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Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003

Panax ginseng C.A. Mey. (Ginseng extract CoE 318)

(FAD-2010-0308; CRL/100286)

European Union Reference Laboratory
Feed Additives

Evaluation Report on the Analytical Methods submitted in connection with the Application for Authorisation of a Feed Additive according to Regulation (EC) No 1831/2003

Dossier related to:	**FAD-2010-0308 - CRL/100286**
Name of Feed Additive:	***Panax ginseng C.A. Mey.*** ***(Ginseng extract CoE 318)***
Rapporteur Laboratory:	**European Union Reference Laboratory for Feed Additives (EURL-FA)** **JRC Geel, Belgium**
Phytochemical marker	**Total ginsenosides**
Report prepared by:	**Stefano Bellorini**
Report checked by: Date:	**Zigmas Ezerskis** **19/01/2021**
Report approved by: Date:	**Christoph von Holst** **19/01/2021**

EXECUTIVE SUMMARY

In the current application an authorisation is sought under Article 10(2) for the botanically defined *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* under the category / functional group (2 b) "sensory additives"/"flavouring compounds", according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, the *feed additive* is sought to be used for cats and dogs.

The Applicant indicated *total ginsenosides* (expressed as *ginsenoside* Rg1) as phytochemical marker for *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* specifying a range of its relative mass fraction in the *feed additive* corresponding to 27 - 30 %.

The *feed additive* is intended to be incorporated directly into *feedingstuffs* or through *premixtures*. The Applicant did not propose a minimum or a maximum level of the *feed additive.* However, a maximum content of 20 mg *feed additive* / kg *feedingstuffs* was suggested by the Applicant.

For the determination of the phytochemical marker in the *feed additive* the Applicant submitted a spectrophotometric method described in the journal Deutsche Apotheker-Zeitung, which is equivalent to the procedure described in the "Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition)", where the *total ginsenosides* are determined and expressed as *ginsenoside* Rg1.

The EURL recommends for official control the spectrophotometric method proposed by the Applicant for the quantification of *total ginsenosides* (phytochemical marker) in the *feed additive*.

As the unambiguous determination of the *feed additive* added to *premixtures* and *feedingstuffs* is not achievable experimentally, the EURL cannot evaluate or recommend any method for official control for the determination of *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* in these matrices.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.

KEYWORDS

Panax ginseng C.A. Mey. (Ginseng extract CoE 318), total ginsenosides, sensory additives, flavourings compounds, cats and dogs

1. BACKGROUND

In the current application an authorisation is sought under Article 10(2) (re-evaluation of additives already authorised under the provisions of the Council Directive 70/524/EEC) for the botanically defined *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* under the category / functional group (2 b) "sensory additives"/"flavouring compounds", according to the classification system of Annex I of Regulation (EC) No 1831/2003 [1,2]. Specifically, the *feed additive* is sought to be used for cats and dogs [2,3].

The *feed additive* is a yellow/brown fine powdered extract of ginseng root consisting of a mixture of chemical components naturally present [4,5]. *Ginseng extract* is a natural product and thus the marker component content may vary depending on its geographical origin and/or from harvest to harvest [4]. Nevertheless, the ginseng root extract mainly contains a special group of triterpenoid saponins named *ginsenosides* Rb1, Rb2, Rc, Rd, *Rg1*, Re and Rg2 [6]. The Applicant indicated *total ginsenosides* (expressed as *ginsenoside Rg1*) as phytochemical marker for *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* specifying a range of its relative mass fraction in the *feed additive* corresponding to 27 - 30 % [4,5].

The *feed additive* is intended to be incorporated directly into *feedingstuffs* or through *premixtures*. The Applicant did not propose a minimum or a maximum level of the *feed additive.* However, a maximum content of 20 mg *feed additive* / kg *feedingstuffs* was suggested by the Applicant [7].

2. TERMS OF REFERENCE

In accordance with Article 5 of Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761, on detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the duties and the tasks of the European Union Reference Laboratory concerning applications for authorisations of feed additives, the EURL is requested to submit a full evaluation report to the European Food Safety Authority for each application or group of applications. For this particular dossier, the methods of analysis submitted in connection with *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* and their suitability to be used for official controls in the frame of the authorisation were evaluated.

3. EVALUATION

Description of the analytical methods for the determination of the active substance in the feed additive, premixtures, feedingstuffs and when appropriate water (section 2.6.1 of the dossier - Annex II of Commission Regulation (EC) No 429/2008)

For the determination of the phytochemical marker in the *feed additive* the Applicant submitted a spectrophotometric method where the *total ginsenosides* are determined and

expressed as *ginsenoside Rg1* [8]. According to the Applicant the method is described in the journal Deutsche Apotheker-Zeitung (Dtsch. Apoth. 119, 1843 (1979)) and is equivalent to the procedure described in the "Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition)" [8-10].

According to the method, the extracted *ginsenosides* are treated with a colouring reagent producing a red colour which is measured at 520 nm against a blank solvent mixture. The content of the phytochemical marker is quantified as ginsenoside Rg1 (i) by comparison with a standard solution obtained from a "pure" *ginsenosides* extract prepared as a sample or (ii) by measuring the optical density and applying a specific molecular extinction coefficient of ginsenoside Rg1.

The Applicant declared a routine use of the method for the analysis of *ginsenosides* in the additive [6]. Furthermore, the method was successfully applied in the frame of the supporting studies presented within the current dossier (i.e. batch-to-batch variation) [11].

The EURL recommends for official control the spectrophotometric method described in the journal Deutsche Apotheker-Zeitung which is equivalent to the method described in the "Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition)" for the quantification of *total ginsenosides* (phytochemical marker) in the *feed additive*.

As the unambiguous determination of the *feed additive* added to *premixtures* and *feedingstuffs* is not achievable experimentally, the EURL cannot evaluate or recommend any method for official control for the determination of *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* in these matrices.

Methods of analysis for the determination of the residues of the additive in food (section 2.6.2 of the dossier - Annex II of Commission Regulation (EC) No 429/2008)

Evaluation of corresponding methods of analysis is not relevant for the present application.

Further testing or validation of the methods to be performed through the consortium of National Reference Laboratories as specified by Article 10 (Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761) is not considered necessary.

4. CONCLUSIONS AND RECOMMENDATIONS

In the frame of this authorisation the EURL recommends for official control the spectrophotometric method described in the journal Deutsche Apotheker-Zeitung which is equivalent to the procedure described in the "Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition)" for the quantification of the *total ginsenosides* (phytochemical marker) in the *feed additive.*

As the unambiguous determination of the *feed additive* added to *premixtures* and *feedingstuffs* is not achievable experimentally, the EURL cannot evaluate nor recommend any method for official control for the determination of *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* in these matrices.

Recommended text for the register entry (analytical method)

For the quantification of the phytochemical marker (*total ginsenosides*) in the *feed additive*:

- spectrophotometry at 520 nm expressing the *total* content as *ginsenoside Rg1* equivalent - Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition)

5. DOCUMENTATION AND SAMPLES PROVIDED TO EURL

In accordance with the requirements of Regulation (EC) No 1831/2003, reference samples of *Panax ginseng C.A. Mey. (Ginseng extract CoE 318)* have been sent to the European Union Reference Laboratory for Feed Additives. The dossier has been made available to the EURL by EFSA.

6. REFERENCES

[1] *Application, Reference SANTE_E5_FWD. APPL. 1831-0017-2018

[2] *Application form, Annex 1, Submission No. 1288800277285-1386

[3] *Application, Proposal for Register Entry – Annex A

[4] *Technical dossier, Section II: II.1.3. Qualitative and quantitative composition

[5] *Technical dossier, Section II: II.2.1.1. Chemical substances

[6] *Technical dossier, Section II: ANNEX_II_6_02_Method statement of supplier.pdf

[7] *Technical dossier, Section II: II.5. Condition of use of the additives

[8] *Technical dossier, Section II: II.6. Method of analysis and reference samples

[9] *Technical dossier, Section II: ANNEX_II_6_01_Analytical method Ginseng root.pdf

[10] Farmacopea Ufficiale della Repubblica Italiana / Pharmacopoea Italica (X edition) – monografia Ginseng (1523)

[11] *Technical dossier, Section II: ANNEX_II_1_02_Analysis batches.pdf

*Refers to Dossier no: FAD-2010-0308

7. RAPPORTEUR LABORATORY & NATIONAL REFERENCE LABORATORIES

The Rapporteur Laboratory for this evaluation is the European Union Reference Laboratory for Feed Additives, JRC, Geel, Belgium. This report is in accordance with the opinion of the consortium of National Reference Laboratories as referred to in Article 6(2) of Commission Regulation (EC) No 378/2005, as last amended by Regulation (EU) 2015/1761.

8. ACKNOWLEDGEMENTS

The following National Reference Laboratories contributed to this report:

- Państwowy Instytut Weterynaryjny, Pulawy (PL)
- Laboratori Agroalimentari, Departament d'Agricultura, Ramaderia, PESCA, Alimentació i Medi Natural. Generalitat de Catalunya, Cabrils (ES)
- Instytut Zootechniki — Państwowy Instytut Badawczy, Krajowe Laboratorium Pasz, Lublin (PL)
- Centro di referenza nazionale per la sorveglienza ed il controllo degli alimenti per gli animali (CReAA), Torino (IT)
- Ústřední kontrolní a zkušební ústav zemědělský (ÚKZÚZ), Praha (CZ)
- Wageningen Food Safety Research (WFSR), Wageningen (NL)[1]
- Österreichische Agentur für Gesundheit und Ernährungssicherheit (AGES), Wien (AT)
- Laboratoire de Rennes (SCL L35), Service Commun des Laboratoires DGCCRF et DGDDI, Rennes (FR)

[1] Name and address according to according COMMISSION IMPLEMENTING REGULATION (EU) 2015/1761: RIKILT Wageningen UR, Wageningen (NL).