Scientific Committee on Health and Environmental Risks

SCHER

Final Opinion

on

Potential risks to human health and the environment from the use of calcium cyanamide as fertiliser

SCHER adopted this Opinion at its plenary meeting on 22 March 2016.

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SCHER

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All Declarations of Working Group members and supporting experts are available at the following webpage:
http://ec.europa.eu/health/scientific_committees/environmental_risks/members_committee/index_en.htm

ABSTRACT

The purpose of this Opinion is to assess potential risks to human health and the environment from the use of calcium cyanamide as fertiliser. Where appropriate, data on hydrogen cyanamide were also considered as this substance is a primary intermediate formed by the degradation of calcium cyanamide when applied as fertiliser or after organisms have been exposed to it. The SCHER has collected available data on physicochemical properties, agricultural practices and (eco) toxicology of this substance. These were used to derive an acceptable operator exposure level (AOEL) as well as the predicted no effect concentrations (PNECs). Subsequently the SCHER calculated predicted environmental concentrations (PECs) using the common application rates of the fertiliser and exposure models. The resulting PECs were compared to the PNECs to calculate the risk characterization ratios (RCRs) for environmental compartments.

With regard to human health, the SCHER has calculated human health risks using worker exposure models for the use of calcium cyanamide as fertiliser, based on approaches used for registration of plant protection products. Exposure calculations were performed for both professional and private use scenarios and additionally for by-standers and residents, including children.

The 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.

Keywords: calcium cyanamide, fertiliser, human toxicity, environmental effects, risk assessment

Opinion to be cited as:

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EXECUTIVE SUMMARY

The purpose of this Opinion was to assess potential risks to human health and the environment from the use of calcium cyanamide as fertiliser.

Information has primarily been obtained from the dossier presented by the manufacturer to support its request for registration of the substance calcium cyanamide as a fertiliser in the European Union and the evaluation of the pesticide hydrogen cyanamide prepared by European Food Safety Authority (EFSA) in 2010. Other relevant scientific papers from the literature were also used if judged relevant with regard to the questions asked. Where appropriate, data on hydrogen cyanamide were also considered as this substance is a primary intermediate formed by the degradation of calcium cyanamide when applied as fertiliser or after organisms have been exposed to it.

The SCHER notes 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 has chosen to apply, as far as possible, the methodology developed for the registration of plant protection products.

The SCHER has collected available data on physicochemical properties, agricultural practices and (eco)toxicology. These were used to derive an acceptable operator exposure level (AOEL) as well as predicted no-effect concentrations (PNECs) for the environmental risk assessment. Subsequently the SCHER calculated predicted environmental concentrations (PECs) using the common application rates of the fertiliser and exposure models. The resulting PECs were compared to the PNECs to calculate risk characterisation ratios (RCRs).

The SCHER addressed potential uncertainties in the risk assessment that relate to the use of exposure models, physicochemical characteristics of the particles and some missing data on chronic (eco)toxicity. However, the SCHER concluded that this does not influence the outcome of the risk assessment. Based on kinetic data available, the SCHER concluded that calcium cyanamide is transformed into cyanamide after oral administration to experimental animals, as well as to humans, as a result of hydrolysis, and that toxic effects observed for calcium cyanamide were mainly attributable to cyanamide toxicity. The SCHER adopted a lowest observed adverse effect level (LOAEL) of 1.3 mg calcium cyanamide/kg bw/d based on a published rat study and derived a provisional AOEL of 4.3 µg/kg bw/d using a safety factor of 300.

With regard to human health, the SCHER has calculated human exposure using worker exposure models. The use of calcium cyanamide as fertiliser was based on data measured for inhalatory exposure as well as on default values attributed to exposure calculation models judged appropriate for granulated materials. Exposure calculations were performed for both professional and private use scenarios and additionally for bystanders and residents, including children.

For the environmental risk assessment, the SCHER derived a $PNEC_{short\text{-}term}$ value of 60 µg/L for the aquatic environment, based on an assessment factor of 100 and a lowest reported 48h-EC50 of 6 mg/L (using ecotoxicity data for three distinct taxonomic groups). For the terrestrial environment a PNEC of 17.3 mg/kg soil dw was derived from earthworm toxicity data using an assessment factor of 10.

Based on available data the SCHER has estimated the PECs in soil, groundwater and surface water using the FOCUS scenario approach originally designed for the evaluation of pesticides.

The SCHER concluded that harmful effects for humans and for the environment cannot be excluded. Risks were identified for the end-users (farmers, as well as private users) and for residents and bystanders including children, if the formulation with 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. In addition, the SCHER identified risks for the contamination of the aquatic environment.

Recommendations for protective measures provided by the manufacturer are not considered sufficient to ensure a safe application of calcium cyanamide for the operator. It is unlikely that additional measures will lead to safe use for the operators due to increased inconveniences experienced during application. Furthermore, no protective measures are available for bystanders and residents who are also exposed. Private use of calcium cyanamide as fertiliser is not recommended by the SCHER.

To reduce the risk to the aquatic compartment to a RCR < 1, the most common application rate of calcium cyanamide needs to be lowered by a factor of 56. Similarly the reduction factor needed for protecting the soil environment would have to be 17.

The SCHER was also asked to identify major gaps in scientific knowledge. Gaps identified are described in paragraph 4.4.

1. BACKGROUND

On 8 March 2013, DG ENTR requested DG SANCO to consult the SCHER for its opinion on the potential risks for human health and the environment from the use of calcium cyanamide as fertiliser. In May 2014, the SCHER delivered an Opinion to the Commission, and gave the company manufacturing the substance the opportunity to comment on the Opinion by the end of July 2014. In September 2014, the company submitted a revised chemical safety report to ECHA in the context of the REACH Regulation.

DG GROW asked the company to list all the relevant available background information in its possession for the finalisation of the SCHER Opinion. A cut-off date of 31.03.2015 for submission of new data was accepted by the company.

Following receipt of the information provided by the company on the date of 31.03.2015, the data were submitted to the SCHER for its assessment.

The SCHER is asked now to re-evaluate two main issues in this assessment:

(1) the application rates used should be based on consumer instructions or recommendations, provided by the company to DG GROW before 1 April 2015 and

(2) the choice of assessment model shall clearly be justified in the SCHER Opinion. Furthermore, the use and/or calculation of model parameters should be explained and justified: in particular, this applies to threshold values (which type of value, selection and interpretation of underlying toxicity test, assessment factor), the dermal absorption rate, the inhalable fraction, the particle size and any other parameters that the SCHER may identify in the course of its assessment as being relevant.

2. TERMS OF REFERENCE

The SCHER is requested to answer the following questions:

1. *Taking into account all relevant information that is available before 1 April 2015, can the use of both the powdered and granulated form of calcium cyanamide be considered safe for human health and the environment?*
2. *In case of risks identified by the SCHER, are the protective measures recommended by the manufacturer sufficient to ensure a safe use of calcium cyanamide as fertiliser?*
3. *In case of potential risk for the environment, which application rate per concerned crops would not create any detrimental effect under the relevant soil and climatic conditions?*
4. *In case major gaps are identified in the scientific knowledge of the hazard or exposure associated with the use of calcium cyanamide, how does the SCHER suggest closing those gaps within a reasonable period of time?*

3. SCIENTIFIC RATIONALE

3.1. Introduction and scope

In order to be able to answer the questions, the SCHER studied the extensive REACH dossier presented by the manufacturer to support its request for registration of the substance calcium cyanamide as a fertiliser in the European Union. The SCHER also assessed several papers from the scientific literature. The Committee reviewed these and made an inventory of the documentation before preparing the Opinion. The SCHER selected the main documents from the literature to underpin the Opinion with respect to the questions asked. Therefore, the SCHER took only into account the papers and documents that related directly to the problem posed. Other documents have been judged and evaluated by the SCHER as being of secondary usefulness compared to the documents of main importance. Basic documents used were the dossier (AlzChem Trostberg, 2010 and Pusch, 2014) presented by the manufacturer and the evaluation of the pesticide hydrogen cyanamide prepared by the European Food Safety Authority – EFSA (EFSA, 2010).

In April 2015, DG GROW submitted new Terms of Reference requesting the SCHER to take into account the revised registration dossier (SCC, 2015).

Section 3.2 of the SCHER Opinion presents the knowledge available on the physico-chemical properties of the substance, including its fate and behaviour, the intended use of the substance in the formulation as a fertiliser and an overview of the toxicological and ecotoxicological information. Section 3.3 presents the risk assessment based on the final selection of the data, whilst section 3.4 provides a summary of the results. Finally, Chapter 4 presents the opinion of the SCHER with respect to the questions asked.

For some endpoints, studies on calcium cyanamide are limited. Additionally, some of the studies were not performed in line with internationally accepted test guidelines and are in many cases not publicly available. The SCHER focussed on data and information on kinetics and toxicity of calcium cyanamide but, if appropriate, data on cyanamide were also considered. All data were evaluated with regard to reliability, relevance and scientific validity according to internationally accepted criteria. Data considered being of the highest reliability included data from studies carried out according to valid, internationally or nationally accepted testing guidelines - preferably performed according to Good Laboratory Practice (GLP) - or in which all parameters described were closely related and comparable to a guideline method. In addition peer-reviewed information was taken into account. Data were used for an overall weight of evidence approach.

3.2. State-of-the-art

3.2.1. Some history on calcium cyanamide

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 low analysis (1 - <12%) excreta deposits. It is produced in 1,000 to >3,000°C electric arc furnaces by burning black coal and white limestone in the presence of atmospheric nitrogen. Energy costs represent the bulk of the cost of production of calcium cyanamide. The main use of calcium cyanamide is in agriculture as a fertiliser. Because calcium cyanamide is in general slow acting, one application at a rate of about 1,000 kg/ha, according to the application information (worst case) can last the length of the growing season. However, when calcium cyanamide is applied at this rate,

particularly in cool and/or dry conditions, it is necessary to delay planting until the high concentrations of plant-penetrating 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. The observation that calcium cyanamide exhibits phytotoxicity led to its use as a herbicide (Hartmann, 2000). The SCHER focuses its considerations on doses recommended in manufacturer's information sheets taking an application rate of 1,000 kg of formulation/ha as a realistic worst case scenario and 500 kg/ha as a normal scenario.

3.2.2. Basic compound properties

General data:

- Name: calcium cyanamide.
- Other names: cyanamide calcium salt, Kalkstickstoff, Lime Nitrogen, Nitrolime, calcium carbimide
- Molecular formula: $CaCN_2$
- Molecular structure: $[NCN]^{2-}$ Ca^{2+}; $[Ca^{2+}]$ $[^{-}N=C=N^{-}]$
- Molecular weight: 80.11 g/mol
- CAS Number: 156-62-7

Relevant physico-chemical properties:

- Melting range (according DIN 51004): 1145 to 1217°C, 1340°C (EpiSuite 3.10)
- Density pure: 2.36 g/cm^3 at 25°C
- Water solubility: 29.4 g/L at 20°C, 19.3 g/L at 25°C; pH of aqueous solutions are strongly alkaline
- log P_{ow}: -0.20 for $CaCN_2$ (calculated with EpiWin 3.10).
- Vapour pressure (mm Hg, 25°C) 4.58E-19 (EpiSuite 3.10) or 0 Pa
- Adsorption/desorption: The log K_{oc} was measured to be <1.25 at pH 5.5 and 7.5. This was equivalent to a K_{oc} of 17.8 dm^3/kg. The corresponding K_{om} was 10.5 dm^3/kg.

Calcium cyanamide is a white solid. Calcium cyanamide technical grade is a solid grey to black powder with a characteristic odour at 20°C and 1,013 hPa. In granular form the product is known as PERLKA. Industrial-grade calcium cyanamide contains, in addition to $CaCN_2$, ca. 20% CaO and 10 – 12% free carbon, which gives the product its grey-black colour. It can also contain a small amount of nitrides formed from silica and alumina. The total nitrogen content varies from 22 – 25%, depending on the raw materials used. Of the total nitrogen, 92 – 95% is present as cyanamide and 0.1 – 0.4% as dicyandiamide; the remainder is present as nitrides (Güthner and Mertschenk, 2006).

The silica and alumina nitride, dicyandiamide, and other minor impurities are not expected to contribute to the toxicological properties of the formulations, thus it was justified to treat the substance as mono-constituent. The formulation PERLKA has a calcium cyanamide content of 44 to 45%. The SCHER used a content of 45% in PERLKA as PERLKA accounts for 98.5 % of all calcium cyanamide fertilisers sold. Other environmentally relevant properties of calcium cyanamide are discussed in the sections below.

PERLKA is a solid, granular formulation and has a typical particle size distribution as shown in Table 1 (AlzChem Trostberg, 2010).

Table 1: Typical particle size distribution of PERLKA (AlzChem Trostberg, 2015).

No.	Size (µm)	Cumulative Distribution (%)
#1	<160	0.1
#2	<315	0.2
#3	<500	0.3
#4	<1000	1.5
#5	<1700	23.5
#6	<2500	71.6
#7	<3550	99.3
#8	>3550	100

From these data the median particle diameter was established at 2100 µm. The SCHER selected a fraction of 0.2 percent as the relevant drift percentage for the calculations for human exposure, taking into account the values in Table 1 and also the information available in the CSR report.

Wherever relevant the SCHER used these physico-chemical characteristics in the calculations carried out.

3.2.3. Production process and reactivity

Calcium cyanamide or $CaCN_2$ is formed when calcium carbide reacts with nitrogen:

$$CaC_2 + N_2 \rightarrow CaCN_2 + C$$

There is only one manufacturer of calcium cyanamide-containing fertilisers in the European Union (EU).

When calcium cyanamide dissolves in water it produces calcium ions (Ca^{2+}) and cyanamide ions (NCN^{2-}) as products. The cyanamide ion is very basic and reacts with water to form the acid cyanamide ion ($HNCN^-$). The acid cyanamide ion is amphoteric, i.e. it can act as either an acid or a base. When it acts as an acid it will revert to the cyanamide ion and when it acts as a base it will react to form molecular cyanamide (H_2NCN). The form that cyanamide takes in solution depends on the pH of the solution, but molecular cyanamide is favoured at pH values typically measured in soils. Molecular cyanamide can then undergo hydrolysis to form urea, which can further react to form ammonium ions, which in turn can be converted to volatile ammonia or to nitrate. The acid cyanamide ion is available to plants and organisms. Once absorbed by plants, the acid cyanamide ion lasts only 2-4 h before it forms urea, which can stay in this form for 4-8 h (Hartmann, 2000).

In contact with water calcium cyanamide decomposes and liberates ammonia:

$$CaCN_2 + 3\ H_2O \rightarrow 2\ NH_3 + CaCO_3$$

Through hydrolysis, calcium cyanamide produces cyanamide and lime ($CaCO_3$), which can in turn proceed to the formation of CaO:

$$CaCN_2 + H_2O + CO_2 \rightarrow CaCO_3 + H_2NCN$$

$$CaCN_2 + H_2O \rightarrow (CaO + H_2NCN) + CO_2 \rightarrow CaCO_3 + H_2NCN$$

In the human body, the hydrolysis of calcium cyanamide is thought to proceed as follows (Brien and Loomis, 1983):

$$2\ CaCN_2 + 2\ H_2O \rightarrow Ca(HNCN)_2 + Ca(OH)_2$$

$$Ca(HNCN)_2 + 2\ H_2O \rightarrow 2\ H_2CN_2 + Ca(OH)_2$$

The hydrogen cyanamide can further react with water to produce urea:

$$H_2CN_2 + H_2O \rightarrow (H_2N)_2CO$$

Calcium cyanamide is stable and does not decompose if stored normally in dry conditions. If in contact with water, ammonia and ethyne gas can be formed (Scottish EPA, 2014).

During the process of decomposition of lime-nitrogen in the soil, dicyandiamide (DCD), a nitrification inhibitor, was formed by dimerization (Nagumo, *et al.*, 2009). Therefore, lime-nitrogen application could mitigate nitrous oxide (N_2O) emission from the soil (Yamamoto, *et al*., 2012). See scheme in section 3.2.5.

3.2.4. Uses and way of application

Two formulations containing calcium cyanamide, i.e. the granulate (PERLKA = Pearled calcium cyanamide) and the powder (Kalkstickstoff), are sold in the EU. Under normal use conditions, one application per year per crop is required. A small part of the granulate produced is packed by retailers in 5 kg bags for private use. The maximum frequency of application for private use is 2 – 3 per year.

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).

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 $CaCN_2$ during cow manure composting significantly shortens the time to inactivate foodborne pathogens (Simujide, *et al*., 2012).

Recent developments in urea fertilisers have used a calcium cyanamide core within urea granules to stabilise nitrogen against nitrification. Calcium cyanamide is also used to control animal pests on pasture. When applied to grassland, it kills the dwarf water snail, which is the intermediate host of the liver fluke. It also kills eggs and larvae of gastric and intestinal parasites in the grass and controls *Salmonella* in liquid sewage (Güthner and Mertschenk, 2006). In considering these side effects, the SCHER is of the opinion

that the substance calcium cyanamide in itself should be evaluated as a pesticide. This has not been done before, since no manufacturer supports this use.

The SCHER is aware of the existence of two formulations, a powdered and a granulated form which have different particle size distributions. As the information on the particle distribution (see Table 1) is only available for the granulated form, the SCHER based its evaluation on the granulated form.

As a consequence, the SCHER used different exposure assessment approaches for formulations that were spread by spraying from a device mounted on a tractor for professional use or by spreading the granules by hand in the garden for private use. The main difference was that the emission of calcium cyanamide to surface water did not occur by drift but only by runoff or drainage in the second case. The active substance hydrogen cyanamide as evaluated by EFSA (EFSA, 2010a) is a formulation using water as a solubilising agent that was spread on land. The environmental risk assessment as well as the human exposure assessments for both forms of this substance could therefore not directly be compared in this Opinion or in the EFSA document (EFSA, 2010b).

Application of calcium cyanamide may lead to reduced emission of N_2O (Hirono and Nonaka, 2014, Yamamoto, *et al.*, 2013) as a result of the inhibition of nitrification by dicyandiamide, which is formed in the soil.

Cyanamide itself has been shown to be a natural product that can be found in vetch (*Vicia villosa subs. varia Roth*) and is known to suppress growth of weeds (Kamo, *et al.,* 2003). It is considered an allelochemical (Soltys, *et al*., 2011).

Calcium cyanamide has also been used therapeutically. It is known to inhibit the endogenous formation of oxalic acid by inhibiting the conversion of glycolaldehyde to glycolic acid. For this reason it has been used with varying success in the treatment of primary hyperoxaluria (oxalosis). The main therapeutical use, however, is as a so-called anti-alcohol, or alcohol-sensitising drug in the treatment of chronic alcoholism as calcium cyanamide interferes with the hepatic biotransformation of ethanol by inhibiting the aldehyde dehydrogenase enzymes. In humans, the increased blood acetaldehyde concentration has been correlated with several physiological changes (MAK Commission, 1979).

For some EU countries examples are given of the different crops with associated application rates of PERLKA (Table 2).

Table 2 Recommended application rates of PERLKA in some EU countries

ITALY			
From Vegetable leaflet – translation			
Crop	**Dose kg/ha PERLKA**	**Period**	**Remarks**
Carrots, spinach, celery, fennel	400 – 500	8 – 10 days	before the sowing/planting
Garlic, onions, leeks	400 – 500	8 – 10 days	before the sowing/planting
Cabbage, cauliflower, broccoli	400 – 500	8 – 10 days	before the sowing/planting
Melon, watermelon, zucchini	400 – 500	8 – 10 days	before the sowing/planting
Eggplants, cucumbers	400 – 500	8 – 10 days	before the sowing/planting
Potatoes	350 – 400	7 – 8 days	before the sowing
Tomatoes, pepper	350 – 400	7 – 8 days	before the planting

Green beans, beans	250 – 300	5 – 6 days	before the sowing
Artichoke	350 – 400	15 days	before the restart of the growth

BENELUX

From Vegetable leaflet BENELUX –translation

Crop	**Dose kg/ha PERLKA**	**Period**	**Remarks**
Potatoes	300 – 500		Before planting or after planting until just before emergence
Asparagus	400 – 500		after the cutting, when ploughing the beds and as long as the asparagus fields can be driven through without damaging the plants
Pickles	300 – 500	2 – 3 weeks	before sowing or planting
Beans	200 – 300	1 – 2 weeks	before sowing or after sowing until shortly before emergence
Peas	200 – 300	1 – 2 weeks	before sowing or from emergence to about 10 cm height
Cabbage crops	500 – 1000	2 weeks	against club root: before planting 500 kg/ha and after planting 500 kg/ha
		2 weeks	against weeds: until 500 kg/ha 2 weeks before planting or 500 kg/ha after planting
		Comment: after planting on Chinese cabbage and cauliflower max. 350 kg/ha	
Leeks	300 – 500	before sowing or planting or 2 – 4 weeks after planting	
Rhubarb	400 – 500	in spring before restart of the growth	
Red radish	400 – 500	8 – 10 days before sowing or planting Incorporation 5 – 10 cm into the soil, if needed keep the soil moist for some days	
Radish	300 – 500	in spring 2 to 3 weeks before sowing, in summer 1 week before sowing	
Ramenas (*Raphanus sativus* subsp. *niger*)	300 – 500	in spring 2 to 3 weeks before sowing, in summer 1 week before sowing	
Salsify	200 – 300	3 – 4 weeks	before sowing
Celery	400 – 500	3 weeks	before planting
Lettuce	300 – 500	lettuce until 400 kg/ha PERLKA, 2 – 3 weeks before planting lamb's lettuce up to 500 kg/ha PERLKA, 2 – 3 weeks before planting	
Spinach	300 – 500	2 – 3 weeks	before sowing
Tomatoes	400 – 500	3 weeks	before planting
Onions	300 – 500	2 – 3weeks	before sowing or as top-dressing for well–developed plants (5 – 10 cm)
Fennel	300 – 400	2 – 3 weeks	before sowing or 300 kg/ha as top-dressing on hand high crops

in light soils use always the lowest dose

top-dressing with PERLKA granular calcium cyanamide is only possible on dry plants, preferentially when the soil itself is still moist.

GERMANY

From Vegetable leaflet – translation

Crop	**Dose kg/ha PERLKA**	**Period**	**Remarks**
Rape	200 – 250	autumn	just before sowing or at the 4–leaf stage
	200 – 400	spring	after a starter-fertilisation with an N / S fertilizer as the second N application on the dry stock
Winter crops	200	autumn	directly before sowing or after emergence or at the 3–leaf stage
	200 – 400	spring	at the end of tilling
Summer crops	200 – 300		incorporate superficially before sowing or after emergence or from 3–leaf stage to tilling, for malting barley only before sowing!
Corn	300 – 500		incorporate superficially before sowing or between sowing and after emergence
	150		root-level placement alone or mixed with DAP
Potatoes	300 – 500		Before planting
	60 – 100		Before emergence
Sugar beets	300 – 500		Approximately 14 days before sowing
	60 – 100		
Sunflower	250 – 300		at 20 to 30 cm height spread on the dry stock
Fruit trees, vines	200 – 400		In early spring until shortly before sprouting
Hop	300 – 400		Before uncovering and cutting
Grassland and meadows	300 – 400		Early spring on the dried sod, 14 days waiting time to grazing!

SLOVAKIA

From vegetable leaflet - translation

Crop	**Dose kg/ha PERLKA**	**Remarks**
Rape	200 – 300 300 – 400	Basic fertilisation before seeding by incorporation into soil Regenerative fertilisation
Winter cereals	200 – 250 250 – 300	Basic fertilisation before seeding by incorporation into soil Regenerative fertilisation

Spring cereals	250 – 300	Basic fertilisation before seeding by incorporation into soil
Corn	100 – 150 300 – 400	By seeding under the base Before seeding by incorporation into soil
Peas	200 – 300	1 – 2 weeks before seeding or from germination to approximately 10 cm of the plant height
Beans	200 – 300	1 – 2 weeks before seeding or after seeding until shortly before germination
Bush beans	300 – 400	In between seeding and germination
Lettuce	200 – 500	In spring 2 – 3 weeks, in summer 1 week before planting
Valerianella locusta	300 – 500	2 – 3 weeks before seeding, by container planting 1 week before the planting
Carrots	300 – 400	2 – 3 weeks before seeding
Spinach	300 – 500	2 – 3 weeks before seeding
Cucumbers	300 – 600	Always 2 – 3 weeks before planting, also as row fertilisation before putting foil down. Attention when used after putting down foil, the plants must not come in contact with calcium cyanamide
Leeks, chives	300 – 600	2 – 3 weeks before seeding or planting or 300 – 500 kg after germination
Celery, tomatoes,	600 – 1000	3 weeks before planting
Fennel	300 – 400	2 – 3 weeks before seeding
Cabbage family *(Brassicaceae*) (while cabbage, red cabbage, kale, cauliflower, (Brussels) sprout	300 – 1000 300 – 400	In spring around 3 weeks, in summer 1 week before planting/seeding. As the main fertiliser for dry plants (not for Chinese cabbage), after germination until rows are covered
Radish	300 – 500	In spring 2–3 weeks, in summer 1 week before seeding
Asparagus	400 – 500	immediately after germination of weeds until asparagus is accessible without the risk of damage. As fertiliser into rows to heap up before covering.
Onion Spring onion	300 – 500 300 – 500	2 – 3 weeks before seeding or at the germination (from 5 – 10cm of the plant height) or 2 – 3 weeks after plantation evenly applied on the plant bed.

		The plants must be absolutely dry.
Rhubarb	400 – 800	Early in spring before sprouting
Strawberries	300 – 500	14 days before planting or after picking. In spring on dry plants 300kg/ha or 500kg/ha after picking
Potatoes	300 – 500	For reduction of nematodes (wireworms) before preparing hillocks (when it's dry already before planting). For protection against weeds from planting until shortly before germination: apply on mounds of dirt during the time of the biggest weed growth.

Based on the information presented in Table 2, the SCHER concludes that a dosage of 1000 kg PERLKA/ha is recommended for a few crops in The Netherlands and in Slovakia and therefore the SCHER has decided to use this as realistic worst case scenario. The SCHER uses an application rate of 500 kg PERLKA/ha as the normal dosage.

The SCHER selects, for human exposure, a drift percentage for granulated calcium cyanamide of 0.2 % based on information in the new CSR and considers this value to be realistic. This percentage is reported to cover particles up to 200 µm. For environmental exposure it is common practice in the evaluation of Plant Protection Products to estimate the drift of granular formulations to the environment to be 0%. Therefore, the SCHER agrees with this value for fertilisers in this case and has subsequently used it in this evaluation.

3.2.5. Fate and behaviour in the environment

The substance, incorporated within a formulation, is applied on the agricultural field as a fertiliser. The SCHER has assumed that the formulation is applied to the field by a tractor mounted with suitable equipment to distribute the formulation equally. After application there are two possibilities for further action: 1) the formulation is superficially incorporated in the soil to prevent runoff or 2) the formulation is incorporated in the upper 20 cm of the soil to allow slow release of the active substance, calcium cyanamide (Tewari, *et al.*, 2004).

3.2.5.1. Transformation scheme

The possible transformations of calcium cyanamide in the environment are summarised in Figure 1.

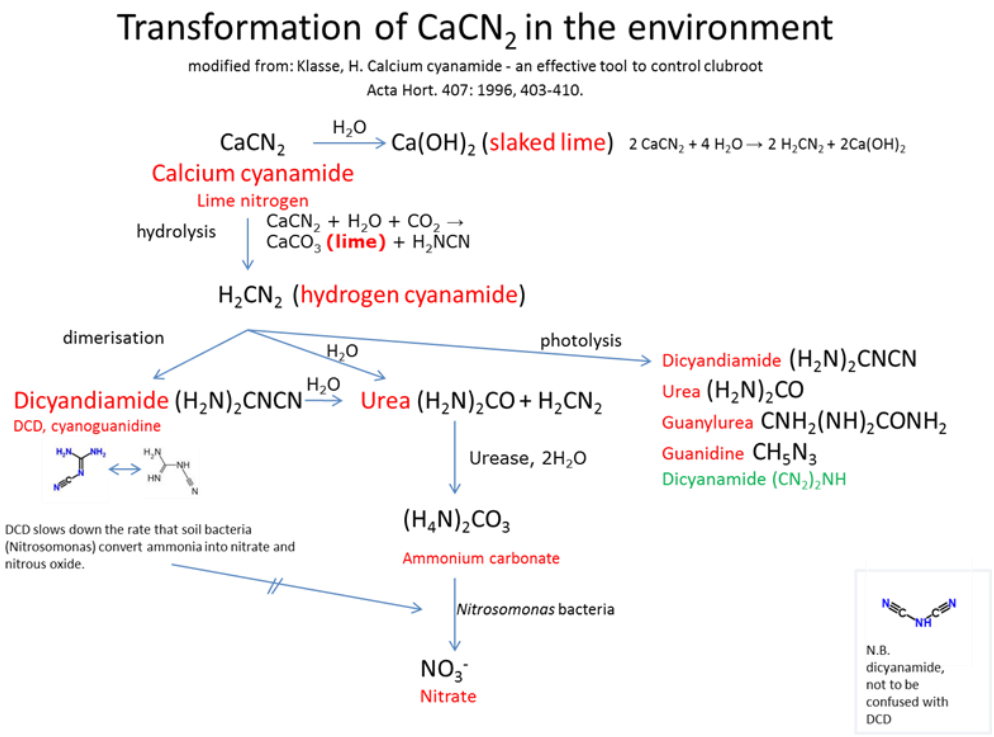

Figure 1 Scheme presenting possible transformation routes of calcium cyanamide in the environment. (modified from Klasse, 1996)

The SCHER considered that the most important degradation route was the hydrolytic pathway leading to hydrogen cyanamide, followed by further hydrolysis to urea:

$$CaCN_2 + H_2O + CO_2 \rightarrow CaCO_3 + H_2CN_2$$

$$H_2CN_2 + H_2O \rightarrow (H_2N)_2CO$$

3.2.5.2. Environmental transformation rates in soil and water

Abiotic degradation

Calcium cyanamide hydrolyses very rapidly to hydrogen cyanamide. Results from a hydrolysis study at pH 1.2 and 5 showed that hydrogen cyanamide was released from its calcium salt within a few minutes (AlzChem Trostberg, 2010).

Phototransformation data are available only for the hydrolysis product (hydrogen cyanamide) in soil and water (Limacher, 2009), and details are provided below.

In soil, with DT50 values (single first order) of 2.4 and 2.0 h in irradiated samples and in the dark, respectively, cyanamide degraded quickly in both types of tests, indicating that the degradation was caused by biodegradation. The rate of degradation due to photolysis was negligible compared to that caused by biodegradation. Cyanamide was almost completely mineralised to CO_2 over the study period. Bound residues were < 5 % at the end of the study period. No major metabolites of cyanamide were encountered in the higher tier soil photolysis study. (AlzChem Trostberg, 2010).

In another study for cyanamide, DT50 values of 1.45 d (irradiated samples) and 4.22 d (dark control) were observed (Burri, 2000).

In water, photolysis has been calculated to be slower with half-lives of 29 d (pH=5) and 38 d (pH=7); in the dark: >100d (AlzChem Trostberg, 2010).

Biodegradation in water and sediment

Results from biodegradation in water and sediment (simulation tests) are described below.

The aerobic aquatic degradation of [^{14}C]-cyanamide was studied in two disparate water/sediment systems: a pond and a river system. Results showed that the elimination of [^{14}C]-cyanamide from the water/sediment systems proceeded mainly via mineralisation to CO_2. Degradation of cyanamide to other metabolites and incorporation into the organic matter of the sediment were of minor importance. The estimated half-life (DT50) of cyanamide from the water phase of the aquatic systems was 2.3 d for the river system and 4.3 d for the pond system, respectively, and the DT90-values were determined to be 7.7 d and 14.4 d, respectively. In the total water sediment systems, cyanamide degraded with half-lives of 2.5 d (river) and 4.8 d (pond). The DT90 values for the total systems were calculated to be 8.2 d in the river system and 15.8 d in the pond system (AlzChem Trostberg, 2010).

One major metabolite was detected in the pond system (13.4% of applied radioactivity) and identified as urea. The DT50- and DT90-values of urea were also calculated using first-order kinetics. The DT50 values in the water phase were calculated to be 2.7 and 7.5 d for the river and pond systems, respectively, and the DT90-values were determined to be 9.1 d and 11.6 d, respectively. In the total water sediment systems, urea was degraded with half-lives of 2.9 d (river) and 8.0 d (pond). The DT90-values for the total systems were calculated to be 9.6 d in the river system and 26.7 d in the pond system (Völkl, 2000).

Biodegradation in soil

According to the OECD 301B test (technical grade), $CaCN_2$ cannot be classified as readily biodegradable (no degradation was observed after 28d of incubation between 21.0 and 23.1 °C) because of insufficient CO_2 evolution and therefore the biodegradability criterion was not fulfilled (Ipser, 2010a).

As shown in the hydrolysis study, calcium cyanamide in contact with water rapidly hydrolyses to hydrogen cyanamide. In addition it should be noted that the use of calcium cyanamide as fertiliser is generally confined to soils which – at the time of application – exhibited aerobic conditions. Therefore the aerobic soil metabolism of calcium cyanamide is best characterised by using its hydrolysis metabolite cyanamide.

The aerobic soil metabolism of [^{14}C]-cyanamide (Schmidt, 1990/91) was investigated in air-dried sandy loam soil, collected from land located near Ashland, Nebraska, USA. The rate of degradation of cyanamide in soil was determined using linear regression assuming first-order reaction kinetics. The primary aerobic pathway by which the parent compound disappears from soil was the final degradation to [^{14}C]-CO_2 (complete mineralisation). This fraction accounted for approximately 94.6% of applied radioactivity after 14 days. The half-life of cyanamide was calculated (using a first order kinetic) to be 1.26 d. The calculated time to 90 % degradation was 1.94 d. One minor degradation product was identified as dicyandiamide accounting for 0.43% of applied radioactivity at maximum.

On the basis of the cyanamide concentrations in soil at various time points after application, regression curves were fitted and the DT50-values were calculated from the regression curves using a graphical estimation method. The DT50-values of the two

loamy sand soils ranged from 1 to 3 d. These results were in good agreement with the values obtained in the aerobic soil metabolism study and during the aerobic phase of the anaerobic soil metabolism study where the DT50-values ranged from 0.52 to 1.26 d. Only in sandy soil with very low organic carbon content did the DT50-values range from 6 to 12 d.

An anaerobic degradation DT50 value in soil under laboratory conditions was calculated to be 34.7 d (AlzChem, 2015).

The results showed that the degradation of cyanamide in soil is influenced by the organic carbon content, indicating that biotic degradation prevails in soils. Furthermore, the degradation rate of cyanamide in the test soils depended on the application rate with a faster degradation observed in the test soils receiving the lowest application rate (Rieder and Heß, 1978).

In another soil study, it was suggested that cyanamide was rapidly degraded in 2 weeks, but nitrification was depressed for a long period (Ohyama, *et al.*, 2010).

Cyanamide degradation in soil is influenced by the organic carbon content of soils. DT50 values up to 12 d were found in sandy soil with a very low organic C content.

The SCHER concluded that calcium cyanamide is rapidly degraded into hydrogen cyanamide and further into urea and/or completely converted to CO_2 in the sediment and soil with DT50 value of a maximum of 12 d and a mean value of a few d in soil and 1.4 d in water.

The SCHER chose a DT50 of 2 d in soil and 1.4 d in water as typical values for calcium cyanamide degradation based on the above information. These values were used in the calculations presented below.

Bioaccumulation and sorption

From its physical-chemical characteristics (see 3.2.2), calcium cyanamide is expected to have a low potential for bioaccumulation and for adsorption to soil.

The adsorption coefficient, K_{oc}, of $CaCN_2$ has been estimated using a HPLC retention time method. At any pH, the compound dissociates in water because it is a salt. The adsorption coefficient of the non-ionised form could not be determined. HPLC based values of log K_{oc} were estimated to be < 1.25 (which was outside the method's scope). Calculated values range between 0.9 and 1.2 (EpiSuite, see Annex 1).

Bioaccumulation is generally considered to be related to the octanol – water partition coefficient. With a log P_{ow} of - 0.20 the substance was classified as not bioaccumulative as bioaccumulation is considered a relevant process at a Log P_{ow} value of > 3. For sorption, if it is assumed that the log K_{oc} is 1.25, the K_{oc} itself can be estimated at 17.8 dm^3/kg and the K_{om} at 10.5 dm^3/kg, which is indicative of a low adsorption capacity to soil. According to the SCHER, biomagnification, as a follow-up process of bioconcentration, was not considered a relevant process for calcium cyanamide.

For its calculations the SCHER selected a K_{om} value of 10.5 dm^3/kg.

3.2.6. Ecotoxicological assessment

3.2.6.1. Aquatic ecotoxicity

Most aquatic ecotoxicity data used by the SCHER originated from the manufacturer's dossier (AlzChem Trostberg, 2010); these are the same as those in the CSR (AlzChem Trostberg, 2015). The studies were generally carried out according to internationally accepted guidelines and using GLP.

A brief description of the main studies is given hereunder.

In a 96-h acute toxicity study, zebra fish (*Danio rerio*) were exposed to calcium cyanamide (technical grade) at nominal concentrations ranging from 25.0 to 401 mg/L. All fish exposed to 401 mg/L died within the first 2 hours of testing. Organisms exposed to 200 mg/L exhibited decreased mobility after 2 hours and, after 24 hours mortality started to occur. After 48 hours of exposure the remaining fish showed loss of equilibrium and bleeding around the mouth and the chest, and 3 of these fish were recorded as having died. The remaining fish in this group were dead 24 hours later. None of the fish in the other test groups or in the control group exhibited any adverse effects throughout the study. The calculated 96h-LC50 of calcium cyanamide (technical grade, Kalkstickstoff) in this study was 140 mg/L (based on nominal concentrations). The derived (96h) NOEC was 100 mg/L (AlzChem Trostberg, 2010).

For several aquatic organisms, e.g. invertebrates and algae, the toxicity of urea is less (by a factor 100 or more) than that of calcium cyanamide. For fish, however, the toxicity of urea and calcium cyanamide are in the same range (i.e. 128 mg/L for urea and 140 mg/L for calcium cyanamide).

In a 48-h toxicity study with *Daphnia magna* (Crustacea, Cladocera), neonates were exposed to $CaCN_2$ at nominal concentrations ranging from 1.32 to 42.8 mg/L calcium cyanamide. The calculated 48h-EC50 (immobility as endpoint) was 6 mg $CaCN_2$/L and the derived 48h-NOEC (based on immobilization) was 1.8 mg/L (AlzChem Trostberg, 2010).

In a 72-h growth inhibition test study, the unicellular algae *Pseudokirchneriella subcapitata* was exposed to calcium cyanamide (technical grade) at nominal concentrations ranging from 0.74 to 200 mg/L. The NOEC and EC50 values based on growth rate were 13.7 and 27.5 mg/L, respectively (AlzChem Trostberg, 2010).

Other algae toxicity data (with exposure periods up to 8 days) available from a public available literature source (IUCLID4 from ECB website) were also considered by the SCHER, but were not retained as critical ecotoxicity values.

From all ecotoxicity data available, the SCHER chose the L(E)C50 data presented in Table 3 as the critical values to be used in the risk assessment for calcium cyanamide.

Table 3. Ecotoxicity values used for the risk assessment of calcium cyanamide performed in this Opinion.

Organism	**Short term (L(E)C50) (mg/L)**		
	calcium cyanamide	**cyanamide**	**urea**
Fish	140	43.1	128
Crustaceans	6	3.2	10,000
Algae	28	0.65	10,000

The SCHER notes that no chronic toxicity data are available. The SCHER is, however, of the opinion that chronic exposure and toxicity 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. In the CSR it is argued that chronic data are not needed as the substance degrades rapidly. This is contradictory to recent regulatory developments. Indeed, it should be noted that the European Chemicals Agency's RAC recently classified cyanamide as harmful to aquatic life with long lasting effects (RAC, 2015), thus implying that chronic effects can be expected.

3.2.6.2. Terrestrial ecotoxicity

Birds

The acute oral toxicity of PERLKA to Japanese quail (*Coturnix coturnix japonica*) was assessed during a single dose 14-day assay. Clinical observations during the first 4 post-treatment hours revealed sluggishness and slight diarrhoea. Most of the deaths occurred between 3 and 20 h after treatment. One cock died on the fifth day post-treatment. The survivors subsequently recovered gradually and looked quite healthy again at the end of the observation period. The individual body weights indicated retarded growth or weight loss in the first week post-treatment. Macroscopic examination of the survivors at autopsy did not reveal any treatment-related gross alteration. From the mortality data the calculated oral LD50 of PERLKA was 1,665 mg/kg bw/d with 1,575 and 1,763 as the 95% confidence limits (AlzChem Trostberg, 2010).

No other toxicity studies with birds were available in the information presented to the SCHER. Although the SCHER recognises the limited number of terrestrial toxicity studies available, the committee is of the opinion that due to the rather high LD50-values determined and the feed avoidance behaviour, additional toxicity studies (including chronic) for birds are not required (especially if during application the granulated product was incorporated into the soil).

Earthworms

The acute toxicity of calcium cyanamide (using PERLKA) to the earthworms *Eisenia foetida* and *Lumbricus terrestris* was determined in 14-day toxicity tests conducted according to OECD Guideline 207. Worms were assessed for mortality and sublethal effects after 7 and 14 days of exposure. The 14d-LC50 of calcium cyanamide was 169 mg/kg dry soil for *Eisenia foetida* and 182 mg/kg dry soil for *Lumbricus terrestris* (AlzChem Trostberg, 2010).

Another acute toxicity with PERLKA and earthworms (E. fetida), i.e. also a 14-day soil exposure laboratory study conducted according to OECD Guideline 207, reported a 14d-LC50 of AlzChem173 mg/kg soil dw for calcium cyanamide. (AlzChem Trostberg, 2010)

Based on the latter LC50-value the SCHER derived a PNEC for soil organisms of 17.3 mg/kg dw using an AF of 10.

Beetles

A laboratory study was carried out to determine the toxicity of PERLKA to the carabid beetle *Bembidion lampros*. No toxicity was observed up to a concentration of 450 kg formulation/ha, i.e. the highest concentration tested (AlzChem Trostberg, 2010).

The SCHER notes that toxicity tests with concentrations reflecting application rates of PERLKA (in several crops) of 500 to 1000 kg formulation/ha are not available.

Microorganisms

To determine effects to microorganisms, a nitrification and dehydrogenase activity study has been carried out with dosages of 1,000 and 5,000 kg formulation/ha. At a dosage of 1,000 kg formulation/ha, i.e. the highest application concentration considered in this opinion, no effects on nitrification and dehydrogenase activity were observed (AlzChem Trostberg, 2010). The SCHER concluded that the fertiliser PERLKA exhibits a low toxicity to microorganisms.

Plants

Calcium cyanamide did not exhibit toxicity to higher plants. It was reported to have positive effects on plant growth (AlzChem Trostberg, 2010). Hydrolysis product(s) of calcium cyanamide, however, were reported to exhibit some toxicity to seeds and seedlings.

Bees

Toxicity data of calcium cyanamide to bees were not available to the SCHER. Therefore, the SCHER was not able to perform a risk assessment for bees. However, the SCHER is of the opinion that bees will not be exposed during the time of application.

3.2.7. Mammalian toxicology

Kinetics (Absorption, distribution, metabolism, excretion)

Although calcium cyanamide had been clinically available for decades, only a few scientific studies, if any, on pharmacokinetics were available in the literature. It had been demonstrated that calcium cyanamide was quantitatively hydrolysed to cyanamide at different pH and also under simulated gastric conditions within minutes or in 1h (Rust, 1987; Brien and Loomis, 1983; Mertschenk, *et al.*, 1991). Calcium cyanamide in tablet formulation, however, hydrolysed to cyanamide to an extent of 60% within 1 hour and quantitatively within 10 hours (Brien and Loomis, 1983). Hydrolysis of calcium cyanamide was reported to be required for drug absorption and it could be assumed that calcium cyanamide follows mainly the same kinetic pathways as cyanamide.

In rats, absorption of cyanamide after oral application was calculated to be approximately 90% with slightly higher values for fasted animals (EFSA, 2010a; Obach, 1986). Also in humans, absorption was fast after oral administration of therapeutic doses of 0.3 (low dose), 1 (medium dose), and 1.5 (high dose) mg/kg bw/d and highest blood levels (T_{max}) were reached after 13 minutes. The substance was widely distributed and the highest amounts were observed in liver and kidney, however, there was no evidence for bioaccumulation. In humans, bioavailability increased from 46% after oral administration of low doses to 70% or 81% for the medium and high doses, respectively, indicating a saturable first pass metabolism (Colom, 1999). Elimination was rapid in rats (>67% within first 24 hours post dose) as well as in humans. Plasma half-life (T1/2) of cyanamide was reported to be of about one hour in rats after oral administration of 35 mg/kg bw and 40 to 60 minutes in humans after oral administration of the different therapeutic doses. Excretion in rats occurs mainly via urine (80 – 98%), while 2 – 4% was excreted via faeces and 4 – 10% via respiratory air. Biliary excretion was increased following intravenous administration. 43 – 55% (rats) or 28 – 58% (humans) of the substance applied were excreted as N-acetylcyanamide, which was the main metabolite in rats, dogs, rabbits and humans (Shirota, 1984; Obach, 1986; Obach, 1989; Gloxhuber, 1989; Mertschenk, *et al.*, 1991; Colom, 1999).

Mechanistic studies regarding the inhibition of aldehyde dehydrogenases showed that cyanamide itself was not active *in vitro* and has to be activated by the mitochondrial catalase enzyme. This resulted in the formation of an unstable N-hydroxycyanamide intermediate that decomposed to cyanide (CN) and nitroxyl (HNO). While cyanide and thiocyanate had not been found in significant amounts in human blood and urine, respectively, nitroxyl had been identified as the active metabolite responsible for the inhibition of aldehyde dehydrogenases and active levels where reached at therapeutical doses of 0.3 mg/kg bw/d (DeMaster, *et al.*, 1998).

Mechanisms of cyanamide toxicity were not fully understood but the inhibition of aldehyde dehydrogenases could also play a role with regard to undesired side-effects of the drug. Additionally, activation of the hypothalamo-pituitary-adrenal axis by cyanamide resulting in an increase of circulating glucocorticoids seemed to be correlated to cyanamide toxicity and its effects on thyroid and testis function in rats and dogs, as well as in the reduction of fertility in rats.

Dermal absorption

Information on dermal absorption was based on data for cyanamide. Calculated on the urinary excretion of the main metabolite N-acetylcyanamide after oral and dermal exposure in humans, maximum dermal absorption from a 1% aqueous cyanamide solution following a 6 h exposure period was reported to be 3.5% (Gloxhuber, 1989). In rats, dermal absorption amounted to 14.3% for a 10% and to 8.2% for a 0.1% solution after 10 h exposure. For cyanamide EFSA concluded on a dermal absorption of 5% for 1% dilution, a dermal absorption of 14.3% for 2.5% dilution and 100% dermal absorption for the cyanamide concentrate (EFSA, 2010a).

In a dermal absorption with 6 human volunteers, 10 mg cyanamide (0.1% aqueous solution) was applied topically over a 6-hour period to the skin, about 7.7% was found as acetylcyanamide in the urine 48 hours after application (Mertschenk, 1991).

The German Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) concluded that skin penetration contributes considerably to internal, systemic exposure and compliance with the relevant occupational exposure limit did not guarantee sufficient protection (MAK Commission, 1979, 1997).

Acute Toxicity

In rats for calcium cyanamide (purity 68%) an LD50 of 765 mg/kg bw has been reported, while the LD50 for the pure substance or the tablet formulation was 690 mg/kg bw and for the commercial formulation (with a calcium cyanamide content of 45%) the LD50 was 711 mg/kg bw for males and 492 mg/kg bw for females, respectively (de Groot, 1976; Berger, 1966; Osheroff, 1990). In mice the LD50 for calcium cyanamide, (purity 63.5%) was 1800 mg/kg bw (Allan, 1992).

In a study with the commercial formulation, an acute inhalation LD50 of >5.1 mg/L was derived (Terrill, 1990). In further studies acute LD50 was above the concentrations tested (155 mg/m^3 non-oiled or 132 mg/m^3 oiled calcium cyanamide) (Appelman, 1978, 1979).

The acute median lethal dermal dosage was established at >2000 mg/kg bw (Osheroff, 1990; Liggett, 1989).

Irritation, Corrosion

Calcium cyanamide was not irritating or corrosive to the skin when tested *in vitro* (Ipser, 2010) or *in vivo* (Liggett, 1989). Dermal exposure to 2000 mg/kg bw, however, induced erythema and necrosis (Osheroff, 1990, Liggett, 1989).

Calcium cyanamide induced severe eye damage *in vitro* (Ipser, 2010) as well as *in vivo* (technical grade: Liggett, 1989, commercial formulation: Mercier, 1989).

Sensitisation

Calcium cyanamide (technical grade) was positive in a modified guinea pig maximisation test (GPMT, OECD test guideline 406). The test was modified due to the poor solubility of the test substance in solvents. Occupational studies in 65 workers showed no evidence that calcium cyanamide was a human skin sensitiser or a respiratory sensitiser (MAK Commission, 1997). In an occupational health examination, calcium cyanamide was negative in a Finn-Chamber test (Mertschenk, *et al.*, 1991).

Repeated dose toxicity

Target organs for systemic effects of calcium cyanamide observed in experimental animals were liver, thyroid gland, pituitary gland and the reproductive system (Benitz, *et al.,* 1965; Benitz and Cavallo, 1960). The morphological activation of the thyroid was to be expected, as calcium cyanamide was known as an anti-thyroid agent and administration of calcium cyanamide in combination with thyroid powder minimised the effect of calcium cyanamide on bodyweight gain (Pridgen, 1966).

In a 4-week dose range finding study with rats the NOAEL was reported for the group which received daily doses of 8.3 – 12.6 mg/kg bw/d (Benitz and Tonelli, 1957).

In a chronic study, 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; Cavallo, 1960). Because of the high mortality rate, treatment was reduced to 7 months for surviving animals of the highest dosage level. In the 0.05% and in the 0.012% dosage groups two animals and one animal died, respectively. 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. As the thyroid was one of the main target organs affected by calcium cyanamide, any effects on this organ have to be considered as long as a possible relationship to calcium cyanamide administration cannot be excluded. In the study, no data on clinical chemistry were provided. The haematological values of rats receiving 0.05% calcium cyanamide in their feed for 1 year were reported. Mean values do not seem to be remarkably different from those of control rats, however no statistical analysis of the data was given. Based on the information available from this study, the SCHER derived a LOAEL of 0.003% corresponding to a daily intake of 1.3 – 3.8 mg/kg bw/d.

The 0.012% dose level (about 11 mg/kg/d) did not cause any morphological changes attributable to treatment with the exception of a few cases of thyroid hyperplasia with the occurrence of thyroidectomy cells and the decrease of acidophilic cells in the anterior pituitary. The thyroid hyperplasia was in rare instances noticeable in animals receiving the 0.003% diet.

A 6-month oral toxicity study was performed in dogs with calcium cyanamide (pharmaceutical grade) (Benitz and Takesue, 1960). Two animals per group (one male, one female) were treated at 2, 10 or 30 mg/kg bw/d. Since the two animals of the highest dosage group died on days 9 and 13, respectively, these animals were replaced

and an additional group of two dogs was added which received 7.5 mg/kg bw/d of calcium cyanamide. Treatment at the highest dosage of 30 mg/kg bw/d caused severe toxic symptoms like ulcers in the upper gastrointestinal tract, fatal lung edema, increased weight of the thyroid and leukopenia. A considerable increase in lung weight was already noted in the two animals of the highest dosage group which were found dead 9 and 13 days after start of treatment, respectively. In addition, the male animal showed increased weight of the testes. Dogs receiving 10 mg/kg bw/d showed a decrease in bodyweight of 6% in the male and 14% in the female animal. Significant changes in some organ weights were noted for all treated animals and include reduced absolute thymus weight in males (10, 7.5 and 2 mg/kg bw/d), increased relative spleen weight in males (10, 7.5 mg/kg bw/d), decreased in relative heart weight in males (10, 7.5 and 2 mg/kg bw/d), reduced relative pancreas weight in males (10, 7.5 mg/kg bw/d), slightly increased absolute and relative thyroid weights in males (10, 7.5 mg/kg bw/d), considerably decreased absolute and relative liver weights in females (10, 7.5 and 2 mg/kg bw/d), reduced absolute pituitary gland weight in females (10, 7.5 and 2 mg/kg bw/d), as well as considerably decreases in relative and absolute ovaries and uterus weights (10, 7.5 and 2 mg/kg bw/d). However, weight of the sexual organs in females might not be completely comparable, as the control female animal was reported to be "in heat" from one to one and a half weeks. A decrease of the total white blood count during the study was noted in all groups but in the highest dose group at an earlier stage than in control animals and in other treatment groups. This observation could not be explained by the authors and findings cannot be evaluated with regard to drug effects. Atypical leucocytes with band-like nuclei and very bizarre and irregular shapes, however, were reported for dosage groups of 7.5 mg/kg bw/d and higher but not for controls and might indicate an effect of calcium cyanamide on white blood cells.

In the opinion of the SCHER, the reliability of this study was limited because bone marrow seems to be a human-relevant target for calcium cyanamide toxicity but for this study definite interpretation for occurrence of leucopoenia in all groups was not feasible. Based on effects on body weight as well as on organ weights (thymus in males and ovaries and uteri in females) the SCHER concluded that the LOAEL from this study is 2 mg/kg bw/d.

Genotoxicity

Calcium cyanamide was evaluated for its mutagenic and genotoxic potential. Ames tests were negative both in the absence and in the presence of metabolic activation (Willems, 1978; Haworth, *et al.*, 1983). A non-guideline bacterial mutation test with calcium cyanamide in *Aspergillus nidulans* was positive in the absence of S9-mix, but negative in its presence (Vallini *et al.,* 1983). Both a mammalian chromosomal aberration test as well as an UDS test in a human cell line on calcium cyanamide were shown to be negative (De Raat, 1979; Lohman, 1981). In an *in vivo* micronucleus test, no mutagenic activity of calcium cyanamide was observed (Willems, 1979).

Carcinogenicity

In chronic studies with rats and mice, no tumours occurred at incidences that could clearly be related to the administration of calcium cyanamide. In male mice, hemangiosarcomas were increased as well as lymphomas and leukaemia in female mice, however, the incidences of these tumours were reported to be in the range of values for historical controls. In subchronic studies performed with rats, calcium cyanamide was found to cause diffuse follicular hyperplasia of the thyroid, with periglandular fibrosis and prominent periglandular vascularity (NCI, 1979).

In an additional study, the probability of calcium cyanamide leading to reticulum cell carcinoma was reported to be very low after oral application of 100 mg /kg bw/d for 18 month to mice (Kotin, 1968).

Developmental and Reproductive toxicity

A study on developmental toxicity (Wil research, 2014) was performed in Sprague-Dawley rats that received 0, 7, 21 or 49 mg/kg bw/d (nominal conc.) of calcium cyanamide in corn oil daily by gavage between G6 and G19. Dose related reductions in body weight and food consumption were observed in the mothers from 21 mg/kg bw/d on. The NOAEL was set at 7 mg/kg bw/d for maternal toxicity. At these dose levels (21 and 49 mg/kg bw/d) both the uterus weight and foetal weight were also slightly reduced. The SCHER selected 7 mg/kg bw/d as the NOAEL for developmental toxicity. There were 1 and 2 malformed foetuses in the control and lowest dose group respectively that were not considered as being associated with the treatment. No other effects on the offspring were even observed. The NOAEL for teratogenicity can be set at > 49 mg/kg bw /d. The following litter parameters were recorded: number of foetuses (dead/alive), uterus weight, foetal weight, macroscopic effects and external abnormalities.

Neither a two-generation reproduction study (OECD 416) or an extended one-generation study in rats is currently available.

The German Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area evaluated the reproductive toxicity of calcium cyanamide on the base of data for cyanamide and classified calcium cyanamide as embryotoxic substance, for which effects on reproduction were not suspected if specific exposure limits for workplace were not exceeded (MAK-Commission, 2007, 2012). For cyanamide EFSA concluded that the relevant maternal and developmental NOAELs were <5 mg/kg bw/d and 5 mg/kg bw/d in rats, respectively, as well as 6 mg/kg bw/d in rabbits. For parental and reproductive toxicity, the NOAEL was 3.75 mg/kg bw/d, based on the reduced body weight gain and fertility impairment. For offspring toxicity, the NOAEL was <1.25 mg/kg bw/d, based on neonate mortality. Cyanamide was considered as having an effect on testis development of the F1 males during the late lactation period, leading to interstitial cell proliferation and tubular atrophy. Fertility reduction was seen at a dose of 15 mg/kg bw/d, inducing general toxicity. The NOAEL for teratogenicity was 45 mg/kg bw/d (EFSA, 2010a).

Human experience

Many studies reported on the so-called nitrolime-disease, the effects of calcium cyanamide after the consumption of alcohol. The dose for long-term therapy was 50 mg calcium cyanamide every 12 hours. Daily ingestion of 50 mg calcium cyanamide for 20 days in a double blind study led to frequent abdominal symptoms, allergic skin reactions, dizziness, nausea, sleepiness, headache and eye symptoms (MAK Commission, 1979).

Also for healthcare workers, generalised symptoms of acute toxicity were reported. After occupational skin contact with calcium cyanamide, severe erythema, inflammation, ulcers and lesions on the skin and mucous membranes were reported (MAK Commission, 1979). Six percent of workers exposed to >2.5 mg calcium cyanamide/m^3 developed conjunctivitis (Schiele, *et al.*, 1981). A case study with 65 employees revealed no evidence of exposure-related adverse effects on health. The workplace concentrations of calcium cyanamide were in the range between 0.23 and 8.36 mg/m^3. Employees from a calcium cyanamide production plant were investigated for hormonal changes. No changes in blood levels were detected in the group of exposed compared to unexposed workers

(Mertschenk, 1993). Extent of exposure to calcium cyanamide, however, varied considerably within the group of workers and no individual data for the hormone levels in blood was provided so possible trends in hormonal variations for highly exposed persons cannot be identified. The MAK Commission recommended a health-based occupational exposure level of 1 mg/m^3 for calcium cyanamide derived from therapeutic doses and set the occupational exposure limit (OEL) at 10% of a daily dose of 100 mg/person which is equal to 1 mg/m³ assuming a total inhaled air volume of 10 m³ per shift (MAK Commission, 1979).

Classification of cyanamide

With regard to health hazards, the RAC concluded on the following Hazard Statements and Hazard Class Categories for cyanamide (RAC, 2015):

H 301:	Toxic if swallowed (Acute Tox. 3)
H 311:	Toxic in contact with skin (Acute Tox. 3)
H 314:	Causes severe skin burns and eye damage ((Skin Corr. 1)
H 317:	May cause an allergic skin reaction (Skin Sens. 1)
H 351:	Suspected of causing cancer (Carc. 2)
H 361 fd:	Suspected of damaging fertility or the unborn child (Repr. 2)
H 373 (thyroid):	May cause damage to organs through prolonged or repeated exposure (STOT RE 2)

The RAC supported the classification as STOT RE 2, based on thyroid effects in the rat and supported by some findings in dog studies. This conclusion takes into account the particular sensitivity of rats as well as evidence of probable higher sensitivity of dogs compared to humans.

Overall conclusion on toxicity

Based on kinetic data available, the 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.

For cyanamide, the main target organs following repeated oral administration were the thyroid (rat, dog) and the testes (dog) as well as red blood cells (rat, dog). Testicular lesions have been reported in young immature beagle dogs at 0.6 mg/kg bw/d in a 90-day study. EFSA used this study to derive a LOAEL of 0.6 mg/kg bw/d for regulatory purposes. For adult dogs, a NOAEL of 1 mg/kg bw/d was derived as well as a NOAEL of 1.5 mg/kg bw/d for rats. The RAC supported a LOAEL of 4.5 mg/kg bw/d in rats based on significant effects on the thyroid observed in males and females of two strains. In the 90-day and 1-year dog studies, hypothyroidism was reported at doses of 2-6 mg/kg bw/d.

These findings were considered to have toxicological significance and to be of relevance to human health (RAC, 2015).

For calcium cyanamide, effects were comparable after repeated exposure with the thyroid and the reproductive system reported to be main target organs affected. From the information available from a rat study (Benitz and Salamandra, 1960, Cavallo 1960), the SCHER derived a LOAEL of 0.003%, corresponding to a daily intake of 1.3-3.8 mg/kg bw/d. From the 6-month study with dogs a LOAEL of 2 mg/kg bw/d could be derived, however, this study was considered to be of limited reliability. A recent developmental study in rats showed reduced maternal weight gain and food consumption as well as reduced foetal weight but no excess foetal mortality. The SCHER selected a NOAEL of 7 mg/kg bw/day for developmental toxicity and a NOAEL of 49 mg/kg bw /d for teratogenicity, since no such effects were observed at the dose levels that were used. Calcium cyanamide did not seem to be a potent human skin sensitiser although the substance showed sensitising properties in experimental animals. In contrast, skin irritating properties of this substance seemed to be more pronounced in humans than in animals.

To summarise, the SCHER uses for its assessment the LOAEL of 1.3 mg/kg bw/d together with following assessment factors to derive the AOEL of 0.0043 mg/kg bw/d:

3	for the extrapolation from LOAEL to NOAEL
4	for allometric scaling (rats to humans)
2.5	for other interspecies differences
10	for intraspecies differences

3.2.8. Operator, bystander and residential exposure estimates

Exposure assessment for operators, professional use:

The manufacturer provided measured inhalatory exposure data for operators. For mixing and loading of calcium cyanamide fertiliser, handling six bags of 600 kg net content for 18 minutes or handling 12 bags with 50 kg net content for 12 minutes resulted in concentrations of 0.21 or 0.13 mg/m^3 air, respectively. Data were generated by a personal air sampling system, measured as cyanamide and recalculated to the corresponding calcium cyanamide concentrations. Additionally, a worker equipped with a personal air sampling system applied 350 kg PERLKA/ha on a field of 5.1 ha for 60 minutes. Calcium cyanamide concentrations reported for this application were 0.06 mg/m^3 in an open tractor and below detection limit of 0.01 mg/m^3 in a closed cabin approach (AlzChem Trostberg, 2013, see also Table 3, manufacturer scenario).

The SCHER uses these data in a first approach to assess operator inhalatory exposure to calcium cyanamide during mixing, loading and application. Therefore the measured data from the manufacturer scenario were used to calculate inhalatory exposure for different scenarios: a realistic worst case with an application rate of 1,000 kg formulation/ha as well as a normal case with an application rate of 500 kg formulation/ha. For both scenarios the exposure was calculated considering different field sizes: a small field of 3 ha, and a large field of 48 ha taking into account greater fields used e.g. for cabbage in certain parts of the EU. The SCHER used an expected concentration in the air of 0.21 mg/m^3 for calculations of exposure during mixing and loading as well as an expected concentration in the air of 0.06 mg/m^3 for the calculation of exposure during application. The SCHER acknowledges, that the use of tractors with dust – tight cabins would reduce

the inhalative exposure for workers during application of the granules to the field. However, the SCHER has no information on use and availability of such tractors for farmers within all European member states. For small fields rotators with a working width of 12 m were considered and for large fields rotators with a working width of 24 m. Factors were applied in order to address different amounts of dust from the different rotators.

The SCHER's estimation of inhalatory exposure for operators resulted in values exceeding the AOEL for the realistic worst case and the normal case scenarios (for further details see Table 4). It has to be kept in mind, that the realistic worst case (1000 kg/ha) and the normal case (500 kg/ha) scenarios were based on data measured for a much lower application rate (350 kg/ha). Measured values can also not be used for the exposure assessment of private users, bystanders and residents.

Table 4: Exposure assessment for operators, inhalation only, approach based on data measured by the manufacturer.
M: mixing, L: loading, Appl: application, AF: assessment factor.

	Abbr.	Formula		Scenario				
				manufacurer	realistic worst case		normal case	
					small field	large field	small field	large field
Treated area			ha/d	5.1	3	48	3	48
Application rate			kg formulation/ha	350	1000	1000	500	500
Active substance			%	45	45	45	45	45
Frequency			-	1	1	1	1	1
Working width			m	15	12	24	12	24
M/L time	TML		min	9	60	81	60	81
Application time	AT		min	60	60	420	60	420
Breathing volume	BV		L/min	20	20	20	20	20
M/L, measured concentration in air			mg/m^3	0.21	-	-	-	-
M/L, expected concentration in air	MLECA		mg/m^3	-	0.21	0.21	0.21	0.21
Expected dose during M/L	MLED	MLECA(1000/350) or MLECA(500/350)	mg/m^3	-	0.6	0.6	0.3	0.3
Appl. measured concentration in air (open cabin)			mg/m^3	0.06	-	-	-	-
Appl. measured concentration in air (closed cabin)			mg/m^3	0	-	-	-	-
Appl. expected concentration in air *	AECA		mg/m^3		0.048	0.0768	0.048	0.0768
Expected dose during application	AED	AECA(1000/350) or AECA(500/350)	mg/m^3		1.37E-01	2.19E-01	6.86E-02	1.10E-01
Body weight	BW		kg	70	70	70	70	70
Exposure calculation only for inhalation		(MLED*BV*TML)+(AED*BV*AT)/(BW/1000)	**mg/kg bw/d**	**5.40E-04**	**1.26E-02**	**4.02E-02**	**6.32E-03**	**2.01E-02**
LOAEL			mg/kg bw/d	1.30E+00	1.30E+00	1.30E+00	1.30E+00	1.30E+00
AF			-	3.00E+02	3.00E+02	3.00E+02	3.00E+02	3.00E+02
Systemic AOEL			**mg/kg bw/d**	**4.33E-03**	**4.33E-03**	**4.33E-03**	**4.33E-03**	**4.33E-03**
% AOEL for inhalation only			-	**1.25E+01**	**2.92E+02**	**9.28E+02**	**1.46E+02**	**4.64E+02**

Besides inhalatory exposure, for mixing and loading but also for application of fertilisers, dermal exposure has to be considered appropriately. For granular formulations the dermal exposure is considered to be relevant. A second approach to model exposures was therefore performed by the SCHER taking into account dermal exposure as well. A dermal penetration rate of 10% is considered appropriate to calculate the dermal exposure of calcium cyanamide when used as fertiliser.

At present there are no internationally harmonised and accepted exposure models for fertilisers available. The SCHER therefore used models developed in the UK[1] for granule pesticide formulations which were considered to be also appropriate for fertilisers. The model used for operators took into account data from a large number of field studies on dermal and inhalatory exposure. This model selected appropriate data from its database

[1] For further information see http://www.pesticides.gov.uk/guidance/industries/pesticides/topics/pesticide-approvals/pesticides-registration/applicant-guide/the-applicant-guide-completing-an-application-overview-for-operator-and-consumer-exposure

to estimate dermal and inhalational exposure for professional operators when handling and applying granular pesticides. The 75th percentile exposure values from these data subsets were used to estimate operator exposure resulting from uses of granular formulations assuming that gloves and working clothes were worn for all activities. However, this model does not foresee using specific values on particle size distribution or drift percentage as input values.

Details on the exposure calculations for the different scenarios are given in Annex 2. Table 5 summarises the results. The AOEL is exceeded in all scenarios.

Table 5: Exposure assessment for workers, inhalation and dermal absorption, based on an operator exposure model for granular formulations; gloves and normal work wear were worn during loading and application operations and respiratory protection equipment was considered for mixing/loading.

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT					
		Realistic Worst Case		Normal Case	
		small field	large field	small field	large field
Total systemic exposure	mg/kg bw/d	0.08	1.21	0.04	0.60
Percent of AOEL	%	**1,755**	**28,072**	**877**	**14,036**

Exposure estimation for private use

Currently there are no exposure models available for predicting exposure for amateur users applying granules. In the absence of specific exposure data for granule products, the Puffer pack model for users applying dustable powder formulations via puffer packs was recommended by the UK as surrogate data for this exposure scenario. This model was used by the SCHER for the exposure assessment of calcium cyanamide fertilisers for private use. Details are provided in Annex 3, table 3.1. Exposure was assumed to be 0.12 mg/kg bw/d (>2700% of AOEL). In addition, the Operator exposure model for granular formulations using hand-held application equipment was used, based on the assumptions of a 500 m² garden, 180 kg active substance applied per ha and the use of protective equipment (see table 3.2). This approach resulted in exposure exceeding the AOEL by 32,821%.

Exposure scenarios for bystanders and residents

Professional use

As there were no models available for fertilisers or for granular pesticides, the approach for sprayed pesticides was used assuming a 0.2% drift to calculate exposure for bystanders and residents (Martin, *et al.*, 2008). This percentage was chosen according to information provided for the particle size distribution (see Table 1) and on information on the amount of fine particles from the CSR.

Details for bystanders are provided in Annex 4, table 4.1. The values calculated for bystanders were considerably high, exceeding the systemic AOEL for adults and for children when assuming exposure duration of 5 minutes as well as 10% dermal absorption (Table 6).

Table 6: Bystander exposure calculation based on 0.2% drift, a duration of 5 minutes and 10% dermal uptake

Bystanders		realistic worst case				normal case			
		small field		large field		small field		large field	
		Adults	Children	Adults	Children	Adults	Children	Adults	Children
Total Systemic Exposure	mg/kg bw/d	11.40	24.14	180.15	384.44	5.70	12.07	90.08	192.22
Percent of AOEL	%	265,116	561,338	4,189,535	8,940,581	132,558	280,669	2,094,767	4,470,291

Calculations for residents included inhalation and dermal exposure. For children oral uptake (hand-to-mouth and object-to-mouth transfer) was also estimated. Based on the calculations, the uptake of calcium cyanamide was high for all scenarios, exceeding the AOEL. Results were given in Table 7 (for 10% dermal absorption), details of the calculations were provided in Annex 4, Table 4.2.

Table 7: Residential exposure calculation based on 0.2% drift, a duration of 2 h and 10% dermal uptake

Residents		realistic worst case				normal case			
		small field		large field		small field		large field	
		Adults	Children	Adults	Children	Adults	Children	Adults	Children
Total Systemic Exposure	mg/kg bw/d	0,015	0,036	0,015	0,036	0,010	0,022	0,010	0,022
Percent of AOEL	%	351	840	351	840	224	510	224	510

Private use

No models were available for bystanders during private use, however, it is expected that exposure for bystanders would not exceed the exposure predicted for persons applying the product. In a worst case assumption, exposure values for users might also be used for bystanders (see above, Exposure estimation for private use).

Also for private use, inhalation and dermal exposure had to be considered for residents. As there were no models available, estimated exposure values for residents after professional use might be considered. A possible scenario of exposure during re-entry into the treated areas and/or using treated areas as playgrounds, sunbathing meadows etc. was not taken into account.

For children, oral uptake also has to be considered for products applied as granules as there is a potential for granules to be ingested by children who may enter treated areas soon after the they have been applied. The UK developed a model for oral uptake of granules by children. This model was used by the SCHER to estimate the additional oral exposure for children after private use of calcium cyanamide as fertiliser. According to the amount applied, the additional oral exposure for children was calculated to be 0.04 mg/kg bw/d (868% of AOEL) or 0.02 mg/kg bw/d (434% of AOEL) depending on the application rate. For details see table 4.3 in Annex 4. The ingestion of granules would be higher for children with pica[2] behaviour.

[2] Pica is an eating disorder typically defined as the persistent eating of non-nutritive substances like clay, sand, stones and pebbles.

Due to high exposure, the SCHER does not recommend the use of calcium cyanamide as fertiliser for private use.

3.2.9. Soil, groundwater and surface water, exposure estimates

3.2.9.1. Justification Pesticides model used for fertilisers

The SCHER notes that specific mathematical models for fertilisers are not available in the scientific literature or regulatory frameworks. It should also be recognized that it is not with the remit of the SCHER to develop such models for fertilisers. Therefore, the SCHER is of the opinion that suitable analogous procedures/models should be used to describe the behaviour and fate of fertilisers. The best available possibility is to use models that are specifically developed to describe the behaviour and fate of chemicals. In fact, a fertiliser, as a chemical substance, is subject to the same degradation, sorption and leaching processes as all chemicals. The most advanced models have been developed specifically for pesticides as their behaviour and fate is of great importance for the registration of these chemicals. In the EU, the US and several other countries, mathematical models have been developed to help the registration authorities in the risk assessment process of pesticides. Examples of these pesticides models can be found on the FOCUS-website of the EU (http://focus.jrc.ec.europa.eu/) and for the US on the EPA-website (http://www.epa.gov/pesticides/science/models_pg.htm). These models are based on the best available scientific knowledge on the fate and behaviour of chemicals and make use of generally applicable, accepted, principles.

The SCHER appreciates the difference between fertilisers and pesticides. Pesticides are used to protect the growth of the plant and to remove any inhibition of the plant development by pests, e.g. weeds, fungi, insects, etc., whilst fertilisers are intended to allow the full development of the crop and to increase the yield of the harvest. If, however, the type of chemical is considered, there are no principal differences between a fertiliser or a pesticide, in the sense that both are mostly (in)organic chemicals that obey the general principles of the conservation of mass. Moreover, the application techniques used for fertilisers and pesticides are similar. Both are applied with the same kinds of spraying equipment. Therefore, processes relevant for pesticides, like (spray) drift, leaching, runoff, also apply for fertilisers and the same holds for molecular processes like degradation and sorption. In addition to these analogies, it should be noted that the environmental fate and behaviour of chemicals is determined by and can be predicted from their physico-chemical characteristics, like molecular weight, solubility, vapour pressure, Henry's Law constant, pKa, polarity and, of course, the dose of the substance. For fertilisers, all these data are available and the application of the models thus leads to predictable outcomes. Recognizing these common principles for fertilisers and pesticides, the SCHER concluded that the use of pesticide models provides the best available approach to describe the fate and behaviour of fertilisers in the environment.

To estimate the concentrations in soil, groundwater and surface water after the application of calcium cyanamide in cabbage, the same calculation methods have been used by the SCHER as normally applied in the evaluation of pesticides in the European Union. This methodology was called the FOCUS scenarios approach and it had especially been developed specifically for this purpose (FOCUS, 2014). The following two sections summarise the results for calcium cyanamide.

3.2.9.2. Estimated PEC in soil

The SCHER has calculated PEC in soils based on two application rate scenarios.

The SCHER applied the normal calculation for the determination of the PEC in soil using the areic application rate of 225 kg a.s./ha and a depth of 5 cm. Therefore, the resulting PEC_{soil} was 0.44 kg calcium cyanamide/m^3 or 440 mg/dm^3 or assuming a soil density of 1,500 kg/m^3 a PEC of 300 mg/kg soil. If the amount of fertiliser was ploughed into the soil, assuming a plough depth of 20 cm, the PEC was a factor of 4 lower: 75 mg/kg soil. Based on a DT50 in soil of 2 d, the PEC_{soil} and the Time Weighted Average (TWA_{soil}) was estimated and the results are presented in Table 8.

Table 8 PEC_{soil} and TWA_{soil} for cyanamide in mg/kg soil for the normal scenario (application rate 225 kg a.s./ha) and the realistic worst case scenario (application rate 450 kg a.s./ha)

	Normal scenario		Worst case scenario	
Day	PEC	TWA	PEC	TWA
0	300	-	600	-
1	215	255	430	510
2	105	155	210	310
4	27	60	54	120
7	2.6	10	5.2	20
14	0	0.5		

3.2.9.3. Estimated PEC in groundwater

The concentrations in groundwater after the application of calcium cyanamide in cabbage were calculated using the FOCUS scenarios. The relevant models applicable to groundwater were downloaded from the FOCUS website (FOCUS, 2014) (MACRO_GW, PEARL, PELMO and PRZM_GW). In the following sections the results for calcium cyanamide are summarised for seven different representative agricultural areas in the EU. Although several models could be used for the estimation of the concentration of a pesticide in groundwater, the SCHER has chosen to apply the PEARL model. The input data for the model are presented in Table 9.

Table 9. Input data for model calculations on calcium cyanamide

Parameter	**Value**
Crop	Cabbage
Location	Châteaudun, Hamburg, Jokioinen, Kremsmuenster, Porto, Sevilla, Thiva
Substance Name	$CaCN_2$
Molecular mass (g mol^{-1})	80.11
DT_{50} (d)	2
K_{om} (L kg^{-1})	10.5
Vapour pressure (Pa)	0
Solubility in water (mg L^{-1})	29400
Dose (kg.ha^{-1}) as active substance	225/450
Interception (-)	0.0

The results of the PEARL calculations are given in Table 10.

Table 10. PEARL Calculations for calcium cyanamide

Location	Estimated groundwater concentration (µg/L) at normal scenario	Estimated groundwater concentration (µg/L) at realistic worst case scenario
CHATEAUDUN	0.10	0.20
HAMBURG	22	44
JOKIOINEN	5	10
KREMSMUENSTER	2.7	5.4
PORTO	0.18	0.36
SEVILLA	0.01	0.02
THIVA	0.7	1.4

According to the registration criteria in the European Union, there should be at least one safe use for the substance available in all the European scenarios. The criterion in the case of groundwater was < 0.1 µg/L. This was the case for Sevilla and Chateaudun. From the viewpoint of safety for groundwater the substances could be registered in the EU. In other areas the application of the substance may be limited at the national level to reduce the contamination of groundwater as all other estimated concentrations were a factor of 7 to 220 higher than the registration criterion.

A lysimeter study with calcium cyanamide was carried out from 1991 to 1994 (Kubiak, 1996) using a dosage of 400 kg PERLKA/ha. The study was carried out according to the German Guideline on lysimeters (BBA, 1990). The soil used was loamy sand with 1.5% organic matter in the upper 30 cm. All residues in the leachate of the lysimeters were below 0.1 µg/L.

The SCHER concludes from these results that application of the formulation PERLKA at the recommended dosage does not result in unacceptable concentrations in groundwater.

3.2.9.4. Predicted Environmental concentration in surface water

The FOCUS-models for the surface water compartment were downloaded from the same website (http://focus.jrc.ec.europa.eu/). It concerned the models SWASH, MACRO_SW, PRZM_SW and TOXSWA. As the formulation PERLKA is a solid that is applied to the soil as a granular product (AlzChem Trostberg, 2010) drift input should not add to the contamination of surface water. This is an accepted approach in the registration of pesticides and in the SCHER's opinion it is also applicable for granulated fertilisers. Some emission by runoff or drainage will take place. Therefore, calculations were carried out with the FOCUS methodology excluding drift. With the exception of the locations mentioned in Table 10, the SCHER used the same input data for the surface water calculation as for the groundwater estimation. The FOCUS surface water scenarios distinguished drainage (D) and run-off (R) scenarios which could contain a ditch (d), a pond (p) or a small stream (s) as the relevant receiving water bodies.

The results of the surface water calculations are summarised in the Tables 11, 12, 12A, 13, 13A, 14, 14A and 15, 15A.

Table 11. PECsw – FOCUS modelling results for $CaCN_2$ in surface waters at normal and realistic worst case scenarios

Scenario	Maximum PECsw (µg/L) at normal scenario	Maximum PECsw (µg/L) at realistic worst case scenario
D3,d	0.0	0.0
D4,p	0.006	0.012
D4,s	0.028	0.056
D5,p	0.0	0.0
D5,s	0.0	0.0
D6,d	7.5	15
R1,p	0.12	0.24
R1,s	6.6	13
R2,s	220	440
R3,s	2300	4600
R4,s	3400	6800

D = drainage scenario, R- run-off scenario, d = ditch, p = pond and s = stream, no cabbage was grown in the other D-scenarios.

More detailed results are provided in the Tables 12, 12A and 13, 13A where the concentrations at the different time points are presented for the normal and the realistic worst case scenarios. The D- and R-scenarios are given in the Tables 12, 12A and 13, 13A respectively.

Table 12. Detailed calculation results for the PEC in surface waters in drainage scenarios in µg/L for the normal application scenario.

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
0	0.00E+00	5.95E-03	2.76E-02	0.00E+00	0.00E+00	7.35E+00
1	0.00E+00	5.95E-03	1.65E-02	0.00E+00	0.00E+00	7.35E+00
2	0.00E+00	5.95E-03	1.44E-02	0.00E+00	0.00E+00	7.30E+00
4	0.00E+00	5.90E-03	1.54E-02	0.00E+00	0.00E+00	7.15E+00
7	0.00E+00	5.75E-03	1.75E-02	0.00E+00	0.00E+00	6.90E+00
14	0.00E+00	5.35E-03	2.21E-02	0.00E+00	0.00E+00	5.80E+00
21	0.00E+00	4.80E-03	2.38E-02	0.00E+00	0.00E+00	5.95E+00
28	0.00E+00	4.65E-03	2.45E-02	0.00E+00	0.00E+00	3.70E+00
42	0.00E+00	5.15E-03	2.29E-02	0.00E+00	0.00E+00	5.10E+00
50	0.00E+00	5.40E-03	1.89E-02	0.00E+00	0.00E+00	4.85E+00
100	0.00E+00	1.85E-03	1.90E-02	0.00E+00	0.00E+00	4.12E+00

Table 12A. Detailed calculation results for the PEC in surface waters in drainage scenarios in µg/L for the realistic worst case application scenario.

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
0	0.00E+00	1.19E-02	5.50E-02	0.00E+00	0.00E+00	1.47E+01
1	0.00E+00	1.19E-02	5.50E-02	0.00E+00	0.00E+00	1.47E+01
2	0.00E+00	1.19E-02	5.49E-02	0.00E+00	0.00E+00	1.47E+01

4	0.00E+00	1.19E-02	5.48E-02	0.00E+00	0.00E+00	1.46E+01
7	0.00E+00	1.17E-02	5.42E-02	0.00E+00	0.00E+00	1.42E+01
14	0.00E+00	1.15E-02	5.33E-02	0.00E+00	0.00E+00	1.34E+01
21	0.00E+00	1.12E-02	5.10E-02	0.00E+00	0.00E+00	1.32E+01
28	0.00E+00	1.06E-02	4.66E-02	0.00E+00	0.00E+00	1.22E+01
42	0.00E+00	1.05E-02	4.69E-02	0.00E+00	0.00E+00	1.15E+01
50	0.00E+00	1.02E-02	4.33E-02	0.00E+00	0.00E+00	1.03E+01
100	0.00E+00	1.19E-02	5.50E-02	0.00E+00	0.00E+00	1.47E+01

Table 13. Detailed calculation results for the PEC in surface waters in run-off scenarios in µg/L for the normal application scenario.

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
0	1.20E-01	5.65E+00	2.63E+02	2.28E+03	3.39E+03
1	1.02E-01	2.30E-03	4.44E-02	2.43E+02	9.35E+00
2	8.65E-02	5.50E-04	1.71E-02	2.32E+00	7.85E-01
4	6.25E-02	2.00E-04	6.15E-03	5.80E-01	2.41E-01
7	3.84E-02	5.00E-05	2.70E-03	2.26E-01	7.50E+01
14	1.05E-02	5.00E-05	1.10E-03	6.60E-02	1.62E-02
21	2.15E-03	0.00E+00	5.50E-04	3.47E-02	8.45E-03
28	4.50E-04	0.00E+00	3.50E-04	2.23E-02	5.45E-03
42	5.00E-05	0.00E+00	2.00E-04	1.23E-02	2.95E-03
50	0.00E+00	0.00E+00	1.50E-04	1.04E-02	5.60E-03
100	0.00E+00	0.00E+00	5.00E-05	3.55E-03	1.90E-03

Table 13A. Detailed calculation results for the PEC in surface waters in run-off scenarios in µg/L for the realistic worst case application scenario.

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
0	2.40E-01	1.13E+01	5.26E+02	4.56E+03	6.77E+03
1	2.04E-01	4.60E-03	8.88E-02	4.85E+02	1.87E+01
2	1.73E-01	1.10E-03	3.41E-02	4.63E+00	1.57E+00
4	1.25E-01	4.00E-04	1.23E-02	1.16E+00	4.82E-01
7	7.68E-02	1.00E-04	5.40E-03	4.52E-01	1.50E+02
14	2.09E-02	1.00E-04	2.20E-03	1.32E-01	3.24E-02
21	4.30E-03	0.00E+00	1.10E-03	6.93E-02	1.69E-02
28	9.00E-04	0.00E+00	7.00E-04	4.46E-02	1.09E-02
42	1.00E-04	0.00E+00	4.00E-04	2.46E-02	5.90E-03
50	0.00E+00	0.00E+00	3.00E-04	2.08E-02	1.12E-02
100	0.00E+00	0.00E+00	1.00E-04	7.10E-03	3.80E-03

The tables 14, 14A and 15, 15A provide detailed results of the calculation of the time-weighted average concentrations for the same scenarios and the same application scenarios. The TWA concentration represents the mean concentration over the specified period.

Table 14. Detailed calculation results for the TWA in surface waters in drainage scenarios in µg/L for the normal application scenario.

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d

1	0.00E+00	5.95E-03	2.75E-02	0.00E+00	0.00E+00	7.35E+00
2	0.00E+00	5.95E-03	2.75E-02	0.00E+00	0.00E+00	7.35E+00
4	0.00E+00	5.95E-03	2.75E-02	0.00E+00	0.00E+00	7.35E+00
7	0.00E+00	5.95E-03	2.74E-02	0.00E+00	0.00E+00	7.30E+00
14	0.00E+00	5.85E-03	2.71E-02	0.00E+00	0.00E+00	7.10E+00
21	0.00E+00	5.75E-03	2.67E-02	0.00E+00	0.00E+00	6.70E+00
28	0.00E+00	5.60E-03	2.55E-02	0.00E+00	0.00E+00	6.60E+00
42	0.00E+00	5.30E-03	2.33E-02	0.00E+00	0.00E+00	6.10E+00
50	0.00E+00	5.25E-03	2.35E-02	0.00E+00	0.00E+00	5.75E+00
100	0.00E+00	5.10E-03	2.17E-02	0.00E+00	0.00E+00	5.15E+00

Table 14A. Detailed calculation results for the TWA in surface waters in drainage scenarios in µg/L for the worst case application scenario.

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
1	0.00E+00	1.19E-02	5.50E-02	0.00E+00	0.00E+00	1.47E+01
2	0.00E+00	1.19E-02	5.50E-02	0.00E+00	0.00E+00	1.47E+01
4	0.00E+00	1.19E-02	5.49E-02	0.00E+00	0.00E+00	1.47E+01
7	0.00E+00	1.19E-02	5.48E-02	0.00E+00	0.00E+00	1.46E+01
14	0.00E+00	1.17E-02	5.42E-02	0.00E+00	0.00E+00	1.42E+01
21	0.00E+00	1.15E-02	5.33E-02	0.00E+00	0.00E+00	1.34E+01
28	0.00E+00	1.12E-02	5.10E-02	0.00E+00	0.00E+00	1.32E+01
42	0.00E+00	1.06E-02	4.66E-02	0.00E+00	0.00E+00	1.22E+01
50	0.00E+00	1.05E-02	4.69E-02	0.00E+00	0.00E+00	1.15E+01
100	0.00E+00	1.02E-02	4.33E-02	0.00E+00	0.00E+00	1.03E+01

Table 15. Detailed calculation results for the TWA in surface waters in run-off scenarios in µg/L for the normal application scenario.

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
1	1.12E-01	2.93E+00	1.23E+02	1.86E+03	2.42E+03
2	1.04E-01	1.47E+00	6.10E+01	9.65E+02	1.21E+03
4	8.95E-02	7.35E-01	3.06E+01	4.82E+02	6.05E+02
7	7.35E-02	4.19E-01	1.75E+01	2.76E+02	3.46E+02
14	4.87E-02	2.10E-01	9.10E+00	1.38E+02	1.77E+02
21	3.44E-02	1.40E-01	6.05E+00	9.20E+01	1.18E+02
28	2.61E-02	1.05E-01	4.54E+00	6.90E+01	8.85E+01
42	1.75E-02	7.00E-02	3.03E+00	4.60E+01	5.90E+01
50	1.47E-02	5.85E-02	2.54E+00	3.87E+01	4.95E+01
100	7.35E-03	2.94E-02	1.27E+00	1.93E+01	2.48E+01

Table 15A. Detailed calculation results for the TWA in surface waters in run-off scenarios in µg/L for the worst case application scenario.

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
1	2.23E-01	5.86E+00	2.45E+02	3.72E+03	4.83E+03
2	2.07E-01	2.93E+00	1.22E+02	1.93E+03	2.42E+03
4	1.79E-01	1.47E+00	6.12E+01	9.64E+02	1.21E+03
7	1.47E-01	8.38E-01	3.50E+01	5.51E+02	6.91E+02
14	9.73E-02	4.19E-01	1.82E+01	2.76E+02	3.54E+02

21	6.87E-02	2.79E-01	1.21E+01	1.84E+02	2.36E+02
28	5.21E-02	2.10E-01	9.08E+00	1.38E+02	1.77E+02
42	3.49E-02	1.40E-01	6.05E+00	9.20E+01	1.18E+02
50	2.93E-02	1.17E-01	5.08E+00	7.73E+01	9.90E+01
100	1.47E-02	5.87E-02	2.54E+00	3.86E+01	4.95E+01

These tables show that especially in scenarios D6, R2, R3 and R4, the concentration of calcium cyanamide is high compared to that in the other scenarios. This is mainly caused by the low organic carbon content of these scenarios, except for R2 where the steep slope of the field, which leads to higher run off rates, is the main reason for the high concentration.

3.2.9.5. Estimated concentration in air

The formulation PERLKA was applied to soil as a granulated product. The vapour pressure of the a.s. calcium cyanamide was very low (estimated with EpiSuite: 4.58E-19 Pa). Therefore, the SCHER concluded that the air compartment is not relevant and should therefore not be considered in estimating exposures except for the scenarios discussed in paragraph 3.2.8.

3.3. Risk Assessment

3.3.1. Human Health Risk Assessment

The SCHER evaluated data available on toxicity of calcium cyanamide as well as on cyanamide in an overall weight of evidence approach in order to assess possible effects on the human health from the use of calcium cyanamide as a fertiliser. As calcium cyanamide was hydrolysed to cyanamide after oral administration in experimental animals as well as in humans, toxic effects observed for calcium cyanamide were mainly attributable to cyanamide toxicity. The SCHER has selected a LOAEL of 1.3 mg calcium cyanamide/kg bw/d from a rat study and derived a provisional AOEL of 4.3 µg/kg bw/d based on a safety factor of 300. Developmental toxicity with reduced foetal weight has been observed above doses of 7 mg/kg bw/d, but with no excess mortality and no signs of teratogenicity at doses as high as 49 mg/kg bw/day.

For the exposure assessment, the SCHER calculated scenarios for the different uses of calcium cyanamide as a fertiliser, based on data measured for inhalation exposure as well as on the basis of default values attributed to exposure calculation models judged appropriate for granulated materials. Exposure calculations were performed for both professional and private use scenarios and additionally for bystanders and residents, including children. For all scenarios, the AOEL is exceeded (see Table 16). Some of the model scenarios might overestimate the actual exposure, but on the other hand, on the basis of measured data, the AOEL is already exceeded when considering the inhalation exposure only.

Table 16: Percent of AOEL for different exposure scenarios

[1] calculated with the UK models

[2] calculated on base of data measured (inhalatory exposure only)

[3] oral uptake of treated soil and granulate only

i = inhalatory, d = dermal, o = oral, n.d. = no data from models

	Exposure	Professional use				Private use	
		realistic worst case		normal case		Operator Model	Puffer Pack Model
		small field	large field	small field	large field		
operator[1]	i, d	1,755	28,072	877	14,036	32,821	2,761
operator[2]	i	292	928	146	464	-	-
bystander adult	i, d	265,116	4,189,535	132,558	2,094,767	n.d.	n.d.
bystander child	i, d	561,338	8,940,581	280,669	4,470,291	n.d.	n.d.
resident adult	i, d	351	351	224	224	n.d.	n.d.
resident child	i, d, o	840	840	510	510	n.d.	n.d.
resident child[3]	o	-	-	-	-	434-868	

3.3.2. Environmental Risk Assessment

Soil

Several organisms were considered for the soil compartment: birds, earthworms, non-target arthropods and microorganisms.

For birds, the toxicity test on feed avoidance behaviour showed that birds did not feed on the PERLKA granules. In the evaluation of hydrogen cyanamide by EFSA (EFSA, 2012) a risk for birds was identified due to the soluble formulation used. The SCHER, however, is of the opinion that because of the granular formulation and the birds' feeding avoidance, exposure is unlikely to occur and therefore birds are not considered at risk.

The risk assessment for earthworms was based on the estimated environmental concentrations given in Table 9 and the ecotoxicity data presented in section 3.2.6.2. An assessment factor of 10 as normally used in the registration procedure for plant protection products in the EU was applied to the ecotoxicity data. The SCHER concluded that for this compartment risks cannot be excluded after the application of cyanamide at the recommended dosage of 225 kg a.s./ha (Table 17). RCRaAF and RCRtwaAF stand for the calculated risk characterisation ratio after acute exposure or time weighted average exposure. The time-weighted average concentration at t = 0 was not defined. A reduction by a factor of about 15 to 20 would reduce the risk to a level without concern.

Table 17. Risk assessment for earthworms

	At normal application rates		At realistic worst case applications	
Day	RCRaAF	RCRtwaAF	RCRaAF	RCRtwaAF
0	17.40		35.52	
1	12.30	14.70	25.12	30.02
2	6.15	8.87	12.56	18.12
4	1.54	3.33	3.14	6.79
7	0.14	0.58	0.28	1.18
14	0.00	0.03	0.00	0.06

In a field study carried out in 1991 and 1992 (Bauchhenß, 1994) with a somewhat lower application rate (400 kg formulation/ha compared to the normal application rate of 500 or the worst-case application rate of 1000 kg formulation/ha) no effects on earthworms were observed. Despite this shortcoming of the study the SCHER is of the opinion that most probably effects on earthworms may be considered negligible.

The SCHER's opinion with respect to exposures to beetles is that the risks cannot yet be completely excluded as only 1 dosage had been tested at 450 kg formulation/ha. The

normal dosage was however 500 kg/ha. The SCHER considered the normal dose and the tested dose sufficiently close that effects may be not likely. A new study at normal application rates is recommended.

No toxicity data of calcium cyanamide to bees were available to the SCHER. Therefore no risk assessment could be carried out. However, the SCHER is of the opinion that bees will not be exposed during the time of application.

Finally, the SCHER concluded that for microorganisms risks were not expected as effects have only been determined at rates 5 times higher than the normal dosage.

Groundwater

Table 10 presents data for several locations across the European Union which were considered representative for the cultivation of cabbage. This table indicates that the concentration in groundwater may exceed the allowable concentration in groundwater of 0.1 μg/L. In areas with low organic matter contents the exceedance might be more than a factor of 200 in the normal application scenario (e.g. 22 μg/L has been calculated in the Hamburg scenario; Table 10) and even more than 400 in the situation of a realistic worst case application scenario. Therefore, the SCHER concluded that concentrations in groundwater occur after the application of calcium cyanamide (according to normal application rates) may pose a risk. SHER notes that even at much lower application rates, in some areas, existing guideline values will be exceeded.

However, a lysimeter study with calcium cyanamide was carried out that showed all concentrations in the leachate below the guideline value of 0.1 μg/L. (AlzChem Trostberg, 2015) Therefore, the SCHER concludes that groundwater will not be at risk after the application of calcium cyanamide at normal application rates.

Surface water

The environmental risk assessment conducted here used the methodology described in the EFSA Guidance Document on aquatic ecotoxicology (EFSA, 2013). In section 3.2.6.1 the relevant acute endpoints for three aquatic species were determined. The PNEC was derived by dividing the lowest L(E)C50 of the three test species by 100. The lowest short-termL(E)C50 in Table 2 is 6 mg/L. the SCHER thus derived a PNEC of 60 μg/L and used this value in the further risk calculations

Tables 18 to 21, using normal applications rates, and Tables 18A to 21A, using the realistic worst case applications rates, present the results of the risk assessment for calcium cyanamide based on the PEC established with the FOCUS surface water scenarios and the derived PNEC. The safe values are indicated in green, and the values representing a risk in red. The SCHER concludes that the application of calcium cyanamide as a fertiliser might lead to risk for aquatic organisms, especially as the Risk Characterisation Ratios (RCRs) > 1 by more than a factor of 10 in many cases.

Table 18A. Risk Characterisation Ratios for the PECs in drainage scenarios at normal application scenario

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
0	0.00	0.00	0.00	0.00	0.00	0.12
1	0.00	0.00	0.00	0.00	0.00	0.12
2	0.00	0.00	0.00	0.00	0.00	0.12
4	0.00	0.00	0.00	0.00	0.00	0.12
7	0.00	0.00	0.00	0.00	0.00	0.12
14	0.00	0.00	0.00	0.00	0.00	0.10
21	0.00	0.00	0.00	0.00	0.00	0.10
28	0.00	0.00	0.00	0.00	0.00	0.06
42	0.00	0.00	0.00	0.00	0.00	0.09
50	0.00	0.00	0.00	0.00	0.00	0.08
100	0.00	0.00	0.00	0.00	0.00	0.07

Table 18B. Risk Characterisation Ratios for the PECs in drainage scenarios at realistic worst case application scenario

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
0	0.00	0.00	0.00	0.00	0.00	0.25
1	0.00	0.00	0.00	0.00	0.00	0.25
2	0.00	0.00	0.00	0.00	0.00	0.24
4	0.00	0.00	0.00	0.00	0.00	0.24
7	0.00	0.00	0.00	0.00	0.00	0.23
14	0.00	0.00	0.00	0.00	0.00	0.19
21	0.00	0.00	0.00	0.00	0.00	0.20
28	0.00	0.00	0.00	0.00	0.00	0.12
42	0.00	0.00	0.00	0.00	0.00	0.17
50	0.00	0.00	0.00	0.00	0.00	0.16
100	0.00	0.00	0.00	0.00	0.00	0.14

Table 19A. Risk Characterisation Ratios for the PECs in runoff scenarios at normal application scenario

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
0	0.00	0.09	4.38	38.00	56.42
1	0.00	0.00	0.00	4.04	0.16
2	0.00	0.00	0.00	0.04	0.01
4	0.00	0.00	0.00	0.01	0.00
7	0.00	0.00	0.00	0.00	1.25
14	0.00	0.00	0.00	0.00	0.00
21	0.00	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00	0.00
50	0.00	0.00	0.00	0.00	0.00
100	0.00	0.00	0.00	0.00	0.00

Table 19B. Risk Characterisation Ratios for the PECs in runoff scenarios at realistic worst case application scenario

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
0	0.00	0.19	8.77	76.00	112.83
1	0.00	0.00	0.00	8.08	0.31
2	0.00	0.00	0.00	0.08	0.03
4	0.00	0.00	0.00	0.02	0.01
7	0.00	0.00	0.00	0.01	2.50
14	0.00	0.00	0.00	0.00	0.00
21	0.00	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00
42	0.00	0.00	0.00	0.00	0.00
50	0.00	0.00	0.00	0.00	0.00
100	0.00	0.00	0.00	0.00	0.00

Table 20A. Risk Characterisation Ratios for the TWAs in drainage scenarios at normal application scenario

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
1	0.00	0.00	0.00	0.00	0.00	0.12
2	0.00	0.00	0.00	0.00	0.00	0.12
4	0.00	0.00	0.00	0.00	0.00	0.12
7	0.00	0.00	0.00	0.00	0.00	0.12
14	0.00	0.00	0.00	0.00	0.00	0.12
21	0.00	0.00	0.00	0.00	0.00	0.11
28	0.00	0.00	0.00	0.00	0.00	0.11
42	0.00	0.00	0.00	0.00	0.00	0.10
50	0.00	0.00	0.00	0.00	0.00	0.10
100	0.00	0.00	0.00	0.00	0.00	0.09

Table 20B. Risk Characterisation Ratios for the TWAs in drainage scenarios at realistic worst case application scenario

Time (d)	D3,d	D4,p	D4,s	D5,p	D5,s	D6,d
1	0.00	0.00	0.00	0.00	0.00	0.25
2	0.00	0.00	0.00	0.00	0.00	0.25
4	0.00	0.00	0.00	0.00	0.00	0.25
7	0.00	0.00	0.00	0.00	0.00	0.24
14	0.00	0.00	0.00	0.00	0.00	0.24
21	0.00	0.00	0.00	0.00	0.00	0.22
28	0.00	0.00	0.00	0.00	0.00	0.22
42	0.00	0.00	0.00	0.00	0.00	0.20
50	0.00	0.00	0.00	0.00	0.00	0.19
100	0.00	0.00	0.00	0.00	0.00	0.17

Table 21A. Risk Characterisation Ratios for the TWAs in runoff scenarios at normal application scenario

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
1	0.00	0.05	2.04	31.00	40.25
2	0.00	0.02	1.02	16.08	20.17
4	0.00	0.01	0.51	8.03	10.08
7	0.00	0.01	0.29	4.59	5.76
14	0.00	0.00	0.15	2.30	2.95
21	0.00	0.00	0.10	1.53	1.97
28	0.00	0.00	0.08	1.15	1.48
42	0.00	0.00	0.05	0.77	0.98
50	0.00	0.00	0.04	0.64	0.83
100	0.00	0.00	0.02	0.32	0.41

Table 21B. Risk Characterisation Ratios for the TWAs in runoff scenarios at realistic worst case application scenario

Time (d)	R1,p	R1,s	R2,s	R3,s	R4,s
1	0.00	0.10	4.08	62.00	80.50
2	0.00	0.05	2.03	32.17	40.33
4	0.00	0.02	1.02	16.07	20.17
7	0.00	0.01	0.58	9.18	11.52
14	0.00	0.01	0.30	4.60	5.90
21	0.00	0.00	0.20	3.07	3.93
28	0.00	0.00	0.15	2.30	2.95
42	0.00	0.00	0.10	1.53	1.97
50	0.00	0.00	0.08	1.29	1.65
100	0.00	0.00	0.04	0.64	0.83

The SCHER concludes on the basis of the results of tables 18A to 221A and 18B to 21B that after application of PERLKA up to a dosage of 500 kg/ha in drainage regions probably no risk for aquatic organisms will occur. However, in runoff areas the SCHER concludes that risks for aquatic organisms cannot be excluded as exceedance of risk characterisation ratios up to a factor of 56 may occur.

3.4. Conclusions on data

3.4.1. Human health

Overall, the SCHER is of the opinion that at the present rate of application common in agricultural practice, there is a risk for operators using calcium cyanamide as a fertiliser. The models used for the exposure calculation for professional use took into account the use of protective gloves and work clothes. The use of masks during application might reduce the risk of operators but was not recommended as:

- the use of masks might not be practical under real conditions when applying fertilisers;
- the use of masks during professional use was irrelevant for protection of private users, bystanders or residents;
- the professional application of calcium cyanamide as fertiliser additionally posed a risk for bystanders and residents.

The private use of calcium cyanamide as fertiliser should be avoided, also with respect to the toxic properties of cyanamide. The risk for bystanders as well as for residents re-entering treated areas could not be calculated. For children playing on treated areas, exposure was estimated to pose a risk. The exposure to calcium cyanamide from a possible oral uptake of granules by children was calculated and exceeded the AOEL.

3.4.2. Environment

The environmental data in the registration dossier for the fertiliser calcium cyanamide are considered by the SCHER to be of sufficient quality to be used in a risk assessment as carried out in this opinion. The SCHER accepts the waivers of the manufacturer on the chronic toxicity for aquatic organisms based on the rather quick degradation of the active substance calcium cyanamide into cyanamide and urea with the final degradation products CO_2, NO_3 and H_2O (see the degradation scheme in Figure 1). The SCHER has chosen to use the toxicity data for calcium cyanamide as the most appropriate for the risk assessment, mainly because the effects of the substance after application were shown in the first couple of days, although some do prolong as far as 50 days after application. The application took place only once a year and before sowing. The information provided by the manufacturer in leaflets, however, shows that in several applications a dosage before and after sowing is recommended.

Based on the dossier provided by the manufacturer the SCHER concluded that potential risks for aquatic organisms cannot be excluded. For other terrestrial organisms, like birds and non-target arthropods no risks are expected at normal application rates of calcium cyanamide. Also risks to microorganisms were not expected. No information was available about the toxicity and potential risks of calcium cyanamide to bees.

According to the SCHER, normal risk mitigation measures, like reduction of the dose, and drift reduction are expected to be insufficient to reduce all risks indicated. It is especially difficult to reduce the risk to groundwater contamination in all scenarios. However, a lysimeter study carried out between 1991 and 1994 indicated that the concentration in the leachate in the soils applied was below 0.1 µg/L. Probably, groundwater contamination might be lower than expected, although in other soils, e.g. with less organic matter, groundwater contaminations at levels that can pose risks may still occur. The SCHER is of the opinion that additional studies may provide more insight into the realism of the anticipated risks. This would imply that for the aquatic compartment field studies or mesocosm studies could be carried out to prove that no effects for aquatic organisms detected. For bees, the basic toxicity tests were missing and appropriate testing should be carried out. In addition, field studies would be required to demonstrate that no adverse effects to beetles occur.

3.4.3. Uncertainties

The primary data as presented by the manufacturer in the registration dossier might have some inherent uncertainty. The SCHER has taken into account uncertainties in the usual manner that uncertainties are accounted for in regulatory risk assessment, i.e. by using appropriate assessment factors and adopting common risk assessment methodologies. However, the risk assessment methods used by the SCHER and developed for estimating environmental exposure and human exposure to pesticides might also have some inherent uncertainty. Nevertheless, the SCHER is of the opinion that based on the information and tools available, the best possible risk assessment approach has been used in this opinion.

4. OPINION OF THE SCHER

4.1. Question 1 of ToR

Taking into account all relevant information that was available before 1 April 2015, can the use of both the powdered and granulated form of calcium cyanamide be considered safe for human health and the environment?

The SCHER concluded after receiving additional information from the manufacturer that a dosage of 1,000 kg PERLKA/ha is a realistic worst case scenario whilst the normal dosage is considered to be 500 kg PERLKA/ha. The results of the risk assessment presented are based on both application rates. The SCHER based its evaluation on the granulated form and was not able to exclude potential effects for human health nor for the environment. In the case of the powdered form the SCHER considered that the risk for human health would increase because of a higher fraction of small size particles in the powdered form. For the environment, the risks identified for the powdered form are the same as those identified for the granulated form because of the assumption of no drift.

Currently there are no exposure/risk models available for the evaluation of fertilisers. Therefore, the SCHER calculated the exposure based on measured data and in addition used exposure models developed for pesticides as the most appropriate tools available. Using these models, the SCHER concluded that harmful effects for humans and for the environment could not be excluded at normal and at the realistic worst-case applications. Risks were identified in both scenarios for the end-users (famers as well as private users) and for residents and bystanders including children. For the environment, the SCHER identified risks for the aquatic compartment in both scenarios.

4.2. Question 2 of ToR

In case of risks identified by the SCHER, are the protective measures recommended by the manufacturer sufficient to ensure a safe use of calcium cyanamide as fertiliser?

The manufacturer provided recommendations for using gloves and work clothes to protect operators. Despite the use of these protective measures, risks have been identified as all models used by the SCHER for the exposure calculation for professional and private use took into account the use of protective gloves and work clothes. The use of masks by operators during application might further reduce the risk of operators but might not be practical under real use conditions.

In addition to the risks to operators, the SCHER identified health risks to bystanders and residents. In contrast to operators, there were no protective measures available for these groups.

Although the SCHER also used some conservative approaches for its exposure assessment, the assumptions made were not unrealistic. In all scenarios the AOEL was exceeded considerably. On the basis of the current available knowledge, a concentration of calcium cyanamide in a fertiliser formulation not posing a health risks for humans could not be derived. Additionally it needs to be kept in mind, that the main metabolite of calcium cyanamide is hydrogen cyanamide, which was already restricted for use as a pesticide due to health risks.

The private use of calcium cyanamide as fertiliser should be avoided for several reasons, *i.e.* (1) AOEL was exceeded in all scenarios even when considering the use of gloves and work clothes, (2) there were no additional protective measures available for private users, (3) there was an unknown risk regarding re-entry and use of treated garden areas, (4) oral uptake of treated soil and granulate by children already exceeded the AOEL.

The manufacturer did not provide recommendations for protecting the environment.

4.3. Question 3 of ToR

In case of potential risk for the environment, which application rate per concerned crops would not create any detrimental effect under the relevant soil and climatic conditions?

The SCHER calculated risks based on an application rate of 500 kg formulation/ha on several crops. For lower and higher application rates, the models predicted a linear exposure relationship.

To ensure environmental safety, the SCHER first considered the RCRs obtained. The RCRs calculated were different for the different environmental compartments taken into account. In order to reduce the risk characterisation ratio to 1 (*i.e.* to avoid any detrimental effect to the aquatic compartment) an application rate of 4 kg of a.s./ha is required (9 kg of formulation/ha).

4.4. Question 4 of ToR

In case major gaps are identified in the scientific knowledge of the hazard or exposure associated with the use of calcium cyanamide, how does the SCHER suggest to close those gaps within a reasonable period of time?

With regard to human health risks, exposure data measured under normal use conditions (application of 500 kg formulation/ha, treatment of a field with an adequate size, determination of drift) should be generated in order to refine the exposure assessment for operators, bystanders and residents.

The SCHER recommends chronic toxicity studies to be conducted which will provide robust data that allow the derivation of a NOAEL.

For the environment, the SCHER identified a lack of appropriate models for the evaluation of exposure to fertilisers. For example, an adapted version of the FOCUS models relevant for fertilisers could be developed and would be highly relevant for future risk evaluation of fertilisers in general.

As the risks for the aquatic compartment identified by the SCHER are based solely on acute toxicity data (no other reliable ecotoxicological data were available), the SCHER recommends additional chronic and higher tier ecotoxicity testing to allow a reduction of the uncertainties in the current effect assessment. It should be noted that for all the additional studies, recommended test guidelines or protocols are available for pesticides and can be adapted for use with fertilisers.

In this respect, the SCHER considers 2 years as a reasonable period of time to close the gaps.

5. MINORITY OPINION

None.

6. COMMENTING PERIOD

A commenting period on this Opinion was opened on the website of the non-food scientific committees from 6 November 2015 to 10 January 2016.

Contributions from 4 stakeholders were received in this commenting period. Each contribution was carefully considered by the SCHER and where appropriate, the text of the Opinion has been modified or explanations have been added to take account of relevant comments. The reference list has been accordingly updated with relevant publications. The scientific rationale and the Opinion section were clarified and strengthened. In cases where the SCHER, after consideration and discussion of the comments, decided to maintain its initial views, the Opinion (or the section concerned) has remained unchanged.

7. LIST OF TERMS AND ABBREVIATIONS

AOEL	Acceptable Operator Exposure Level
a.s.	Active Substance
BCOP	Bovine Corneal Opacity and Permeability Study in vitro
bw	body weight
Cah	cyanamide hydratase
$CaCN_2$	calcium cyanamide
CAS	Chemical Abstract Services
d	day
dw	dry weight
DCD	dicyandiamide
DT50	Time to degrade 50% of the substance (d)
DT90	Time to degrade 90% of the substance (d)
EC	European Commission
ECDC	European Centre for Disease prevention and Control
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EMA	European Medicines Agency
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
GPMT	modified guinea pig maximisation test
h	hour
ha	Hectare
HPLC	High-performance liquid chromatography
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
MAK	Maximale Arbeitsplatz-Konzentration (German: maximum workplace concentration)
NCI	National Cancer Institute

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
RCR	Risk Characterization Ratio
REACH	Registration, Evaluation and Authorisation of Chemicals
SCCS	Scientific Committee on Consumer Safety
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SCHER	Scientific Committee on Health and Environmental Risks
ToR	Terms of Reference

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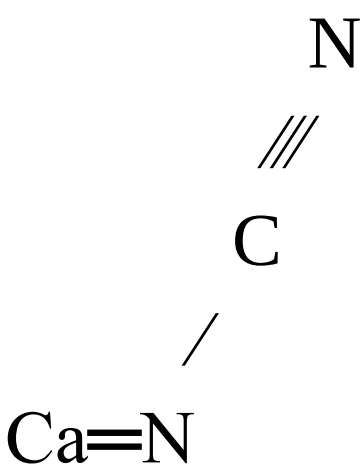
9. ANNEXES

Annex 1: EPISUITE results for calcium cyanamide

Formula:



```
SMILES : [Ca]=NC(#N)
CHEM : Calcium Cyanamide
CAS NUM: 000156-62-7
MOL FOR: C1 N2 Ca1
MOL WT : 80.10
------------------------------ EPI SUMMARY (v3.10) ------------------------
--
Physical Property Inputs:
Water Solubility (mg/L): ------
Vapor Pressure (mm Hg) : ------
Henry LC (atm-m3/mole) : ------
Log Kow (octanol-water): ------
Boiling Point (deg C) : ------
Melting Point (deg C) : ------
Log Octanol-Water Partition Coef (SRC):
Log Kow (KOWWIN v1.66 estimate) = -0.20
Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.40):
Boiling Pt (deg C): 167.04 (Adapted Stein and Brown method)
Melting Pt (deg C): -3.45 (Mean or Weighted MP)
VP(mm Hg,25 deg C): 4.58E-019 (Modified Grain method)
MP (exp database): 1340 deg C
Water Solubility Estimate from Log Kow (WSKOW v1.40):
Water Solubility at 25 deg C (mg/L): 1.934e+005
log Kow used: -0.20 (estimated)
no-melting pt equation used
ECOSAR Class Program (ECOSAR v0.99g):
Class(es) found:
Neutral Organics
Henrys Law Constant (25 deg C) [HENRYWIN v3.10]:
Bond Method : Incomplete
Group Method: Incomplete
Henrys LC [VP/WSol estimate using EPI values]: 2.496E-025 atm-m3/mole
Probability of Rapid Biodegradation (BIOWIN v4.00):
```

Linear Model : 0.7094
Non-Linear Model : 0.8666
Expert Survey Biodegradation Results:
Ultimate Survey Model: 3.0222 (weeks)
Primary Survey Model : 3.7322 (days-weeks)
Readily Biodegradable Probability (MITI Model):
Linear Model : 0.4738
Non-Linear Model : 0.5531
Atmospheric Oxidation (25 deg C) [AopWin v1.90]:
Hydroxyl Radicals Reaction:
OVERALL OH Rate Constant = 0.0000 E-12 cm3/molecule-sec
Half-Life = -------
Ozone Reaction:
No Ozone Reaction Estimation
Soil Adsorption Coefficient (PCKOCWIN v1.66):
Koc : 8.3
Log Koc: 0.919
Aqueous Base/Acid-Catalyzed Hydrolysis (25 deg C) [HYDROWIN v1.67]:
Rate constants can NOT be estimated for this structure!
BCF Estimate from Log Kow (BCFWIN v2.14):
Log BCF = 0.500 (BCF = 3.162)
log Kow used: -0.20 (estimated)
Volatilization from Water:
Henry LC: 2.5E-025 atm-m3/mole (calculated from VP/WS)
Half-Life from Model River: 2.099E+021 hours (8.748E+019 days)
Half-Life from Model Lake : 2.29E+022 hours (9.543E+020 days)
Removal In Wastewater Treatment:
Total removal: 1.85 percent
Total biodegradation: 0.09 percent
Total sludge adsorption: 1.76 percent
Total to Air: 0.00 percent
Level III Fugacity Model:
Mass Amount Half-Life Emissions
(percent) (hr) (kg/hr)
Air 1.59e-005 1e+005 1000
Water 45.1 360 1000
Soil 54.9 360 1000
Sediment 0.0755 1.44e+003 0
Persistence Time: 421 hr

Annex 2: Operator exposure calculations using UK models for granular formulations

Table 2.1: Operator exposure model for granular formulations, realistic worst case, small field, assuming 10% dermal absorption, gloves and normal work wear were worn during loading and application operations

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	3	ha/day	**RPE**	
Application rate	450	kg a.s./ha	**Loading**	EN149 FFP3
Dermal absorption	10	%	**Application**	EN149 FFP3
Inhalation absorption	100	%		
Systemic AOEL	0.0043	mg/kg bw/day		

	75th PERCENTILE VALUES	
LOADER		
Dermal exposure		
PHED surrogate - hands ADE	0.0014	mg/kg a.s.
PHED surrogate - body ADE	0.0161	mg/kg a.s.
kg a.s. loaded	1350	kg a.s./day
dermal exposure	23.6224	mg a.s./day
absorbed dose	2.3622	10%
Inhalation exposure		
PHED surrogate	0.0208	mg/kg a.s.
kg a.s. loaded	1350	kg a.s./day
potential inhalation exposure	28.0937	mg a.s./day
transmission through RPE	5	%
absorbed dose	1.4047	100%
APPLICATOR		
Dermal exposure		
PHED surrogate - hands ADE	0.0003	mg/kg a.s.
PHED surrogate - body ADE	0.0048	mg/kg a.s.
kg a.s. applied	1350	kg a.s./day
dermal exposure	6.9224	mg a.s./day
absorbed dose	0.6922	10%
Inhalation exposure		
PHED surrogate	0.0010	mg/kg a.s.
kg a.s. applied	1350	kg a.s./day
potential inhalation exposure	1.3491	mg a.s./day
transmission through RPE	5	%
absorbed dose	0.0675	100%
TOTAL SYSTEMIC	0.0754	mg/kg bw/d
EXPOSURE AS % OF AOEL	1,754.51	%

Table 2.2: Operator exposure model for granular formulations, realistic worst case scenario, large field, assuming 10% dermal absorption, gloves and normal work wear were worn during loading and application operations

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	48	ha/day	**RPE**	
Application rate	450	kg a.s./ha	**Loading**	EN149 FFP3
Dermal absorption	10	%	**Application**	EN149 FFP3
Inhalation absorption	100	%		
Systemic AOEL	0.0043	mg/kg bw/day		

	75th PERCENTILE VALUES		
LOADER			
Dermal exposure			
PHED surrogate - hands ADE	0.0014	mg/kg a.s.	
PHED surrogate - body ADE	0.0161	mg/kg a.s.	
kg a.s. loaded	21600	kg a.s./day	
dermal exposure	377.9587	mg a.s./day	
absorbed dose	37.7959	10%	
Inhalation exposure			
PHED surrogate	0.0208	mg/kg a.s.	
kg a.s. loaded	21600	kg a.s./day	
potential inhalation exposure	449.5000	mg a.s./day	
transmission through RPE	5	%	
absorbed dose	22.4750	100%	
APPLICATOR			
Dermal exposure			
PHED surrogate - hands ADE	0.0003	mg/kg a.s.	
PHED surrogate - body ADE	0.0048	mg/kg a.s.	
kg a.s. applied	21600	kg a.s./day	
dermal exposure	110.7590	mg a.s./day	
absorbed dose	11.0759	10%	
Inhalation exposure			
PHED surrogate	0.0010	mg/kg a.s.	
kg a.s. applied	21600	kg a.s./day	
potential inhalation exposure	21.5854	mg a.s./day	
transmission through RPE	5	%	
absorbed dose	1.0793	100%	
TOTAL SYSTEMIC	1.2071	mg/kg bw/d	
EXPOSURE AS % OF AOEL	28,072.11	%	

Table 2.3: Operator exposure model for granular formulations, normal case, small field, assuming 10% dermal absorption, gloves and normal work wear were worn during loading and application operations

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	3	ha/day	**RPE**	
Application rate	225	kg a.s./ha	**Loading**	EN149 FFP3
Dermal absorption	10	%	**Application**	EN149 FFP3
Inhalation absorption	100	%		
Systemic AOEL	0.0043	mg/kg bw/day		

	75th PERCENTILE VALUES	
LOADER		
Dermal exposure		
PHED surrogate - hands ADE	0.0014	mg/kg a.s.
PHED surrogate - body ADE	0.0161	mg/kg a.s.
kg a.s. loaded	675	kg a.s./day
dermal exposure	11.8112	mg a.s./day
absorbed dose	1.1811	10%
Inhalation exposure		
PHED surrogate	0.0208	mg/kg a.s.
kg a.s. loaded	675	kg a.s./day
potential inhalation exposure	14.0469	mg a.s./day
transmission through RPE	5	%
absorbed dose	0.7023	100%
APPLICATOR		
Dermal exposure		
PHED surrogate - hands ADE	0.0003	mg/kg a.s.
PHED surrogate - body ADE	0.0048	mg/kg a.s.
kg a.s. applied	675	kg a.s./day
dermal exposure	3.4612	mg a.s./day
absorbed dose	0.3461	10%
Inhalation exposure		
PHED surrogate	0.0010	mg/kg a.s.
kg a.s. applied	675	kg a.s./day
potential inhalation exposure	0.6745	mg a.s./day
transmission through RPE	5	%
absorbed dose	0.0337	100%
TOTAL SYSTEMIC	0.0377	mg/kg bw/d
EXPOSURE AS % OF AOEL	877.25	%

Table 2.4: Operator exposure model for granular formulations, normal case, large field, assuming 10% dermal absorption, gloves and normal work wear were worn during loading and application operations

EXPOSURE TO GRANULAR FORMULATIONS: VEHICLE-MOUNTED EQUIPMENT				
VARIABLES				
Work rate	48	ha/day	**RPE**	
Application rate	225	kg a.s./ha	**Loading**	EN149 FFP3
Dermal absorption	10	%	**Application**	EN149 FFP3
Inhalation absorption	100	%		
Systemic AOEL	0.0043	mg/kg bw/day		

	75th PERCENTILE VALUES		
LOADER			
Dermal exposure			
PHED surrogate - hands ADE	0.0014	mg/kg a.s.	
PHED surrogate - body ADE	0.0161	mg/kg a.s.	
kg a.s. loaded	10800	kg a.s./day	
dermal exposure	188.9793	mg a.s./day	
absorbed dose	18.8979	10%	
Inhalation exposure			
PHED surrogate	0.0208	mg/kg a.s.	
kg a.s. loaded	10800	kg a.s./day	
potential inhalation exposure	224.7500	mg a.s./day	
transmission through RPE	5	%	
absorbed dose	11.2375	100%	
APPLICATOR			
Dermal exposure			
PHED surrogate - hands ADE	0.0003	mg/kg a.s.	
PHED surrogate - body ADE	0.0048	mg/kg a.s.	
kg a.s. applied	10800	kg a.s./day	
dermal exposure	55.3795	mg a.s./day	
absorbed dose	5.5379	10%	
Inhalation exposure			
PHED surrogate	0.0010	mg/kg a.s.	
kg a.s. applied	10800	kg a.s./day	
potential inhalation exposure	10.7927	mg a.s./day	
transmission through RPE	5	%	
absorbed dose	0.5396	100%	
TOTAL SYSTEMIC	0.6036	mg/kg bw/d	
EXPOSURE AS % OF AOEL	14,036.05	%	

Annex 3: Exposure during private use based on puffer pack model of the UK

Table 3.1: Exposure assessment for private use, puffer pack model assuming 10% dermal absorption.

PUFFER PACK MODEL					
PRODUCT NAME	**PERLKA**				
ACTIVE SUBSTANCE	**Calciumcyanamide**				
ACTIVE CONTENT	**450 g/kg**				
DERMAL ABSORPTION	**10 %**				
AOEL	**0.0043 mg/kg bw/day**				
	Rate of exposure mg/min	Exposure Duration (mins)	Estimated exposure to spray mg/day		
Hand and forearm	**2.83**	**30**	**84.9**		
Legs, feet and face	**2.15**		**64.5**		
TOTAL DERMAL EXPOSURE TO POWDER (mg/day)				**149.4**	
ABSORPTION				**10.0**	
ABSORBED DERMAL DOSE (mg/day)				**6.723**	
	Rate of exposure mg/min	Exposure Duration (mins)	Estimated exposure to spray mg/day		
Breathing rate = 1m^3/h	**0.02960**	**30**	**0.88800**		
INHALATION EXPOSURE - 100% ABSORPTION (mg/day)				**0.3996**	
			All data refer to the 75th percentile values		
DERMAL (mg/day)	**6.723**				
INHALATION (mg/day)	**0.3996**				
TOTAL (mg/day)	**7.1226**				
BODYWEIGHT (kg)	**60**				
OPERATOR EXPOSURE (mg/kg bw/day)		**0.11871**			
THIS IS	**2760.7%**	**OF THE AOEL FOR**		**Calciumcyanamide**	
THE ESTIMATE FOR	**PERLKA**		**EXCEEDS ACCEPTABLE LEVELS**		

Table 3.2: Operator exposure model for granular formulations, private use assuming 10% dermal absorption, protective measures considered

EXPOSURE TO GRANULAR FORMULATIONS: HAND-HELD EQUIPMENT				
VARIABLES				
Work rate	0.05	ha/day	**RPE**	
Application rate	180	kg a.s./ha	**Load/Apply**	EN149 FFP3
Dermal absorption	10	%		
Inhalation absorption	100	%		
Systemic AOEL	0.0043	mg/kg bw/day		

	75th PERCENTILES	
LOADER/APPLICATOR		
Dermal exposure		
PHED surrogate - hands ADE	28.5320	mg/kg a.s.
PHED surrogate - body ADE	65.3203	mg/kg a.s.
kg a.s. loaded/applied	9	kg a.s./day
dermal exposure	844.6705	mg a.s./day
absorbed dose	84.4671	10%
Inhalation exposure		
PHED surrogate	0.4677	mg/kg a.s.
kg a.s. loaded/applied	9	kg a.s./day
potential inhalation exposure	4.2096	mg a.s./day
transmission through RPE	5	%
absorbed dose	0.2105	100%
TOTAL SYSTEMIC	1.4113	mg/kg bw/d
EXPOSURE AS % OF AOEL	32820.75	%

Annex 4: Exposure calculation for bystander, residents and children

Table 4.1: Operational use, exposure calculation for bystanders assuming 0.2% drift, a duration of 5 minutes and 10% dermal absorption.

Bystanders (adults and children)			realistic worst case				normal case			
			small field		large field		small field		large field	
			Adults	Children	Adults	Children	Adults	Children	Adults	Children
Application rate (AS)	AR	mg/m2	45000	45000	45000	45000	22500	22500	22500	22500
Drift	D	%	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Exposed Body Surface Area	BSA	m2	1	0.21	1	0.21	1	0.21	1	0.21
Dermal absorption	DA	%	10	10	10	10	10	10	10	10
Bodyweight	BW	kg	60	16.15	60	16.15	60	16.15	60	16.15
Specific inhalation exposure	IA*	mg/kg d	0.001000	0.000575	0.001000	0.000575	0.001000	0.000575	0.001000	0.000575
Area treated	A	ha	3	3	48	48	3	3	48	48
Duration	T	min	5	5	5	5	5	5	5	5
Inhalation Absorption	IA	%	100	100	100	100	100	100	100	100
Systemic Dermal Exposure Bystanders (ARxDxBSAxDA)/BW	SDEB	mg/kg bw d	0.150	0.117	0.150	0.117	0.075	0.059	0.075	0.059
Systemic Inhalation Exposure Bystanders (IA*xARxAxTxIA)/BW	SIEB	mg/kg bw d	11.250	24.020	180.000	384.328	5.625	12.010	90.000	192.164
Systemic Exposure total		**mg/kg bw d**	**11.400**	**24.138**	**180.150**	**384.445**	**5.700**	**12.069**	**90.075**	**192.222**
syst AOEL		mg/kg bw d	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03
Exposure		%AOEL	2.65E+05	5.61E+05	4.19E+06	8.94E+06	1.33E+05	2.81E+05	2.09E+06	4.47E+06

Table 4.2: Operational use, exposure calculation for residents (adults and children) assuming 0.2% drift, a duration of 2 hours and 10% dermal absorption.

Residentials Dermal and Inhalative Exposure			realistic worst case				normal case			
			small field		large field		small field		large field	
			Adults	Children	Adults	Children	Adults	Children	Adults	Children
Application rate (AS)	AR	mg/cm2	4.5	4.5	4.5	4.5	2.25	2.25	2.25	2.25
Drift	D	%	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Turf Transferable Residues	TTR	%	5	5	5	5	5	5	5	5
Transfer Coefficient	TC	cm2/h	7300	2600	7300	2600	7300	2600	7300	2600
Duration	H	h	2	2	2	2	2	2	2	2
Dermal absorption	DA	%	10	10	10	10	10	10	10	10
Bodyweight	BW	kg	60	16.15	60	16.15	60	16.15	60	16.15
Airbourne Concentration Vapour	ACV	mg/m3	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015
Inhalation Rate	IR	m3/d	16.57	8.31	16.57	8.31	16.57	8.31	16.57	8.31
Inhalation Absorption	IA	%	100	100	100	100	100	100	100	100
Systemic Dermal Exposure Residentials (ARxDxTTRxTCxHxDA)/BW	SDER	mg/kg bw d	0.011	0.014	0.011	0.014	0.005	0.007	0.005	0.007
Systemic Inhalation Exposure Residentials (ACVxIRxIA)/BW	SIER	mg/kg bw d	0.004	0.008	0.004	0.008	0.004	0.008	0.004	0.008
Residentials Oral Exposure (children) Application rate (AS)	AR	mg/cm2		4.5		4.5		2.25		2.25
Drift	D	%		0.2		0.2		0.2		0.2
Turf Transferable Residues	TTR	%		5		5		5		5
Saliva Extraction Factor	SE	%		50		50		50		50
Surface Area Hands	SA	cm2		20		20		20		20
Frequency	Freq	events/h		20		20		20		20
Exposure Duration	H	h		2		2		2		2
Oral absorption	OA	%		100		100		100		100
Body Weight	BW	kg		16.15		16.15		16.15		16.15
Dislodgeable Foliar Residues	DFR	%		20		20		20		20
Ingestion Rate Mouthing Grass/Day	IGR	cm2		25		25		25		25
Systemic Oral Exposure - Hand to Mouth (ARxDxTTRxSExSAxFreqxHxOA)/BW	SOEH	mg/kg bw d		0.011		0.011		0.006		0.006
Systemic Oral Exposure - Object to Mouth (ARxDxDFRxIGRxOA)/BW	SOEO	mg/kg bw d		0.003		0.003		0.001		0.001
Total Residential Exposure Adults SDER+SIER	SERa	**mg/kg bw d**	**0.015**		**0.015**		**0.010**		**0.010**	
Children SDER+SIER+SOEH+SOEO	SERc	**mg/kg bw d**		**0.036**		**0.036**		**0.022**		**0.022**
syst AOEL		mg/kg bw d	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03	4.30E-03
%AOEL			3.51E+02	8.40E+02	3.51E+02	8.40E+02	2.24E+02	5.10E+02	2.24E+02	5.10E+02

Table 4.3: Residential exposure, private use, uptake of granules by children

Children daily ingestion of granulate material				
Formulation/ha		kg	1000	500
Active Substance		%	45	45
Formulation/m2		g	100	50
Active Substance/m2		g	45	22.5
Active Substance/cm2	AR	mg	4.5	2.25
Soil Density Factor	SDF		0.67	0.67
Uptake	U	g/d	0.2	0.2
Bodyweight		kg	16.15	16.15
Ingestion (AR*SDF*U)/BW		mg/kg bw d	0.04	0.02
AOEL		mg/kg bw d	4.30E-03	4.30E-03
Exposure		%AOEL	8.68E+02	4.34E+02