Feed additives

Annual Report 2009
of the National Reference Laboratory

J.J.M. Driessen, W.M.J. Beek, J. de Jong

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Summary

This report of the National Reference Laboratory (NRL) for feed additives describes the activities employed in 2009. The main tasks of the NRL are: giving assistance to the CRL on their request and advice and support the competent authority, the Dutch Ministry of Economic Affairs, Agriculture and Innovation - Department of Food, Animal Health and Welfare and Consumer Policy (EL&I-VDC).

NRL activities on request of the CRL

In 2009 the NRL commented on three initial evaluation reports prepared by the rapporteur laboratory. This concerned one histomonostat, one zootechnical feed additive and a zinc source additive.
In June 2009 an employee of RIKILT participated and actively contributed to a workshop in discussions regarding the implementation of the verification-concept as laid down in Reg. (EC) No 429 (2008).
A second employee of RIKILT attended to the training course "Training Course for NRL Rapporteurs 'Coccidiostats and Histomonostats'" organized May 2009 by JRC-IRMM regarding the evaluation on "the suitability of analytical methods determining the content of active substance in product per se, in premixtures and in feedingstuffs for official controls".
A questionnaire to all the NRLs in order to allow the CRL to check and update the information in their database was completed and sent back. The questionnaire related to several NRL activities, among others about contributions to international projects or international committees in the field of feed additives.

Advices and support

The NRL gave 16 advices to the competent authority regarding temporary use exemptions of feed additives in The Netherlands. The requests concerned among others enzymes, probiotics and amino acids.

Several times advices were given by E-mail on issues related to the registration or use of feed additives. The majority of the advices concerned information regarding the status of a feed additive in relation with the analytical composition, description of the production process and/or EU regulations. Among others advice was given about the need to get a temporary use exemption for the addition of mycotoxin binders to feed in experimental trials.

Furthermore RIKILT was asked by the competent authority to give their opinion about the establishment of a new functional group of feed additives in Regulation (EC) 1831/2003 for reduction of contamination by mycotoxins. Among others the question has been raised if, after the addition of these mycotoxin binders, it is still possible to detect the mycotoxins in feed materials and compound feeds. If the binding is very strong, this could lead to a low recovery when normal extraction procedures are applied. Work has been initiated by the CRL to investigate this issue. After a

favourable opinion of the Standing Committee on the Food Chain and Animal Health the new functional group has been established through Commission Regulation (EC) No 386/2009.

Other activities

This year the set up of a decision tree was continued to find in a harmonized and in a repeatable way the answer to the question: what is the status/functionality of a new substance.
Unfortunately it was concluded that it is very difficult to realize a universal decision tree. Because this difficulty is recognized by the European partners new guidelines are under development enabling the Member States to find answers case-by-case on the issue of doubtful or double listed products. The Netherlands will comply with these guidelines aiming to offer contributions case-by-case and therefore the development of a national decision tree will be abandoned.

Contents

1 Introduction

Within the EU livestock production occupies a very important place in the agriculture. Satisfactory results depend to a large extent on the use of safe and good-quality feedingstuffs. In order to protect human health, animal health and the environment, feed additives should undergo a safety assessment through a Community procedure before being placed on the market, used or processed within the Community. The applicant (producer of the additive) has to submit a dossier containing all relevant information regarding safety of the product. The details of the application procedure are described in Regulation (EC) 1831/2003. The European Food Safety Authority, established by Regulation (EC) no. 178/2002 carries out scientific assessment of feed additives (including premixes).

Within the EU, the Community Reference Laboratory (CRL) and a consortium of National Reference Laboratories (NRLs) play an important role in the evaluation and authorisation process to place a feed additive on the market. The Joint Research Centre (JRC in Geel, Belgium) is the CRL. Within the Netherlands RIKILT and RIVM are the NRLs for feed additives (Commission Regulation (EC) No 378/2005) .
In EU regulation 1831/2003 the tasks and duties of the CRL are defined. It is also described in this regulation that for all tasks and duties of the CRL the NRLs may be asked by the CRL for assistance.
The CRL is responsible for:
The reception, preparation, storage and maintenance of the reference samples.
The testing and evaluation or validation of the method for detection.
Evaluating the data provided by the applicant for authorization to place the feed additive on the market, for the purpose of testing and evaluation or validation of the method for detection
Submitting full evaluation reports to the Authority.
Next to these tasks the CRL shall play a role in dispute settlements between Member States concerning the analytical results of testing additives for use in animal nutrition.

Commission regulation (EC) 378/2005 describes in more details the activities and organization of CRL and NRLs. During an application evaluation process it is possible that an NRL is requested to act as the rapporteur of the application (the rapporteur laboratory) or to participate in the consortium. The rapporteur laboratory has to :
Draft an initial evaluation report concerning the data submitted in each application and submitting it for comments to the other laboratories.
Compile the comments received from the other laboratories and prepare a revised evaluation report.
Submit the revised evaluation report to the CRL. The CRL submits the full evaluation report to the Authority.

For doing research on the use of a feed additive that has not yet been registered as such or for a specific application, the applicant needs to have a 'temporary use exemption' for the feed additive. These permissions are obtained by the Dutch 'Bureau Diergeneesmiddelen' under supervision of the Dutch Ministry of Economic Affairs, Agriculture and Innovation - Department of Food, Animal and Consumer (EL&I-VDC). EL&I-VDC is the competent authority in The Netherlands for authorisation of feed additives. RIKILT advices the Dutch government regarding the temporary use exemption of specific feed additives, more specific about issues related to the application of feed additives in feed,

e.g. cross-contamination, stability and homogeneity. Furthermore on request RIKILT as a NRL advices EL&I regarding other issues concerning feed additives.

This report describes the activities employed in 2009 by RIKILT regarding the functions as described above viz:
a. as the NRL for feed additives,
b. advices given regarding temporary use exemptions,
c. other advices and support of EL&I.

Starting in 2008, last year the set up of a decision tree was continued to find in a harmonized and in a repeatable way the answer to the question: What is the status/functionality of a feed additive. It was concluded that it is very difficult to realize a universal decision tree. Because this difficulty is recognized by the European partners new guidelines are going to be developed enabling the Member States to find answers case-by-case on the issue of doubtful or double listed products. It was decided to that The Netherlands will comply with these guidelines aiming to offer contributions case-by-case. In doing so the development of a national decision tree will be abandoned.
This report also presents the activities performed by the NRL to keep up expertise on the analysis of feed additives like participation in proficiency tests and presenting (posters, abstracts, publications) analytical research.

2 NRL activities

2.1 Dossier evaluation

In 2009 the NRL commented on three initial evaluation reports prepared by the rapporteur laboratory. The advices were described in evaluation reports and included the following additives:

HistoBloc 80 Microgranulate: authorisation as feed additive under the category 'histomonostats' is sought; evaluation of HPLC-methods for the determination of the active substance paromomycin sulphate in the feed additive and in feedingstuffs respectively.
Formi LHS: authorisation is sought to use Formi LHS as zootechnical feedadditive for sow; evaluation of an iodometric titration method for the determination of the active substance potassium diformate in the feed additive and of an ion chromatography method for the determination of the active substance potassium diformate in feedingstuffs.
Biokey Zn: authorisation is sought to use Biokey Zn as a source of zinc (zinc chelate of amino acids) for all animal species; evaluation of an atomic absorption spectrometry method for the determination of Zinc in the feed additive, premixtures and feedingstuffs. However this (accepted) method can not distinguish between Zinc from Zn chelate of amino acids and inorganic Zn. Because the applicant claims a better bio-availability of Zn chelate of amino acids hydrate RIKILT advised to ask the company to deliver a method that can distinguish between inorganic and organic forms of Zinc.

2.2 CRL workshop

In 2009 an employee of RIKILT participated to the following workshop:
CRL-Workshop 11-12 June 2009, JRC-IRMM in Geel, Belgium.
J. de Jong actively contributed to this workshop in discussions regarding the implementation of the verification-concept as laid down in Regulation (EC) No 429/2008, which means that the performance of methods of analysis, developed and validated in one laboratory must be checked by a second accredited and independent laboratory and that the results of this check must be included in the dossier. The needs of the EFSA - FEEDAP panel for advanced analytical methods have been presented by prof. Gropp, member of the FEEDAP-panel. In relation to this presentation the question was raised why, until now, there is no obligation for applicants to include methods of analysis in the dossier that give evidence that active substances are present in specific forms, e.g. as metal chelates. New guidance documents for applicants and NRL's have been discussed. New methods of analysis for flavourings and vitamins A & E have been presented. Developments within CEN-Technical Committee 327 “Animal Feedingstuffs” regarding European harmonization of methods of analysis for feed additives have been presented by J. de Jong, chairman of this committee.

2.3 Training for NRL rapporteurs

In 2009 an employee of RIKILT attended to the following training course:
* Training Course for NRL Rapporteurs "Coccidiostats and Histomonostats" 06-08 May 2009, JRC-IRMM in Geel, Belgium.
W. Beek participated to this course regarding the evaluation on "the suitability of analytical methods determining the content of active substance in product per se, in premixtures and in feedingstuffs for official controls".
The course consisted of two exercises, one using a previously evaluated coccidiostat dossier (Cycostat 66G) and another dossier that was not evaluated before (Avatec). As a result of the second case, the Avatec dossier, an evaluation report has been provided to the CRL-FA.

2.4 Questionnaire to NRLs

In 2009 the CRL has sent a questionnaire to all the NRLs in order to allow the CRL to check/update the information in their database. The questionnaire related to NRL participation to proficiency testing schemes and method validation collaborative trials, NRL contribution to international projects or international committees in the field of feed additives, a description/list of NRL methods of analysis (i.e. analytes, matrix, instrumental techniques) and a list of international or national standard documents applied (i.e. ISO, CEN, AOAC). The questionnaire was completed and sent back to the CRL.

3 Advices on temporary use exemptions

In 2009 a number of 16 national requests for permission to use substances -which are not authorised at Community level- as additives for experiments for scientific purposes (according to Regulation (EC) No 1831/2003, article 3.2, handled by EL&I-VDC / Bureau Diergeneesmiddelen) have been assessed. The requests concerned among others enzymes, probiotics and amino acids.

4 Communications and advices

One of the tasks of the NRL is to communicate with the Competent Authority on issues regarding the control and use of feed additives. The communication and advice activities employed by the NRL in 2009 are described below.

4.1 Advices on product registration

In The Netherlands the Advising Committee for Registration of Feed Additives ('Adviescommissie Product Registratie' (APR)) advices the competent authority about issues related to the registration or use of feed additives. In 2009 RIKILT was asked several times by E-mail to give advice.
The majority of the advices concerns information regarding the status of the product in relation with the analytical compositions, description of the production processes and intended use. Among others, advice was given about the need to get a temporary use exemption for the addition of mycotoxin binders to feed in experimental trials.
Advice on the establishment of a new functional group of feed additives for reduction of contamination by mycotoxins
RIKILT was asked by the competent authority to give their opinion about the establishment of a new functional group of feed additives in Regulation (EC) 1831/2003 for reduction of contamination by mycotoxins. Among others the question has been raised if, after the addition of these mycotoxin binders, it is still possible to detect the mycotoxins in feed materials and compound feeds. If the binding is very strong, this could lead to a low recovery when normal extraction procedures are applied. Work has been initiated by the CRL to investigate this issue. After a favourable opinion of the Standing Committee on the Food Chain and Animal Health the new functional group has been established through Regulation (EC) No 386/2009.

4.2 Advice on maximum levels for carry-over of coccidiostats

RIKILT was asked in 2008 by the competent authority to give their opinion about draft SANCO proposals to amend Annex I to Directive 2002/32/EC as regards maximum levels of unavoidable carry-over of coccidiostats or histomonostats in non-target feed. Maximum levels of 1 % and 3 % carry-over in non-target feeds have been established in 2009 through Directive 2009/8/EC. There is a need for further method development and international harmonization (CEN) of methods of analysis that allow the detection of these low carry-over levels. Initiatives have been taken in 2009 within the CEN network to include this work in a possible future mandate from the European Commission for CEN/TC 327.

5 Other activities

The set up of a decision tree was continued to find in a harmonized and in a repeatable way the answer to the question: What is the status/functionality of a feed additive. It was concluded that it is very difficult to realize a universal decision tree. Because this difficulty is recognized by the European partners new guidelines are going to be developed enabling the Member States to find answers case-by-case on the issue of doubtful or double listed products. With respect to these new guidelines it can be referred to two meetings of the Standing Committee on the Food Chain and Animal Health, section Animal Nutrition:
- July 2009, agenda item 3,
http://ec.europa.eu/food/committees/regulatory/scfcah/animalnutrition/sum_2324062009_en.pdf
- November 2009, agenda item 3.1,
http://ec.europa.eu/food/committees/regulatory/scfcah/animalnutrition/sum_2324112009_en.pdf
It was decided that The Netherlands will comply with these guidelines aiming to offer contributions case-by-case. In doing so the development of a national decision tree will be abandoned.

6 Participation in collaborative studies

Due to the scope of the NRL task assigned, RIKILT participated in two collaborative studies organized by CEN/TC 327 “Animal Feedingstuffs” Working group 3 (Feed Additives and Drugs) as part of harmonization of methods of analysis.

1. Animal feeding stuffs - Determination of Decoquinate by HPLC-fluorescence
2. Animal feedingstuffs - Determination of semduramicin content - Liquid chromatographic method using mass spectrometry detection

The results are currently evaluated and will be discussed this year in the working group.

7 Publications, presentations and posters

7.1 Publications

A.A.M. Stolker and T. Zuidema, Annual Report: Feed Additives; Annual Report 2008 of the Dutch National Reference Laboratory, RIKILT-report 2009.009

7.2 Presentations

The following presentations are related to but have not been produced within the NRL project:
J. de Jong, S. Weigel and M.W.F. Nielen; CONffIDENCE in Food and Feed: a new European Research Project; Keynote lecture, Rapid Methods Europe 2009; 26 – 28 January 2009, Noordwijkerhout, The Netherlands
J. de Jong, S. Weigel and M.W.F. Nielen; Rapid methods for feed safety ; the CONffIDENCE project; 3rd International FEED SAFETY conference - Methods and Challenges, 6 – 7 October 2009, Wageningen, The Netherlands
J. de Jong, S. Weigel and M. Nielen; Rapid Methods for Food Quality and Safety Control; Invited Lecture, 4th International Symposium on Recent Advances in Food Analysis; 4-6 November 2009, Prague (CZ)

7.3 Posters

The following posters are related to but have not been produced within the NRL project:
T. de Rijk et al; The influence of mycotoxin binders on the performance and validity of an LC-MSMS multi-mycotoxin method; Symposium World-wide mycotoxin reduction in food and feed chains, Tulln, Austria, 9-11 September 2009

Posters presented at the 3rd International FEED SAFETY conference - Methods and Challenges, Wageningen (NL), 6 – 7 October 2009. Page numbers refer to the Book of Abstracts.
Theo de Rijk, Ed Boers, Paul Zomer, Hans Mol, Jörg Stroka; The influence of mycotoxin binders on the performance and validity of an LC-MSMS multi-mycotoxin method; page 68
T. Zuidema, E. Oosterink, W. Schutte, L. Stolker and J. de Jong; Development of a method for the analysis of coccidiostats in animal feed according to Commission Directive 2009/8/EC; page 62

8 Plan for NRL activities 2010

The participation of the NRL in the dossier evaluation procedure will be continued for the coming year. The NRL will also advice the competent authority regarding all kind of upcoming questions and temporary use exemptions.
Furthermore the yearly CRL meeting will be attended.

9 References

Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003.On additives for use in animal nutrition, L 268 page 29-43.

Commission Regulation (EC) No 378/2005 of 4 March 2005 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 tasks of the Community Reference Laboratory concerning applications for authorisations of feed additives.

Commission Directive 2009/8/EC of 10 February 2009 amending Annex I to Directive 2002/32/EC of the European Parliament and of the Council as regards maximum levels of unavoidable carry-over of coccidiostats or histomonostats in nontarget feed, L 40 page 19-25.

Commission Regulation (EC) No 386/2009 of 12 May 2009 amending Regulation (EC) No 1831/2003 of the European Parliament and of the Council as regards the establishment of a new functional group of feed additives.