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NSF International Standard for Dietary Supplements —

Dietary supplements

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5.3.4 **Aristolochic acid**~~Natural toxins~~

Raw materials and finished products shall not contain botanicals in the Aristolochiaceae family (e.g., species in the following genera: *Aristolochia*; *Asarum*; *Asiphonia*; *Hexastylis*; *Thottea*; etc.) unless such materials or products are confirmed to be free of aristolochic acid at a limit of detection of 0.5 ppm.

Raw materials and finished products containing any botanicals listed in Annex A shall be confirmed to be free of aristolochic acid at the above-stated limit of detection according to 7.4 ~~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 tetrandia* shall not contain *Aristolochia fangchi*.~~

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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~~ AOAC Official Method 2007.05, Aristolochic Acid I in Botanicals and Dietary Supplements Potentially Contaminated with Aristolochic Acid I (LC-UV with Confirmation by LC/MS), a modification of this method or another scientifically valid method which has been shown to be fit for purpose for the particular sample matrix being tested.

Sources for methods may include AOAC International, AHP, USP and other compendial methods. An existing method may need to be modified to better suit the sample under test or improved technology may allow for a more accurate and precise method to be developed. The use of any modified or new method shall require that an assessment be performed which

includes evaluation of the specificity, linearity, reproducibility, accuracy, spike recovery, and method detection limit.

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.

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Annex A (normative)

Table A1 List of botanicals known or suspected to contain which require testing for aristolochic acid¹

† <i>Aristolochia</i> spp. spp.	† <i>Asarum splendens</i>
† <i>Aristolochia acuminata</i>	† <i>Asarum</i> <i>Asaum</i> <i>forbesii</i>
† <i>Aristolochia argentina</i>	† <i>Asarum heterotropoides</i> <i>heterotrpoides</i>
† <i>Aristolochia baetica</i>	† <i>Asarum sieboldii</i>
† <i>Aristolochia bracteata</i>	<i>Akebia</i> spp. spp.
† <i>Aristolochia chilensis</i>	* <i>Akebia quinata</i>
† <i>Aristolochia cinnabarina</i>	* <i>Akebia trifoliata trifoliata</i>
† <i>Aristolochia clematidis</i>	† <i>Thottea siliquosa</i> (syn. <i>Bragantia wallichii</i>)
† <i>Aristolochia contorta</i>	<i>Clematis</i> spp. spp.
† <i>Aristolochia cymbifera</i>	* <i>Clematis armandii</i>
† <i>Aristolochia debilis</i>	* <i>Clematis chinensis</i>
† <i>Aristolochia elegans</i>	* <i>Clematis hexapetala</i>
† <i>Aristolochia esperanzae</i>	* <i>Clematis terniflora</i> var. <i>mandshurica</i>
† <i>Aristolochia fangchi</i>	* <i>Clematis montana</i>
† <i>Aristolochia fimbriata</i>	<i>Clematis uncinata</i>
† <i>Aristolochia indica</i>	<i>Cocculus</i> spp. spp.
† <i>Aristolochia kaempferi</i>	<i>Cocculus carolinus</i>
† <i>Aristolochia kwangsiensis</i>	<i>Cocculus diversifolius</i>
† <i>Aristolochia macrophylla</i>	<i>Cocculus hirsutus</i>
† <i>Aristolochia manshuriensis</i> <i>manschuriensis</i>	<i>Cocculus indicus</i>

¹ The source of this table is *FDA Alert: Aristolochic Acid: Listing of Botanical Ingredients of Concern* <<http://www.fda.gov/Food/DietarySupplements/Alerts/ucm095283.htm>>. The lists provided by FDA have been revised where needed for taxonomic accuracy. One additional species, *Clematis terniflora* var. *mandshurica*, is included here as it, along with *C. chinensis* and *C. hexapetala*, is an acceptable source of Radix et Rhizoma Clematidis (Chinese Pharmacopoeia Commission. *Pharmacopoeia of the People's Republic of China*, Volume I. Beijing: People's Medical Publishing House. 2005. Listed as *C. manshurica*). an April 19, 2004 U.S. FDA correspondence from the Office of Nutritional Products, Labeling and Dietary Supplements (www.cfsan.fda.gov/~lrm/dms/dc-bot14.html)

† <i>Aristolochia maurorum</i>	<i>Cocculus laurifolius</i>
† <i>Aristolochia maxima</i>	<i>Cocculus leaeba leaeba</i>
† <i>Aristolochia mollissima</i>	<i>Cocculus madagascariensis</i>
† <i>Aristolochia pistolochia</i>	* <i>Cocculus orbiculatus</i> (syn. <i>C. trilobus</i>)
† <i>Aristolochia rigida</i>	<i>Cocculus palmatus</i>
† <i>Aristolochia rotunda</i>	<i>Cocculus pendulus</i>
† <i>Aristolochia serpentaria</i>	<i>Cocculus thunbergii</i>
† <i>Aristolochia watsoni</i>	<i>Diploclisia affinis</i> (syn. <i>D. chinensis</i>)
† <i>Aristolochia watsonii</i>	<i>Diploclisia chinensis</i>
<i>Aristolochia westlandi</i>	<i>Menispermum</i> <i>Menispermum dauricum</i>
† <i>Aristolochia westlandii</i>	* <i>Saussurea costus</i> (syn. <i>S. lappa</i>) <i>lappa</i>
† <i>Aristolochia zollingeriana</i>	<i>Sinomenium acutum</i> (syn. <i>Cocculus diversifolius</i>)
† <i>Asarum canadense</i>	<i>Stephania</i> spp. spp.
† <i>Asarum himalaicum</i> <i>himalacium</i>	* <i>Stephania tetrandra</i>
<i>Asarum himalaycum</i>	* <i>Vladimiria souliei</i>

NOTE - The potential for aristolochic acid contamination in an herb listed in this table is highly variable. Those marked with a dagger symbol (†) are species in the Aristolochiaceae family and should be assumed to contain aristolochic acid unless scientifically valid analysis shows otherwise. Authoritative references (e.g., Upton R., *Characterization of selected plants that may contain or be adulterated with aristolochic acid*. Scotts Valley: American Herbal Pharmacopoeia, 2006) have confirmed that those marked with an asterisk(*) have some history of substitution with one or another species of *Aristolochia*. All other listed taxa are included here because they have been identified by FDA as “botanicals which may be adulterated with aristolochic acid,” but may not be likely to contain this contaminant. The specific contamination and adulteration risk factors that apply in a certain situation should be considered in the development of specifications according to good manufacturing practices.

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