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Safety and efficacy of a feed additive consisting of *Streptococcus salivarius* DSM 13084/ATCC BAA 1024 for dogs and cats (BLIS Technologies Limited)

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP), Vasileios Bampidis, Giovanna Azimonti, Maria de Lourdes Bastos, Henrik Christensen, Birgit Dusemund, Mojca Durjava, Maryline Kouba, Marta López-Alonso, Secundino López Puente, Francesca Marcon, Baltasar Mayo, Alena Pechová, Mariana Petkova, Fernando Ramos, Yolanda Sanz, Roberto Edoardo Villa, Ruud Woutersen, Miguel Prieto, Kettil Svensson, Luca Tosti, Montserrat Anguita, Rosella Brozzi, Matteo Lorenzo Innocenti, Elisa Pettenati, Joana Revez, Maria Vittoria Vettori and Fabiola Pizzo

Abstract

Following a request from the European Commission, EFSA was asked to deliver a scientific opinion on the safety and efficacy of *Streptococcus salivarius* DSM 13084/ATCC BAA 1024 as a technological additive (functional group: acidity regulators) in feed for dogs and cats. The additive is intended for use at a proposed minimum concentration of 1×10^{11} CFU/l or kg liquid feed for dogs and cats. Due to the lack of adequate data, the FEEDAP Panel could not conclude on the safety of the additive for the target species. The additive was considered a respiratory sensitiser, but not irritant to skin. No conclusions could be drawn on the potential of the additive to be an eye irritant or a skin sensitiser. No environmental risk assessment is necessary for the use of the additive in feeds for pets. The Panel concluded that the additive has the potential to be efficacious in feeds for dogs and cats at the proposed conditions of use.

Keywords: technological additives, acidity regulator, *Streptococcus*, safety, efficacy, cats and dogs

Requestor: European Commission

Question number: EFSA-Q-2021-00501

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1. Introduction

1.1. Background and Terms of Reference

Regulation (EC) No 1831/2003[1] 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 BLIS Technologies Limited[2] for the authorisation of the additive consisting of *Streptococcus salivarius* DSM 13084/ATCC BAA 1024,[3] when used as a feed additive for dogs and cats (category: technological additives; functional group: acidity regulators).

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 of 7 December 2021.

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, user and on the efficacy of the additive consisting of a preparation of *Streptococcus salivarius* DSM 13084/ATCC BAA 1024, when used under the proposed conditions of use (see Section 3.1.5).

1.2. Additional information

Streptococcus salivarius DSM 13084/ATCC BAA 1024 is not authorised as a feed additive in the European Union.

2. Data and methodologies

2.1. Data

The present assessment is based on data submitted by the applicant in the form of a technical dossier[4] in support of the authorisation request for the use of *Streptococcus salivarius* DSM 13084/ ATCC BAA 1024, as a feed additive.

The dossier was received 1/6/2021 and the general information and supporting documentation is available at https://open.efsa.europa.eu/questions/EFSA-Q-2021-00501.

The confidential version of the technical dossier was subjected to targeted consultation of the interested Member States from 9 December 2021 to 9 March 2022 for which received comments that were considered for the assessment.

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.

EFSA has verified the European Union Reference Laboratory (EURL) report as it relates to the methods used for the control of the agent in animal feed.[5]

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the council of 22 September 2003 on the additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] BLIS Technologies Limited, 81 Glasgow street, South Dunedin, Dunedin 9,012, New Zealand (represented in the EU by Pen & Tech Consulting S.L.U, Plaza Ausias March 1, 4ª D01, Barcelona, Sant Cugat del Vallès 08195, Spain).
[3] Originally designated as *Streptococcus salivarius*.
[4] FEED dossier reference: FAD-2021-0060.
[5] The full report is available on the EURL website: 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 *Streptococcus salivarius* DSM 13084/ATCC BAA 1024 is in line with the principles laid down in Regulation (EC) No 429/2008[6] and the relevant guidance documents: Guidance on studies concerning the safety of use of the additive for users/workers (EFSA FEEDAP Panel, 2012), Guidance on the identity, characterisation and conditions of use of feed additives (EFSA FEEDAP Panel, 2017a), Guidance on the assessment of the safety of feed additives for the target species (EFSA FEEDAP Panel, 2017b), Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018a), Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA FEEDAP Panel, 2018b) and Guidance on the assessment of the safety of feed additives for the environment (EFSA FEEDAP Panel, 2019).

3. Assessment

This opinion assesses the safety and efficacy of an additive consisting of *Streptococcus salivarius* DSM 13084/ATCC BAA 1024 as a technological additive (functional group: acidity regulators) for cats and dogs.

3.1. Characterisation

3.1.1. Characterisation of the active agent

The additive contains a non-genetically modified strain of *S. salivarius* which is deposited [redacted][7] It will be hereafter referred to DSM 13084. The active agent was originally isolated from the saliva of a healthy child. The whole genome of the strain was sequenced and used for identification purposes. [redacted].

Three approaches were used to establish the taxonomic identification of the active agent. [redacted].

Altogether, the identification results allocate the strain DSM 13084 within the species *S. salivarius*.

The susceptibility of the active agent to the antibiotics recommended by FEEDAP was tested [redacted] following the FEEDAP guidance (EFSA FEEDAP Panel, 2018b).[8] All the minimum inhibitory concentration (MIC) values determined were equal to or fell below the corresponding cut-off values defined by the FEEDAP Panel for the closest related species *S. thermophilus*.

The whole genome sequence (WGS) data of the active agent [redacted][9] [redacted]. No hits of concern were identified. [redacted]

[6] Commission 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.
[7] Technical dossier/Section II/Annex II.2.2.1.4.
[8] Technical dossier/Section II/Annex II. 2.2.2.2.1.1.
[9] Technical dossier/Section II/Annex II. 2.2.1.2.9.

[redacted] The strain *S. salivarius* DSM 13084 was predicted as non-pathogenic. The WGS data was also interrogated for the presence of virulence factors [redacted] None was considered of concern.

To exclude the capacity of the active agent to produce antimicrobials, [redacted].[10] No inhibition was observed, denoting the lack of antimicrobial production by *Streptococcus salivarius* DSM 13084.

3.1.2. Manufacturing process

[redacted][11]

3.1.3. Characterisation of the additive

The applicant has described a preparation as freeze-dried powder which consists of *Streptococcus salivarius* DSM 13084 [redacted], maltodextrin [redacted], trehalose dihydrate [redacted] and lactitol anhydrous [redacted].

The minimum concentration of the active agent in the additive is specified to be 1×10^{11} colony forming unit (CFU)/g. Analysis of five batches of the additive showed a mean value of 4×10^{11} CFU/g (range: 2.7–5.8 $\times$ 10^{11} CFU/g), demonstrating compliance with the proposed specifications.[12]

The same batches were analysed for chemical and microbiological contaminants. Levels of cadmium ranged from < 0.005 to < 0.01 mg/kg, lead and mercury were < 0.01 mg/kg and arsenic ranged from 0.01 to < 0.03 mg/kg.[13]

Total coliforms, coagulase positive *Staphylococcus* spp. and *Escherichia coli* were not detected in 1 g, *Salmonella* spp. was not detected in 25 g, Enterobacteriaceae were < 1 CFU/g, total yeasts, filamentous fungi and mesophilic aerobic spores were < 10 CFU/g in all batches tested.[12]

Three additional batches of the additive were analysed for aflatoxins (B1, B2, G1, G2), deoxynivalenol, fumonisins (B1 and B2), ochratoxin A, HT-2 toxin, T-2 toxin and zearalenone.[14] All the values were below the respective limits of quantification (LOQs) of the analytical methods.[15]

The same three batches were also analysed for dioxins. The concentration of dioxins and the sum of dioxins and dioxin-like PCBs were < 0.002 ng WHO-PCDD/F-TEQ/kg and < 0.005 ng WHO-PCDD/F-PCB-TEQ/kg, respectively, in all the batches tested.

The detected amounts of the above described impurities do not raise safety concerns.

The tapped and bulk density, measured in duplicate in three batches of the additive, was on average 720 kg/m^3 (range 600–780 kg/m^3) and 550 kg/m^3 (range 470–600 kg/m^3), respectively.[16]

The dusting potential of the same three batches of the additive (four replicates), determined using the Stauber–Heubach method, showed an average value of 3,800 mg/m^3 (range 2,350–4,990 mg/m^3).

The particle size distribution was measured by dry dispersion laser diffraction in five batches of the additive. The results showed that 90% of the particles had diameter < 391 μm.[12]

[10] Technical dossier/Section II/Annex II. 2.2.2.2.2.
[11] Technical dossier/Section II/Annexes II.3.1.1. and II.3.1.2.Conf.
[12] Technical dossier/Section II/Annex II.2.1.3.2.
[13] Technical dossier/Section II/Annex II.2.1.3.2. LOQ: Hg: 0.025 μg/kg, Cd: 0.02 μg/kg, Pb: 0.025 μg/kg and arsenic: 0.05 μg/kg, LOD: Hg: 0.01 mg/kg, Cd: 0.01 mg/kg, Pb: 0.01 mg/kg and arsenic: 0.03 mg/kg.
[14] Technical dossier/Section II/ Annexes II.2.1.4.2.2, II.2.1.4.2.3 and II.2.1.4.2.4.
[15] LOQ: aflatoxins (B1, B2, G1, G2) < 1 μg/kg; deoxynivalenol < 100 μg/kg, fumonisins (B1 and B2) < 5 μg/kg, ochratoxin A < 1 μg/kg, HT-2 toxin < 20 μg/kg, T-2 toxin < 50 μg/kg and zearalenone < 5 μg/kg.
[16] Technical dossier/Section II/Annex II.2.1.5.1.

3.1.4. Stability and homogeneity

The shelf life of the additive was evaluated in three batches when stored at 5°C ± 3°C in aluminium foil bags up to 6 months. Losses at the end of the storage period were negligible (< 0.05 $\log_{10}$ CFU/g).[17]

For technological additives, stability in feed can be demonstrated by the persistence of the intended technological effect. The applicant provided evidence of the stability in feed in the efficacy studies done with several feeds for up to 24 h. The studies are described in the efficacy section (see Section 3.3).

The homogeneous distribution of the additive was studied in 10 subsamples of reconstituted milk replacer for cats at an inclusion level of 3×10^{11} CFU/L. The coefficient of variation (CV) was 6.55%.[18]

3.1.5. Conditions of use

The additive is intended for use at a proposed minimum level of 1×10^{11} CFU/L or kg liquid feed for dogs and cats (e.g. liquid milk and gravy and/or wet pet feed with gravy (> 70% moisture)).

3.2. Safety

3.2.1. Safety of the active agent

The active agent was shown to belong to the species *Streptococcus salivarius*. *S. salivarius* is not a species eligible for the qualified presumption of safety (QPS) approach of safety assessment due to the ability of some strains to cause bacteraemia and systemic infections that result in a variety of morbidities (EFSA BIOHAZ Panel, 2023). Based on the data provided, the active agent does not harbour acquired AMR genes and is not expected to be virulent or to produce any toxic compounds. Moreover, the active agent did not show the ability to produce antimicrobial compounds of relevance for human and animal health.

3.2.2. Safety for the target species

For microorganisms not satisfying the requirements of the QPS approach to safety assessment (EFSA, 2007; EFSA BIOHAZ Panel, 2023), or when its biology is not sufficiently well known to allow pathogenic/toxigenic strains to be excluded by direct testing, data should be submitted to support the safety for the target species.

No tolerance studies performed in the target species were submitted by the applicant.

To support the safety of the additive for the target species, the applicant provided a publication by Burton et al. (2010) which includes results of an Ames test, an acute toxicity study (dose-range finding study) and a 28-day oral toxicity study, conducted with the additive under assessment. These studies were claimed as Good Laboratory Practice (GLP) compliant. The Ames test and the subacute toxicity study are briefly described below.

The Ames test reported by Burton et al. (2010), is performed following OECD Testing Guideline (TG) 471 and showed no mutagenic effects either in the absence or presence of metabolic activation. However, no quantitative data are reported in the publication and only the conclusions are available in the text.

In a subacute toxicity study, not fully in compliance with the OECD TG 407, 160 mature Sprague–Dawley rats (20/sex per group) were fed diets providing 7.5, 100, or 5,000 mg/kg body weight (bw) per day of test item for a period of 28 days. These levels provided a corresponding daily intake of 1.25×10^8, 1.67×10^9, or 8×10^{10} CFU per kg bw, respectively. Animals in the control group were fed a diet providing 7.5 mg lyoprotectant/kg bw/day.

A fifth group, consisting of 5 males and 5 females, was designed to collect tissue and blood on Day 0 to establish baseline parameters for the animals.

No adverse effects were reported in any dose group up to the highest level 5,000 mg/kg bw per day during the administration period.

The FEEDAP Panel noted some limitations in the dataset provided: no results were available as raw data but only mentioned in tables as group mean values including standard errors and standard

[17] Technical dossier/Section II/Annex II.2.4.1.1.
[18] Technical dossier/Section II/Annex II.2.4.2.1.

deviations, results on food consumption, histopathology and organ weights were only mentioned briefly in the text, results from functional observational battery (FOB) and from tests for endocrine activity were not available.

Although these studies do not show any adverse effects, due to the several limitations identified, they cannot be used for the risk assessment of the additive under assessment.

3.2.2.1. Conclusions on the safety for the target species

The dataset provided showed several limitations which precluded any conclusion. In the absence of adequate data, the Panel is not in the position to conclude on the safety of the additive for the target species.

3.2.3. Safety for the user

Based on the dusting potential data (up to 4,990 mg/m^3), the FEEDAP Panel considered that the exposure through inhalation is very likely. No specific information was submitted on possible effects at the level of respiratory system. However, considering the proteinaceous nature of the active agent, the additive should be considered a respiratory sensitiser.

The skin irritation potential of the additive under assessment was evaluated in an *in vitro* test conducted following the OECD TG 439.[19] Based on the results obtained, the additive is classified as non-irritant to the skin (UN GHS 'No Category').

The eye irritation potential of the additive under assessment was evaluated in an *in vitro* test conducted following the OECD TG 492.[20] The interaction of the test item with the test procedures (the live bacteria reduced the MTT to purple formazan interfering with the MTT endpoint analysis) prevented a valid conclusion being obtained.

The FEEDAP Panel notes that the OECD test guidelines available at present are designed to assess the skin sensitisation potential of chemical substances only and that currently no validated assays for assessing the sensitisation potential of microorganisms are available.[21] Therefore, no conclusion can be drawn on the skin sensitisation potential of the additive.

3.2.3.1. Conclusions on the safety for the users

Considering the proteinaceous nature of the active agent, the FEEDAP Panel concluded that the additive should be considered a respiratory sensitiser. The additive is not a skin irritant. No conclusions can be drawn on its potential to be an eye irritant or a skin sensitiser.

Once an active agent has been authorised, different formulations can be placed on the market with reference to that authorisation. The applicant listed excipients which would allow multiple formulations of the additive to be produced and, consequently, the Panel cannot conclude on other formulations that might be placed on the market.

3.2.4. Safety for the environment

The additive under assessment is intended to be used in feed for dogs and cats only. No environmental risk assessment is necessary for such use (EFSA FEEDAP Panel, 2019).

3.3. Efficacy

The applicant provided two sets of three *in vitro* studies[22,23] to demonstrate the ability of the additive to reduce the pH in liquid feeds for cats and dogs. The same studies were also used to demonstrate the stability of the additive, in terms of CFU concentration.

Three liquid matrices (milk replacers for cats and dogs and a gravy from canned food for cats) were used. The additive was added at three different inclusion levels: 0 (control), 1–3 $\times$ 10^{11} CFU/L and 1–3 $\times$ 10^{12} CFU/L. The milk replacers were diluted with water (50°C at the inclusion of the milk replacer) and supplemented with the additive to reach the intended concentration. The gravy was supplemented with the additive after mechanical separation from the meat chunks.

[19] Technical dossier/Section III/Annex_III.3.3.1.2.1.
[20] Technical dossier/Section III/Supplementary Information (October 2022)/Annex_III.3.3.1.2.
[21] https://www.efsa.europa.eu/sites/default/files/2022-07/feedap20220629-30_m.pdf
[22] Technical dossier/Section IV/Annex II.4.1.1, Annex IV.4.1.2 and Annex IV.4.1.3.
[23] Technical dossier/Supplementary Information (October 2022)/Annex_IV_4_1_4, Annex_IV_4_1_5 and Annex_IV_4_1_6.

Two samples of each feed used in the first set of studies and three samples of each feed used in the second set of studies were stored in Schott glass bottles at room temperature (22°C ± 2°C) for 24 h. The pH values of the samples were measured (in duplicate) at the start of the experiment and at three incubation time points (3, 6 and 24 h) and compared to the control. The supplemented samples were also analysed for the enumeration of *Streptococcus salivarius* DSM 13084 at 0, 3, 6 and 24 h (triplicate analysis each) in the first set, and at 0 and 24 h (triplicate analysis at time 0 and one analysis at 24 h) in the second set.

The data were subjected to an analysis of variance (ANOVA) and group means were compared with Tukey's test. Significance level was set at $p \leq 0.05$. The results on the effects of the additive on the pH of the feeds and on stability up to 24 h are shown in Tables 1 and 2 for the first and second set of studies, respectively.

Table 1: Effects of the additive on pH in feeds (milk replacers for cat and dog and a gravy (from canned food) for cat) and DSM 13084 enumeration in the first set of studies

Study number (matrix)	Inclusion level (CFU/l)	Mean pH at different time points (DSM 13084 count (CFU/L)) (2 replicates)			
		Time 0	Time 3 h	Time 6 h	Time 24 h
1 (cat milk)	0	6.96	7.04^{a}	7.05^{a}	7.03^{a}
	3×10^{11}	7.01 (2.9×10^{11})	6.51^{b} (3.7×10^{11})	6.18^{b} (4.2×10^{11})	5.12^{b} (9.1×10^{11})
	3×10^{12}	6.84 (2.8×10^{12})	5.29^{c} (2.7×10^{12})	5.02^{c} (2.6×10^{12})	4.6^{c} (2.9×10^{12})
2 (puppy milk)	0	7.00^{a}	7.09^{a}	7.08^{a}	6.98^{a}
	3×10^{11}	7.02^{a} (3×10^{11})	6.23^{b} (5.3×10^{11})	5.79^{b} (7.1×10^{11})	4.79^{b} (1.3×10^{11})
	3×10^{12}	6.90^{b} (2.8×10^{12})	4.98^{c} (3×10^{12})	4.76^{c} (2.4×10^{12})	4.62^{b} (1.9×10^{12})
3 (cat gravy)	0	6.25	6.26	6.29^{a}	6.29^{a}
	1×10^{11}	6.31 (1×10^{11})	6.13 (1.8×10^{11})	5.77^{ab} (1.7×10^{11})	5.57^{b} (0.6×10^{11})
	1×10^{12}	6.27 (9.2×10^{12})	5.55 (1.5×10^{12})	5.05^{b} (1.7×10^{12})	4.68^{c} (0.9×10^{12})

CFU: colony forming unit.
a,b,c: Mean values within a study and within a column with a different superscript are significantly different ($p < 0.05$).

In the first set of studies, the pH of the treated groups in milk replacer for cats or dogs showed a significant dose-dependent effect at any of the time points with the exception of the milk replacer for dogs at 24 h, where both groups supplemented with the additive showed lower pH than the control. In the gravy for cats, no difference among the groups were observed after 3 h; after 6 h, only the high concentration group had pH values lower than the control. After 24 h, a dose-dependent difference in pH values was observed.

Table 2: Effects of the additive on pH in feeds (milk replacers for cat and dog and a gravy (from canned food) for cat) and DSM 13084 enumeration in the second set of studies

Study number (matrix)	Inclusion level (CFU/l)	Mean pH at different time points (DSM 13084 (CFU/L)) (3 replicates)			
		Time 0	Time 3 h	Time 6 h	Time 24 h
1 (cat milk)	0	6.96^{a}	6.97^{a}	6.97^{a}	6.96^{a}
	1×10^{11}	6.97^{a} (1.4×10^{11})	6.78^{b}	6.59^{b}	5.65^{b} (1.9×10^{11})
	1×10^{12}	6.81^{b} (1.3×10^{12})	5.73^{c}	5.30^{c}	4.68^{c} (8.1×10^{12})

Study number (matrix)	Inclusion level (CFU/l)	Mean pH at different time points (DSM 13084 (CFU/L)) (3 replicates)			
		Time 0	Time 3 h	Time 6 h	Time 24 h
2 (puppy milk)	0	7.05[a]	7.05[a]	7.03[a]	7.05[a]
	3×10^{11}	7.03[b] (1.5×10^{11})	6.90[b]	6.71[b]	6.16[b] (9.4×10^{10})
	3×10^{12}	6.90[c] (1.7×10^{12})	5.86[c]	5.23[c]	4.60[c] (8.3×10^{11})
3 (cat gravy)	0	6.19[b]	6.23[a]	6.24[a]	6.23[a]
	1×10^{11}	6.22[a] (1.9×10^{11})	5.84[b]	5.42[b]	4.79[b] (1.4×10^{11})
	1×10^{12}	6.24[a] (1.7×10^{12})	4.99[c]	4.70[c]	4.45[c] (8.7×10^{11})

CFU: colony forming unit.
a,b,c: Mean values within a study and within a column with a different superscript are significantly different ($p < 0.05$)

In the second set of studies, in all feeds, a significant dose-dependent effect on pH was observed at all the time points.

The counts of the active agent, in both set of studies, showed generally no losses (< 0.5 log) at the end of the storage period.

3.3.1. Conclusions on efficacy

The additive has the potential to be efficacious as acidity regulator at the recommended concentration of 1×10^{11} CFU/L or kg liquid feed for dogs and cats.

4. Conclusions

Due to the lack of adequate data, the FEEDAP Panel could not conclude on the safety of the additive for the target species.

Considering the proteinaceous nature of the active agent, the additive is considered a respiratory sensitiser. The additive is not a skin irritant. No conclusions can be drawn on its potential to be an eye irritant or a skin sensitiser.

Since the additive under assessment is intended to be used in feed for dogs and cats only, no environmental risk assessment is necessary.

The additive has the potential to be efficacious as acidity regulator at the recommended concentration of 1×10^{11} CFU/l or kg liquid feed for dogs and cats.

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Abbreviations

ANOVA	analysis of variance
ATCC	American Type Culture Collection
BW	body weight
CFU	colony forming unit
DM	dry matter
EURL	European Union Reference Laboratory
GLP	Good Laboratory Practice
FEEDAP	EFSA Scientific Panel on Additives and Products or Substances used in Animal Feed
LOD	limit of detection
LOQ	limit of quantification
NCBI	National Center for Biotechnology Information
OECD	Organisation for Economic Co-operation and Development
PCB	polychlorinated biphenyl
PCDD	polychlorinated dibenzo(*p*)dioxin
PCDF	polychlorinated dibenzofuran
QPS	Qualified presumption of safety
TEQ	toxic equivalents
WGS	whole genome sequences
WHO	World Health Organization