A PRELIMINARY ASSESSMENT IF THE USE OF CALCIUM CYANAMIDE AS A FERTILISER POSES AN UNACCEPTABLE RISK TO HUMAN HEALTH OR THE ENVIRONMENT

IUPAC NAME(S): Calcium cyanamide

EC NUMBER(S): 205-861-8

CAS NUMBER(S): 156-62-7

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Summary

This preliminary note concerns the use of calcium cyanamide as a fertiliser and its potential to pose an unacceptable risk to human health and/or the environment.

Calcium cyanamide is listed in Annex I to Regulation (EC) No 2003/2003 as an EC fertiliser and hence benefits from free circulation in the Single Market. Under REACH, the substance is registered in the range of greater than 1 000 tonnes and it has already been examined by the ECHA Member State Committee in the context of a testing proposal in relation to a data gap on reproductive toxicity. Cyanamide also has been reviewed by ECHA's Committee for Risk Assessment (RAC) and a harmonised classification and labelling decision has been adopted by the Commission. Cyanamide has been positively reviewed by ECHA's Biocidal Products Committee (BPC) for use in certain biocidal products. The use of cyanamide as an active substance to be used in plant protection products was not supported by the Commission in 2008.

Based on concerns for human health and environment due to its use as a fertiliser, the Commission requested SCHER to provide an opinion on its potential risks. SCHER concluded that harmful effects for humans and for the environment could not be excluded when calcium cyanamide is used at the current rates of application. This conclusion raised concerns whether safe use as a fertiliser is demonstrated in the REACH registration dossier.

The European Commission therefore requested ECHA to carry out a preliminary assessment, taking into account information in the REACH registration dossier for the substance, in the SCHER opinion and in dossiers submitted for other regulatory processes (e.g. under the Biocidal Products Regulation and the Plant Protection Products Regulation). This assessment will be used by the Commission to determine whether the use of calcium cyanamide as a fertiliser could pose an unacceptable risk to human health and/or the environment.

In this note, ECHA describes its preliminary assessment of the use of calcium cyanamide as a fertiliser – both for professional and consumer use. Based on this, further work is necessary to adequately characterise the risk for the environment and human health.

Related to the **environmental concerns** of the substance, ECHA has used a more comprehensive ecotoxicity dataset than SCHER (read-across from cyanamide) and this is likely to improve the robustness (and reduce the uncertainty) of the subsequent environmental assessment. The PNEC values derived as part of the evaluation of cyanamide as a biocidal active substance are significantly (up to two orders of magnitude) lower than those derived by SCHER for calcium cyanamide. This suggests that whilst SCHER identified risks to the environment on the basis of their assessment, these risks may have been underestimated.

A preliminary re-assessment of the risk characterisation for the aquatic compartment presented in the SCHER opinion using the PNEC values from the biocides assessment of cyanamide suggests that risks would be identified in a greater number of aquatic scenarios. In addition, the risks in these scenarios (which already have an RCR>1) would occur over a longer period of time after application.

Furthermore, the potential for risks to aquatic sediments and the appropriateness of FOCUS modelling approaches to fertilisers needs to be clarified. Risks to the terrestrial compartment may also benefit from re-evaluation and if considered relevant, the assessment could also be

extended to take account of the risks posed by metabolites and breakdown products of cyanamide in the environment.

Concerning **human health assessment**, there are uncertainties related to the derivation of the benchmark level used by SCHER: instead of the AOEL of 0.0043 mg/kg bw/d, potentially higher AOEL and DNEL values could have also been justified. In addition, there are also a number of uncertainties related to the exposure assessment conducted by SCHER. These uncertainties were associated with the justifications for the use of specific assumptions (e.g. size of the fields, duration of application, effect of the RMMs on the modelled exposure levels). The assumptions made are likely to result in the overestimation of the exposure. The uncertainties are further identified in the sections describing the elements of the evaluation of the exposure assessment.

As a result of these concerns, the assessment of human health risks by SCHER would benefit from further refinement, potentially based on alternative methodologies or using a different set of benchmarks and input parameters. Such further analysis may support the conclusions drawn by SCHER, or indicate an alternative outcome.

Although a much smaller proportion of the total use, the risk of the powdered form of calcium cyanamide needs to be assessed. The majority of the data available to ECHA are primarily based upon the use of the granulated form of calcium cyanamide. The risk associated with the powdered form, with a significantly smaller particle size, so far has not been characterised.

In addition, the issue of other toxicological endpoints assessed for cyanamide – corrosivity, skin sensitisation, carcinogenicity and toxicity for reproduction – if taken into account based on read across – may also affect the risk characterisation of the use of calcium cyanamide as a fertiliser.

Glossary of terms

AOEL	Acceptable Operator Exposure Level
a.s.	Active substance
BPR Regulation	Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products.
BPC	ECHA's Biocidal Products Committee
bw	Body weight
CaCN2	Calcium cyanamide
CAS	Chemical Abstract Services
CLP Regulation	Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures
CSA	Chemical safety assessment
CSR	Chemical safety report
d	Day
dw	Dry weight
EC	European Communities
ECHA	European Chemicals Agency
EOGRTS	Extended one-generation reproductive toxicity study
EPIWIN	US-model to determine chemical properties
EU	European Union
FOCUS	Forum for the coordination of pesticide models and their use
GLP	Good Laboratory Practice
h	Hour
ha	Hectare
Kalkstickstoff	Formulation name of calcium cyanamide in powder form
LC50	Lethal concentration for 50% of the population
LD50	Lethal dose for 50% of the population
LOAEL	Lowest observed adverse effect level
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
OECD	Organization for Economic Cooperation and Development
PEC	Predicted Environmental Concentration
PERLKA	Formulation name of calcium cyanamide in granular form
PNEC	Predicted No Effect Concentrations
PPP	Plant Protection Product
RAC	ECHA's Committee for Risk Assessment
RCR	Risk Characterization Ratio
REACH Regulation	Regulation (EC) No 1907/2006 on registration, evaluation and authorisation of chemicals
SCHER	Scientific Committee on Health and Environmental Risks

Report

The identified problem

Introduction

Calcium cyanamide, which comprises 44% calcium and 24% nitrogen, was first made in the late 1800s, as part of a search for a high analysis nitrogen source for industry and agriculture to replace excreta deposits. It is produced by burning black coal and white limestone in the presence of atmospheric nitrogen (at 1 000 to >3 000°C in electric arc-furnaces). Energy costs represent the bulk of the cost of production. The main use of calcium cyanamide is in agriculture as a fertiliser. Because calcium cyanamide releases nitrogen slowly, one application at a rate of about 1 000 kg/ha, according to the application information (worst case), is sufficient to last the whole length of the growing season, particularly in cool and/or dry conditions[1]. However, it is necessary to delay planting until the high concentrations of initial hydrolysis products of calcium cyanamide, which are phytotoxic, dissipate. The phytotoxic characteristics of calcium cyanamide also make repeated dry applications at lower rates impractical.

Two formulations containing calcium cyanamide, i.e. the granulated form (PERLKA = granulated or pearled calcium cyanamide) and the powdered form (Kalkstickstoff), are sold by AlzChem in the EU for use as a fertiliser. In addition, AlzChem, the manufacturer and registrant of calcium cyanamide, has confirmed a small part of the granulated form produced is sold in local DIY stores in 5 kg bags for private use to fertilise home and garden vegetables and as a minor use, for lawns.

Calcium cyanamide is used in agriculture and horticulture predominantly in Europe and Asia as a slow-release nitrogen fertiliser, which exhibits side effects against soil borne plant diseases, slugs and germinating weeds. The fertiliser is broken down by soil moisture into highly reactive lime and free cyanamide. The latter is responsible for the fertiliser's fungicidal and herbicidal effects. Within a few days after application, soil microbes and/or fungi, e.g. *Myrothecium verrucaria* (Maier-Greiner, et al., 1991) convert the cyanamide to urea and then to ammonia. Calcium cyanamide has to be applied prior to sowing and so-called deep placement in soil (at 20 cm depth) has been advocated (Kaushal, et al., 2006a). Under normal use conditions, one application per year per crop is required. For lawns, several applications are possible.

A second known breakdown pathway leads to the production of dicyandiamide, which acts as a nitrification inhibitor in soil. In this way, the conversion of ammonia nitrogen into nitrate is slowed down for several weeks (Kaushal, et al., 2006b), and leaching of fertiliser nitrogen is prevented. Calcium cyanamide is claimed to be particularly valuable for intensively used soils that are highly infested with soil borne pathogens that cause root and stem rot (Scottish EPA, 2014; Bourbos, et al., 1997; Shi, et al., 2009). Addition of calcium cyanamide during cow manure composting significantly shortens the time to inactivate foodborne pathogens (Simujide, et al., 2013).

[1] Based on a comment by AlzChem, in order to ensure a well-balanced nitrogen supply according to good agricultural practice application rates above 500 kg/ha are not recommended any more.

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Calcium cyanamide is listed in Annex I to the Fertiliser Regulation (EC) No 2003/2003 as an EC fertiliser and hence benefits from free circulation in the Single Market.

Besides being a component in a fertiliser, cyanamide is an existing active substance under the Biocides Review Programme and an application was evaluated by the German competent authority and peer-reviewed by the Biocidal Products Committee. Applications for approval of cyanamide for use in insecticides, acaricides and products to control other arthropods (PT18) and as a veterinary biocidal products (PT3) were submitted in 2006 under Directive 98/8/EC by AlzChem. The risk assessment identified risks to groundwater under some exposure scenarios (metabolite thiourea). Final opinions were adopted by the BPC in June 2016 and decisions are currently pending from the Commission.

In June 2015 RAC adopted its opinion on harmonised classification and labelling at EU level of cyanamide (carbamonitril). In terms of environmental-related classification, the proposal provided justification for a classification of Aquatic Chronic 1 on the basis of chronic aquatic toxicity. However, in the RAC opinion a classification of Aquatic Chronic 3 was considered to be appropriate, recognising there was evidence of rapid degradation of cyanamide in environmentally relevant water/sediment model systems. It is perhaps noteworthy that the lowest reported NOEC (0.104 mg cyanamide/L) is only marginally greater than the trigger threshold for an Aquatic Chronic 2 classification (≤0.1 mg/L). Rounding of the NOEC value (consistent with number of significant figures used in the classification criteria) would have resulted in a classification of Aquatic Chronic 2, requiring the use of the 'hazardous for the environment' GHS pictogram on packaging.

AlzChem AG has confirmed it is the sole registrant of calcium cyanamide under REACH, although it is aware that several other companies offer calcium cyanamide for the EU market (their REACH status is unknown). Several companies preregistered calcium cyanamide and AlzChem has started negotiations on a possible substance information forum (SIEF) arrangement. Calcium cyanamide was registered in the greater than 1 000 tonnes/year tonnage range (130 000 tonnes were manufactured in 2014) by AlzChem AG (Dr.-Albert-Frank-Straße 32 83308 Trostberg Bayern Germany).

Calcium cyanamide has been examined by the ECHA Member State Committee in the context of a testing proposal in relation to a data gap on reproductive toxicity, specifically for a pre-natal developmental toxicity (PNDT) and an extended one-generation reproductive toxicity study (EOGRTS). After examination of the testing proposals under REACH dossier evalution, ECHA issued a decision in 2013 in which the PNDT study was requested (according to OECD 414), however the decision on the proposed EOGRTS remains pending. Currently, the registrant is - as recently requested by the Commission - updating its dossier to include a study proposal (according to OECD 443). The updated dossier has been be submitted on 27 October 2017.

A Commission decision was made on 18 September 2008[2] not to include cyanamide in the list of approved active substances for use in plant protection products. The grounds for this decision were clear indications that harmful effects on human health may occur and in

[2] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008D0745&from=EN

particular on operators. SCHER in its opinion of 22 March 2016[3] on calcium cyanamide noted 'calcium cyanamide in itself should be evaluated as a pesticide. This has not been done before, since no manufacturer supports this use'.

Based on concerns for human health and environment due to its use as a fertiliser, in April 2015 the Commission requested SCHER to provide an opinion on its potential risks taking into account all the relevant information that was available to SCHER before 1 April 2015. In its opinion of 22 March 2016 SCHER concluded that harmful effects for humans and for the environment could not be excluded when calcium cyanamide is used at the current rates of application. In its opinion, SCHER also noted that no specific risk assessment methodology has been developed for fertilisers in the European Union that could be applied to the questions posed to the SCHER. Therefore, the SCHER applied as far as possible, the methodology developed for the registration of plant protection products. SCHER's conclusion raises the question whether safe use as a fertiliser is demonstrated in the REACH registration dossier.

The European Commission therefore requested ECHA on 24 February 2017 to carry-out a preliminary assessment, taking into account information in the REACH registration dossier for the substance, in the SCHER opinion and in dossiers submitted for other regulatory processes (e.g. under the Biocidal Products Regulation and the Plant Protection Products Regulation). This assessment is to determine whether the use of calcium cyanamide as a fertiliser could pose an unacceptable risk to human health and/or the environment. An interim draft report summary was provided to the Commission on 22 June 2017 for comments.

Hazard, exposure/emissions and risk

2.1 Identity of the substance(s), and physical and chemical properties

2.1.1 Substance Identity

This report concerns the substance calcium cyanamide.

Table 1. Identifiers for calcium cyanamide

EC number	205-861-8
EC name	Calcium cyanimide
CAS number	156-62-7
Molecular formula	CN2.Ca
Molecular weight range	80.1021
Structural formula	Ca^{2+} N^{-}=C=N^{-}

[3] https://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_169.pdf

Pure calcium cyanamide is a white solid. The two formulations of calcium cyanamide that are used as fertilisers in the EU are the granulated form PERLKA and the powdered form, Kalkstickstoff (also referred to as calcium cyanamide 20.5 – on account of its nitrogen content). PERLKA is a grey-black solid granule and 20.5 is a grey-black powder at 20°C and 1 013 hPa[4]. In addition to 44% calcium cyanamide, PERLKA also contains amongst other things 2.8% urea, calcium nitrate (11.1%) and calcium dihydroxide (13.4%). 20.5 contains 58% calcium cyanamide, calcium oxide (11.1%) and magnesium carbonate (5.8%).

AlzChem has confirmed in stakeholder consultation, that approximately 98.5% of the calcium cyanamide used as a fertiliser is sold in the granulated form (51 200 tonnes/year) and less than 1.5% (800 tonnes/year) in the powdered form. Of this 1000 tonnes/year are used by consumers for private crops and lawns, exclusively in the PERLKA form. In addition to its use as a fertiliser, calcium cyanamide is used in industry for the manufacture of basic metals and bulk chemicals. Cyanamide itself is used as a biocide to control certain arthropods (PT18) and as a veterinary biocidal product (PT3). Application for the use of cyanamide as an active substance in plant protection products was not supported by the Commission in 2008 (see section 1.1). The characteristics of the granulated and powdered forms are summarised on AlzChem's website – see Table 2.

Table 2. Chemical properties of calcium cyanamide (source: AlzChem website)

Chemical properties	Ground calcium cyanamide	PERLKA®
Total nitrogen	20.5%	19.8%
Nitrate nitrogen	-	1.8%
Cyanamide nitrogen	> 19.5%	> 15%
Dicyandiamide nitrogen	-	approx. 0.5%
Neutralising value (CaO)*	> 60%	> 50%
Physical properties	**Ground calcium cyanamide**	**PERLKA®**
appearance and Composition	Gray-black powder	Gray-black granulate
Pouring density	1000kg/m³	1000kg/m³
Grain size	0.01 - 1.0 mm	0.8 - 3.5 mm

[4] According to the registrant, the registered substance as well as the two formulations of calcium cyanamide that are used as fertilisers in the EU are grey-black due to their high graphite content.

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The REACH registration dossier is entitled 'calcium cyanamide/kalkstickstoff' and the accompanying chemical safety report (CSR) is entitled 'calcium cyanamide'. The studies described in the CSR have used a variety of forms of calcium cyanamide. The registrant reported 'if available, studies with….technical grade kalkstickstoff are used for evaluation of the toxicological properties. Nevertheless also studies with pure calcium cyanamide are used…and studies with a mixture of calcium cyanamide with other main components, PERLKA are used for read across. In addition read across to hydrogen cyanamide was used in rare cases….especially for environmental fate parameters'.

SCHER reported that the granulated form, PERLKA has a median particle diameter size of 2100µm (2142µm in the REACH registrant's CSR and); although 1.5 - 23.5 % of the cumulative distribution of the particles have a size of 1000 - 1700µm (see SCHER opinion) and from technical data provided by the registrant to ECHA (see Table 2 and Annex 1) a size range of 800-3500 µm. The powdered form has a much smaller diameter size distribution: 10-1000 µm (Annex 1) and the mass median diameter of calcium cyanamide as reported in the CSR for Kalkstickstoff was 40 µm as measured by dry sieve analysis.

In its CSR, the registrant states: 'the typical concentration of calcium cyanamide in Kalkstickstoff is about 68 %'. 'Other main impurities are CaO and C with a typical content of about 13.8 % and 13 % respectively'. 'These and other minor impurities are not expected to contribute to the toxicological properties of 'Kalkstickstoff', thus it is justified to treat the substance as mono-constituent'. The SCHER opinion also states that the impurities are not toxicologically active.

AlzChem reports in the CSR: *'in a technical process the powder calcium cyanamide will be formulated into commercial product PERLKA. Due to this formulation process the particle size of calcium cyanamide will changed. The form of the substance changed from powder to granulate. It was shown that in the commercial product PERLKA the mass median diameter is greater than in the technical product calcium cyanamide. Thus, for industrial applications the particle size of calcium cyanamide, technical grade Kalkstickstoff and for professional and consumer application the particle size of PERLKA will be used in risk assessment*'. Therefore, the risk assessment under REACH conducted for the use of calcium cyanamide as a fertiliser does not take into account the powdered form.

The key physicochemical properties of calcium cyanimide are summarised below, based on information extracted from REACH registration dossier.

Table 3. Relevant physicochemical properties of calcium cyanamide

Property	**Results**	**Value used for CSA / Discussion**
Physical state at 20°C and 1013 hPa	Kalkstickstoff (calcium cyanamide, technical grade) is a solid grey to black powder with a characteristic odour.	Solid.
Melting / freezing point	The melting range was determined to be 1145°C to 1217°C.	Two endothermic thermal decompositions and continuous loss of mass were observed. Significant increase of mass loss at a temperature above 1040°C and 1124°C was measured.
Boiling point	Study waived.	Not applicable.
Relative density	The density of pure and technical grade Kalkstickstoff was determined to be 2.36 g/cm3 and 2.3 g/cm3 at 25°C, respectively.	2.3 at 20°C

Property	**Results**	**Value used for CSA / Discussion**
Granulometry	The mass median diameter of technical grade Kalkstickstoff was determined to be 40 µm; and for PERLKA was determined to be 2142 µm as measured by dry sieve analysis.	Kalkstickstoff: 40 µm PERLKA: 2142 µm
Vapour pressure	Study waived.	Not applicable.
Partition coefficient n-octanol/water (log value)	Study waived as technical grade Kalkstickstoff hydrolyses rapidly and quantitatively thus the test cannot be performed. A very low partition coefficient is expected for technical grade Kalkstickstoff based on other available physical and chemical parameters like high water solubility.	Not applicable.
Water solubility	The water solubility of Kalkstickstoff was determined to be 29.4 g/L calcium cyanamide at 20°C. The elemental carbon remains undissolved.	29400 mg/L at 20 °C
Flammability	In the key study technical grade Kalkstickstoff was categorised in category 1 of 6 regarding flammability. Local burning or glowing without further extension. Thus, the substance is not regarded highly flammable. The lower explosive level in a dust explosion test was determined to be 125g/m3. In addition, no flammability in contact with water and no pyrophoric abilities are expected. These studies are thus waived.	Non-flammable.
Explosive properties	Study waived.	Not applicable.
Oxidising properties	Study waived.	Not applicable.

Concerning Annex I to the Fertilisers Regulation, AlzChem has confirmed (see Annex 1):

1) Kalkstickstoff (calcium cyanamide 20.5) falls into Annex I category 3(a) of the EC Fertiliser Regulation as it contains calcium cyanamide as its essential ingredient. Kalkstickstoff meets the requirements of the EC fertiliser regulation for type 3(a) as its declared total nitrogen content exceeds the minimum content set in the fertiliser regulation (i.e. min 18% total N);

2) PERLKA® falls into Annex I category 3(b) of the EC Fertiliser Regulation as it is a nitrogenous type of calcium cyanamide due to the fact that nitrate is added to the calcium cyanamide during the formulation process. PERLKA meets the requirements of the EC fertiliser regulation for type 3(b) as its declared total nitrogen as well as its nitric (=nitrate) content exceed the minimum contents set in the fertiliser regulation (i.e. min 18% total N and 1% - 3% nitric nitrogen N).

Table 4. Calcium cyanamide and Annex I of the Fertilisers Regulation (EC) No 2003/2003

No	**Type designation**	**Data on method of production and essential ingredients**	**Minimum content of nutrients (percentage by weight)** **Data on the expression of nutrients** **Other requirements**	**Other data on the type designation**	**Nutrient content to be declared** **Forms and solubilities of the nutrients** **Other criteria**
3(a)	Calcium cyanamide	Chemically obtained product containing calcium cyanamide as its essential ingredient, calcium oxide and possibly small quantities of ammonium salts and urea.	18 % N. Nitrogen expressed as total nitrogen, at least 75 % of the nitrogen declared being bound in the form of cyanamide.		Total nitrogen
3(b)	Nitrogenous calcium cyanamide	Chemically obtained product containing calcium cyanamide as its essential ingredient, and calcium oxide and possibly small quantities of ammonium salts and urea, plus added nitrate.	18 % N. Nitrogen expressed as total nitrogen, at least 75 % of the non-nitric nitrogen declared being bound in the form of cyanamide. Nitric nitrogen content: - min: 1% N - max: 3% N		Total nitrogen Nitric nitrogen.

2.1.2 Classification and labelling

Calcium cyanamide is classified in Annex VI of CLP:

- Acute tox 4,
- STOT SE 3,
- Eye Dam.1.

Cyanamide has a current harmonised classification under the CLP Regulation as:

- Acute Tox. 3 *;
- Acute Tox. 4 *;
- Eye Irrit. 2;
- Skin Irrit. 2;
- Skin Sens. 1.

The following harmonised classifications were adopted for cyanamide by RAC on 5 June 2015 and have been incorporated into the CLP Regulation, due to enter into force on 1 December 2018:

- Acute Tox. 3 (H311, H301);
- Skin Corr. 1 (H314);
- Skin Sens. 1 (H317);
- Eye damage 1 (H318)
- Carc. 2 (H351);
- Repr. 2 (H361fd);
- STOT RE 2 (H373, thyroid);
- Aquatic Chronic 3 (H412).

It is important for the purposes of this evaluation to take into account that the properties of cyanamide can be read-across to calcium cyanamide (as the former is the breakdown product of the latter). At pH 1.2 and pH 5 the hydrolysis is reported to take place within a few minutes but information is not available on the hydrolysis rate at pH 7 and 9. This rationale was used in the registration dossier as justification for a read-across strategy from calcium cyanamide to cyanamide. Similarly this justification was used in the dossiers for cyanamide submitted under the Biocidal Products Regulation, in the harmonised classification and labelling proposed submitted under the CLP Regulation and by SCHER.

In addition to any restriction, a revision of the harmonised classification for calcium cyanamide should also be considered. This is especially important considering the classification agreed by RAC for cyanamide (Carc 2, Aquatic Chronic 3, Skin Corr. 1 and Skin Sens. 1).

2.1.3 Hazard assessment

2.1.3.1 Human Health Hazard

SCHER 2017 gives a comprehensive overview of the human health hazards from calcium cyanimide. The key health endpoint is identified as effects on the thyroid after repeated exposure.

Animal data

In the key study identified by SCHER, rats were fed for 17 – 50 weeks with dosages of 0.003%, 0.012%, 0.05% and 0.2% **calcium cyanamide** in the diet (Benitz and Salamandra, 1960; Benitz and Cavallo, 1960). At 0.012%, morphological activation of the thyroid and thyroidectomy cells in the pituitary were observed. Also for the 0.003% dosage group, cases of moderate morphological activation of the thyroid were reported. This low dose groups corresponds to a daily intake of 1.3 – 3.8 mg/kg bw/d. The SCHER defined this low dose level as **LOAEL of 1.3 mg calcium cyanamide/kg bw/day**.

For **cyanamide**, RAC identified the LOAEL for effects on the thyroid in a 1-year study with dogs as 2 – 6 mg cyanamide/kg bw/d and in a 90-day study in rats with 4.5 mg cyanamide/kg bw/d as a basis for STOT classification. From those studies, the corresponding **NOAELs are 1 and 1.5 mg cyanamide/kg bw/day**.

SCHER indicated that 'b*ased on kinetic data available, SCHER concludes that calcium cyanamide hydrolysed to cyanamide after oral administration to experimental animals as well as to humans and that toxic effects observed for calcium cyanamide were mainly attributable to cyanamide toxicity. Kinetic parameters showed that relevant cyanamide blood levels were reached later and cyanamide elimination was slower after calcium cyanamide exposure rather than after exposure to cyanamide itself. Delay in systemic bioavailability of cyanamide after oral administration of calcium cyanamide would also explain lower acute toxicity of calcium cyanamide: Oral LD50 values for calcium cyanamide were in the range of 400 to 1,800 mg/kg bw while for cyanamide the oral LD50 was 142 to 223 mg/kg bw (EFSA, 2010a).* ***However, after subchronic and chronic exposure, values for NOAEL seemed to be in the same range for both substances'****.*

AOEL and DNELs for the general population

Based on the LOAEL of 1.3 mg/kg bw/d (0.003%) SCHER applied the following assessment factors (AF): AF 3 (LOAEL to NOAEL), AF 1 (exposure duration: chronic study) AF 4 (allometric scaling rat human), AF 2.5 (other interspecies differences), AF 10 (intraspecies differences) resulting in an **AOEL of 0.0043 mg/kg bw/d.**

With respect to extrapolation from rat to human, RAC stated that the *'particular sensitivity of the rat to antithyroid substances should be taken into account*'. *'The mechanism proposed is relevant to humans but humans are likely to be significantly less sensitive than rodents and probably also less sensitive than dogs'.* Taking into consideration the higher sensitivity of rats and probably dogs to antithyroid substances as explained by RAC and based on human experiences with this substance (see below), the interspecies assessment factor 4 (allometric scaling) does not need to be applied.

Hence, based on the chronic LOAEL of 1.3 mg calcium cyanamide/kg bw/d and by applying AF 3 (extrapolation LOAEL to NOAEL), AF 1 (allometric scaling rat human), AF 2.5 (other interspecies differences), AF 10 (intraspecies differences), an **oral DNEL for the general public of 0.017 mg calcium cyanamaide/kg bw/d** would result.

For cyanamide, RAC identified NOAELs with 1 and 1.5 mg cyanamide/kg bw/d. By applying AF 2 (for extrapolating from sub-chronic to chronic), AF 1 (allometric scaling rat human), AF 2.5 (other interspecies differences), AF 10 (intraspecies differences), an oral **DNEL for the general public of 0.03 mg/kg bw/d could also be justified**.

DNEL for workers

The registrant has developed DNELs for workers and the general public based on the same study and using a NOAEL of 0.012% corresponding to 11 mg/kg bw/day based on the histopathological findings in thyroid and liver observed at the next higher dosage level. Dermal and inhalation DNELs were calculated from the oral dose descriptor.

Table 5. DNELs developed by the registrant

	Worker			**General public**		
	Oral	***Dermal***	***Inhalation***	***Oral***	***Dermal***	***Inhalation***
(modified) Dose descriptor	-	110 mg/kg bw/day	9.70 mg/m^3 (from oral rat study)	11 mg/kg bw/day	110 mg/kg bw/day	4.1 mg/m^3 (from oral rat study)

		(from oral rat study)			(from oral rat study)	
AF	-	50	12.5	100	100	25
DNEL	-	2.2 mg/kg bw/day	0.78 mg/m^3	0.11 mg/kg bw/day	1.1 mg/kg bw/day	0.16 mg/m^3
Comments	-	10% dermal absorption used			10% dermal absorption used	

It is to be noted that **the point of departure (NOAEL of 11 mg/kg bw/d) as used by the registrant for calcium cyanamide is not considered appropriate**.

By using the LOAEL of 1.3 mg/kg bw/d as identified by SCHER, and considering that no AF for allometric scaling from rat to human is required, the following DNELs result:

Table 6. Derived DNELs

	Worker			**General public**		
	Oral	***Dermal***	***Inhalation***	***Oral***	***Dermal***	***Inhalation***
(modified) Dose descriptor	-	13 mg/kg bw/day (from oral rat study)	1.15 mg/m^3 (from oral study)	1.3 mg/kg bw/d (from oral study)	13 mg/kg bw/day (from oral rat study)	1.95 mg/m^3 (from oral rat study)
AF	-	37.5	37.5	75	75	75
DNEL	-	**0.35 mg/kg bw/d**	**0.03 mg/m^3** [*SCOEL OEL of 1 mg/m^3 might also be applied*]	**0.017 mg/kg bw/d**	**0.17 mg/kg bw/d**	**0.026 mg/m^3**
Comments	-	10% dermal absorption used			10% dermal absorption used	

The derivation of DNEL values, including the starting points and assessment factors used, is presented in the Annex 3.

Human data

In the RAC classification and labelling background document, the following is stated: *'calcium cyanamide has been worldwide intensively used as drug to deter drinking in alcoholics. The*

consumption of alcoholic beverages after intake of cyanamide leads to intolerances. This is probably due to an inhibition of acetaldehyde dehydrogenase thus leading to a retardation in ethanol breakdown, which stops on the stage of acetaldehyde accumulating in the blood. Intolerance reactions towards alcohol occur in man after daily cyanamide doses higher than 20 mg.

In general daily doses of more than 0.4 – 1 mg/kg bw cyanamide have been used in the alcohol aversion therapy. The duration of the treatment ranges from a few months to a few years. In some cases, patients have taken cyanamide for more than 10 years'.

The SCHER AOEL of 0.0043 mg/kg bw/d corresponds to 1% of the lowest therapeutic dose of 0.4 mg/kg bw/d (enzyme inhibition).

An oral DNEL for the general public (based on RAC criteria) of 0.017 or 0.03 mg/kg bw/d would correspond to 4 or 7.5% of the lowest therapeutic dose of 0.4 mg/kg bw/d (enzyme inhibition) which could be considered as sufficiently protective.

Summary

In the SCHER opinion (22 March 2016) on calcium cyanamide, an AOEL of 0.0043 mg/kg bw/d was derived on the basis of thyroid effects in rats.

However, using the methodology applied by SCHER, DNELs of 0.017 or 0.03 mg/kg bw/d for the general public could also be justified based on the type of effects observed in the studies with experimental animals administered calcium cyanamide or cyanamide and based on available human experiences with therapeutic use of this substance.

It is proposed that the following DNELs would be taken forward to any subsequent the risk assessment:

- Worker
    - inhalation 0.03 mg/m^3
    - dermal 0.35 mg/kg bw/d
- General population
    - oral 0.017 mg/kg bw/d
    - inhalation 0.026 mg/m^3
    - dermal 0.17 mg/kg bw/d

2.1.3.2 Environmental hazard assessment

Fate, behaviour and transformation in the environment

Calcium cyanamide (CAS no. 156-62-7) hydrolyses to cyanamide (also known as hydrogen cyanamide - CAS no. 420-04-2). At pH 1.2 and pH 5 the hydrolysis is reported to take place within a few minutes but information is not available on the hydrolysis rate at pH 7 and 9.

In the REACH registration dossier for cyanamide it is stated that 'calcium cyanamide is rapidly and quantitatively converted to hydrogen cyanamide upon contact with water'. This rationale was used as justification for a read-across strategy from calcium cyanamide to cyanamide for the registration. Similar statements are made in the dossiers for cyanamide submitted under

the Biocidal Products Regulation and in the harmonised classification and labelling proposed submitted under the CLP Regulation.

SCHER, in its assessment of the risk from the use of calcium cyanamide as a fertiliser, provide justification for a similar read-across, but in this case from hydrogen cyanamide to calcium cyanamide.

From these various independent assessments, it appears that (as long as results are expressed accordingly) there is a broad consensus that the use of ecotoxicity data for hydrogen cyanamide can be used as part of an assessment of the risks of calcium cyanamide (and *vice versa*). However, despite justifying a read-across approach in the introduction to their opinion SCHER (as well as the REACH Registrants) did not use available ecotoxicity data from hydrogen cyanamide in their assessments. The implications of this are elaborated further in the sections below.

In the REACH Registration dossier for calcium cyanamide it is observed that ready biodegradation was not observed after 28 days in an OECD 301B test. However, the read-across substance cyanamide is rapidly degraded in natural water-sediment systems and in soil (typical half-life of 2 days in soil and 1.4 days in water). Therefore, although the substance is not considered as 'readily biodegradable' it can be regarded as 'rapidly biodegradable'.

Information is available on the transformation pathways of the substance and on the intermediate transformation products. The substance is ultimately mineralised to CO_2 and nitrate.

The biocides risk assessment stated that, despite low to moderate persistence in aquatic and soil compartments, cyanamide is considered to be very mobile in soil.

Aquatic toxicity

Only short-term data, based on tests with calcium cyanamide, are reported in registration dossiers:

- LC_{50} fish: 140 mg/L
- EC_{50} *Daphnia*: 6 mg/L
- EC_{50} algae: 28 mg /L

Long-term (chronic exposure) data requirements are waived by the Registrant on the basis that the substance degrades rapidly in the environment.

No data are provided in the registration dossier from ecotoxicity tests with hydrogen cyanamide. If hydrolysis occurs as rapid as described then, according to ECHA R.7 Guidance, data on the hydrolysis product, i.e. cyanamide, should also have been included in the Registration dossier.

The Committee for Risk Assessment (RAC) opinion on a harmonised classification and labelling proposal for cyanamide (carbamonitril) submitted by Germany (adopted June 2015) evaluated a proposal for a classification of Aquatic Chronic 1 on the basis of chronic aquatic toxicity data (21-day NOEC for *Daphnia magna* of 0.104 mg/L) in combination with the absence of evidence for 'ready biodegradability'.

After evaluating the submitted information and the comments submitted in the public consultation, RAC considered (with the support of the dossier submitter) that a classification

of Aquatic Chronic 3 would be more appropriate, recognising there was evidence of rapid degradation of cyanamide in environmentally relevant water/sediment model systems. It is perhaps noteworthy that the lowest reported NOEC (0.104 mg cyanamide/L) is only **marginally** greater than the trigger threshold for an Aquatic Chronic 2 classification (≤0.1 mg/L). Rounding of the NOEC value (consistent with number of significant figures used in the classification criteria) would have resulted in a classification of Aquatic Chronic 2, which is a more stringent classification, requiring the use of the 'hazardous for the environment' GHS pictogram on packaging.

The biocides review discussed the short-term tests with fish, daphnids and algae that were available for cyanamide. The lowest acute toxicity was found for daphnids (EC_{50} = 3.2 mg a.s./L). Long-term tests are available for daphnids (NOEC = 0.1044 mg a.s./L) and algae (NOE_rC = 2.6 mg a.s./L) and aquatic plants (NOE_rC = 0.43 mg a.s./L), the prolonged toxicity study with fish could not be used as long-term test since it does not examine a sensitive stage in the fish life cycle or sub-lethal endpoints.

As two long-term NOEC values from species representing two trophic levels were available, an assessment factor of 50 would normally be used to derive a PNEC. However, in short-term tests, fish were approximately a factor of 10 less sensitive to cyanamide than the most sensitive species (*Daphnia magna).* Therefore, it was concluded that the NOEC from a long-term fish test would not be lower than the NOEC for *Daphnia* (NOEC = 0.1044 mg a.s./L).

Terrestrial toxicity

SCHER reports acute terrestrial ecotoxicity data for Japanese quail (*Coturnix coturnix japonic*a) two earthworm species (*Eisenia fetida* and *Lumbriculs terrestris*) and a species of beetle (*Bembidion lampros*). The $PNEC_{soil}$ used for the assessment of risks to the terrestrial compartment was based on a 14-day LC50 for *Eisenia fetida* of 173 mg/kg dw and an assessment factor of 10; resulting in a $PNEC_{soil}$ of 17.3 mg calcium cyanamide/kg dw.

The Registration dossier includes studies on short-term toxicity to earthworm and to soil micro-organisms. No data is reported for terrestrial plants.

- Short-term earthworm: 14d LC_{50}: 169 mg/kg dw
- Soil micro-organisms: NOEC: 1 300 mg/kg dw

No data are reported for terrestrial plants. However, as the substance is used as a fertiliser it is perhaps surprising that no relevant data are reported (based on testing with cyanamide).

In the biocides review of cyanamide, tests with plants (short-term and long-term), earthworms (short-term), collembolans (long-term) and soil-microorganisms are provided. In short-term tests the plant species *Allium cepa* was most sensitive to cyanamide. The lowest long-term effect was found in a reproduction study with the collembolan *Folsomia candida* (EC_{10} = 1.5 mg a.s./kg soil dw).

Sediment

In the biocides review the $PNEC_{sediment}$ for cyanamide was derived from the $PNEC_{aqua}$ using equilibrium partitioning, resulting in **$PNEC_{sediment}$ for cyanamide of 9.16 µg a.s./kg ww.**

PNEC derivation

No PNEC is derived in the Registration dossier and no environmental exposure assessment or risk characterisation has been reported. The following justification is provided in the dossier:

'According to Regulation (EC) No 1907/2006 Article 14(4) no exposure assessment for the environment is required, as calcium cyanamide, technical grade is not classified as toxic or harmful for the environment according to Annex I to Directive 67/548/EEC or Regulation (EC) No 1272/2008 (CLP-Regulation) and does not meet the criteria as PBT- or vPvB-substance. As no environmental hazard was identified no environmental-related exposure assessment and risk characterisation was performed. In conclusion derivation of PNECs is not required'.

However, based on the proposal for harmonised classification Aquatic Chronic 3 (H412) and the availability of long-term data on cyanamide, environmental exposure assessment should have been provided and PNECs derived.

Aquatic compartment

As observed in the registration dossier, only a 'base-set'[5] of acute aquatic ecotoxicity data for calcium cyanamide were reported in the SCHER opinion. The aquatic PNEC used for surface water risk assessment was based on the most sensitive of the reported data, a 48-hour EC_{50} for *Daphnia magna* of 6 mg/L, and an assessment factor of 100; resulting in a **$PNEC_{aqua}$ of 60 µg calcium cyanamide/L**.

No chronic data were reported by SCHER. However, the SCHER opinion notes that chronic exposure and toxicity of calcium cyanamide cannot be excluded as the formulation releases the active substance slowly and it can therefore be present in the environment for considerable periods during the growing season[6].

Based on the data for cyanamide in the biocides review, as two long-term NOEC values from species representing two trophic levels were available, an assessment factor of 50 would normally be used to derive a PNEC. However, in short-term tests fish were approximately a factor of 10 less sensitive to cyanamide than the most sensitive species *Daphnia magna*, it was concluded that the NOEC from a long-term fish test would not be lower than the NOEC for *Daphnia* (NOEC = 0.1044 mg a.s./L). Thus, an assessment factor of 10 was used, resulting in a **$PNEC_{aqua}$ for cyanamide of 10.44 µg a.s./L**

Terrestrial compartment

In the biocides review of cyanamide, tests with plants (short-term and long-term), earthworms (short-term), collembolans (long-term) and soil-microorganisms are provided. In short-term tests the plant species *Allium cepa* was most sensitive to cyanamide. The lowest long-term effect was found in a reproduction study with the collembolan *Folsomia candida* (EC_{10} = 1.5 mg a.s./kg soil dw). Therefore, this value is used for the derivation of the $PNEC_{soil}$. As long-term tests with species from three trophic levels were available, an assessment factor of 10 was used; resulting in a **$PNEC_{soil}$ for cyanamide of 0.15 mg a.s./kg soil.**

Sediment

No PNEC for the sediment compartment was derived by SCHER.

In the biocides review the $PNEC_{sediment}$ for cyanamide was derived from the $PNEC_{aqua}$ using equilibrium partitioning, resulting in **$PNEC_{sediment}$ for cyanamide of 9.16 µg a.s./kg ww.**

[5] Ecotoxicity dataset comprising three studies: aquatic invertebrate, algae and fish.

[6] The registrant has explained the apparent 'slow release effect' of calcium cyanamide is a 'stabilised nitrogen effect' and most of the nitrogen is preserved for several weeks in the form of ammonium.

Table 7. Summary of PNECs derived from the available risk assessments

	Aquatic environment **$PNEC_{aqua}$**	**Terrestrial environment** **$PNEC_{soil}$**	**Sediment** **$PNEC_{sediment}$**
SCHER (calcium cyanamide)	60 µg/L	17.3 mg/kg dw.	-
Biocides (cyanamide)	10.44 µg/L	0.15 mg a.s./kg soil	9.16 µg a.s./kg ww
Registration Dossier (calcium cyanamide)	-	-	-

2.1.4 Exposure assessment

2.1.4.1

Human health

SCHER assessed the exposure to calcium cyanamide related to the application of this substance as a fertiliser (representing approx. 40% of the total volume manufactured and imported) assuming calcium cyanamide as the fertilising agent was applied at the recommended dose of 450 kg a.s./ha in the realistic worst case and 225 kg a.s./ha in the normal case. The registrant also carried out an exposure assessment in their CSR. The main differences between the two assessments and ECHA's evaluation are described below.

Physical form of the applied fertiliser

According to the registration CSR, for application as a fertiliser, calcium cyanamide is used in the granular form in formulation – trade name PERLKA, in the concentration of approximately 44-45%. SCHER used the upper level of calcium cyanamide 45% (the same as reported in the REACH registration dossier) in PERLKA as the basis for its report.

According to the registrant, the mass median diameter of granulate was calculated to be 2142 µm. This value was also used by SCHER. The SCHER report acknowledges use of powder form as fertiliser as well – in approximately 1.5% of total tonnage used for this purpose. However, as the information on the particle distribution (see Table 1) was only available for the granulated form, SCHER based its evaluation on the granulated form (section 3.2.4). The information provided by the manufacturer (see Annex 1) in response to ECHA's question indicates that indeed, powder form is also used as a fertiliser. However, use of powder form is not assessed in the exposure scenarios developed by the registrant for its REACH registration and this would be the worst-case situation for the exposure assessment. Regarding the use of the powder form of calcium cyanamide as fertiliser the registrant (AlzChem) recently (14 Dec 2017) informed ECHA of its commitment to discontinue use of the powder form as a fertiliser from 1 January, 2018.

The granulate is treated with wax, to reduce the presence of fine particles which would result in inhalatory and dermal exposure. The ratio of fine particles <100 µm - 0.0268% (CSR, p 161) was used by the registrant. SCHER in its assessment uses the value of 0.2% representing the content of particles up to 315µm ('This percentage is reported to cover particles up to

200 µm' – p19). The value selected is based on the particle size distribution assessment performed by the registrant.

The difference in the selected particle size responsible for the exposure does have an impact on the exposure levels for both workers and general public (bystanders and consumers). However, it is not an input parameter for the exposure modelling tools used by SCHER and the registrant. SCHER did not adjust the modelling results for the content of the low-particle size dust for neither the workers, nor consumers or bystanders.

The registrant in its CSR, however, did adjust the modelling results for the particle size distribution. This approach is also argued for by the registrant in its comments to the SCHER report, as mentioned also in the section on exposure estimation.

SCHER also states: 'a small share of granulates produced is packed by retailers in 5 kg bags for private use', whereas for agricultural & horticultural producers, normal parcel size is larger e.g. 50kg/600kg sacks in Finland. This information was confirmed by the manufacturer in its responses to ECHA's questions.

Volume of the substance used and the rate of its application

SCHER has performed an assessment for use of PERLKA by professional workers on a small field of 3 ha, and a large field of 48 ha. For both field sizes, two application rates were evaluated: realistic worst case - rate of 1 000 kg formulation/ha and a normal case - rate of 500 kg formulation/ha were used. For consumers – the application of 400 kg/ha of PERLKA on 500m^2 was considered (20 kg on 500m^2). The registrant in it CSR has used the application rate of 500 kg/ha for professional use and the same application rate on 0.02 ha for consumer use (10 kg on 200 m^2 – slightly more than rate considered by SCHER).

SCHER has based its input parameters on the information included in the brochures provided for the industry use: the use of 1 000 kg of the product per hectare is recommended on some crops (cabbage, tomatoes, celery) in some of the countries (e.g. Benelux, Slovakia). 'The realistic worst case' of SCHER does not cover all cases, as for instance in Finland 1 500 (even up to 1 900) kg per hectare for cabbage has been recommended[7]. However, the vast majority of the crops require lower application rate - below 500 kg/ha.

The market information on the distribution of the volume of substance used at various rates is not available. The precise information on the use rate by consumers is also not available. In response to ECHA's question the manufacturer has stated, that the consumers on average apply 2 to 5 kg of PERLKA per 100m^2, once per crop. Lawns may be fertilised multiple times per year, with the application rate of 2 kg per 100m^2. According to the manufacturer, consumers usually purchase only one 5kg bag of PERLKA per year, based on this the application area per consumer would be close to 100 - 250m^2. This information is in line with the registration CSR, and indicates lower use and comparable use rate than described in the SCHER report.

[7] http://kasvinsuojelu.berner.fi/tuotteet/typpilannoitteet/perlka-kalkkityppi: cabbage, 3 weeks before planting 400-1500 kg/ha, 3 weeks after the planting 300-400 kg/ha. The registrant (AlzChem) informed ECHA that it has now requested the reseller in Finland to amend (decrease) its use recommendation with immediate effect. In all other European Member states the use recommendations have already been amended. Any use rate exceeding 500 kg/ha is no longer recommended as it is not in line with good agricultural practice.

As it seems that the higher rate used by SCHER for workers exposure is recommended by the registrant for some crops, its use as the realistic worst case seems to be justified. The use rate for consumers used by the SCHER, lower than assumed for professional use but within the recommended use rates for various crops is also acceptable.

Duration of exposure

There are two types of tasks potentially resulting in exposure of the workers identified both by the registrant and SCHER in their assessments: transfer or mixing and loading of the fertiliser and its application.

Transfer / mixing and loading

SCHER considers that mixing and loading of the product needed to apply to a small field (3 ha) takes 60 min, while for the large field - 81 minutes, irrespectively of the application rate per hectare and the volume of the fertiliser needed.

SCHER also provides data submitted by the manufacturer: for the application rate of 350 kg / ha onto 5.1 ha - the mixing and loading duration was 9 minutes. There is no justification provided for the specified durations of the tasks used by the SCHER and the difference in durations between the volumes to be mixed / loaded for the application rates and field sizes considered is not clear.

The registrant describes transfer of substance (REACH registration use descriptors: PROC 8a and PROC 8b) as a task taking > 4 hours, which can be interpreted also as up to 8 hours. The volume of substance transferred during this time is not described (not an input parameter for the exposure modelling tool used).

The application of the fertiliser

In its CSR, the registrant has provided the exposure assessment for the application of 500kg / ha of the product over 20ha per day, not specifying the exact duration of spreading the fertiliser (2.5 ha per hour, assuming 8 hours of application time).

The application duration considered in its calculation by the SCHER was 60 min for the 3 ha and 420 min for 48 ha, irrespective of the application rate. The SCHER in its assessment has assumed the application with open tractor and use of rotators with a working width of 12 m for small fields, and use of rotators with a working width of 24 m for large fields. It is not explained how the equipment used affects the area of application per hour, however, it is clear that the time needed for the application of fertiliser over a specified area would vary depending on size and style of equipment being used as well as on the geometry of the fields in question and access to them. The data from the manufacturer states that application of the product on 5.1 ha took 60 min using 15m wide rotator.

Discussion

The form of the substance – powder or granulate – affects the exposure of workers, bystanders and consumers. Due to the higher concentration of the active substance and lower particle size – it may be assumed that the exposure resulting from use of powder form could be higher. The effect of the form of the substance however has not been discussed in the SCHER report, and would require an assessment to be performed. Neither the CSR nor the SCHER report include justifications for the durations allocated to individual tasks.

It is not clear, what is the basis for the assumed duration of exposure for mixing and loading for the small field – 3 ha and 60 min, and large field – 48 ha and 81 min (ratio of areas :

1:16, ratio of durations: 1:1.35) and for application - 60 min and 420 min (ratio of 1:7). SCHER in its assessment describes mixing and loading and application duration as tasks of the same duration, regardless of the application rate – whether it is 1 000 kg or 500 kg per ha. Considering the volumes of the substance needed – this may not be an accurate assumption, overestimating the transfer / mixing / loading task durations for some 'rate vs area' combinations, underestimating for other.

Considering that the data provided by the manufacturer quoted in the SCHER report is linked to the exposure monitoring – it could be assumed that the application rate of 5 ha per hour is feasible (with 15 m rotator).

Therefore, the application durations for specified field sizes assumed by SCHER may need to be reconsidered: 60 min per 3 ha may be an overestimation of the duration of the task, but application of the fertiliser to 48 ha in 7 hours may not be possible by single operator. The registrant in its comment reflected that the loading of the product into the equipment and driving time to the field also need to be taken into consideration in the assessment, effectively reducing the duration and area of application. Using a rate of 5 ha in 60 min (specified in the monitoring report), application of the product to 48 ha alone would take almost 10 hours – not considering loading and driving time. Assuming the application rate adopted for the small field – 3 ha in 60 min – the time needed for 48 ha would be 16 hours. The SCHER report does mention use of different types of spreading equipment – but the effect on the time needed for the application of fertiliser per ha is not described. In addition, the information on the types of rotators used for smaller and bigger fields is not available (e.g. there is no guarantee that for the application on all bigger fields wider boom equipment is used).

The registrant in its comment provides also an operational / practical justification for 48 ha not being a realistic area of application within one day: 10 ha can be planted within one day, therefore considering the time suitable for planting in relation to the fertiliser application –the fertiliser should not be applied to more than 20 ha within a day. It is possible however that a larger area could be planted, for example using additional resources (equipment and manpower), or a specialised fertiliser spreader may be contracted, so this justification of limiting the application of fertiliser to 20ha per day may not be valid in all cases.

Taking into account all of the above, it can be considered therefore that SCHER's calculation presented in the Table 4 of its opinion, based on the measured inhalatory exposure **represents an overestimation of exposure resulting from the use of PERLKA in granular form**. Nevertheless, the following aspects also need to be considered: the use of the wide-boom equipment may enable application of the product over larger area in a designated time; and whether the professional worker performing mixing and loading is also applying the product.

RMMs used and their effect on exposure

It seems that the main risk management measure, applicable for both professional and consumer use, is the specific formulation of the product – granulate with wax coating, reducing the effects of attrition and generation of dust, described by application of standard Heubach method (Sarawinski, 2014). The results of this assessment are used by the registrant to modify the outputs of the PHED modelling (see below). However, SCHER uses a more conservative value for the drift factor, based on the typical size distribution assessment.

The use of powder form as fertiliser is acknowledged by the SCHER (approx. 1.5% of the tonnage used for this purpose), however an exposure assessment was not performed for this

form. In their CSR the registrant only presented exposure scenarios for the granulate, which is consistent with the information provided on the physicochemical properties of the substance. This indicates, that the use of the powder form as a fertiliser is not recognised by the registrant. This, however, is in conflict with the information presented at the registrant's website, and in the answers provided to ECHA by the manufacturer, as discussed above.

The registrant in its CSR specifies also use of gloves with 90% effectiveness. SCHER describes the same approach.

However, while in the CSR the effectiveness of gloves (90%) is described as being taken into account in the exposure assessment, the input parameters listed by the SCHER do not include the effect of dermal protection. So it is not clear, if the dermal exposure is modified for the effect of gloves.

It is assumed that the application by workers is conducted by use of tractors with open cabins, acknowledging, that a closed cabin would reduce the exposure level. However, as it is not known if the closed cabin is used by all operators – open cabin appears to be more appropriate for both the SCHER and the registrant.

Use of the respiratory protection, even for the short-duration tasks such as mixing and loading is not considered in either of the assessments[8]. However, its effect is described in the annexes to the SCHER report presenting input parameters for workers' exposure.

Methodology used for exposure assessment

Worker exposure

For the assessment of workers' exposure via inhalation due to mixing and application of the PERLKA fertiliser SCHER used measured data provided by the manufacturer. The linear relationship between the volume of the substance used and the air concentration was assumed. It was also assumed that the air concentrations provided by the manufacturer were 8h time weighted average (TWA) values and were directly compared to the calculated AOEL value.

The report states, that the use of different type of rotators (width of 12 m and 24 m) was assumed for small and large fields (the manufacturer used rotator of 15m), and assessment factors were applied to account for the differences in the volume of the dust generated. Linear relationship between the width of the rotator and level of exposure was assumed. The justification for such approach was not provided.

As dermal exposure is also relevant for the product, SCHER has used the UK model for granulate pesticide formulations (PHED)[9]. This tool was considered to be appropriate, although SCHER has acknowledged that the specific properties of the PERLKA - low dustiness – are not taken into consideration (the input parameters for this tool were presented in the annex). It is difficult to interpret the assessment results, as the information on the RMMs applied is unclear: in the report, it is stated that the use of gloves and working clothes was assumed. The tables 2.1 - 2.4 presented in Annex 2 of the SCHER opinion include the

[8] The registrant has informed ECHA that the use of respiratory protection is recommended for mixing and loading tasks.

[9] The UK has developed a model for operator exposure which is a surrogate for the US model the Pesticides Handlers Exposure Database (PHED).

information on the effectiveness of RPE (95%), but no information on the effectiveness of skin protection equipment.

The registrant in its CSR used the same exposure modelling tool - PHED. However, the registrant has adjusted its exposure estimations to reflect the particle distribution of the applied product, basing their dustiness evaluation on the standard test results published in reports (Sarawinski, 2014). This approach is also argued for by the registrant in its comments of the SCHER opinion.

The registrant in its comments on the SCHER opinion provides a discussion on the unsuitability of PHED for worker and consumer exposure assessment. One aspect mentioned is the scope of applicability to a specific type of product, which is also mentioned in the SCHER opinion. As opposed to the registrant in CSR, SCHER did not account for this issue in its assessment.

The manufacturer has recently submitted to ECHA a monitoring report, describing inhalatory and dermal exposures measured at 12 locations in UK (the executive summary report is included as Annex 2) while activities related to the daily application of 20 000 kg of PERLKA on 40-50 ha, with an application rate of 400-500 kg PERLKA/ha at each farm studied . It is noted in the monitoring report, that the monitored scenario is considered to represent an unrealistic worst case – use of double the volume that is considered by the manufacturer to be a realistic worst case. The report describes the exposures measured for workers loading the fertiliser hoppers and workers applying the substance using commercial spreaders separately. The systemic exposure values - combining the inhalatory and dermal exposures are for application – 0.000324 mg/kg bw/day, and for loading – 0.0171 mg/kg bw/day. These results of the exposure monitoring are significantly lower than those described in the Table 5 of the SCHER opinion.

Exposure of bystanders

The same methodology for exposure assessment to bystanders, based on the model by Martin et al. (2008), was used by SCHER and the registrant. The differences in the results are due to the use of differing drift percentage, area treated and application rate. The uncertainties related to these factors were discussed in the sections above.

Consumer exposure

The Puffer Pack Model recommended by UK was used by SCHER for the assessment of exposure of consumers applying PERLKA to their gardens. This model however is appropriate for the use of dustable powder formulations. In addition, an operator exposure model for granular formulations (PHED) was used. It is not clear – from the input parameters presented in the annexes to the SCHER opinion – what RMMs were used: while there is an indication of the effect of RPE, there is no mention of skin protection. The specificity of the product used (fraction of the low size particle) was not considered. The registrant in its comments on the SCHER opinion reflected on these shortcomings.

The REACH registrant in its CSR used the same assessment tool as used for modelling of exposure to workers – PHED, changing the method of the application to rotary grinder.

The same adjustments were made by the registrant as for the workers' exposure – the specificity of the product (its low content of small particles) was taken into consideration, with justification included.

SCHER also took into consideration the exposure of children – not considered specifically by the registrant, and exposure to residents following the application. The exposure of children was assessed as exceeding the level of AOEL.

Conclusions

There is a number of uncertainties related to the exposure assessment conducted by SCHER. These include the justifications for the use of specific assumptions (e.g. size of the fields, duration of application, effect of the RMMs on the modelled exposure levels) as well as unclarities on how the particle size was taken into account – on one hand a certain amount sold in powder form and on the other hand the use of a PHED modelling tool and how particle size is taken into account. Nevertheless, some of the assumptions made are likely to result in the possible overestimation of the exposure.

The monitoring results recently presented by the manufacturer, differing benchmark – DNEL values, derived in accordance with the REACH guidance and uncertainties related to the input parameters indicate, that the conclusions of the assessment need to be re-considered.

A reassessment has not been carried out at present due to the lack of access to the appropriate modelling tools, but based on the level of uncertainty the exposures are likely to be less than reported by SCHER.

2.1.4.2 Environment

Exposure assessment reported by SCHER was made under both 'normal' and 'reasonable worst case' application rates of PERLKA of 500 and 1000 kg formulation/ha, respectively. This corresponds to application rates of 225 kg a.s./ha and 450 kg a.s/ha, respectively.

Exposure modelling was based on the standard methodologies and models that are typically used for the risk assessment of plant protection products and biocidal products i.e. a standard set of 'FOCUS' modelling scenarios estimating exposure in soil, groundwater and in adjacent surface waters through either run-off or drainage.

2.1.5 Risk characterisation

2.1.5.1 Human health

Based on the AOEL) of 0.0043 mg/kg bw /day, the conclusion of the SCHER assessment is that harmful effects for humans and for the environment cannot be excluded. Risks were identified for the end-users (professional users as well as consumer users) and for residents and bystanders including children, if the formulation with Ca-cyanamide as the fertilising agent was applied at the recommended dose of 450 kg a.s./ha in the realistic worst case and 225 kg a.s./ha in the normal case.

Given the uncertainties in the DNEL derivation and the exposure assessment, the conclusion of SCHER would need to be reviewed in more detail in any further work. This conclusion is further strengthened by the results of the monitoring of inhalatory and dermal exposure submitted by the manufacturer, indicating that there is no risk for professional workers applying the product, comparing to the AOEL developed by SCHER. Should DNEL values derived for workers be used – the exposure level would be lower than DNEL values for both

groups of workers. It is likely, that the exposure of general public would also be lower than the relevant DNEL values.

It needs to be remembered that the above conclusions are applicable to the granular form of calcium cyanamide: the assessment of exposure for the powder form, representing, according to the manufacturer 1.5% of the volume used, may result in different conclusions.

In addition, the issue of other toxicological endpoints assessed for cyanamide – corrosivity, skin sensitisation, carcinogenicity and toxicity for reproduction may need to be taken into consideration in the risk assessment, affecting the conclusion on risk characterisation

2.1.5.2 Environment

Based on the PNEC value of 60 µg/L reported above, SCHER identified risks (RCR >1) in several of the surface water FOCUS scenarios, after both normal and realistic application rates of calcium cyanamide. Specifically, risk characterisation ratios >1 were observed in the R2(s), R3(s) and R4(s) run-off scenarios up to 28 days after application at normal application rates and up to 50 days after application at realistic worst case application rates. Risk characterisation ratios were <1 in all drainage scenarios.

SCHER concluded that, on the basis of the modelling performed, application of PERLKA up to a rate of 500 kg/ha is unlikely to pose a risk to surface waters via drainage. However, risks to surface waters via run-off cannot be excluded. Risk characterisation ratios >1 were also calculated for the terrestrial compartment. Despite RCR values >1 for the terrestrial compartment, SCHER concluded that adverse effects to earthworms were unlikely to occur in practice.

The risk assessment carried out according to the biocides regulation did not identify risks from cyanamide to the aquatic (surface water or sediment) compartment, terrestrial compartment or groundwater, but did predict risks to groundwater (defined as concentrations > 0.1 µg/L at 1m soil depth) for some FOCUS scenarios (representative locations) based on the concentration of the metabolite thiourea.

However, according to the practice followed under the BPR, cyanamide was recommended for approval on the basis that safe use could be demonstrated for at least one representative location. Final opinions on the use of cyanamide in PT3 and PT18, recommending its approval, were adopted by the BPC in June 2016. Final decisions on these applications are currently pending from the Commission.

No chronic data were reported by SCHER. However, the SCHER opinion notes that chronic exposure and toxicity of calcium cyanamide cannot be excluded as the formulation releases the active substance slowly and it can therefore be present in the environment for considerable periods during the growing season. No PNEC for the sediment compartment was derived in the SCHER opinion.

<u>Discussion</u>

The SCHER conclusion that there are unacceptable risks for the aquatic compartment under some of the FOCUS scenarios assessed appears to be reliable (surface water run-off scenarios R2 [stream], R3 [stream] and R4 [stream] up to 50 days after application), particularly noting that the aquatic PNEC used (60 µg/L) was derived from acute toxicity data only and that a

large reduction in application rate would be needed to result in RCR values <1 in the relevant FOCUS scenarios. On this basis, **the use of calcium cyanamide as a fertiliser could pose an unacceptable risk to the environment.**

There are notable differences in the ecotoxicological dataset for calcium cyanamide used by SCHER to derive PNEC values and the ecotoxicity datasets collated in recent CLP and Biocidal Product Authorisation dossiers for the active substance cyanamide, which is the hydrolysis product of calcium cyanamide. As hydrolysis is acknowledged to occur rapidly in the environment it would have been appropriate for SCHER to read-across ecotoxicity data for cyanamide when deriving PNEC values for the risk assessment of calcium cyanamide.

The use of the more comprehensive ecotoxicity dataset for cyanamide to derive aquatic and terrestrial PNEC values for calcium cyanamide is likely to improve the robustness (and reduce the uncertainty) of any subsequent environmental risk assessment. In relation to this, a key observation is that the PNEC values derived as part of the evaluation of cyanamide as a biocidal active substance are significantly (up to two orders of magnitude) lower than those derived by SCHER for calcium cyanamide. This suggests that whilst SCHER identified risks to the environment on the basis of their assessment, these risks may have been underestimated.

A preliminary re-assessment of the risk characterisation for the aquatic compartment presented in the SCHER opinion using the PNEC values from the biocides assessment of cyanamide suggests that risks would be identified in a greater number of aquatic scenarios than those identified by SCHER, specifically drainage scenario D6 (ditch) and run-off scenarios R1 (stream). In addition, risks in the scenarios already associated with RCR>1 would occur up to 100 days after application, rather than up to 50 days.

However, this preliminary assessment requires further consideration, notably in relation to ensuring the appropriateness of the physico-chemical parameters and the application rates of calcium cyanamide used for modelling (and any necessary conversions between exposures and effects data expressed as cyanamide or calcium cyanamide). It is also notable that the SCHER assessment did not explicitly address the potential for risks to aquatic sediments. The appropriateness of FOCUS modelling approaches to fertilisers (rather than plant protection products and biocides), also needs to be ensured.

Risks to the terrestrial compartment, whilst considered negligible by SCHER, may also benefit from re-evaluation given the availability of additional relevant information on the chronic effects of cyanamide to soil arthropods (such as the collembolan *Folsomia* spp.) and plants, which are associated with PNEC values several orders of magnitude lower than the PNEC value derived by SCHER for calcium cyanamide from acute ecotoxicity data for earthworms.

Further, the assessment under the biocides regulation incorporated an assessment of the risk from the metabolite thiourea. If considered relevant, the assessment of the use of calcium cyanamide as a fertiliser could also be extended to take account of the risks posed by metabolites and breakdown products of cyanamide in the environment.

Justification for an EU wide restriction measure

Calcium cyanamide, as discussed in this review, falls within the scope of the EC Fertiliser Regulation Annex I, which as such allows it to be placed on the EU market as a fertiliser in

any Member State[10]. As pointed out in this report, calcium cyanamide as a fertiliser is widely available and used in EU Member States. Because it is widely used in the EU a potential restriction would address the risk the substance poses to the environment, and possibly to human health on a Union-wide basis. At the same time an EU-wide restriction would avoid any risk of creating unequal market conditions and ensure a 'level playing field' among the EU Member States.

Baseline

4.1 Manufacture and uses

Calcium cyanamide is the inorganic compound with the formula $CaCN_2$. This calcium derivative of cyanamide (CN_2^{2-}) was first synthesized in 1898 by Adolph Frank and Nikodem Caro (Frank-Caro process). One of its main uses is a fertiliser use and this use has been well-known since the start of the last century. Calcium cyanamide is also commercially known as nitrolime.

Based on the registration dossier CSR 130 000 tonnes of calcium cyanamide has been annually manufactured in 2010-2014, reportedly on 1-10 sites. In addition to this 100 tonnes was imported and 7 000 tonnes exported in the same time period. Furthermore, 52 000 tonnes/year of calcium cyanamide was reported to be used by professional users as a fertiliser and more than the same amount by industry. 1 000 tonnes/year are used by private individuals as a fertiliser for their home crops and lawns.

Table 8. Uses of calcium cyanamide (source: REACH registration dossier)

Activity	Tonnes/year
Manufacture	130 000
Formulation (incl. fertiliser.)	130 000
Industrial use - steel, metal industry	44 500
Industrial use- intermediate in chemical manufacture	25 000
Professional use as a fertiliser	52 000
Consumer (fertiliser) use in private properties	1000

As mentioned above, there are two known calcium cyanamide fertiliser products in the EU, both manufactured by AlzChem AG: 'Kalkstickstoff', the powdered form with typical concentration of calcium cyanamide about 58-68 %, and PERLKA, a granulated mixture of calcium cyanamide with other main components. The product with the trade name PERLKA is sold in granulated form, a calcium cyanamide content of about 45 % w/w and widely available in Europe. According to SCHER PERLKA accounts for 98.5%.

[10] Regulation (EC) No 2003/2003 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 13 October 2003 was introduced to ensure the free circulation on the Internal Market of "EC Fertilisers" i.e. those fertilisers that meet the requirements of the legislation in terms of nutrient content, safety, and absence of adverse effects on the environment.

AlzChem, a manufacturer of PERLKA, advertises calcium cyanamide as a fertiliser and for its ability to deliver phytosanitary benefits, i.e. help to reduce pests and increase soil fertility. Calcium cyanamide is stated to provide slow- and sustained-release nitrogen[11] and to inhibit the resting spores of soil-borne pathogens on germination. Recommended use for winter cereals is 100-200kg/ha before sowing, 150-300kg/ha after sowing and 200-300kg/ha as a top-dressing in spring when vegetation starts. For summer cereals and malting barley the amounts are 200-300kg/ha before sowing and 300 and 200-300kg/ha respectively after sowing/emerging. For potatoes, the recommended amount is 300-500kg/ha before laying and 300-500kg/ha between and emerging. https://www.alzchem.com/en/agriculture/calcium-cyanamide-perlka/application/agriculturefarming.

The proposed per-hectar-amounts are in the same range as listed in the SCHER opinion. A larger recommendation was found in Finland, where suggested applications rates for cabbage appear to be 400-1500kg/ha before and 300-400kg/ha after the planting, whereas for other crops the recommendations appeared alike elsewhere (e.g. for rapeseed 250kg/ha at fall when seeding) https://viljelijanberner.fi/perlka-kalkkityppi-600kg.html.

Impact assessment

Calcium cyanamide is commonly used as a fertiliser for agricultural and horticultural crops and nutrients may be added in alternative combinations. There are other fertiliser mixes providing somewhat similar effect. Calcium cyanamide is advertised as a multipurpose fertilizer. According to AlzChem it is the only fertilizer, containing the nutrient element nitrogen in the so-called NCN binding form, which helps ensure that plants are supplied with nitrogen over a longer time period as and when needed. Trenkel (2010) discusses different ways and alternatives for controlling release of fertilisers in soil. Additionally, AlzChem states that fertilizing with calcium cyanamide also increases the biological activity of the soil and forces soil-borne pathogens into retreat by the stronger natural competition.

The second nutrient element that calcium cyanamide contains, calcium, is mostly water-soluble and so is immediately available to the plants. Calcium cyanamide improves the lime balance of the soil. Based on the description by AlzChem, on soils that are fertilised with calcium cyanamide plants receive the ideal amount of nitrogen, the structure of the soil is improved through the addition of valuable lime, and the soil hygiene is improved at the same time.

Commonly in agriculture lime and nutrients are added separately. Such an option should be readily available, however, it includes an additional application and as such requires more labour and potentially additional machinery. As such, the use could end up being more costly.

There has also been hints towards positive phytosanitary effect of calcium cyanamide. Based on a brief web search some scientific studies can be found testing phytosanitary impacts of calcium cyanamide e.g. inhibitory effect of calcium cyanamide on foodborne pathogens and use of it as an alternative to methyl bromide in soil fumigation see e.g. Simujide et.al. (2013) and Bletsos (2005) respectively. This suggests, that it may indeed have some effect on soil

[11] Recently, also dicyandiamide (DCD) has been discussed as a possible substance capable to slow down and control release of fertilizers and nitirification.
https://www.fertilizer.org//images/Library_Downloads/2010_Trenkel_slow%20release%20book.pdf

hygiene besides fertilizer effect which has to be taken into account when alternatives are sought for.

Assumptions, uncertainties and sensitivities

As part of the stakeholder consultation the registrant has provided an executive summary on the results obtained from a recent (GLP compliant) OPEX study. The whole study has not been used for this review. The registrant has also informed ECHA that based on request by the Commission it has included in its dossier a proposal for an extended one-generation reproductive toxicity study and updated the dossier accordingly (by 27 October 2017). For a complete human health assessment of calcium cyanamide the results of these studies should also be considered if further work on the topic is to be undertaken.

It is obvious that in the Member States there are numerous resellers and both, professional and consumer users. Resellers tend to have their own recommendations for use rates based on specific local conditions depending on e.g. soil types, length of the growing season, typical crop varieties, etc. Resellers are supposed to acknowledge and follow the practises described in the CSR. A common regulation e.g. via a restriction would be a way to harmonise and guide the ways resellers prepare their recommendations. On the user side, non-professionals may currently be less aware of potential human health and environmental threats of their fertiliser applications and a common regulation could enhance safe use practises and use levels among them.

Conclusion

Based on its preliminary assessment, ECHA advises further work on assessing the need for a restriction for calcium cyanamide used as a fertiliser. ECHA's assessment is based upon the data used by SCHER in preparing its opinion, and also data available to ECHA from the REACH, CLP and BPR regulatory processes.

Risks to the aquatic environment under some exposure scenarios appear likely and may have been underestimated in previous assessments. Risks to the terrestrial compartment should also be reconsidered.

There are also a number of uncertainties associated with the potential risks for human health of using the granulated form of calcium cyanamide as fertiliser. The risk associated with the use of the powdered form of calcium cyanamide as a fertiliser has not been considered.

For these reasons further work is required to assess the risks for the environment and human health in more detail. ECHA makes several recommendations to clarify the areas of uncertainty.

ECHA has evaluated the risks to human health and to environment from the use of calcium cyanamide as a fertiliser. This preliminary assessment was carried out at the request of the Commission[12] following an opinion by SCHER which 'raises serious concerns about the safe use of calcium cyanamide as a fertiliser'. ECHA was therefore asked to carry out its preliminary

[12] https://echa.europa.eu/documents/10162/13641/calcium_cyanamide_request_to_echa.pdf/6ccd9451-52fd-abab-f9cd-04030ae2b19d

assessment taking into account additional information it has from the REACH, CLP and BPR processes. This preliminary assessment is based upon the evidence available to ECHA.

ECHA's preliminary assessment has found that the use of calcium cyanamide as a fertiliser could pose an unacceptable risk for the environment. This is consistent with SCHER's opinion that 'harmful effects for [] the environment cannot be excluded'. ECHA has reached the same conclusion utilising not only the ecotoxicological datasets that have been used by SCHER, but also considering the data available from the REACH registration for calcium cyanamide and the review of cyanamide in the CLH and BPR processes. Cyanamide is the hydrolysis product of calcium cyanamide and since hydrolysis is acknowledged to occur rapidly in the environment it is appropriate to read-across ecotoxicity data for cyanamide when deriving PNEC values for the environmental risk assessment of calcium cyanamide.

The further use of a more comprehensive ecotoxicity dataset for cyanamide to derive aquatic and terrestrial PNEC values for calcium cyanamide is likely to improve the robustness (and reduce the uncertainty) of any subsequent environmental assessment. In relation to this, a key observation is that the PNEC values derived as part of the evaluation of cyanamide as a biocidal active substance are significantly (up to two orders of magnitude) lower than those derived by SCHER for calcium cyanamide. This suggests that whilst SCHER identified risks to the environment on the basis of their assessment, these risks may have been underestimated.

A preliminary re-assessment of the risk characterisation for the aquatic compartment presented in the SCHER opinion using the PNEC values from the biocides assessment of cyanamide suggests that risks would be identified in a greater number of aquatic scenarios and that the risks in these scenarios (which already have an RCR>1) would occur over a longer period of time after application.

Furthermore, the potential for risks to aquatic sediments and the appropriateness of FOCUS modelling approaches to fertilisers needs to be clarified. Risks to the terrestrial compartment may also benefit from re-evaluation and if considered relevant, the assessment could also be extended to take account of the risks posed by metabolites and breakdown products of cyanamide in the environment.

Concerning **human health assessment**, there are a number of uncertainties associated with the exposure assessment conducted by SCHER. In addition, there are also uncertainties related to the derivation of the benchmark level used: instead of the AOEL of 0.0043 mg/kg bw/d which was used, it appears that potentially higher AOEL and DNEL values could have also been justified. The uncertainties include lack of justifications for the use of specific assumptions (e.g. size of the fields, duration of application, effect of the RMMs on the modelled exposure levels). The assumptions made are likely to result in the overestimation of the exposure. The uncertainties are further identified in the sections describing the elements of the evaluation of the exposure assessment.

As a result of these concerns, the assessment of human health risks by SCHER would benefit from further refinement, potentially based on alternative methodologies or using a different set of benchmarks and input parameters. Such further analysis may support the conclusions drawn by SCHER, or indicate an alternative outcome.

Although a much smaller proportion of the total use, the risk of the powdered form of calcium cyanamide needs to be assessed. The majority of the data available to ECHA are primarily based upon the use of the granulated form of calcium cyanamide. The risk associated with

the powdered form, with a significantly smaller particle size, has thus far not been adequately characterised.

In addition, the issue of other toxicological endpoints assessed for cyanamide – corrosivity, skin sensitisation, carcinogenicity and toxicity for reproduction – if taken into account – may affect the risk characterisation of the use of calcium cyanamide as a fertiliser.

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Annex 1: Stakeholder consultations

During the preparation of the report, the only registrant, AlzChem was consulted. AlzChem provided further information as requested.

Annex 2: Monitoring results – executive summary (source: provided to ECHA by AlzChem 10 August 2017)

Executive summary of preliminary results obtained from the study 'Determination of operator exposure during typical activities associated with mixing/loading and application of PERLKA® (a granular formulation containing 450 g/kg calcium cyanamide at farm locations in Europe.

In order to determine the exposure of agricultural workers to the granulated formulation of calcium cyanamide (PERLKA®) used as fertiliser, a GLP compliant OPEX study was performed (see reference 3). As SCHER calculated the highest AOEL utilisation for a large field scenario the study was designed to represent such a large field scenario as worst case. To enable the spreading of these high quantities of PERLKA the study was conducted in co-operation with some of the largest vegetable growers in the UK.

At each of the farm locations approximately 20,000 kg formulated product (PERLKA®) equivalent to approximately 9000 kg calcium cyanamide was handled on a single working day. The application rate ranged from 400 to 500 kg PERLKA/ha and the work rate per day from 40 to 50 ha. It should be noted that in our opinion this scenario still represents an unrealistic worst case as it involves two times the volume we consider a reasonable worst-case application rate per day (reference 2).

In the OPEX study the dermal and inhalation exposure to operators was determined during typical activities associated with loading and application of PERLKA®. Twelve operators (loaders) were monitored during loading of the fertiliser hoppers and twelve operators (applicators) were monitored during the application using commercial spreaders. All operators were wearing a cotton/polyester blend coverall as outer dosimeter. The inner dosimeter consisted of a full length cotton underwear garment covering the arms, legs and torso. Nitrile gloves were worn during handling the product and safety glasses and dust masks during loading. Hand exposure was assessed by the hand wash procedure. Exposure of the head was assessed by face/neck wipes. Potential inhalation exposure was assessed using Xad-2 OVS filters connected via a tube to a suitable air sampling pump.

As the exposure values for applicators and loaders differed substantially the statistical calculations were done separately for operators 1 to 12 (applicators) and 13 to 24 (loaders). Individual operator exposure results can be found in the summary tables (reference 4). All results are corrected for field recovery when <70% as explained in the tables in detail.

According to the EFSA guidance on assessment of exposure for operators the 75th percentile is considered as appropriate for the assessment of medium- /long-term operator exposure. In addition, the 95th percentile is provided because PERLKA is used only once per crop, i.e. usually before sowing or planting, and thus represents an acute exposure scenario.

The conversion of the actual dermal exposure values into systemic exposure values assumes a dermal absorption of 10 %, which is considered appropriate by SCHER for the use of calcium

cyanamide as fertiliser. For the inhalation exposure 100 % absorption is used for applicators and 10 % for loaders because for loaders wearing a dust mask (90 % protection factor) is considered mandatory.

For a revised operator risk assessment the systemic exposure values derived from the exposure values determined in the OPEX study are compared with relevant acceptable exposure levels (AELs).

As AELs for cyanamide were established in 2016 in the framework of the EU biocide regulation (see reference 1, page 17), these AELs were translated into calcium cyanamide by using a conversion factor of 1.905 taking into account the respective molecular mass (80.1/42.04). This calculation is based on the conservative assumption that 100 % of the calcium cyanamide is converted into cyanamide.

Consequently, the medium-/long-term AEL for cyanamide (0.01 mg/kg bw/d) is equivalent to 0.019 mg/kg bw/d calcium cyanamide. The acute AEL for cyanamide (0.05 mg/kg bw/d) equals 0.095 mg/kg bw/d calcium cyanamide.

Total systemic exposure in mg/kg bw/ was calculated as follows:
Applicators 75th percentile:
[2.341 µg/kg bw/day (actual Dermal exposure) x 0.1 (10 % dermal absorption) + 0.08268 µg/kg bw/day (Inhalation exposure)]/1000 = 0.000324 mg/kg bw/day.

Loaders 75th percentile:
[148.03 µg/kg bw/day (actual Dermal exposure) x 0.1 (10 % dermal absorption) + 23.3 µg/kg bw/day (Inhalation exposure) x 0.1 (90 % protection from mandatory dust mask)]/1000 = 0.0171 mg/kg bw/day.

From the 75th and 95th percentile exposure values it is obvious that the exposure of the loaders is substantially higher compared to the exposure of the applicators. Despite this, the systemic exposure of all operators is below the respective Acceptable Exposure Level. In addition, it can be seen from the individual loader exposure values that there is a high variation between the individual loaders. We are currently analysing the possible reasons for this high variability and are confident that by implementing additional risk mitigation measures the exposure for the loaders can be reduced further.

It may be concluded that based on the results of the OPEX study the exposure of operators to calcium cyanamide used as fertiliser is well below the acceptable operator exposure level (AOEL). The exposure of applicators is generally much lower than the exposure of loaders. For the relevant acute exposure scenario applicator exposure accounted for 2.03 % of the systemic AOEL and loader exposure for 29.8 % of the systemic AOEL. Additional risk mitigation measures are likely to further reduce loader exposure.

Annex 3: Derivation of DNEL values

DNELs

Long-term DNEL derived in the CSR of the REACH registration for Ca-cyanamide and the long-term DNEL that would result when applying the LOAEL of 1.3 mg/kg bw/d instead the NOAEL of 11 and by not applying AF for allometric scaling:

	CSR of the REACH registration	Proposed by ECHA
Inhalation, worker	NOAEL 11 mg/kg bw/d Modification starting point: x 1/0.38 m^3/kg bw/d x 50/100 (absorption) x 6.7 m^3/10 m^3 Dose descriptor: 9.70 mg/m^3 Assessment factors: 12.5 - 1 duration (chronic) - 2.5 interspecies - 5 intraspecies workers **DNEL: 0.78 mg/m^3** **SCOEL OEL 1 mg/m^3**	LOAEL 1.3 mg/kg bw/d Modification starting point: x 1/0.38 m^3/kg bw/d x 50/100 (absorption) x 6.7 m^3/10 m^3 Dose descriptor: 1.15 mg/m^3 Assessment factors: 37.5 - 3 LOAEL to NOAEL - 1 duration (chronic) - 2.5 interspecies - 5 intraspecies workers **DNEL: 0.03 mg/kg bw/d**
Dermal, worker	NOAEL 11 mg/kg bw/d Modification starting point: x 10 (absorption 10%) Dose descriptor:110 mg/kg bw/d Assessment factors: 50 - 1 duration (chronic) - 4 allometric scaling - 2.5 interspecies - 5 intraspecies workers **DNEL: 2.2 mg/kg bw/d**	LOAEL 1.3 mg/kg bw/d Modification starting point: x 10 (absorption 10%) Dose descriptor: 13 mg/kg bw/d Assessment factors: 37.5 - 3 LOAEL to NOAEL - 1 duration (chronic) - 1 allometric scaling - 2.5 interspecies - 5 intraspecies workers **DNEL: 0.35 mg/kg bw/d**
Inhalation, general population	NOAEL 11 mg/kg bw/d Modification starting point: x 1/4 (allometric scaling) x 60 kg bw x 1/20 m^3 x 50/100 (absorption) Dose descriptor: 4.13 mg/m^3 Assessment factors: 25 - 1 duration (chronic) - 2.5 interspecies - 10 intraspecies population **DNEL: 0.16 mg/m^3**	LOAEL 1.3 mg/kg bw/d Modification starting point: x 1/1 (allometric scaling) x 60 kg bw x 1/20 m^3 x 50/100 (absorption) Dose descriptor:1.95 mg/m^3 Assessment factors: 75 - 3 LOAEL to NOAEL - 1 duration (chronic) - 2.5 interspecies - 10 intraspecies population **DNEL: 0.026 mg/m^3**
Dermal, general population	NOAEL 11 mg/kg bw/d Modification starting point: x 10 (absorption 10%) Dose descriptor: 110 mg/kg bw/d Assessment factors: 100 - 1 duration (chronic) - 4 allometric scaling	LOAEL 1.3 mg/kg bw/d Modification starting point: x 10 (absorption 10%) Dose descriptor: 13 mg/kg bw/d Assessment factors: 75 - 3 LOAEL to NOAEL - 1 duration (chronic)

	- 2.5 interspecies - 10 intraspecies population **DNEL: 1.1 mg/kg bw/d**	- 1 allometric scaling - 2.5 interspecies - 10 intraspecies population **DNEL: 0.17 mg/kg bw/d**
Oral, general population	NOAEL 11 mg/kg bw/d Dose descriptor: 11 mg/kg bw/d Assessment factors: 100 - 1 duration (chronic) - 4 allometric scaling - 2.5 interspecies - 10 intraspecies population **DNEL: 0.11 mg/kg bw/d**	LOAEL 1.3 mg/kg bw/d Dose descriptor: 1.3 mg/kg bw/d Assessment factors: 75 - 3 LOAEL to NOAEL - 1 duration (chronic) - 1 allometric scaling - 2.5 interspecies - 10 intraspecies population **DNEL: 0.017 mg/kg bw/d**