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Consultation: Proposed amendments to the Poisons Standard - Joint ACMS/ACCS meetings, June 2020 - Consultation for a delegate initiated proposal to amend the scheduling for cannabidiol

Public submission on scheduling proposals from Aurora Cannabis Enterprises Inc., Global Cannabis Leader – May 21, 2020

Executive Summary:

- Aurora Cannabis Enterprises Inc. (Aurora) is a global leader in providing high-quality, safe, and effective medical cannabis products to patients around the world. As one of largest cannabis companies in the world, Aurora is at the forefront of product development, research, and policy work surrounding medical cannabis.
- A growing body of scientific research on medical cannabis, and cannabidiol (CBD) in particular, suggests its safety and efficacy in a wide range of treatments and potential symptomatic relief to patients for a variety of medical conditions. This has led health authorities around the world, to either create or revise regulatory frameworks concerning medical cannabis.
- The TGA's request for feedback on the proposal to amend the scheduling for CBD is an important step forward in differentiating the regulatory requirements between CBD and tetrahydrocannabinol (THC), two very different active ingredients found in cannabis.
- The inconsistencies or lack of clarity in global regulatory requirements concerning CBD has created confusion in the marketplace for these products. Aurora, as a global cannabis company who currently exports cannabis medical products to Australia, welcomes the TGA's effort in defining parameters around the use of CBD as a Schedule 4 and now, a proposed Schedule 3 product. Ultimately, this will provide ease of access and increased safety for consumers in purchasing CBD products in Australia, through a legal and controlled pathway.
- Aurora does observe first-hand, the challenges and opportunities in educating healthcare professionals on cannabis products. We do feel that this should be addressed in TGA's proposal to introduce CBD as a Schedule 3 product, since TGA's regulation requires professional advice from a pharmacist to assess appropriate use. Healthcare professionals inadequate understanding of cannabis products presents difficulties for both the professional in providing advice as well as consumers who require education on CBD products. There is a growing repository of scientific literature and educational tools available to healthcare professionals regarding CBD. In order to ensure healthcare professionals have the understanding and confidence to incorporate a CBD product as part of a patient's

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treatment regimen, the TGA should help to ensure that there are adequate information sources and forums for information sharing for healthcare professionals.

- Overall, Aurora supports the amendment to re-define CBD as a Schedule 4 product and add CBD as a Schedule 3 product (Pharmacist Only Medicine).

Introduction:

Aurora Cannabis Enterprises Inc. is a Canadian licensed cannabis producer, headquartered in Edmonton, Canada. Aurora is one of the largest cannabis companies in the world by market capitalization. As of May 2020, Aurora has 13 Canadian cannabis production facilities, 9 of which with processing licenses for sale (including four that are EU GMP certified). Aurora also has international facilities in Germany, Denmark and Uruguay. Aurora has successfully received import permits for medical cannabis products from the Cayman Islands, Brazil, Germany, Denmark, Italy, Malta, Luxembourg, Poland, Czech Republic, the United Kingdom, Ireland, South Africa and Australia.

Aurora's main priority is to serve patients who require high quality cannabis products for medical purposes. To be a licensed producer of cannabis in Canada, each site is approved and continually inspected by Health Canada (Canada's federal health authority). In addition, as Aurora is now operating in several countries across the globe, we continue to have direct interactions with regulatory authorities in order to meet the regulatory requirements in each jurisdiction where we operate.

Scheduling change for CBD

Aurora supports the amendment to change the CBD Schedule 4 definition and add to add a New Entry for CBD as a Schedule 3 product (Pharmacist Only Medicine) – new text highlighted in red. Below we have provided requests for clarification or suggestions for modification in the specific elements of the New Entry.

Schedule 4 - Amend Entry
CANNABIDIOL in preparations for therapeutic use where:

a. **cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation and 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, except when included in Schedule 3; or**

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b. **cannabidiol is a synthetic or semi-synthetic copy of the molecule and comprises 98 per cent or more of the total cannabinoid content of the preparation and any other synthetic or semi-synthetic cannabinoids, other than cannabidiol, must comprise 2 per per cent or less of the total cannabinoid content of the preparation.**

except when cannabidiol comprises 98 per cent or more of the total cannabinoid content and the tetrahydrocannabinol (THC) content is less than or equal to 0.2 per cent of the total cannabinoid content of the preparation.

Schedule 3 - New 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 of the preparation; 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.

Aurora Comments on the Scheduling Change

Change a. the cannabidiol is either plant derived, or when synthetic only contains the (-) CBD enantiomer

Aurora comment:

Aurora recommends further clarification on 'plant derived', as to whether this would include different processes to purify CBD such as extraction, isolation, distillation. These were added in the proposed changes to CBD products with less than or equal to 0.2 percent THC, outlined in the Public Notice of 17 April 2020 (item 2.2).

Aurora also recommends clarification as to whether the product can include a mixture of CBD derived via different production processes, e.g. extracted cannabis product combined with concentrated or isolated CBD.

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Change b. the maximum recommended daily dose is 60 mg or less of cannabidiol

Aurora comment:

TGA has stated that "*Concerns about potential drug-CBD interactions can be handled effectively through limiting the amount of CBD able to be sold in a month's supply and the inclusion of appropriate warning labels.*". As noted by the TGA on The Safety of Low Dose Cannabidiol report (https://www.tga.gov.au/sites/default/files/review-safety-low-dose-cannabidiol.pdf; April, 2020), peer reviewed studies exploring the safety and toxicity of CBD are scarce. CBD has been assessed by the FDA and the EMA as a pharmaceutical drug "Epidiolex/Epidyolex", and deemed safe and effective for the treatment of severe epilepsy in children at doses ranging from 5 to 20 mg/kg/day; however, a full clinical evaluation of all cannabis products containing plant-derived or synthetic CBD has not been conducted.

Aurora feels that there is not enough scientific data on all CBD products to form a general conclusion on a maximum daily dose. Since Schedule 3 products will be require a pre-approval assessment from the TGA of efficacy, safety and quality, there should not be a maximum daily dose set for all products but instead allow for an approved recommended dose for individual products. A safe and efficacious dose is very dependent on individual characteristics, pre-existing medical conditions, concomitant medications (including CBD from other products), as well as product characteristics (plant derived or synthetic CBD). The TGA's report on The Safety of Low Dose Cannabidiol, only reviewed the safety of CBD in clinical studies assessing the low dose (60 mg) but did not compare to the safety of CBD in higher doses. In addition, if more data on a safe and efficacious daily dose of CBD reveals that 60 mg is not the ideal dose for all consumers, the Schedule 3 recommendation would need to be modified.

Aurora therefore recommends that no maximum dose is currently set for a Schedule 3 CBD product, but instead, a limitation on the total amount of CBD allowed per package (or per unit in a discrete form such as a capsule or tablet), recommended child-resistant packaging, as well as specific warning messages set by the TGA on the product label, Product Information or Consumer Medicine Information that could convey i) the product is not a prescription product, ii) consumers should inform their healthcare professionals that they are taking this product as well as other CBD products, iii) potential drug-drug interactions with CBD, etc. As Aurora has extensive experience operating under Health Canada's *Cannabis Regulations*, many of these concepts concerning limitations on packaging as well as specific warning messages, are a part of these regulations (https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/laws-regulations/regulations-support-cannabis-act.html).

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Change c. in packs containing not more than 30 days' supply; and

Aurora comment:

Similar to the above recommendation for point b., Aurora suggests the maximum dose should be removed from the list of criteria, a 30 days' supply would be different for different consumers. Therefore, Aurora recommends to remove the 30 days' supply criteria and instead limit the amount of CBD allowed per package (or per unit in a discrete form such as a capsule or tablet), recommended child-resistant packaging, as well as provide TGA required Product Information that includes specific warnings and recommendations for use.

Education and awareness are critical for consumers of CBD products to understand that the potential effects of high doses of CBD have not been extensively studied in all patient populations. Introducing a limit on the amount of CBD per package as well as child-resistant packaging would discourage chronic use in adults and prevent accidental ingestion by children. A limitation with 30 days' supply would be difficult to enforce and monitor at the pharmacy level, especially when a consumer may be able to access more CBD products at a different pharmacy or be taking other medicinal cannabis products simultaneously that contain CBD. Also, a 30 days' supply would not necessarily reduce the chance of accidental over-consumption.

Change d. cannabidiol comprises 98 per cent or more of the total cannabinoid content of the preparation; 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

Aurora comment:

Aurora's high CBD medical cannabis oil/extract products that are currently sold in Canada, as well as the specific products sold in Australia have approximately 30 mg/mL CBD and 1 mg/mL THC. With the total cannabinoid content being approximately 35 mg/mL, this current product would be 86% CBD and 3% THC. In order to achieve a 98% CBD content as well as less than 2% THC content, the cannabis product would likely need to undergo a different process, such as isolation or distillation. Aurora would like to understand further why the Schedule 3 product would need to have such a high CBD percentage and a low percentage of other cannabinoids, when there is no conclusive evidence that a high CBD percent (98%) product is less harmful than a medical cannabis product with 86% CBD, 3% THC and 11% other cannabinoids.

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In addition, as Aurora's current medical cannabis products fall under TGA's Special Access Scheme, it would be important for the TGA to provide clear guidance on the newly proposed CBD products under Schedule 3 and what all the necessary requirements will be concerning quality requirements (i.e., Good Manufacturing Practices) as well as what specific data is required to demonstrate efficacy (specific indications recommended) and safety.

Impact of Proposed Change – Potential Benefits and Costs to Aurora

1. Import of Aurora's Products, into Australia - Benefit

As Australia's current availability of medical cannabis products does rely to some degree on imported product, Aurora welcomes the proposal to classify CBD products as Schedule 3. This will present Canadian Licensed Producers with more opportunities to expand our market of CBD products in Australia and will also open up the availability of these products via a non-prescription route to consumers through a controlled and legal pathway.

2. Recommendation for TGA Guidance on Product Labelling and Product Information to be supplied with CBD products - Benefit

Unlike other global regulators, such as Canada and European countries, which have provided clear guidance on labelling and product information for medical cannabis products, Australia currently lacks clear guidance in this regard for medical cannabis products under the Special Access Scheme. In order to move towards offering CBD products as Schedule 3, there needs to be specific labelling guidance from the TGA. This will help promote healthcare professional and consumer education on these products, and in Aurora's opinion, will be more effective than limiting the dose or monthly quantities of products being offered.

3. Packaging Change and Testing Requirements - Cost

There would be cost incurred with labelling and packaging changes needed for the proposed changes of the 30 day limit and the 60 mg daily dose maximum. Licensed Producers who are currently selling CBD-only oils in Australia will incur additional costs having to order new bottles or syringes in order to accommodate these specific changes. Whereas Aurora's suggestion of a maximum mg/CBD per container could require no changes to the actual packaging/product. From a patient perspective, any change in the potency or packaging of their medicine could lead

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to confusion when dosing this product. If there are no changes to the packaging, they will continue to use the same CBD product, but accessed through a de-scheduled pathway.

TGA's current testing requirements for medical cannabis are in many instances, more specific and extensive than the requirements in other countries. Aurora does incur additional costs in testing products for the Australian market, in order to meet the specific requirements of TGA. Aurora would recommend that for CBD as a Schedule 3 product, the TGA clearly outline and consider greater flexibility of testing requirements (aligning with how the product is currently tested for other markets). Manufacturers such as Aurora, can demonstrate i) batch to batch consistency during the review of a Schedule 3 product and ii) current testing specifications performed for other markets are posing no potential risk to consumers.

4. Importance of Educating Healthcare Professionals – Cost with Long-term Benefits

Around the world an increasing number of doctors are recognizing both the symptom-relieving benefits of cannabis and the remarkably limited potential for harm. To date, no reports of human death directly caused by the overconsumption of cannabis have been reported and thus, many doctors are comfortable in providing access to medical cannabis for those patients most desperate to get relief from their chronic, uncontrolled conditions. Any healthcare professional, albeit a pharmacist, nurse, or doctor, who will observe the increased use of CBD products in Australia with this change in Scheduling, must also become familiar with the evidence supporting its use, with its possible untoward effects. Without this level of education, especially at the level of a pharmacist to provide the Schedule 3 required "professional advice to assess appropriate use", Aurora questions whether the more appropriate Scheduling for CBD should be Schedule 2 "accessible on pharmacy shelves. Purchase does not require advice from a pharmacist".

It would be important to ensure that Australian healthcare professionals are provided with the proper resources, so they can effectively utilize and understand the emerging scientific evidence around medical cannabis, and specifically CBD. Certified continuing education initiatives for doctors that focus on medical cannabis is the best way to achieve this. In addition, a forum in which Australian healthcare professionals can communicate with Canadian healthcare professionals that have prescribed cannabis would facilitate the exchange of up-to-date and accurate information related to medical cannabis and CBD.

Having the support of the TGA will be instrumental in assisting with the education of Australian healthcare professionals about medical cannabis and CBD.

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Conclusion

Aurora supports TGA's proposal to change the scheduling of CBD but has advised on further examination of the Schedule 3 criteria. When advancing this proposal, the TGA should place an emphasis on educating healthcare professionals as well as patients around the evidence showing that CBD can be a safe and effective, when certain precautions are taken. This will increase the confidence of healthcare professionals as well as patients, thereby improving outcomes and access.

Aurora applauds the TGA for this proposal, paving the pathway for other regulators to observe and learn, hopefully progressing the regulation of CBD and decoupling it from THC. Aurora would be happy to help the TGA with any inquiries or questions on our written feedback.

List of Contributors

Aurora's Global Regulatory Affairs, International Partnerships (Medical Sales), Clinical Science, Medical Affairs, Government Relations, Communications, Product Development and Legal Affairs team members.

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