

Response to *Pre-review: Extracts and tinctures of cannabis*.

Authored by Americans for Safe Access and International Medical Cannabis Patients Coalition

4 June 2018

40<sup>th</sup> Meeting of ECDD

Thank you for allowing us to address World Health Organization's Expert Committee on Drug Dependence (ECDD). We are encouraged to see the agenda of the 40<sup>th</sup> meeting of ECDD dedicated to carrying out pre-reviews of cannabis and cannabis-related substances. Americans for Safe Access (ASA), the leading medical cannabis patient advocacy organization in the United States, represents over 100,000 individuals that are using medical cannabis and the International Medical Cannabis Patient Coalition (IMCPC) represents patients from thirty four countries.

We were engaged in United Nations General Assembly Special Session on Drugs in 2016 (UNGASS) meetings where the member states reiterated their "strong commitment to improving access to controlled substances for medical and scientific purpose by appropriately addressing existing barriers." We are grateful to have the opportunity to share our experiences and offer the assistance of our international coalition to ECDD. Below you will find our review, suggestions and response to the critical review document entitled *Pre-review: Extracts and tinctures of cannabis*.

## **Section 1 Chemistry**

Overall, we agree with the authors section on Chemistry. We suggest using common and currently accepted terminology to avoid confusion. As it is unclear exactly what products the authors are actually discussing.

No systematic overview on the composition of the various products discussed is provided, and no percentages (max., min., typical values) of the main constituents in the various extracts are provided – except for BHO (the most problematic and least representative of these products).

## **Section 2 Pharmacology**

This section provides a comprehensive but basic overview of cannabis extracts and their pharmacology. In general, we agree with this subsection. Although it is thorough, it is hampered by a lack of precision when it comes to providing definitions (such as "dabbing") or

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### **National Office**

1624 U St. NW, Suite 200, Washington DC 20009  
PHONE: 202.857.4272 FAX: 202.857.4273

### **California Office**

770 L St., Suite 950, Sacramento, CA 95814  
PHONE: 916.449.3975

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to address important trends in consumption patterns (such as the use of existing dosing guidelines on cannabis extracts in harm reduction, or in tobacco cessation). Other data that balance the presented research outcomes seem to be missing:

*MacCallum, C. A., & Russo, E. B. (2018). Practical considerations in medical cannabis administration and dosing. European Journal of Internal Medicine, 49, 12–19. <http://doi.org/10.1016/j.ejim.2018.01.004>*

Furthermore, although several mentions of "edibles" (ingested preparations made out of Cannabis extracts) are made, a definition and a specific description of their pharmacological effects are absent. Yet the report on "Cannabis plant and cannabis resin", states that the pharmacology of edibles is addressed in the Pharmacology section of "Extracts and tinctures".

Finally, the author of the pharmacology section notes that "users who smoke or vape products with higher  $\Delta 9$ -THC contents than their regular product tend to up-titrate, resulting in greater overall exposure." However, more detailed scrutiny into the published literature shows ample evidence to the contrary to the author's narrative:

*L D Chait and K A Burke, "Preference for High- Versus Low-Potency Marijuana," Pharmacology, Biochemistry, and Behavior 49, no. 3 (November 1994): 643–47, doi:10.1016/0091-3057(94)90082-5.*

*T H Kelly et al., "Are Choice and Self-Administration of Marijuana Related to Delta 9-THC Content?," Exp Clin Psychopharmacol 5, no. 1 (1997): 74–82.*

*C H Ashton, "Adverse Effects of Cannabis and Cannabinoids.," British Journal of Anaesthesia 83, no. 4 (October 1, 1999): 637–49, doi:10.1093/bja/83.4.637.*

*S J Heishman and M L Stitzer, "Effect of D-Amphetamine, Secobarbital, and Marijuana on Choice Behavior: Social Versus Nonsocial Options," Psychopharmacology (Berl) 99, no. 2 (1989): 156–62.*

*Louisa Degenhardt and Wayne Hall, "The Association Between Psychosis and Problematical Drug Use Among Australian Adults: Findings From the National Survey of Mental Health and Well-Being," Psychological Medicine 31, no. 4 (May 17, 2001): 659–68, doi:10.1017/S0033291701003865*

Lastly on page 7, under 1.1.4 *Nabiximols (Sativex®)* the authors incorrectly refer to a pump from Sativex or a nabiximols as a "puff". This is completely inaccurate. Sativex and nabiximols are not inhaled in puffs, they are sprayed under the tongue or on the buccal mucosa. Simply put, when

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drugs are inhaled there are puffs, when applied under the tongue or on the buccal mucosa in a liquid it is a spray.

### **Section 3 Toxicology**

In general, we agree with the author's reporting of cannabis toxicology. However, several points of concern arise from this section as it appears the authors are not familiar with the field's accepted terminology or the difference between inhaled or oral-mucosal administration. It also seems there is unnecessary information regarding explosions, which distracts from the topic. The first is the strange framing of the different sub-taxa of the category (addressed below in §51-58), which includes "cannabis resin" (yet explicitly excluded from the terms of reference provided to the author), and agglomerates into "concentrates" what other authors divided into up to 5 categories.

It is also confusing to read concerns about "*disastrous fires and explosions*" in a report about the toxicology of drugs. It is fair to say that explosions due to home production of cannabis concentrates are certainly more likely to be associated with the lack of a regulated and standardized legal retail market than the toxicology of cannabis extracts per se. We recommend removing non-scientific information regarding explosions from manufacturing illicit substances; it does not fit within the science of toxicology. Lastly, the list of market authorization for Sativex is missing 19 countries under *3.1 Extent of therapeutic use*.

### **Section 4 Therapeutic applications and extent of therapeutic use and epidemiology of medical use**

We are in agreement with the section on the efficacy of nabiximols and cannabis extracts. We strongly support the conclusion of the authors that, "*There were few adverse events and no evidence of abuse, misuse, or addiction...*" The process for monitoring the abuse and diversion of a licensed pharmaceutical like Sativex, and there has simply been none evident from this rigorous process that involves monitoring the Internet and other reporting Poison Indexes.

However, this section does appear incomplete as it only addresses nabiximols. Yet, other extracts and tinctures of cannabis are available on the pharmaceutical market (such as in Germany, Netherlands, Australia, Malta, Canada, etc.), although often only marketed legally as products in compounding pharmacies. The section could be enhanced by discussing the above.

### **Section 5 Epidemiology**

We completely disagree with the authors' proposal that the researchers "*did not yield any articles related to licit production, consumptions and international trade of cannabis extracts*

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*and tinctures” and that “Overall, the use of tinctures is not widespread today, and evidence supporting the therapeutic use of tinctures is limited (Nabiximols are a sub-type of tinctures).”*

Lastly, the authors equate the manufacturing of extracts and tinctures to use and abuse of these products under the subsection *Nature and magnitude of public health problems related to misuse, abuse and dependence*, while leaving out relevant information about the effect these products actually have in humans. This section demonstrates a complete lack of understanding or due diligence to generate this report.

A basic search in a web browser, however, shows dozens of results, such as the 2017 annual report of the UN International Narcotics Control Board stating that globally, *“[the] licit use of cannabis has been increasing considerably since 2000. Before 2000, licit use was restricted to scientific research [...] In 2000, total licit production was 1.4 tons; by 2016 it had increased to 211.3 tons.”*

The committee experts might have been interested in knowing that this international agency explained that *“The United Kingdom [where Sativex® is manufactured] continued to be the main exporter of cannabis (2.1 tons, or 67.7 per cent of the total)”* and that *“the large majority of the stocks were held by the United Kingdom (93.1 tons, or 78.2 per cent).”* Much more data is widely available through the internet.

This subsection ignores the immense amount of information available about the illicit manufacture and traffic of the different extracts or tinctures included. The authors only acknowledge the “negligible role” of the *“seizures of tinctures”* – although it is broadly recognized that seizures are among the least representative metrics of illicit markets – and totally omits oils, concentrates, and other extracts.

## **Additional Resources**

International Medical Cannabis Patient Coalition (IMCPC)’s UNGASS 2016 Declaration delivered to the UN Commission on Narcotic Drugs in Vienna March 2015: <http://bit.ly/1TV0gNi>

Cannabis and Cannabis Resin- Critical Review Preparation Document 2016 prepared by the Americans for Safe Access at their National Unity Conference  
[https://www.safeaccessnow.org/critical\\_review](https://www.safeaccessnow.org/critical_review)

Testimony from WHO ECDD November 2015 Meetings:

Global Patient Populations Need International Medical Cannabis Policies to Evolve:  
<http://bit.ly/1TV0G6I>

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[pdf, 272kb Steph Sherer, Executive Director, Americans for Safe Access]

Cannabis, an irreplaceable botanical medicine of long standing human use <http://bit.ly/1TV0vbf>  
[pdf, 50kb Michael Krawitz, Executive Director, Veterans For Medical Cannabis Access:  
<http://bit.ly/1TV0vbf>]

The WHO cannabis background document: <http://bit.ly/1TV0nID>

### **Acknowledgments**

ASA would like to acknowledge the contribution of the following individuals:

Core Author:

Jahan Marcu, Ph.D.

*Corresponding author: [jahan@safeaccessnow.org](mailto:jahan@safeaccessnow.org)*

Contributing Authors:

Ethan Russo, MD

Kenzi Riboulet Zemouli

Tomas Sadilek

Pavel Kubu, MD

Steph Sherer

Debbie Churgai

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