SCIENTIFIC OPINION

Scientific Opinion on the safety and efficacy of Urea for ruminants[1]

EFSA Panel on Additives and Products or Substances used in Animal Feed (FEEDAP)[2,3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Urea supplementation to feed for ruminants provides non-protein nitrogen for microbial protein synthesis in the rumen and thus in part replaces other dietary protein sources. Urea supplementation of feed for ruminants at doses up to 1 % of complete feed DM (corresponding to 0.3 g/kg bw/day) is considered safe when given to animals with a well adapted ruminal microbiota and fed diets rich in easily digestible carbohydrates. Based on the metabolic fate of urea in ruminants, the use of urea in ruminant nutrition does not raise any concern for consumers' safety. Urea is considered to be non irritant to skin and eyes and its topical use suggests that it is not a dermal sensitiser. The risk of exposure by inhalation would be low. The substitution of protein by urea in well balanced feed for ruminants would not result in an increased environmental nitrogen load. Urea is an effective source of non-protein nitrogen substituting for dietary protein in ruminants.

KEY WORDS

Nutritional additives, urea, non-protein nitrogen, ruminant nutrition, safety, efficacy

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SUMMARY

Following a request from European Commission, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) was asked to deliver a scientific opinion on the use of urea in ruminants from the beginning of the rumination. Urea supplementation to feed for ruminants provides nitrogen for microbial protein synthesis in the rumen and thus in part replaces other dietary protein sources.

Urea supplementation of feed for ruminants at doses up to 1 % of complete feed DM (corresponding to 0.3 g/kg bw/day) is considered safe when given to animals with a well adapted ruminal microbiota and fed diets rich in easily digestible carbohydrates.

Based on the metabolic fate of urea in ruminants, the use of urea in ruminant nutrition does not raise any concern for consumers' safety.

Urea is considered to be non irritant to skin and eyes and its topical use suggests that it is not a dermal sensitiser. The risk of exposure by inhalation would be low.

The substitution of protein by urea in well balanced feed for ruminants would not result in an increased environmental nitrogen load.

Urea is an effective source of non-protein nitrogen substituting for dietary protein in ruminants.

The Panel included a recommendation for a more precise definition of the term "the beginning of rumination".

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BACKGROUND

Regulation (EC) No 1831/2003[4] establishes the rules governing the Community authorisation of additives for use in animal nutrition. In particular, Article 10(2) of that Regulation specifies that for existing products within the meaning of Article 10(1), an application shall be submitted in accordance with Article 7, at the latest one year before the expiry date of the authorisation given pursuant to Directive 70/524/EEC for additives with a limited authorisation period, and within a maximum of seven years after the entry into force of this Regulation for additives authorised without time limit or pursuant to Directive 82/471/EEC.

The European Commission received a request from the company UREAC/EEIG – Urea Authorisation Consortium[5] for authorisation and re-evaluation of the product Urea as a feed additive for ruminants (category: nutritional additives; functional group d: urea and its derivates) under the conditions mentioned in Table 1.

According to Article 7(1) of Regulation (EC) No 1831/2003, the Commission forwarded the application to the European Food Safety Authority (EFSA) as an application under Article 10(2)/(7) (re-evaluation of an authorised feed additive). EFSA received directly from the applicant the technical dossier in support of this application.[6] According to Article 8 of that Regulation, EFSA, after verifying the particulars and documents submitted by the applicant, shall undertake an assessment in order to determine whether the feed additive complies with the conditions laid down in Article 5. The particulars and documents in support of the application were considered valid by EFSA as of 18 November 2010.

In EU, urea is currently authorised as feed additive for ruminants from the beginning of the rumination without limitations on its maximum content in feedingstuffs (Dir. 84/433/EEC). The applicant asks for the re-evaluation of the use of urea as additive to feed for ruminants from the beginning of the rumination.

TERMS OF REFERENCE

According to Article 8 of Regulation (EC) No 1831/2003, EFSA shall determine whether the feed additive complies with the conditions laid down in Article 5. EFSA shall deliver an opinion on the safety for the target animal(s), consumer, user and the environment and the efficacy of the product Urea for ruminants when used under the conditions described in Table 1.

[4] Regulation (EC) No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L 268, 18.10.2003, p. 29.
[5] UREAC/ EEIG Amino Acids Authorisation Consortium – Avenue Louise 120, Box 13 – 1010 – Brussels, Belgium; Companies: Borealis Agrolinz Melamine GmbH, GPN, Aliphos, Yara France, SKW Stickstoffwerke Piesteritz GmbH.
[6] EFSA Dossier reference: FAD-2010-0113.

Table 1: Description and conditions of use of the additive as proposed by the applicant

Additive	Urea technically pure (see attached Appendix for more details on the urea forms detailed in this application)			
Registration number/EC No/No (if appropriate)	3d.xx			
Category(-ies) of additive	3. Nutritional additives			
Functional group(s) of additive	d. Urea and its derivatives			
Description				
Composition, description	Chemical formula	Purity criteria (if appropriate)	Method of analysis (if appropriate)	
Urea content: minimum 97% Nitrogen content: 46%	**(NH2)2CO**	**Complies with EU law on undesirable substances**	**Commission Regulation (EC) n° 152/2009**	
Trade name (if appropriate)	Not appropriate			
Name of the holder of authorisation (if appropriate)	UREAC EEIG			
Conditions of use				
Species or category of animal	Maximum Age	Minimum content	Maximum content	Withdrawal period (if appropriate)
		mg or Units of activity or CFU/kg of complete feedingstuffs (select what applicable)		
Only for all ruminants (large, small) (from the beginning of rumination)	-	-	-	Not appropriate
Other provisions and additional requirements for the labelling				
Specific conditions or restrictions for use (if appropriate)	Do not exceed the dose of 30g urea(solid)/100 kg bw/day adult ruminant.			
Specific conditions or restrictions for handling (if appropriate)	Not appropriate			
Post-market monitoring (if appropriate)	Not appropriate (existing feed additive)			
Specific conditions for use in complementary feedingstuffs (if appropriate)	Not appropriate			
Maximum Residue Limit (MRL) (if appropriate)				
Marker residue	Species or category of animal	Target tissue(s) or food products	Maximum content in tissues	
Not appropriate	Not appropriate	Not appropriate	Not appropriate	

ASSESSMENT

This opinion is based in part on data provided by a consortium of five companies involved in the production/distribution of urea. It should be recognised that this data covers only a fraction of existing additives containing urea. The composition of the additives is not subject of the application.

The application contains data on three urea solid products.[7]

1. Introduction

Urea as a source of non-protein nitrogen (NPN) has been used worldwide in ruminant nutrition for decades. In the EU, urea is authorised as feed additive for ruminants from the beginning of rumination (Dir. 84/433/EEC).

Urea supplementation to feed for ruminants provides nitrogen for microbial protein synthesis in the rumen and thus in part replaces other dietary protein sources. After oral intake, urea is almost immediately hydrolysed in the rumen to ammonia and CO_2 by the bacterial enzyme urease. Ammonia from urea or from degraded dietary protein is used by the ruminal microbiota for synthesis of microbial proteins which are subsequently digested in the intestine. Approximately 70 % of crude protein entering the small intestine is of microbial origin.

Urea has a GRAS status (Generally Recognised as Safe) in the USA. Urea is also widely used as a fertilizer (EC 2003/2003), as a de-icing agent, in food (E 927b), as a detergent, in cosmetics, and also as a biocide (EC 1451/2007).

2. Characterisation

The active substance is identical to the additive.

Urea, EINECS No. 200-315-5, CAS number: 57-13-6 (synonyms: carbamide or carbonyldiamide, IUPAC name: diaminomethanone, CAS number 58069-82-2), has the molecular weight of 60.06 g/mol, its chemical formula is $(NH_2)_2CO$. The molecular structure is shown in Figure 1.

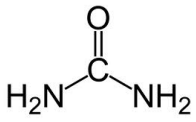

Figure 1. Molecular structure of urea

According to the specification, the additive contains > 97 % urea. Based on analysis of at least five batches from each producer (a total of 44 batches), the mean analysed urea content was 99.3 % (range: 98.6 to 99.8 %).[8] The analysed mean biuret content ($(CONH_2)_2$-NH), a condensation product of urea, was 0.7 % (range: 0.4 to 1.0 %). Water content ranged from 0.1 to 0.7 %.

Four companies provided analyses of heavy metals and As from 20 batches,[9] of dioxins (11 batches) and the sum of dioxins plus dioxin like PCBs (six batches).[10] All values for heavy metals and As were below the LOQ (Pb < 0.3, Hg < 0.03, Cd < 0.3 and As < 0.3 mg/kg).[11] The dioxins were ≤ 0.08 ng WHO-PCCD/F-TEQ/kg, the sum of dioxins and dioxin-like PCBs was ≤ 0.1 ng WHO-PCCD/F-PCB-

[7] During the assessment the applicant decided to withdraw the application for the liquid form and for its use in water for drinking.
[8] Technical dossier/Section II/Annex II.2.1.7 to II.2.1.10.
[9] Technical dossier/Section II/Annex II.2.1.12 to II.2.1.15.
[10] Technical dossier/Section II/Annex II.2.1.17 to II.2.1.20.
[11] Technical dossier/Supplementary information February 2012/Annex I.1.

TEQ/kg. There are no specified limits for urea set by Regulation EC No 2002/32, however the analysed values are low.

The additive is produced in three forms: spheric prills,[12] micro-prills and powder. Particle size analysis done by sieving of 25 batches (at least three per each product) showed that predominant diameter of prills was in the range from 1.5 to 2.5 mm with only 1.7 % particles < 1 mm, for microprills from 0.2 to 1.3 mm with no particles < 0.15 mm whereas in powder form the majority of particles was < 1 mm with only 0.5 % particles being <50 µm.[13] Consequently no data on dusting potential of the products are required.

The bulk density ranged from 710-785 kg/m^3, specific weight was 1,320 kg/m^3, water solubility 1080 g/L at 20° C and melting point 133° C.

Urea is manufactured by chemical synthesis.[14] The first step in which ammonium carbamate is obtained by reaction of ammonia and carbon dioxide (material safety data sheets [MSDS] for all raw materials provided) is followed by dehydration leading to urea. The side reactions leading to formation of biuret, isocyanic acid and urea decomposition to ammonia and CO_2 depend on temperature and overall conditions. The various industrial processess differ only with regard to separation, and decomposition of unconverted ammoniun carbamate as well as recovery of NH_3 and CO_2. The obtained ca 70 % urea solution is several times diluted with demineralised water and again concentrated in order to remove residual ammonia, followed by prilling procedure in evaporator.

2.1. Stability and homogeneity

The stability of urea was studied on a total of 14 batches (at least three batches from each producer) for one to 23 months (10 batches ≥ 12 months) stored in original closed packages or plastic bottles under ambient conditions.[15,16] The full recovery of urea stored for 12 to 18 months supports the proposal of the applicant for shelf life of 18 months. The water content monitored in six batches of additive remained constant (0.1 to 0.4 %).

Due to its relatively high supplementation rates, urea is not incorporated in premixtures. Stability of urea was studied in both mash and pelleted feed for four products at a supplementation level of 3 %. One was added to a complementary feed based on soybean meal, rapeseed and soya hulls, and the other three products to a complete feed for ruminants based mainly soya hulls, palm kernel expeller, citrus pulp, dried distilled wheat grains and canola and containing already 0.03 % urea. Initial values in the complementary feed were 81 and 90 % and after three months 92 and 87 % of the intended value for the mash and the pelleted complementary feed, respectively.[17] Similar stability data were obtained for the other three products incorporated in mash (110 % of the initial value) and pelleted complete feed for ruminants (97 % of the initial value).[18]

The ability of urea to be homogeneously distributed in mash and pelleted feeds for ruminants was investigated for four products using the same feedingstuffs as described above. A micro-tracer was used to determine the mixing accuracy of the equipment. In the complementary mash (n = 20) and pelleted (n = 15) feed, homogeneity of one product (presumably a powder) was given by CVs of 8.2 % and 5.3 %, respectively.[19] In the studies with the complete feed, a urea powder showed CVs of 11.5

[12] A prill or Fert Tower is a small aggregate of a material, most often a dry sphere, formed from a melted liquid. The material to be prilled must be a solid at room temperature and a low viscosity liquid when melted. Prills are formed by allowing drops of the melted prill substance to congeal or freeze in mid-air after being dripped from the top of a tall prilling tower. Fertilizers (ammonium nitrate, urea, NPK fertilizer) and some detergent powders are commonly manufactured as prills.
[13] Technical dossier/Section II/Annex II.2.2.6 to 2.2.9.
[14] Technical dossier/Section II.2.3.
[15] Technical dossier/Section II/Annex II.2.4.1 and II.2.4.2.
[16] Technical dossier/Supplementary information February 2012/Annex II.3.3 and II.3.4.
[17] Technical dossier/Section II/Annex II.2.4.4.
[18] Technical dossier/Supplementary information February 2012/Annex III.5.
[19] Technical dossier/Section II/Annex II.2.4.4.

and 1.9 % in mash and pelleted diet, respectively. The prilled products showed CVs of 30 and 23 % in the mash diet, but only 3.3 and 5.4 % in the pelleted diet.[20]

2.2. Conditions of use of the additive

Urea is intended to be used in feedingstuffs for ruminants with functional rumen. Due to potential toxic effects of urea added to feed, the applicant recommends that in adapted ruminants, the following urea concentrations in feed should not be exceeded: (i) 30 g urea/100 kg bw/day, (ii) 30 % of total nitrogen in the daily ration from urea-N, (iii) 1 % urea in DM of complete feedingstuffs, and (iv) 3 % urea in complementary feed.[21]

2.3. Evaluation of the analytical methods by the European Union Reference Laboratory (EURL)

EFSA has verified the EURL report as it relates to the methods used for the control of the urea in animal feed. The Executive Summary of the EURL report can be found in the Appendix.

3. Safety

3.1. Safety for the target species

Urea as a final metabolite of protein catabolism is a physiological compound and is well tolerated even when given parenterally. However, in ruminants with a functional microbiota in forestomachs, urea after oral intake is almost immediately hydrolysed into ammonia (NH_3) and carbon dioxide (CO_2) by bacterial enzyme urease. High ammonia levels in blood are known to have neurotoxic effects.

Ammonia absorbed into blood is detoxified by synthesis of endogenous urea in liver. A significant portion of endogenous urea recycles back into the digestive tract via the rumen wall, saliva, bile, and pancreatic juice where undergoes again the hydrolysis into ammonia and CO_2 (Varady *et al*., 1979). The surplus of endogenous urea is excreted by urine.

Ammonia from urea or degraded protein is used by ruminal microbiota for the synthesis of microbial protein and any surplus is absorbed to portal blood. The excessive amount of ingested urea by ruminants leads to a huge production of ammonia exceeding the ability of ruminal microbiota to utilize it in protein synthesis as well as its detoxification by liver in urea cycle synthesis. Under conditions of normal rumen pH value (6.5-6.7) almost all rumen ammonia occurs in its ionic ammonium form (NH_4^+) which is well soluble in water but insoluble in lipids. During urea overdosage, in addition to very high ammonia level in rumen, the situation is further worsen by increasing of ruminal pH above 7 and under these conditions the ion ammonium (NH_4^+) is converted into ammonia (NH_3) which is highly soluble in lipids. Large amounts of NH_3 can then rapidly cross the cellular membrane and be absorbed into the blood stream, thus leading to hyperammonemia (Chalupa, 1968; Hogan, 1975).

Normal ammonia levels in peripheral blood are below 5 mg/L. In ruminants the clinical signs of neurotoxicity due to urea overdose appear when the systemic blood ammonia level reaches 10 mg/L. Early signs of ammonia toxicity are muscle tremors (especially of the face and the ears), exophtalmia, abdominal pain, increased salivation, polyuria, and bruxism, more serious intoxications may lead to tetany. Ammonia level in peripheral blood higher than 50 mg/L may prove lethal (Davidovich *et al*., 1977).

Dietary exposure of unadapted ruminants to urea doses of 0.3-0.5 g/kg bw usually results in adverse effects due to inability of ruminal microbiota to utilize the large amounts of ammonia produced and doses of 1.0-1.5 g urea/kg bw may be lethal. In general, ruminants require days or weeks for a total

[20] Technical dossier/Supplementary information February 2012/Annex III.5.
[21] Technical dossier/Section II.2.5.

adaptation before rumen microbiota can utilize the gradually increasing dietary amounts of ammonia originating from rapid rumen urea hydrolysis. This ability of ruminal microbiota is lost within a few days when urea as a source of non-protein nitrogen (NPN) is removed from diet. It has been well established that ruminants fed high energy diets rich in easily digestible carbohydrates show a considerably better tolerance to urea than those fed diets with only high fibre content (NAS, 1976).

Conclusions on the safety for target species

Urea supplementation of feed for ruminants at doses up to 1 % of complete feed DM (corresponding to 0.3 g/kg bw/day) is considered safe when given to animals with a well adapted ruminal microbiota and fed diets rich in easily digestible carbohydrates.

3.2. Safety for the consumer

Urea is the final metabolite of protein catabolism in mammals and is evenly distributed in the body water with the exception of kidneys, where higher concentrations occur. Due its metabolic fate, the substitution of dietary protein by urea in feeding of ruminants would not lead to a significant increase of urea and/or ammonia in edible tissues and products.

Based on the metabolic fate of urea in ruminants, the use of urea in ruminant nutrition does not raise any concern for consumers' safety.

3.3. Safety for the users/workers

Since none of the products contained > 1 % of particles < 50 µm, the inhalation hazard is considered to be minimal and a study of respiratory toxicity is not required.

A study conducted in rabbits according to OECD guideline 404 found urea to be non-irritant to skin.[22] A study of penetration enhancers in mice included urea and showed no irritancy of a 10 % w/v solution in water.[23] The study included histological examination of the skin to which the product had been applied.

A brief report of an eye irritation study in rabbits conducted according to OECD guideline 405 showed irritant effects at 24 hours which, although quite mild, extended to the conjunctiva, cornea and iris, which had cleared by eight days after treatment.[24] It is non irritant.

3.4. Safety for the environment

The substitution of protein by urea in well balanced feed for ruminants would not result in an increased environmental nitrogen load.

4. Efficacy

Urea is an effective source of non-protein nitrogen (NPN) substituting for dietary protein in ruminants.

5. Post-market monitoring

The FEEDAP Panel considers that there is no need for specific requirements for a post-market monitoring plan other than those established in the Feed Hygiene Regulation[25] and Good Manufacturing Practice.

[22] Technical dossier/Supplementary information February 2012.
[23] Technical dossier/Supplementary information February 2012.
[24] Technical dossier/Supplementary information February 2012.
[25] Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene. OJ L 35, 8.2.2005, p. 1.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Urea supplementation of feed for ruminants at doses up to 1 % of complete feed DM (corresponding to 0.3 g/kg bw/day) is considered safe when given to animals with a well adapted ruminal microbiota and fed diets rich in easily digestible carbohydrates.

Based on the metabolic fate of urea in ruminants, the use of urea in ruminant nutrition does not raise any concern for consumers' safety.

Urea is considered to be non irritant to skin and eyes and its topical use suggests that it is not a dermal sensitiser. The risk of exposure by inhalation would be low.

The substitution of protein by urea in well balanced feed for ruminants would not result in an increased environmental nitrogen load.

Urea is an effective source of non-protein nitrogen substituting for dietary protein in ruminants.

RECOMMENDATION

The current authorisation of urea specifies the species or categories of animals as: "ruminants from the beginning of rumination." Since rumination starts considerably earlier than the full functionality of the rumen is developed, the FEEDAP Panel proposes to modify the text above as follows: "ruminants with a fully functional rumen."

DOCUMENTATION PROVIDED TO EFSA

1. Dossier FAD-2010-0113. October 2010. Submitted by UREAC EEIG – Urea Authorisation Consortium.
2. Dossier FAD-2010-0113. Supplementary information. January 2012. Submitted by Erawan Consulting.
3. Evaluation report of the Community Reference Laboratory for Feed Additives on the methods(s) of analysis for urea.
4. Comments from Member States received through the ScienceNet.

REFERENCES

Chalupa W, 1968. Problems in feeding urea to ruminants. Journal of Animal Science, 27, 207-219.

Davidovich A, Bartley EE, Bechtle RM and Dayton AD, 1977. Ammonia toxicity in cattle. III. Absorption of ammonia gas from the rumen and passage of urea and ammonia from the rumen to the duodenum. Journal of Animal Science, 45, 551-558.

Hogan JP, 1975. Quantitative aspects of nitrogen utilization in ruminants. Journal of Dairy Science, 58, 1164-1177.

Varady J, Tashenov KT, Boda K., Fejes J, Kosta K, 1979. Endogenous urea secretion into the sheep gastrointestinal tract. Physiologia Bohemoslovaca, 28, 551-559.

NAS, 1976. Urea and other nonprotein nitrogen sources in animal nutrition. National Academy of Sciences, Washington, D.C.

APPENDIX

Executive Summary of the Evaluation Report of the European Union Reference Laboratory for Feed Additives on the Method(s) of Analysis for Urea technically pure.[26]

In the current application authorisation is sought for *urea technically pure* under Articles 4(1) (new use of a feed additive in water) and 10(2) (re-evaluation of the already authorised feed additive – Council directive 70/524/EEC), category of 'nutritional additives' functional group 3(d), 'urea and its derivatives' according to Annex I of Regulation (EC) No 1831/2003. Specifically, authorisation is sought for the use of the *feed additive* for ruminants. According to the Applicant *urea technically pure* is available as a solid and a liquid formulation. The *feed additive* is intended to be mixed to *premixtures, feedingstuffs* and *water* at maximum doses of 30 g solid *urea* or 70 g liquid *urea* per 100 kg body weight of adult ruminant per day.

For the determination of *urea* in the *feed additive* the Applicant proposed the ISO 22241-2 method. However, two ring-trial validated Community methods exist for the determination of the *urea* in fertilizers: - the titrimetric method for the determination of the total nitrogen content in the *urea* and - the spectrophotometric method for the determination of the nitrogen content in *biuret*. The content of *urea* is then derived from the total nitrogen in *urea* corrected for the nitrogen content in *biuret*. The performance characteristics of the Community methods are:

(i) For the determination of total nitrogen in the *feed additive*:
- a standard deviation for *repeatability* (RSD_r) of 0.3 %; and

- a standard deviation for *reproducibility* (RSD_R) of 0.6 %.

(ii) For the determination of the nitrogen content in *biuret*:

- RSD_r of 1.7% and

- RSD_R of 8.9%.

Based on the performance characteristics presented, the EURL recommends for official control the two ring-trial validated titrimetric and spectrophotometric Community methods, to determine *urea* in the *feed additive*.

For the determination of the *feed additive* in *feedingstuffs* and *water*, the Applicant suggests the spectrophotometric official Community method specifically designed for the determination of *urea* in *feedingstuffs*.

For the determination of *urea* in *premixtures*, the Applicant did not submit any analytical methods. The EURL suggests diluting the *premixtures* samples with ground cereal feed and apply the abovementioned Community method for the determination of *urea* in *feedingstuffs*.

Based on these considerations the EURL recommends for official control, the spectrophotometric Community method, to determine *urea* in *premixtures, feedingstuffs* and *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.

During the assessment of the dossier the applicant decided to withdraw the application for the

[26] The complete report is available online: http://irmm.jrc.ec.europa.eu/SiteCollectionDocuments/FinRep-FAD-2010-0113.pdf

liquid form and for its use in water for drinking.