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 4th CBD Meeting held on the 17th of January 2023

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 4th 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 17th of January 2023, online using Microsoft Teams.

Attendance

Committee Chair

Dr Camilla Alexander-White - Chair of ACNFP

Committee Members

Professor Alan Boobis - Chair of COT

Mrs Alison Austin - ACNFP

Dr Cheryl Scudamore - COT

Dr Stella Cochrane - COT

Dr Lesley Stanley - ACNFP

Dr Mac Provan - COT

Professor Shirley Price - COT

Dr James Coulson - COT

Professor Gunter Kuhnle - COT

Prof. Gary Hutchinson - COT

Apologies

Dr Simon Wilkinson - COT

Observers (FSA)

Mr. Will Smith - ACNFP Secretariat

Observers BEIS

Ms. Frances Hill

Secretariat

Mr Ben Haynes - Lead Secretariat for Subgroup

Mrs Ruth Willis - Technical Secretary ACNFP

Dr Tahmina Khan - ACNFP Secretariat

Mrs Afielia Choudhry - ACNFP Secretariat

Dr Cath Mulholland - Technical Secretary COT

Dr Olivia Osborne - COT Secretariat

Miss Victoria Balch - ACNFP and subgroup Administrative Secretariat

Executive summary

The Joint Subgroup of the Advisory Committee on Novel Foods and Processes (ACNFP) and Committee on Toxicity (COT) on CBD and Hemp Derived Products considered a data update on the EIHA Consortium of CBD applications during their meeting on 17th January 2022. They identified several areas requiring further evaluation that need to be considered in order to progress with the safety assessment of CBD Novel Food applications.

1. Apologies and Announcements

Apologies were received from Dr. Simon Wilkinson.

2. Minutes from the 1st, 2nd and 3rd meetings

CBD/01/02/03/MINS

The Chair welcomed the members, representatives from the FSA, the observers and the Secretariat team. The Chair noted that the status of minutes from the previous subgroup meetings was to be addressed by the lead Secretariat.

The lead Secretariat thanked the members for their continued patience whilst awaiting the package containing the minutes which had been reviewed by FSA staff. The Secretariat explained that the package was circulated in December and was therefore available to Subgroup members for further commentary. The Secretariat explained that the deadline for comments had passed and as such, the final minutes are ready to be presented during this meeting.

The three sets of minutes were presented, and further comments were raised by members and updated accordingly in the draft with the agreement of the Chair and Subgroup members present. It was concluded that the minutes documents were completed.

3. EIHA Consortium CBD Paper (Reserved Business)

CBD/04

Background to the CBD working group - refresher

Upon request from the Chair, both the lead secretariat and the ACNFP Technical Secretary provided a refresher to the Subgroup members on the goals and focus of the CBD working group in the coming months. The workplan for the group for the next six to nine months was outlined and accepted.

How any conclusions reached would be used by the ACNFP in reviewing the novel food dossiers was discussed. It was explained there are also wider issues beyond the toxicology that will need to be considered in the applications review.

The next areas of work for the Subgroup were considered. Following the review of the high purity CBD ingredient the next dataset for review will be the ingredients with a greater range of cannabinoids followed by the broad-spectrum data packages.

Work on these data packages had already commenced. The Secretariat are currently also considering which other aspects of the CBD assessment it would be beneficial to make use of the Subgroups expertise in supporting the applications review. For example, understanding the proposed level from the advisory Committee on the Misuse of Drugs recommendations for THC in CBD products and how this links to food safety considerations.

The Chair and Members agreed that the FSA should prioritise organising future meeting dates and having the topics of these meetings recorded at the nearest opportunity, to ensure continuity and efficient use of time and schedules of the Subgroup members.

Action; Secretariat to provide a plan for the topics to be considered at forth coming meetings.

Detailed review of the updated data package.

The Subgroup were provided with a toxicological study data for the EIHA Consortium covering products with greater than 98% CBD. A separate study is being generated for products with a wider range of cannabinoids. The study is intended to add to the existing body of evidence for CBD isolate/pure form products, incorporating new information as provided by the applicants.

The identification of the reserved ADI for isolates by the Subgroup during the previous subgroup meetings, allowed the group to make some initial conclusions and build upon the advice already provided to consumers. For this meeting the FSA provided the new data to test whether it would support the reserved ADI based on the body of toxicological evidence. The FSA also requested that the

Subgroup provide an indication as to whether on its own, the data package could support data read across to the wide number of consortium members who are using it to maintain their products on the market.

Members reviewed the new study considering the information on the toxicological parameters and whether the whole body of evidence would provide further support for the previously derived toxicological point of departure, for which toxicological effects/endpoints and whether there were any outstanding evidence gaps. Considerations were made by the Subgroup on the new study data as follows:

of the applicant had identified a No Observed Adverse Effect Level (NOAEL) of 25 mg/kg bw/day, which was considerably lower than the previous datasets presented to the Subgroup for review. The Subgroup reviewed the study and the identified NOAEL. It was noted that the NOAEL was based on the observations in the ovaries and adrenal glands which differed from the endpoints used in the other studies reviewed. Based on the evidence presented and the commentary from those running the toxicological study, the Subgroup agreed the NOAEL was 25mg/kg bw/day for this study.

The subgroup utilised the new dataset to test the provisional ADI of 0.15mg/kg/bw/day which is equivalent to 10mg/day for a 70kg adult. The Secretariat informed the Subgroup that the EIHA consortium had already proposed their own ADI in a summary statement which suggested an ADI of 17.5 mg/day for a 70kg adult. It was debated amongst members that there is potential that any effects seen in humans may be different from those effects seen in the animal models. As such, further discussion into ADI calculations using this dataset were taken offline and explored via correspondence to consider the new study in the context of the additional data.

It was also noted that two members of the subgroup declared conflicts of interest when discussing the dataset. These conflicts of interest were related to having connections with those undertaking CBD projects of interest, however the members in question declared that they were not involved with them directly. As such, both members declared having nothing to do with the projects and therefore they continued to play an active role in Subgroup discussions.

Subchronic 90-day study general commentary overview

The 90-day study was deemed to be generally good; the applicant had provided further detail and commentary on every observable parameter that was

measured. As a result, the 90-day supporting evidence was considered adequate to based conclusions on the toxicological aspect of the assessment.

The Subgroup discussed the potential of whether a conclusion could be drawn on the accumulation of CBD in tissues over time from the data. The reason for this was because the study? suggested CBD has a half-life longer than 24 hours. At the end of the 90-day study recovery period the applicant reported that there were significant levels of CBD in tissues which was higher than levels in the blood.

The Subgroup noted that the applicant mentioned the disproportionate accumulation of CBD in reproductive tissues and kidneys but did not explain the basis of it. They also had not follow up by assessing lipophilic tissues in the study, where CBD would be expected to accumulate. This limited the interpretation of the data to some extent, when regarding the ability to extrapolate and use the data.

Specific organs

- Thyroid

The Subgroup reviewed data considered by the applicant as adverse on the impact of their test item on thyroid induction. Members agreed with each other that from the thyroid observations, the effects seen were an adaptive response alongside the observations seen in the liver. One outlying observation by the applicant was highlighted by members. The applicants TSH and T4 hormone levels as well as T3 hormone level observations were inconsistent with the function changes observed. Once the applicant detected a change in T4 hormone level, they saw no change in TSH hormone levels. Members suggested that this unexpected finding was most likely the result of the analytical method used being insufficiently sensitive enough. One possible explanation was that the drive for the thyroid changes observed was an elevation of TSH.

- Adrenal

The Subgroup noted an accumulation of the test item in the adrenal gland that was observed by the applicant. It was debated whether this observation may or may not be adverse. Members agreed with the applicant that the observations made when observing the adrenal glands and the ovaries would correctly lead to

a NOAEL of 25mg/kg bw/day.

However, members noted that the there remains a data gap from the study on why those effects were seen. It was concluded that there was no evidence that the effects seen were important. The effects appeared to be a transient observation, ultimately suggesting that there was not an issue to influence wider conclusions on CBD.

- Reproductive toxicology

The subgroup noted the ongoing data gap on reproductive toxicology for CBD. Members agreed that in the absence of new data the current advice for consumers that women and men who are wanting to conceive should not be exposed to CBD would remain.

From the observations for reproductive related parameters, the effects observed were judged to be a transient effect. The ongoing data need to understand what the long-term implications are for the ovary from exposure to CBD remained. Additionally, members commented that the applicant's data suggested that there was no inflammation in the ovary, which would be expected where the other findings observed were present.

The Subgroup considered the comment from the applicant that there was no impact on the menstruation of the rats from exposure to CBD. Reproductive toxicology specialists on the group highlighted that the Wistar Rat only has a four-day menstrual window, which would make observation of any impact more difficult. As such this was not seen as evidence that the CBD was not having impacts on reproductive function and continued to consider this a data gap.

Toxicokinetics

The Subgroup reviewed the quality of the toxicokinetic data that was provided both alongside the 90-day study and as a separate single kinetic study report by the applicant, as part of their dossier application.

Members agreed that the toxicokinetic data provided did not fully address this aspect of the review. It was suggested that this was on going data gap and may be mitigated in part by the applicant providing the data that appeared to be missing from the data reported.

Conclusions

From the review of the data the Subgroup agreed that the NOAEL from the study was level of 25mg/kg bw/day. This was based on their adrenal and ovary results correctly reflected the observations they had made throughout their study.

The subgroup took an action to put the new data into context of the wider dataset for highly pure CBD ingredients to test the provisional ADI that had previously been identified.

The Subgroup commented that the focus of their review of the data is to set a generic ADI for pure form >98% CBD products which is most likely to be relevant to CBD in oil supplements. For individual food product dossiers reviewed under the novel food regime, the ACNFP will have to consider whether the ADI is applicable to the food matrix i.e. are the UFs enough to account for any increase in bioavailability from the matrix and given all the other things that create uncertainty in the risk assessment through lack of data.

4. Item 2: Position Paper for >98% pure form CBD products

The Secretariat introduced item 2 on the agenda; the >98% pure form CBD position paper skeleton which collates all of the progress made thus far throughout the Subgroup meetings on whether there is sufficient data to identify a provisional ADI. Members views were sought on the content of the paper and whether the proposed structure would adequately capture of the work of the subgroup.

It was explained that the position paper will eventually be cleared by the wider parent committees for approval through the agreed governance measures. The main ACNFP and COT committees will be the chosen committees who will further scrutinise and where agreeing the position adopt the draft paper before publication. This reflects that the Subgroup serves the interest both committees. To support review the Secretariat was requested to circulate the original position paper from the COT on CBD in order to understand the starting point for the new paper.

Action: Secretariat to circulate original CBD position paper from the COT to inform Subgroup review of the new position paper.

Following initial discussion, it was agreed that Members would have a commenting period on the draft until the 24th of January. Initial comments were received that included that some sections of the draft need to be more detailed, particularly the uncertainties updates and the path taken to determine a suitable Point of Departure from each study to form the ADI.

It was also noted that the FSA should be careful about how they talk about the term ‘uncertainties’ to allow for human sensitivity within a population.

Action: Members to comment on the skeleton to inform the first draft of the statement for further input.

5. Date of the next meeting

The next meeting is scheduled for Wednesday 8th March 2023. It will be held online via Microsoft Teams.