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Australian Government

Department of Health and Ageing
Therapeutic Goods Administration

Draft Compositional Guideline for XXXX

[with changes; additions in pink, deletions highlighted in yellow with strikethrough]

Name of the ingredient

XXXX (AAN) (check the ARTG permitted ingredients list for the correct name and type of substance)

Definition of the ingredient

The substance should be defined as to its origin (eg, genus, species, part of the organism, geographical location of harvest) and method of manufacture (cultivated or wild, extracted, dried, distilled purified by ion-exchange chromatography etc). This must be the same as the process against which the safety/toxicology data was evaluated by the TGA.

Molecular formula (*if applicable*):

CAS Number (*if applicable*):

Table 1. Ingredient specific requirements

Test	Method reference	Acceptance criteria
Description *This should include all physical properties ~~which may be assessed without testing~~, such as appearance, colour, odour~~, particle size~~ etc.*	*Where there is no formal testing regime required e.g. appearance or ~~smell~~ odour, a description such as 'organoleptic' or 'visual' is satisfactory.*	*~~Criteria should be such that an incorrectly labelled substance could be identified as non-compliant~~* *Complies*

Test	Method reference	Acceptance criteria
Characteristics *Properties of the substance that ensure its quality. Pharmacopeial tests and limits for comparable substances should be considered when determining what to include. Some examples include:* ~~Residue on ignition~~ ~~Sulfated ash~~ ~~Loss on drying~~ ~~Solubility~~ ~~Melting Point~~ ~~Peroxide Value~~ ~~pH of solution~~ becomes Loss on drying *Residue on ignition** *Sulfated ash** Solubility Melting Point pH of solution	 *Add in* *Refer to pharmacopoeial methods (attach details of proprietary methods).*	~~*Limits should be declared as a percentage, e.g. < 1 % w/w.*~~ ~~*Ranges with more significant figures are preferable to single values with fewer significant figures, e.g. pH 3.5 – 4.5 is preferable to pH 4.*~~ ~~*Limits*~~ *Amounts should be declared as a percentage, e.g. < 1 % w/w.* *Ranges should be stated rather than single values. Consideration should be given to the number of significant figures, e.g. pH 3.5 – 4.5 is preferable to pH 4, in line with pharmacopoeial practice.*
Identification *The identification test(s) must be able to unambiguously ~~identify~~ distinguish the substance from any other substance, ~~especially related substances,~~ and may include 'fingerprint' tests such as ~~tlc~~ TLC, HPLC or FT-IR which must be compared to an authenticated reference material. More than one test may be appropriate. For pure substances, chromatographic retention time alone is generally considered inadequate as a method of identification.*	*Add in* *List methods of identification. Refer to pharmacopoeial methods where possible (attach details of proprietary methods).*	*E.g. Matches spectrum of authenticated reference material* *becomes* *Complies, e.g. matches spectrum of authenticated reference material.*

Test	Method reference	Acceptance criteria
Assay		
~~*In the case of complex mixtures (eg herbal extracts) where the active(s) are unknown or cannot be assayed 'marker' compounds may be used as proxies. See EMEA guideline 815/00.*~~	~~*Where the method is proprietary information, a statement of the type of method is adequate - details are not required for the guideline, but are expected in the application.*~~	~~*Ranges, not limits should be stated unless justified.*~~
becomes	*becomes*	*becomes*
Describe specific tests that determine the presence and quantity of a specific substance. In case of herbal materials, preparations, or other complex mixtures (e.g. herbal extracts), appropriate marker compounds may be assayed.	*State and if necessary describe methods of assay or provide brief details.*	*Limits for assay(s) taking into account practical but reasonable biological, physical and chemical variation.*
Notes ** the test is valid when performed on inorganic material. For organic substances, the test should be included under "Other organic or inorganic impurities or toxins".*		

Table 2. Incidental constituents

Where justified, ~~C~~certain ~~incidentals~~ tests for incidental constituents may be excluded based on the origin and processing of the substance, e.g. a dried leaf, otherwise unprocessed, may be exempted from residual solvent testing. Other incidentals, such as ~~PCBs,~~ scheduled contaminants (e.g. bromides, ephedrine) or radioactivity should be included ~~as~~ where appropriate.

Test	Method reference	Acceptance criteria
Solvent residues	~~*For example*~~ ~~*BP* (Vol IV, Appendix VIII L, Residual solvents; *Ph. Eur.* method 2.4.24)~~	Complies
Add in	*becomes*	*becomes*
Specifically address solvents that may be present.	*List methods of assay, e.g. BP 2011 (Appendix VIII L, Residual solvents; Ph Eur method 2.4.24)*	*Limits of total solvents*
Address any additional solvents that may be used in the production, preparation, manufacturing or formulation.		*Solvent specific limits*
Incidental metals and non-metals ~~*The four metals specified below should always be tested for. Other metals such as tin, copper, etc should be tested for if they are expected to be present in substantial quantities.*~~		
~~Total heavy metals~~	~~*BP* (Vol IV, Appendix VII Limit test for heavy metals; *Ph. Eur.* method 2.4.8) or in-house.~~	~~<5 ppm~~
~~Lead~~ ~~Arsenic~~ ~~Cadmium~~ ~~Mercury~~ ~~*Copper*~~ ~~*Silicon*~~		~~<0.5 ppm~~ ~~<0.5 ppm~~ ~~<0.1 ppm~~ ~~<0.5 ppm~~ ~~*Or otherwise justified*~~
becomes		
Specifically address the metals in the current BP or other default standard (Ph Eur, USP) limit tests for heavy metals.	*List methods of assay e.g. BP 2011 (Appendix VII); Ph Eur method 2.4.8 or in-house*	*Limits of total heavy metals*
Include any limits for specific metals or non-metals e.g. cadmium, arsenic, lead, mercury		*Metal specific limits*

Test	Method reference	Acceptance criteria
Pesticide residues and environmental contaminants: (including agricultural and veterinary substances) Add in *Specifically address the limits stipulated in the current BP (or Ph Eur, USP), and whether the product would comply with these limits. In addition, state any additional residue limits that may be relevant.*	~~*BP* (Vol IV, Appendix XI L, Pesticide residues; *Ph. Eur.* method 2.8.13)~~ *List methods of assay e.g. BP 2011 (Appendix XI L, Pesticide residues; Ph Eur method 2.8.13)*	Complies
Other organic or inorganic impurities or toxins *Include other substances that may pose a risk on safety or may be of therapeutic significance.* *What specific substance are assayed ? E.g. dioxins, PCBs, mycotoxins* *Give consideration to related substances such as by-products, co-extracted substances, inactive isomers and degradation products.* *Ash* *Residue on Ignition* *Sulfated ash* *Peroxide value*	*List methods of assay, refer to pharmacopoeial methods where possible, e.g. BP, Ph Eur, USP.*	*Limit of impurities in substance* *Impurity specific limits* *Amounts should be declared as a percentage, e.g. < 1 % w/w.*
Microbiology	While substance manufacturers are encouraged to include limits for objectionable microorganisms, it is the product into which those substances are formulated that is subjected to a legally binding set of criteria. The Therapeutic Goods Order No. 77 *'Microbiological Standards for Medicines'* mandates that any finished product which contains the ingredient, alone or in combination with other ingredients, must comply with the microbial acceptance criteria set by Clause 9 of the Order.	
Notes		

Key to abbreviations: - insert any additional from above

BP = British Pharmacopoeia (currently promulgated edition);

FT-IR = Fourier transform infrared spectroscopy;

HPLC = ~~H~~high-pressure liquid chromatography;

Ph. Eur = European Pharmacopoeia;

TLC = Thin layer chromatography

USP = United States Pharmacopoeia;