EMINEX® – PROBABILITY OF TRANSFER TO MILK OR MEAT

Scientific Report from DCE – Danish Centre for Environment and Energy no. 710 2026

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Erkin Gözdereliler
Patrik Fauser
Mohamed Fathi Abdallah
Pedro Carvalho
Hans Sanderson
Carsten Suhr Jacobsen

Aarhus University, Department of Environmental Science

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Data sheet

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Authors: Erkin Gözdereliler, Patrik Fauser, Mohamed Fathi Abdallah, Pedro Carvalho, Hans Sanderson & Carsten Suhr Jacobsen
Institution: Aarhus University, Department of Environmental Science

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Abstract: This report assesses the probability of residue transfer to milk or meat following the use of Eminex® in dairy slurry management. Eminex® is a calcium cyanamide-based slurry additive, which can be used to reduce methane formation during slurry storage and improve manure handling. The assessment considers product formulation, degradation pathways, environmental fate, food-chain transfer, mammalian toxicity, analytical methods, and relevant scientific and regulatory evidence. Overall, the available evidence supports the conclusion that Eminex® does not pose a credible residue risk in milk or meat when used correctly, provided that good agricultural practice and appropriate handling measures are maintained. Further investigations are recommended to strengthen understanding of low-level exposure scenarios, transformation processes, and ecological interactions under dairy production conditions.

Keywords: Eminex®; calcium cyanamide; dairy slurry management; greenhouse gas emissions; milk and meat residues; food-chain transfer; environmental fate; food safety.

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Preface

This report was prepared at the request of Arla and Royal FrieslandCampina. It provides a scientific advisory assessment of the probability that the use of Eminex® in dairy slurry management may lead to residues in milk or meat.

Eminex® is a calcium cyanamide-based slurry additive intended to reduce methane formation during slurry storage and improve manure handling under farm conditions. Its direct application to slurry, followed by the potential agricultural use of treated slurry, makes it relevant to assess product composition, degradation behaviour, environmental fate, and possible transfer through the dairy production chain.

The assessment is based on available scientific literature, regulatory information, manufacturer-provided product data, environmental fate considerations, food-chain transfer evidence, mammalian toxicity data, and analytical detection methods. Where relevant, the assessment distinguishes between the absence of available residue measurements and cases in which measurements have been performed without detection. This distinction is important for evaluating the strength and limitations of the available evidence.

The report is intended to support informed decision-making regarding the potential use of Eminex® under recommended agricultural conditions. It presents a structured evaluation of the available evidence, identifies remaining knowledge gaps, and outlines areas where further investigation may strengthen understanding of low-level exposure scenarios, transformation processes, and ecological interactions in dairy production systems.

1 Background

Eminex® is a commercial slurry additive produced by the German company Alzchem. The active component in Eminex® is calcium cyanamide ($CaCN_2$). The product delays the degradation of volatile fatty acids (VFA) and their conversion to methane. Through this mode of action, the use of Eminex® can reduce greenhouse gas emissions from slurry storage and thereby help to lower the carbon footprint of livestock farming.

Eminex® is approved for use throughout Europe. It is promoted by Alzchem and its distributors in several countries as a product that supports climate-friendly livestock farming. Eminex® main active ingredient is $CaCN_2$, a compound that has been used for many years as a nitrogen fertilizer (e.g. product known as Perlka®).

Eminex® is already used by some farmers to control foaming in slurry storage. Its use improves the utilization of available storage capacity and prevents foaming on the barn floors, which can otherwise create handling and hygiene issues. The additive is applied directly to slurry and is compatible with standard manure management practices on dairy farms.

Royal Friesland Campina (RFC) and Arla Foods (Arla) are currently considering whether to encourage their member farmers to use Eminex®.

One of the known degradation products of Eminex® is dicyandiamide (DCD), a compound known to act as a nitrification inhibitor. DCD has previously been detected in milk in New Zealand following its use on grasslands used for dairy feed (non-peer-reviewed information).

It is therefore important to determine whether the large-scale use of Eminex® on dairy farms could lead to the presence of $CaCN_2$, DCD, or other degradation products in milk or meat, and whether such use poses any risks to animals, humans, the environment, or nature.

2 Assessment of EMINEX® Composition, Formulation and Batch Variability

The specific components included in Eminex®, along with their respective percentages in the commercial formulation, are presented in Table 1. These data are provided by the Alzchem Trostberg GmbH, the producer of Eminex®, and reflect the typical formulation of the product as marketed for agricultural use. The composition may include both the active substance, calcium cyanamide ($CaCN_2$, CAS 156-62-7), and various by-products, formulation aids or stabilizing agents that are formed or added during manufacturing to ensure product stability, safe handling, and consistent performance across batches. These include calcium dihydroxide (CAS 1305-62-0), graphite (CAS 7782-42-5) and melamine (CAS 108-78-1). According to the manufacturer, melamine is not intentionally added but is formed as a by-product during the granulation process, and measures are currently being assessed and implemented to reduce melamine levels in the commercial product to well below 0.1%. This information is based on manufacturer communication and has not been independently verified within the scope of this assessment.

Variations between different batches are expected within the composition ranges provided for the product, as shown in Table 1, and include differences in the concentration of known compounds such as dicyandiamide (DCD, CAS 461-58-5). These variations depend on the specific chemical components, and the data is further used as a representation of the chemical profile of Eminex® as currently applied in agricultural settings.

Table 1. Detailed composition of EMINEX®.

Component	Chemical ID	% in Eminex®
Calcium cyanamide, $CaCN_2$	CAS 156-62-7 SMILES: C(#N)N=[Ca]	> 40[1]
Calcium hydroxide	CAS 1305-62-0 SMILES: [OH-].[OH-].[Ca+2]	15 – 20[1]
Graphite	CAS 7782-42-5 SMILES: C	≥ 7 - ≤ 10[1]
Melamine	CAS 108-78-1 SMILES: C1(=NC(=NC(=N1)N)N)N	≤ 0.15[1]
Dicyandiamide, aka DCD, cyanoguanidine, $(H_2N)_2CNCN$, *TP2 in this report*	CAS 461-58-5 SMILES: C(#N)N=C(N)N	< 2[2] (1.9 – 2.3)[3]

[1] based on the Safety Data Sheet from Alzchem group.

[2] based on document 2024-08_Arla_DCD in Gewässern_Entwurf.pdf.

[3] based on document AZ Eminex®_2025_10_10_BK_Sha.pdf.

- Cyanamide calcium is also known as cyanamide calcium salt, Kalkstickstoff, Lime Nitrogen, Nitrolime, or calcium carbamide.
- Dicyandiamide is also known as dicyanodiamide, cyanoguanidine or 2-Cyanoguanidine.

3 Predicted Degradation Pathways, Transformation Products, and Environmental Persistence of EMINEX®

The expected degradation products of Eminex® throughout its environmental pathway, from manure storage and application to soil and within the rumen, are described per each individual chemical component of the commercial product (Table 1).

Calcium cyanamide ($CaCN_2$) undergoes well-documented reactions and transformation processes in the environment, as summarized in Figure 1 and Table 2. $CaCN_2$ is known to form a total of eight transformation products (labeled TP1 to TP8 below), several of which are naturally occurring compounds involved in the nitrogen cycle (e.g. urea, ammonium carbonate, nitrate) and contribute to the environmental nitrogen balance. DCD, besides being present in the Eminex® formulation, is also a known transformation product of $CaCN_2$, can further transform into urea (TP3), ammonium carbonate (TP7), and nitrate (TP8) and is also known to degrade into melamine, guanidine salts, and poly(triazine imide).

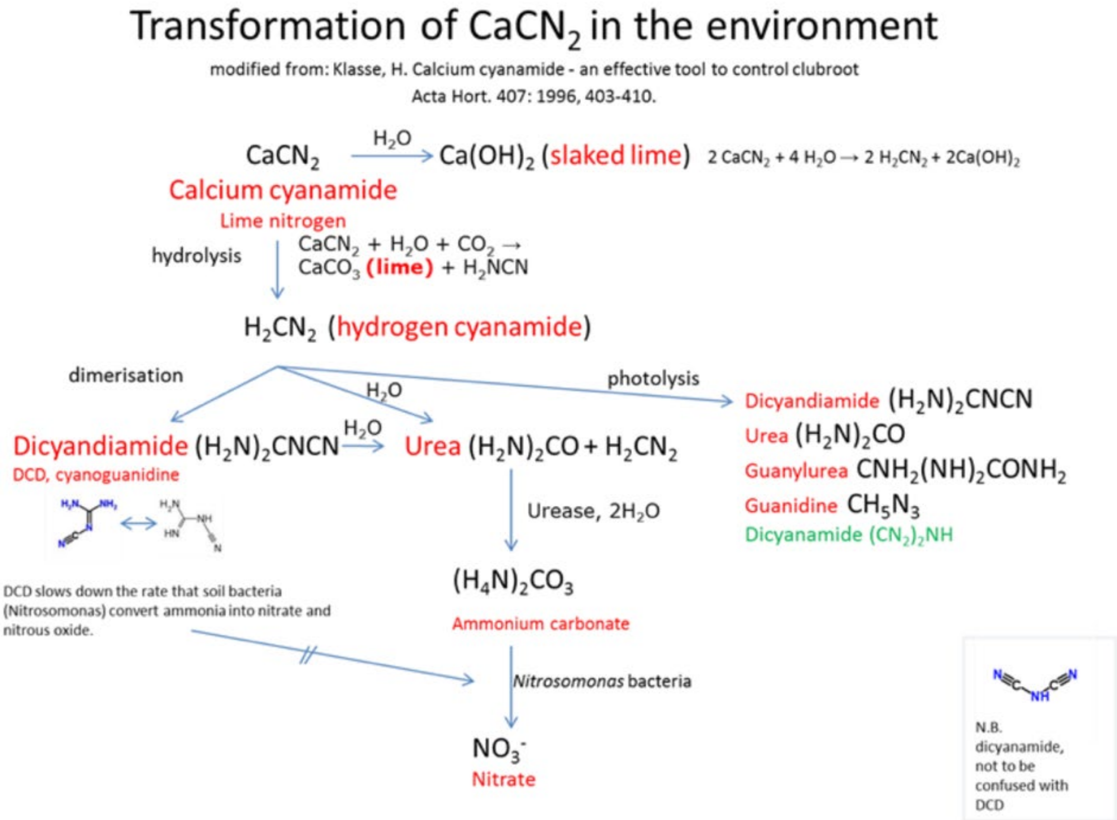

Figure 1. Known environmental transformation pathways of calcium cyanamide, the main active ingredient of Eminex®. Figure from the SCHER report.

Table 2. Known transformation products of Calcium cyanamide, CaCN2.

TP ID	Known TPs	Chemical ID	Known effects	Known TPs?
1	Hydrogen cyanamide, CH_2N_2	CAS 420-04-2 SMILES: C(#N)N	-	TP 2 – 8
2	Dicyandiamide, aka DCD, cyanoguanidine, $(H_2N)_2CNCN$	CAS 461-58-5 SMILES: C(#N)N=C(N)N	nitrification inhibitor	TP 3, 7 and 8
3	Urea $(H_2N)_2CO$	CAS 57-13-6 C(=O)(N)N	-	-
4	Guanylurea $CNH_2(NH)_2CONH_2$	CAS 141-83-3 SMILES: C(=NC(=O)N)(N)N	-	-
5	Guanidine CH_5N_3	CAS 113-00-8 SMILES: C(=N)(N)N	-	-
6	Dicyanamide $(CN_2)_2NH$	CAS 504-66-5 SMILES: C(#N)NC#N	-	-
7	Ammonium carbonate $(H_4N_2)_2CO_3$	CAS 506-87-6 SMILES: C(=O)([O-])[O-].[NH4+].[NH4+]	-	-
8	Nitrate NO_3^-	CAS 14797-55-8 SMILES: [N+](=O)([O-])[O-]	-	-

Calcium dihydroxide (CAS 1305-62-0) and graphite (CAS 7782-42-5) are considered endpoints with no further transformation. Melamine (CAS 108-78-1), present in the formulation, is a known endpoint from several different compounds that can be present in the environment.

In addition to the literature search, potential unknown transformation products were screened using two online open access prediction in-silico tools: i) the EAWAG-BBD Pathway Prediction System and ii) Biotransformer 3.0 Environmental Microbial Transformation module. All compounds listed above, including the ingredients from Eminex® and the known transformation products were computed. Results are summarized in Table 3. All predicted compounds, to the best of our knowledge, have never been detected before and should be considered in future studies to elucidate if plausible or not.

Table 3. Predicted Transformation products from all compounds listed above, including Eminex® ingredients and known transformation products of calcium cyanamide.

Compound	Predictions	Chemical ID
Calcium cyanamide (Eminex®)	N/A	-
Calcium hydroxide (Eminex®)	N/A	-
Graphite (Eminex®)	N/A	-
Melamine (Eminex®)	4 predicted products[1] 1 biotransformations[2]	C1(=NC(=NC(=O)N1)N)N, Ammeline () C1(=NC(=O)NC(=O)N1)N, Ammelide (TP10) C1(=O)NC(=O)NC(=O)N1, Cyanuric acid (TP11) C(=O)(N)NC(=O)N, biuret (TP12)
Hydrogen cyanamide (TP1)	1 predicted products[1] 0 biotransformations[2]	C(=O)(N)N, Urea, TP3
Dicyandiamide, DCD (TP2)	3 predicted products[1] 1 biotransformations[2]	C(=NC(=O)N)(N)N, Guanylurea (TP4) C(=O)(N)[O-], Carbamate (TP13) C(=N)(N)N, Guadinine (TP5)
Urea $(H_2N)_2CO$ (TP3)	0 predicted products[1] 0 biotransformations[2]	- -
Guanylurea $CNH_2(NH)_2CONH_2$ (TP4)	2 predicted products[1] 1 biotransformations[2]	C(=O)(N)[O-], Carbamate (TP13) C(=N)(N)N, Guadinine (TP5) C(=NC(=O)[O-])(N)N, N-(diaminomethylidene)carbamate (TP14)
Guadinine CH_5N_3 (TP5)	0 predicted products[1] 0 biotransformations[2]	- -
Dicyanamide $(CN_2)_2NH$ (TP6)	5 predicted products[1] 1 biotransformations[2]	CNC(=O)N, methylurea (TP15) C(=O)(N)NC(=O)N, biuret (TP12) C(=O)(N)[O-], Carbamate (TP9) [C-]#N, cyanide (TP16) C(=O)(N)N, Urea, TP3 C(#N)NC(=O)N, cyanourea (TP17)
Ammonium carbonate $(H_4N_2)_2CO_3$ (TP7)	N/A [1] 0 biotransformations[2]	- -
Nitrate NO_3^- (TP8)	N/A	-

[1] EAWAG-BBD: Pathway Prediction Results.

[2] BioTransformer 3.0.

N/A stands for not applicable, or outside the applicability domain of the model.

Data on whether compounds are persistent, their degradation times, and their potential to accumulate in milk or meat were collected or predicted and were summarized in Table 4. This exercise was conducted for all ingredients in Eminex®, as well as for the known and predicted transformation products reported above.

Table 4. Degradability and bioconcentration/bioaccumulation factors for all compounds reported.

Components	Readily Biodegradable?	Bioconcentration/Bioaccumulation Factor
Calcium cyanamide (Eminex)	No[1] Yes[2]	0.5 (Log BCF)[1] -0.04 (Log BAF)[1] Not relevant[2]
Calcium hydroxide (Eminex)	N/A	N/A
Graphite (Eminex)	N/A	N/A
Melamine (Eminex)	No[1] > 10000 days[3]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Hydrogen cyanamide (TP1)	Yes[3] DT50 of 2.4 h to 1.45 d in irradiated soil (abiotic)[2] DT50 of 2.7 d in river[2] DT50 of 0.7 to 4.6 d in aerobic soil[3] DT50 of 34.7 d in anaerobic soil[3]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
DCD (TP2)	No[1] DT50 > 1000 days in surface water[3] DT50 11.1 days in soil[3]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Urea (TP3)	N/A	N/A
Guanylurea (TP4)	N/A	N/A
Guanidine (TP5)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Dicyanamide (TP6)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.04 (Log BAF)[1]
Ammonium carbonate (TP7)	N/A	N/A
Nitrate (TP8)	N/A	N/A
Ammeline (TP9)	No[1] 3.7 days[1]	0.5 (Log BCF) -0.05 (Log BAF)
Ammelide (TP10)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Cyanuric acid (TP11)	No[1] 3.7 days[1] Yes[3]	0.96 (Log BCF)[1] -0.33 (Log BAF)[1]
Biuret (TP12)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Carbamate (TP13)	N/A	N/A
N-(diaminomethylidene)carbamate (TP14)	N/A	N/A
Methylurea (TP15)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]
Cyanide (TP16)	No[1] 3.8 days[1] readily biodegraded[3]	0.5 (Log BCF)[1] -0.04 (Log BAF)[1] not bioaccumulative[3]
Cyanourea (TP17)	No[1] 3.7 days[1]	0.5 (Log BCF)[1] -0.05 (Log BAF)[1]

[1] Prediction from EPI-Suite.

[2] SCHER report.

[3] ECHA dossier.

The application of Eminex® introduces three key compounds of concern, $CaCN_2$, melamine, and DCD, into manure and consequently into agricultural soils, giving rise to up to seventeen potential transformation products in the environment. Out of the transformation products, several are naturally occurring, such as urea and organic acids including carbamate and cyanuric acid. While none of these compounds are readily biodegradable, they are generally not considered persistent, with most expected to degrade within a few days, whereas melamine and DCD may require further monitoring. A laboratory simulation study (Fraunhofer IME, 2023) evaluated the anaerobic degradation of $CaCN_2$ from the product Eminex® in liquid cattle manure. The study monitored the concentrations of $CaCN_2$, its primary metabolite cyanamide, and DCD over time to assess their persistence under anaerobic conditions. $CaCN_2$, the active ingredient, was rapidly transformed to cyanamide, which declined from 95.6% of the initial amount at day 0 to 0.3% after 27 days and was not detectable at day 43. In contrast, DCD exhibited greater persistence, with concentrations ranging from 24.8 mg/kg at day 0 to a peak of 29.9 mg/kg at day 13, followed by a gradual decrease to 22.8 mg/kg at day 43. These findings demonstrate that cyanamide, the metabolite of $CaCN_2$, degrades quickly under anaerobic conditions, whereas DCD remains present at low but measurable levels throughout the study period. While DCD and cyanamide are generally short-lived in the environment, melamine, present at low levels as a formulation component, requires further attention. Melamine is of particular concern due to its suspected carcinogenicity and ongoing assessment by ECHA for persistent, bioaccumulative, and toxic properties as well as potential endocrine-disrupting effects. In 2019, the International Agency for Research on Cancer (IARC) classified melamine as a substance that is "possibly carcinogenic to humans" (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2019). Further investigation is recommended to assess the possible presence of melamine, DCD, and their transformation products in milk and meat.

4 Occurrence and Exposure Levels of EMINEX® and Its Degradation Products in Milk and Meat

Based on a literature review, a scientific evaluation has been conducted to assess the occurrence and potential exposure of $CaCN_2$, cyanamide, DCD, urea and melamine in milk and meat from dairy animals, as well as the likelihood of human exposure through consumption. The objective of this assessment was to determine whether any of these compounds are measurable in edible animal products following the agricultural use of Eminex®. The evaluation integrates measured empirical data from controlled feeding trials and analytical detection studies with model-based data derived from environmental exposure and food-chain transfer models. These data were drawn from European and international regulatory assessments, including ECHA, European Food Safety Authority (EFSA), Food and Agriculture Organization/World Health Organization (FAO/WHO), SCHER, and other scientific documents. A summary of the evaluated data and key findings is presented in Table 5. It is important to distinguish between situations where *no measurements* were made, meaning no sampling or published data are available for that compound or matrix, and situations where measurements were conducted but the compound was *not detected* above the laboratory limit of detection or quantification. Both types of information were considered in this assessment.

DCD has been reported at trace levels in some New Zealand milk powder batches manufactured in September 2012, which prompted the suspension of on-farm use and extensive follow-up testing. Subsequent surveillance conducted by MPI and the dairy industry, involving nearly 2,000 dairy product samples, found no traces of DCD in milk collected from farms after mid-November 2012. The authorities concluded that the small traces initially detected in the milk powders posed no food safety risk at the measured levels, and public updates and assurance letters were issued to communicate these findings. Controlled dosing and feeding studies consistently demonstrate that DCD is primarily excreted in urine (>80%), with only a small fraction appearing in milk (1,2%) (Welten et al., 2016). Modeling studies, including those by Ray et al. (2023), predict milk DCD concentrations in the microgram per kilogram range, with mean values of approximately 0.005 mg/kg for granular applications and approximately 0.05 mg/kg for liquid applications, resulting in predicted human intakes between 1×10^{-5} and 1×10^{-4} mg/kg body weight per day, which are orders of magnitude below the reference tolerable daily intake of 1 mg/kg body weight per day. Taken together, these data indicate that although DCD can be detected at very low levels in milk, it does not pose a significant risk under recommended application rates.

For $CaCN_2$, regulatory and review documents, including ECHA (2023), do not report measured residue data in milk, muscle, or liver from dairy animals. These documents primarily focus on environmental fate, groundwater, and ecotoxicity rather than food-product residues. $CaCN_2$ rapidly hydrolyzes to cyanamide in water and soil, which itself is a short-lived intermediate with a half-life of less than one day. No peer-reviewed or regulatory reports were found that have measured for calcium cyanamide in milk or meat.

Cyanamide, a short-lived intermediate in the degradation pathway of calcium cyanamide ($CaCN_2$), has a reported half-life of less than one day (ECHA, 2023). No peer-reviewed or regulatory studies have reported measurements of cyanamide in milk or meat. While analytical methods have been developed for the detection of cyanamide in plant and food matrices, published residue data for animal products are currently lacking (Hiradate et al.,2005). In conclusion, cyanamide has not been detected in either meat or milk.

Urea, as an endogenous metabolite, is normally present in milk and animal tissues and is routinely measured in milk quality analyses (e.g., milk urea nitrogen). Because urea is produced by the animal, it is classified as measured endogenous material rather than a contaminant residue resulting from Eminex® application.

Melamine has been measured in milk and milk powder during high-profile adulteration events, most notably in China in 2008. It serves as an endpoint or a transformation product of several $CaCN_2$-related compounds. These historical detections in milk powder have prompted continued monitoring by authorities (Ball and Quirke, 2019). While melamine is relevant in the context of adulteration of milk powder and has been historically been measured in such products, it has not been considered relevant as a degradation product of $CaCN_2$.

To place the above-described degradation pathways and compound profiles into a quantitative exposure context, a conservative estimate of the potential DCD and melamine loads associated with recommended Eminex® use via slurry application was calculated. Based on the upper-range composition values for Eminex® (melamine content 0.15% and DCD content 2%) and the manufacturer recommended application rate of 1 kg Eminex® per cubic meter of final slurry volume, a slurry application rate of 30 m^3/ha would correspond to an application of approximately 30 kg Eminex® per hectare via slurry. Under these conservative assumptions, the calculated melamine load introduced via slurry would be approximately 0.045 kg/ha, and the corresponding DCD load approximately 0.6 kg/ha. These calculations intentionally represent a worst-case scenario, as they do not account for degradation, transformation, or dilution processes occurring during slurry storage prior to land application or following incorporation into soil. For context, the intentional use of DCD as a nitrification inhibitor in manure or mineral fertilizers typically results in substantially higher DCD inputs, on the order of 10–15 kg/ha, while the application of DCD-inhibited urea at a nitrogen fertilization rate of 80 kg N/ha would correspond to a DCD input of approximately 4 kg/ha.

Collectively, these findings indicate that among the compounds assessed, only DCD has been observed at trace levels in milk, while $CaCN_2$ and cyanamide degrade rapidly and do not bioaccumulate in edible animal products. Urea is naturally occurring in milk and is not considered a contaminant residue resulting from Eminex® application, and melamine is a by-product being formed during product granulation and is not considered relevant as a degradation product of $CaCN_2$. Regulatory and scientific literature confirm that under recommended agricultural practices, Eminex® does not lead to measurable residues in milk or meat, and human exposure through these food products is negligible. Environmental and metabolic degradation pathways further indicate that nitrogen compounds from Eminex® are transient, non-persistent, and effectively excreted, supporting the conclusion that residues in edible animal products are unlikely to pose a risk to consumers. Studies such as Holtkamp et al. (2023) support the efficacy of $CaCN_2$ in emission reduction while emphasizing the need for ongoing research into microbial and ecological impacts, ensuring that both environmental and food safety considerations are addressed.

Table 5. Summary of measurements and modelling.

Compound	Reported measurements in milk or meat	Comments on measurements	No measurements vs no detections
Dicyandiamide (DCD)	Measured in milk powder in New Zealand. 1.2% of ingested DCD transferred to milk; >80% excreted in urine; <2% in faeces. Milk concentrations 0.005–0.05 mg/kg. None detected in meat or organs.	Trace DCD detected in some NZ milk powder. Later surveillance found no DCD in milk collected after 2012. Feeding studies report small transfer to milk (μg/kg).	Measured (some early positive cases). Subsequent surveillance: measured but not detected in later milk samples. Analytical capability exists at low μg/kg.
Calcium cyanamide ($CaCN_2$)	No published measurements in milk or meat.	Regulatory dossiers and reviews do not present residues in edible tissues. Hydrolysis complete prior to uptake.	Not measured (data gap).
Cyanamide (hydrogen cyanamide)	No published measurements in milk or meat.	Methods exist; residue data for animal products not found in the literature. Rapid hydrolysis to urea and ammonium carbonate.	Not measured (data gap).
Urea	Routinely measured (but endogenous).	Milk urea nitrogen is standard milk-quality analytics. Urea is a normal metabolite. Natural milk constituent at 20–30 mg/dL.	Measured as endogenous compound. Not a contaminant in the same sense.
Melamine	Historically measured (adulteration cases)	High-profile melamine detections in milk powder. Authorities monitor for melamine when concern exists.	Measured in past adulteration events, not as a result of Eminex® or $CaCN_2$ application.

5 Mammalian Toxicity and Human Health Risks of EMINEX® and Its Transformation Products

A recent REACH registration presents findings regarding the mammalian toxicity and human health risks of $CaCN_2$ and its transformation products. In water, $CaCN_2$ rapidly hydrolyses to cyanamide, and environmental studies often use cyanamide as a test substance, with results read across to $CaCN_2$. Although $CaCN_2$ has been clinically available for decades, only pharmaceutical data exist, indicating that in rats' excretion occurs primarily via urine (80–98%) as N-acetylcyanamide. Target organs for systemic effects in experimental animals include the liver, thyroid gland, pituitary gland, and reproductive system. Morphological activation of the thyroid was expected, as $CaCN_2$ functions as an anti-thyroid agent. Based on repeated dose studies, SCHER derived a LOAEL of 0.003%, corresponding to 1.3–3.8 mg/kg body weight per day. The mechanisms underlying cyanamide toxicity are not fully understood; however, inhibition of aldehyde dehydrogenases may contribute to some of the compound's adverse effects. Cyanamide also activates the hypothalamo-pituitary-adrenal axis, increasing circulating glucocorticoids, which correlate with effects on thyroid and testis function in rats and dogs, as well as with reduced fertility in rats. Studies found no evidence of mutagenicity or carcinogenicity. SCHER determined NOAEL values of 7 mg/kg bw/day for developmental toxicity and 45 mg/kg bw/day for teratogenicity.

Many studies have documented the so-called nitrolime disease, which occurs in humans after consuming alcohol following exposure to calcium cyanamide ($CaCN_2$) or cyanamide. Kinetic data indicates that after oral administration in both experimental animals and humans, $CaCN_2$ is rapidly hydrolyzed to cyanamide, and the observed toxic effects are primarily due to cyanamide. $CaCN_2$ is classified as Acute Tox. 4, STOT SE 3, and Eye Dam 1. For cyanamide, SCHER used a LOAEL of 1.3 mg/kg bw/day, together with appropriate assessment factors, to derive an Acceptable Operator Exposure Level (AOEL) of 0.0043 mg/kg bw/day. The following hazard statements and classifications apply for cyanamide: H301: Toxic if swallowed (Acute Tox. 3); H311: Toxic in contact with skin (Acute Tox. 3); H314: Causes severe skin burns and eye damage (Skin Corr. 1); H317: May cause an allergic skin reaction (Skin Sens. 1); H351: Suspected of causing cancer (Carc. 2); H361fd: Suspected of damaging fertility or the unborn child (Repr. 2); H373 (thyroid): May cause damage to organs through prolonged or repeated exposure (STOT RE 2); H412: Harmful to aquatic life with long-lasting effects.

Cyanamide is used as a representative substance for $CaCN_2$ in REACH registration assessments due to the rapid hydrolysis of $CaCN_2$ in the environment. $CaCN_2$ is harmful to humans and animals, primarily because it breaks down into cyanamide, and can adversely affect the liver, thyroid, and reproductive system. It also poses environmental risks. The European Commission recommends phasing out $CaCN_2$ as a fertiliser due to these health and ecological concerns. The Dossier Submitter has determined that the use of $CaCN_2$ as a fertiliser, when applied according to the Registrant's recommended rates and methods, results in risks that are not adequately controlled, particularly for surface water adjacent to fertilised fields. These risks are mainly attributable to cyanamide, one of the primary transformation products of $CaCN_2$. Notably, cyanamide has been identified as an endocrine disruptor affecting both human health and non-target organisms by the Biocidal Products Committee (BPC) in December 2019.

The mammalian toxicity profile of Hydrogen cyanamide (CAS 420-04-2) is the same as that for CAS 156-62-7, as reported in the REACH registration.

The REACH registration reported that DCD is stable to hydrolysis at pH 4.0, 7.0 and 9.0. It is not readily biodegradable in an OECD 301E screening test, although degradation was observed in an OECD 302B test. DCD is degradable in soils through both abiotic and biotic processes, and a weight-of-evidence soil DT_{50} of 11.1 days at 20 °C was determined as key value. In contrast, pelagic surface-water testing according to OECD 309 showed no biological degradation, with a DT_{50} for primary biodegradation greater than 1000 days. Due to its log octanol–water partition coefficient of −1.0, high water solubility, polar nature and pK_a, DCD is not expected to adsorb to soil or sediment and is therefore considered mobile in the environment. It is also not expected to bioaccumulate. The chemical safety assessment under REACH Annex I concluded that no further investigation of the environmental fate and behaviour of DCD or its degradation products is required. A DNEL of 6.5 mg/kg bw/day was derived, with repeated dose toxicity identified as the most sensitive endpoint. No evidence of CMR effects was reported, and overall DCD is considered to have a low hazard potential.

Melamine is classified as a substance of very high concern, with harmonized classifications for carcinogenicity and repeated-dose toxicity. In 2019, the International Agency for Research on Cancer (IARC) classified melamine as a substance that is “possibly carcinogenic to humans (IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, 2019). It is included in the REACH candidate list, requiring authorization for use, and assessment regarding endocrine-disrupting properties is ongoing.

Urea is naturally produced in mammals as part of normal physiological processes, primarily through the detoxification of ammonia generated during protein catabolism via the urea cycle. It is formed in the liver from ammonia, a deamination product of amino acids. Urea is generated in large quantities in the human body as a normal metabolic product and is excreted unchanged in the urine. In a 12-month carcinogenicity screening study, F-344 rats and C57BL/6 mice (50 per sex per group) were exposed to urea in the diet at concentrations of 4,500, 9,000 or 45,000 ppm. Five animals per sex per group were sacrificed at the end of the 365-day exposure period, and an extensive list of tissues was examined histopathologically. Interim deaths were evaluated in the same manner. The remaining animals were sacrificed after a 4-month recovery period and examined histopathologically. No signs of toxicity were observed. Survival and body weight were unaffected by treatment, and gross and microscopic pathology revealed no treatment-related findings. The study concluded that urea has very low chronic toxicity. Using default conversion factors, the highest dietary concentration (45,000 ppm) corresponds to approximately 2,250 mg/kg bw/day in rats and 6,750 mg/kg bw/day in mice. Overall, urea is considered a non-toxic compound that is naturally produced in the body.

6 Analytical Methods and Detection Limits for EMINEX® and Its Degradation Products in Milk and Meat

This section focuses on mass spectrometry–based methods for the accurate measurement of DCD contamination at low concentrations (ppb levels) in dairy products and other animal-by-products. Analytical methods developed for detecting intentional adulteration of milk with DCD or other nitrogen-rich adulterants, where concentrations are much higher and used to increase apparent protein content, are not described here because they fall outside the scope of this report.

Quantitative determination of DCD in milk and milk-based matrices has mainly relied on liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) (Abernethy & Higgs, 2013; X.-H. Chen et al., 2014; Draher et al., 2014; Inoue et al., 2014; Shen et al., 2013; SHIMADZU, 2013). For trace-level analysis (ppb), DCD can be extracted using a dilute-and-shoot approach involving liquid–liquid extraction with dilute formic acid (2–2.5%), followed by acetonitrile. This procedure provides satisfactory LOD values (0.01–20 ng/g), LOQ values (0.05–60 ng/g), and recovery rates of 80–110% (Inoue et al., 2014; Shen et al., 2013; SHIMADZU, 2013). To minimize matrix effects, stable-isotope-labelled DCD (such as $^{15}N_4$-DCD or DCD-$^{15}N_2{}^{13}C_2$) can be used as internal standards, improving quantification accuracy (Draher et al., 2014; Frank et al., 2017; Inoue et al., 2014; Shen et al., 2013). Solid phase extraction (SPE) has also been used for clean-up, although the literature reports no substantial improvement in sensitivity when internal standards are employed (X.-H. Chen et al., 2014; Frank et al., 2017). Given the high polarity of DCD, separation is typically achieved using hydrophilic interaction liquid chromatography (HILIC). The methods developed in the literature have used several HILIC column types, including TSKgel Amide-80, Acquity UPLC BEH Amide, and ZIC-HILIC (X.-H. Chen et al., 2014; Inoue et al., 2014; Shen et al., 2013). Reversed-phase HPLC has been applied to calcium cyanamide, although derivatization with dansyl chloride was required to enable detection (S. Chen et al., 1991).

A summary of the available LC-MS/MS methods for DCD quantification in milk, milk powder, and infant formula is presented in Table 6. When these methods were applied to real samples, DCD contamination (not adulteration) was generally not detected (<LOQ) in dairy milk or infant formula from several countries (Draher et al., 2014; Shen et al., 2013). One study from Japan detected DCD in a single infant formula powder sample (79.1 ± 1.2 ng/g out of 23 samples) using a stable isotope dilution ESI+ HILIC–MS/MS method. The reported LOD and LOQ for the method were 0.01 and 0.05 ng/mL, respectively (Inoue et al., 2014).

For edible animal tissues (chicken, beef, mutton, pork, and pig liver), DCD determination has been demonstrated using the method developed by Ge et al. (2016). Extraction relied on accelerated solvent extraction (ASE), followed by clean-up with melamine molecularly imprinted polymer solid-phase extraction (MISPE). Separation was performed using an Acquity UPLC BEH-HILIC column with UPLC-DAD detection. The method provided low LOD and LOQ values and acceptable recovery rates without the use of internal standards. No DCD was detected (<LOQ) in the tissue samples analyzed in that study (Ge et al., 2016).

In addition to mass spectrometry, other analytical techniques such as infrared spectroscopy (Da Costa Filho et al., 2022; Nanayakkara et al., 2023) and Raman spectroscopy (Lin et al., 2015; Muhammad et al., 2020; Nieuwoudt et al., 2016) have been used to detect DCD and related metabolites. However, these methods function primarily as screening tools for economic adulteration with nitrogen-rich compounds and are not suitable for quantifying DCD contamination at ppb levels. For this reason, they are not appropriate for the objectives of this report.

Table 6. Summary of the reported LC-MS/MS method for detection and quantification of DCD and other compounds in dairy products.

Target	Matrix	Extraction	Clean-up	IS	LOD (ng/g)	LOQ (ng/g)	Recovery rate (%)	P/N	Detected Conc	Year	Country	Reference
DCD	Infant formula powder	LLE (Dilute and shoot)	_	$^{15}N_4$- DCD	0.01	0.05	110.8	1/23	79.1 ± 1.2	2014	Japan	Inoue et al., 2014
DCD	Infant formula powder	LLE (Microwave-assisted extrac-tion)	Sep-Pak AC-2 SPE	$^{15}N_4$- DCD	3	10	83.6 - 95.7	0/100	_	2013	China	Shen et al., 2013
DCD	Infant formula powder	LLE (Dilute and shoot)	_	_	0.05	0.1	102.9	_	_	2013	Japan	SHIMADZU, 2013
DCD	infant formula, liquid milk, dairy ingredient, high protein meal, cereal, infant cereal, and meat/fish powder	LLE (Dilute and shoot)	Supelclean™ PSA SPE and discovery® DSC-18 SPE	$^{15}N_4$- DCD	_	50	80-110	_	_	2017	Switzerland	Frank et al., 2017
DCD	Milk powder	LLE	_	$^{15}N_4$- DCD	400	1100	94–97	0/15	_	2014	USA	Draher et al., 2014
DCD	Milk powder	CS-NR-MP d-*μ*-SPE purification	d-μ-SPE)	DCD-$^{15}N_2{}^{13}C_2$	0.02	0.06	99– 105	0/30	_	2014	China	Chen et al., 2014

Note: All methods mentioned above used HILIC column for separation. The MS/MS was operated in ESI+ mode. IS: Internal standard; LLE, liquid-liquid extraction; dispersive micro-solid-phase extraction (d-μ-SPE). P/N: number of the positive (contaminated samples) over the total analyzed samples. Recovery rate is referred to the apparent recovery.

7 Risk Assessment of Misuse and Food Transfer Scenarios for EMINEX®

This section investigates the potential risks to human health if Eminex® is not used correctly, specifically in cases of accidental ingestion by cattle or overdosing at ten times the recommended rate. The review draws on international and regulatory assessments, including ECHA (2023), SCHER (2016), EFSA (2015), FAO/WHO (2009), and the New Zealand EPA (2024), complemented by key experimental and modelling studies (Welten et al., 2016; Ledgard et al., 2008; Ray et al., 2023).

$CaCN_2$ hydrolyses rapidly in aqueous environments, converting first to cyanamide and subsequently to urea and DCD. These transformation products are non-persistent and are integrated into the nitrogen cycle. Hydrogen cyanamide is acutely toxic and an irritant, with an LD_{50} of 140–200 mg/kg in rodents, whereas DCD exhibits low toxicity and no evidence of mutagenicity or carcinogenicity (EFSA, 2015).

Two primary misuse scenarios are considered: direct ingestion of Eminex® or calcium cyanamide ($CaCN_2$) by livestock and overdosing of slurry at ten times the recommended application rate, which could potentially increase DCD transfer to milk. A summary of compounds and risk levels is presented in Table 7. Direct ingestion of $CaCN_2$ or cyanamide poses acute toxicity concerns to both animals and humans, including gastrointestinal distress, systemic toxicity, and irritation of the skin or mucous membranes. Occupational exposures to hydrogen cyanamide have previously caused poisoning incidents (ECHA, 2023; SCHER, 2016).

Table 7. Summary of compounds and risk levels.

Compound	Milk Level (normal / 10×)	TDI / Guidance	Risk considerations	Key References
Calcium cyanamide	Not measured	Not applicable	Hydrolyses rapidly; acute hazard if ingested	ECHA, 2023; SCHER, 2016
Cyanamide	Not measured	Not applicable	Transient; low persistence	ECHA, 2023
Dicyandiamide (DCD)	0.005–0.05 / 0.05–0.5 mg/kg	1 mg/kg bw/day	Negligible dietary risk	Ray et al., 2023; Welten et al., 2016
Urea	20–30 mg/dL	Physiological	No change with misuse	EFSA, 2015
Melamine	≤0.001 mg/kg	0.2 mg/kg bw/day	Not related to Eminex® according to references	FAO/WHO, 2009

Chronic human dietary exposure is primarily associated with DCD residues in milk. Under normal conditions, milk DCD levels are estimated to range from 0.005 to 0.05 mg/kg, corresponding to an estimated daily intake (EDI) of 1×10^{-5} to 1×10^{-4} mg/kg bw/day. Even assuming a tenfold misuse scenario, predicted milk DCD levels would be 0.05 to 0.5 mg/kg, yielding EDIs up to 1×10^{-3} mg/kg bw/day, which remains approximately 1000 times below the EFSA tolerable daily intake of 1 mg/kg bw/day.

8 Conclusion

Based on this evaluation of Eminex® composition, degradation pathways, environmental fate, toxicology, and food-chain transfer, the evidence indicates that the use of Eminex® in dairy production, when applied according to recommended agricultural practices at a dose not exceeding 1 kg per ton of manure, is highly unlikely to result in detectable or harmful residues in milk or meat. However, this is based on our best educated guess since the literature on this subject is very scarce.

Calcium cyanamide ($CaCN_2$), the active component, rapidly hydrolyses to cyanamide and subsequently at a slower rate degrades to common nitrogen-cycle compounds such as urea and ammonium, which do not bioaccumulate in animal tissues. Among all assessed substances, only dicyandiamide (DCD) has been detected historically at trace levels in milk, and extensive empirical data and modelling consistently show that transfer to milk is minimal, transient, and results in consumer exposure via milk and meat several orders of magnitude below established health-based guidance values.

$CaCN_2$ and cyanamide themselves have not been measured in milk or meat in the very few cases it has been looked for, and urea is an endogenous constituent of animal metabolism rather than a contaminant. Melamine, present at low levels as a by-product of the production process, has been historically observed in milk and milk powder only during high-profile adulteration events.

Conservative estimates suggest that introduction via slurry application of Eminex® is likely to result in minimal environmental loading and low potential for exposure via milk and meat, although data remain limited. Under misuse or overdosing scenarios, direct ingestion of the product by livestock, which constitutes misuse, could pose acute toxicity risks to animals. In the same scenarios, predicted consumer exposure via milk and meat remains well below safety thresholds. Occupational exposure risks could increase for farm workers handling the concentrated product directly, primarily via dermal or inhalation contact, in situations of accidental misuse or insufficient protective measures.

Despite these considerations there is a pending case within the REACH committee regarding a potential total ban on the use of $CaCN_2$ as a fertilizer. This is based on well documented side effects recorded for the compound in two scenarios. i) in soil $CaCN_2$ has a toxic impact on springtails, and ii) in water, $CaCN_2$ has a toxic impact on daphnia. When used as a fertilizer, $CaCN_2$ is applied in high concentrations, and there is no current knowledge of the effects at the application rate used when Eminex® is applied to control methane emissions from manure.

Overall, the available scientific and regulatory evidence supports the conclusion that Eminex® does not pose a credible risk of residues in milk or meat when used correctly, and its use in dairy production is compatible with food safety requirements, good agricultural practice and appropriate handling measures are maintained. Nevertheless, further investigations are recommended to enhance understanding of potential low-level exposures, transformation products, and ecological interactions in dairy production systems.

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EMINEX® – PROBABILITY OF TRANSFER TO MILK OR MEAT

This report assesses the probability of residue transfer to milk or meat following the use of Eminex® in dairy slurry management. Eminex® is a calcium cyanamide-based slurry additive, which can be used to reduce methane formation during slurry storage and improve manure handling. The assessment considers product formulation, degradation pathways, environmental fate, food-chain transfer, mammalian toxicity, analytical methods, and relevant scientific and regulatory evidence. Overall, the available evidence supports the conclusion that Eminex® does not pose a credible residue risk in milk or meat when used correctly, provided that good agricultural practice and appropriate handling measures are maintained. Further investigations are recommended to strengthen understanding of low-level exposure scenarios, transformation processes, and ecological interactions under dairy production conditions.

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