

Safety and efficacy of a feed additive consisting of tartrazine for its use in baits for freshwater fish (GIFAP)

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Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of tartrazine as sensory additive (functional group: (a) colourants: (i) substances that add or restore colour in feeding-stuffs). Tartrazine is intended to be incorporated in fishing baits up to a maximum of 30 mg/kg in complementary feed in order to colour them and attract fish in freshwater (ponds, rivers), for both recreational and competitive fishing. The additive is not intended for use in aquaculture. Tartrazine is already authorised for use with cats and dogs, ornamental fish, grain-eating ornamental birds and small rodents. The EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) concluded that the use of tartrazine in the preparation of baits for freshwater fish under the proposed conditions of use is of no concern for the target animals. The use of tartrazine as a feed additive under the proposed conditions of use is considered safe for the consumer and the environment. Regarding the user safety, the additive should be considered a dermal and respiratory sensitiser. Inhalation and dermal exposure are considered a risk. The FEEDAP Panel could not conclude on the irritation potential of the additive. In absence of data, no conclusion can be reached on the efficacy of tartrazine in freshwater fish baits.

KEYWORDS

colourant, efficacy, freshwater fish, safety, sensory additive, tartrazine

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1 | INTRODUCTION

1.1 | Background and Terms of Reference

Regulation (EC) No 1831/2003 establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 4(1) of that Regulation lays down that any person seeking authorisation for a feed additive or for a new use of feed additive shall submit an application in accordance with Article 7.

The European Commission received a request from GIFAP¹ for the authorisation of the additive consisting of tartrazine, when used as a feed additive for freshwater fish (category: sensory additives; functional group: (a) colourants: (i) substances that add or restore colour in feedingstuffs).

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 4(1) (authorisation of a feed additive or new use of a feed additive). EFSA received directly from the applicant the technical dossier in support of this application. The particulars and documents in support of the application were considered valid by EFSA as 31st March 2023.

According to Article 8 of Regulation (EC) No 1831/2003, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animals, consumer, user and the environment and on the efficacy of the feed additive consisting of tartrazine, when used under the proposed conditions of use (see Section 3.1.3).

1.2 | Additional information

Tartrazine is authorised as a feed additive for cats and dogs, ornamental fish, grain-eating ornamental birds and small rodents (2a102).² The EFSA FEEDAP Panel issued in 2016 an opinion on the safety of this additive when used in feed for cats and dogs, ornamental fish, grain-eating ornamental birds and small rodents (EFSA FEEDAP Panel, 2016).³

2 | DATA AND METHODOLOGIES

2.1 | Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier⁴ in support of the authorisation request for the use of tartrazine as a feed additive. The dossier was received on 7 November 2022 and the general information and supporting documentation is available at <https://open.efsa.europa.eu/questions/EFSA-Q-2022-00779>.

The confidential version of the technical dossier was subject to a target consultation of the interested Member States from 31 March 2023 to 30 June 2023 for which the received comments were considered for the assessment.

In accordance with Article 38 of the Regulation (EC) No 178/2002⁵ and taking into account the protection of confidential information and of personal data in accordance with Articles 39 to 39e of the same Regulation, and of the Decision of EFSA's Executive Director laying down practical arrangements concerning transparency and confidentiality,⁶ a non-confidential version of the dossier.

According to Article 32c(2) of Regulation (EC) No 178/2002 and to the Decision of EFSA's Executive Director laying down the practical arrangements on pre-submission phase and public consultations, EFSA carried out a public consultation on the non-confidential version of the technical dossier from 30 January to 20 February 2024 for which no comments were received.

The FEEDAP Panel used the data provided by the applicant together with data from other sources, such as previous risk assessments by EFSA or other expert bodies, peer-reviewed scientific papers, other scientific reports and experts' knowledge, to deliver the present output.

The European Union Reference Laboratory (EURL) considered that the conclusions and recommendations reached in the previous assessment regarding the methods used for the control of the tartrazine in animal feed are valid and applicable for the current application.⁷

¹GIFAP, BP 25 Saint-Laurent Médoc - France, France.

²Commission Implementing Regulation (EU) 2020/157 of 5 February 2020. OJ L 34, 6.2.2020, p. 15.

³Commission Regulation (EU) No 231/2012. OJ L 83, 22.3.2012, p. 1.

⁴Dossier reference: FEED-2022-7830.

⁵Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–48.

⁶Decision available at: <https://www.efsa.europa.eu/en/corporate-pubs/transparency-regulation-practical-arrangements>.

⁷Evaluation report received on 14/3/2019 and available on the EU Science Hub https://joint-research-centre.ec.europa.eu/eurl-fa-eurl-feed-additives/eurl-fa-authorisation/eurl-fa-evaluation-reports_en.

2.2 | Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of tartrazine is in line with the principles laid down in Regulation (EC) No 429/2008⁸ and the relevant guidance documents: Guidance on the assessment of the safety of feed additives for the consumer (EFSA FEEDAP Panel, 2017a), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017c), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018), Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019) and Guidance on the assessment of the safety of feed additives for the users (EFSA FEEDAP Panel, 2023).

3 | ASSESSMENT

Tartrazine is intended to be used as a sensory additive (functional group: (a) colourants: (i) substances that add or restore colour in feedingstuffs) in baits for freshwater fish. Tartrazine is intended to be incorporated in fishing baits in order to colour them and attract fish in freshwater (ponds, rivers), for both recreational and competitive fishing. The additive is not intended for use in aquaculture.

3.1 | Characterisation

3.1.1 | Characterisation of the additive

Tartrazine is a disulfonated mono azo dye and consists of trisodium-5-hydroxy-1-(4-sulfonatophenyl)-4-(4-sulfonatophenylazo)-H-pyrazole-3-carboxylate (chemical formula $C_{16}H_9N_4Na_3O_9S_2$, Chemical Abstracts Service (CAS) number 1934-21-0, molecular weight 534.37) and subsidiary colouring matters together with sodium chloride and/or sodium sulfate as the principal uncoloured components. Tartrazine is described as the sodium salt.

Tartrazine is produced by chemical synthesis.⁹ It is prepared from 4-amino benzenesulfonic acid, which is diazotised using hydrochloric acid and sodium nitrite. The resulting diazo compound is then coupled with 4,5-dihydro-5-oxo-1-(4-sulfophenyl)-1H-pyrazole-3-carboxylic acid or with the methyl ester, the ethyl ester or a salt of the carboxylic acid. The resulting dye is purified and isolated as the sodium salt.

The applicant states that the specifications of tartrazine comply with those of the additive already authorised for use in dogs, cats and ornamental fish, grain-eating ornamental birds and small rodents¹⁰: colouring matter calculated as the sodium salt $\geq 85\%$, subsidiary colouring matter $\leq 1\%$, organic compounds other than colouring matters¹¹ $\leq 0.5\%$, unsulfonated primary aromatic amines $\leq 0.01\%$ and ether extractable matter under neutral conditions $\leq 0.2\%$. These specifications are also in line with those set for the use of tartrazine as a food additive.¹²

Five batches of tartrazine were analysed for their specified components.¹³ They all complied with the specifications as follows: 91.1% total colouring matter (range 90.7%–91.6%); 0.1% subsidiary colouring matter; 0.30% sum of organic compounds other than colouring matters (0.05%–0.34%), $< 0.01\%$ unsulfonated primary aromatic amines and $< 0.20\%$ ether extractable matter.

The applicant has set specifications for arsenic (< 3 mg/kg), lead (< 2 mg/kg), mercury and cadmium (< 1 mg/kg), which align with the established limits for tartrazine when used as a food additive. The levels analysed in the same five batches above were: 0.01 mg arsenic/kg (0.005–0.029), 0.44 mg lead/kg, (0.005–0.77), 0.006 mg mercury/kg (0.005–0.008) and 0.05 mg cadmium 0.04–0.10.

The additive is an odourless light orange powder, with a bulk density of 500–700 kg/m³. Tartrazine is freely soluble¹⁴ in water; a solubility test in accordance with the OECD Test Guideline (TG) 105 was submitted,¹⁵ resulting in 200–1000 g/L.

The dusting potential, as determined by the Stauber-Heubach method, was evaluated in two independent batches, yielding results of 1658 mg/m³ and 7375 mg/m³, respectively.¹⁶ For a third batch, the measurement was unfeasible due to the inability to retrieve all the dust from the filter.¹⁷

⁸Commission Regulation (EC) No 429/2008 of 25 April 2008 on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the preparation and the presentation of applications and the assessment and the authorisation of feed additives. OJ L 133, 22.5.2008, p. 1.

⁹Technical dossier/Annex_11.

¹⁰Commission Implementing Regulation (EU) 2020/157 of 5 February 2020 concerning the authorisation of tartrazine as a feed additive for dogs, cats, ornamental fish, grain-eating ornamental birds and small rodents. OJ L 34, 6.2.2020, p. 15.

¹¹4-hydrazinobenzene sulfonic acid, 4-aminobenzene-1-sulfonic acid, 5-oxo-1-(4-sulfophenyl)-2-pyrazoline-3-carboxylic acid, 4,4'-diazaminodi(benzene sulfonic acid), Tetrahydroxysuccinic acid.

¹²Commission Regulation (EU) No 231/2012. OJ L 83, 22.3.2012, p. 1.

¹³Technical dossier/Annex_3, Annex_4, Annex_5, Annex_6 and Annex_7.

¹⁴For solubility terms, see Table 2 of the Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (EFSA Scientific Committee, 2021).

¹⁵Technical dossier/Annex_50.

¹⁶Technical dossier/Annex_50 and Annex_52.

¹⁷Technical dossier/Annex_76.

3.1.2 | Stability and homogeneity

The shelf life of the additive stored for 8 years at 15–45°C and 40%–90% relative humidity was evaluated in three batches for their colour content by measuring the extinction coefficient.¹⁸ After 9 years, average losses in pure dye content was 3.7%, moisture content increased by 4.1% and total dye content increased by 0.6% in two batches and decreased by 0.5% in the third one.

No data were submitted on the stability of the additive when incorporated in feed. The applicant states that tartrazine is generally unstable in the presence of oxidising or reducing agents (e.g. sugars and acids).

3.1.3 | Conditions of use

The additive tartrazine is intended to be incorporated in fishing baits for freshwater fish up to a maximum of 30 mg/kg in complementary feed. The applicant stated that it can be used either as small fish baits of approximately 4 g attached to the hooks or fishing lines or as small pellets (ground bait) which are cast in water to attract fish to the fishing area. It is not intended for use in aquaculture feed.¹⁹

3.2 | Safety

Tartrazine is intended to be used in the preparation of baits for freshwater fish only. According to the proposed conditions of use, it can be used either as small fish baits of approximately 4 g attached to the hooks or fishing lines or as small pellets (ground bait) which are cast in water to attract fish to the fishing area (Section 3.1.3). Therefore, the FEEDAP Panel considers that the safety assessment of this additive should consider this peculiar use, which will likely result in an occasional exposure of the target animals to tartrazine, and not to a continuous exposure during their whole life, as it is normally the case with other feed additives.

The safety of tartrazine was previously evaluated by the Joint FAO/WHO Expert Committee on Food Additives in 1966 and 2016 (JECFA, 1966, 2016), by the Scientific Committee on Food (SCF) (European Commission, 1975, 1984), by EFSA in 2009 when re-evaluating tartrazine as a food additive (EFSA ANS Panel, 2009) and in 2016 as a feed additive for cats, dogs, ornamental birds, ornamental fish and small rodents (EFSA FEEDAP Panel, 2016).

No new studies were submitted in support of the safety of the additive, but the applicant performed a literature search on the safety of tartrazine for the target species, consumers and users, covering the period up to October 2023 and for the safety for the environment up to November 2022, to identify any relevant information that might be available since the previous evaluations. The literature search was conducted using the Google Scholar, PubMed and EFSA publications databases. A total of 53 publications were retrieved (20 on the safety for the target species, 27 for the consumer, four for the users and two for the environment).

3.2.1 | Absorption, distribution, metabolism and excretion and residues

No data on absorption, distribution, metabolism, excretion (ADME) and residues of tartrazine in fish was made available to the FEEDAP Panel.

The ADME of tartrazine in laboratory animals have been previously reviewed by EFSA (EFSA ANS Panel, 2009; EFSA FEEDAP Panel, 2016) and JECFA (JECFA, 2016) which considered that the absorption of tartrazine in humans and laboratory animals is typically less than 5%. Once absorbed, tartrazine is primarily excreted unchanged in the urine. The unabsorbed portion undergoes reductive metabolism by the intestinal microbiota. Small amounts of some metabolites (e.g. sulfanilic acid and 4-amino-3-carboxy-5-hydroxy-1-(4-sulfophenyl)pyrazole (SCAP) and aniline derivatives) are then absorbed by the intestine and excreted via urine.

The applicant provided a literature search (see Section 2.2) to support that the anatomical organisation of the intestine, the gene expression regulated by gut microbes and the core gut microbiota assembly are similar in fish and mammals (Tyagi & Shukla, 2002; Rawls et al., 2004; Roeselers et al., 2011; Wu et al., 2012; Turnbaugh & Gordon, 2009; Turnbaugh et al., 2009, cited in Li et al., 2014). Although these findings might suggest a commonality of the enteric metabolism in fish and mammals, the FEEDAP Panel considered that the information provided by the applicant is of limited relevance for the characterisation of the ADME profile of tartrazine in fish.

No data on possible residues of tartrazine in fish was made available to the FEEDAP Panel. Considering the conditions of use of tartrazine in freshwater fish (as described in Section 3.1.3), the Panel considers that the use of the additive for recreational or sportive fishing would result in a limited consumption of baits before the animals are caught. Therefore, considering the limited amount ingested by the animals over a short period of time, the deposition of tartrazine in fish flesh is considered unlikely.

¹⁸Technical dossier/Annex_13, Annex_45 and Annex_51.

¹⁹Technical dossier/Conditions_of_use.pdf.

3.2.2 | Toxicological profile

Based on the results from long-term carcinogenicity studies and in vivo genotoxicity studies, described in the above-mentioned assessments (EFSA ANS Panel, 2009; EFSA FEEDAP Panel, 2016; JECFA, 2016), tartrazine was considered not carcinogenic nor genotoxic and not a reproductive/developmental toxicant. In 2009, the ANS Panel confirmed the existing acceptable daily intake (ADI) for tartrazine of 7.5 mg/kg body weight (bw) which was previously established by JECFA based on a no observed adverse effect level (NOAEL) of 1.5% (corresponding to 750 mg/kg bw per day), which was the highest dose tested in a repeated dose study in (Mannell et al., 1958). In 2016, JECFA updated the safety evaluation of tartrazine (JECFA, 2016) and withdrew the previous ADI and established a new one of 0–10 mg/kg bw, which was derived from a NOAEL of 984 mg/kg bw per day, based on the reduction in body weight observed in a chronic study in rats and applying an uncertainty factor (UF) of 100.

The literature search retrieved five papers (Ai-Mashhedy & Fijer, 2016; Boussada et al., 2017; de Souza et al., 2022; Ghonimi & Elbaz, 2015; Ismail & Rashed, 2022) which were not considered in the previous assessments. Three papers describe toxicological studies with oral administration in rats and report adverse effects in liver, testes (including sperm quality and testosterone levels), brain, kidney, stomach over a repeated dose exposure (Boussada et al., 2017; Ghonimi & Elbaz, 2015; Ismail & Rashed, 2022). However, given the specific use of the additive in fishing bait, which likely results in an occasional exposure of the animals, the FEEDAP Panel considers that the effects of repeated dose exposure to tartrazine described in these publications are not relevant for the current assessment. One paper (De Souza et al., 2022) reported positive genotoxicity results obtained testing a tartrazine of unknown purity. However, the relevance of the test item used in this study for the additive under assessment is not established and therefore, this paper was not further considered for the current assessment.

The paper by Ai-Mashhedy and Fijer (2016) evaluated the acute oral toxicity of tartrazine (E102) in male mice. The median lethal dose (LD_{50}) of tartrazine was found to be greater than 6250 mg/kg bw, with no observed mortality following single-dose administration across all dosage groups (ranging from 125 to 6250 mg/kg bw). The FEEDAP Panel considers the results of this study relevant for the assessment of the safety of the additive for the target species. The FEEDAP Panel also noted that a LD_{50} of 6375 mg/kg bw for tartrazine, when orally administered in rats, was reported in the paper by Boussada et al. (2017). This result is in line with the study by Ai-Mashhedy and Fijer (2016).

3.2.3 | Safety for the target species

Tartrazine is intended to be used only in the preparation of fishing baits for freshwater fish. The Panel considers that this use will likely result in an occasional exposure of the animals to the additive, and not to a continuous exposure during the whole life. In addition, for those fish that are caught and killed after capture, the assessment of the safety of the additive is irrelevant. Therefore, the Panel considers that the assessment of the safety for the target species is relevant only for those fish that are either caught and released in the water, or those that eat the ground baits and are not caught. In both cases, it is not possible to make an accurate estimate of the actual consumption of the additive, which, as mentioned before, is going to be occasional, in a very short time and not continuous during long periods of the life of the animals. In addition, the number of baits ingested represents a small fraction of the total feed intake of fish during a given day.

The FEEDAP Panel noted that the literature search performed by the applicant identified two papers reporting adverse effects in fish after exposure to tartrazine. Wu et al. (2021) fed crucian carp with various tartrazine concentrations (1.4, 5.5 and 10 mg/kg bw) for 2 months, noting alterations in intestinal and liver structure, oxidative stress and microbiota composition; Athira and Ds (2022) exposed carp to tartrazine concentrations of 5 and 10 mg/L for 75 days, observing behavioural changes, decreased body weight, mucosal coating and altered enzyme activity. Due to the specific use of tartrazine as fishing bait and the brief interval between ingestion and capture, these findings were considered not relevant for the current assessment by the FEEDAP Panel.

The FEEDAP Panel considered appropriate to make an estimation of the potential exposure to tartrazine from its use in baits. In that regard, the applicant proposed as a worst-case scenario for the consumer safety assessment that a 300 g fish might eat 20 baits (total of 80 g). The FEEDAP Panel considers this scenario can be appropriate for the assessment of the safety for the target animals. Under these conditions, considering the maximum use level of 30 mg tartrazine/kg complementary feed, a single fish would ingest approximately 2.4 mg tartrazine. Considering an average weight of the fish of 300 g, that would result in an exposure of 8 mg tartrazine/kg bw.

The FEEDAP Panel also noted that tartrazine is already authorised in feed for ornamental fish at 1924 mg/kg complete feed.

Considering that tartrazine is of low acute toxicity in mammalian species (LD_{50} , rats and mice), and the peculiarity of the conditions of use which would likely result in an occasional exposure, the FEEDAP Panel concludes that the use of tartrazine in the preparation of baits for freshwater fish under the proposed conditions of use (maximum use level of 30 mg/kg complementary feed) is of no concern for the target animals.

3.2.4 | Safety for the consumer

Considering that tartrazine is already authorised for use as food additive in several food categories and the conditions of use of the feed additive as proposed by the applicant, the FEEDAP Panel considers that the exposure to residue of tartrazine from fish for recreational or sportive fishing would not significantly contribute to the overall exposure to tartrazine via food for the consumers (EFSA ANS Panel, 2009). Therefore, the FEEDAP Panel concludes that the use of tartrazine under the proposed conditions of use is safe for the consumers.

3.2.5 | Safety for the user

The highest dusting potential measured was 7375 mg/m³. Therefore, the FEEDAP Panel considered that the exposure of users by inhalation is likely.

For the current dossier, the applicant submitted two papers (Kalender, 2000; Safford & Goodwin, 1985) which suggest that tartrazine is a skin sensitiser. In addition, the applicant referred to eye and skin irritation studies submitted to the European Chemicals Agency (ECHA). However, since the full reports of these studies were not made available, the FEEDAP Panel could not conclude on the eye and skin irritation potential.

The additive should be considered a dermal and respiratory sensitiser. Inhalation and dermal exposure are considered a risk. The FEEDAP Panel could not conclude on the eye irritation potential of the additive.

3.2.6 | Safety for the environment

Tartrazine is intended to be used only in fishing baits for freshwater fish, and the additive will not be used in aquaculture operation involving the use of cages. Therefore, surface water is considered the environmental compartment potentially at risk.

In line with the requirements of the FEEDAP Panel guidance on the safety of the additive for the environment (EFSA FEEDAP Panel, 2019) the applicant calculated the predicted environmental concentration for surface water (PEC_{sw}) using the FERA calculation tool,²⁰ assuming that 100% of the ingested dose is excreted as the parent compound.

At the maximum concentration of tartrazine used in fishing baits (30 mg/kg complementary feed), the PEC_{sw} does not exceed the threshold value of 0.1 µg/L for aquaculture from land-based fish farms. Thus, the use of tartrazine in the feed of freshwater fish does not present a risk of contamination of surface waters and the assessment stops in Phase I of the FEEDAP guidance on the safety of the additive for the environment (EFSA FEEDAP Panel, 2019). The FEEDAP Panel considers that the use of tartrazine, according to the proposed conditions of use, is not expected to pose a risk for the environment.

3.3 | Efficacy

Tartrazine is intended to be used to colour the fishing baits of freshwater fish. Tartrazine is authorised as a food additive. In principle, where the function requested for feed is the same as that used in food, no further demonstration of efficacy is necessary, provided that the effect seen when used in food could reasonably be expected to be seen when used in feed at the recommended concentration, and that food and feed matrices are of comparable nature. However, considering the uncertainty in the equivalence of the food and feed matrices and the use levels, efficacy demonstration for this use as feed additive was considered necessary.

No data on efficacy were submitted by the applicant. Therefore, no conclusion on the efficacy of tartrazine to be used in freshwater fish baits can be reached.

4 | CONCLUSIONS

The FEEDAP Panel concludes that the use of tartrazine in the preparation of baits for freshwater fish under the proposed conditions of use (maximum use level of 30 mg/kg complementary feed) is of no concern for the target animals.

The use of tartrazine as a feed additive under the proposed conditions of use is considered safe for the consumer and the environment.

Regarding the user safety, the additive should be considered a dermal and respiratory sensitiser. Inhalation and dermal exposure are considered a risk. The FEEDAP Panel could not conclude on the irritation potential of the additive.

In absence of data no conclusion can be reached on the efficacy of tartrazine in freshwater fish baits.

²⁰FERA calculation tool available online: <https://www.efsa.europa.eu/en/applications/feedadditives/tools>.

ABBREVIATIONS

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and excretion
ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
BW	body weight
CAS	Chemical Abstracts Service
ECHA	European Chemicals Agency
EURL	European Union Reference Laboratory
FAO	Food and Agricultural Organization
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LD ₅₀	median lethal dose
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
SCF	Scientific Committee on Food
UF	uncertainty factor
WHO	World Health Organization

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REQUESTOR

European Commission

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