

AHPA Guidance Policy

AHPA develops guidance policies to promote responsible commerce in herbal supplements. These policies address a variety of labeling and manufacturing issues and reflect the consensus of AHPA's members and its board of trustees. AHPA encourages its members and non-member companies to adopt these policies to establish consistent and informed trade practices.

Residual Solvents in Extracts (adopted October 2010, revised July 2011)

AHPA recommends that herbal extracts marketed in the U.S. limit any contained residual solvents to the levels established by the current International Conference on Harmonization's (ICH's) document, [Impurities: Guideline for Residual Solvents](#), except that this guidance does not apply to the ICH limit of 50 mg per day for the class 3 solvent ethanol when it is present in liquid extracts formulated to contain ethanol, or for the class 3 solvent acetic acid when it is present in liquid extracts formulated to contain acetic acid or vinegar.

With regard to this guidance, solvents identified in the cited ICH document as class 1 solvents (benzene;* carbon tetrachloride;* 1,2-dichloroethane;* 1,1-dichloroethene; and 1,1,1-trichloroethane), which are considered by ICH as unacceptably toxic or an environmental hazard, are not appropriate for use, and should not be used, in the manufacture of herbal extracts.

With regard to this guidance, solvents identified in the cited ICH document as class 2 solvents, which are considered by ICH to be inherently toxic, are listed in the table below with the ICH recommended upper limits for Permissible Daily Exposures (PDE) and concentration limits given in ppm assuming a 10 gram daily dose.

<i>Class 2 Solvent</i>	<i>PDE (mg/day)</i>	<i>limit (ppm)</i>
Acetonitrile	4.1	410
Chlorobenzene	3.6	360
Chloroform*	0.6	60
Cyclohexane	38.8	3880
1,2-Dichloroethene	18.7	1870
Dichloromethane*	6.0	600
1,2-Dimethoxyethane	1.0	100
N,N-Dimethylacetamide*	10.9	1090
N,N-Dimethylformamide	8.8	880
1,4-Dioxane*	3.8	380
2-Ethoxyethanol	1.6	160
Ethyleneglycol	6.2	620
Formamide	2.2	220
Hexane	2.9	290
Methanol	30.0	3000
2-Methoxyethanol	0.5	50
Methylbutyl ketone*	0.5	50
Methylcyclohexane	11.8	1180
N-Methylpyrrolidone*	5.3	530
Nitromethane*	0.5	50
Pyridine*	2.0	200
Sulfolane	1.6	160
Tetrahydrofuran	7.2	720
Tetralin	1.0	100
Toluene*	8.9	890
1,1,2-Trichloroethene	0.8	80
Xylene	21.7	2170

With regard to this guidance, solvents identified in the cited ICH document as class 3 solvents, which are considered by ICH as having low toxic potential, should be limited to 50 mg/day,[†] which equates to 5000 ppm or 0.5% in 10 grams. Their use should be limited by good manufacturing practice (GMP) or other quality based requirements. They are identified as the following:

Class 3 Solvents

Acetic acid	Ethanol*	3-Methyl-1-butanol
Acetone	Ethyl acetate	Methylethyl ketone
Anisole	Ethyl ether	Methylisobutyl ketone
1-Butanol	Ethyl formate	2-Methyl-1-propanol
2-Butanol	Formic acid	Pentane
Butyl acetate	Heptane	1-Pentanol
tert-Butylmethyl ether	Isobutyl acetate	1-Propanol
Cumene*	Isopropyl acetate	2-Propanol
Dimethyl sulfoxide	Methyl acetate	Propyl acetate

†This limit does not apply for ethanol when it is present in liquid extracts formulated to contain ethanol or for acetic acid when it is present in liquid extracts formulated to contain acetic acid or vinegar.

Adherence to this AHPA guidance does not infer compliance with California Proposition 65. Several of these solvents are listed by the State of California as chemicals known to the State to cause cancer or reproductive toxicity, including, as of the date of the last revision of this guidance, at least those solvents marked with an asterisk (*). The listing of ethanol with regard to California Proposition 65 refers only to its presence in alcoholic beverages.