

NATURAL HEALTH PRODUCT

COGNITIVE FUNCTION PRODUCTS

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLAs) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredients described within.

Notes

- ▶ Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion.
- ▶ The solidus (/) indicates that the terms and/or the statements are synonymous. Either term or statement may be selected by the applicant.

Date

August 16, 2017

Proper name(s), Common name(s), and Source material(s)

Table 1 Proper names, common names and source materials of medicinal ingredients

Proper name(s) ¹	Common name(s) ¹	Source material(s) ²
Group 1: Ingredients with nervine action		
<i>Avena sativa</i>	<ul style="list-style-type: none"> • Common oat • Oat 	Seed
<i>Nepeta cataria</i>	<ul style="list-style-type: none"> • Catmint • Catnip 	As per NNHPD Catnip monograph
<i>Pulsatilla vulgaris</i>	<ul style="list-style-type: none"> • European pasqueflower • Pasqueflower • Pulsatilla 	Dried herb top *Do not use the fresh plant
<i>Tilia cordata</i>	<ul style="list-style-type: none"> • Linden • Small-leaf linden • Tilia 	As per NNHPD Small-leaf linden monograph
<i>Tilia platyphyllos</i>	<ul style="list-style-type: none"> • Large-leaf linden • Linden • Tilia 	As per NNHPD Large-leaf linden monograph
<i>Tilia x europaea</i>	<ul style="list-style-type: none"> • European linden • Linden • Tilia 	As per NNHPD European linden monograph
<i>Turnera diffusa</i>	Damiana	<ul style="list-style-type: none"> • Leaf • Leaf and stem



<i>Withania somnifera</i>	<ul style="list-style-type: none"> • Asgandh • Ashwagandha • Asvagandha • Winter-cherry • Withania 	As per NNHPD Ashwagandha monograph
Group 2: Ingredients with sedative action		
<i>Eschscholzia californica</i>	California poppy	As per NNHPD California poppy monograph
<i>Humulus lupulus</i>	Hops	As per NNHPD Hops monograph
<i>Hypericum perforatum</i>	<ul style="list-style-type: none"> • Hypericum • St. John's wort 	As per NNHPD St John's wort monograph
L-5-Hydroxytryptophan/ 5-Hydroxy-L-tryptophan	<ul style="list-style-type: none"> • L-5-HTP • L-5-Hydroxytryptophan 	As per NNHPD 5-HTP monograph
<i>Matricaria chamomilla</i>	<ul style="list-style-type: none"> • Chamomile • German chamomile 	As per NNHPD German Chamomile-Oral Monograph
<i>Melissa officinalis</i>	<ul style="list-style-type: none"> • Lemon balm • Melissa 	As per NNHPD Lemon balm monograph.
<i>Panax quinquefolius</i>	American ginseng	As per NNHPD American ginseng monograph
<i>Passiflora incarnata</i>	Passionflower	As per NNHPD Passionflower monograph
<i>Scutellaria lateriflora</i>	<ul style="list-style-type: none"> • Scullcap • Skullcap 	As per NNHPD Skullcap monograph
<i>Stachys officinalis</i>	<ul style="list-style-type: none"> • Bishop's-wort • Purple betony • Wood betony 	Herb top
<i>Valeriana officinalis</i>	<ul style="list-style-type: none"> • Garden valerian • Valerian 	As per NNHPD Valerian monograph
<i>Withania somnifera</i>	<ul style="list-style-type: none"> • Asgandh • Ashwagandha • Asvagandha • Winter-cherry • Withania 	As per NNHPD Ashwagandha monograph
Group 3: Ingredients with cognitive support action		
(2R)-2-(Acetyloxy)-3-carboxy-N,N,N-trimethyl-1-propanaminium	Acetylcarnitine	<ul style="list-style-type: none"> • N-Acetyl L-carnitine hydrochloride

inner salt		<ul style="list-style-type: none"> • Acetyl-L-carnitine arginate dihydrochloride
<i>Schizochytrium spp.</i>	Schizochytrium Oil	<i>Schizochytrium spp.</i>
<i>Bacopa monnieri</i>	<ul style="list-style-type: none"> • Bacopa • Moneywort • Water hyssop 	Herb top
Cod liver oil	Cod liver oil	As per NNHPD Cod liver oil monograph
<i>Eleutherococcus senticosus</i>	<ul style="list-style-type: none"> • Eleuthero • Siberian ginseng 	As per NNHPD Eleuthero monograph
Fish oil	Fish oil	As per NNHPD Fish oil monograph
<i>Ginkgo biloba</i>	<ul style="list-style-type: none"> • Ginkgo • Ginkgo biloba • Maidenhair tree 	As per NNHPD Ginkgo biloba monograph
L-alpha-Glycerolphosphorylcholine/ 2-[[[(2R)-2,3-Dihydroxypropoxy]hydroxyphosphinyl]oxy]-N,N,N-trimethylethanaminium hydroxide inner salt/ d-Choline hydroxide 2,3-dihydroxypropyl hydrogen phosphate inner salt	Choline alfoscerate	Choline alfoscerate
<i>Panax ginseng</i>	<ul style="list-style-type: none"> • Asian ginseng • Chinese ginseng • Hong shen • Korean (red) ginseng • Oriental ginseng • Panax ginseng • Red ginseng • Renshen 	As per NNHPD Panax ginseng monograph
Phosphatidylserine	Phosphatidylserine	As per NNHPD Phosphatidylserine AbLS
<i>Rhodiola rosea</i>	<ul style="list-style-type: none"> • Rhodiola • Roseroot 	As per NNHPD Rhodiola rosea monograph
Group 4: Caffeine/Ingredients containing caffeine		
1,3,7-trimethylxanthine/ 3,7-Dihydro-1,3,7-trimethyl-1H-purine-2,6-dione	Caffeine	As per NNHPD Caffeine monograph
<i>Ilex paraguariensis</i>	<ul style="list-style-type: none"> • Brazilian tea • Mate 	Leaf



	<ul style="list-style-type: none"> • Paraguayan tea • Paraguay tea • St Bartholomew's tea • Yerba mate 	
<i>Paullinia cupana</i>	Guarana	Seed
Group 5: Ingredients with action on cognitive fatigue		
L-Tyrosine	<ul style="list-style-type: none"> • L-Tyrosine • Tyrosine 	As per NNHPD L-Tyrosine monograph
Group 6: Ingredients with action on memory		
<i>Bacopa monnieri</i>	<ul style="list-style-type: none"> • Bacopa • Moneywort • Water hyssop 	<ul style="list-style-type: none"> • Whole plant • Herb top
<i>Withania somnifera</i>	<ul style="list-style-type: none"> • Asgandh • Ashwagandha • Asvagandha • Winter-cherry • Withania 	As per NNHPD Ashwagandha monograph
Group 7: Ingredients with relaxation action		
Gamma-Aminobutyric acid	<ul style="list-style-type: none"> • GABA • gamma-Aminobutyric acid 	Glutamic acid
L-Theanine/ N-Ethyl-L-glutamine	L-Theanine	As per NNHPD L-Theanine AbLS
Group 8: Ingredients with adaptogen action		
<i>Asparagus racemosus</i>	<ul style="list-style-type: none"> • Shatamuli • Shatavari 	Root
<i>Astragalus membranaceus</i>	<ul style="list-style-type: none"> • Astragalus • Membranaceus milk vetch • Milk vetch root 	As per NNHPD Astragalus Monograph
<i>Eleutherococcus senticosus</i>	<ul style="list-style-type: none"> • Eleuthero • Siberian ginseng 	<ul style="list-style-type: none"> • Root • Root and rhizome • Root and stem bark
<i>Ganoderma lucidum</i>	<ul style="list-style-type: none"> • Ganoderma • Reishi 	As per NNHPD Reishi monograph
<i>Glycyrrhiza glabra</i>	Licorice	<ul style="list-style-type: none"> • Root

		<ul style="list-style-type: none"> • Root and stolon
<i>Ocimum tenuiflorum</i>	<ul style="list-style-type: none"> • Holy basil • Sacred basil • Tulsi • Tulasi 	As per NNHPD Holy basil-Leaf monograph
<i>Panax ginseng</i>	<ul style="list-style-type: none"> • Asian ginseng • Chinese ginseng • Hong shen • Korean (red) ginseng • Oriental ginseng • Panax ginseng • Red ginseng • Renshen 	As per NNHPD Panax ginseng monograph
<i>Panax quinquefolius</i>	<ul style="list-style-type: none"> • American ginseng • Occidental ginseng • Sang • Shang • Xi yang shen 	<ul style="list-style-type: none"> • Root • Root and leaf
<i>Rhodiola rosea</i>	<ul style="list-style-type: none"> • Rhodiola • Roseroot 	As per NNHPD Rhodiola rosea monograph
<i>Schisandra chinensis</i>	<ul style="list-style-type: none"> • Chinese magnoliavine • Schisandra • Wu wei zi 	Fruit
<i>Tinospora cordifolia</i>	Guduchi	<ul style="list-style-type: none"> • Stem • Stem and root • Stem, root and leaves
<i>Withania somnifera</i>	<ul style="list-style-type: none"> • Asgandh • Ashwagandha • Asvagandha • Winter-cherry • Withania 	<ul style="list-style-type: none"> • Root • Whole plant

¹ Proper names and common names: NHPID: Natural Health Products Ingredient Database

² Source materials: Group 1: At least two of the following references were consulted per source material: Bone 2003; Hoffman 2003; Bradley 1992; Williamson et al. 1988; BHP 1983; Remington and Wood 1918; BPC 1911.

Group 2: The following two references were consulted per source material: Hoffman 2003; Williamson et al. 1988.

Group 3: At least one of the following references was consulted per source material: Yurko-Mauro et al. 2010; Calabrese et al. 2008; Bone 2003; De Jesus Moreno Moreno 2003; Parnetti et al. 2001; Barbagallo et al. 1994; Parnetti et al. 1993; Canal et al. 1991.

Group 4: At least three of the following references were consulted per source material: EMA 2013; ESCOP 2009; Bradley 2006; Kennedy et al. 2004; Taylor 2003; Barnes et al. 2002; BHP 1983.

Group 6: At least one of the following references was consulted per source material: Bone 2003; API 2001.

Group 7: The following four references were consulted per source material: Kanehira et al. 2011; Abdou et al. 2006; Yamakoshi et al. 2006; NHPID: Natural Health Products Ingredient Database.

Group 8: At least one of the following references was consulted per source material: Upton 2012; Winston and Kuhn 2008; Winston and Maimes 2007; WHO 2004; Bone 2003; Hoffman 2003; Thomsen 2002; Williamson 2002; Blumenthal et al. 2000; Upton 1999a; WHO 1999; Bradley 1992; BHP 1983.



Route of administration

Oral

Dosage form(s)

- ▶ The acceptable pharmaceutical dosage forms include, but are not limited to capsules, chewables (e.g., gummies, tablets), gels, liquids, powders, strips or tablets.
- ▶ This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s) and doses

Subpopulation

Adults (≥ 18 years)

Quantity(ies)

Refer to Table 2 below.

Table 2 Cognitive function use or purpose statements and associated daily doses

Use or Purpose ¹	Medicinal Ingredient	Dose ²
Group 1: Ingredients with nervine action		
Traditionally used in Herbal Medicine as a nervine to help relieve nervousness and restlessness	<i>Avena sativa</i> (Oat)	Preparation: Powdered, fluid extract, tincture 0.6-20 g dried seed per day
	<i>Nepeta cataria</i> (Catnip)	As per NNHPD Catnip monograph
	<i>Pulsatilla vulgaris</i> (Pasqueflower)	Preparation: Powdered, fluid extract, tincture 0.03-0.6 g dried plant per day Preparation: Decoction/infusion 0.1-0.9 g dried plant per day *Note: Do not use the fresh plant

	<i>Tilia cordata</i> (Small-leaf linden)	As per NNHPD Small-leaf linden monograph
	<i>Tilia platyphyllos</i> (Large-leaf linden)	As per NNHPD Large-leaf linden monograph
	<i>Tilia x europea</i> (European Linden)	As per NNHPD European linden monograph
	<i>Turnera diffusa</i> (Damiana)	Preparation: Powdered, fluid extract, tincture 1.5-4 g dried leaf per day
Traditionally used in Ayurveda to balance aggravated Vata (nervine tonic, sedative)	<i>Withania somnifera</i> (Ashwagandha)	As per NNHPD Ashwagandha monograph
Group 2: Ingredients with sedative action		
Traditionally used in Herbal Medicine to help relieve nervousness (sedative and/or calmative) OR Traditionally used in Herbal Medicine as a sleep aid (in cases of restlessness or insomnia due to mental stress)	<i>Eschscholzia californica</i> (California poppy)	As per NNHPD California poppy monograph
	<i>Humulus lupulus</i> (Hops)	As per NNHPD Hops monograph
	<i>Hypericum perforatum</i> (St John's wort)	As per NNHPD St John's wort monograph
	<i>Matricaria chamomilla</i> (German chamomile)	As per NNHPD German chamomile-Oral monograph
	<i>Melissa officinalis</i> (Lemon balm)	As per NNHPD Lemon balm monograph
	<i>Panax quinquefolius</i> (American ginseng)	As per NNHPD American ginseng monograph
	<i>Passiflora incarnata</i> (Passionflower)	As per NNHPD Passionflower monograph
	<i>Scutellaria lateriflora</i> (Skullcap)	As per NNHPD Skullcap monograph
	<i>Stachys officinalis</i>	Preparation: Powdered, fluid extract, tincture

	(Wood betony)	2-4 g dried plant per day
	<i>Valeriana officinalis</i> (Valerian)	As per NNHPD Valerian monograph
Used in Herbal Medicine as a sleep aid and/or to help relieve restlessness and/or nervousness (sedative and/or calmative)	<i>Matricaria chamomilla</i> (German chamomile)	As per NNHPD German chamomile-Oral monograph
	<i>Panax quinquefolius</i> (American ginseng)	As per NNHPD American ginseng monograph
Used as a sleep aid and/or helps to relieve nervousness (calmative/sedative)	L-5-Hydroxytryptophan (L-5-HTP)	As per NNHPD 5-HTP monograph
	<i>Valeriana officinalis</i> (Valerian)	As per NNHPD Valerian monograph
Traditionally used in Ayurveda as a sleep aid and/or to balance aggravated Vata (nervine tonic, sedative)	<i>Withania somnifera</i> (Ashwagandha)	As per NNHPD Ashwagandha monograph
Group 3: Ingredients with cognitive support action		
Helps to support cognitive health and/or brain function	Acetyl-L-Carnitine (Acetylcarnitine)	1.5- 4 g per day
	Schizochytrium oil	200-2000 mg DHA per day
	<i>Bacopa monnieri</i> (Bacopa)	Preparation: Standardised extract 300 mg extract per day, standardized to 40-55% bacosides
	Cod liver oil	As per NNHPD Cod liver oil monograph
	Fish oil	As per NNHPD Fish oil monograph
	L-alpha-Glycerophosphorylcholine (Choline alfoscerate)	1.2 g per day
	Phosphatidylserine	As per NNHPD Phosphatidylserine AbLS
Used in Herbal Medicine to help improve mental performance after periods of mental exertion	<i>Eleutherococcus senticosus</i> (Eleuthero)	As per NNHPD Eleuthero monograph

Helps to enhance cognitive function and/or memory in adults	<i>Ginkgo biloba</i> (Ginkgo)	As per NNHPD Ginkgo biloba monograph
(Used in Herbal Medicine to) help(s) support cognitive function and/or reduce mental fatigue (in cases of mental stress)	<i>Panax ginseng</i> (Panax ginseng)	As per NNHPD Panax Ginseng monograph
	<i>Rhodiola rosea</i> (Rhodiola)	As per NNHPD Rhodiola monograph
Group 4: Caffeine/Ingredients containing caffeine		
Helps to temporarily promote alertness and wakefulness, and to enhance cognitive performance Helps (temporarily) to relieve fatigue	1,3,7-trimethylxanthine (Caffeine)	100-400 mg per day, not to exceed 200 mg per single dose *Note: A maximum daily dose of 1000 mg from the NNHPD Caffeine monograph does not apply for the Cognitive Monograph as this maximum dose is not acceptable for prolonged use and this may conflict with other ingredient requirements.
	<i>Ilex paraguariensis</i> (Yerba mate)	Preparation: Powdered, fluid extract, tincture, decoction, infusion Up to 6 g dried leaf per day providing at least 100 mg caffeine per single dose and up to 150 mg caffeine per day *Note: This ingredient must be standardized to caffeine
	<i>Paullinia cupana</i> (Guarana)	Preparation: Powdered, fluid extract, tincture Up to 3 g dried seed per day, providing at least 100 mg caffeine per single dose and up to 200 mg caffeine per day *Note: This ingredient must be standardized to caffeine
Used in Herbal Medicine to help temporarily promote alertness and wakefulness, and to enhance cognitive performance	<i>Ilex paraguariensis</i> (Yerba mate)	Preparation: Powdered, fluid extract, tincture 3-6 g dried leaf per day, not to exceed 150 mg caffeine per day Decoction, infusion: 2-6 g dried leaf per day, not to

		exceed 150 mg caffeine per day
	<i>Paullinia cupana</i> (Guarana)	Preparation: Powdered, fluid extract, tincture 1-3 g dried seed per day, not to exceed 200 mg caffeine per day
Group 5: Ingredients with action on cognitive fatigue		
Helps to decrease cognitive fatigue due to physically stressful situations (e.g. extended wakefulness, exposure to cold, excessive noise)	L-Tyrosine	As per NNHPD L-Tyrosine monograph
Group 6: Ingredients with action on memory		
Traditionally used in Ayurveda for memory enhancement	<i>Bacopa monnieri</i> (Bacopa)	Preparation: Powdered, fluid extract, tincture 1-6.5 g dried plant per day
	<i>Withania somnifera</i> (Ashwagandha)	As per NNHPD Ashwagandha monograph
Helps support memory	<i>Bacopa monnieri</i> (Bacopa)	Preparation: Standardised extract 300 mg extract per day of dried whole plant, standardized to 40-55% bacosides
Group 7: Ingredients with relaxation action		
Helps to temporarily promote relaxation	Gamma-Aminobutyric acid (GABA)	50-750 mg per single dose, not to exceed 3000 mg per day
	L-Theanine	As per NNHPD L-Theanine AbLS
Group 8: Ingredients with adaptogen action		
Used in Herbal Medicine as an Adaptogen to help increase energy and resistance to stress (e.g. in case of mental and physical fatigue related to stress)	<i>Asparagus racemosus</i> (Shatavari)	Preparation: Powdered, fluid extract, tincture 2-6 g dried root per day



	<i>Astragalus membranaceus</i> (Astragalus)	Preparation: Powdered, fluid extract, tincture 2.3-4.8 g dried root per day
	<i>Eleutherococcus senticosus</i> (Eleuthero)	Preparation: Powdered, fluid extract, tincture 1-6 g dried root per day Preparation: Decoction, infusion 2-3 g dried root in 150 ml of water
	<i>Ganoderma lucidum</i> (Reishi)	As per NNHPD Reishi monograph
	<i>Glycyrrhiza glabra</i> (Licorice)	Preparation: Powdered, fluid extract, tincture 0.6-6 g dried root per day
	<i>Ocimum tenuiflorum</i> (Holy basil)	As per NNHPD Holy Basil-Leaf monograph
	<i>Panax ginseng</i>	Preparation: Powdered, fluid extract, tincture 0.5-3 g dried root per day Preparation: Decoction, infusion 0.5-2 g dried root per day
	<i>Panax quinquefolius</i> (American ginseng)	Preparation: Powdered, fluid extract, tincture 1-3 g dried root per day Preparation: Decoction, infusion 1-2 tsp. dried cut/sifted root to 360 ml water. Taken in divided doses (120ml) 3 times per day.
	<i>Rhodiola rosea</i> (Rhodiola)	As per NNHPD Rhodiola monograph.
	<i>Schisandra chinensis</i> (Schisandra)	Preparation: Powdered, fluid extract, tincture 1.2-6 g dried fruit per day Preparation: Decoction, infusion 1.5-6 g dried fruit per day
	Guduchi	Preparation: Powdered, fluid extract, tincture 0.9- 3 g dried plant per day

		Preparation: Decoction 20-30 g dried stem per day
	<i>Withania somnifera</i> (Ashwagandha)	Preparation: Powdered, fluid extract, tincture 2.5-6.5 g dried root per day
(Used as an Adaptogen) (to help(s) (to) temporarily relieve symptoms of stress (such as mental fatigue and sensation of weakness))	<i>Rhodiola rosea</i> (Rhodiola)	As per NNHPD Rhodiola monograph
Traditionally used in Ayurveda as Rasayana (rejuvenative tonic)	<i>Asparagus racemosus</i> (Shatavari)	Preparation: Powdered, fluid extract, tincture 3-6 g dried root per day
<p>¹ Uses or Purposes: Group 1: At least two of the following references were consulted per use or purpose: Bone 2003; Hoffman 2003; Ellingwood 1983; Felter and Lloyd 1983; Grieve 1971. Group 2: The following two references were consulted per use or purpose: Toby et al. 2010; Williamson et al. 1988. Group 3: At least one of the following references was consulted per use or purpose: Morgan and Stevens 2010; Yurko-Mauro et al. 2010; Calabrese et al. 2008; Malaguanera et al. 2008; De Jesus Moreno Moreno 2003; Parnetti et al. 2001; Stough et al. 2001; Thal et al. 2000; Barbagallo et al. 1994; Pettegrew et al. 1994; Parnetti et al. 1993; Sano et al. 1992; Canal et al. 1991; Spagnoli et al. 1991. Group 4: At least three of the following references were consulted per use or purpose: EMA 2013; EMA 2010; ESCOP 2009; Bradley 2006; Christopher et al. 2005; Kennedy et al. 2004; Taylor 2003; Barnes et al. 2002; Kamimori et al. 2000; Zwyghuizen-Doorenbos et al. 1990. Group 6: The following two references were consulted per use or purpose: Murthy 2004; API 2001. Barbhaiya et al. 2008; Raghav et al. 2006; Roodenrys et al. 2002; Stough et al. 2008. Group 7: The following two references were consulted per use or purpose: Kanehira et al. 2011; Abdou et al. 2006. Group 8: At least two of the following references were consulted per use or purpose: API 2004; Upton 2012; Winston and Maimes 2007; Mills and Bone 2005; WHO 2004; Bone 2003; Hoffman 2003; Thomsen 2002; Williamson 2002; Blumenthal et al. 2000; Upton 1999a; WHO 1999; Bradley 1992.</p> <p>² Doses: Group 1: At least two of the following references were consulted per daily dose: CNF 2012; Bone 2003; Hoffman 2003; Bradley 1992; Williamson et al. 1988; BHP 1983; Ellingwood 1983; Felter and Lloyd 1983; Remington and Wood 1918; BPC 1911. Group 2: The following reference was consulted per daily dose: Williamson et al. 1988. Group 3: At least three of the following references were consulted per daily dose: Jensen et al. 2010; Morgan and Stevens 2010; Quinn et al. 2010; Yurko-Mauro et al. 2010; Calabrese et al. 2008; Malaguanera et al. 2008; De Jesus Moreno Moreno 2003; Parnetti et al. 2001; Stough et al. 2001; Thal et al. 2000; Barbagallo et al. 1994; Pettegrew et al. 1994; Parnetti et al. 1993; Sano et al. 1992; Canal et al. 1991; Spagnoli et al. 1991. Group 4: At least one of the following references was consulted per daily dose: EMA 2013; Health Canada 2012; EMA 2010; ESCOP 2009; Bradley 2006; Taylor 2003; NNHPD caffeine monograph. Group 6: The following two references were consulted per daily dose: Bone 2003; API 2001. Group 7: The following three references were consulted per daily dose: Kanehira et al. 2011; Powers et al. 2007; Yamakoshi et al. 2006. Group 8: At least one of the following references was consulted per daily dose: API 2004; Upton 2012; Winston and Maimes 2007; Mills and Bone 2005; WHO 2004; Bone 2003; Hoffman 2003; Thomsen 2002; Williamson 2002; Blumenthal et al. 2000; Upton 1999a; WHO 1999; Bradley 1992.</p>		

Direction(s) for use

See Table 4 below.

Combination rules and restrictions

All medicinal ingredients included in this monograph may be combined across all groups, with the following restrictions:

Use or Purpose Restrictions

- ▶ A use or purpose statement is only acceptable if at least one medicinal ingredient associated with that statement is present at a dose at or above the minimum daily dose listed in Table 2.
- ▶ Medicinal ingredients which do not meet the minimum daily dose for a use or purpose statement will be considered as acceptable complementary medicinal ingredients in product formulations.
- ▶ Traditional with non-traditional use or purpose: When traditional and non-traditional claims are both made, the traditional claim must be preceded with the medicinal ingredient that supports it, unless it is a single medicinal ingredient product.
- ▶ Combination of paradigms: When traditional Herbal Medicine and traditional Ayurvedic claims are both made, each claim must be preceded with the medicinal ingredient that supports it.
- ▶ If products contain caffeine (Group 4), sedative/relaxation claims are not permitted.
- ▶ If products contain sedatives (Group 2), alertness claims are not permitted.

Rules for Caffeine

- ▶ The maximum amount of caffeine permitted from all ingredients in the product is 400mg/day, and 200mg per single dose.
- ▶ The maximum daily amount of caffeine permitted for each medicinal ingredient must be respected. Please see Table 2 above.
- ▶ If the total amount of caffeine provided by the combination of ingredients in the product (e.g. Yerba mate and Guarana) is equal to or higher than 100 mg/day, risk statements from the NNHPD Caffeine Monograph are required. Please see Table 4 below.
- ▶ Additional synthetic caffeine added to Guarana and/or Yerba mate extracts must be represented as a separate medicinal ingredient.

Rules for Sedatives

- ▶ When combining L-5-HTP, St. John’s Wort, and/or Passionflower, an additional risk statement is required. Please see Table 4 below.
- ▶ If ingredients are combined within Group 2 (Ingredients with sedative action), the sum of the percentages of the maximum daily reference dose must not exceed 100%, for all ingredients contributing to support the claim. Please see Table 3 below.

Table 3 Combination Table to assess Safety of Group 2 Ingredients

Additive Indication:	Group 2 (e.g. Traditionally used in Herbal Medicine as a sleep aid)		
Medicinal Ingredient	Maximum Daily Recommended Dose on PLA form	Maximum Daily Monograph Reference Dose	Percentage of the Maximum Daily Monograph Reference



			Dose (%)
<i>Eschscholzia californica</i> (California poppy)	0.5 g	3 g	0.5/3 = 16.67%
<i>Humulus lupulus</i> (Hops)	4 g	6 g	4/6 = 66.66%
<i>Hypericum perforatum</i> (St John's wort)	0.5 g	12.6 g	0.5/12.6 = 3.96%
Sum of Percentages			87.3%

The calculations are performed as follows:

- Percentage of the Maximum Daily Monograph Reference Dose = $[(\text{Maximum Daily Recommended Dose on PLA form}) / (\text{Maximum Daily Monograph Reference Dose})] \times 100\%$

Safety assessment - Sum of Percentages:

- In the example above, the sum of Percentages of the Maximum Daily Monograph Reference Dose is 87.3%, which is less than 100%. Safety of the combination of ingredients is therefore supported.

Duration of use

See Table 4 below.

Risk information

Consult Table 4 for appropriate statements related to each medicinal ingredient. The medicinal ingredients of Table 4 are associated with the required numbered statements below.

Conditions of Use:

- As per the respective NNHPD monograph/abbreviated labelling standard.

Duration of Use:

- Ayurvedic bacopa claim only: Use for a minimum of 6 weeks to see beneficial effects.
- Doses $\geq 300 - 3000$ mg GABA per day: For use beyond 4 weeks, consult a health care practitioner.

Caution(s) and warning(s)

- If symptoms persist or worsen, consult a health care practitioner.
- If you are pregnant or breastfeeding, consult a health care practitioner prior to use.
- If you are pregnant, consult a health care practitioner prior to use.
- If you are breastfeeding, consult a health care practitioner prior to use.
- If you experience severe stomach and/or intestinal irritation, discontinue use.
- If you have gastrointestinal irritation, do not use.



10. If you have a urinary tract disorder and/or kidney disease, consult a health care practitioner prior to use.
11. If you have liver disease, kidney disease and/or a seizure disorder, consult a health care practitioner prior to use.
12. If you have high blood pressure, consult a health care practitioner prior to use.
13. Doses \geq 300 mg GABA per day: Do not use with alcohol.
14. If you have glaucoma, and/or detrusor instability (overactive bladder syndrome), consult a health care practitioner prior to use.
15. Consumption with natural health products (e.g. bitter orange extract, synephrine, octopamine, ephedra) or other drugs (e.g. ephedrine) which increase blood pressure is not recommended.
16. Consumption with other caffeine-containing products (e.g. medications, coffee, tea, colas, cocoa) is not recommended.
17. Consult a health care practitioner prior to use if you are taking lithium.
18. This product is not intended as a substitute for sleep.
19. If you experience any of the following symptoms within a few hours after taking this product, discontinue use and consult a health care practitioner: changes in mental state such as restlessness or confusion, increased heart rate, enlarged pupils, loss of muscle coordination, sweating, shivering and/or gastrointestinal symptoms such as nausea, vomiting, diarrhea.

Contraindication(s):

20. Do not use if you are pregnant or breastfeeding.
21. Do not use if you are pregnant.

Known adverse reaction(s):

22. May cause digestive problems

Table 4 Risk information, durations of use, and directions for use associated with medicinal ingredients

Medicinal Ingredient	Risk Information	Duration of Use	Direction(s) for use
1,3,7-trimethylxanthine (Caffeine)	1		
Acetyl-L-Carnitine (Acetylcarnitine)	5,11,22		
<i>Asparagus racemosus</i> (Shatavari)	6		
<i>Astragalus membranaceus</i> (Astragalus)	1		
<i>Avena sativa</i> (Oat)	4		
<i>Bacopa monnieri</i> (Bacopa)	5,22	2	
Cod liver oil	1		
<i>Eleutherococcus senticosus</i> (Eleuthero)	1	1	
<i>Eschscholzia californica</i> (California poppy)	1		
Fish oil	1		
Gamma-Aminobutyric acid (GABA)	4,5,13	3	
<i>Ganoderma lucidum</i> (Reishi)	1	1	1
<i>Ginkgo biloba</i> (Ginkgo)	1	1	
<i>Glycyrrhiza glabra</i> (Licorice)	1	1	
<i>Humulus lupulus</i> (Hops)	1		
<i>Hypericum perforatum</i> (St. John's wort)	1	1	
<i>Ilex paraguariensis</i> (Yerba mate)	5,12		

L-5-Hydroxytryptophan (L-5-HTP)	1		1
L-alpha-Glycerophosphorylcholine (Choline alfoscerate)	5		
L-Theanine	1		
L-Tyrosine	1	1	1
<i>Matricaria chamomilla</i> (German chamomile)	1		
<i>Melissa officinalis</i> (Lemon balm)	1		
<i>Nepeta cataria</i> (Catnip)	1		
<i>Ocimum tenuiflorum</i> (Holy basil)	1		
<i>Panax ginseng</i> (Asian ginseng)	1	1	
<i>Panax quinquefolius</i> (American ginseng)	1		
<i>Passiflora incarnata</i> (Passionflower)	1		
<i>Paullinia cupana</i> (Guarana)	5,12		
Phosphatidylserine	1		
<i>Pulsatilla vulgaris</i> (Pasqueflower)	4,8,9,10,20		
<i>Rhodiola rosea</i> (Rhodiola)	1		
<i>Schisandra chinensis</i> (Schisandra)	7,21		
<i>Scutellaria lateriflora</i> (Skullcap)	1		
<i>Stachys officinalis</i> (Wood Betony)	4,5		
<i>Tilia cordata</i> (Small-leaf linden)	1		
<i>Tilia platyphyllos</i> (Large-leaf linden)	1		
<i>Tilia x europaea</i> (European linden)	1		
<i>Tinospora cordifolia</i> (Guduchi)	5		
<i>Turnera diffusa</i> (Damiana)	4,7,21		
<i>Valeriana officinalis</i> (Valerian)	1		
<i>Withania somnifera</i> (Ashwagandha)	1		
Combination of ingredients resulting in a total caffeine content of 100 mg/day or more (e.g. Yerba mate and Guarana)	5,12,14,15,16,17,18		
Combination of two or more of the following ingredients: L-5-HTP, St John's Wort, and/or Passionflower	19		
The following references were consulted for the above statements: AMR 2010; Arya et al. 2000; Avisar et al. 2002; Bain et al. 2006; Barnes et al. 2002; Berardi et al. 2002; Bone 2003; Bradley 1992; Brinker 2001; Bouchard et al. 2005; Bradley 2006; Bui et al. 2006; Calabrese et al. 2008; Chandrasekaran et al. 2005; CPS 2008; Cornelis and El-Sohehy 2007; Creighton and Stanton 1990; EMA 2013; Erner et al. 2003; ESCOP 2009; FDA 1988; FDA 2004; Fiebich et al. 2011; Gardner and McGuffin 2013; Haller et al. 2005; Jee et al. 1999; Jefferson 1988; Mester et al. 1995; Mills et al. 2006; Morgan and Stevens 2010; Nathan et al. 2001; Nathan et al. 2004; Noordzij et al. 2005; Okun et al. 2010; Powers et al. 2007; Rai et al. 1990; Shils et al. 2006; Stough et al. 2001; Thomsen 2002; Turner et al. 2006; Vahedi et al. 2000; Zimmerman 1992 .			

Non-medicinal ingredients

Must be chosen from the current Natural Health Products Ingredients Database (NHPID) and must meet the limitations outlined in that database.



Storage conditions

Products containing Cod liver oil, Fish oil or Schizochytrium oil

- ▶ Refrigerate after opening (except when encapsulated) (Senanayake and Fichtali 2006; Wille and Gonus 1989).
- ▶ Store in airtight container, protected from light (Ph.Eur. 2012; USP 35).

Products containing Reishi

Store in a dry place at room temperature (PPRC 2010)

Specifications

- ▶ The finished product specifications must be established in accordance with the requirements described in the NNHPD's Quality of Natural Health Products Guide.
- ▶ The medicinal ingredient must comply with the requirements outlined in the NHPID.
- ▶ For the following ingredients please see the respective NNHPD monograph/AbLS for additional quality requirements: Astragalus, Cod liver oil, Eleuthero, Fish oil, German chamomile-Oral, Ginkgo biloba, American ginseng, Panax ginseng, Hops, Licorice, St John's wort, L-Tyrosine, Valerian, L-Theanine.

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