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SCIENTIFIC OPINION

Safety evaluation of synthesised DNA oligonucleotides as a food additive

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Abstract

The EFSA Panel on Food Additives and Flavourings (FAF) was requested to evaluate the safety of synthesised DNA oligonucleotides as a new food additive, in accordance with Regulation (EC) No 1331/2008. Considering that the additional information requested by the Panel during the risk assessment was not provided by the applicant, the assessment was concluded on the basis of the sole information available in the application. The proposed food additive consists of purified synthetic DNA sequences intended to be used for traceability purposes, alone or combined with carriers. Information provided by the applicant on the identity, characterisation and production process of the proposed food additive was considered insufficient. The Panel considered that the product specifications as proposed by the applicant do not adequately define and characterise the proposed food additive. The applicant proposed for the food additive the maximum use levels of 0.001 mg/kg for a variety of food categories. The food additive was also proposed as a Group I additive at a specific maximum level of *quantum satis*. The applicant did not provide exposure estimates according to the EFSA ANS Panel guidance (2012). No biological or toxicological data were provided by the applicant for the proposed food additive. Considering the inadequate information available and the uncertainty introduced by the proposal at *quantum satis*, along with the insufficient specifications, the Panel could not conclude on the safety of the food additive as proposed and described by the applicant.

KEYWORDS

quantum satis, synthesised DNA oligonucleotides

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SUMMARY

The EFSA Panel on Food Additives and Flavourings (FAF) was requested to evaluate the safety of synthesised DNA oligonucleotides as a new food additive, in accordance with Regulation (EC) No 1331/2008.

Considering that the additional information requested by the Panel during the risk assessment was not provided by the applicant, the assessment was concluded solely on the basis of the information available in the application.

The proposed food additive consists of purified synthetic DNA sequences of [redacted] bases intended to be used for traceability purposes, alone or combined with carriers.

DNA oligonucleotides are obtained through chemical synthesis based on phosphoramidite chemistry, followed by the purification of DNA sequences. The resulting DNA oligonucleotides are lyophilised and can be ultimately combined with carriers. Additional information on reagents and raw materials used in the manufacturing process, experimental conditions, chemical or physical decontamination methods were not provided.

Overall, the information provided by the applicant on the production process and characterisation of the proposed food additive was considered insufficient.

The Panel considered that the product specifications as proposed by the applicant do not adequately define and characterise the proposed food additive.

The applicant suggested for DNA oligonucleotides the maximum use level of 0.001 mg/kg for a variety of food categories. The product was also proposed as a Group I additive at a specific maximum level of *quantum satis*, thus preventing the Panel from calculating the exposure to the proposed food additive itself and to potential impurities.

The proposed food categories were not clearly specified, and the exposure estimates provided by the applicant did not account for the anticipated exposure for average and 95th percentile of the European population for different age groups, according to the EFSA ANS Panel guidance (2012).

No biological or toxicological data were provided by the applicant for the proposed food additive.

Considering (1) the absence of an appropriate characterisation of the identity, sufficient specifications and of a comprehensive description of the manufacturing process, which could potentially enable the production of substantially different product(s) to that presented here and (2) the uncertainty introduced by the proposal at *quantum satis* which prevents estimating the exposure to the proposed food additive itself and to potential impurities, the Panel could not conclude on the safety of the food additive as proposed and described by the applicant.

1 | INTRODUCTION

The present scientific opinion deals with the safety evaluation of synthesised DNA oligonucleotides, namely SafeTracers®, proposed as a food additive for traceability purposes.

1.1 | Background and Terms of Reference as provided by the European Commission

1.1.1 | Background

The use of food additives is regulated under the European Parliament and Council Regulation (EC) No 1333/2008[1] on food additives. Only food additives that are included in the Union list, in particular in Annex II to that regulation, may be placed on the market and used in food under the conditions of use specified therein. Moreover, food additives shall comply with the specifications as referred to in Article 14 of that Regulation and laid down in Commission Regulation (EU) No 231/2012.[2]

An application has been introduced for the authorisation of the use of synthesised DNA oligonucleotides, made of [redacted] base pairs,[3] as a food additive for traceability purposes.

According to the applicant DNA oligonucleotides, added to foodstuffs during processing, enable traceability by providing a unique code, that can be linked to a database containing a set of information, for example, on harvest date, lot number or packaging location and thus offering benefits for food safety and supply chain management.

1.1.2 | Terms of Reference

The European Commission requests the European Food Safety Authority (EFSA) to provide a scientific opinion on the safety of the proposed use of synthesised DNA oligonucleotides, made of [redacted] base pairs, as a food additive, in

[1]Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives. OJ L 354, 31.12.2008, p. 16.

[2]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.

[3]The Panel noted an inconsistency between the information provided in the dossier and the one reported in the mandate.

accordance with Regulation (EC) No 1331/2008[4] establishing a common authorisation procedure for food additives, food enzymes and food flavourings.

1.2 | Information on existing evaluations and authorisations

There are no existing authorisations or risk assessments by EFSA for synthesised DNA oligonucleotides in the EU.

However, in the EU, there are several authorised food additives in Regulation (EC) No 1333/2008 which mentions the following single nucleotides under the group of 'Ribonucleotides': guanylic acid (E 626); disodium guanylate (E 627); dipotassium guanylate (E 628); calcium guanylate (E 629); inosinic acid (E 630); disodium inosinate (E 631); dipotassium inosinate (E 632); calcium inosinate (E 633); calcium 5′-ribonucleotides (E 634) and disodium 5′-ribonucleotides (E 635).

The authorisations of ribonucleotides (E 626–635) were based on the risk assessment by the Scientific Committee on Foods (SCF) in 1990, when a group acceptable daily intake (ADI) 'not specified' was established.

The re-evaluation of ribonucleotides under Regulation (EU) No 257/2010[5] is ongoing.[6]

The Panel noted that nucleotides listed in Reg (EC) 1333/2008 are monomers or dimers of nucleotides in which the sugar moiety is ribose rather than deoxyribose.

2 | DATA AND METHODOLOGIES

2.1 | Data

The applicant has submitted a dossier to support the safety evaluation of the present application on synthesised DNA oligonucleotides proposed as a food additive for traceability purposes (Documentation provided to EFSA No. 1).

During the risk assessment, additional information (indicated further in the opinion) was requested from the applicant but no additional information was submitted to EFSA within the deadline given.

2.2 | Methodologies

This opinion was formulated following the principles described in the EFSA Guidance of the Scientific Committee on transparency with regard to scientific aspects of risk assessment (EFSA Scientific Committee, 2009) and following the relevant existing Guidance documents from the EFSA Scientific Committee.

The current 'Guidance for submission for food additive evaluation' (EFSA ANS Panel, 2012) has been followed by FAF Panel for evaluating this application. The 'Guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use' (EFSA GMO Panel, 2011) and the 'Scientific Guidance for the submission of dossiers on Food Enzymes' (EFSA CEP Panel, 2021) have been also considered.

3 | ASSESSMENT

3.1 | Technical data

3.1.1 | Identity of the proposed food additive

The proposed food additive, indicated by the applicant with the commercial name SafeTracers®, consists of DNA oligonucleotides that are DNA sequences, made up of [redacted] bases, that are synthesised and purified and are intended to be used for traceability purposes (Documentation provide to EFSA No. 1).

The proposed food additive is described by the applicant as a white to off-white powder that can be used in combination with a variety of authorised carriers (e.g. starches and sugars), depending on the food category in which is to be applied. The DNA oligonucleotides are intended to be added to food during standard food processing procedures, which may include adding them to automated filling lines, incorporating them into washes or using them as part of a product coating, at a concentration of up to 0.001 mg/kg in the final food product. The applicant has also proposed the inclusion of synthesised DNA oligonucleotides as a Group I additive at a specific maximum level of *quantum satis*, which in view of the Panel conflicts with the proposal for maximum permitted levels (MPLs) for specific food categories.

[4]Regulation (EC) No 1331/2008 of the European Parliament and of the Council of 16 December 2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings. OJ L 354, 31.12.2008, p. 1.

[5]Commission Regulation (EU) No 257/2010 of 25 March 2010 setting up a programme for the re-evaluation of approved food additives in accordance with Regulation (EC) No 1333/2008 of the European Parliament and of the Council on food additives. OJ L 80, 26.3.2010, p. 19.

[6]See https://open.efsa.europa.eu; EFSA Question numbers: from EFSA-Q-2011-00691 to EFSA-Q-2011-00700.

According to the applicant, the assessed impurities of the proposed food additive are mostly oligonucleotides of unwanted length, arising from unexpected elongation or truncation of the oligomers, as well as salts. According to the applicant, these do not raise safety concerns and do not affect the toxicological evaluation of the proposed food additive (Documentation provided to EFSA No. 1).

The DNA oligonucleotides are obtained through chemical synthesis and subsequent purification. The manufacturing process complies with ISO 14001:2015 and follows the procedures described in the documents submitted to EFSA (Documentation provided to EFSA No. 1). The applicant has developed a standard operating procedure (SOP) to produce the proposed food additive using synthetic DNA bases.

According to the applicant, the particle size distribution is not relevant for the safety assessment, given the characteristics of DNA oligonucleotides (Documentation provided to EFSA No. 1) and for this reason, no further information was provided. The Panel agreed with the applicant and no additional data were required.

The technical dossier specifies that the sequences of DNA oligonucleotides are derived from non-GMO sources, in accordance with the provisions of the United States National Institutes of Health (NIH) (Documentation provided to EFSA No. 1). The applicant also states that, based on the definition of GMO laid down in EU legislation,[7] the proposed food additive is not to be considered a GMO.

The Panel considered that the information provided on the identity of DNA oligonucleotides was not sufficient, and therefore requested the applicant to provide additional data. The additional information requested was not provided by the applicant and therefore the assessment was concluded solely on the basis of the information available in the application.

3.1.2 | Proposed specifications

The specifications for synthesised DNA oligonucleotides, as proposed by the applicant, are presented in Table 1.

TABLE 1 Specifications for synthesised DNA oligonucleotides as proposed by the applicant (Documentation provided to EFSA No. 1).

Parameter	Specification
Definition	Synthetic deoxyribonucleic acid
Colour Index No	Colourless
Chemical names	Deoxyribonucleic Acid (DNA)
Chemical formula	[redacted]
Molecular weight	[redacted]
Particle size of powder	[redacted]
Assay	Absorbance wave 260/280 OD reading
Spectrophotometry, spectrometry, chromatography, Infra Red, X-ray diffraction	Spectrophotometry
Density/specific gravity	1.7 g/cm^3
pH	Buffer dependent, Neutral pH
Precipitation reaction	Precipitation by ethanol when suspended in solution
Colour reaction	Sybr green chemistry is used for detection of the DNA
Solubility	100% in Water
Specific identification tests and parameters	Quantitative PCR (qPCR) is used to detect, characterise and quantify the DNA using non specific Sybr Green Chemistry

The applicant claimed that synthesised DNA oligonucleotides are manufactured in compliance with the proposed specifications. However, the Panel noted that some of the parameters indicated in the proposed specifications (e.g. chemical formula, molecular weight) are relevant to a single sequence only, while the application covers potentially other nucleotides with different sequences.

The applicant provided certificates of analysis for seven batches of the proposed food additive (Documentation provided to EFSA No. 1). The Panel noted that the parameters analysed were consistent in the tested batches with relative standard deviations (RSDs) of ~ 10% or lower.

According to the information provided by the applicant, the purity of five out of the seven tested batches was consistently [redacted], while for the last (in time/date of production) two batches, data on purity were not provided. The purity of DNA oligonucleotides was expressed as area % and was determined through reversed-phase high-performance liquid chromatography (RP-HPLC) analysis (Documentation provided to EFSA No. 1). A complete description of the method used

[7]Directive 2001/18/EC of the European Parliament and if the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC. OJ L 106, 17.4.2001, p. 1.

to determine the purity of DNA oligonucleotides was not provided. The Panel noted that a purity value has not been included in the proposed specifications.

According to the information provided, the number of bases was consistently below ■. However, the Panel noted that the proposed specifications did not include any requirement for the sequence length.

The average molecular weight of the DNA oligonucleotides, determined by electrospray ionisation–mass spectrometry (ESI–MS), was 20.9 kDa across the seven batches. The Panel noted that the figure given under the 'particle size of powder' seems to refer to molecular weight which has no relevance to the particle size.

No data were submitted by the applicant on the analysis for toxic elements in the proposed food additive or of other potential impurities.

The Panel considered the specifications proposed by the applicant to be inadequate and unclear. Therefore, EFSA requested the applicant to provide additional information, supported by analytical data, on proposed specifications. The additional information requested was not provided by the applicant and therefore the assessment was concluded solely on the basis of the information available in the application.

The Panel considered that the information available does not adequately define and characterise the proposed food additive.

3.1.3 | Manufacturing process

The manufacturing process of the proposed food additive includes a first phase where DNA oligonucleotides are synthesised. Details of the production process were submitted to EFSA (Documentation provided to EFSA No. 1). The process follows a solid phase phosphoramidite synthesis. The synthesis cycle consists of the following steps: deblocking, coupling, capping and oxidation. The resulting crude oligonucleotide is then purified using anion exchange HPLC with sodium-based buffers, obtaining a purified oligonucleotide in its sodium salt form. Subsequently, the product undergoes desalting and evaporation, followed by lyophilisation to produce oligonucleotides in their sodium form as a white powder.

The lyophilised DNA oligonucleotides can undergo further processing by mixing with carriers authorised in the European Union.

The Panel noted that details on the reagents and raw materials used in the manufacturing process, experimental conditions, chemical or physical decontamination methods, were not provided in the dossier. Therefore, EFSA requested the applicant to provide additional information. The additional information requested was not provided by the applicant and therefore the assessment was concluded solely on the basis of the information available in the application.

The Panel considered the description of the manufacturing process to be insufficient as it lacked specific information about the identity of reagents, raw materials and substances entering the process, as well as the experimental conditions applied.

Based on the manufacturing process provided, the Panel could not conclude on the similarity between the manufactured material and natural single-stranded DNA. However, based on the method used for analysis in food (i.e. qPCR – quantitative polymerase chain reaction), the Panel anticipates that the DNA oligonucleotides are linear and are similar to natural single-stranded DNA.

3.1.4 | Method(s) of analysis in food

DNA oligonucleotides can be detected and quantified using qPCR. Method description and validation were provided to EFSA (Documentation provided to EFSA No. 1).

3.1.5 | Stability, reaction and fate in food of the proposed food additive

The applicant indicated that the proposed food additive has an expiration date up to 24 months and it can be stored at room temperature (Documentation provided to EFSA No. 1). However, no data were provided to support this statement.

Tests were conducted on one production batch of synthesised DNA oligonucleotides of ■ bases on different foods (wheat, wheat flour and palm oil) using the food additive combined with a carrier (acacia gum – E414). The food additive was mixed with the food matrix, and its concentration was assessed periodically. DNA oligonucleotides were detected and quantified by qPCR, following the method described in the dossier (Documentation provided to EFSA No. 1). The tests included both normal storage conditions (room temperature) and accelerated storage conditions (32°C) for wheat and wheat flour, while palm oil was tested under accelerated conditions (55°C) only. A paper was provided that outlined some stability tests conducted on waxes for fruit coating.

The data indicated that the proposed food additive remained stable for the whole duration of the tests applied: up to 378 days in wheat and wheat flour and up to 90 days in palm oil under accelerated conditions, corresponding to 1200 days at ambient storage conditions.

The applicant stated that the proposed food additive meets the appropriate shelf-life requirements for each food, allowing it to effectively fulfil its technological function. According to the applicant, potential degradation products resulting

from any degradation of the proposed food additive consist of shorter DNA fragments (Documentation provided to EFSA No. 1).

The Panel considers that the stability tests presented were adequate to assess the stability in low water content matrices. Moreover, the Panel considers that if the original DNA sequence is not of safety concern, then the degradation products would also not be of safety concern.

3.2 | Proposed uses and use levels

The Panel noted that the applicant has submitted proposed maximum use levels of 0.001 mg/kg for a variety of food categories, including whole, broken or flaked grain, flour, fats and oils, fruit and vegetables (Documentation provided to EFSA No. 1). However, the Panel noted that the proposed food categories were not always clearly specified according to Part D of Annex II of Regulation (EC) No 1333/2008, or to the FoodEx2 classification system used by EFSA, as outlined in the applicable Guidance for submission for food additive evaluations (EFSA ANS Panel, 2012).

The applicant has also proposed inclusion of synthesised DNA oligonucleotides as a Group I additive at a specific maximum level of *quantum satis*. It is noted that according to the EFSA ANS Panel Guidance (2012), the Panel was not able to conclude on the safety of the food additive since an exposure assessment from proposed uses at *quantum satis* could not be calculated, for the proposed food additive itself and its potential impurities.

EFSA requested the applicant to indicate the proposed uses as well as the maximum and the typical use levels of the proposed food additive in food using either the food classification system defined in Part D, Annex II of Regulation (EC) No 1333/2008 or the FoodEx2 classification system used by EFSA. The additional information requested was not provided by the applicant and therefore the assessment was concluded solely on the basis of the information available in the application.

3.3 | Exposure data

3.3.1 | Exposure to SafeTracers® from its proposed use as food additive

The applicant provided a dietary exposure assessment based on US average food consumption figures and assuming that 25% of fruits and vegetables consumed (corresponding to 310 g/day) contain the proposed food additive at a concentration of 0.001 mg/kg (Documentation provided to EFSA No. 1). Based on these assumptions, the average daily dietary intake of synthesised DNA oligonucleotides as calculated by the applicant would be of 0.005 μg/kg body weight (bw) per day for an individual weighting 60 kg.

The Panel noted that the estimation provided by the applicant was not based on the Food Additive Intake Model 2.0 (FAIM) tool and it did not cover the exposure at the 95th percentile for the different age groups. Moreover, since the proposed uses and use levels of the proposed food additive were not presented following the indications of the Guidance for submission for food additive evaluations (EFSA ANS Panel, 2012), the Panel was not able to perform the exposure assessment using the FAIM tool.

EFSA requested the applicant to provide a dietary exposure assessment using the dedicated FAIM tool. The additional information requested was not provided by the applicant and therefore the assessment was concluded solely on the basis of the information available in the application.

3.3.2 | Anticipated exposure to potential impurities

The Panel noted that the applicant did not provide information on potential impurities coming from the manufacturing process, thus preventing an evaluation of the anticipated exposure to impurities potentially present in the proposed food additive.

3.4 | Biological and toxicological data

No biological or toxicological data were provided by the applicant for the proposed food additive.

4 | DISCUSSION

The European Commission requests the European Food Safety Authority (EFSA) to provide a scientific opinion on the safety of synthesised DNA oligonucleotides, proposed as a new food additive, in accordance with Regulation (EC) No 1331/2008 establishing a common authorisation procedure for food additives, food enzymes and food flavourings.

The proposed food additive, indicated by the applicant with the commercial name SafeTracers®, consists of purified synthetic DNA sequences of [redacted] bases intended to be used for traceability purposes.

DNA oligonucleotides are obtained through chemical synthesis based on phosphoramidite chemistry, followed by the purification of DNA sequences. The resulting DNA oligonucleotides are lyophilised and can be ultimately combined with carriers. The Panel considered the description of the manufacturing process to be insufficient as it lacked specific information about the identity of reagents, raw materials and substances entering the process, as well as the experimental conditions applied. Additional information was requested from the applicant. However, this was not provided.

Analytical data on some parameters listed in the proposed specifications were provided for seven batches of the proposed food additive, showing that results remained consistent across different batches. Data on purity were provided for five batches out of the seven analysed. The Panel considered the specifications proposed by the applicant to be inadequate and unclear as regards the identity of the proposed food additive. The applicant did not reply to the EFSA additional data request.

The Panel noted that the applicant has submitted proposed maximum use levels of 0.001 mg/kg for a variety of food categories. The applicant has also proposed the inclusion of synthesised DNA oligonucleotides as a Group I additive at a specific maximum level of *quantum satis*. It is noted that, according to the EFSA ANS Panel Guidance (2012), the Panel was not able to conclude on the safety of the food additive since an exposure assessment from proposed uses at *quantum satis* could not be calculated.

Furthermore, the proposed use level up to *quantum satis*, without knowledge of potential impurities, would create a large uncertainty in the risk assessment.

The proposed food categories were not clearly specified according to the criteria set in the Guidance for submission for food additive evaluations (EFSA ANS Panel, 2012). Therefore, the applicant was requested to identify the food categories according to the classification method used in Part D of Annex II of Regulation (EC) No 1333/2008, or following the FoodEx2 classification system, as specified in the applicable Guidance (EFSA ANS Panel, 2012). The Panel did not receive any reply to this request. Therefore, exposure could not be estimated by the Panel.

The Panel noted that the applicant did not provide dietary exposure estimation based on the FAIM tool, and that the exposure assessment proposed by the applicant did not account for the anticipated exposure for average and 95th percentile of the European population for different age groups.

No biological or toxicological data were provided by the applicant for the proposed food additive.

5 | CONCLUSIONS

Considering (1) the absence of an appropriate characterisation of the identity, sufficient specifications and of a comprehensive description of the manufacturing process, which could potentially enable the production of substantially different product(s) to that presented here and (2) the uncertainty introduced by the proposal at *quantum satis* which prevents estimating the exposure to the food additive itself and to potential impurities, the Panel could not conclude on the safety of the food additive as proposed and described by the applicant.

6 | DOCUMENTATION AS PROVIDED TO EFSA

1. Application for authorisation of SafeTracers® as a food additive. Technical Dossier. SafeTraces, Inc. July 2021.

ABBREVIATIONS

ADI	acceptable daily intake
AMP	adenosine 5′-phosphoric acid
ANS Panel	Panel on Food Additives and Nutrient Sources added to Food
bw	body weight
CEP Panel	Panel on Food Contact Materials, Enzymes and Processing Aids
CMP	cytidine 5′-monophosphoric acid
CONTAM Panel	Panel on Contaminants in the Food Chain
ESI–MS	electrospray ionisation–mass spectrometry
FAF Panel	Panel on Food Additives and Flavourings
FAIM	Food Additives Intake Model
FDA	Food and Drug Administration
GMO	genetically modified organisms
GRAS	generally recognised as safe
HPLC	high-performance liquid chromatography
ISO	International Organization for Standardization
MPLs	maximum permitted levels
NIH	United States National Institutes of Health
OD	optical density

qPCR	quantitative polymerase chain reaction
RP-HPLC	reversed-phase high-performance liquid chromatography
RSD	relative standard deviation
SOP	standard operating procedure

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CONFLICT OF INTEREST
If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

REQUESTOR
European Commission

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LEGAL NOTICE
The full opinion will be published in accordance with Article 12(3) of Regulation (EC) No 1331/2008 once the decision on confidentiality will be received from the European Commission.

REFERENCES
EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to Food). (2012). Guidance for submission for food additive evaluations. *EFSA Journal*, *10*(7), 2760. https://doi.org/10.2903/j.efsa.2012.2760

EFSA CEP Panel (EFSA Panel on Food Contact Materials, Enzymes and Processing Aids). (2021). Scientific guidance for the submission of dossiers on food enzymes. *EFSA Journal*, *19*(10), 6851. https://doi.org/10.2903/j.efsa.2021.6851

EFSA GMO Panel (EFSA Panel on Genetically Modified Organism). (2011). Guidance for the risk assessment of genetically modified microorganism and their products intended for food and feed use. *EFSA Journal*, *9*(6), 2103. https://doi.org/10.2903/j.efsa.2011.2

EFSA Scientific Committee. (2009). Guidance of the scientific committee on transparency in the scientific aspects of risk assessments carried out by EFSA. Part 2: General principles. *EFSA Journal*, *7*(7), 1051. https://doi.org/10.2903/j.efsa.2009.1051

SCF (Scientific Committee on Foods). (1990). *Food-science and techniques. Reports of the Scientific Committee for Food (Twenty-fifth series)*. https://aei.pitt.edu/40834/1/25th_food.pdf

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