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Safety and efficacy of a feed additive consisting of butylated hydroxyanisole (BHA) for use in cats (FEDIAF)

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Abstract

Following a request from the European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the safety and efficacy of butylated hydroxy anisole (BHA) when used as a technological additive (antioxidant) in feed for cats. BHA is a waxy solid consisting for > 98.5% of the active substance, a mixture of 3-*tert*-butyl-4-hydroxyanisole and 2-*tert*-butyl-4-hydroxyanisole and is currently authorised for use in all animal species except in cats. In support of the safety of the additive for the target species, the applicant has submitted a tolerance study which demonstrated that BHA is tolerated by cats at a concentration up to 150 mg/kg complete feed. The additive should be considered a skin, eye irritant and a potential skin sensitiser. Exposure of the user via inhalation was considered unlikely; therefore, a risk is not expected. BHA is authorised as an antioxidant for food use at comparable use levels; therefore, no studies were required to demonstrate the efficacy of BHA as an antioxidant in complete feed for cats.

Keywords: technological additive, antioxidants, butylated hydroxyanisole, BHA, cats, safety, efficacy

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

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 a feed additive shall submit an application in accordance with Article 7.

The European Commission received a request from FEDIAF[2] for authorisation of the additive consisting of butylated hydroxyanisole (BHA), when used as a feed additive for cats (category: technological additive; functional group: antioxidants).

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). The particulars and documents in support of the application were considered valid by EFSA as of 26 February 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 and user and on the efficacy of the product butylated hydroxyanisole (BHA), when used under the proposed conditions of use (see Section 3.1.1).

1.2. Additional information

The additive butylated hydroanisole (BHA), hereinafter referred to as BHA, is currently authorised as a technological additive in feed for all animal species other than cats with a maximum content of 150 mg/kg complete feed.[3]

In 2018, EFSA issued an opinion on the safety and efficacy of BHA when used as a feed additive for all animal species (EFSA FEEDAP Panel, 2018a,b) and another opinion on the safety of BHA in cats (EFSA FEEDAP Panel, 2019).

BHA is authorised according to Directive 95/2/EC1[4] as a food additive (antioxidant), up to a maximum level of 400 mg/kg. The Scientific Committee on Food (SCF), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and EFSA ANS Panel have delivered several opinions on the use of BHA as a food additive (JECFA, 1974, 1976, 1982, 1986, 1987, 1989, 1999, 2006; SCF, 1989; EFSA ANS Panel, 2011, 2012).

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[5] in support of the authorisation request for the use of BHA as a feed additive.

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 BHA in animal feed are valid and applicable for the current application.[6]

2.2. Methodologies

The approach followed by the FEEDAP Panel to assess the safety and the efficacy of BHA is in line with the principles laid down in Regulation (EC) No 429/2008[7] and the relevant guidance documents:

[1] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[2] FEDIAF, Avenue Louise 89, Brussels (Belgium).
[3] Commission Implementation Regulation (EU) 2020/1399 of 5 October 2020 concerning the authorisation of butylated hydroxyanisole as a feed additive for all animal species except cats. OJ L 324, 6.10.2020, p. 3.
[4] European Parliament and Council Directive No 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61, 18.3.1995, p. 1.
[5] FEED dossier reference: FAD-2020-0089.
[6] The full report is available on the EURL website: https://ec.europa.eu/jrc/sites/jrcsh/files/FinRep-FAD-2010-0132.pdf
[7] 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.

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) and Guidance on the assessment of the efficacy of feed additives (EFSA FEEDAP Panel, 2018a,b).

3. Assessment

The additive under assessment, BHA, is intended to be used as a feed additive (category: technological additives; functional group: (b) antioxidants) in complete feed for cats.

The additive is currently authorised for use in feeding stuffs for all animal species other than cats.

3.1. Characterisation

The active substance BHA is identical to the additive. BHA is a white, waxy solid (white to cream coloured flakes) with a characteristic odour and consists of a mixture of 3-*tert*-butyl-4-hydroxyanisole and 2-*tert*-butyl-4-hydroxyanisole.

The additive has been characterised in a previous opinion of the FEEDAP Panel (EFSA FEEDAP Panel, 2018a,b). New information has been submitted on the composition and impurities, which is presented below.

The additive is specified to contain at least 98.5% of BHA (International Union of Pure and Applied Chemistry (IUPAC) name: 2-*tert*-butyl-4-hydroxyanisole and 3-*tert*-butyl-4-hydroxyanisole, Chemical Abstracts Service (CAS) number 25013-16-5, chemical formula $C_{11}H_{16}O_2$, and molecular weight 180.25 Da) and not less than 85% of the 3-*tert*-butyl-4-hydroxyanisole isomer. These specifications are in line with the current authorisation of BHA as a feed additive for all animal species except cats[8] and also as food additive.[9]

The analysis of six batches of the additive resulted in a mean content of BHA [redacted] and of 3-*tert*-butyl-4-hydroxyanisole of [redacted][10] in compliance with the existing specifications.

The same batches were analysed for possible presence of impurities, including heavy metals. Arsenic, lead, mercury, cadmium and fluorine were below the respective limit of detection (LOD) [redacted] in all the batches analysed. [redacted] Based on the results obtained, no concern is expected from the possible presence of the tested impurities.

3.1.1. Conditions of use

BHA is intended to be used as an antioxidant in complete feed for cats with a maximum content of 150 mg/kg complete feed (alone or in combination with butylated hydroxytoluene (BHT)).

3.2. Safety

3.2.1. Safety for cats

In its previous opinion (EFSA FEEDAP Panel, 2018a,b), the Panel concluded that 'a weight of evidence' of the limited data supports that 150 mg BHA/kg complete feed would be a safe dose for all animal species. However, a possible exception could be the cat, with its known lower capacity for glucuronidation of phenolic compounds and for which no specific data were available.' Following the submission of new information to support the safety for cats (a review of the literature on of the metabolism of phenolic compounds in cats and an *in vivo* study with cats), the FEEDAP Panel issued another opinion on BHA (EFSA FEEDAP Panel, 2019) and concluded that 'No specific information on metabolic fate of BHA has been made available for the feline species'. The lack of knowledge is of particular relevance considering the additional load of phenolic compounds by dietary BHA for the full lifetime expectancy of cats. Considering the lack of information on the metabolism of BHA in cats and

[8] Commission implementing Regulation (EU) 2020/1399 of 5 October 2020 concerning the authorisation of butylated hydroxyanisole as a feed additive for all animal species except cats, OJ L 324/29, 6.10.2020, p. 1–3.

[9] Commission Regulation (EU) No 231/2012 of 9 March 2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council, OJ L 83, 22.3.2012, p. 1–295.

[10] Technical dossier/Section II/Annex_II_1_3.

the absence of a well-designed tolerance study, the FEEDAP Panel confirms its previous assessment on the safety of BHA for cats. Consequently, the Panel reiterates that no safe concentration of BHA in complete feed for cats could be established'.

In the current application, the applicant has submitted a tolerance study conducted in cats.[12]

Sixty healthy cats (both males and females, aged 3–10 years, body weight at start: 2–7 kg) were allocated to four experimental groups (15 animals/group) which were balanced for body weight, age, gender and housing room.[13] The cats were group housed in common rooms, but at the time of feeding (twice a day) they were housed individually. Water was available for ad libitum intake. An acclimatisation period of 4 weeks took place prior to the start of the study where the same diet was offered to all cats. The groups were fed a control diet (without supplemental BHA), or diets supplemented with BHA at 150 mg BHA/kg feed (1× maximum proposed level), 450 mg BHA/kg feed (3×) or 750 mg BHA/kg feed (5×), respectively. The intended BHA levels were analytically confirmed (< 10, 202, 451 and 857 mg/kg as average of 3 samples taken at start, middle and end of production). The trial lasted 28 days.

All four treatment diets were identical in composition (same batch) except for the inclusion level of BHA which was applied as spray post-extrusion. [redacted]

General health status and behaviour of the cats was observed at least twice a day. Faecal consistency was monitored and scored (using a 1–5 classification scale)[15] at the group level throughout the study, any vomiting was recorded. Feed intake was recorded daily. Body weight and body condition scores were recorded weekly. Blood samples were taken from fasted animals before start of the study, and at days 7, 14 and 28. All samples were analysed for biochemistry parameters,[16] the samples before start and from day 28 also for additional biochemistry parameters[17] and for haematology.[18]

Alanine aminotransferase (ALT) and alkaline phosphatase (ALP), considered as key liver health markers, and symmetric dimethyl arginine (SDMA), creatinine and urea, kidney health markers, were the primary parameters for the study. Body weight and feed intake were considered secondary parameters.

The study was powered to detect a 1.6-fold change[19] between control and test diets at the final sampling occasion for the primary parameters and a 1.2-fold change within each diet between baseline and final sample for the secondary parameters. The P-values were unadjusted and then tested against 10% significance divided by the number of test diets (3). Equivalence tests in the form of TOST (two-one-sided T-tests) were carried out for primary and secondary parameters. Equivalence was defined as when both p-values ≤ 0.033.

No mortality was recorded during the study. An initial not significant decrease in feed intake of the 5 × BHA overdose group was observed; however, this was transient, recovering over the 28-day study

[12] Technical dossier/Section III/Annex_III_1_1.

[13] Power analysis showed that 10 cats are required per group to see a 1.6x fold change in ALT and ALP and a 1.2x fold change for feed intake and bodyweight to meet the EFSA guidelines requirement of a 10% significance level and a target power of 75% (EFSA FEEDAP Panel, 2017a,b). The decision was made to use 15 cats per diet group to allow for any removal from the study.

[redacted]

[15] 1: Hard, dry and crumbly, 'bullet-like'; 1.5: Hard and dry; 2: Well formed, does not leave a mark, 'kickable'; 2.5: Well formed, slightly moist surface, leaves a mark, sticky to touch; 3: Moist, beginning to lose form, leaving a definite mark when picked up; 3.5: Very moist, but still has some definite form; 4: The majority, if not all of the form is lost, poor consistency, viscous; 4.5: Diarrhea with some areas of consistency; 5: Watery diarrhea.

[16] Glucose; SDMA; creatinine; urea (BUN); phosphorus; calcium; magnesium; sodium; potassium; Na:K ratio; chloride; bicarbonate; total protein; albumin; globulin; albumin:globulin ratio; alanine aminotransferase (ALT); aspartate-aminotransferase (AST); alkaline phosphatase (ALP); gamma-glutamyl transferase (GGT); bilirubin total; bilirubin conjugated; cholesterol; triglyceride; amylase; lipase; creatine kinase.

[17] Serum amyloid A (SAA) and lactate dehydrogenase (LDH).

[18] Red blood cells, haematocrit; haemoglobin (g/L); mean corpuscular volume; mean corpuscular haemoglobin; mean corpuscular haemoblogin concentration; red cell distribution width; reticulocytes; reticulocyte haemoglobin; white blood cells; neutrophils; lymphocytes; monocytes; eosinophils; basophils; platelets; fibrinogen; prothrombin time; partial thromboplastin time.

[19] This level of difference has been selected as it represents the measured variation in ALT and ALP levels observed in healthy cats over a long-term (6-month) feeding study conducted at the institution where the tolerance study has been made.

period. Two cats from 5× BHA were removed from the study (at days 4 and 17, due to reduced feed intake, reduction > 10% compared to baseline, data not provided). The applicant suggested that the effect on feed intake could be probably due to a palatability issue. Faecal scores remained consistent for all the cats during the whole study, except for one cat (in the treated group 150 mg/kg feed) that had several occasions of poor faeces, lasting not more than 1 day. Only one case of vomiting was reported in a cat in the control group.

ALP and ALT remained with their 95% confidence intervals below the upper reference ranges for all cats throughout the full study period. Within each group, results of ALP and ALT were equivalent between the values measured before study start and at study end ($p \leq 0.033$). Comparisons with each BHA supplemented group to the control (before the study: 24.2; study end: 24.6 IU/L) revealed equivalence for all groups for ALP ($p \leq 0.033$). For ALT, equivalence was seen for both the BHA use level and BHA 5× overdose groups when compared to the control ($p \leq 0.033$) (before the study: 47.8; study end: 40 IU/L for BHA use level and before the study: 44.3 and study end: 47.4 IU/L for BHA 5 ×); but was not significant for the 450 mg BHA diet (3 ×) (before the study: 45; study end: 54.9 IU/L) ($p > 0.033$). The latter finding is not considered BHA-related since equivalence for the higher dose group was shown.

Creatinine and urea, expressed as blood urea nitrogen (BUN), remained with their 95% confidence intervals within the normal reference ranges, and within individual groups both parameters were equivalent between study start and study end ($p \leq 0.033$). Comparisons between the BHA supplemented groups and the control group indicated equivalence (BUN, before the study: 7.9; study end: 8.2 mmol/L; creatinine, before the study: 135; study end: 128 μmol/L) ($p \leq 0.033$).

SDMA levels for some cats were above the upper reference range throughout the study, this was seen already before study start, across all sampling occasions and was not unique to a single group. Equivalence analysis confirmed that there was no change of SDMA values before study start (11.4 μg/dL) to those at study end (11.5 μg/dL), nor were differences detected between the groups with BHA supplemented feed and the control group ($p \leq 0.033$) (Table 1).

All other additional biochemistry and haematology parameters including their 95% confidence limits were, with few and not relevant exceptions (for the lower and upper 95% confidence limits), within the reference ranges.

Equivalence testing did not identify differences in feed intake during the test period ($p \leq 0.033$) for any group. Comparisons of feed intake between BHA supplemented groups and the control group indicated equivalence too ($p \leq 0.033$). These findings were also reflected in the body weight data during the test period, with no differences within or between group detected (before the study: 4.7; study end: 4.7 kg) ($p \leq 0.033$) (Table 2).

Table 1: Liver and kidney health marker before study start and at study end (n = 15/group, except the group with 750 mg supplemental BHA/kg with n = 13)

Parameters evaluated		Intended supplemental BHA (mg/kg feed)			
		0	150	450	750
ALP (IU/L)[(a)]	Before study start	24.2	26.1	25.2	21.9
	Study end	24.6	27.6	27.8	23.3
ALT (IU/L)[(b)]	Before study start	47.8	41.1	45.0	44.3
	Study end	40.0	38.3	54.9	47.4
Urea (BUN in mmol/L)[(c)]	Before study start	7.9	8.3	8.2	7.4
	Study end	8.2	8.7	8.8	8.4
Creatinine (μmol/L)[(d)]	Before study start	135	148	143	133
	Study end	128	133	132	132
SDMA (μg/dL)[(e)]	Before study start	11.4	12.1	11.3	10.4
	Study end	11.5	11.7	11.6	11.4

ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; SDMA: symmetric dimethyl arginine.
(a): Parameter reference range: ALP 12–59 IU/L.
(b): Parameter reference range: ALT 27–158 IU/L.
(c): Parameter reference range: BUN 5.7–13.2 μmol/L.
(d): Parameter reference range: creatinine 80–221 μmol/L.
(e): Parameter reference range: SDMA 0–14 μg/dL.

Table 2: Feed intake (weekly average) and body weight (n = 15/group, except the group with 750 mg supplemental BHA/kg with n = 13)

Parameters evaluated		Intended supplemental BHA (mg/kg feed)			
		0	150	450	750
Feed Intake (g/kg bw)	Before study start	10.1	10.0	9.2	10.4
	Week 1	11.4	11.1	9.7	8.9
	Week 2	11.6	11.1	9.9	9.9
	Week 3	11.2	11.0	10.0	9.9
	Week 4	11.5	11.1	10.4	10.0
Body weight (kg)	Before study start	4.7	4.9	5.3	4.5
	Week 1	4.8	4.9	5.3	4.4
	Week 2	4.8	4.9	5.3	4.4
	Week 3	4.8	4.9	5.3	4.4
	Week 4	4.7	4.9	5.3	4.4

bw: body weight.

3.2.1.1. Conclusions on safety for cats

The results of the tolerance study indicate that dietary BHA levels up to the fivefold overdose were tolerated by cats. Therefore, the FEEDAP Panel concludes that 150 mg BHA/kg complete feed, the highest proposed feed concentration, is safe for cats.

3.2.2. Safety for user

The safety of BHA has been evaluated in a previous EFSA opinion (EFSA FEEDAP Panel, 2018a,b). No new data have been submitted that would allow to reconsider the conclusions previously reached. The additive should be considered a skin and eye irritant and a potential skin sensitiser. Exposure of the user via inhalation is considered unlikely due to the lack of dusting potential; therefore, a risk is not expected.

3.3. Efficacy

BHA is authorised to be added as an antioxidant to foods with a wide range of moisture content at concentrations of 40–400 mg/kg. Since the same effect can be reasonably assumed for complete feed, no studies are required to demonstrate the efficacy of BHA as an antioxidant in complete feed for cats.

4. Conclusions

The FEEDAP Panel considers the use of BHA at concentrations up to 150 mg/kg complete feed to be safe for cats.

The additive should be considered a skin and eye irritant and a potential skin sensitiser. Exposure of the user via inhalation is considered unlikely; therefore, a risk is not expected.

Since BHA is authorised as an antioxidant for food use at comparable use levels, no studies are required to demonstrate the efficacy of BHA as an antioxidant in complete feed for cats.

5. Documentation as provided to EFSA/Chronology

Date	Event
22/09/2020	Reception of the Evaluation report of the European Union Reference Laboratory for Feed Additives
10/11/2020	Dossier received by EFSA. Butylated hydroxyanisole (BHA) for cats. Submitted by FEDIAF.
20/11/2020	Reception mandate from the European Commission
26/02/2021	Application validated by EFSA – Start of the scientific assessment
27/05/2021	Comments received from Member States
23/06/2021	Opinion adopted by the FEEDAP Panel. End of the Scientific assessment

References

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2011. Scientific Opinion on the re-evaluation of butylated hydroxyanisole – BHA (E 320) as a food additive. EFSA Journal 2011;9(10):2392, 12 pp. https://doi.org/10.2903/j.efsa.2011.2392

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food), 2012. Statement on the safety assessment of the exposure to butylated hydroxyanisole E 320 (BHA) by applying a new exposure assessment methodology. EFSA Journal 2012;10(7):2759, 34 pp. https://doi.org/10.2903/j.efsa.2012.2759

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), 2012. Guidance on studies concerning the safety of use of the additive for users/workers. EFSA Journal 2012;10(1):2539, 5 pp. https://doi.org/10.2903/j.efsa.2012.2539

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J and Innocenti ML, 2017a. Guidance on the identity, characterisation and conditions of use of feed additives. EFSA Journal 2017;15(10):5023, 12 pp. https://doi.org/10.2903/j.efsa.2017.5023

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J, Innocenti ML and Martino L, 2017b. Guidance on the assessment of the safety of feed additives for the target species. EFSA Journal 2017;15(10):5021, 19 pp. https://doi.org/10.2903/j.efsa.2017.5021

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, López-Alonso M, López Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J, Innocenti ML and Martino L, 2018a. Guidance on the assessment of the efficacy of feed additives. EFSA Journal 2018;16(5):5274, 25 pp. https://doi.org/10.2903/j.efsa.2018.5274

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Kolar B, Kouba M, Lopez-Alonso M, Puente SL, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Lundebye A-K, Nebbia C, Renshaw D, Innocenti ML and Gropp J, 2018b. Scientific Opinion on the safety and efficacy of butylated hydroxyanisole (BHA) as a feed additive for all animal species. EFSA Journal 2018;16(3):5215, 18 pp. https://doi.org/10.2903/j.efsa.2018.5215

EFSA FEEDAP Panel (EFSA Panel on Additives and Products or Substances used in Animal Feed), Bampidis V, Azimonti G, Bastos ML, Christensen H, Dusemund B, Kouba M, Kos Durjava M, Lopez-Alonso M, Lopez Puente S, Marcon F, Mayo B, Pechova A, Petkova M, Ramos F, Sanz Y, Villa RE, Woutersen R, Aquilina G, Bories G, Gropp J, Nebbia C and Innocenti ML, 2019. Scientific Opinion on the safety of butylated hydroxy anisole (BHA) for all animal species. EFSA Journal 2019;17(12):5913, 8 pp. https://doi.org/10.2903/j.efsa.2019.5913

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1974. Butylated hydroxyanisole (BHA). Toxicological evaluation of some food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers and thickening agents. Prepared by the Joint FAO/WHO Expert Committee on Food Additives at the meeting in Geneva, 25 June - 4 July 1973. WHO Food Additives Series 5. Available online: http://www.inchem.org/documents/jecfa/jecmono/v05je22.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1976. 416. Butylatedhydroxyanisole (BHA). Toxicological evaluation of certain food additives. Prepared by the Joint FAO/WHO Expert Committee on Food Additives at the meeting in Rome, 21-29 April 1976, WHO Food Additives Series 10. Available online: http://www.inchem.org/documents/jecfa/jecmono/v10je02.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1982. 489. Butylated hydroxyanisole (BHA). Toxicological monograph of BHA. Prepared by the Joint FAO/WHO Expert Committee on Food Additives. WHO Food Additives Series 15. Available online: http://www.inchem.org/documents/jecfa/jecmono/v15je04.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1986. 558. Butylated hydroxyanisole (BHA). Toxicological monograph. Prepared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series 18. Available online: http://www.inchem.org/documents/jecfa/jecmono/v18je05.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1987. 608. Butylated hydroxyanisole (BHA). Toxicological evaluation of certain food additives and contaminants. Prepared by the thirtieth meeting of the Joint FAO/WHO Expert Committee on Food Additives, Cambridge (GB): Cambridge University Press. WHO Food Additives Series: 21. Available online: http://www.inchem.org/documents/jecfa/jecmono/v21je02.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1989. 652. Butylated hydroxyanisole (BHA), Toxicological monograph of BHA. Prepared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series, 24, 3-22. Available online: http://www.inchem.org/documents/jecfa/jecmono/v024je02.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 1999. 949. Butylated hydroxyanisole (BHA). Safety evaluation of certain food additives. Evaluation of national assessments of intake of butylated hydroxyanisole (BHA). Prepared by the Fifty-first meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series 42, 415–28. Available online: http://www.inchem.org/documents/jecfa/jecmono/v042je23.htm

JECFA (Joint FAO/WHO Expert Committee on Food Additives), 2006. Butylated hydroxyanisole (BHA), Analytical Method, Specifications for identity and purity. Prepared at the 33rd JECFA (1988), published in FNP 38 (1988) and in FNP 52 (1992). Metals and arsenic specifications revised at the 61st JECFA (2003). Codex Alimentarius' specifications. Available online: http://www.fao.org/ag/agn/jecfa-additives/details.html?id=68

SCF (Scientific Committee on Food), 1989. Butylated hydroxyanisole. Reports of the Scientific Committee for Food (Twenty-second series). Commission of the European Communities. Available online: http://ec.europa.eu/food/fs/sc/scf/reports/scf_reports_22.pdf

Abbreviations

ALP	alkaline phosphatase
ALT	alanine aminotrasferase
ANS	EFSA Scientific Panel on Additives and Nutrient Sources added to Food
BHA	butylated hydroxy anisole
BHT	butylated hydroxytoluene
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
FEEDAP	Panel on Additives and Products or Substances used in Animal Feed
IUPAC	International Union of Pure and Applied Chemistry
JECFA	The Joint FAO/WHO Expert Committee on Food Additives
LOD	limit of detection
SCAN	Scientific Committee on Animal Nutrition
SCF	Scientific Committee on Food
SDMA	symmetric dimethyl arginine
WHO	World Health Organization