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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**

**Methyl Cellulose**  
*(FAD-2016-0063; CRL/100323)*

**Hydroxypropyl Methyl Cellulose**  
*FAD-2016-0066; CRL/100323)*



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Dossier related to: **FAD-2016-0063 - CRL/100323**  
**FAD-2016-0066 - CRL/100323**

Name of Feed Additive: ***Methyl Cellulose***  
***Hydroxypropyl Methyl Cellulose***

Active Agent (s): -

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

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Date: **18/07/2019**

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Date: **18/07/2019**

## EXECUTIVE SUMMARY

In the current application authorisation is sought under Article 10 for *methyl cellulose* and *hydroxypropyl methyl cellulose* under the category / functional group 1 (c,d,e,f) "technological additives" / "emulsifiers, stabilisers, thickeners and gelling agents" 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 animal species.

*Methyl cellulose* and *hydroxypropyl methyl cellulose* are white to off-white powders. The Applicant states that the specific purity criteria set in Commission Regulation (EU) 231/2012 for the use of *methyl cellulose* and *hydroxypropyl methyl cellulose* as food additives are also applicable when using them as *feed additives*.

The *feed additives* are intended to be included into *feedingstuffs* through *premixtures* with no minimum or maximum dose indicated by the Applicant.

For the identification/characterisation of the *feed additives*, the Applicant referred to Commission Regulation (EU) 231/2012, where the criteria and specific qualitative and quantitative tests/methods are indicated for checking the compliance with the criteria specified for *methyl cellulose* and *hydroxypropyl methyl cellulose*.

For the identity check of *methyl cellulose* tests for solubility and pH have to be performed. In addition, the methods for purity include determination of the loss on drying and sulfated ash. Finally, the determination of the content of methoxy and hydroxyethoxy groups is specified by the above mentioned Regulation. For the identity check of *hydroxypropyl methyl cellulose* the tests for solubility and pH are outlined. The methods for purity include measurements of the loss on drying, sulfated ash and the content of propylene chlorohydrins. Finally, the determination of the content of methoxy and hydroxypropoxy groups by gas chromatography is required according to the above mentioned Regulation. All of the above mentioned tests/methods are described in the FAO JECFA '*methyl cellulose*' and '*hydroxypropylmethyl cellulose*' monographs, the '*volume 4*' of the FAO JECFA combined compendium for food additives specifications [9] and the European Pharmacopoeia monographs (01/2016:0345 [10] and 01/2016:0348 [11]).

The EURL recommends for the identification/characterisation of the *feed additives* the above mentioned methods described in the FAO JECFA '*Methyl cellulose*' and '*Hydroxypropyl methyl cellulose*' monographs, the '*volume 4*' of FAO JECFA combined compendium for food additives specifications and the European Pharmacopoeia monographs (01/2016:0345 and 01/2016:0348).

As the accurate quantification of *methyl cellulose* and *hydroxypropyl methyl cellulose* added to *premixtures* or *feedingstuffs* is not achievable experimentally the EURL cannot evaluate

nor recommend any method for official control to quantify *methyl cellulose* and *hydroxypropyl methyl cellulose* in *premixtures* or *feedingstuffs*.

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

*Methyl cellulose, hydroxypropyl methyl cellulose*, technological additives, emulsifiers, stabilisers, thickeners, gelling agents, all animal species

## 1. BACKGROUND

In the current application authorisation is sought under Article 10 (re-authorisation of an existing feed additives) for *methyl cellulose* and *hydroxypropyl methyl cellulose* under the category / functional group 1 (c,d,e,f) "technological additives" / "emulsifiers, stabilisers, thickeners and gelling agents" according to the classification system of Annex I of Regulation (EC) No 1831/2003 [1]. Specifically, authorisation is sought for the use of the *feed additives* for all animal species [2,3].

*Methyl cellulose* and *hydroxypropyl methyl cellulose* are white to off-white powders [4,5]. The Applicant states [4,5] that the specific purity criteria set in the Commission Regulation (EU) 231/2012 [6] for the use of *methyl cellulose* and *hydroxypropyl methyl cellulose* as food additives are also applicable when used them as *feed additives*.

The *feed additives* are intended to be included into *feedingstuffs* through *premixtures* with no minimum or maximum dose indicated by the Applicant [2,3,4,5].

## 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 *methyl cellulose* and *hydroxypropyl methyl cellulose* 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)***

An evaluation of corresponding methods of analysis is not relevant for the current application.

***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)***

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

***Identification/Characterisation of the feed additive (section 2.6.3 of the dossier - Annex II of Commission Regulation (EC) No 429/2008)***

For the identification/characterisation of the *feed additives*, the Applicant referred to Commission Regulation (EU) 231/2012 [6], where the criteria and specific qualitative and quantitative tests/methods are indicated for checking the compliance with the criteria specified for *methyl cellulose* and *hydroxypropyl methyl cellulose*.

For the identity check of *methyl cellulose* tests for solubility and pH have to be performed. In addition, the methods for purity include determination of the loss on drying and sulfated ash. Finally, the determination of the content of methoxy groups is specified by the above mentioned Regulation [6].

For the identity check of *hydroxypropyl methyl cellulose* the tests for solubility and pH are outlined. The methods for purity include measurements of the loss on drying, sulfated ash and the content of propylene chlorohydrins. Finally, the determination of the content of methoxy and hydroxypropoxy groups by gas chromatography is required according to the above mentioned Regulation [6].

These tests/methods are described in the FAO JECFA '*methyl cellulose*' [7] and '*hydroxypropylmethyl cellulose*' [8] monographs, the '*volume 4*' of the FAO JECFA combined compendium for food additives specifications [9] and the European Pharmacopeia monographs (01/2016:0345 [10] and 01/2016:0348 [11]).

In the frame of the identification/characterisation of *methyl cellulose* when performing a solubility test, water, ethanol, chloroform and glacial acetic acid are used [6,7,9].

For pH measurements the 1 % colloidal solution is used [6,7].

For the determination of the loss on drying, an accurate amount of sample (1 to 2 g) is placed in an oven at 105 °C and kept for 3 h. After cooling down to room temperature the sample is weighed again, and the difference of the mass is defined as loss on drying [6,7,9].

For the determination of sulfated ash, a diluted sulfuric acid is added to the sample (1 g). The sample is then gently heated until most of it is volatilised. The insoluble matter is ignited at

800 ± 25 °C for 15 min at least. The residue is then cooled down and weighed to determine the amount of sulfated ash [6,7,9].

For the determination of the content of methoxy groups, the sample (65 mg) is mixed with adipic acid, an internal standard (a solution of *ortho*-xylene in octane) and hydroiodic acid. The reaction mixture is heated at 130 °C for 60 min under continuous stirring. After cooling down, the upper layer is taken for further analysis by gas chromatography coupled to flame ionisation or to thermal conductivity detection. The determination of the content of methoxy groups is performed by calibration with *iso*-propyl iodide as a standard substance [10].

In the frame of the identification/characterisation of *hydroxypropyl methyl cellulose* water and ethanol are used when performing a solubility test, while pH measurements are performed with 1 % of colloidal solution of *hydroxypropyl methyl cellulose* [6,8,9].

For the determination of the loss on drying and sulfated ash, the procedures described above are used [6,8,9].

For the determination of propylene chlorohydrins, the sample (1 g) is mixed with the internal standard (*ortho*-xylene-d<sub>10</sub>) solution in diethyl ether, sonicated for 10 min and centrifuged. The layer of diethyl ether is used for further analysis by gas chromatography-mass spectrometry (GC-MS). A single ion monitoring mode (SIM) and an internal standard calibration is used for the quantification of the analyte [8].

For the determination of the content of methoxy and hydroxypropoxy groups in *hydroxypropyl methyl cellulose*, a similar procedure as the one described above for the determination of the content of methoxy groups in *methyl cellulose* is used [11].

The EURL recommends for the identification/characterisation of the *feed additives* the above mentioned methods described in the FAO JECFA '*Methyl cellulose*' and '*Hydroxypropyl methyl cellulose*' monographs, the '*volume 4*' of FAO JECFA combined compendium for food additives specifications and the European Pharmacopoeia monographs (01/2016:0345 and 01/2016:0348).

As the accurate quantification of *methyl cellulose* and *hydroxypropyl methyl cellulose* added to *premixtures* or *feedingstuffs* is not achievable experimentally the EURL cannot evaluate nor recommend any method for official control to quantify *methyl cellulose* and *hydroxypropyl methyl cellulose* in *premixtures* or *feedingstuffs*.

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 the identification/characterisation of the *feed additives* the above mentioned methods described in the FAO JECFA '*Methyl cellulose*' and '*Hydroxypropyl methyl cellulose*' monographs, the '*volume 4*' of FAO JECFA combined compendium for food additives specifications and the European Pharmacopoeia monographs (01/2016:0345 and 01/2016:0348).

As the accurate quantification of *methyl cellulose* and *hydroxypropyl methyl cellulose* added to *premixtures* or *feedingstuffs* is not achievable experimentally the EURL cannot evaluate nor recommend any method for official control to quantify *methyl cellulose* and *hydroxypropyl methyl cellulose* in *premixtures* or *feedingstuffs*.

##### ***Recommended text for the register entry (analytical method)***

For the identification/characterisation of *methyl cellulose* in the *feed additive*:

- The FAO JECFA '*Methyl cellulose*' monograph, the '*volume 4*' of FAO JECFA combined compendium for food additives specifications and the European Pharmacopoeia monograph 01/2016:0345

For the identification/characterisation of *hydroxypropyl methyl cellulose* in the *feed additive*:

- The FAO JECFA '*Hydroxypropyl methyl cellulose*' monograph, the '*volume 4*' of FAO JECFA combined compendium for food additives specifications and the European Pharmacopoeia monograph 01/2016:0348

#### 5. DOCUMENTATION AND SAMPLES PROVIDED TO EURL

In accordance with the requirements of Regulation (EC) No 1831/2003, reference samples of *methyl cellulose* and *hydroxypropyl methyl cellulose* 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. 1831-0018-2019 & Annex I – submission number 1288338704054-1270
- [2] \*Application, proposal for Register entry – Annex A
- [3] +Application, proposal for Register entry – Annex A
- [4] \*Technical dossier, Section II: Identify, characterisation and conditions of use of the additive; methods of analysis



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- [5] +Technical dossier, Section II: Identify, characterisation and conditions of use of the additive; methods of analysis
- [6] 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
- [7] FAO JECFA Combined Compendium of Food Additive Specifications, '*Methyl cellulose*', Monograph No. 1 (2006)  
[http://www.fao.org/fileadmin/user\\_upload/jecfa\\_additives/docs/Monograph1/Additive-277.pdf](http://www.fao.org/fileadmin/user_upload/jecfa_additives/docs/Monograph1/Additive-277.pdf)  
(last visited on 03/06/2019)
- [8] FAO JECFA Combined Compendium of Food Additive Specifications, '*Hydroxypropyl methyl cellulose*', Monograph No. 11 (2011)  
[http://www.fao.org/fileadmin/user\\_upload/jecfa\\_additives/docs/monograph11/additive-233-m11.pdf](http://www.fao.org/fileadmin/user_upload/jecfa_additives/docs/monograph11/additive-233-m11.pdf)  
(last visited on 03/06/2019)
- [9] FAO JECFA Combined Compendium for Food Additive Specifications - Analytical methods, test procedures and laboratory solutions used by and referenced in the food additive specifications, Vol. 4  
<http://www.fao.org/docrep/pdf/009/a0691e/a0691e.pdf> (last visited on 28/05/2019)
- [10] European Pharmacopoeia monograph, 01/2016:0345
- [11] European Pharmacopoeia monograph, 01/2016:0348
- \*Refers to Dossier no: FAD-2016-0063
- +Refers to Dossier no: FAD-2016-0066

## 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)
- Ústřední kontrolní a zkušební ústav zemědělský (ÚKZÚZ), Praha (CZ)
- Laboratori Agroalimentari, Departament d'Agricultura, Ramaderia, PESCA, Alimentació i Medi Natural. Generalitat de Catalunya, Cabrils (ES)
- Österreichische Agentur für Gesundheit und Ernährungssicherheit (AGES), Wien (AT)
- Staatliche Betriebsgesellschaft für Umwelt und Landwirtschaft. Geschäftsbereich 6 — Labore Landwirtschaft, Nossen (DE)