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 1st CBD Meeting held on the 27th of July 2022

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 1st 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 27th of July 2022, online using Microsoft Teams.

Attendance

Committee Chair

Professor Alan Boobis - Chair of COT

Committee Members

Mrs Alison Austin - ACNFP

Dr Cheryl Scudamore - COT

Dr Lesley Stanley - ACNFP

Dr Simon Wilkinson - COT

Professor Shirley Price - COT

Dr Stella Cochrane - COT

Dr James Coulson - COT

Secretariat

Mr Ben Haynes - Lead Secretariat for Subgroup

Dr Cath Mulholland - Technical Secretary COT

Dr Olivia Osbourne - COT Secretariat

Mrs Priscilla Wanjiru - ACNFP Secretariat

Mrs Ruth Willis - Technical Secretary ACNFP

Dr Tahmina Khan - ACNFP Secretariat

Mrs Afielia Choudhry - ACNFP Secretariat

Mrs Jenny Lika - ACNFP Secretariat

Miss Victoria Balch - ACNFP and subgroup Administrative Secretariat

1 . Apologies and Announcements

1. Apologies for absence were received from the joint Chair Dr Camilla Alexander White, Gary Hutchinson who will providing expertise as needed and Mac Provan. It was agreed that Dr Rene Crevel would participate in the group on an ad hoc basis following his retirement from the Committee on Toxicity earlier this year.

2. Record of potential conflicts of interest

2. It was noted that Professor Boobis is part of the external advising committee- for Centre for research on Ingredient Safety (CRIS) at Michigan University. The organisation has a research project on CBD. Professor Boobis has no direct

involvement in the project or benefit from the work and as such while noted no further action was considered necessary.

3. Similarly, Dr Stella Cochrane, highlighted that the organisation she works for, Unilever, has a CBD project, but Dr Cochrane has no involvement. As such while the potential conflict was noted no further actions was considered necessary.

3. Introductions

4. The technical Secretary for the ACNFP Ruth Willis introduced the background to the formation of the subgroup. It was explained it had been noted that the COT had looked at the evidence on the safety of Cannabidiol (CBD) as substance safety back in 2020. The consumer advice had provided the backbone to the consideration of the significant number of applications for CBD containing ingredients received in early 2021. However, it was recognised that the data provided by the applicants represented an additional data set that could further develop thinking on what would represent a safe upper intake level of CBD.

5. The group had been formed to consider the additional evidence and consider if this could provide a framework for the assessment of individual dossiers on their own merits. To support facilitation of the subgroups consideration of the data these will be presented on the basis of their composition so similar test substances can be considered together if relevant.

6. It was explained that the key questions for the group were:

- Whether it was possible to identify a safe upper intake level for CBD based on the additional data
- Whether there were new conclusions based on the dataset that could be reached to inform policy making and consumer use of the products and
- Whether further data was required to address any remaining data gaps and uncertainties.

The work of the subgroup will take place as reserved business and will be published routinely once publication plans are in place.

4. CBD Isolate Update Paper – (Reserved Business)

7. The subgroup began the discussion by highlighting the most immediate uncertainties and conclusions that could be extracted from the paper. The committee considered each toxicological adverse effect one at a time. These informed discussions on the further data to be collected and analysed from the dataset at future meetings. It was noted that areas identified for deeper consideration include Repro/Immunotoxicity, Hepatotoxicity, Thyroid toxicity, and Genotoxicity. From the data presented the key points raised are detailed below.

8. The subgroup considered that a detail review of each study and the supporting data was needed verify where there are adverse effects ad at what doses. It would not be possible to reach conclusions until this work had been undertaken. The possibility of a meta-analysis to support this work was considered.

9. The possibility of pulling data from additional external data sets was also a notable discussion point. Members noted the anecdotal data from the yellow card reporting system. This included both medicinal and food supplement uses of CBD containing products. It was discussed that the minimum dosages were not known for these cases and therefore difficult to draw any conclusions from these to support the wider review.

10. Clinical data was identified as a potential useful data source particularly where it could address datagaps on immunotoxicology data. The subgroup concluded that the Secretariat could explore whether there are additional datasets to be considered.

11. It was noted that the quality of the studies provided to support authorisation was variable. It was agreed that the quality of the studies should be reviewed in detail to understand how they form a dataset on which to base conclusions. Compositional data was heavily discussed at this meeting – it was noted that as there is the potential for interconversion as well as analytical uncertainty in the testing methodologies which adds an uncertainty when seeking to compare data from test material that are not the same purity. This is important from a reproductive toxicology point of view because there is evidence that THC 9/8 can induce reproductive adverse effects. This could make interpreting data where the extract is less pure more difficult. The possibility of lab-to-lab variability needs to be considered, for example, the way applicants conduct the study can affect this. It was questioned whether applying international quality standards would minimise the uncertainty with this data.

12. Stability – The subgroup recognised that while data on stability is provided as part of the regulatory data package it is difficult to replicate the future consumer

behaviour in the home. This was recognised as a potential source of uncertainty to be considered by the subgroup in their work. However, it was noted that there is no systematic way of looking at the impact of storing things differently throughout the food chain from a scientific point of view.

13. Members expressed the need for more toxicokinetic data sets. These data sets need to be assessed and determined if they are reliable enough.

14. For reproductive toxicology, whilst there are indications in the evidence of something that should be reviewed further in 90-day studies and their subsequent follow ups, the committee does not have enough evidence to reach conclusions on this point.

15. When concluding on Immunotoxicology, the subgroup decided that the evidence indicates some impact from CBD but the nature of the impact is difficult to identify. The subgroup suggested that a immunotoxicologist be asked to comment on the data that is presented to the subgroup.

16.The degree of regulation to be considered via immunotoxicology is dependent on who and when the changes in immune systems are occurring. The subgroup provided examples of scenarios to consider for example the immunosuppressed and the linkage this may have to any consumer advice on co-consumption of CBD with some medicines.

17. It was concluded that this aspect should be considered further. Another point for consideration in discussing the CBD was the importance of the administration vehicle and the impact on the uptake and impact of CBD. This would need to be consider for each study as it may account for difference in individual studies with similar test materials. The subgroup wished to see tabulated data for each study report and in an evaluative format which includes the nature of the material to inform discussions at next meeting.

18. It was also discussed whether there was a role in considering data on the experience of consumers / post market monitoring. The subgroup was keen to make best use of any available data and noted that for example, considering reversibility as an endpoint in light of clinical data could help monitor post marketing. This was recognised as a data gap that needed further consideration once the current datasets had been explored further.

Conclusions from the meeting

19. It was agreed that based on the data as presented it was not possible to reach conclusions or comment on the need for further data. It was agreed to further analyse the dataset to allow a deeper review of the data at the next meeting.

20. Areas of uncertainty for further consideration were identified in relation to TK data and the implications this may have for interpretation of bioavailability. This will be particularly important for CBD which is currently sold in a range of food types which could influence CBD's uptake and action. As highlighted in the COT review of the published data it was recognised there was a potential for different effects in different organisms and it was noted that this would need to be considered in more detail as part of the deeper review at the next meeting.

21. The subgroup also requested to see the entirety of the hepatotoxicity raw data, in order to understand the potential signals for adverse toxicological effects in humans, the provided data does not currently cover this enough to warrant a decision/conclusion to be made regarding the hepatotoxic nature of CBD isolates.

22. The subgroup provided no conclusions on long term effects at this point, but there were lingering concerns surrounding durational exposure and whether members were content with the information obtained from 90-day studies being sufficient or if this represents a datagap for some parameters.

23. Chronic exposure and mixture effects were also identified as potential uncertainties to be explored as part a wider review of the dataset at the next meeting.

5. Date of next meeting

The next meeting is scheduled for 28th September 2022. It will be an online meeting only via teams.