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The BfR recommends acute reference dose as basis for assessing hemp-containing foodstuff

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Tetrahydrocannabinol (THC or Δ^9 -THC) is a psychoactive cannabinoid that can be found in hemp-containing foods. Above a certain intake, the substance can have undesirable health consequences, such as mood swings and fatigue. In order to avoid the occurrence of such effects, the Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV) recommended guidance values for maximum THC levels in various food groups in 2000. The guidance value for beverages was given as 0.005 mg/kg, for edible oils with 5 mg/kg and for all other foods with 0.150 mg/kg. In 2018, the BfR came to the conclusion that these values no longer correspond to current scientific knowledge.

Instead, the BfR recommends that the toxicological assessment of hemp-containing foods be carried out on the basis of the acute reference dose (ARfD) of 1 microgram Δ^9 -THC/kg body-weight derived by the European Food Safety Authority (EFSA) in 2015. The ARfD specifies the estimated maximum quantity of a substance that can be consumed with food in the course of one day—either during one meal or during several meals—without a detectable risk to health. From the point of view of the BfR, whether the ARfD can possibly be exceeded should be checked on a case-by-case basis for each product under assessment. The measured THC levels and the estimated consumption quantities are used for this assessment. Information on the latter can be found in the “EFSA Comprehensive European Food Consumption Database”.

1 Subject of the assessment

The Federal Institute for Risk Assessment (BfR) comments from the perspective of scientific risk assessment on the guideline values for $\Delta 9$ -tetrahydrocannabinol ($\Delta 9$ THC) in hemp-containing foodstuffs established by the former Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV). The BfR points out that the setting of guidance values is the responsibility of the risk management authorities.

2 Result

In 2018, the BfR came to the conclusion (Opinion No. 034/2018, 08 November 2018) that the THC guidance values recommended by the former BgVV in 2000 are no longer suitable for the assessment of hemp-containing foods according to current standards. In addition, it is currently considered not feasible to issue scientifically robust general recommendations concerning the maximum thresholds for $\Delta 9$ -THC concentrations in foodstuff which would rule out the ARfD being exceeded. The ARfD stands for acute reference dose, i.e. the amount of substance per kg of bodyweight that can be ingested through food over a day without any identifiable risk for the consumer.

The BfR therefore recommends that the toxicological assessment of hemp-containing foods be carried out on the basis of the ARfD of 1 microgram $\Delta 9$ -THC/kg bodyweight (BW) derived by the European Food Safety Authority (EFSA) in 2015. In an individual case, taking into account the measured concentrations and consumption data for the relevant food category (e.g. from the “EFSA Comprehensive European Food Consumption Database”, and in the case of food supplements, as a rule, from the legally prescribed information on the recommended consumption amount), it is possible to calculate whether consumption of the products under assessment may result in the ARfD being exceeded.

Exceeding the ARfD is undesirable from a toxicological point of view, since adverse health effects can no longer be ruled out with the required degree of certainty. For comparison with the ARfD, it seems reasonable from a toxicological point of view to use the value for the total measured THC, i.e. the sum of the measured concentrations of $\Delta 9$ -THC and $\Delta 9$ -THC acid ($\Delta 9$ -THCA).

3 Rationale

3.1 Basic considerations

3.1.1 Starting position

$\Delta 9$ -Tetrahydrocannabinol ($\Delta 9$ -THC) is a psychoactive cannabinoid. It is formed in glandular hairs that are found all over the hemp plant with the exception of seeds and roots. The glandular hairs are located in a particularly high density on the leaves and in the area of the inflorescences. Cannabinoids are not found in the seeds due to the lack of glandular hair. The concentration of $\Delta 9$ -THC in hemp seeds and products obtained from hemp seeds thus represent a contamination that is probably caused by contact with cannabinoid-containing plant parts during harvest or further processing (BfR 2018).

A large selection of hemp-containing foods is available in retail stores. In addition to hemp seeds and the hemp seed oil obtained from them, various other hemp-containing foods such as baked goods, beer or tea-like products are offered. The latter products consist partly or exclusively of hemp leaves and possibly hemp flowers (BfR 2018).

The fibre hemp usually used for food production may contain up to 0.2% total THC in accordance with legal regulations, so that THC can often be found in foods made from fibre hemp, including naturally cannabinoid-free hemp seeds or products obtained from hemp seeds such as hemp seed oil. Since the occurrence of cannabinoids in hemp seeds and products obtained from hemp seeds represents a contamination, the concentration can generally be kept low by ensuring suitable conditions during harvest and further processing. In the case of hemp-containing products that contain hemp leaves and possibly hemp flowers, however, Δ 9-THC is an ingredient. The Δ 9-THC content is subject to large fluctuations depending on the type of hemp and various environmental factors. From the BfR's point of view, it is therefore doubtful whether the concentrations in these foods can be reduced reliably (BfR 2018).

3.1.2 Toxicological basis

In 2015, EFSA assessed the health risks that might be associated with the consumption of hemp-containing foods. In this report, the available and relevant data on the hazard potential of Δ 9-THC were described and assessed in detail. According to this, effects on the central nervous system and the cardiovascular system are to be expected in humans after oral intake of low Δ 9-THC doses. Effects on the central nervous system (e.g. mood swings and fatigue) were identified as the most sensitive endpoint for the effects mediated by the cannabinoid Δ 9-THC. The effects were already observed at an oral dose of 2.5 mg/person (corresponding to about 0.036 mg/kg bodyweight assuming a bodyweight of 70 kg) - both after single and repeated intake. This dose was regarded as the lowest-observed adverse effect level (LOAEL). Using a factor of 30 (factor 3 for extrapolation from a LOAEL to a NOAEL (no observed adverse effect level), factor 10 for inter-individual variations), EFSA derived an ARfD of 1 microgram Δ 9-THC/kg bodyweight (EFSA 2015). The ARfD indicates the estimated maximum amount of Δ 9-THC that can be ingested with one meal or several meals in the course of a day without any identifiable health risk. Higher intake levels are undesirable from a toxicological point of view, since adverse health effects can no longer be ruled out with the required degree of certainty. The BfR also considers the ARfD, which was derived by EFSA in 2015, as protective and therefore employs it as a suitable health-based guidance value in its Δ 9-THC risk assessments.

3.2 Guidance values for THC in hemp-containing foods

3.2.1 Assessment of the guidance values recommended in 2000 by the former Federal Institute for Health Protection of Consumers and Veterinary Medicine

In a press release in 2000, the former BgVV published preliminary guidance values for maximum levels of total THC as the sum of Δ 9-THC and Δ 9-THC acid (Δ 9-THCA) with respect to ready-to-eat foods. For non-alcoholic and alcoholic beverages, the guidance value was 0.005 mg/kg, for edible oils 5 mg/kg and for all other foods 0.150 mg/kg (BgVV 2000). These guidance values were drawn up as a risk management measure on the basis of toxicological knowledge, market knowledge concerning the hemp products available at the time and other criteria.

As part of the BfR Opinion No. 034/2018 of 08 November 2018, the BfR checked whether these guidance values are still suitable to guarantee an appropriate level of protection for consumers from the perspective of scientific risk assessment and while accounting for the current state of the art. For this purpose, model calculations were performed for the three above-mentioned food groups which worked out from which consumption quantities the ARfD derived by the EFSA would be fully exhausted if the corresponding foods had total

THC contents at the level of the guidance values. These consumption quantities were compared with the actual consumption quantities determined in consumption studies for similar foods that do not necessarily contain hemp. For the exact methodological approach and the associated uncertainties, see BfR Opinion No. 034/2018. The comparison showed that the consumption of hemp-containing foods can lead to the ARfD being exceeded even if the guidance values recommended by the BgVV in 2000 are adhered to - at least for high consumers of products from the group of edible oils or all other foods. From the BfR's point of view, these guidance values are therefore unsuitable for ensuring an adequate level of protection. The guidance value for non-alcoholic and alcoholic beverages, on the other hand, appeared to be sufficiently conservative based on these model calculations (BfR 2018).

An additional difficulty, however, is the fact that the group "all other foods" currently includes a large number of different hemp-containing foods that were not on the market when the guidance values were established in 2000 and therefore could not be taken into account, which is why the relevance of this guidance value is also questionable.

Overall, the guidance values recommended by the BgVV appear to be no longer suitable for assessing hemp-containing foods according to today's standards.

3.2.2 Update of the guidance values for THC in food

The determination of guidance values for the occurrence of undesirable substances in food is the responsibility of risk management authorities. In contrast to the BgVV, which has carried out risk management tasks in addition to the scientific risk assessment, the BfR is exclusively entrusted with the task of scientific risk assessment due to its legal mandate.

In addition, it is currently considered not feasible to issue scientifically robust general recommendations concerning the maximum thresholds for $\Delta 9$ -THC concentrations in foodstuff which would rule out the ARfD being exceeded. The reason is that hemp-containing foods are among those seldom consumed foods that are not included in the currently available consumption data for children and adults, which were determined on the basis of representative consumption studies.

3.2.3 Recommendations on the possible procedure for the toxicological assessment of food

From the point of view of the BfR, the toxicological assessment of hemp-containing foods should be based on the ARfD of 1 microgram $\Delta 9$ -THC/kg bodyweight derived by EFSA in 2015. It should be examined on the basis of the measured levels, in each individual case, whether the consumption of the products under assessment is likely to result in the ARfD being exceeded. Exceeding the ARfD is undesirable from a toxicological point of view, since adverse health effects can no longer be ruled out with the required degree of certainty.

To estimate the intake of the products under assessment, the respective levels of consumption should be estimated in each individual case. As a basis, the following are used among other things:

- Data from the "EFSA Comprehensive European Food Consumption Database",
- Alternatively, consumption data for analogous foods that do not necessarily contain hemp can be taken into account. These data were published for various relevant food categories, e.g. in BfR Opinion No. 034/2018 of 08 November 2018 (BfR 2018).

- In the case of dietary supplements, the expected amount of consumption can usually be determined directly from the legally prescribed information on the recommended amount of consumption.

For the comparison with the ARfD, it appears reasonable from a toxicological point of view to use the value for the total THC determined, i.e. the measured sum of $\Delta 9$ -THC and $\Delta 9$ -THCA.

3.3 Analytical aspects

In 2018, taking into account all relevant aspects, the BfR came to the conclusion that at the time it was justified to determine the $\Delta 9$ -THC content in food using the official test method ASU L 47.00-9: 2004-12 and to use it as a basis for assessment (BfR 2018). It should be noted that this procedure determines the total THC content, i.e. the sum of $\Delta 9$ -THC and the biosynthetic precursor $\Delta 9$ -THCA, which can also be found in hemp-containing foods, but does not itself have any psychoactive effects. Among other things, this recommendation was based on:

- 1.) Methods for the separate detection of $\Delta 9$ -THC and $\Delta 9$ -THCA in food matrices were available at the time, but were not yet very widespread,
- 2.) The fact that ratios of $\Delta 9$ -THC and $\Delta 9$ -THCA in hemp-containing foods can be variable and
- 3.) The fact that heat-dependent conversion of $\Delta 9$ -THCA into $\Delta 9$ -THC in food processing is possible under certain circumstances.

In the meantime, however, methods are almost exclusively used in food analysis that allow the separate detection of $\Delta 9$ -THC and $\Delta 9$ -THCA in food matrices. This applies to methods based on liquid chromatographic separation in combination with mass spectrometric detection (LC-MS or LC-MS/MS), but also to gas chromatographic methods (GC-MS), provided $\Delta 9$ -THCA is derivatised before detection. A method based on LC-MS is also established at the National Reference Laboratory for Mycotoxins and Plant Toxins in Feed and Food at the BfR, which enables the separate determination of $\Delta 9$ -THC and $\Delta 9$ -THCA as well as other cannabinoids.

Even if a separate detection of the analytes $\Delta 9$ -THC and $\Delta 9$ -THCA is now generally recommended, from a toxicological point of view it still makes sense to use total THC, i.e. the sum of $\Delta 9$ -THC and $\Delta 9$ -THCA, for the toxicological assessment, provided that the measured values depend on the starting products. This procedure is also intended for assessing the regulatory maximum levels, which are currently being discussed at European level. This is due to the fact that it can usually not be ruled out that the majority of the available hemp-containing starting products undergo thermal treatment as part of further food processing, e.g. roasting of hemp seeds or use of hemp seed oil for frying. In the case of thermal treatment, it must be assumed that the $\Delta 9$ -THCA determined in the starting product is partially or completely converted into $\Delta 9$ -THC in ready-to-eat food. Therefore, it seems appropriate to use the total content of $\Delta 9$ -THC and $\Delta 9$ -THCA determined in the starting product for assessments and to compare it directly with the ARfD. From the point of view of the BfR, however, this basic approach should be derogated from in individual cases, if it is not expected that a particular product will undergo further thermal treatment. This would be the case, for example, with dietary supplements in the form of capsules or tablets. In these cases only the measured $\Delta 9$ -THC content should be used for comparison with the ARfD. In this respect, separate analytical detection of $\Delta 9$ -THC and $\Delta 9$ -THCA is required.

For further information, please visit the BfR website:

Tetrahydrocannabinol concentrations are too high in many hemp-containing foods (Opinion No. 034/2018, 08 November 2018)

<https://www.bfr.bund.de/cm/349/tetrahydrocannabinol-levels-are-too-high-in-many-hemp-containing-foods-health-impairments-are-possible.pdf>

BgVV recommends guidance values for THC in hemp-containing foods (BgVV Press Release 07/2000, 16 March 2000)

https://www.bfr.bund.de/de/presseinformation/2000/07/bgvv_emp-fiehlt_richtwerte_fuer_thc_tetrahydrocannabinol_in_hanfhaltigen_lebensmitteln-884.html



BfR “Opinions app”

4 References

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EFSA (European Food Safety Authority: Scientific Panel on Contaminants in the Food Chain (CONTAM)) (2015). Scientific Opinion on the risks for public health related to the presence of tetrahydrocannabinol (THC) in milk and other food of animal origin. EFSA Journal 13: 4141.

About the BfR

The German Federal Institute for Risk Assessment (BfR) is a scientifically independent institution within the portfolio of the Federal Ministry of Food and Agriculture (BMEL) in Germany. It advises the German federal government and German federal states (“Laender”) on questions of food, chemical and product safety. The BfR conducts its own research on topics that are closely linked to its assessment tasks.

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