Notice of Draft Guideline for Comment

Draft Voluntary Guideline: Standardized Information on Dietary Ingredients (SIDI) Protocol

Summary: The SIDI Work Group is announcing an opportunity for comment on its draft voluntary guideline titled "Draft Voluntary Guideline: Standardized Information on Dietary Ingredients (SIDI) Protocol." This Guideline is being updated from a previous version published in 2008. The SIDI™ Protocol is intended to assist dietary ingredient suppliers in preparing information packages on dietary ingredients to provide to their customers (supplement manufacturers). The SIDI™ Protocol defines the type and scope of information that manufacturers typically seek from ingredient suppliers. The primary goal of the SIDI™ Protocol is to provide a standard format for the presenting dietary ingredient information in an efficient manner. This guideline will be an open access tool for the dietary supplement industry, when finalized. Template forms will be developed based on the final SIDI™ Protocol.

Dates: Submit written comments by **July 3, 2017**.

Comments: Interested persons are encouraged to submit comments to the SIDI Work Group by filling out the Comment Form. Comments must be submitted by e-mail to info@sidiworkgroup.com.

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Comment Form

Draft Voluntary Guideline: Standardized Information on Dietary Ingredients (SIDI) Protocol

Submitter information: Please provide the information below.

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Position/Title:	**Vice President, Dietary Supplements and Herbal Medicines**
Company/Organization:	**United States Pharmacopeial Convention**
Type of company/organization (supplier, manufacturer, distributor, association, etc):	**Scientific non-profit standards setting organization**

Comment: You are encouraged to focus your comments to address one or more of the questions listed below but all feedback is welcomed.

	Question	Comment
1	*Is the purpose of this document clear (i.e., to provide a standardized format for development of information packets or dossiers on dietary ingredients)? If not, what should be removed or added to make this clear?*	No concerns regarding clarity.
2	*Is the organization of the draft guideline appropriate? If not, what modification(s) is needed to the organization of the document?*	No concerns regarding the organization.
3	*Does the draft guideline make clear that dietary ingredient data sheets developed based on the SIDI Protocol are customizable?*	The guideline explicitly states, e.g., on p. 2, that it is customizable but publishing some examples with the guideline would help clarify this point.
4	*Does the draft guideline include the minimum type and scope of information that dietary supplement manufacturers need on dietary ingredients? If not, what other type(s) of information is needed?*	*In section A2 – please add* Method(s) of identification for the non-botanical starting material • Source of reference standard *In section A3and B3* – Method of analysis should also include a description of method validation or citation of a validated method such as a USP method.

		A3, Bullet 6 – Please Add "Adopt USP monograph or General Chapter methods where available" at the end of the sentence A3, please add Certificate of Analysis to the list of information required *Section B6* - No mention was made of retained samples, which are an important aspect of cGMPs. Explicit information in Part 2 of the retention of samples for future examination if needed would provide assurance for buyers in the event of a need for analysis associated with traceability and recall.
5	*Does the draft guideline recommend inclusion of information on dietary ingredients that are irrelevant or out of scope? If yes, what information should be removed?*	No concerns regarding relevance or scope.
6	*Are the terms used in the draft guideline adequately defined? If not, what specific terms need to be defined and what definitions would be appropriate?*	*Section A5* – The term pre-DSHEA status is not clear. There is currently no CFR reference or approved list of pre-DSHEA (grandfathered) ingredients. If the ingredient was in use pre-DSHEA, the evidence supporting that claim needs to be cited or provided Some specific comments on definitions in the glossary are provided below.
6	*Would firms be able to easily use the SIDI Protocol to develop their own dietary ingredient datasheets? What factors might impact the ability of firms to use the SIDI Protocol? Indicate how feasible it would be for firms to use the SIDI Protocol on a scale of 1 to 10 with 1 being highly unfeasible and 10 being extremely feasible.*	Yes, firms can easily use the SIDI Protocol to develop their own DIS. Time and qualified human resource availability to complete forms appropriately and systematically will impact ability of firms to use this protocol. Feasibility should generally be around 9.
7	*What are the appropriate methods for measuring usage of the SIDI Protocol by the dietary supplement industry?*	Setting up a training and mentoring program through industry umbrella groups, followed by periodic voluntary auditing, will allow measurement of usage and changes in usage over time. This evaluation needs to be made globally, especially in countries that export dietary ingredients to the US, e.g., China.
8	*Other comments: Please be certain to include a reference to the draft guideline section and sub-section as applicable.*	Please see the attached table.

Page	**Section**	**Comment**
	General Comment	The purpose of the SIDI format is to promote "exchange of relevant and required information between ingredient suppliers and dietary supplement manufacturers." It is a good attempt to list common requirements between ingredient suppliers and DS manufacturers. The protocol provides a checklist of the desirable topics, but it does not identify the minimum expectation that the methods should be scientifically valid. Without this minimum expectation, the checklist cannot achieve its stated purpose to help buyers and sellers communicate clearly or to meet the DS cGMP requirements for specifications (the identity, purity, strength, composition, and limits on potential

		contaminants). If the method cited references the supplier's in-house method, the supplier needs to indicate whether or not the method had been properly validated. The majority of FDA GMP warning letters are related to specifications, because either they are not set or because they are deficient (such as the use of particle size, pH or color for the ID test). The protocol could be strengthened by making reference to USP monographs, USP General Chapters (such as <1225> *Validation of Compendial Procedures*), and guidelines (such as nomenclature guidelines).
	A.3, B.3	The CAS number is used as the identifier -- CAS numbers can be ambiguous; there are better codes such as the FDA UNII (Unique Ingredient Identifier) which could be used as an alternative. In addition, to ensure clear communication, use of the USP compendial names for ingredients produced or sold for US use is recommended. If there is no compendial name, USP nomenclature guidelines and General Chapter <1121> *Nomenclature* provide guidance. Also in these sections, USP specifications can be provided if the product meets USP requirements.
z	A.5, B. 5	Should GE status be listed as GE/GMO status since GMO is the more common term and is used outside of the US?
5	A.6	For safety information, in addition to safety studies and history of use, safety evaluations in the USP Dietary Supplements Compendium could provide useful information.
6	B.1	It is not clear why the International Code is cited here. This source provides information about the genus, species and author but it would not be as useful to industry as, for example, sources to verify the correct Latin binomial and author (not "authority"). Suggest the following: "Latin binomial (genus and specific epithet) and its author (if not in *Herbs of Commerce*, see *Kew Medicinal Plant Names Services* at http://mpns.kew.org/mpns-portal/); variety or strain, if applicable". Part of the plant used should also be identified. Depending on the nature of the extract, and the concentration of major constituents, the appropriate nomenclature is very important for communication between the buyer and the seller. USP nomenclature guidelines could be used to appropriately label the ingredients. USP General Chapters *<561> Articles of Botanical Origin*, *<563> Identification of Articles of Botanical Origin*, and *<565> Botanical Extracts* could be consulted.
7	B.2	We propose an alternative to "List known or potential economically motivated adulterants". First, there is an evolving list of such substances; and second, no entity should sell a product with a known adulterant. Instead, it would be more helpful to state "List potential economically motivated adulterants and the steps taken to ensure they are not present. Contaminants should be tested on risk-based approach and quantitated to limit the levels. USP General Chapters provide the methods and limits for these contaminants."
7	B.2	If the botanical ingredient is subject to trade restrictions such as listing on one of the Appendices to the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), then information and supporting evidence should be provided regarding relevant permits and certificates establishing that the sourcing of the ingredient is compliant with the requirements of the Convention. See https://www.cites.org/ and https://www.fws.gov/international/cites/.
7	B.3	Part 1 – B relates to botanical dietary ingredients, and the information in B.3 should not just be cut from A.3 and pasted here; instead we recommend copying from B.1. For example, the common or usual name should refer, as in B.1, to *Herbs of Commerce* and not FD&C colors, repeat correction for Latin binomial and author, probiotics are not botanicals so delete ref to CFU, etc.
8	B.3	Some physical parameters such as pH are useful only in the finished product with

		regard to the likelihood for growth of food-borne pathogens. Most bioassay methods, while potentially useful, have not been adequately standardized and validated for botanical ingredients. A reference to the USP monograph approach for identity, purity and strength would be useful here. For botanical ingredients, as per USP General Chapter <561> *Articles of Botanical Origin* and WHO (2011) *Quality Control Methods for Herbal Materials*, ash values should be retained as they help in the determination of foreign matter such as sand and soil. The total ash method is designed to measure the total amount of material remaining after ignition. This includes both "physiological ash", which is derived from the plant tissue itself, and "non-physiological" ash, which is the residue of the extraneous matter (e.g. sand and soil) adhering to the plant surface. Acid-insoluble ash is the residue obtained after boiling the total ash with dilute hydrochloric acid, and igniting the remaining insoluble matter. This measures the amount of silica present, especially as sand and siliceous earth. Water-soluble ash is the difference in weight between the total ash and the residue after treatment of the total ash with water.
16	Glossary	Extract ratio: a couple of examples would help to clarify that the quantity of botanical raw material should always be the first number and the quantity of the extract the second number in the ratio. "For example, for a liquid extract, a ratio of 1:5 means that 1 g of botanical raw material was used to prepare 5 mL of liquid extract; for a solid extract, a ratio of 5:1 means that 5 g of botanical raw material was used to prepare 1g of solid extract."
19	Glossary	Organic solvent: It would be more accurate to state "but most are manufactured synthetically (e.g., acetone, hexane, methanol)." Acetone occurs naturally in plants and animals, methanol is produced by bacteria, and hexane occurs naturally as a component of petroleum.