FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Supporting document 3

Commentary on studies relating to oral fluid and urine testing (at Approval) – Application A1039

Low THC Hemp as a Food

Biological matrices relevant for THC testing in this context are oral fluid and urine. For both of these matrices there are Australian Standards that specify procedures for specimen collection, the detection and quantitation of THC and/or its metabolites, and cut-off levels for declaring positive tests. The published literature has been searched for human studies most relevant to the issue. A recent unpublished study is also considered below.

Oral fluid

Australian Standard AS 4760-2006 specifies a positive test cut-off of 25 ng/mL for screening of oral fluid samples (e.g. when using an immunoassay method of detection) and a 10 ng/mL cut-off for confirmatory tests which are typically conducted using gas chromatography-mass spectrometry (GC-MS) or liquid chromatography-mass spectrometry (LC-MS) methods.

For smoked cannabis, evidence to date indicates that THC may be found in oral fluid primarily as a result of direct deposition in the oral cavity rather than from transfer from blood. No published data have been located on oral fluid levels of THC resulting from hemp food consumption. An unpublished study investigated the saliva levels of THC following smoking of cannabis, passive exposure to cannabis smoke, and consumption of cookies made using cannabis as an ingredient (Fitzmaurice 2012). The cookie test samples had a minimum THC content of around 23 mg per 30 g cookie (i.e. 766 mg/kg). This is well in excess of the maximum levels in hemp foods proposed by FSANZ (a maximum of 10 mg/kg). The oral fluid levels of THC exceeded the test cut-off of 10 ng/mL immediately after consumption of a cookie and for up to three hours after consumption. Based on the maximum levels of THC proposed by FSANZ, a hypothetical 30 g cookie made entirely from hempseeds would contain a maximum THC level of 0.15 mg. By extrapolation, consumption of such a cookie gives an estimated THC level in oral fluid of 0.86 ng/mL, which is about 12-times lower than the test cut-off. The above calculation assumes the maximum level of THC for hempseeds applies to the whole cookie – this results in an overestimate given that hempseeds would constitute only a small proportion of the final product, typically no more than 20%. Moreover, the actual levels of THC in hemp food products are expected to be much lower than the proposed MLs.

Published human studies have investigated oral fluid levels of THC resulting from oral administration of a pharmaceutical formulation of THC (Marinol®, a THC solution in sesame oil in soft gelatin capsules). In a recent well-designed study, 10 male participants over an 8 day period each received 37 oral doses of 20 mg THC with increasing frequency (every 4–8 h around the clock, with frequency adjusted for each participant to minimise adverse effects) (Milman et al 2010). The participants were daily cannabis smokers; however no cannabis smoking was permitted during the study in which participants were housed in a secure clinical research facility.

The resulting total doses of THC were 40 to 120 mg/day (0.5-1.5 mg/kg bw/day[1]) which are 150 to 460 times greater than the highest dietary exposure estimated to result from consumption of low-THC hemp foods: 3.2 µg/kg bw/day.[2]

Oral fluid samples were analysed using a validated GC-MS method. The limit of quantification (LOQ) was 0.5 ng/mL which is similar to LOQs quoted in other recently published GC-MS methods for analysis of THC in oral fluid. The highest concentrations of THC in oral fluid were observed immediately following admission due to previously self-administered smoked cannabis. The mean concentration of THC in oral fluid observed during oral administration of THC was 1.1 ng/mL with a range of 0.6 to 8.0 ng/mL. Thus, despite the use of oral THC doses at least 150-times higher than the highest estimated dietary exposure, the highest level of THC measured was below the 10 ng/mL limit specified by the Australian Standard. For comparison, controlled studies on smoked cannabis have resulted in oral fluid THC levels of several thousand ng/mL shortly after smoking a single cannabis cigarette and up to ~90 ng/mL six hours after smoking (Huestis and Cone 2004; Milman et al 2012).

It is acknowledged that direct transfer into oral fluid of THC administered in a gelatin capsule is likely to be negligible unless the capsule contents are released or partially released in the mouth. Direct transfer into oral fluid of THC present in food is likely to occur; however a large fraction of the oral fluid will be swallowed along with the food resulting in minimal accumulation of THC in the oral cavity. This in combination with the low maximum THC levels proposed for hemp foods suggests that it would be unlikely for positive oral fluid tests to be attributable to the consumption of such hemp foods.

Urine

Australian/New Zealand Standard AS/NZS 4308-2008 specifies a positive test cut-off of 50 ng/mL (for “cannabis metabolites”) for screening of urine samples and a 15 ng/mL cut-off for confirmatory tests (for the major THC metabolite in urine, carboxylic acid THC: THC-COOH).

Several published studies from the late 1990s reported urine levels of THC metabolites resulting from hemp food consumption, however no information was provided on levels of THC in the hemp foods and/or the amount of the hemp food consumed (e.g. Struempler et al 1997; Fortner et al 1997; Costantino et al 1997). A follow up paper reported levels of THC in some marketed hemp oils of up to 150 mg/kg which is 15-fold higher than the ML currently proposed (Alt and Reinhardt 1998).

A study which did report THC levels in hemp oil, the amount of hemp oil consumed and resulting concentrations of THC metabolites in urine was considered in the Assessment Report (Leson et al 2001). It was shown in this study that daily oral administration of hemp oil, resulting in THC doses of 0.6 mg/day for 10 days, resulted in urine levels of THC-COOH that were well below the cut-off for confirmatory tests (15 ng/mL). The highest THC-COOH concentration found in urine was 5.2 ng/mL. A THC intake of 0.6 mg/day is equivalent to the consumption of 60 g of hemp oil containing THC at the maximum proposed level of 10 mg/kg or 120 g of hempseeds containing THC at the maximum proposed level of 5 mg/kg.

[1] Bodyweights and heights of participants were not reported; however the mean body mass index was 26.0 kg/m^2. Assuming a mean height of 1.76 m results in a mean bodyweight of 80 kg.

[2] The Dietary Exposure Assessment indicates that the 97.5th percentile exposure for the population group with the highest predicted exposure (that includes individuals of driving and working age) is 3.2 µg/kg bw/day (for New Zealanders 15-19 years of age). Dietary exposures are likely to be overestimated as discussed in the Risk Assessment Supporting Document.

An additional relevant study involved the oral administration of known doses of THC in hemp oil (Gustafson et al 2003). In this study, 7 individuals received 0, 0.39, 0.47, 7.5, and 14.8 mg THC/day for 5 days. These correspond to bodyweight relative doses of 5.2, 6.2, 99 and 196 µg/kg bw/day (i.e. 1.6, 1.9, 31 and 61-times the highest predicted dietary exposure of 3.2 µg/kg bw/day). Dosing occurred three times per day with meals. No other subsequent studies have been identified which use dose level(s) similar to the highest predicted dietary exposure to THC from hemp foods. The 0.39, 0.47 and 14.8 mg THC doses were administered as hemp oil while the 7.5 mg/kg dose was administered as the THC pharmaceutical product Marinol®. Each participant followed each of the 5 dosing regimens with 10-day washout periods between regimens. All urine voids were collected separately over a 10-week period and tested using 3 different commercially available immunoassays and by GC-MS. A total of 4381 urine samples were analysed.

One participant of 7 had three positive immunoassay results (i.e. > 50 ng/mL) at the low dose of 0.39 mg/day. This participant had two positive samples with one of the immunoassays and one with an alternate immunoassay giving detection rates of approximately 0.2% and 0.1%, respectively. After daily ingestion of 0.47 mg THC, three participants produced one, two, and two positive specimens, respectively, with one of the immunoassays. All participants produced positive specimens after administration of the higher doses (7.5 and 14.8 mg/day).

The 0.39 and 0.47 mg/day doses produced GC-MS positive specimens in 4/7 and 2/7 participants, respectively. The respective C_{max} mean values (and ranges) were 19.8 ng/mL (range: 7.3-38.2 ng/mL) and 12.2 ng/mL (range 5.4-31.0 ng/mL). These data show that THC doses 1.6 to 1.9 times greater than the highest predicted dietary exposure to THC from hemp foods resulted in only a small fraction of urine specimens with THC-COOH concentrations greater than the Australia/New Zealand Standard positive cut-off of 15 ng/mL.

The predicted chronic dietary exposure to THC at the 90th percentile for consumers of foods containing hemp (FSANZ assessment) is likely to be an overestimate because of the conservative assumptions used in the modelling. Although there are some uncertainties in the risk assessment due to the lack of data on consumption of hemp foods, the lowest dose tested by Gustafson et al is 1.6-times greater than this likely overestimate of high dietary exposure. It is therefore considered unlikely that an individual could return a positive urine test due to the consumption of hemp foods complying with the proposed maximum levels of THC.

Conclusions

Published and unpublished results from studies on human volunteers indicate that it is unlikely that consumption of hemp foods containing THC at the proposed maximum levels could result in any positive tests when oral fluid or urine samples are analysed according to Australian Standards (AS 4760-2006 & AS/NZS 4308-2008). These Australian Standards specify a positive THC result for oral fluid of 25 ng/mL (immunoassay) and 10 ng/mL (GC-MS, LC-MS) and for urine of 50 ng/mL (immunoassay) and 15 ng/mL (GC-MS, LC-MS).

References

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