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Complementary Medicines Reform Section
Complementary and OTC Medicines Branch
Therapeutic Goods Administration
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WODEN ACT 2606

January 21, 2019

Re: TGA Consultation: Remaking Therapeutic Goods Order No. 78 - Standard for Tablets and Capsules and reintroducing pills into the remade Order.

On behalf of Sun Herbal Pty Ltd, I welcome this opportunity to respond to the TGA Consultation: Remaking Therapeutic Goods Order No. 78 - Standard for Tablets and Capsules and reintroducing pills into the remade Order.

About Sun Herbal

Sun Herbal Pty Ltd (SH) is a small proprietary company employing 4 full time and 3 part time staff, supplying a range of Chinese herbal medicines to Australian healthcare professionals, predominantly registered practitioners of Acupuncture and Traditional Chinese Herbal Medicine. SH has been in business since 2004.

Summary and introductory comments

We welcome the inclusion of pills into the remade order together with the recognition that the quality standards for pills are different from those for tablets in the BP. Moreover, we agree with the decision to align the standards for pills with those of the Pharmacopoeia of the Peoples Republic of China (CP). Additionally, we would welcome the future addition of the CP as a default standard for all of the herbal medicines and formulations used within the Traditional Chinese Medicine (TCM) paradigm.

Clarity on a uniform standard for limits of the heavy metals: As, Cd, Hg and Pb in herbal medicines is of critical importance, owing to the highly toxic nature of these elements and their long half-life in the body once ingested. Set limits are based on estimates of Tolerable Daily Intake (TDI) for each of these elements. However, there are many issues concerning the calculation of TDI, which lead to a significant degree of inaccuracy (always erring on the side of excessive caution). Moreover, the limit value itself is arrived at through a process, which must take into account several variables, and it too must err on the side of excessive caution. Thus, the limit value is an estimate, which in turn is based on an estimate, and it cannot be regarded as a strict measurement. Therefore, in an herbal product, small deviations from any of these limits are highly unlikely to have an impact on human health. Unfortunately, if too rigidly enforced, the establishment of fixed limits for heavy metals may have an impact on the ability of a sponsor to continue to supply TCM herbal medicines, and on the broader availability of TCM herbal products in Australia.

COMMENTS ON THE PROPOSED CHANGES TO TGO 78

How the reintroduction of pills to the remade Order will affect your business?
No change

If the 12-month transition period for the inclusion of pills is suitable.
Yes

Which impurity limits should apply to medicines not following an individual monograph?
Schedule 1, Item 3, OPTION 1
These limits are more closely aligned with the limits that have been established by authorities that are specifically concerned with herbal medicines, which are generally consumed in much smaller quantities than food and drinking water.
For comparison:

WHO Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues. (WHO, 2007) For crude herbal drugs only.
Pb ≤ 10 ppm
Cd ≤ 0.3 ppm
Hg not specified
As not specified

Green Trade Standards of Importing & Exporting Medicinal plants & Preparations China Chamber of Commerce for Import and Export of Medicines and Health Products. (Wu & Xue, 2013)
Pb ≤ 5.0 ppm
Cd ≤ 0.3 ppm
Hg ≤ 0.2 ppm
As ≤ 2.0 ppm

ASEAN Guidelines on Limits of Contaminants for Health Supplements (TMHSPWG, 2015):
Lead: ≤ 10.0 ppm
Arsenic: ≤ 5.0 ppm
Mercury: ≤ 0.5 ppm
Cadmium: ≤ 0.3 ppm

How the introduction of heavy metal limits in the remade Order will affect your business?
While SH will have no difficulty meeting the BP standards (Option 1), the standards of USP (Option 2) are set too low to be consistently achieved using our current chain of supply and manufacturing methods. Adoption of the Option 2 limits would result in additional costs to our business. At present we are unable to quantify these costs, as they may include the following: cancelling some, or all, of our products from the ARTG; increased costs for raw materials; increased production costs.

The suitability of the requirements specified in the remade Order.
The other requirements for pills and hard capsules are reasonable and present no difficulties for the continued supply of our herbal medicine products.

The exclusion of unapproved goods from the application of the remade Order.
Agree.

The usefulness of the proposed guidance document
The document is clear and has proven to be very useful

Suggested improvements to either document.
None

Alternative options if you do not support the proposal.
N/A

An assessment of how the proposal will positively and adversely impact on you.
Pls see response to item No.4, above

Additional comments re limits for heavy metals.
Limits for heavy metals are derived from estimates of tolerable daily (or weekly) intake, defined as the maximum amount of a chemical that can be ingested daily *over a person's lifetime* with no appreciable health risk. Moreover, this level of intake is calculated by applying a safety or uncertainty factor, which results in an "estimate with uncertainty *spanning perhaps an order of magnitude* of a daily exposure for the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime." (Becking, Nordberg & Nordberg, 2007). (critical phrases italicised by me)
Thus, all of the proposed limits for concentration of heavy metals in herbal medicine preparations contain an inbuilt margin of safety of at least an order of magnitude. This, together with the fact that these preparations are generally only taken for short periods of time, supports the notion that the given figure should be regarded more as an indication of a range of values within which daily intake is highly likely to be safe, rather than a fixed value, which, if exceeded by only a very small amount poses an imminent health risk to the consumer. As an example, if the limit, say, for Arsenic is set 2 ppm and chemical analysis of an herbal preparation finds 2.5 ppm, this would not present a significant increase in the health risk to the consumer. Moreover, the deviation above the set limit would have been due to expected variations in a natural product and not contamination. Based on this line of reasoning, it seems fair to propose that the newly introduced limits for heavy metals be assessed in a similar way to the assessment procedures for uniformity of weight for herbal pills, allowing a small degree of leeway for products that are well within one order of magnitude of the limit.

Sincerely,

Tony Reid
Director,
Technical and Regulatory Affairs Officer
January 21, 2019

REFERENCES

ACCSQ Traditional Medicines and Health Supplements Product Working Group (TMHSPWG), 2015. ASEAN Guidelines on Limits of Contaminants for Health Supplements. From ASEAN website, ASEAN Economic Community/Sectoral Bodies under the Purview of AEM/Standards and Conformance/Policy and Guidelines. Retrieved 16th Jan, 1019 from: https://asean.org/asean-economic-community/sectoral-bodies-under-the-purview-of-aem/standards-and-conformance/policy-and-guidelines/asean-guidelines-on-limts-of-contaminants-hs-v2-0-with-disclaimer/

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Becking, G., Nordberg, M., Nordberg, G. (2007), Ch. 9 - Essential Metals: Assessing Risks from Deficiency and Toxicity, in *Handbook on the Toxicology of Metals (Third Edition)*, pp. 163-176. Burlington, MA: Academic Press.