



JRC.F.5/UV/ZE/AS/Ares

Subject: Amendment of the EURL evaluation report

References:

FAD-2010-0148, FAD-2010-0223, FAD-2010-0231 and FAD-2010-0370 – *potassium iodide*, *calcium iodate anhydrous* (JRC.D.5/FSQ/CvH/PRO/ago/ARES(2012)454413)

Upon a recent publication of the ring-trial validated method EN 17050 [1], dedicated for the determination of *iodine* in animal feedingstuffs, the EURL considered appropriate to evaluate its suitability for official control in the frame of the above-mentioned *feed additive* dossiers.

Meanwhile, the titrimetry methods described in Food Chemical Codex (FCC) monographs for *potassium iodide* [2] and *calcium iodate* [3] and the older version [4] of European Pharmacopeia monograph for *potassium iodide* [5] have been already recommended for official control in the frame of previous EURL evaluation [6] for the determination of *potassium iodide* and *calcium iodate* in the *feed additives*. In the current addendum, the EURL also re-iterates the titration method from the Applicant [7] based on the procedure described in the FCC monograph of *calcium iodate* [3] for the determination of *iodine* content in the coated granulated preparation of *calcium iodate*. Concerning the determination of total *potassium* and total *calcium* in the corresponding *feed additives*, the two ring-trial validated methods, namely EN ISO 6869 [8] and EN 15510 [9] in its older version [10] have been previously recommended for official control [6].

This addendum aims to provide up-to-date EURL recommendations, including all the available analytical methods complying with the highest requirements as stated in Annex II of Regulation (EC) No 429/2008 [11], which would allow Member States' official control laboratories full flexibility regarding the selection of methods of analysis.

According to the EN 17050 method [1], iodine compounds are extracted from the sample with tetramethyl ammonium hydroxide (TMHA) at 90 °C for 3 h. The extract is filtered or centrifuged and further analysed by inductively coupled plasma-mass spectrometry (ICP-MS). The elemental *iodine* is detected by ICP-MS at mass-to-charge (m/z) of 127. The quantification is performed using potassium iodate solutions as calibration standards with tellurium (m/z of 125, 126 or 128) as an internal standard.

The EN 17050 method was ring-trial validated for *iodine* content ranging from 0.7 to 631 mg/kg of different matrices, such as mineral *premixture*, seaweed meal, fish meal, plant

based ingredient and *complete feed*. The following performance characteristics were reported in the frame of the validation studies: a relative standard deviation for *repeatability* (RSD_r) ranging from 2.3 to 14.1 %; and a relative standard deviation for *reproducibility* (RSD_R) ranging from 7.7 to 22.2 %. In addition, in the frame of the previous evaluation [6], the Applicant demonstrated the applicability of another equivalent CEN method, namely EN 15111 dedicated for the determination of *iodine* in foodstuffs [12], to determine *iodine* in *premixtures* and *compound feed* at the levels ranging from 4 to 1000 mg/kg. Furthermore, the limit of quantification (LOQ) of 0.05 mg *iodine* /kg *compound feed* was reported [6].

Based on overall experimental evidence available, the EURL recommends for official control the EN 17050 method based on ICP-MS, for the determination of *iodine* in *premixtures* and *compound feed*.

Recommended text for the registry entry (analytical method) (replacing the previous recommendations)

For the determination of *potassium iodide* in the *feed additive (potassium iodide)*:

- Titrimetry – Food Chemicals Codex “Potassium Iodide” monograph; or
- Titrimetry – European Pharmacopoeia monograph 0186

For the determination of *calcium iodate* in the *feed additive (calcium iodate anhydrous)*:

- Titrimetry – Food Chemicals Codex “Calcium Iodate” monograph

For the determination of *iodine* in the *feed additive (coated granulated calcium iodate anhydrous)*:

- Titrimetry

For the determination of *total potassium* and *total calcium* in the *feed additives*:

- Atomic Absorption Spectrometry, AAS (EN ISO 6869); or
- Inductively Coupled Plasma Atomic Emission Spectrometry, ICP-AES (EN 15510)

For the determination of *iodine* in *premixtures* and *compound feed*:

- Inductively Coupled Plasma-Mass Spectrometry, ICP-MS (EN 17050)

References

- [1] EN 17050:2017 – Animal feeding stuffs: Methods of sampling and analysis - Determination of iodine in animal feed by ICP-MS
- [2] Food Chemical Codex monograph “Potassium Iodide”, FCC 7 (2010), p. 851
- [3] Food Chemical Codex monograph “Calcium Iodate”, FCC 7 (2010), p. 139
- [4] European Pharmacopoeia monograph (Eur. Ph., 01/2008:0186)
- [5] European Pharmacopoeia monograph (Eur. Ph., 01/2023:0186)

- [6] EURL Report – FAD-2010-0148, FAD-2010-0223, FAD-2010-0231 and FAD-2010-0370 – potassium iodide, calcium iodate anhydrous (JRC.D.5/FSQ/CvH/PRO/ago/ARES(2012)454413)
- [7] *Technical dossier, Section II – Annex_II_22
- [8] EN ISO 6869:2000 Animal feeding stuffs – Determination of the contents of calcium, copper, iron, magnesium, manganese, potassium, sodium and zinc – Method using atomic absorption spectrometry
- [9] EN 15510:2017 – Animal feeding stuffs: Methods of sampling and analysis – Determination of calcium, sodium, phosphorus, magnesium, potassium, iron, zinc, copper, manganese, cobalt, molybdenum and lead by ICP-AES
- [10] EN 15510:2007 – Animal feeding stuffs - Determination of calcium, sodium, phosphorus, magnesium, potassium, iron, zinc, copper, manganese, cobalt, molybdenum, arsenic, lead and cadmium by ICP-AES
- [11] 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 authorisations of feed additives, OJ L 133 22.5.2008, p. 1
- [12] EN 15111:2007 – Foodstuffs - Determination of trace elements - Determination of iodine by ICP-MS (inductively coupled plasma-mass spectrometry)

*Refers to FAD-2010-0370

Addendum

- Prepared by Zigmantas Ezerskis
 - Reviewed and approved by María José González de la Huebra and Ursula Vincent (EURL-FA), respectively, Geel, 25/03/2024
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JRC.D.5/FSQ/CvH/PRO/ago/ARES(2012)454413

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

Dossier related to: FAD-2010-0148 – CRL/100162
FAD-2010-0223 – CRL/100310
FAD-2010-0231 – CRL/100204
FAD-2010-0370 – CRL/100267

Feed Additive Name: Potassium iodide
Calcium iodate, anhydrous

Active Substance(s): E 2
Iodine

Rapporteur Laboratory: European Union Reference Laboratory
for Feed Additives (EURL-FA)
Geel, Belgium

Report prepared by: Piotr Robouch (EURL-FA)

Report revised by: Dijana Mitic & Stefano Bellorini
Date: (EURL-FA)
12/04/2012

Report approved by: Christoph von Holst
Date: 13/04/2012

EXECUTIVE SUMMARY

In the current application authorisation is sought under articles 4(1) and 10(2) for *Potassium iodide* and *Calcium iodate anhydrous* under the category/functional group (3b) "nutritional additives"/"compounds of trace elements", according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of the *feed additives* for all categories and species.

According to the Applicants *Potassium iodide* is a white to yellow crystalline powder with a minimum content of 67 % total iodine and 21 % potassium, while *Calcium iodate anhydrous* is a white crystalline powder with a minimum content of 63 % total iodine and 10 % calcium.

The *feed additives* are intended to be incorporated into *premixtures*, *feedingstuffs* and *water* (only for KI). All Applicants proposed the maximum total iodine levels in *feedingstuffs* set in the previous legislation: 4 mg/kg for equine; 5mg/kg for dairy cows and laying hens; 20 mg/kg for fish and 10 mg/kg for other species and categories.

For the characterisation of *Potassium iodide* in the *feed additive*, Applicants (FAD-2010-0148 and FAD-2010-0231) suggested the titrimetric method described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:0186) and in the Food Chemicals Codex (FCC) monographs. For the characterisation of *Calcium iodate* in the *feed additive*, all Applicants suggested the same titrimetric method, based on the iodate conversion to tri-iodide as described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:20504) and in the FCC monographs. Even though no performance characteristics are available, the EURL recommends for official control the titrimetric methods described in the European Pharmacopoeia and the FCC monographs for the characterisation of *Potassium iodide* and *Calcium iodate* in the *feed additives*.

For the quantification of total calcium, and total potassium in the *feed additives*, the EURL identified two ring-trial validated methods - EN ISO 6869:2000, based on atomic absorption spectrometry (AAS) after dilution in hydrochloric acid; and - EN 15510:2007, based on inductively coupled plasma atomic emission spectrometry (ICP-AES) after dilution in hydrochloric acid, for which relative precisions were reported ranging from 4 to 25 %. Based on these performance characteristics, the EURL recommends for official control the two methods (EN ISO 6869:2000 and EN 15510:2007) for the quantification of total calcium and total potassium in the *feed additives*.

For the quantification of total iodine in *premixtures* and *feedingstuffs*, Applicant (FAD-2010-0148) submitted the ring-trial validated CEN method EN 15111:2007 designed for the quantification of iodine in foodstuffs by inductively coupled plasma mass spectrometry (ICP-

MS). The following performance characteristics are reported for a total iodine concentration ranging from 0.2 to 40 mg/kg:

- a relative standard deviation for *repeatability* (RSD_T) ranging from 0.7 to 7.8 %; and
- a relative standard deviation for *reproducibility* (RSD_R) ranging from 6.2 to 19 %.

The Applicant applied the above mentioned CEN method to analyse *premixtures* and two *feedingstuffs* (including a mineral feed) containing *Potassium iodide* or *Calcium iodate* with iodine concentrations ranging from 4 to 1000 mg/kg. The reported recovery rates range from 95 to 105 % while the reported relative precisions (ranging from 2 to 15%) are in good agreement with those of the EN 15111:2007 method. This demonstrates the applicability (cf. extension of scope) of the CEN method to *premixtures* and *feedingstuffs*. Based on the experimental evidence provided, the EURL recommends for official control the EN 15111:2007 method for the quantification of total iodine in *premixtures* and *feedingstuffs*.

Applicant FAD-2010-0231 provided no experimental data for the quantification of total iodine in *water*. Hence, the EURL could not evaluate nor recommend any method for official control to determine total iodine in *water*.

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) is not considered necessary.

KEYWORDS

E2 iodine, Potassium iodide, Calcium iodate anhydrous; nutritional additive; compounds of trace elements; all animal species and categories.

1. BACKGROUND

In the current application authorisation is sought under articles 10(2) (authorisation of an existing product) [1-4] for *Potassium iodide* and *Calcium iodate anhydrous* and 4(1) (new use in water) [3] for *Potassium iodide* under the category/functional group (3b) "nutritional additives"/"compounds of trace elements" [1-4], according to the classification system of Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of the *feed additives* for all categories and species [1-8].

According to the Applicants (FAD-2010-0148; FAD-2010-0223; FAD-2010-0231):

- *Potassium iodide* (KI) is a white to yellow crystalline powder with a minimum content of 67 % total iodine and 21 % potassium [9,11];
- *Calcium iodate anhydrous* (Ca(IO₃)₂) is a white crystalline powder with a minimum content of 63 % total iodine and 10 % calcium [9-11].

The *feed additives* are intended to be incorporated into *premixtures*, *feedingstuffs* [9-12] and *water* (only for KI) [3,11]. All Applicants propose the maximum total iodine levels in *feedingstuffs* set in the previous legislation: 4 mg/kg for equine; 5mg/kg for dairy cows and laying hens; 20 mg/kg (or 30 mg/kg [7]) for fish and 10 mg/kg for other species and categories [5-8].

Furthermore, Applicant (FAD-2010-0370) intends to market a film granulated preparation of *Calcium iodate anhydrous* containing 10 % total iodine [20]. The preparation consists of a defined carrier granulate (containing calcium and magnesium carbonate with corn cobs) to which the active agent is fixed using filming agents such as dispersants and non-ionic surfactants (i.e E423, E484 and E420ii).

2. TERMS OF REFERENCE

In accordance with Article 5 of Regulation (EC) No 378/2005, as last amended by Regulation (EC) No 885/2009, 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 *Potassium iodide* and *Calcium iodate anhydrous*, and their suitability to be used for official controls in the frame of the authorisation, were evaluated.

3. EVALUATION

Qualitative and quantitative composition of impurities in the additive

When required by EU legislation, analytical methods for official control of undesirable substances in the additive (e.g. arsenic, cadmium, lead, dioxins and dioxin like PCBs) are available from the respective European Union Reference Laboratories [13].

Description of the analytical methods for the determination of the active substance in the feed additives, premixtures, feedingstuffs and water

While no analytical method allows the direct determination of *Potassium iodide* and *Calcium iodate anhydrous* in *feed additives, premixtures* and *feedingstuffs*, several methods could be used for the quantification of *total potassium*, *total calcium* and *total iodine* in the matrices of concern.

For the characterisation of *Potassium iodide* in the *feed additive*, Applicants (FAD-2010-0148 and FAD-2010-0231) suggested the titrimetric method described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:0186) [19] and in the Food Chemicals Codex (FCC) [14] monographs. Hydrochloric acid is added to the potassium iodide dissolved in water. The solution is then titrated with potassium iodate until the colour changes from red to yellow. Chloroform is then added and titration is continued till the organic phase is decolorised.

For the characterisation of *Calcium iodate* in the *feed additive*, all the Applicants suggested the same titrimetric method, based on the iodate conversion to tri-iodide [14,17,18,21]. This method is described in the European Pharmacopoeia (Eur.Ph. 6 01/2008:20504) [18] and in the FCC [14] monographs. Calcium iodate is first dissolved and diluted in water and perchloric acid. The solution is then titrated with sodium thiosulfate and a starch indicator solution is added just before the end point is reached.

Even though no performance characteristics are available, the EURL recommends for official control the titrimetric methods described in the FCC monographs and in the European Pharmacopoeia ones for the characterisation of *Potassium iodide* and *Calcium iodate* in the *feed additives*.

For the quantification of *total calcium* and *total potassium* in the *feed additives*, the EURL identified two ring-trial validated methods - EN ISO 6869:2000, based on Atomic Absorption Spectrometry (AAS) after dilution in hydrochloric acid [22], and - EN 15510:2007, based on Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) after dilution in hydrochloric acid [23], for which relative precisions were reported ranging from 4 to 25 %.

Based on these performance characteristics, the EURL recommends for official control the AAS and ICP-AES methods (EN ISO 6869:2000 and EN 15510:2007) for the quantification of *total calcium* and *total potassium* in the *feed additives*.

For the quantification of *total iodine* in *premixtures* and *feedingstuffs*, Applicant (FAD-2010-0148) submitted the ring-trial validated CEN method (EN 15111:2007) [15] designed for the determination of iodine in foodstuffs by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Iodine compounds are extracted from the samples with a strong alkaline reagent (tetramethyl ammonium hydroxide) at elevated temperature (90 °C for 3 hours). After

removing the undissolved components, extracts are analysed by ICP-MS with tellurium as internal standard and using an external calibration.

The following performance characteristics are reported, for a total iodine concentration ranging from 0.2 to 40 mg/kg:

- a relative standard deviation for *repeatability* (RSD_T) ranging from 0.7 to 7.6 %; and
- a relative standard deviation for *reproducibility* (RSD_R) ranging from 6.2 to 19 %.

The Applicant applied the CEN method mentioned above to analyse *premixtures* and two *feedingstuffs* (including a mineral feed) containing *Potassium iodide* or *Calcium iodate* with iodine concentrations ranging from 4 to 1000 mg/kg [16]. The reported recovery rates range from 95 to 105 % while the reported relative precisions (ranging from 2 to 15%) are in good agreement with those of the EN 15111:2007 method. This demonstrates the applicability (cf. extension of scope) of the CEN method to *premixtures* and *feedingstuffs*. Furthermore, the Applicant reported a limit of quantification (LOQ) of 0.05 mg/kg.

Based on these experimental evidence and performance characteristics provided, the EURL recommends for official control the EN 15111:2007 method based on ICP-MS, for the quantification of *total iodine* in *premixtures* and *feedingstuffs*.

Applicant FAD-2010-0231 provided no experimental data for the quantification of *total iodine* in *water*. Hence, the EURL could not evaluate nor recommend any method for official control to determine *total iodine* in *water*.

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) is not considered necessary.

4. CONCLUSIONS AND RECOMMENDATIONS

In the frame of this authorisation the EURL recommends for official control:

- the titration methods described in the Food Chemicals Codex and the European Pharmacopoeia monographs (Eur.Ph. 6 01/2008:0186 and Eur.Ph. 6 01/2008:20504) for the characterisation of *Potassium iodide* and *Calcium iodate* in the *feed additives*;
- the ring trial validated CEN methods EN ISO 6869, based on Atomic Absorption Spectrometry (AAS) or EN 15510, based on Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES), for the quantification of *total calcium* and *total potassium* in the *feed additives*; and

- the ring trial validated CEN method EN 15111:2007, based on Inductively Coupled Plasma Mass Spectrometry (ICP-MS), for the quantification of total iodine in *premixtures* and *feedingstuffs*.

Applicant FAD-2010-0231 provided no experimental data for the quantification of total iodine in *water*. Hence, the EURL could not evaluate nor recommend any method for official control to determine total iodine in *water*.

Recommended text for the register entry (analytical method)

For the determination of *Potassium iodide* in the *feed additive*:

- Titrimetry - Food Chemicals Codex monograph; or
- Titrimetry - European Pharmacopoeia monograph (Eur.Ph. 6 01/2008:0186)

For the determination of *Calcium iodate* in the *feed additive*:

- Titrimetry - Food Chemicals Codex monograph; or
- Titrimetry - European Pharmacopoeia monograph (Eur.Ph. 6 01/2008:20504)

For the quantification of *total calcium* and *total potassium* in the *feed additives*:

- Atomic Absorption Spectrometry, AAS (EN ISO 6869:2000); or
- Inductively Coupled Plasma Atomic Emission Spectrometry, ICP-AES (EN 15510:2007)

For the quantification of *total iodine* in *premixtures* and *feedingstuffs*:

- Inductively Coupled Plasma Mass Spectrometry, ICP-MS (EN 15111:2007)

5. DOCUMENTATION AND SAMPLES PROVIDED TO EURL

In accordance with the requirements of Regulation (EC) No 1831/2003, reference samples of *Potassium iodide* and *Calcium iodate anhydrous* 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] ^a Application, Reference SANCO/D/2 Forw. Appl. 1831/7050-2010
- [2] ^b Application, Reference SANCO/D/2 Forw. Appl. 1831/7088-2010
- [3] ^c Application, Reference SANCO/D/2 Forw. Appl. 1831/10461-2010
- [4] ^d Application, Reference SANCO/D/2 Forw. Appl. 1831/7161-2010
- [5] ^a Application, Proposal for Register Entry – Annex A.
- [6] ^b Application, Proposal for Register Entry – Annex A
- [7] ^c Application, Proposal for Register Entry – Annex A

- [8] ^d Application, Proposal for Register Entry – Annex A
- [9] ^a Technical dossier, Section II – Identity; Conditions of use of the additive
- [10] ^b Technical dossier, Section II – Identity; Conditions of use of the additive
- [11] ^c Technical dossier, Section II – Identity; Conditions of use of the additive
- [12] ^d Technical dossier, Section II – Identity; Conditions of use of the additive
- [13] Commission Regulation (EC) No 776/2006 amending Annex VII to Regulation (EC) No 882/2004 of the European Parliament and of the Council as regards to Community Reference Laboratories
- [14] ^a Technical dossier, Section II – 2-6-1_Analytical method FCC
- [15] EN 15111:2007 - *Foodstuffs – Determination of trace elements – Determination of iodine by ICP-MS (inductively coupled plasma mass spectrometry)*
- [16] ^a Technical dossier, Section II – 2-6-4_UT2A_Validation iodine in feed
- [17] ^b Technical dossier, Section II – Annex_II_15_Analytical method Calcium Iodate
- [18] ^c Technical dossier, Section II – Ref_II_6_01 (Ph.Eur. 6.0 01/2008:20504-Iodine value)
- [19] ^c Technical dossier, Section II – Ref_II_6_02 (Ph.Eur. 6.0 01/2008:0186-KI)
- [20] ^d Technical dossier, Section II – Annex_II_1_2.1.3.a & Annex_II_1_2.1.3.b
- [21] ^d Technical dossier, Section II – Annex_II_22_2.6.1.a & Annex_II_22_2.6.1.b
- [22] EN ISO 6869:2000 - *Animal feedingstuffs - Determination of the contents of calcium, copper, iron, magnesium, manganese, potassium, sodium and zinc - Method using atomic absorption spectrometry*
- [23] EN 15510:2007 – *Animal feedingstuffs – Determination of calcium, sodium, phosphorus, magnesium, potassium, iron, zinc, copper, manganese, cobalt, molybdenum, arsenic, lead and cadmium by ICP-AES*
- ^a Refers to Dossier No. FAD-2010-0148
- ^b Refers to Dossier No. FAD-2010-0223
- ^c Refers to Dossier No. FAD-2010-0231
- ^d Refers to Dossier No. FAD-2010-0370

7. RAPPORTEUR LABORATORY & NATIONAL REFERENCE LABORATORIES

The Rapporteur Laboratory for this evaluation was European Union Reference Laboratory for Feed Additives, IRMM, 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 (EC) No 885/2009.

8. ACKNOWLEDGEMENTS

The following National Reference Laboratories contributed to this report:

- Plantedirektoratet, Laboratorium for Foder og Gødning, Lyngby (DK)
- Instytut Zootechniki w Krakowie, Krajowe Laboratorium Pasz, Lublin (PL)
- Centro di referenza nazionale per la sorveglianza ed il controllo degli alimenti per gli animali (CReAA), Torino (IT)
- Państwowy Instytut Weterynaryjny, Puławy (PL)
- Thüringer Landesanstalt für Landwirtschaft (TLL), Abteilung Untersuchungswesen. Jena (DE)
- Laboratoire de Rennes, SCL L35, Service Commun des Laboratoires, Rennes (FR)
- Ústřední kontrolní a zkušební ústav zemědělský (ÚKZÚZ), Praha (CZ)