

ADVISORY COMMITTEE FOR NOVEL FOODS AND PROCESSES

REQUEST FOR ADVICE FOR CBD APPLICANTS

Issue

1. As with many naturally derived plant extracts, cannabidiol (CBD) based products and extracts may contain several known components that can potentially be harmful for the consumer.
2. Given the complexity of the CBD industry with a wide spread of small and medium sized companies, several companies applying to place CBD products in the UK market are aiming to jointly submit their applications for authorisation. Whilst each manufacturer is planning to submit individual manufacturing processes and composition analyses, they propose to share results from the relevant toxicology studies to prove the safety of CBD-based novel food products. Applicants question whether this approach will be accepted to demonstrate the safety of the product.
3. Applicants of small and medium-sized companies have also requested a reference range of acceptable levels of cannabinoids and other components of their products to account for variability between company's batches. This would include chemical and microbiological contaminants such as heavy metals, pesticides and mycotoxins. The Committee is asked whether it is willing to consider the proposition, and, if so, if it is willing to provide referential numerical values.

Background

4. CBD was confirmed as a novel food in January 2019 and as yet, there are no authorised CBD products on the UK market. In February 2020, the FSA set a deadline of 31st March 2021 by which businesses already selling CBD must have submitted a dossier to the FSA which must be complete enough for the FSA to validate these products enabling them to remain on the market. Any companies not achieving this will be required to remove their products from the market or face potential prosecution. Following validation, applications received will be presented to the ACNFP for consideration.
5. CBD is one of more than 113 well known cannabinoids. In the production process of CBD extracts, a purifying stage aims at minimising the presence of unwanted cannabinoids that may cause harmful and unwanted effects in the consumer. Amongst these cannabinoids lies tetrahydrocannabinol, or THC, which is known to cause psychotropic effects in consumers. Scientific literature suggests that the reported side effects of CBD-extract-based products occur due to THC contamination rather than CBD hydrolytic conversion in the stomach of the consumer¹.

¹ Lachenmeier, Dirk W et al. "Are side effects of cannabidiol (CBD) products caused by tetrahydrocannabinol (THC) contamination?" *F1000Research* vol. 8 1394. 8 Aug. 2019

6. In the UK, the Home Office classes any product that contains more than 1mg of THC per unit as a controlled substance and therefore appropriate licenses would be required to handle such products.
7. As an extract from a natural source, there is also the potential for the presence of contaminants such as heavy metals, mycotoxins and extraction solvents. In *Cannabis sativa* L. plants, *Aspergillus spp.*, *Penicillium spp.* and *Cladosporium spp.* are described as the main cause of mycotoxin formation. Arsenic, cadmium and mercury appear as the main heavy metals of concern, reported at high levels in several studies. In the case of pesticides, due to the illegal nature of growing *Cannabis sativa* in many countries, it is not uncommon to find plantations treated with pesticides not approved for food plants, increasing the risk of consumers being exposed to harmful chemicals ². While most of these contaminants are a higher cause for concern when cannabis is consumed through inhalation, there is a risk that they may remain in the CBD extract if it is produced and purified incorrectly.

Cannabinoid content

8. In Table 1, average levels of cannabinoids reported by applicants in CBD extracts are presented. These offer members a reference of the percentage values present in current applications in order to guide the discussion:

Table 1: Average levels of cannabinoids reported by applicants in CBD extracts

Cannabinoid	Ap. 1 (Extract)	Ap. 2 (Extract)	Ap. 3 (Oil 10%)	Ap. 4 (Extract)	Ap. 5 (Extract)	Ap. 6 (Oil 5%)
CBD (%)	98.7	98.7	11.2	>70	98.5	9.1
THC (%)	<0.010	<0.005	<0.005	N/A	<0.05	<0.04
THCA (%)	<0.010	-	<0.0025	-	-	<0.04
CBDA (%)	<0.010	-	<0.0025	-	-	<0.04
CBN (%)	<0.010	<0.002	<0.0025	<20	-	<0.04
CBG (%)	<0.010	N/A	<0.0025	<20	0.1	<0.04
CBDV (%)	<0.030	0.18	0.024	-	0.3	-
Butyl-CBD (%)	0.054	-	-	-	-	-
CBDB (%)	-	0.16	-	-	-	-
CBDVA (%)	-	-	<0.0025	-	-	-

9. According to Lachenmeier et al. (2019), CBD products analysed in the market retrieved concentrations of THC above the LOAEL and above the German guideline value for total THC content. The table summarising these results is presented in Annex A for reference.

² McPartland J.M., McKernan K.J. (2017) Contaminants of Concern in Cannabis: Microbes, Heavy Metals and Pesticides. In: Chandra S., Lata H., ElSohly M. (eds) *Cannabis sativa* L. - Botany and Biotechnology. Springer, Cham. https://doi.org/10.1007/978-3-319-54564-6_22

Other components

10. Other components of interest and likely to vary between products from different manufacturers would include:

- Heavy metals (cadmium, mercury, nickel, lead, arsenic, chromium, zinc, copper)
- Aflatoxins, ochratoxin
- E. coli, salmonella, total aerobic microorganism count, total yeast and mould
- Dioxins, PCB's, PAH's
- Pesticides (permitted and non-permitted)
- Extraction solvents

We would anticipate manufacturers providing certificates of analysis for these components and providing details of their manufacturing process for each CBD product or ingredient they propose to market. Manufacturers are hoping to select a 'representative product' and to use this product to carry out the ADME and toxicological studies as this is a large financial commitment and could reduce the numbers of animals necessary to undertake toxicological studies.

Committee Action Required

- Members are asked whether it is possible to establish acceptable ranges of CBD and other components in the product to account for company batch variability in joint applications.
- If so, members are asked whether it is possible to provide a numerical range, in absolutes or percentage.
- Members are asked whether they are willing to accept evidence from relevant toxicology studies and evidence of safe use across different producers in joint applications.

**Secretariat
August 2020**

Annexes to the dossier

Annex A: Table 2 from Lachenmeier, Dirk W et al. "Are side effects of cannabidiol (CBD) products caused by tetrahydrocannabinol (THC) contamination?" F1000Research vol. 8 1394. 8 Aug. 2019