Minutes

Joint Subgroup of the Advisory Committee on Novel Foods and Processes (ACNFP) and Committee on Toxicity (COT) on CBD and Hemp Derived Products. Minutes of the 9th CBD Meeting held on the 1st of February 2024

These minutes are subject to confirmation by the Subcommittee.

Members are required to declare any personal interest in matters under discussion; where Members have a particularly close association with any item, the Chairman will limit their involvement in the discussion. In cases where an item is to be discussed in their absence, a Member may make a statement before leaving.

Minutes of the 9th meeting of the Joint Subgroup of the Advisory Committee on Novel Foods and Processes (ACNFP) and Committee on Toxicity (COT) on CBD and Hemp Derived Products, held on 1st February, in person at Clive House and online using Microsoft Teams.

Attendance

Committee Chair

Dr Camilla Alexander-White - Chair of ACNFP

Professor Alan Boobis - Chair of COT

Committee Members

Mrs Alison Austin - ACNFP

Dr Mac Provan - COT

Dr Stella Cochrane - COT

Professor Gunter Kuhnle - COT

Dr Cheryl Scudamore - COT

Prof. Gary Hutchinson - COT

Dr Lesley Stanley - ACNFP

Dr Simon Wilkinson - COT

Dr James Coulson - COT

Professor Shirley Price - COT

Apologies

None

Secretariat

Mr Ben Haynes - Lead Secretariat for Subgroup

Mrs Ruth Willis - Technical Secretary ACNFP

Dr Tahmina Khan - ACNFP Secretariat

Mrs Afielia Choudhry - ACNFP Secretariat

Mr. Will Smith - ACNFP Secretariat

Dr Olivia Osborne - COT Secretariat

Dr. Cath Mulholland - Technical Secretary COT

Mr. David Franklin - Scientific Sampling and Laboratory Policy Team Lead

Miss Victoria Balch - ACNFP and subgroup Administrative Secretariat

Miss Sophy Wells - ACNFP and subgroup Administrative Secretariat

Observers

Mr. Michael Dickinson - Regulated Products Team Lead

Executive summary

The Joint Subgroup of the Advisory Committee on Novel Foods and Processes (ACNFP) and Committee on Toxicity (COT) on cannabidiol (CBD) and Hemp Derived Products met on the 1st February in a hybrid meeting to further progress the review of wider cross cutting questions on CBD and THC safety. In the meeting, the sub-group reviewed the analytical data recently obtained by the FSA in conjunction with a discussion of the possible further actions for management of the group B CBD ingredients (i.e. with 98% pure CBD plus other cannabinoids).

An update to the previously discussed literature review on the toxicological effects of tetrahydrocannabinol (THC), and how this can be applied to assessing THC as a contaminant in CBD products, was also explored. Progress was made on the consideration of the analytical data to support chemical characterisations and toxicological evaluation of CBD, and on the safety considerations of low levels of THC as a contaminant. Consideration of the group B CBD novel foods will continue at the next available meeting.

1. Apologies and Announcements

No apologies were received from any members or observers.

2. Welcome and introduction

The Chair welcomed the members, representatives from the FSA, the observers and the Secretariat team.

3. Minutes from the November meeting

CBD/08/MINS

The Chair reviewed the draft minutes with the Subgroup. These were agreed as an accurate record subject to minor amendments.

4. Item 1 – Analytical data workshop and round table discussion (Reserved Business)

CBD/09/01

A presentation from the FSA was provided that outlined the work supported by the FSA on analytical detection and quantification of CBD and other cannabinoids. The potential challenges in detecting cannabinoids in some matrices was explored. The presentation highlighted the need to use appropriate quality data in considering the composition of cannabinoid-containing novel foods and the potential issues for stability and interconversions.

It was clear from a recent interlaboratory study, that there was potential for high variability in the data from some analytical methods use to quantify cannabinoids. Interlaboratory trials had shown this for CBD and THC. The subgroup commented that it was important for applicants to use accredited laboratories wherever possible, and when internal methods were being used, they should be well described and validated. Limits of detection and limits of quantification of all analytical methods used by applicants should be clearly demonstrated and high-quality certificates of analysis sought from applicants. LOD and LOQ values should then relate clearly to product specifications.

Following the presentation, members raised concerns regarding the stability of CBD and associated cannabinoids in varying environments and storage conditions. The Subgroup noted evidence that degradation of CBD to THC can occur over time and at temperatures that could occur in food manufacturing. Further discussions were held regarding the available batch to batch data for products and the matrices in which the data has been generated. It was suggested that matrix could affect both the reliability of the data but also the stability of the novel food. This had been allowed for in the assessment factors used to derive the provisional ADI for Group A pure form CBD but was more complex for Group B with variable cannabinoids in a mixture.

As a general recommendation the subgroup suggested that better characterisation data should be generated for all CBD products, in terms of knowing the cannabinoid profile in the novel food. At present, in many Group B applications, there remained a significant proportion of the novel food for which the composition is unknown. This should include cannabinoids and their major degradation products and impurity profiles. It was suggested that to support this, a guidance document that provides a specification of the analytical data required

by applicants for identifying and quantifying CBD or other cannabinoids should be generated. Following this, members discussed whether the analytical uncertainties and need for data would have implications for consortium applications which might be more variable in the specification than other novel foods.

It was agreed that it is unlikely that data from a toxicology study performed for one Group B product could simply be read-across to another Group B product *in the absence of good composition data on the cannabinoid profiles* of the test item used in the toxicology study and those cannabinoids present in the novel food products for the market.

Actions from this item – The Secretariat is requested to consider producing a guidance document for applicants which requests laboratory validation data, detection limits of methods being used, alongside proof of accreditation.

Secretariat to request further analytical data from the group B and C applications.

5. Item 2 – Group B CBD Novel Foods – Approach to managing the group of applications paper (Reserved Business)

CBD/09/02

Members were asked to advise on a document which outlined two possible approaches the FSA could take when managing the group B CBD ingredient applications. Members were also reminded and presented with a summary of the current datasets for group B which had been discussed during prior meetings. Advice from the Subgroup was sought on whether the group B applications should be managed individually or whether it was possible to group them together based on the compositional data available for the cannabinoid profile of the ingredients. The possibility for read-across between the studies was a key consideration in deciding which approach would be appropriate for this data.

Members discussed each approach, and that the absence of human data for group B continued to be a data gap. By comparison Group A pure form CBD had adverse effects information from human studies that could be used together with toxicology data in a weight-of-evidence approach to deriving a provisional

acceptable daily intake (ADI). That would not be the case for Group B. The safety evaluation of other cannabinoids in Group B products would largely rely on in vivo toxicology data available in the public domain or submitted by applicants. The presence of a range of different cannabinoids in different novel foods made interpreting the study results from mixtures more difficult, especially in the context of the lack of data on effects individually for other common cannabinoids present in the mix. Overall, while study to study variability was high, members agreed that the pattern of liver effects for high level CBD (e.g. 60-98% w/w) in Groups B products were similar to those seen for Group A studies, with liver effects occurring at similar doses once the data was corrected for CBD content.

Given the FSA have published the consumer advice for pure form CBD in October 2023, which states a provisional ADI of 10 mg CBD per day, this could be used to assess the safety of the CBD component in a Group B product, where intakes are calculable. Depending upon the quantity of other cannabinoids in a mix, the possibility of simply applying an additional uncertainty factor to the provisional ADI for the missing human data for group B cannabinoids and the unknown effects of the other cannabinoids was considered. To take such an approach of applying an extra assessment factor would be invoking the precautionary principle in the absence of scientific evidence. Applicants' toxicology studies that related directly to a Group B product can be used to determine a point of departure on a case by case basis, if data quality allows. Reading across from one Group B product to another, without characterisation data on the different products, was not considered possible.

The Chair proposed that to support comparison of all available studies on cannabinoids, the effects data and point of departures seen for Group A and Group B CBD products to date could be standardised and mapped. The approach could be used to visualise the possible data gaps, the relative potency of Group A and B cannabinoid ingredients and begin to predict the effects that could be seen for particular formulations. This could provide a route, rather than simple one-to-one read across, to make better use of the data as it is generated. Such a view of the CBD toxicological data landscape, similar to toxicological endpoint reviews produced by the US ATSDR, could help to defend the use of the ADI for CBD to cover broad spectrum effects of CBD, and inform making decisions on the validity of read-across from studies on different cannabinoid ingredients, inform future data collection to minimise the use of animals and consider relative potency of different cannabinoids. However, it was noted that read across will be especially difficult for consortium applications with varying degrees of composition between Group B products.

Actions from this item – The Secretariat is requested to produce a NOAEL mapping exercise for each subchronic endpoint, in the first instance for CBD data, allowing members to readily compare and update data when required. This will provide insight into the data gaps and uncertainties for this group of applications.

6. Item 3 – THC Literature Review (Reserved business)

CBD/09/03

The Subgroup reviewed additional data on the toxicity of tetrahydrocannabinol (THC) consumed orally, identified through a literature search. The Subgroup was asked to consider whether a safe upper intake could be identified for THC as a contaminant to support the assessment of CBD novel foods with trace levels of THC. This would provide a food safety context to the work of the Advisory Council on the Misuse of Drugs (ACMD) recommendation to set maximum levels of THC allowable in CBD products for the purpose of exempting them from drugs legislation.

Following the previous discussions of the scientific opinion published by the European Food Safety Authority (EFSA) on THC as a contaminant of milk and foods of animal origin, the Subgroup agreed the uncertainty factors applied by EFSA were reasonable and agreed that the Acute Reference Dose extracted from the literature was applicable. However, members raised further concerns regarding the data gaps surrounding chronic exposure to THC as the ARD failed to consider specifically the accumulation of THC within the body with more chronic daily use.

The recommendations of the Advisory Council on the Misuse of Drugs (ACMD) for THC in CBD novel food products was also discussed. Following the actions set by members of the Secretariat during the previous meeting, further evaluation by the sub-group regarding *how the recommendations of the ACMD compare to the LOAEL derived from the toxicology data review* were sought by the Secretariat. This reflects that the ACMD recommendations, if adopted by the Home Office in law, would provide criteria for the exclusion of foods derived from *Cannabis sativa* from the Misuse of Drugs Act but this is not intended to set a safe level of consumption for the exempt products.

Discussions were held around whether the recommendations of the ACMD would be sufficiently protective in the context of food safety. The level set in the ACMD recommendation is on a serving basis and was compared to potential exposure to THC from the proposed novel food uses. It was noted that the ACMD level would be protective of safety if one unit of consumption containing 10mg of CBD was consumed per day. However, food intakes were more variable and as such the Subgroup recommended that a level of THC in products was set as a proportion of CBD based on the toxicological data available.

Given that any novel food authorisation would set a level for contaminants such as THC in the specification, defining a specification for THC as lower than a specific value or THC as a proportion of the CBD content would be more practical to apply to assure safety of novel foods.

Actions from this item – The Secretariat is requested to consider setting a specification for THC concentrations in CBD novel food products.

7. Date of the next meeting

The next meeting is scheduled for Wednesday 22nd May 2024. It will be held online via Microsoft Teams as a virtual meeting.