be run after every 10 sample preparations and/or at the end of the run. The recovery for the CCV shall be between ~~within the uncertainty of the method for the data to be acceptable~~80-120% of the theoretical standard value. CCV standards, which are run to confirm an existing calibration, must show recovery of 90-110%. If the result falls outside this range, a new calibration shall be run.

Voting Results from 173i29

Voter		Vote	Section	Subject	Comment	Proposal	Status	Company Name
Jo Ann	Peterson	NO		warrants more discussion	Based on the comments posted at this time, I am casting a negative vote to indicate my belief that more discussion should take place to resolve some of the detailed points.		Assigned to KL	National Enzyme Company
Katherine	Sharpless	NO	6.2.5.1.4	Accuracy	My main comments (and the reasons for my negative vote) relate to section 6.2.5.1.4. First is the statement that spike recovery is indicative of accuracy. Spike recovery indicates that the method is capable of recovering analyte that may or may not be incorporated in the matrix in the same way as the naturally occurring analyte. If you're evaluating reproducibility, you probably need to identify reproducibility conditions in the standard, otherwise I suspect people will be assessing their repeatability. Re: the information in the note, a control sample should always be analyzed, regardless of whether a spike is economically feasible or not. The control material, especially if it's traceable to a natural-matrix certified reference material, will be indicative of your accuracy. Editorial comment: In 6.2.5.1.1., correlation coefficient should be r squared. In 6.2.5.1.2, the relative standard deviation of what? the instrument response? between runs shall not exceed 2%?	1. Don't say that spike recovery indicates accuracy. 2. Specify reproducibility conditions. 3. Recomend analysis of a certified reference material (CRM) or in-house control material (traceable to a CRM if possible) for demonstration of accuracy.	Assigned to KL	NIST
Darryl	Sullivan	NO	6.2.2, 6.2.3,	Justification for my negative vote	I disagree with specifying USP methods for Botanical, Vitamin and Mineral testing. These sections should specify USP, AOAC, or other appropriate compendial test methods.		Assigned to KL	Covance Inc.
Michael	McGuffin	ABSTAIN	173i29	Reason for my abstention	I see that the group is split on this vote, with those who understand these details best in disagreement. I do not have sufficient familiarity with the issue to make a decision without some guidance. I have therefore abstained with the hope that there will be another opportunity to discuss and resolve the points raised.	More discussion.	Addressed	American Herbal Products Assoc.
Heather	Arnold	NO		Reason for negative vote.	I agree with Darryl regarding specifying only USP. The sections should specify USP, AOAC, or other appropriate compendial test methods.		Assigned to KL	Access Business Group LLC
Leila	Saldanha	NO		Reason for negative vote	I agree with Darryl and Heather regarding specifying only USP. The sections should specify USP, AOAC, or other appropriate compendia test methods --- consistent with the new CGMPs.		Assigned to KL	NutrIQ LLC
Michael	Bradley	NO	General Comment	173i29r1	I agree with the comments that refer to a general compendial reference versus a single compendial reference. All official compendia should be considered to be included in the Standard by reference. We also believe that some of the specific limits identified in the issue paper may be justifiably modified, and that should be left up to the individual companies or Third Party Testing Laboratories as long as they can justify amending the specific limit.	Change the language to include a general statement concerning compendial references and include language that allows the changing of the specific limits, if justifiable.	Assigned to KL	Perrigo of South Carolina

Jim	Roza	NO	173i29	Methods	I concur with my other colleagues who registered a negative vote that methods other than USP i.e. AOAC or AOCS should be allowed.		Assigned to KL	Source One Global Partners
Anthony	Windust	NO	6.2.5.1.5 and 6.2.4	Agree with neg comments and CCV section requires revision	CCV's may or may not be applicable dependent on the mode of calibration e.g., using I.S. further "and/or at end of run" is imprecise wording. Further do not understand use of "recovery" in context of checking instrument calibration with, presumably, pure standards. In 6.2.4 "claims" should be qualified as quantitative to differentiate from e.g. health claims.		Assigned to KL	National Research Council Canada
Staci	Eisner	NO	6.2.5.1.1 - 6.2.5.1.5	data quality requirements	I can only comment from the perspective of the work in my own lab and in the independent labs whom I use; but the proposed data quality requirements seem rather loose to me. 6.2.5.1.1 R of 0.995 correponds to R2 of 0.990, which is rather low for chromatographic work (even with a manual injector). I personally prefer to see R2 > 0.995 and R > 0.997. But I guess it is ok. Not as egregious as some of the other proposals below. 6.2.5.1.2 Should single-level calibrations even be allowed? The better independent analytical labs that I know of use 3 to 5 point calibrations, and certainly the better manufacturer's labs do the same 6.2.5.1.3 A peak in the blank at 5% the response of the target analyte seems very large – this could lead to the analyte content being overstated by 5%, no? I personally prefer to see NMT 0.5% or even NMT 0.1%. Maybe that is not realistic for an independent lab's samples, but 5% seems too high to me. 6.2.5.1.4 a) Spike recovery of 70-130% may be ok for potency tests (however I would prefer to see 90-110% or at least 80-120%), but it is too tight fo	More discussion!!	Assigned to KL	BBS/Plusp harma

Allison McCutcheon	NO	6.2.4 and 6.2.5.1	Minor amendments	6.2.4 Other dietary supplement ingredients Should be amended to include quantification based upon bioactivity. For many DS the putative "active ingredients" have not been conclusively idenified, and in these cases quantification based on relevant bioactivity may be superior. In this context "micro-assays" would be better described as micro-chemical assays. 6.2.5.1 Calibration The term "certified reference materials" (CRMs) has a specific meaning and CRMs are not available for many DS. Suggest deleting the word "certified" or amending the wording to better reflect the intent. MINOR EDITORIAL QUIBLES 6.2.5.1.4 Reproducibility/accuracy Define "unfamiliar"? 6.2.1-6.2.4 Listing of other guidelines should be alphabetical, otherwise it implies an order of preference. 6.2.4 Insert word "pharmacopoeial"; I.e The source of these methods may include AOAC International, or AHP, European, German, Japanese, USP-NF etc. pharmacopoeial monographs. 6.2.5.1.5 Insert space between word acceptable and 80-120%		Assigned to KL	University of British Columbia