22 May 2020

Via Email

Secretary of the Department of Health
Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606
medicines.scheduling@health.gov.au

Re: Elixinol Global Limited's Submissions Concerning the TGA's Proposed Amendments to the Poisons Standard (Medicines/Chemicals); Cannabidiol Scheduling

Dear Secretary,

Elixinol Global Limited ("**EXL**") thanks the Therapeutic Goods Administration ("**TGA**") for its proposal to amend the Poisons Standard as concerns the scheduling of cannabidiol ("**CBD**") and we appreciate the opportunity to provide these comments.

EXL is a Sydney-based, industry-leading hemp grain and hemp extract / hemp-derived CBD company through our subsidiary businesses, Elixinol USA and Hemp Foods Australia. Elixinol USA, founded in 2014 and based in Colorado, USA, is a manufacturer and global distributor of hemp extract / CBD dietary supplements and skin care products in nearly 50 countries. Hemp Foods Australia, founded in 1999, is a leading hempseed-based food wholesaler, retailer, manufacturer and exporter of bulk and branded raw materials and finished products with operations based out of Bangalow, New South Wales. EXL is publicly listed and our team is comprised of some of the most internationally respected professionals in the hemp and *Cannabis* industries.

These comments address the matters raised in section 52E of the *Therapeutic Goods Act 1989* (Cth). With the exception of items addressed herein as a recommendation and request to amend the proposed amendment, EXL broadly supports the TGA's proposal to amend the scheduling of CBD.

SAFETY PROFILE OF CBD

The available scientific evidence demonstrates that CBD is generally well tolerated, even at high doses, in both healthy and non-healthy populations.[1] In June 2018, the World Health Organization ("**WHO**") concluded there are no public health-related concerns associated with the use of CBD nor is there any evidence of CBD recreational use. As described in the report, the WHO also concluded CBD is generally well tolerated with a good safety profile and recognized that CBD does not produce the highs that are seen with delta-9 tetrahydrocannabinol ("**THC**"), and in experimental models of abuse liability, CBD exhibited no effects indicative of any abuse or dependence potential.[2]

[1] Iffland, K. and F. Grotenhermen, An Update on Safety and Side Effects of Cannabidiol: A Review of Clinical Data and Relevant Animal Studies. *Cannabis Cannabinoid Res.*, (2017), 2(1)., available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5569602/.

[2] World Health Organization Expert Committee on Drug Dependence Critical Review Report on Cannabidiol (June 2018), available at https://www.who.int/medicines/access/controlled-substances/WHOCBDReportMay2018-2.pdf?ua=1.

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The U.S. Food & Drug Administration's ("**FDA**") scheduling recommendation to the U.S. Drug Enforcement Administration on CBD concludes that based on clinical and available epidemiological data, "there is little indication that CBD has abuse potential or presents a significant risk to the public health."[3] The FDA went on to state, "if this [reliance on the 1961 Single Convention on Narcotic Drugs] is so, to maintain treaty obligations, and reflecting on our scientific findings to the extent currently possible, we recommend CBD and its salts [with residual D-9 THC limits] be placed in the least restrictive Controlled Substances Act schedule, Schedule V. If treaty obligations do not require control of CBD, or if the international controls on CBD change in the future, this recommendation will need to be promptly revisited."[4] In 2016, Food Standards Australia New Zealand also evaluated the safety of CBD and determined that CBD is well tolerated at doses greater than 1000 mg per day and that there were no reports of adverse effects of oral CBD in the published literature.[5] These findings regarding the safety and efficacy of CBD are consistent with the TGA's recent review on the safety of low dose CBD.[6]

CBD has been evaluated in healthy adults using a variety of tests for abuse potential as well as physiological effects. In general, clinical studies have reported that even high doses of oral CBD do not produce the same effects that are characteristic of THC (Grotenherman, 2016 and Consoroe, 1979). For example, a single dose administration of CBD at 600 mg did not differ from the placebo on scales used by the Addiction Research Centre Inventory, a 16 item Visual Analog Mood Scale, and subjective measurements of intoxication or psychotic symptoms.[7] In another recent study of CBD in healthy adults, consisting of three arms, CBD was administered in single ascending dose (1500, 3000, 4500, or 6000 mg CBD), multiple dose (750 or 1500 mg twice daily) and with food (1500 mg CBD single dose).[8] The results indicate that CBD was well tolerated with most adverse events being of mild severity with no severe or serious events. The most common adverse events were diarrhea, nausea, headache, and somnolence across all trial arms. We note that this serving size of 1500 mg is anywhere from 10 to 100 times higher than serving sizes recommended in the supplement and nutritional space.

In any event, possible side effects occurring at high level dosages of pure CBD do not justify strict regulatory control as a matter of course. Safety concerns exist for numerous supplements and foods, yet these products are still sold at supermarkets, pharmacies and various online channels, with health care providers such as medical practitioners and pharmacists advising on mitigation of drug-drug and drug-disease interactions. Grapefruit and bitter orange, along with the widely available supplements Kava and St John's Wort, can cause serious drug-drug interactions and side effects, including liver damage, fainting, nausea, low blood pressure and even death. Similarly, inappropriate use of non-prescription medicines such as paracetamol can cause liver failure while high doses or contraindicated

[3] Letter from Brett P. Giroir, U.S. Dept. of Health & Human Services Assistant Secretary of Health to The Honorable Robert W. Patterson, Acting Administrator, U.S. Drug Enforcement Administration (May 16, 2018), at the Letter's single attachment "Basis for the Recommendation to Place Cannabidiol in Schedule V of the Controlled Substances Act" at Page 18, available at https://hempindustrydaily.com/wp-content/uploads/2018/10/DHS-DEA-letter-2018-0014-0002.pdf.

[4] *Id.* at Page 3 of the Letter's attachment.

[5] Food Standards Australia New Zealand, Cannabidiol hazard profile – Proposal P1042 (2016), available at https://www.foodstandards.gov.au/code/proposals/Documents/P1042%20Low%20THC%20hemp%20CFS%20SD2%20Cannabidiol%20hazard.pdf.

[6] Therapeutic Goods Administration, Safety of low dose cannabidiol (April 2020), available at https://www.tga.gov.au/sites/default/files/review-safety-low-dose-cannabidiol.pdf.

[7] Martin-Santos, R., et al., Acute effects of a single, oral dose of d9- tetrahydrocannabinol (THC) and cannabidiol (CBD) administration in healthy volunteers. *Curr Pharm Des,* (2012), 18(32): p. 4966-79, available at https://pubmed.ncbi.nlm.nih.gov/22716148/.

[8] Taylor, *et al*. A Phase I, Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose, Multiple Dose, and Food Effect Trial of the Safety, Tolerability and Pharmacokinetics of Highly Purified Cannabidiol in Heathy Subjects, *CNS Drugs*, (2018): 32:1053-1067, available at https://pubmed.ncbi.nlm.nih.gov/30374683/.

use of ibuprofen can cause gastric bleeding and renal failure.

SPECIFIC COMMENTS TO THE TGA'S PROPOSAL

EXL again wishes to express our support for the TGA's proposal to amend the Poisons Standard, and we submit the following specific comments in relation to the proposed Schedule 3 entry:

- We agree that CBD is appropriately defined by reference to plant-based or synthetic forms (paragraph a).

- We do not disagree that a maximum recommended daily dose of 60 mg or less of CBD is appropriate as research continues, and we support supply in packs containing no more than 30 days' supply (paragraphs b and c).

- We disagree that CBD content should be defined by reference to the "*total cannabinoid content of the preparation*" and recommend instead, that the content be defined by reference to the percentage of CBD within the cannabinoid *profile* of the *finished product*. This clarity in language is necessary to avoid misinterpretation because, taken literally, a final product comprised of 98% CBD is essentially a pure isolate form of CBD that can only be achieved as a powder. Additionally,

    - Extract derived from the floral parts of industrial hemp must be diluted with an excipient (*e.g.*, an oil) to remediate THC and this is performed globally, generally with either coconut oil, MCT oil, hemp seed oil, or olive oil; all of which are known and recognized as safe foods. Additives that are known and already recognized as safe food or dietary supplement products must be allowed; and

    - As Australian lawmakers and regulators expand their scope of understanding and acceptance of cannabinoids as other countries such as the USA are expanding, they will discover that industrial hemp and cannabis extracts containing a variety of cannabinoids – for example, 75% CBD with cannabinoids such as cannabigerol ("**CBG**"), cannabinol ("**CBN**"), and cannabidivarin ("**CBDV**") comprising the remainder of the profile – are often optimal for various needs and uses. Mandating a cannabinoid profile of 98% CBD will limit the ability of manufacturers to supply these often more optimal products in Australia in the future absent another amendment. Hemp varieties with high CBG, CBN and other non-intoxicating cannabinoids are being bred around the world to meet these needs. Perhaps the impetus for mandating a 98% CBD cannabinoid profile within the finished product is to safeguard against the inclusion of THC, which is a cannabinoid capable of resulting in intoxication. To the extent that is the case, future amendment language could include a precise limit of the THC allowed within the cannabinoid profile of the finished product.

In light of the matters raised above, EXL submits that the TGA consider the following alternative wording for the proposed Schedule 3 entry:

> *CANNABIDIOL in preparations for therapeutic use when:*
>
> *a. the cannabidiol is either plant derived, or when synthetic only contains the (-) CBD enantiomer; and*
>
> *b. the maximum recommended daily dose is 60 mg or less of cannabidiol; and*
>
> *c. in packs containing not more than 30 days' supply; and*

d. cannabidiol comprises 98 per cent or more of the total cannabinoid ~~content~~ profile ~~of~~ within the ~~preparation~~ finished product; and

e. any cannabinoids, other than cannabidiol, must be only those naturally found in cannabis and comprise 2 per cent or less of the total cannabinoid content of the preparation; and

f. for adults aged 18 years and over.

AUSTRALIA'S PUBLIC HEALTH & ECONOMIC INTERESTS & THC

The two largest hemp CBD companies (by market cap) in Australia, Ecofibre and Elixinol, are both listed on the ASX, yet only trade in the USA and EU due to the restrictive regulation of CBD based products in Australia. Appropriate, evidence-based relaxation of such regulation would allow:

1. Importation and sale of Ecofibre and Elixinol products in Australia, which is expected to create numerous jobs and stimulate the economy by providing millions of dollars in trade revenue; and

2. Further investment into Australia to process and manufacture these products locally over time, creating local jobs and directly stimulating economic expenditure.

It is also well known that there exists a multi-million-dollar illegal CBD industry in Australia. Part of the reason for the existence of this industry is that stringent regulation of CBD based products has created opportunities for unscrupulous participants to benefit from the production and sale of illegal products. Those products are not quality assured and potentially not safe. Suitable amendments to the Poisons Standard will provide opportunities for new participants in the market and to contribute to the Australian economy. In particular, EXL expects that alignment of Australian regulation with existing EU/USA regulations which state CBD products are legal with up to 0.2% or 0.3% THC maximum, respectively, will provide the greatest economic benefit.

* * *

Thank you for the opportunity to comment on this important subject. Please do not hesitate to contact us if the agency has any questions or would like to discuss our comments in more detail.

Respectfully submitted,

[redacted]

Oliver Horn, Group CEO & Executive Director
On Behalf of Elixinol Global Limited's Board of Directors