SUBMISSION FOR RECLASSIFICATION

HYDROCYANIC ACID

WELEDA NEW ZEALAND LTD.

P.O. BOX 8132

HAVELOCK NORTH

RATIONALE

Preamble

The recent recommendation to set an exemption from scheduling levels has occurred as a result of the move towards harmonisation with Australian schedules. The exemption level set has implications for some homoeopathic medicines that are on the market in New Zealand, that are produced differently to homoeopathic medicines on the market in Australia.

Our aim in this submission is:

- To clarify the classification and schedule exemption levels so that they can be clearly and objectively applied to anthroposophical and homoeopathic medicines.
- To propose classification and schedule exemption levels based on active principle concentration.
- To propose classification and schedule exemption levels that fairly reflect the actual risk of the medicine to the consumer.

To our knowledge, there have been no reports of adverse effects associated with anthroposophical or homoeopathic medicines containing hydrocyanic acid that have initiated this change.

Rationale 1: Reclassification

There are plants that contain Hydrocyanic acid that are used as starting materials in anthroposophical and homoeopathic medicines.

We consider that the general application of a Prescription Only Medicine classification to product containing Hydrocyanic acid up to the schedule exemption level of 1 microgram per litre or per kilogram is not substantiated by toxicity data. We propose that a lower classification be applied to product containing lower concentrations of Hydrocyanic acid.

The therapeutic dose range for hyoscyamine is 0.15 mg to 0.3 mg hyoscyamine (refer to the Hyoscyamus reclassification submission). This dose range appears to have been used in the setting of the classification levels for hyoscyamine, eg.:

Pharmacist Only Medicine: Hyoscyamine; in liquid form for oral use; in solid dose form containing more than **0.3 milligrams per dose** or more than 1 milligram per recommended daily dose

We propose that the same approach be used with the classification of Hydrocyanic acid.

Toxic and therapeutic doses:

> Fatal dose: 50 mg is the lowest fatal dose for an adult of Hydrocyanic acid mentioned. *(Refer Appendix 1, points 3. and 4.)*

5 mg is the lowest fatal dose for a 10 kg child of Hydrocyanic acid based on the LD50 of 0.5 mg/kg. *(Refer Appendix 1, points 5.)*

Therapeutic dose: 2 to 8 mL of Cherry-laurel Water standardized to contain 0.1% HCN (hydrocyanic acid) is referred to as a therapeutic dose *(refer Appendix 1, point 6.)*. This is equivalent to 2 to 8 mg of hydrocyanic acid.
Another therapeutic dose is Cherry Laurel Water, B.P., ½ to 2 fluid drachms *(refer Appendix 1, point 7.)*
Using the definition of a minim "Sixty minims equal 1 fluid dram. One minim equals 0.06 mL." ½ to 2 fluid drachms are equivalent to 1.8 to 7.2 mL, and using the 0.1% concentration this is equivalent to 1.8 to 7.2 mg hydrocyanic acid.

Low concentration, homoeopathic medicines are commonly presented in liquid or powder form, therefore classification based on pack concentration is included.

Proposed reclassifications based on the middle of the therapeutic range – refer Part A, Point 8.

POM: Hydrocyanic acid; for oral use in liquid or powder form in a pack containing more than 4 milligram; in solid dose form containing more than 4 milligram per dose.

PM: Hydrocyanic acid; for oral use in liquid or powder form in a pack containing 4 milligram or less; in solid dose form containing 4 milligram or less per dose.

The effect of this reclassification is that:

Liquid or powder oral preparations, containing plants that contain Hydrocyanic acid, in a pack containing more than a single dose of 4 mg of Hydrocyanic acid, and solid dose forms containing more than 4 mg per dose are classified as Prescription Only Medicines.

Liquid or powder oral preparations, containing plants that contain Hydrocyanic acid, in a pack containing a single dose of 4 mg or less of Hydrocyanic acid, and solid dose forms containing 4 mg or less per dose are classified as Pharmacy Medicines.

Rationale 2: Schedule exemption level based on active principle concentration

The aim is:

To provide a 1000 fold difference between a therapeutic dose and the dose of a product containing the exemption level.

Present Hydrocyanic acid schedule exemption level:
1 microgram per litre or kilogram (0.0000001%)

This exemption level does not equate with the premise of a 1000 fold difference between the therapeutic dose and the dose of a product containing the proposed exemption level – refer following points.

Therapeutic dose: 2 to 8 mL of Cherry-laurel Water standardized to contain 0.1% HCN (hydrocyanic acid) is referred to as a therapeutic dose *(refer Appendix 1, point 6.)*. **This is equivalent to 2 to 8 mg of hydrocyanic acid.**
Another therapeutic dose is Cherry Laurel Water, B.P., ½ to 2 fluid drachms *(refer Appendix 1, point 7.)*
Using the definition of a minim "Sixty minims equal 1 fluid dram. One minim equals 0.06 mL." ½ to 2 fluid drachms are equivalent to 1.8 to 7.2 mL, and using the 0.1% concentration **this is equivalent to 1.8 to 7.2 mg hydrocyanic acid**.

A 1 mL oral dose of a product containing 0.0000001% of hydrocyanic acid would contain 0.001 microgram hydrocyanic acid.

This is approximately a **1,000,000 fold** difference between the therapeutic dose range (1.8 mg to 7.2 mg) and the dose of a product containing the exemption level (0.001 microgram).

We consider that this is an excessive margin.

We would propose the following schedule exemption to meet the premise of a 1000 fold difference between the therapeutic dose and the dose of a product containing the exemption level – refer Part A, Point 8.

Hydrocyanic acid, in preparations containing 1 milligram per litre or per kilogram of hydrocyanic acid (0.0001%)
(As the largest pack size in the market is 100 mL, there is an extra safety factor of ten)

A 1 mL oral dose of a product containing 0.0001% of hydrocyanic acid would contain 0.001 mg (1 microgram) hydrocyanic acid.

This is approximately a **1000 fold** difference between the therapeutic dose range (1.8 mg to 7.2 mg) and the dose of a product containing the exemption level (0.001 mg).

We consider that this is an extremely wide safety margin.

Rationale 3: Safety in the market place

Weleda medicines containing plants that contain Hydrocyanic acid have been on the market since the early 1950's and have had wide use during those years, in the customer base to which they are directed. There have been NO adverse reactions reported.

PART A

1. International Non-proprietary Name of the medicine

Hydrocyanic acid

2. Proprietary name(s)

Non-specific change application for anthroposophical and homoeopathic products.

3. Company requesting reclassification

Weleda New Zealand Ltd.
P.O. Box 8132
Havelock North
NEW ZEALAND

4. Dose form(s) and strength(s)

Not applicable.

5. Pack size and other qualifications

Not applicable.

6. Indications for which change is sought

Not applicable.

7. Present classification of medicine

Prescription Only Medicine: Hydrocyanic acid

Schedule exemption: 1 microgram per litre or per kilogram

8. Classification sought

Prescription Only Medicine: Hydrocyanic acid; for oral use in liquid or powder form in a pack containing more than 4 milligram; in solid dose form containing more than 4 milligram per dose.

Pharmacy Medicine:	Hydrocyanic acid; for oral use in liquid or powder form in a pack containing 4 milligram or less; in solid dose form containing 4 milligram or less per dose.
Schedule exemption:	Hydrocyanic acid, in preparations containing 1 milligram per litre or per kilogram of hydrocyanic acid (0.0001%) *(As the largest pack size in the market is 100 mL, there is an extra safety factor of ten)*

9. Classification status in other countries

Germany:	Hydrocyanic acid not classified.
Australia:	*Schedule 4 (Prescription Only Medicine):* Hydrocyanic acid for therapeutic use *Schedule exemption:* 1 microgram per litre or per kilogram

10. Extent of usage in NZ and elsewhere

Small amounts of Hydrocyanic acid are present in a number of plants, that are used as starting materials for the production of homoeopathic products.

11. Proposed labelling

Not applicable.

12. Proposed warning statements

Not applicable.

13. Other products containing the same active ingredient(s) and which would be affected by the proposed change

Anthroposophical and homoeopathic medicines.

PART B

Reasons for Requesting Classification Change

1. Expected benefits to both the consumer and to the public

Maintains accessibility to safe anthroposophical and homoeopathic medicines that have been used for minor, self-limiting conditions, in NZ for more than 40 years.

2. Ease of self-diagnosis or diagnosis by a pharmacist

Not applicable.

3. Relevant comparative data for like compounds

Not applicable

4. Local data or special considerations relating to NZ

Not applicable

5. Interactions with other medicines

None known.

6. Contraindications

Not applicable.

7. Possible development of drug resistance

None

8. Adverse events

Weleda medicines containing plants that contain very small amounts of Hydrocyanic acid have been on the NZ market since the early 1950's and on the European market since the early 1920's. During these years there have been, to our knowledge, no reports of any adverse events associated with these anthroposophical and homoeopathic medicines.

9. Potential for abuse or misuse

None

Glossary, Appendices and Reference Copies

Glossary

Anthroposophical medicine
The medicines specially made for anthroposophical therapy which contain herbal and homoeopathically produced preparations.

Homoeopathic medicine
Article 1 of the European Guidelines EG 92/73 and EG 92/74 on Homoeopathic Pharmaceuticals for Human respectively Veterinary Use provides the following definition [official within the 15 nations of the E.U.] of the term "homoeopathic medication":

(1) "Within the sense of this Guideline, a homoeopathic (veterinary) medication constitutes any medicinal agent, which has been prepared from products, substances, or compounds designated as homoeopathic source-material in accordance with homoeopathic manufacturing procedure as described in a European pharmacopoeia or – in absence of the corresponding monograph – according to the currently official pharmacopoeia of a member state.

(2) "Homoeopathic medication may contain multiple active constituents"
[Official Journal of European Communities No. L 297/8 of Oct.13, 1992].

Homoeopathic medicines can be the mother tincture right through the range of homoeopathic potencies.

Homoeopathic potency
A homoeopathic potency is produced from one or several source material or mother tinctures, generally followed by potentising: serial dilution and succussion (potentisation). The following are examples of the common attenuation-ratios:

- 1:10 - Decimal or D, DH, or X potencies
- 1:100 - Centesimal or C, CH potencies
- 1:50,000 - Q or LM potencies

Potentisation
Potentisation: serial dilution and succussion - a special form of shaking the liquid dilution, or triturating the powder dilution.

Mother tincture
A mother tincture is a preparation of a substance, that is used as the starting material for the preparation of a homoeopathic potency, and in some cases can also be used as a homoeopathic medicine in its own right.

Appendices

1. Appendix 1: References to Active Principle, Therapeutic and Toxicity Levels
2. Appendix 2: Previous Medsafe classifications of Hydrocyanic acid

Reference Copies

1. Reference Copy 1: pg. 336, Pharmacognosy 14th Ed., by Trease and Evans, published by WB Saunders Company Ltd., ISBN 0-7020-1899-6
2. Reference Copy 2: pg. 755, German Homoeopathic Pharmacopoeia (GHP) (Homoopathisches Arzneibuch HAB) Official Edition, published by Deutscher Apotheker Verlag Stuttgart Govi-Verlag GmbH, Frankfur, ISBN 0946717 05 2, ISBN for German original 3-7692-0932-X
3. Reference Copy 3: pg. 829-830, Medical Toxicology, Diagnosis and Treatment of Human Poisoning (1988), by Matthew J. Ellenhorn and Donald G. Barceloux, published by Elseveier Science Publishing Company, Inc., ISBN 0-444-01129-3
4. Reference Copy 4: pg. 1128, Martindale, 30th Ed., published by The Pharmaceutical Press, ISBN 0 85369 300 5, ISSN 0263-5364
5. Reference Copy 5: pg. 252, Handbook of Poisoning, 12th Edition, published by Appleton & Lange, a Publishing Division of Prentice-Hall, ISBN 0-8385-3643-3
6. Reference Copy 6: pg. 769, The Extra Pharmacopoeia, Martindale, Volume 1, 24th Edition, 1958, published by The Pharmaceutical Press
7. Reference Copy 7: pg. 190, A Modern Herbal, by Mrs M, Grieve, published by Peregrine Books
8. Reference Copy 8: pg. 722, Mosby's Medical and Nursing Dictionary, 2nd Edition, Thomas A. Manning, The C.V. Mosby Company, ISBN 0-8016-5195-6