



**HSE**

# **Draft Assessment Report**

## **Evaluation of Active Substances**

Plant Protection Products

Prepared according to **Regulation (EC) no. 1107/2009**  
as it applies in Great Britain

### **Elemental iron**

### **Volume 1**

Great Britain

January 2024

## Version History

When	What
November 2021	Initial DAR
February 2022	Updated post Expert Committee on Pesticides (ECP) Independent Scientific Advice (ISA) (November 2021 meeting)
October 2023	Updated following submission of additional information on Ecotoxicology
January 2024	Updates made after comments from the applicant

Note that references to "Retained Regulation (EC) 1107/2009", "Retained Regulation (EC) No 396/2005" and "Retained Regulation (EC) No 1272/2008" should now read as "Assimilated Regulation No 1107/2009", "Assimilated Regulation No 396/2005" and "Assimilated Regulation No 1272/2008" respectively as per the Retained EU Law (Revocation and Reform) Act of 2023. Any reference to the former now refers to the respective for the latter.

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# Level 1

## Elemental iron

## **1. STATEMENT OF SUBJECT MATTER AND PURPOSE FOR WHICH THIS REPORT HAS BEEN PREPARED, AND BACKGROUND INFORMATION ON THE APPLICATION**

### **1.1. CONTEXT IN WHICH THIS DRAFT ASSESSMENT REPORT WAS PREPARED**

#### **1.1.1. Purpose for which the draft assessment report was prepared**

This draft assessment report has been prepared following the evaluation of the dossier for the new active substance Elemental iron and for the formulated product ‘Final Bite’. The dossier was submitted by ADAMA Agriculture B.V (affiliate of ADAMA) for the first approval of this substance in Great Britain (GB) under Regulation (EC) No 1107 with the evaluation performed by the Chemicals Regulation Division of the Health and Safety Executive. ADAMA also have an ongoing application for the first approval of elemental iron as a new active substance in the EU, with the evaluation being performed by Austria as EU Rapporteur Member State (RMS).

The new active substance elemental iron is a molluscicide, and the representative formulation, Final-Bite (product code 0402206), is a Ready to Use Bait (RB) containing 10g of active substance/kg (1 % w/w) for use on a range of crops.

ADAMA have requested that elemental iron is considered for approval as a new low-risk active substance and they have stated that the dossier contains data and information to support the representative uses of the new low risk active substance elemental iron, in various crops for which it is intended to demonstrate that the requirements of Regulation (EC) No 1107/2009 can be met.

They state that the dossier has been prepared in accordance with guidance document SANCO/10181/2013 – rev 3, dated 12 December 2014. According to article 22 of Regulation EC No 1107/2009 and its annex II, as well as Commission Regulation (EU) No 2017/1432, request is made to get approval as a low-risk active substance, as elemental iron fulfils all the defined criteria thereof.

This dossier is the application for the first approval of elemental iron in accordance with Regulation (EC) no. 1107. ADAMA have also submitted an application to include elemental iron in Annex IV of Regulation EC 396/2005.

A classification and labelling report – is not required to be prepared under GB CLP by HSE.

#### **1.1.2. Regulatory history for use in Plant Protection Products**

Elemental iron is a new active substance and products containing it have not previously been authorised in Great Britain.

#### **1.1.3. Evaluations carried out under other regulatory contexts**

Elemental iron is a new molluscicide active substance. The applicant submitted a dossier in support of their application for the first approval of this active substance in Great Britain in accordance with Regulation (EC) No. 1107/2009. No registrations or authorisations of elemental iron containing plant protection products currently exist in the UK or EU Member States.

There is also an ongoing application for the approval of elemental iron as a new active substance in the EU, with the evaluation being performed by the Austria as Rapporteur Member State (RMS). The active substance and the product is registered in New Zealand (by the Ministry of Primary Industries) since August 2021. The applicant has not provided details of any information exchange within the

OECD. Furthermore, no other relevant EU-evaluations of the active substance have been carried out under other EU-legislation.

## 1.2. APPLICANT INFORMATION

### 1.2.1. Name and address of applicant(s) for approval of the active substance

Name: ADAMA Agriculture B.V. (affiliate of ADAMA)

Address: Arnhemseweg 87  
3832 GK Leusden  
The Netherlands

Contact: [REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
[REDACTED]  
Telephone number: [REDACTED]  
Fax number: [REDACTED]  
Email: [REDACTED]

### 1.2.2. Producer or producers of the active substance

Confidential information see Volume 4

### 1.2.3. Information relating to the collective provision of dossiers

There is no Task Force involved in the dossier for approval of elemental iron submitted by ADAMA.



**1.3. IDENTITY OF THE ACTIVE SUBSTANCE**

<b>1.3.1. Common name proposed or ISO-accepted and synonyms</b>	Elemental iron
<b>1.3.2. Chemical name (IUPAC and CA nomenclature)</b>	
IUPAC	Iron
CA	Fe
<b>1.3.3. Producer's development code number</b>	None
<b>1.3.4. CAS, EEC and CIPAC numbers</b>	
CAS	7439-89-6
EEC	231-096-4
CIPAC	No CIPAC number is allocated for elemental iron
<b>1.3.5. Molecular and structural formula, molecular mass</b>	
Molecular formula	Fe
Structural formula	-
Molecular mass	55.845 u ± 0.002 u
<b>1.3.6. Method of manufacture (synthesis pathway) of the active substance</b>	Confidential information see Volume 4
<b>1.3.7. Specification of purity of the active substance in g/kg</b>	The minimum purity of elemental iron is 989 g/kg
<b>1.3.8. Identity and content of additives (such as stabilisers) and impurities</b>	
	Confidential information see Volume 4
<b>impurities</b>	Confidential information see Volume 4
<b>mpurities</b>	<p>Elemental iron contains the following toxicologically relevant impurities:</p> <p>Arsenic: Max 0.03 g/kg  Mercury: Max 0.0001 g/kg  Lead: Max 0.003 g/kg  Cadmium: Max 0.001 g/kg  Nickel: Max 0.2 g/kg</p>
<b>1.3.9. Analytical profile of batches</b>	Confidential information see Volume 4

**1.4. INFORMATION ON THE PLANT PROTECTION PRODUCT**

<b>1.4.1. Applicant</b>	Name: ADAMA Agriculture B.V. (affiliate of ADAMA) Address: Arnhemseweg 87 3832 GK Leusden The Netherlands Contact: [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] [REDACTED] Telephone number: [REDACTED] Fax number: [REDACTED] Email: [REDACTED]
<b>1.4.2. Producer of the plant protection product</b>	Confidential information see Volume 4
<b>1.4.3. Trade name or proposed trade name and producer's development code number of the plant protection product</b>	Trade name: Final Bite® Code number: 0402206
<b>1.4.4. Detailed quantitative and qualitative information on the composition of the plant protection product</b>	
<b>1.4.4.1. Composition of the plant protection product</b>	Pure active substance : 10 g/kg (1% w/w) Limits: 7.5 – 12.5 g/kg (0.750-1.250 % w/w) Minimum purity of technical active substance of 98.9%) Technical active substance: 10.11 g/kg (1.011% w/w) Limits: 7.58-12.64 g/kg (0.75-1.27 % w/w)
<b>Information on the active substances</b>	ISO common name: Iron and steel products (77.140) CAS No: 7439-89-6 EC No: 231-096-4 CIPAC No: No CIPAC number is allocated for elemental iron Salt, ester anion or cation present: No
<b>1.4.4.3. Information on safeners, synergists and co-formulants</b>	Confidential information see Volume 4
<b>1.4.5. Type and code of the plant protection product</b>	Ready to use bait [RB]
<b>1.4.6. Function</b>	Molluscicide.
<b>1.4.7. Field of use envisaged</b>	Elemental iron is a molluscicide which is intended to be used on all edible (vegetables, fruit crops and arable

	crops) and none edible crops subjected to snail and slug pressure in the field and greenhouses.
<b>1.4.8. Effects on harmful organisms</b>	Iron causes pest molluscs to stop feeding and then causes paralysis by interfering with oxygen uptake leading to the death of the organism.

## 1.5. DETAILED USES OF THE PLANT PROTECTION PRODUCT

### 1.5.1. Details of representative uses proposed by ADAMA

Crop and/ or situation  (a)	Region	Product name	F G or I  (b)	Pests or Group of pests controlled  (c)	Formulation		Application				Application rate per treatment			PHI (days)  (l)	Remarks:  (m)
					Type	Conc. of as	Method Kind	Growth stage & season  (j)	number min max (k)	interval between applications (days)	kg as/ha min max	water L/ha min max	kg as/ha min max		
All edible and non edible crops (outdoor & protected)	GB	Iron 1% RB	F/G/I	Molluscs	RB	10 g/kg	Spreading	When infestation appears (peak mainly in spring & autumn)	1-6	Minimum 5	Not applicable because the product is intended to be applied as a ready to use granular bait	Not applicable because the product is intended to be applied as a ready to use granular bait	0.08	Not required	Maximum Seasonal application rate  0.48 kg as/ha
Amenity Vegetation	GB	Iron 1% RB	F/G/I	Molluscs	RB	10 g/kg	Spreading	When infestation appears (peak mainly in spring & autumn)	1-6	Minimum 5	Not applicable because the product is intended to be applied as a ready to use granular bait	Not applicable because the product is intended to be applied as a ready to use granular bait	0.08	Not required	Maximum Seasonal application rate  0.48 kg as/ha

<p>(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)</p> <p>(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)</p> <p>(c) <i>e.g.</i> biting and sucking insects, soil born insects, foliar fungi, weeds</p> <p>(d) <i>e.g.</i> wettable (WP), emulsifiable concentrate (EC), granule (GR)</p> <p>(e) CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide</p> <p>(f) All abbreviations used must be explained</p> <p>(g) Method, <i>e.g.</i> high volume spraying, low volume spraying, spreading, dusting, drench</p> <p>(h) Kind, <i>e.g.</i> overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated</p>	<p>(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypry). <b>In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).</b></p> <p>(j) Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application</p> <p>(k) Indicate the minimum and maximum number of applications possible under practical conditions of use</p> <p>(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha)</p> <p>(m) PHI - minimum pre-harvest interval</p>
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### **1.5.2. Further information on representative uses**

#### **1.4.2.1 Application rate and concentration of active substance**

The product is intended to be used at a rate of 8.0 Kg Product/ha

This rate corresponds to a concentration of 0.08 Kg Product/ha

#### **1.4.2.2 Method of application**

The product is intended to be applied as a broadcast treatment.

#### **1.4.2.3 Number and timings of applications and duration of protection**

##### Maximum number of applications and their timings:

6 Applications maximum with 5 days minimum interval. Application must be done according to level of infestation.

##### Growth stages of crops or plants to be protected:

When infestation appears (peak mainly in spring autumn)

Development stages of the harmful organism concerned: The product is ingested by the target pest when eating the baited pellets, and therefore controls the target pest (juvenile and adult slugs and snails) when they are actively feeding. Duration of protection afforded by each application: Each application will afford around 14-28 days control of the target pest; the exact duration of control will depend on environmental conditions e.g. rainfall.

Duration of protection afforded by the maximum number of applications: Duration of protection covers the critical phase of pest control for each target pest. Season long control can be achieved by using the product according to the GAP recommendations.

##### Minimum waiting periods or other precautions between last application and sowing or planting succeeding crops:

No minimum period or other precautions are necessary before sowing or planting succeeding crops.

##### Limitations on choice of succeeding crops:

No limitation on choice of succeeding crops as no phytotoxic effects are expected for Final Bite®

### **Proposed instruction for use**

#### Direction for Final Bite® use

##### Restriction or warnings

Due to the mode of action of Final Bite®, no excessive slime secretions will be evident on, or around, the crop. The slugs retreat underground to die and dead slugs will not be visible. Effectiveness should therefore be measured by the decreased feeding damage to the crop.

It is advisable to test for compatibility and tolerance to crop injury on ornamental crops prior to full scale commercial use.

##### Time of application

Apply as a broadcast treatment as soon as damage is seen or indicated by test baiting. For some crops, e.g. cereals and oilseed rape, where slug activity is present prior to crop emergence, it is advised to treat the crop before emergence and after seed bed preparation is complete.

Application timing should be based on likely pest presence and the part of the crop attacked by the pest e.g seeds, seedling plants or harvestable produce.

Repeat application may be required if pest pressure remains high.

#### Following crops

There are no restrictions on following crops.

#### Application

Final Bite® can be applied by hand or by mechanical applicator.

Applications by hand are suitable when areas to be treated are small e.g. glasshouse crops.

Apply evenly over the plants to be protected.

Take care to ensure pellets do not remain lodged within foliage, florets or other parts of the plants.

Calibrate all equipment before use.

#### Slug Trapping

To establish the need for pellet application on winter wheat or winter oilseed rape, monitor for slug activity. Where bait traps are used, use a foodstuff attractive to slugs e.g. chicken layers' mash which has proven to be particularly effective.

### **1.5.3. Details of other uses applied for to support the setting of MRLs for uses beyond the representative uses**

ADAMA submitted an application to request the inclusion of elemental iron in Annex IV of Regulation (EC) 396/2005, listing active ingredients that do not need a maximum residue limit.

### **1.5.4. Overview on authorisations in EU Member States**

Not applicable, elemental iron is a new active substance.

## **Level 2**

### **Elemental iron**



## **2. SUMMARY OF ACTIVE SUBSTANCE HAZARD AND OF PRODUCT RISK ASSESSMENT**

### **2.1. IDENTITY**

Elemental iron is a new active substance which acts as a molluscicide. The active substance contains the following relevant impurities: arsenic, mercury, lead, cadmium and nickel.

### **2.2. PHYSICAL AND CHEMICAL PROPERTIES**

#### **2.2.1. Summary of physical and chemical properties of the active substance**

Elemental iron is a grey powder. It has a melting point of 1535°C and a boiling point of 2750°C. Elemental iron is not soluble in water therefore properties such as vapour pressure, Henry's law constant, dissociation constant and surface tension were not applicable. Elemental iron is also not soluble in organic solvents. UV/Vis, IR, NMR and MS spectra data were not provided as these techniques are not appropriate for the determination of elemental iron. Highly specific techniques such as ICP-OES are available for the determination and identification of elemental iron. Elemental iron is not flammable, oxidising or explosive.

#### **2.2.2. Summary of physical and chemical properties of the plant protection product**

'Final Bite' is a nearly dust-free Ready to use Bait (RB) formulation, containing 1% of Elemental Iron. It is a blue granular solid, with a synthetic odour. The formulation is not explosive, oxidising or flammable, and therefore no classification is required for the product. A 1% solution of 'Final Bite' has a pH of between 4.2 and 4.5. Its pour and tap density are 0.7668 g/cm<sup>3</sup> and 0.7806 g/cm<sup>3</sup> respectively. On completing a dry sieve test, no inhalation study was required and the formulation has 100% attrition resistance.

The physical and chemical properties of this product indicate that the product fulfils the requirements of a ready to use bait formulation type. The product is not intended to be co-applied in a mixture with other plant protection products, therefore no physical or chemical compatibility data are required. This is acceptable from a chemistry perspective. The formulation demonstrated acceptable physical and chemical properties after accelerated storage at 54 ± 2°C for two weeks in PET/PET bags.

Data must be provided showing satisfactory chemical and physical properties for the product and their retention after ambient storage for two years in the commercial packaging.

### **2.3. DATA ON APPLICATION AND EFFICACY**

In line with the principles established in SANCO/10054/2013 - rev. 3 'Guidance Document on Data Requirements on Efficacy for the Dossier to be Submitted for the Approval of New Active Substances Contained in Plant Protection Products', the 'principal objective of the efficacy evaluation of an active substance is to confirm that the doses are realistic for the GAP submitted for risk evaluation and approval and representative for all subsequent authorisations.'

#### **2.3.1. Summary of effectiveness**

The representative formulation Final bite has been tested in development trials between 2011 - 2018. The results of the trials show acceptable efficacy against target slugs in a range of crops and limited data supports the use against snails in strawberry.

Efficacy trials were conducted in the Maritime or North East EPPO zones, with a case presented by the applicant to support the inclusion of North East zone data. A mix of arena and field trials were presented.

#### Arena trials

Crop	EPPO Code	Number of trials	Year
Chinese chard	BRSCH	1	2017
Oilseed rape	BRSNN	2	2016-2017
Brussels sprouts	BRSEF	2	2017-2018
Cabbage	BRSOL	7	2018
Chrysanthemum	CHYSS	1	2018
Strawberry	FRASS	11	2017-2018
Hosta	HSTSS	2	2011, 2017
Lettuce	LACSA	6	2012, 2018
Marigolds	TAGSS	8	2017-2018
Garden pansy	VIOWH	2	2017

#### Field trials

Crop	EPPO Code	Number of trials	Year
Winter oilseed rape	BRSNW	18	2017-2018
Spring oilseed rape	BRSNS	1	2018
Kohlrabi	BRSEF	2	2017
Cabbage	BRSOL	7	2016-2018
Chinese cabbage	BRSPK	1	2017
Calendula	CLDSS	1	2017
Spring barley	HORVS	2	2018
Winter barley	HORVW	1	2018
Lettuce	LACSA	3	2017
Potato	SOLTU	10	2017-2018
Winter wheat	TRZAW	17	2017-2018

Trials were conducted in the UK, NL, PL, FR, BE, CZ and DE. All trials have been conducted according to EPPO standards by GEP accredited organisations. Trials were designed, conducted and reported in accordance with general EPPO standards PP1/95(4), PP1/135(4), PP1/152(4), PP1/289(1), and PP1/181(4) regarding design, analysis and reporting.

Applications were made at 8kg product/ha (corresponding to 80g elemental iron/ha). 1 Application was made in 41 trials and 2 applications were made in 25 trials, with an interval of 14-49 days depending on pest pressure. Efficacy was tested under a range of environmental conditions.

The effectiveness (based in plant damage assessments) of Final bite applied at the proposed rate was comparable to or higher than that of the commercial standard reference products used. Overall, there is evidence that the proposed dose would be ‘sufficiently effective’ and that the supported GAP is representative.

### **2.3.2. Summary of information on the development of resistance**

The development of resistance is considered unlikely because of the physiological mode of action of elemental iron. The iron salt formed on contact with the low pH gastric digestive fluid of the mollusc interferes with haemocyanin, the respiratory pigment of the snail's haemolymph, interfering with the uptake of oxygen. It is unlikely that a change leading to the possible development of resistance can occur in this biological pathway, which has taken millions of years to evolve and remain stable for gas exchange.

Slugs surviving baits containing elemental iron show no aversion against baits thereafter. As elemental iron is not persistent the selection pressure on the target organisms occurs only temporarily.

Elemental iron is a new active substance to the UK. No resistance to other active substances (ferric phosphate and metaldehyde) has been reported in molluscs, despite years of extensive use. The mode of action of elemental iron is similar to ferric phosphate and no resistance is currently known. Therefore, no specific resistance management strategy is required for the active.

### **2.3.3. Summary of adverse effects on treated crops**

Specific field trials have been conducted to demonstrate the crop safety of Final bite. These trials were carried out on oilseed rape (2 trials), broccoli (1 trial), cabbage (3 trials), strawberry (2 trials), lettuce (2 trials), marigold (2 trials) and winter wheat (2 trials). Observations were also made in 48 efficacy field trials. The trials were designed and conducted according to approved EPPO standards.

The submitted data support crop safety in the proposed crops.

### **2.3.4. Summary of observations on other undesirable or unintended side-effects**

No undesirable or unintended side effects were reported in any of the trials provided. Further, the lack of inherent herbicidal properties, and method of application, makes possible impacts on succeeding or adjacent crops unlikely.

In summary, Effectiveness and crop safety of the representative uses have been demonstrated. This is sufficient to meet the requirements set with Regulation (EC) no. 1107/2009. However, the individual claims and uses will be assessed at product evaluation

## **2.4. FURTHER INFORMATION**

### **2.4.1. Summary of methods and precautions concerning handling, storage, transport or fire**

Store only in the original container. Store the containers sealed, in a well-ventilated place, away from direct sunlight. Avoid leakage of the product into the environment. Do not eat, drink or smoke during use. Remove any contaminated clothes and personal protective equipment before entering places in which people eat.

In the event of fire, conventional extinguishing equipment can be used (carbon dioxide, foam, powder and water spray). Do not breathe combustion products. Use jets of water to cool the containers to prevent product decomposition and the development of substances potentially hazardous for health. Always wear full fire prevention gear. Collect extinguishing water to prevent it from draining into the

sewer system. Dispose of contaminated water used for extinction and the remains of the fire according to applicable regulations.

#### 2.4.2. Summary of procedures for destruction or decontamination

Neat product residues should be considered special non-hazardous waste. Disposal must be performed through an authorised waste management firm, in compliance with national and local regulations. Contaminated packaging must be recovered or disposed of in compliance with national waste management regulations.

#### 2.4.3. Summary of emergency measures in case of an accident

**EYES:** Remove contact lenses, if present. Wash immediately with plenty of water for at least 15 minutes, opening the eyelids fully. If problem persists, seek medical advice.

**SKIN:** Remove contaminated clothing. Wash immediately with plenty of water. If irritation persists, get medical advice/attention. Wash contaminated clothing before using it again.

**INHALATION:** Remove to open air. In the event of breathing difficulties, get medical advice/attention immediately.

**INGESTION:** Get medical advice/attention. Induce vomiting only if indicated by the doctor. Never give anything by mouth to an unconscious person, unless authorised by a doctor.

### 2.5. METHODS OF ANALYSIS

#### 2.5.1. Methods used for the generation of pre-authorisation data

**Active substance and impurities in the technical material:** An ICP-OES analytical method with detection of iron at wavelength 273.955 nm, was considered fully validated in accordance with SANCO/3030/99 rev. 4 and rev. 5 for the determination of active substance content in the technical material. The relevant impurities arsenic, cadmium and nickel were determined using an ICP-OES method, which was considered fully validated in accordance with SANCO/3030/99 rev. 4 and rev. 5 with respect to arsenic. A data gap has been identified to demonstrate the validity of this method with regards to the determination of cadmium and nickel in the technical material. The relevant impurity mercury was determined using an Atomic Fluorescence Spectroscopy method specific to mercury, which was considered fit for purpose. A data gap has been identified to demonstrate the full validity of this method. The relevant impurity lead was determined using a Graphite Furnace Atom Absorption Spectroscopy method specific to lead, which was considered fully validated in accordance with SANCO/3030/99 rev. 4 and rev. 5. Details of the analytical methods for the determination of impurities in the technical material are given in Volume 4 Confidential Information and Volume 3 CA B5.

**Active substance and impurities in the plant protection product:** An XRF spectroscopy analytical method was considered fully validated in accordance with SANCO/3030/99 rev. 4 and rev. 5 for the determination of active substance content in the formulation. The methods used for the determination of the relevant impurities in the technical material were proposed as being suitable for the determination of these impurities in the formulation. However, supporting validation data in relation to the formulation was not provided. Validated analytical methods for the determination of the relevant impurities (mercury, lead, arsenic, cadmium, nickel) in the formulation are also required. This has been set as a data gap.

**Methods used for data generation:** Satisfactory methods of analysis for the detection of iron in relevant matrices to support all areas of the risk assessment (including ecotoxicology) have been provided. These methods have been assessed in accordance with SANCO/3029/99 rev.4. The validation evaluation has been conducted in section B5 of the CA and CP DAR documents. The applicability of these methods is addressed in the respective sections for these studies which these methods support.

### 2.5.2. Methods for post control and monitoring purposes

The active substance, iron, is a stable, non-volatile elemental atomic particle and is insoluble in water. As iron is a natural constituent of soils serving as essential nutrient in animal and plant physiology, relevant residues of iron in food of plant, animal origin, environmental compartments, air and body fluids and tissues, in exceedance of natural background, are not expected to occur. Additionally, there are already numerous international peer validated methods and ring-tested methods available. Therefore, no monitoring methods are required.

## 2.6. EFFECTS ON HUMAN AND ANIMAL HEALTH

This assessment addresses the toxicology and metabolism of elemental iron, in the form [REDACTED] elemental iron. Elemental iron ( $\text{Fe}^0$ , CAS No. 7439-89-6) is a new molluscicidal active substance for application on edible and non-edible crops grown in the field, greenhouses and indoors. The applicant's source of the active substance holds approval in the USA as a food-grade mineral supplement (US CFR (Code of Federal Regulation) 21 184.1375 for elemental iron). The applicant has provided information to support the compliance of their source with the specification for elemental iron (reduced) entry in the US Food Chemical Codex (Regulatory compliance statement July 2019). In the EU, elemental iron is one of a range of iron compounds authorised for use in food or food supplements (Regulations (EC) Nos. 1170/2009 and 53/2009, respectively). The representative product 'Final Bite' is a ready-to-use granular bait, containing 10 g/kg (1 % w/w) elemental iron in a nearly dust-free formulation. The product is used as a bait application during pre- and post-emergence of the crop.

The proposed mode of molluscicidal action of elemental iron in the representative product is as follows:

*Following ingestion of the granular pellet, the acidic gastric environment in the target species causes liberation of solubilised, ionic iron, in the form of  $\text{Fe}^{2+}$ . In the representative product, the ionic form of iron is then available to form a soluble complex with a complexing agent that interferes with the oxygen transport capability of haemocyanin in molluscs - a mode of action irrelevant to humans since humans do not possess this target.*

In considering the toxicological profile of elemental iron as a powdered active substance, it is acknowledged that exposure of humans to poorly soluble metal-containing particles may theoretically result in adverse effects due to the particle surface (particle size, form and surface reactivity), particle uptake or the release of metals from the particle. These potential hazards of elemental iron particles have been addressed by the submission of published literature on iron powders. As elemental iron is an existing food supplement substance with a significant amount of publicly available literature, the toxicological assessment of the substance is also extrapolated from these sources of information. In addition, the EU assessments of iron sulphate ( $\text{FeSO}_4$ ; DAR UK 2008, EFSA conclusion 2012) and ferric phosphate ( $\text{FePO}_4$  RAR, DE 2013, EFSA conclusion 2015) have been used to bridge to the toxicity potential of elemental iron. Iron sulphate and ferric phosphate are approved in the EU for use as pesticidal active substances and HSE also notes that the EU review of ferric pyrophosphate is ongoing (EFSA Final Conclusion 2020). Conclusions on the safety of elemental iron for the currently proposed molluscicidal use can be drawn from the literature on insoluble iron particulate matter and the scientific evaluations of these other – more soluble - forms.

The toxicological data on elemental iron (active substance) generated by the applicant is limited to an acute inhalation toxicity study, driven by concerns over the particle size of the active substance. Data from the literature on elemental iron are also available, but these, although evaluated by HSE where it might be considered relevant to address a data point, are of limited regulatory value. In view of the fact that, following external exposure to elemental iron, and regardless of the route of exposure, any subsequent systemic exposure of iron will be to its ionic forms (see below for justification), in the absence of either substance-specific literature or regulatory studies, the read-across from ferrous and ferric ionic forms has been performed where necessary for all routes of exposure:

- **Oral:** In humans, it is expected that solubilisation of elemental iron – presumed to be  $\text{Fe}^{3+}$  (ferric) - will occur in the acidic environment of the stomach and proximal duodenum, with subsequent uptake of inorganic, ferrous ( $\text{Fe}^{2+}$ ) iron occurring via active, homeostatic processes, mainly in the duodenum and proximal jejunum. Further down the gastrointestinal tract, the alkaline environment of the jejunum reduces the solubility of iron by conversion to the ferric form, lowering the bioavailability of iron released from elemental iron (Hurrell *et al.*, 2002). There is no evidence that particulate or elemental iron will transfer into the blood.
- **Dermal:** Elemental iron ( $\text{Fe}^0$ ) is poorly soluble in aqueous or organic solvents and hence negligible oxidation to either  $\text{Fe}^{2+}$  or  $\text{Fe}^{3+}$  is expected to occur following topical exposure at a skin sweat pH of approximately 4.2-6.5 (Hedberg *et al.*, 2010a; Stefaniak, A. B. *et al.*, 2014). Elemental iron is a micron-sized particulate substance, not a nanomaterial; therefore, it is unlikely that soluble or insoluble elemental iron will partition into the lipid matrix of dermal cellular membranes. A potential for partitioning is even less likely to apply to elemental iron as a large granular PPP. Since it is well known that oral absorption of iron is actively physiologically regulated (Lynch *et al.*, 2018), and iron is ubiquitous in the human environment, the likelihood of passive migration through the stratum corneum to the dermis - and subsequent entry into the systemic circulation - is unlikely. Similarly, no local reactions from exposure to elemental iron in particulate form are predicted, as the surface of the material is not redox-active or corrosive (UK Iron DAR Vol 3 CA\_B.2).
- **Inhalation:** Elemental iron ( $\text{Fe}^0$ ) is incorporated into a nearly dust-free, solid plant protection product of non-respirable size ( $> 50 \mu\text{m}$ ; see UK Iron DAR Vol 3 CP\_B.2) and therefore any significant exposure via inhalation is considered unlikely. Any iron released from the solid matrix can be assumed to be either in an ionised form, or poorly soluble particles. If ionic iron penetrates the protective lung lining fluid – rich in antioxidants - systemic exposure to ionic iron is likely to be negligible due to the innate control of iron absorption. Furthermore, it is expected that insoluble deposited particulate matter will be captured by the mucociliary escalator for elimination via the GIT, with a subsequent solubilisation comparable to the oral route of exposure (described above).

No other data are supplied, and none are considered necessary, for the following reasons:

As iron is not easily metabolized by humans from food sources and since iron deficiency is a widespread condition, iron supplementation of food is a widely accepted practice. Those particularly vulnerable to iron deficiency are infants, toddlers, adolescents, menstruating and pregnant women, the elderly and those consuming foods high in iron absorption inhibitors. As a result, elemental iron (carbonyl, electrolytic and hydrogen-reduced) forms are currently approved for use in the EU in foods or as beneficial food supplements (Reg. (EC) No. 953/2009 on substances that may be added for specific nutritional purposes in foods for particular nutritional uses). In accordance with this legislation, the single entry for elemental iron covers the three forms – reduced, carbonyl and electrolytic. The HSE notes that the applicant's source of elemental iron is compliant with the US Food Chemical Codex specification, permitting its use as a food-additive in the USA, and is therefore suitable for human

consumption. Similarly, ferric diphosphate (pyrophosphate), saccharate, ammonium citrate, sodium diphosphate; and ferrous ascorbate, bisglycinate, carbonate, citrate, fumarate, gluconate, lactate, L-pidolate and sulphate are already approved for use in foods (Reg. (EC) No. 953/2009).

Human exposure to iron and iron compounds is extensive. As highlighted during the EU reviews of iron sulphate and ferric phosphate, iron is ubiquitous in the environment and is essential for plant and animal function, including humans. Soil contains a range from 0.5 to 5 % of iron (Brady<sup>1</sup>, 1974) and dietary sources such liver, kidney, beef, ham, egg yolk and soybeans contain iron concentrations of the order of 30-150 mg Fe/kg fresh weight (Elinder<sup>2</sup>, 1986). Iron is a natural constituent of the human body and is involved in oxygen transport, electron transfer, redox reactions, DNA synthesis and many other cellular functions. Iron deficiency leads to reduced levels of haemoglobin and myoglobin, with reduced cellular ATP. A lack of iron-dependent enzymes may impair RNA synthesis and neurotransmitter metabolism. Iron-deficiency anaemia increases the risk for low birth weight, while the cognitive deficiency symptoms observed with such anaemia include deficits in attention, perceptual motor speed, memory and verbal fluency. There is consensus on the importance of iron for cognitive function, with sufficient evidence of its role in cognitive development (EFSA, 2009).

Elemental iron is poorly soluble, of low bioavailability, non-volatile, and as the formulated product, elemental iron particles are incorporated in the product within a solid matrix that is of a non-respirable size. These physicochemical characteristics mean that systemic exposure via the oral, dermal and inhalation routes to the active substance from the product is low. Despite the low likelihood of exposure via the inhalation route from the representative product, due to the expected particle size of the active substance, the applicant has submitted a study on the acute inhalation toxicity of the active substance; no other data has been generated on the active substance. A data package on the representative product 'Final Bite' has been submitted, comprising of an *in vivo* dermal sensitisation (LLNA) study and *in vitro* dermal and ocular irritancy studies – these have been summarised in Volume 3CP\_B6 document.

The information publicly available has been generated on [REDACTED] elemental iron, which differs from [REDACTED] iron in the manufacturing process, not in composition. Hurrell *et al.* (2002) refer to [REDACTED]

[REDACTED] However, the applicant did not produce data supportive of this hypothesis and regardless of the method of manufacture, it is known that in complex biological media, elemental iron is of low bioavailability compared to ferrous sulphate. In considering the availability of inhalation toxicity data generated on particulate [REDACTED] elemental iron, further information on the physicochemical properties of the particles would need to be known before [REDACTED] elemental iron is considered to be an acceptable surrogate for addressing particle-mediated toxicity of elemental iron.

The data from all scientific peer-reviewed sources, combined with the low toxicity of elemental iron and the proposed read-across of the systemic toxicity of elemental iron from data on ionic iron forms indicate that further testing is not necessary. For each endpoint, where reliable data on elemental iron are available, these will take priority in the evaluation. If these are not available, then data on the less soluble ferric (Fe<sup>3+</sup>) ion form will be considered. If neither are available, then data on the more soluble and bioavailable ferrous (Fe<sup>2+</sup>) ion form will be taken into account. This approach was supported by the advisory scientific committee, the ECP. Therefore, the HSE concludes that an exemption from the requirements of the submission of further toxicological studies is justified.

<sup>1</sup> Brady, NC, 1974, The Nature and Properties of Soils, 8<sup>th</sup> Ed., Macmillan Publishing, NY

<sup>2</sup> Elinder, CG, 1986, Handbook on the toxicology of metals, Friberg *et al.* (Eds), Elsevier



### 2.6.1. Summary of absorption, distribution and excretion in mammals

#### Oral exposure

Iron is an essential metal, and by virtue of its ability to undergo facile 1-electron loss or gain, it is involved in many critical cellular processes fundamental to life which require cytochromes, haemoglobin, myoglobin, metalloenzymes etc. These include oxygen transport, energy production, xenobiotic metabolism and DNA synthesis. Iron is toxic in its redox-active 'free' form and its availability is tightly regulated under normal homeostasis. There are no active routes of excretion and as there is no indication that iron accumulates in the body, it is evident that effective control at the point of absorption is vital. A fraction, estimated at 10 – 18 %, of dietary iron is absorbed, with several factors influencing absorption, mainly chemical form, solubility in the gastrointestinal tract (GIT), interaction with other dietary components and the systemic requirements of the body.

The mechanism of iron absorption is dependent on whether exposure is to haem- or non-haem sources, and in relation to elemental iron, the absorption of non-haem iron shall be the focus of this evaluation.

Inorganic, non-haem iron crosses cell membranes only in the ferrous ( $\text{Fe}^{2+}$ ) state, through an active transport mechanism, not by passive diffusion; ferric ions ( $\text{Fe}^{3+}$ ) in food have to be liberated in the stomach by gastric acid digestion, reduced to the  $\text{Fe}^{2+}$  state, and only thus made available for absorption. Alternatively, Fe which arrives at the duodenum is reduced to the ferrous form by duodenal cytochrome B, a protein found on the surface of the enterocyte. The fraction of elemental iron solubilised in gastric acidic conditions is available for absorption into the intestinal mucosal cells by the divalent metal transporting protein (DMT1) which is expressed on the apical membrane of mature duodenal or proximal jejunum enterocytes.

Once inside the enterocyte, iron of either haem or non-haem form enters the same pool and is either stored intracellularly as ferritin (with up to 4500 ferrous ions per ferritin complex) or it is transported across the basement membrane via the ferroportin protein to the plasma carrier, apotransferrin, thereby forming transferrin. The main pools of ferritin are the liver and reticulo-endothelial cells. Ferritin is soluble, but can degrade into insoluble haemosiderin; the latter is increased during iron overload and in situations following hemorrhage, suggesting that its formation may be related to phagocytosis of red blood cells and haemoglobin.

A small amount of absorbed iron may be retained within the enterocyte for processing into haem within mitochondria. The efflux of iron from enterocytes to apotransferrin is coupled to re-oxidation of  $\text{Fe}^{2+}$  to  $\text{Fe}^{3+}$  by the basement membrane-bound enzyme, hephaestin. Subsequently, transferrin transports ferric iron (2 ferric ions per transferrin molecule) to the liver and reticulo-endothelial cells and releases its iron load into cells via transferrin receptors. Transferrin receptors are most prevalent in certain tissues – primarily the liver erythroid cells, macrophages in the liver, spleen and bone marrow.

It could be proposed that ionisation in the gastric environment may form a pool of inorganic iron for absorption. This could pose a significant hazard if gut integrity was compromised, for example, by corrosive action of elemental iron, but the evidence for this is distinctly lacking from the available human database. Considering that elemental iron has been approved for use as a food additive and dietary supplement for several years, the absence of such reports suggests that an irritant or corrosive action of elemental iron is unlikely; it is reasonable to presume that in the absence of an iron-specific physiological disorder, the absorption and hence bioavailability of ionised iron from elemental iron is going to be regulated by normal intestinal function.

Regulation of systemic iron homeostasis is largely regulated by controlling the rate of iron delivery to circulating transferrin. This is achieved by adjustments to the expression of ferroportin on cell membranes through the action of circulating hepcidin. Hepcidin, a hormone produced in the liver, binds to ferroportin, causing the complex to be ubiquitinated, internalized and degraded in lysosomes,



increasing the intracellular pool of potentially bioavailable iron. Hence, increased iron levels lead to a high concentration of circulating hepcidin, which will reduce the number of ferroportin molecules on enterocytes, eventually decreasing the amount of iron absorbed.

Homeostatic control of iron is largely dependent on the production and degradation of erythrocytes, as most iron in the body is contained within erythrocytes. Iron has no regulated excretion pathway, so absorbed iron is virtually completely utilized for functional or storage proteins. Virtually all of the iron from erythrocytes is recycled for incorporation into haemoglobin and thus only a small amount of iron is excreted daily, except where there is substantial blood loss. Daily basal iron losses are reported to be 0.2 mg in infants, 0.5 mg in children, 1.0 mg in men, 0.64 mg in non-menstruating women and 1.3 mg in menstruating women. Excretion of iron occurs predominantly via faeces, although trace amounts of iron are also excreted in the urine, desquamated gastrointestinal and urinary tract cells at the end of their lifespan, and bile.

Based on comparative absorption and bioavailability, elemental iron [REDACTED] is expected to be less hazardous than other forms of iron compounds, and thus data for any  $\text{Fe}^{2+}$  or  $\text{Fe}^{3+}$  compound is eligible for conservative extrapolation to the derivation of  $\text{Fe}^0$  reference values for human risk assessment. Under previous EU pesticide active substance assessments, an oral absorption value of 50 % has been agreed for ferrous and ferric compounds ( $\text{FeSO}_4$ ; DAR UK 2008, EFSA conclusion 2012), ferric phosphate ( $\text{FePO}_4$  RAR, DE 2013, EFSA conclusion 2015).

#### Dermal and Inhalation routes of exposure

The dermal absorption of elemental iron from its representative product is addressed in CP\_B6, where a dermal absorption value of 10% is proposed for solubilised, ionic iron following its dissolution into sweat.

As one of the basic requirements for cellular life is to maintain osmotic homeostasis and compartmental integrity, the dermal ingress of relatively large, particulate elemental iron or ionised iron are not physiologically plausible. Noting that an extensive body of published literature on human physiology of systemic iron exposure is available for the applicant's review, the evidence indicate that the amount of iron passively shed by natural desquamation is in the order of magnitude of approximately 1 mg/day (Galaris and Pantopoulos, 2008).

The inhalation absorption of elemental iron is not an expected route of systemic exposure. Although a well-established and precautionary UK and EU approach taken with all plant protection product active substances is to assign a default inhalation absorption value of 100 %, this is not applicable to elemental iron in the form supplied. It is expected that insoluble deposited particulate matter will be captured by the mucociliary escalator for elimination via the GIT, with a subsequent dissolution and systemic exposure comparable to the oral route. Inhalation absorption is not expected to be greater than that of oral absorption, therefore, if required, the value proposed for the oral absorption may be used for an inhalation exposure risk assessment.

#### **2.6.2. Summary of acute toxicity**

The acute toxicity of elemental iron powder has been assessed on the basis of information in the public domain, extrapolation from specific studies on ferric phosphate and/or iron sulphate and an acute inhalation toxicity study on a representative source of the active substance. These data confirm that elemental iron is of extremely low oral, dermal and inhalation toxicity and is not a dermal or eye irritant or skin sensitiser. The conclusions on the acute oral toxicity, dermal and eye irritation are based on vertebrate test data generated on ferric phosphate, the need to address acute dermal toxicity with test data was waived, and skin sensitisation was addressed by human data – all of which have been summarised in the existing EU assessments of iron sulphate and ferric phosphate. Regarding the

potential for acute inhalation toxicity, the active substance is not volatile, however a significant proportion of this commercial source of elemental iron powder is  $< 22.4 \mu\text{m}$ ; therefore the applicant has submitted an acute inhalation toxicity study on the active substance, which confirms elemental iron is not hazardous via the inhalation route of exposure.

No phototoxicity studies are required, as due to the poor solubility of the active substance in either aqueous or organic solvent, testing is not technically feasible and the data requirement under Reg EC No. 283/2013 is not triggered.

No classification is warranted for any acute toxicity, irritation or skin sensitisation endpoint, as summarised in the table below.

**Table 2.6.2-1 Acute toxicity of elemental iron – overall summary**

Guideline, reference	Test item	Species	Result	Classification
<b>Acute Oral toxicity</b>				
Whittaker P. <i>et al.</i> , 2002 5.2.1/01 Publication	Fe <sup>0</sup> (carbonyl elemental iron)	Rat	LD <sub>50</sub> >50 g/kg bw, <i>i.e.</i> at least 45 times less (in terms of iron) than that of iron sulphate (1100 mg/kg)	<b>None</b>
EPA Reregistration eligibility document (RED), Iron salts, 1993 Publication	Ferric sulphate  Ferrous sulphate heptahydrate	Rat  Rat, rabbit, mice	LD <sub>50</sub> 1487 mg/kg bw (approx. 300 mg/kg of iron) LD <sub>50</sub> rat 1389 mg/kg bw (approx. 280 mg/kg of iron); rabbit 2778 mg/kg (approx. 550 mg/kg of iron); mice 1520 mg/kg (approx. 300 mg/kg of iron)	<b>None</b>
FePO <sub>4</sub> RAR 2013 OECD 423	FeIII (ferric phosphate)	Rat	LD <sub>50</sub> >5000 mg/kg bw (>1850 mg/kg of iron)	<b>None</b>
<b>Acute Dermal toxicity</b>				
EPA Reregistration Eligibility Document (RED), Iron salts, 1993	Ferric sulphate	Rabbit	LD <sub>50</sub> >2000 mg/kg bw	<b>None</b>
<b>Acute Inhalation toxicity</b>				
Lowe, 2018 OECD 403	Elemental iron powder (NutraFine RS®)	Rat,	LC <sub>50</sub> 4h > 5.15 mg/L nose-only	<b>None</b>
EPA Reregistration Eligibility Document (RED), Iron salts, 1993 Publication	Ferric sulphate	Rat	LC <sub>50</sub> >1.1 mg/L	<b>None</b>
Sayes <i>et al.</i> , 2007 Publication	Fe <sup>0</sup> (carbonyl; 0.8-3 $\mu\text{m}$ )	<i>in vivo</i> : Rat <i>in vitro</i> : Rat primary and immortalised cell	No adverse effects	<b>None</b>

Guideline, reference	Test item	Species	Result	Classification
		cultures, Human erythrocytes.		
Warheit <i>et al.</i> , (2007a)  Publication	Fe <sup>0</sup> (carbonyl; 0.8-3 µm)	Rat	No adverse effects	None
Warheit <i>et al.</i> , (2007b)  Publication	Fe <sup>0</sup> (carbonyl; 0.8-3 µm)	Rat	No adverse effects	None
Kiranmai and Reddy (2012)  Publication	Fe <sup>0</sup> (carbonyl; 4.5-5.2 µm)	Rat	No adverse effects	None
<b>Skin Irritation</b>				
FePO <sub>4</sub> RAR 2013 OECD 404	Ferric phosphate	Rabbit	No observable irritancy	None
<b>Eye Irritation</b>				
FePO <sub>4</sub> RAR 2013 OECD 405	Ferric phosphate	Rabbit	No observable irritancy	None
<b>Skin Sensitisation</b>				
FePO <sub>4</sub> RAR 2013 and FeSO <sub>4</sub> DAR 2008.	none	none	Weight of evidence, absence of positive reports from the published literature for these more soluble forms of iron.	None
EPA Reregistration Eligibility Document (RED), Iron salts, 1993  Publication	Ferric sulphate	Guinea Pig	Not sensitising	None

### 2.6.3. Summary of short-term toxicity

No standard short-term regulatory studies on elemental iron are available. Instead, this data point has been fulfilled by a read-across case to the existing EU assessments of the more bioavailable forms of iron - iron sulphate and ferric phosphate.

*Short-term toxicity summary of iron sulphate (excerpt taken from Vol.1 FeSO<sub>4</sub> DAR 2008):*

*In a published 49-day study in mice at doses of 120, 5000 and 8000 ppm corresponding to 20, 833 or 1333 mg Fe/kg body weight or 100, 4165 or 6665 mg FeSO<sub>4</sub>·7H<sub>2</sub>O/kg body weight there was evidence of liver toxicity at dose levels of ≥ 5000 ppm whilst the significance of any findings at 120 ppm were not clearly reported.*

*Corrosive effects can be expected following large doses related to poisoning and changes in gut flora has been observed with large iron intakes. The effects of iron on the intestinal flora have been noted to be in line with a reported human cohort study in Chile [Yeary *et al.* (1966)]. In this study, adverse effects on the gut flora, including more frequent diarrhoea, have been observed when children consumed iron-fortified milk (12 mg Fe/l) while the control group drank normal cow milk with a content of 1 mg Fe/l.*

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*Short-term toxicity summary of ferric phosphate (excerpt taken from Vol. 1 FePO<sub>4</sub> RAR 2013):*

*In a study with schoolchildren approximately 52.5 mg ferric phosphate per capita were consumed for a period of up to 18 months without adverse effects. Most information on ferric phosphate and other iron salts are based on acute and chronic observations. A special subchronic risk of ferric phosphate has not been identified.*

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The applicant has supplemented the read-across to the existing approved iron-based substances by the provision of peer-reviewed scientific literature on elemental iron, which confirm that data on the more soluble, ionic forms represents a worse-case scenario. The published literature generally focussed on iron-overload conditions in rats or mice via the oral or inhalation routes of exposure.

The main toxicity of iron is secondary to free radical formation, and the generation of reactive oxygen species (ROS); comparable iron toxicity has not been reported under conditions of normal intestinal function. Iron toxicity has been reported under conditions of hereditary genetic disorders and some of the key initiating pathology can be replicated in short-term vertebrate studies.

Under exaggerated oral exposure of elemental iron, there is evidence of accumulation of iron in the liver and an exceedance of the iron-binding capacity of transferrin, leaving free iron circulating in the plasma. These may then reach target organs, resulting in wider tissue damage from increased levels of ROS, e.g. hepatic lipid peroxidation. In one publication, rats dosed for 90 days demonstrated no adverse effects up to a dose of 200 mg/kg bw/d. In contrast, data from another research group indicate increased unbound iron and insoluble deposition (haemosiderosis) in the liver from approximately 35 Fe/kg bw/d in rats (LOAEL), with more widespread organ damage including atrophy at higher dose levels (heart, pancreas and spleen); the NOAEL from this study was 3.2 mg/kg bw/d

Under excessive lung overload conditions induced at high concentration levels of [REDACTED] iron in a published sub-acute inhalation study in rats, effects on sensitive biomarkers of pulmonary toxicity were seen. These findings were noted from 50 mg/m<sup>3</sup>, becoming more severe at the top concentration of 250 mg/m<sup>3</sup>. A NOAEC of 5 mg/m<sup>3</sup> was identified from the study. Following consultation with the ECP, due to the potential for differences in physico-chemistry (including particle size, porosity and other particle characteristics) between [REDACTED] forms of elemental iron particles in the respiratory environment, the reliability of the read-across from [REDACTED] iron to [REDACTED] iron for the inhalation route of exposure was deemed too uncertain. Overall, when combined with the shortcomings in the reporting of the data (including information on immunological parameters in the lungs) from a single publication, derivation of a local effects AOEC for [REDACTED] elemental iron was not supported.

There are no reports of adverse pulmonary effects from the medical surveillance at the manufacturing site from which the 'free' (technical material) active substance is sourced, nor any evidence from the applicant's literature search.

In the absence of any evidence of significantly altered pathology or functional deficiency, HSE does not consider these effects to be sufficiently severe to support classification for specific target organ toxicity in accordance with Regulation (EC) No. 1272/2008.

Table 2.6.3-1: Short-term toxicity of elemental iron – summary of available published vertebrate data

Reference	Route of exposure and duration	Test item, doses	LOAEL mg/kg bw/d	NOAEL mg/kg bw/d	Species	Main adverse effects
Whittaker P. <i>et al.</i> , (1996) Publication	Oral 84 d	Fe <sup>0</sup> (carbonyl) 35 (control), 350, 3500, 20,000 mg iron/kg diet  Approximately equivalent to 3.2, 35, 350, 1850 mg/kg bw/d	35	3.2	Rat	<u>3.2 mg/kg bw/d</u> No observed effects  <u>35 mg/kg bw/d</u> Liver iron deposition (haemosiderosis) and lipid peroxidation  <u>350 mg/kg bw/d</u> Mortality 2/10, liver iron deposition (haemosiderosis) and lipid peroxidation, cardiomyopathy, splenic and pancreatic atrophy  <u>1850 mg/kg bw/d</u> Mortality 5/18, iron deposition (haemosiderosis), cardiomyopathy, splenic and pancreatic atrophy
Zhu Q. <i>et al.</i> , (2016) Publication	Oral 90 d	Fe <sup>0</sup> (carbonyl) 0, 100 or 200 mg/kg bw/d	> 200	200	Rat	No adverse effects observed on a variety of parameters
Akhtar S. <i>et al.</i> , 2011a Publication	Oral 56 d	Fe <sup>0</sup> (carbonyl) 0 or 1.5 mg/kg bw/d	> 1.5	1.5	Rat	No observed adverse effects on clinical chemistry
Akhtar S. <i>et al.</i> , 2011b Publication	Oral 28 & 56 d	Fe <sup>0</sup> (carbonyl) 0 or 1.5 mg/kg bw/d	> 1.5	1.5	Rat	No observed adverse effects on hepatic enzymes and thyroid hormones
Domitrović R., <i>et al.</i> , 2008 Publication	Oral 21 d	Fe <sup>0</sup> (carbonyl) 600 mg/kg bw/d	n/a	n/a	Mice	Mechanistic study, not clearly investigating markers of toxicity. Accumulation of iron in the liver, induction of lipid peroxidation, some evidence of redistribution of antioxidants to the liver.

Reference	Route of exposure and duration	Test item, doses	LOAEL mg/kg bw/d	NOAEL mg/kg bw/d	Species	Main adverse effects
Warheit <i>et al.</i> , 1997  Publication  Not relevant to elemental iron	Inhalation  5 d/wk, 4 weeks	Fe <sup>0</sup> (carbonyl) 0, 5, 50 or 250 mg/m <sup>3</sup>	5 mg/m <sup>3</sup>	50 mg/m <sup>3</sup>	Rat	<p><u>5 mg/m<sup>3</sup></u> No observed adverse effects</p> <p><u>50 mg/m<sup>3</sup></u> Mild and transient pulmonary inflammation (neutrophilic infiltration), deficits in alveolar macrophage function, and particle-laden macrophage aggregates at alveolar/alveoli bifurcations associated with adverse histopathology (mild hyperplasia and hypertrophy)</p> <p><u>250 mg/m<sup>3</sup></u> Lung overload – sustained pulmonary inflammation (neutrophilic infiltration), (terminal bronchioles and pulmonary parenchyma), impaired particle clearance, deficits in macrophage function and large numbers of particle-laden macrophage aggregates at alveolar/alveoli bifurcations associated with adverse histopathology (significant hyperplasia and hypertrophy)</p>

#### 2.6.4. Summary of genotoxicity

Elemental iron is approved for use as a human food supplement in the EU and in comparison with ionic forms, it is relatively insoluble and hence of low potential bioavailability. Following exposure to elemental iron, systemic exposure is expected to be to the ionic forms of iron, hence read-across from the more soluble forms - to address the potential for *in vivo* systemic genotoxicity – has been performed. The EU reviews for both iron sulphate and ferric phosphate conclude that on a range of *in vitro* and *in vivo* data, neither substance is considered mutagenic. Furthermore, the applicant has identified a published *in vitro* Comet assay, generated on elemental iron in an human alveolar cell line, which yielded negative results.

Genotoxicity can also arise as a function of particle surface reactivity; however, no such concerns have been identified for elemental iron powder in the published literature. Based on the negative findings of a published haemolysis assay, elemental iron appears to be of low surface reactivity, with no evidence of direct interaction or generation of reactive oxygen species. In the same study, no genotoxicity was observed in an alveolar cell line using the Comet assay.

Overall, HSE conclude that elemental iron is not genotoxic, nor is there any evidence in the public domain which would indicate a hazard for germ cells. No further data are required.



### 2.6.5. Summary of long-term toxicity and carcinogenicity

Despite the poor bioavailability of elemental iron as a nutritional food supplement, it has been widely used in the EU and on a global scale for several decades, primarily due to its chemical stability in food items, combined with the relatively low cost of bulk production. The applicant's source of elemental iron is currently approved for use as a food-grade supplement in the USA (GRAS).

In the absence of substance-specific data on elemental Fe<sup>0</sup> iron in the public domain, the potential for long term toxicity and carcinogenesis - following exposure to elemental iron - has been extrapolated from the approved EU PPP active substance assessments of FeSO<sub>4</sub> and FePO<sub>4</sub> (EFSA conclusions 2012 and 2015, respectively); both of which - in comparison to elemental iron - are more bioavailable forms of iron and are the forms systemically available following exposure to elemental iron. The WHO (WHO/JECFA, 1983<sup>3</sup>) proposed a provisional maximum tolerable daily intake for a 60 kg human of **0.8 mg/kg bw/day**, based on observations that normal individuals have taken dietary supplements of **50 mg Fe/day** (ferrous iron) for long periods, and that females can - during pregnancy and lactation - meet requirements for iron supplementation with dosages of 30 – 60 mg/day. This therapeutic dose has formed the basis for the EU long-term dietary risk assessments of FeSO<sub>4</sub> and FePO<sub>4</sub>, as approved pesticidal active substances, however details of the WHO database are unavailable to HSE. In relation to the potential local effects of iron particles in the lungs following inhalation exposure, a **NOAEC of 5 mg/m<sup>3</sup>** was identified in rats exposed to iron [REDACTED] dust for 4 weeks (see short-term toxicity section). However, following consultation with the ECP, due to the potential for differences in physico-chemistry (including particle size, porosity and other particle characteristics) between [REDACTED] and [REDACTED] forms of elemental iron particles in the respiratory environment, the reliability of the read-across from [REDACTED] iron to [REDACTED] iron for the inhalation route of exposure was deemed too uncertain. Overall, when combined with the shortcomings in the reporting of the data (including information on immunological parameters in the lungs) from a single publication, derivation of a local effects AOEC for [REDACTED] elemental iron was not supported.

Disorders of iron metabolism – as is seen in hereditary hemochromatosis whereby patients have an excessive gastrointestinal absorption of dietary iron – is directed towards the liver, therefore hepatotoxicity is the most common finding in those affected. Hemochromatosis is characterised by excess systemic iron, leading to excessive intracellular ferritin-bound iron which degrades and deposits throughout the body as insoluble hemosiderin. The hemosiderin eventually degrades, releasing redox-active iron. The catalytic generation of ROS, in particular, the hydroxyl radical via the Fenton reaction ensues, causing damage to lipids and proteins and manifesting as architectural and functional oxidative damage to tissues. The main target organ of iron overload is the liver, as it is the main recipient of excessive iron, with the heart and pancreas also sustaining particularly high levels of damage. Several mechanisms plausibly link iron overload to hepatic toxicity and hepatocellular carcinoma – an excessive accumulation of iron in the liver leads to the generation of ROS from 'free' iron, resulting in tissue damage and modification of proteins and DNA; the generation of ROS depletes the antioxidant status and suppresses host immune defences, thus inducing chronic diseases such as fibrogenesis and cirrhosis; iron may also promote the proliferation of tumour cells by increasing the activity of iron-containing enzymes and proteins, which catalyse cellular metabolism thereby accelerating growth.

There has been no evidence to suggest that these are likely adverse health outcomes following exposure to elemental iron under normal intestinal function, nor even in subjects heterozygous for the genetic condition.

<sup>3</sup> Evaluation of certain food additives and contaminants (27<sup>th</sup> report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696, 1983, and corrigenda.

There is no convincing evidence of either chronic toxicity or carcinogenicity from the long-term use of elemental iron in the epidemiological data provided by the applicant. Elemental iron is very poorly absorbed, therefore with limited systemic exposure from either dietary or non-dietary routes, chronic iron overload is an unlikely outcome of the approval of elemental iron as a molluscicidal plant protection product. No further data are required to support this conclusion.

#### **2.6.6. Summary of reproductive toxicity**

No regulatory reproductive or developmental toxicity studies performed with elemental iron have been submitted by the applicant, nor have any relevant publications been identified by the applicant's literature search. In the absence of substance-specific data on ferric phosphate, the conclusions on this endpoint have been extrapolated from the EU assessment of the more soluble FeSO<sub>4</sub>.

Due to the inefficient and variable absorption of iron from GIT, rather than a risk of excess iron intake, pregnant women are more susceptible to iron deficiency and related anaemia. To meet a total iron demand of approximately 1000 mg during pregnancy (the vast majority of which is destined for the foetus), iron supplementation of 50 mg ferrous iron/day is recommended for all women as standard practice (EFSA 2015<sup>b</sup>). The WHO report (WHO/JECFA, 1983) cites the results of studies on the influence of iron and its compounds on reproduction, which show that no maternal toxicity or developmental effects were observed for doses up to 60 mg/d in non-anaemic pregnant women. Current WHO guidance recommends daily supplementation with 30- 60 mg elemental iron/d, rising to 120 mg/d for those diagnosed with anaemia (WHO recommendations on antenatal care for a positive pregnancy experience, 2016<sup>4</sup>).

There is no evidence of reproductive or developmental toxicity in the applicant's literature review and based on the routine supplementation during pregnancy, HSE conclude that no hazard has been identified with regard to this endpoint.

#### **2.6.7. Summary of neurotoxicity**

No regulatory neurotoxicity studies performed with elemental iron have been submitted in support of its use as a plant protection product. A number of scientific reviews have concluded that there is no convincing evidence that dietary iron is associated with any specific neurotoxicity. Considering the extensive use of iron in the human population and the absence of adverse findings in the published database, HSE conclude that no hazard has been identified with regard to this endpoint and no further studies are required.

#### **2.6.8. Summary of further toxicological studies on the active substance**

There is no requirement to provide additional data on elemental iron.

#### **Endocrine disruption**

Considering the low toxicity in the available database, its poor solubility, its extensive use as a human food supplement, and the absence of evidence of specific endocrine disruption in the published database, it is reasonable to conclude that elemental iron does not pose a hazard to the endocrine system. An assessment in line with the ECHA/EFSA (2018) guidance is not considered necessary and no further investigative data are required. This is in line with the approach taken for the EU assessment of iron pyrophosphate (EFSA conclusion 2020).

#### **Immunotoxicity**

The available evidence in the public domain points to the fundamental role of iron for normal development of the immune system, and no indication of iron overload in a normal human population,

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<sup>4</sup> WHO recommendations on antenatal care for a positive pregnancy outcome (WHO, 2016)



leading to immunotoxic effects, has been found in the public domain. No specific immunotoxic events have been identified in patients suffering from clinical conditions of iron overload, nor in individuals taking dietary iron supplements (SACN, 2010).

### **2.6.9. Summary of toxicological data on impurities and metabolites**

The technical specification of elemental iron is considered to be of food chemical quality and therefore the maximum content of certain heavy metals impurities should comply with the limits established in the EU legislation setting maximum levels for certain metal contaminants in foodstuff (Regulation (EC) No. 1881/2006 as amended by Regulation (EC) No. 629/2008). HSE has also identified the potential presence of toxicologically relevant heavy metal impurities (arsenic (0.03 g/kg), lead (0.003 g/kg), cadmium (0.001 g/kg), nickel (0.2 g/kg)) and the assessment of these requires no further toxicological data.

### **2.6.10. Summary of medical data and information**

Elemental iron has been authorised as an additive in foodstuffs and as a dietary supplement for several decades. There are no reports of serious poisoning resulting from human exposure to elemental iron. In addition, there is no evidence that lung overload has occurred in humans exposed to iron particles at occupationally relevant concentrations.

### **2.6.11. Toxicological end point for assessment of risk following long-term dietary exposure - ADI**

Iron is ubiquitous in the environment, it is the most abundant transition metal in the human body and is essential for a variety of fundamental cellular functions. The applicant has deemed no dietary reference values for elementary iron are necessary.

HSE propose that if required, the **ADI of 0.8 mg/kg bw/d** as previously recommended by EFSA during the EU assessments of iron sulphate ( $\text{FeSO}_4$ ; DAR UK 2008, EFSA conclusion 2012), ferric phosphate ( $\text{FePO}_4$  RAR, DE 2013, EFSA conclusion 2015) and ferric pyrophosphate ( $\text{Fe}_4(\text{P}_2\text{O}_7)_3$  DAR PL, EFSA conclusion 2020) can be applied to elemental iron. The WHO (WHO/JECFA, 1983<sup>5</sup>) proposed a provisional maximum tolerable daily intake of 0.8 mg/kg bw/d, based on observations that healthy individuals (~ 60 kg) have taken dietary supplements of 50 mg Fe/day (ferrous iron) for long periods and that women can - during pregnancy and lactation - meet requirements for iron supplementation with dosages of 30 – 60 mg/day. This therapeutic dose has formed the basis for the EU long-term dietary risk assessments of the afore-mentioned iron-based active substances, noting that details of the WHO database are unavailable to HSE.

It is reassuring that that no regulatory authority has established health-based guidance values on known adversity in humans. It is noted that no consumer risk assessment has been performed for the representative plant protection product.

### **2.6.12. Toxicological end point for assessment of risk following acute dietary exposure - ARfD (acute reference dose)**

An acute reference is not necessary as there is no evidence of acute effects following elemental iron ingestion.

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<sup>5</sup> Evaluation of certain food additives and contaminants (27<sup>th</sup> report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696, 1983, and corrigenda.

### 2.6.13. Toxicological end point for assessment of occupational, bystander and residents risks – AOEL

A systemic AOEL can be derived on the same basis as rationale by which the ADI has been established. However, a correction factor of 50% for oral bioavailability of elemental iron is applied, as previously agreed during the EU assessments of iron sulfate, ferric phosphate and ferric pyrophosphate (EFSA conclusions 2012, 2015 and 2020, respectively). Therefore, the resulting systemic **AOEL is 0.4 mg/kg bw per day.**

There is some limited evidence from the literature, that inhalation of particulate [REDACTED] elemental iron powder may lead to lung overload and local toxicity. However, as the evidence is not extensive (a single publication with limited reporting, leading to some uncertainty), and due to concerns that for the inhalation route of exposure, the [REDACTED] form of iron may not be an appropriate surrogate for [REDACTED] elemental iron, the endpoints from this study were not carried forward to derive a quantitative non-dietary local AOEL.

### 2.6.14. Summary of product exposure and risk assessment

#### Operator exposure

The operator exposure assessment indicates that the proposed uses of 'Final Bite' through vehicle mounted broadcast application will result in acceptable systemic operator exposure equal to 0.71% of the AOEL for elemental iron for an operator that applies the product wearing normal workwear (arms, body and legs covered) and no PPE. For the proposed uses of 'Final Bite' through manual application an acceptable systemic operator exposure is calculated to be equal to 98% of the AOEL for elemental iron for an operator that applies the product wearing normal workwear (arms, body and legs covered) and no PPE. For granule application it is considered that exposure indoors would be equivalent to exposure outdoors.

The product 'Final Bite' is classified for human health effects:

- Skin Irritation 2; H315 (Causes skin irritation)
- Eye Irritation 1; H318 (Causes serious eye damage)

The use of suitable protective clothing (coveralls), suitable protective gloves and face protection (faceshield) when handling the product are therefore required.

### Bystander and resident exposure

The longer term exposure assessment to residents indicates that the proposed outdoor uses of 'Final Bite' will result in an acceptable risk of exposure to an unprotected adult and child. The longer term exposure to residents is acceptable for the surface deposits pathway at 0.03% (child) and 0.01% (adult) of the AOEL for elemental iron respectively. An assessment of exposure to child from ingestion of 'Final Bite' granules has been conducted. The number of granules a child would have to ingest to result in adverse health effects is calculated to be approximately 63 granules. It is considered improbable that a child resident would ingest this amount of product, as such, the risk from ingestion of granules is considered to be acceptable.

Elemental iron does not have significant acute toxicity or the potential to exert toxic effects after a single exposure, therefore no bystander risk assessment is required. Resident/bystander exposure is not expected from the proposed indoor use of 'Final Bite'.

### Worker exposure

Worker re-entry exposure to dislodgeable foliar residues is regarded as being negligible in the context of use of granular plant protection products. An assessment of worker exposure has been undertaken for workers handling treated soil. For the proposed uses of 'Final Bite' the worker exposure is predicted to be equal to <1% of the AOEL for elemental iron for a worker without PPE which is within acceptable limits.

## 2.7. RESIDUE

**Summary:** Elemental iron is a molluscicide which is formulated as a granular bait containing 1.0 % of the active substance. Iron is the fourth most abundant element in the earth's lithosphere, following oxygen, silicon, and aluminium. Most of the iron in the earth's crust is in the form of ferromagnesium silicates. Weathering of such minerals in soil is usually accomplished by combined hydrolysis and oxidation due to reaction with water and air. Most of the iron released by weathering is precipitated as oxides or hydroxides; only a small part of the iron is incorporated into secondary silicate minerals or complexed by soil organic matter.

The plant protection product is applied to the soil surface at a rate of 8 kg/ha per treatment which corresponds to 0.08 kg a.s./ha per treatment (maximum total dose: 0.48 kg a.s./ha).

Compared to the natural abundance, the amount of elemental iron added by application of the molluscicide is by several orders of magnitude smaller than the natural content commonly found in soils. Additionally, iron is applied in considerable amounts to agricultural soils in chelated fertilizers.

The fate of elemental iron, as well as of its component's ferric ions in soil, plants and animal, is well documented in the published literature. No metabolism and distribution studies in plants and animal after soil application are necessary, because elemental iron is a natural constituent of soil, plants and animal diets and cannot be degraded therefore the occurrence of further degradation products can be excluded.

Relevant residues of elementary iron in food of plant and animal origin, in exceedance of natural background, are not expected to occur. Therefore, supervised residue trials in primary and succeeding crops are not necessary.

Uneaten bait does decompose, leaving the active ingredient, elemental iron. The elemental iron does not dissolve as would be conventionally expected with this type of process but reacts with oxygen in the air,

to form insoluble hydrated iron oxide, the major natural constituent of iron in the soil environment, not soluble iron.

Mechanisms exist for the root uptake of iron, principally as ferric ions, but they require special conditions and are very slow. Considering the role of iron as an essential plant nutrient, the immobility of iron as well as its natural occurrence in soil, monitoring of residues originating from soil application of elemental iron is not necessary. Therefore, no residue definition is proposed.

Finally, as the soil application of elemental iron will not result in relevant residues of iron in crops and animal products. Therefore, no estimation of acute and chronic dietary exposure coming from the application of elemental iron as plant protection product will be necessary.

**HSE comment:** It should be noted that no residues studies were submitted to support the registration of elemental iron. Instead, literature was provided to support the case that specific residues trials are not required. The applicant has provided summaries based on text taken directly from the available literature. HSE considers that the literature supports the case that specific residue trials are not required.

It is also noted that the proposed GAP does not specify a pre-harvest interval/latest timing of application. This could be interpreted as a zero-day PHI which is not considered to be appropriate for edible crops. Therefore, for edible crops a 1-day PHI should be stipulated.

#### **2.7.1. Summary of storage stability of residues**

No storage stability study is required as no analysis of residues in plants, plant products and products of animal origin was conducted.

#### **2.7.2. Summary of metabolism, distribution and expression of residues in plants, poultry, lactating ruminants, pigs and fish**

No metabolism and distribution studies in plants are necessary, because elemental iron is a natural constituent of soil and plants.

#### **2.7.3. Definition of the residue**

As described in Volume B.7. of the DAR, application of elemental iron as a plant protection product will not result in relevant residues in plants. Also, the natural concentrations of iron in soil are much higher than the increase caused by the application of elemental iron as plant protection product.

Mechanisms exist for the root uptake of iron, principally as ferric ions, but they require special conditions and are very slow. Considering the role of iron as an essential plant nutrient, the immobility of iron as well as its natural occurrence in soil, monitoring of residues originating from soil application of elemental iron is not necessary. Therefore, residue definitions for plants and products of animal origin are not required.

#### **2.7.4. Summary of residue trials in plants and identification of critical GAP**

Relevant residues of elemental iron in food of plant and animal origin, in exceedance of natural background, are not expected to occur. Therefore, supervised residue trials are not necessary.

#### **2.7.5. Summary of feeding studies in poultry, ruminants, pigs and fish**

As described in Volume B.7. of the DAR, no relevant residues of elemental iron, in exceedance of natural background, are to be expected in plants and feeds based on the proposed representative uses.

Consequently, additional uptake of iron by animals by way of treated feed items is of no concern and livestock metabolism studies are not necessary.

#### **2.7.6. Summary of effects of processing**

No relevant residues of elemental iron are to be expected in crops after application of elemental iron according to the representative uses. Consequently, no processing studies are required.

#### **2.7.7. Summary of residues in rotational crops**

Uneaten bait does decompose, leaving the active ingredient, elemental iron. The elemental Iron does not dissolve as would be conventionally expected with this type of process but reacts with oxygen in the air, to form insoluble hydrated iron oxide (rust), the major natural constituent of iron in the soil environment, not soluble iron.

Application of elemental iron as a plant protection product will therefore not result in relevant residues in succeeding or rotational crops, compared to natural background values, and no further data are required.

#### **2.7.8. Summary of other studies**

Soil application of the compound will not result in relevant residues in plants, pollen or bee products or in drinking water. No additional studies are required.

#### **2.7.9. Estimation of the potential and actual exposure through diet and other sources**

As described in Volume B.7. of the DAR, soil application of the compound will not result in relevant residues in plants. Consequently, the respective crops constitute no source of dietary exposure to iron. This also applies for products of animal origin. Therefore, no estimation of dietary exposure through diet and other means is necessary.

**HSE comment:** Iron is a natural constituent of soils serving as an essential nutrient in animal and plant physiology. The amount of iron added by application according to the GAP will be negligible compared to the natural iron content in soil. Furthermore, it is noted that iron is applied in considerable amounts to agricultural soils in chelated fertilizers.

There are many different potential sources of dietary exposure to iron considering its natural presence in food of animal and plant origin, as well as the fact that it is commonly consumed as a food supplement.

The level of iron found in plants following treatment with the plant protection product are unlikely to be higher than the natural background levels. For this reason, it is considered that a consumer risk assessment is not required to address levels of iron found in food resulting from the proposed use.

#### **2.7.10. Proposed MRLs and compliance with existing MRLs**

Currently no specific MRLs for elemental iron have been established as elemental iron is a new active substance. The default LOQ MRL of 0.01 mg/kg would apply. As described in Volume B.7. of the DAR, the application of elemental iron as a plant protection product will not result in relevant residues in plants. An application to list the active in part 4 of the GB MRL register has been made in this submission.

### 2.7.11. Proposed import tolerances and compliance with existing import tolerances

No Import tolerances have been applied for by the notifier.

## 2.8. FATE AND BEHAVIOUR IN THE ENVIRONMENT

Iron is the fourth most abundant element and the second most abundant metal, accounting for 5.1% (by weight) of the Earth's crust. Elemental iron ( $\text{Fe}^0$ ) is rarely found in nature as it readily undergoes redox reactions to form ions ( $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ ) and compounds (oxides, hydroxides, carbonates, and sulphides). These naturally occur in all terrestrial and aquatic ecosystems.

Due to the nature of this active substance, cases were presented and accepted by the HSE to waive several data requirements for the environmental fate and behaviour risk assessment. As a result, no standard environmental fate laboratory or field studies were performed. The DAR volume 3CA section B.8 reviewed naturally occurring background levels of iron and described its environmental behaviour. The DAR volume 3CP section B.8 presented calculated predicted environmental concentrations (PEC) and compared these to measured background levels.

### 2.8.1. Summary of fate and behaviour in soil

Iron is ubiquitous in all soils, with concentrations ranging from 0.2 to 5%. Iron is present in one of two oxidation states in soils: reduced ferrous iron ( $\text{Fe}^{2+}$ ) and oxidised ferric iron ( $\text{Fe}^{3+}$ ). Under normal environmental conditions, in aerated soils with pH 4-9, most iron is in the oxidised form  $\text{Fe}^{3+}$  or its compounds. The  $\text{Fe}^{3+}$  form, commonly known as rust, is immobile, insoluble and less bioavailable than  $\text{Fe}^{2+}$ .

Iron is an essential nutrient for most organisms. Plants will primarily uptake  $\text{Fe}^{2+}$  ions and use various mechanisms to reduce  $\text{Fe}^{3+}$  ions in order to assimilate them into the roots. Furthermore, microorganisms play a key role in the biogeochemical cycling of iron in the environment. Iron is commonly applied as a fertiliser to agricultural land with recommended quantities ranging from 600 g Fe/ha for preventative measures to 6000 g Fe/ha for cases of iron deficiency in crops. Both these amounts far exceed the maximum total dose of iron in the assessed plant protection product (i.e. 480 g/ha).

It is considered acceptable that environmental fate studies were not performed to assess the route and rate of degradation of iron in soil. Under prolonged anaerobic conditions, such as flooded fields, iron is more likely to be present in the reduced mobile form  $\text{Fe}^{2+}$ . However, the product is unlikely to be applied under such conditions. The HSE considers that the iron applied in granular bait will not behave differently in the soil environment to that which is already present, either from natural sources or derived from human activity (e.g. mining, farming or industrial activity). Furthermore, it would be difficult to distinguish the applied active substance from naturally occurring iron in either laboratory or field studies.

### 2.8.2. Summary of fate and behaviour in water and sediment

Iron is found in natural aquatic systems, particularly in the sediment compartment. The speciation of iron and its bioavailability to aquatic organisms will depend on the redox conditions. Iron will be present as insoluble  $\text{Fe}^{3+}$  oxide and hydroxide complexes in most oxygenated waters at circumneutral pH conditions, which will then precipitate to the sediment layer. Typically, iron undergoes reduction in sediment as a function of depth due to decreasing oxygen levels. Soluble  $\text{Fe}^{2+}$  ions are then uptaken by plants and benthic organisms. All data requirements for the route and rate of chemical, photochemical and biological degradation of iron in water or sediment were waived. The HSE considers this acceptable

as the iron applied in granular bait will not behave any differently to iron which is naturally present in the aquatic environment.

### 2.8.3. Summary of fate and behaviour in air

Elemental iron or its oxidation states ( $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ ) are non-volatile under ambient environmental conditions. The HSE considers it acceptable to waive the data requirements for the fate and behaviour of elemental iron in air.

### 2.8.4. Summary of monitoring data concerning fate and behaviour of the active substance, metabolites, degradation and reaction products

The HSE considers it acceptable for monitoring data to not be provided for a new active substance. Furthermore, in the case of elemental iron it would be difficult to distinguish the applied active substance from the iron present in the environment, either from natural sources or derived from human activity. Therefore, it is considered acceptable to waive the requirements for monitoring.

#### Definition of the residue for monitoring

<i>Compartment</i>	<i>Residue/(s)</i>
Soil	N/A Elemental iron and its two oxidation states are naturally occurring compounds
Sediment	N/A Elemental iron and its two oxidation states are naturally occurring compounds
Water - Surface	N/A Elemental iron and its two oxidation states are naturally occurring compounds
Water – Drinking/Ground	N/A Elemental iron and its two oxidation states are naturally occurring compounds
Air	N/A Elemental iron and its two oxidation states are naturally occurring compounds

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### 2.8.5. Definition of the residues in the environment requiring further assessment

#### Definition of the residue for risk assessment

<i>Compartment</i>	<i>Residue/(s)</i>
Soil	Elemental iron (Fe), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )
Surface Water	Elemental iron (Fe), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )
Sediment	Elemental iron (Fe), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )
Ground Water	Elemental iron (Fe), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )
Air	N/A

### 2.8.6. Summary of exposure calculations and product assessment

#### 2.8.6.1 Soil exposure assessment

The soil exposure assessment was based on the worst-case GAP: a single maximum total dose of 480 g a.s./ha applied to bare soil. A worst-case mixing depth of 5 cm was used in accumulation calculations to account for the wide range of GAP uses, some of which will not involve any cultivation. Additional calculations were performed to account for the uses that will involve some cultivation, and so  $\text{PEC}_{\text{SOIL}}$  accumulation values are presented for 20 cm mixing depth. Degradation in soil was discounted in the

calculations as iron will not degrade in the environment but will transform over time via oxidation and reduction. The  $PEC_{SOIL}$  values represent a combination of  $Fe^0$ ,  $Fe^{2+}$  and  $Fe^{3+}$  compounds that would be naturally found in the soil environment.

Table 2.8.6.1-1  $PEC_{SOIL}$  values for elemental iron following applications of 1x 480 g a.s./ha of 'Final Bite ®' (0 % interception)

$PEC_{SOIL}$ iron	Single application (1x 80 g a.s./ha)		Maximum total dose (1x 480 g a.s./ha)	
	Actual	TWA	Actual	TWA
$PEC_{SOIL}$ initial* (mg/kg)	0.107	0.107	0.640	0.640
$PEC_{SOIL}$ accumulation (mg/kg) after 20 years (based on 5 cm, no tillage)	2.140	-	12.800	-
$PEC_{SOIL}$ accumulation (mg/kg) after 20 years (based on 20 cm tillage)	0.620	-	3.680	-
$PEC_{SOIL}$ accumulation (mg/kg) after 50 years (based on 5 cm, no tillage)	5.350	-	32.000	-

\* $PEC_{SOIL}$  values calculated for days 1-100 are not presented here as no degradation was considered.

The  $PEC_{SOIL}$  accumulation value of 12.8 mg/kg represents a worst-case scenario, assuming no degradation or dissipation of the active substance over 20 years, following year on year applications of the maximum dose i.e. 6 applications of 80 g a.s./ha. However, the  $PEC_{SOIL}$  accumulation from multiple applications of 'Final Bite ®' is still less than the naturally occurring background levels present in the soil environment.

$PEC_{SOIL}$  values considering 20 years of consecutive applications in order to be consistent with the groundwater modelling approach were calculated. Following consultation with the ECP, it was advised that as the active substance cannot degrade, a much longer timeframe than the standard 20 years should be considered in the evaluation of  $PEC_{SOIL}$ . A  $PEC_{SOIL}$  accumulation value of 32 mg/kg for 50 consecutive years of applications without tillage was therefore calculated. This value is still significantly less than natural background levels of iron and its compounds in soil. The ECP were of the opinion that the application of the product is unlikely to disrupt the biogeochemical cycling of iron in soils or significantly alter the concentration of iron in soils.

The HSE compared the  $PEC_{SOIL}$  initial and the  $PEC_{SOIL}$  accumulation values for multiple applications to the observed background levels of iron in European and British soils as shown below.

Table 2.8.6.1-2 Ratios of natural background concentrations of iron in soil with the  $PEC_{SOIL}$  initial and accumulation values for 'Final Bite ®'

Database/ reference	Range min-max (%)	Minimum observed natural background concentration in soil (mg/kg)	Ratio minimum background level/ $PEC_{SOIL}$ initial (0.640 mg/kg) <sup>d</sup>	Ratio minimum background level/ $PEC_{SOIL}$ accumulation (12.8 mg/kg) <sup>d</sup>
FOREGS subsoil (Total XRF extraction)	0.11- 15.6	1100	1718.75	85.938



method <sup>a)</sup>				
FOREGS subsoil ( <i>Aqua regia</i> ICP-AES extraction method <sup>b)</sup> )	0.07- 9.42	700	1093.75	54.688
FOREGS topsoil (Total XRF extraction method <sup>a)</sup> )	0.16- 22.3	1600	2500.00	125.00
FOREGS topsoil ( <i>Aqua regia</i> ICP-AES extraction method <sup>b)</sup> )	0.07- 15.2	700	1093.75	54.688
Scheffer & Schachtschabel (1992)	0.2- 5	2000	3125.00	156.250
UK soil observatory (wavelength dispersive XRF <sup>c)</sup> )	0.014- 4.05	140	218.75	10.938

a Total X-ray fluorescence.

b Digestion by *aqua regia* then analysis by inductively coupled plasma atomic emission spectrometry.

c Wavelength dispersive X-ray fluorescence spectrometry

d Ratios calculated by dividing the minimum observed background concentration value by the calculated initial or accumulation PEC<sub>SOIL</sub> value. Reported to 3 d.p.

The worst-case PEC<sub>SOIL</sub> accumulation value of 12.8 mg/kg considering 20 years of applications is ten-fold lower than minimum observed amount in UK soils (140 mg/kg). This represents the lowest 10<sup>th</sup> %ile of UK soils and so most soils will contain significantly more iron than this. Overall, by comparing the PEC<sub>SOIL</sub> values for granular applications of ‘Final Bite ®’ with the observed background concentrations of iron in soil, it is demonstrated that the natural content of iron in soil is far greater, even after repeated applications over many years. The HSE considers that the additions of iron to the soil from use of ‘Final Bite ®’ will be negligible compared to the background levels of iron present in the soil environment.

The ecotoxicology assessment is driven by the toxicity of the product formulation. Therefore, the HSE has calculated a PEC<sub>SOIL</sub> formulation based on the product application rate 48 kg product/ha. The PEC<sub>SOIL</sub> of ‘Final Bite ®’ is 64 mg/kg.

### 2.8.6.2 Groundwater exposure assessment

Elemental iron is insoluble and unlikely to leach to groundwater; however, it will undergo various redox reactions in soil to form Fe<sup>2+</sup> and Fe<sup>3+</sup> ions and mineral compounds. The two ions behave differently in the environment with regard to solubility, mobility and bioavailability. One of the dominant redox reactions in groundwater is the reduction of largely insoluble Fe<sup>3+</sup> ions to soluble, aqueous Fe<sup>2+</sup> ions under anoxic and acidic conditions. The HSE calculated predicted concentrations in groundwater for the two oxidation states using contrasting physicochemical properties. To represent high solubility and low sorption for Fe<sup>2+</sup> ions, the HSE selected an aqueous solubility of 10,000 mg/L and the FOCUS default K<sub>OC</sub> of 10 mL/g for poorly adsorbing compounds. This represents a worst-case scenario of all the applied iron forming Fe<sup>2+</sup> ions under anaerobic conditions, with no uptake by biota or complexation with other compounds in the soil, followed by leaching to groundwater. For the relatively immobile and insoluble Fe<sup>3+</sup> ions, an aqueous solubility value of 1x10<sup>-9</sup> mg/L was used with the FOCUS default K<sub>OC</sub>

value of 10,000 mL/g for strongly adsorbing compounds. Furthermore, no plant uptake was considered which is conservative as iron is an essential nutrient readily uptaken by plants in large quantities.

A single maximum total dose (1x 480 g a.s./ha, 0% interception) was modelled using FOCUS PELMO v5.5.3, FOCUS PEARL v4.4.4 and MACRO v5.5.4 models for the UK relevant scenarios Châteaudun, Hamburg, Okehampton and Kremsmünster. The 80<sup>th</sup> percentile PEC<sub>GW</sub> for the Fe<sup>2+</sup> and Fe<sup>3+</sup> ions are shown below.

Table 2.8.6.2-1 80<sup>th</sup> percentile PEC<sub>GW</sub> values (µg/L) of iron Fe<sup>2+</sup> ions following application of ‘Final Bite ®’ at 1x 480 g a.s./ha to winter cereals (0% interception) using PELMO v5.5.3

FOCUS scenario	Spring	Summer	Autumn	Winter
Châteaudun	520.326	508.366	512.635	536.115
Hamburg	245.317	239.114	231.502	237.861
Kremsmünster	204.759	195.661	195.199	203.839
Okehampton	148.328	132.794	138.887	143.030

PEC<sub>GW</sub> values should not be relied upon in the risk assessment and are for reference only.

Table 2.8.6.2-2 80<sup>th</sup> percentile PEC<sub>GW</sub> values (µg/L) of iron Fe<sup>3+</sup> ions following application of ‘Final Bite ®’ at 1x 480 g a.s./ha to winter cereals (0% interception) using PELMO v5.5.3

FOCUS scenario	Spring	Summer	Autumn	Winter
Châteaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmünster	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001

PEC<sub>GW</sub> values should not be relied upon in the risk assessment and are for reference only.

Table 2.8.6.2-3 80<sup>th</sup> percentile PEC<sub>GW</sub> values (µg/L) of iron Fe<sup>2+</sup> ions following application of ‘Final Bite ®’ at 1x 480 g a.s./ha to winter cereals (0% interception) using PEARL v4.4.4

FOCUS scenario	Spring	Summer	Autumn	Winter
Châteaudun	497.831	504.756	475.996	496.735
Hamburg	283.139	283.906	276.153	266.004
Kremsmünster	162.317	155.820	165.222	165.577
Okehampton	148.235	136.011	133.512	141.808

PEC<sub>GW</sub> values should not be relied upon in the risk assessment and are for reference only.

Table 2.8.6.2-4 80<sup>th</sup> percentile PEC<sub>GW</sub> values (µg/L) of iron Fe<sup>3+</sup> ions following application of ‘Final Bite ®’ at 1x 480 g a.s./ha to winter cereals (0% interception) using PEARL v4.4.4

FOCUS scenario	Spring	Summer	Autumn	Winter
Châteaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmünster	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001

PEC<sub>GW</sub> values should not be relied upon in the risk assessment and are for reference only.

Table 2.8.6.2-5 80<sup>th</sup> percentile PEC<sub>GW</sub> values (µg/L) of iron Fe<sup>2+</sup> and Fe<sup>3+</sup> ions following application of 'Final Bite ®' at 1x 480 g a.s./ha to winter cereals (0% interception) for the Châteaudun scenario using MACRO v5.5.3

Application season	Fe <sup>2+</sup>	Fe <sup>3+</sup>
Spring	567.000	<0.001
Summer	536.000	<0.001
Autumn	541.000	<0.001
Winter	557.000	<0.001

PEC<sub>GW</sub> values should not be relied upon in the risk assessment and are for reference only.

The maximum 80<sup>th</sup> percentile PEC<sub>GW</sub> value for Fe<sup>2+</sup> ions was 567 µg/L. All PEC<sub>GW</sub> values for Fe<sup>2+</sup> ions were significantly greater than 100 µg/L for all application scenarios and seasons. This represents an absolute worst-case scenario based on worst-case parameters for solubility and mobility. Furthermore, for the entire applied iron to reduce to Fe<sup>2+</sup> ions in the soil and then leach to groundwater, the granules would need to be applied to waterlogged soils under prolonged anaerobic conditions. This scenario is highly unlikely. Although the PEC<sub>GW</sub> values for Fe<sup>2+</sup> ions greatly exceed the drinking water parametric value of 0.1 µg/L for pesticides and in many cases exceed the drinking water standard for iron of 200 µg/L (Drinking Water Inspectorate, 2017), none are unusual compared to background levels of iron present in groundwater which can vary between <10 and >10,000 µg/L. DAR volume 3CA section B.8.2.3.1 describes the processes used by water treatment plants for removal of iron from abstracted water. These processes are adequate to remove any iron from groundwater resulting from the use of 'Final Bite ®', which will be minimal compared to background levels in the environment.

During consultation with the ECP, it was concluded that the environmental fate models typically used for modelling leaching to groundwater (i.e. FOCUS PEARL, PELMO and MACRO) do not accurately describe the behaviour of metals in the environment. These models require parameters that cannot be derived for metals. The HSE acknowledges that the FOCUS groundwater models are limited in their ability to describe the behaviour of metal compounds and that more suitable environmental fate models should be sought for future risk assessments.

The PEC<sub>GW</sub> values, assuming all iron is either in the ferric form (Fe<sup>3+</sup>) or in the ferrous form (Fe<sup>2+</sup>) provide a worst case risk envelope. Actual environmental exposure would be much lower than the PEC<sub>GW</sub> values generated using the ferrous iron assumption but may be higher than those generated using the ferric iron assumption. **Therefore the PEC<sub>GW</sub> values presented here should not be relied upon in the risk assessment and are for reference only.**

### 2.8.6.3 Surface water exposure assessment

A first tier drainflow assessment was performed for the representative product 'Final Bite ®'. The HSE considers that a spray drift assessment is not necessary due to the product formulated as a solid granule scattered to soil via mechanical applicator or by hand. As elemental iron is likely to oxidise or reduce in the soil environment, drainflow calculations were performed for two ions Fe<sup>2+</sup> and Fe<sup>3+</sup>. To represent the high mobility of Fe<sup>2+</sup> ions, the HSE selected the FOCUS default K<sub>OC</sub> of 10 mL/g for poorly adsorbing compounds. For the relatively immobile and insoluble Fe<sup>3+</sup> ions, the FOCUS default K<sub>OC</sub> value of 10,000 mL/g for strongly adsorbing compounds was used. The application rate was modelled as a single maximum total dose of 1x 480 g a.s./ha with no crop interception.

The PEC<sub>SW</sub> value for the more mobile Fe<sup>2+</sup> ions is much greater at 70.154 µg/L than the PEC<sub>SW</sub> Fe<sup>3+</sup> ions at 0.295 µg/L. This is due to the contrasting K<sub>OC</sub> values used for poorly and strongly sorbing compounds; the Fe<sup>2+</sup> PEC<sub>SW</sub> value represents a conservative assessment whereby very little active substance is

retained on soil particles so more is available in water for transport via subterranean drains. The  $PEC_{SED}$  value for  $Fe^{2+}$  ions 323.787  $\mu\text{g/kg}$  is also much greater due to the higher amount entering the water body which then precipitates to the sediment layer. The HSE selected the default  $K_{OC}$  values to represent the relative mobility of the  $Fe^{2+}$  ions compared to the relative immobility of the  $Fe^{3+}$  ions. However, it should be noted that such adsorption parameters are intended to describe the environmental behaviour of organic compounds rather than elemental metals. The iron ions will interact and bond with soil surfaces, however  $K_{OC}$  values cannot adequately describe these processes.

Table 2.8.6.3-1  $PEC_{SW}$  and  $PEC_{SED}$  via drainflow of the iron  $Fe^{2+}$  and  $Fe^{3+}$  ions following applications of 'Final Bite ®' at 1x 480 g a.s./ha (0% interception) using the first tier EXCEL 'PEC sw-sed (drainflow)' spreadsheet

Compartment	$Fe^{2+}$	$Fe^{3+}$
$PEC_{SW}$ ( $\mu\text{g/L}$ )	70.154	0.295
$PEC_{SED}$ ( $\mu\text{g/kg}$ )	323.787	1.363

$PEC_{SW}$  and  $PEC_{SED}$  values should not be relied upon in the risk assessment and are for reference only.

The surface water exposure assessment for  $Fe^{2+}$  represents an extreme worst-case scenario of applications of 'Final Bite ®' to anaerobic soils and 100% conversion of  $Fe^0$  to  $Fe^{2+}$  ions, followed by transport via drainflow to the surface water body. Under normal environmental conditions, in aerobic soils over a pH range 4-9, most iron will be in the oxidised form  $Fe^{3+}$ . Furthermore, any  $Fe^{2+}$  is likely to oxidise and hydrolyse to  $Fe^{3+}$  ions and other insoluble compounds upon entering the surface water compartment, which would then precipitate to the sediment compartment. The HSE considers that granular applications of elemental iron will be applied to the soil surface under aerobic conditions. Most of the iron in the bait which is not consumed will come into contact with oxygen and water and essentially rust, converting to  $Fe^{3+}$  ions.

The HSE compared the  $PEC_{SW}$  and  $PEC_{SED}$  values with observed background concentrations of total iron in European and UK freshwater rivers and streams. The  $PEC_{SW}$  value for  $Fe^{2+}$  ions 70.154  $\mu\text{g/L}$  is slightly higher than the median measured concentration of total iron in European stream water, however the  $PEC_{SW}$  value for the  $Fe^{3+}$  ions (0.295  $\mu\text{g/L}$ ) is much lower. Furthermore, the  $PEC_{SW}$  values for both oxidation states of iron are considerably less than the ecological quality standard of 730  $\mu\text{g/L}$  for iron set by the Water Framework Directive.

Iron typically precipitates from the water column to accumulate in sediments. Table 2.8.6.3-2 shows that both  $PEC_{SED}$  values calculated for the UK drainflow assessment (313.787  $\mu\text{g/kg}$  for  $Fe^{2+}$  and 1.363  $\mu\text{g/kg}$  for  $Fe^{3+}$ ) are much lower than the background levels of iron in European sediment reported in the FOREGS database (2005), which range from 600-358,000  $\mu\text{g/kg}$ .

Table 2.8.6.3-2 Ratios of natural background concentrations of iron in surface water and sediment with PEC<sub>SW</sub> and PEC<sub>SED</sub> values for 'Final Bite ®'

Database/ reference	Range min-max (%)	Median observed natural background concentration (µg/L or µg/Kg)	Ratio average background level/ PEC <sub>SW</sub> (µg/L)	Ratio average background level/ PEC <sub>SED</sub> (µg/Kg)
<b>Surface water</b>				
FOREGS (2005) European stream water (dissolved ICP-MS extraction method) 807 samples	<0.1- 4820 µg/L	67	0.995 (Fe <sup>2+</sup> ) 227.119 (Fe <sup>3+</sup> )	-
WFD (2012) UK 3397 samples	17- 11700 µg/L	730*	10.406 (Fe <sup>2+</sup> ) 2474.58 (Fe <sup>3+</sup> )	-
<b>Sediment</b>				
FOREGS (2005) European stream sediment (total XRF method) 852 samples	0.11- 20.9	35700	-	110.258 (Fe <sup>2+</sup> ) 26192.223 (Fe <sup>3+</sup> )
FOREGS (2005) European stream sediment (Aqua regia ICP-AES method) 845 samples	0.06- 20.0	19700	-	60.842 (Fe <sup>2+</sup> ) 14453.412 (Fe <sup>3+</sup> )
FOREGS (2005) European floodplain sediment (total XRF method) 747 samples	0.25- 35.8	33300	-	102.845 (Fe <sup>2+</sup> ) 24431.401 (Fe <sup>3+</sup> )
FOREGS (2005) European floodplain sediment (Aqua regia ICP-AES method) 747 samples	0.16- 19.5	19500	-	60.225 (Fe <sup>2+</sup> ) 14306.676 (Fe <sup>3+</sup> )

\*Average value not reported. The ecological quality standard for UK freshwaters was set to 730 µg/L as recommended by the WFD.

The ECP acknowledged that standard environmental fate models are also not designed to adequately describe the behaviour of metals in surface water or sediment. As such, the PEC<sub>SW</sub> and PEC<sub>SED</sub> values represent risk envelopes. The actual exposure to the aquatic environment from use of the product is likely to be between the PEC values generated using the two assumptions (all iron in ferric or ferrous form) and would be much lower than the worst-case predictions generated assuming all iron is in the ferrous form (Fe<sup>2+</sup>). The Committee noted that the applicant did not describe any attempts within their assessment summary to find alternative models that may have been more suitable. The ECP recognised that an assessment with alternative models would be difficult unless the model that HSE accepts was specified and guidance on use of the model were provided. Nonetheless, the applicant could consider

providing fate modelling for both drainflow and groundwater using models which are more suitable for metal substances, if this were required to resolve uncertainties in the assessment

The  $PEC_{SOIL}$  accumulation based on 20 consecutive years without tillage is 12.8 mg/kg which is considerably less than the range naturally observed in UK and European soils (140–22,300 mg/kg). The HSE considers that in situations where large amounts of iron naturally transport via drainflow or runoff from soils into adjacent water bodies, the use of ‘Final Bite ®’ will not impact significantly on this. The surface water exposure assessment represents a worst-case scenario for the  $Fe^{2+}$  ions. The HSE considers that it is highly unlikely ‘Final Bite ®’ granules will be applied during flooding events in which anaerobic conditions may prevail. Furthermore, in situations where the soil is under prolonged anaerobic conditions, most of the mobile  $Fe^{2+}$  ions would be naturally occurring. The HSE does not consider the addition of iron from ‘Final Bite ®’ would impact on the natural environmental processes.

Since there is no agreed data set for entry of granule formulations to surface water, this has been addressed by labelling in the past - setting a voluntary ‘no spread zone’ restriction to greatly reduce the risk of direct contamination of adjacent water bodies by pellets during application. Wording could be as follows:

- Pellets should not fall within 6 m of a watercourse or ditch. To achieve this, users should determine the spread width of the applicator with the product to be applied prior to any application (to the rear as well as the side of the applicator).
- Calibrate the applicator before use.

#### 2.8.6.4 Air exposure assessment

Elemental iron is non-volatile under ambient environmental conditions. Furthermore, iron ions and compounds are not expected to undergo significant volatilisation. The HSE considers it acceptable that  $PEC_{AIR}$  values have not been calculated for elemental iron.

#### 2.8.6.5 Predicted environmental concentrations from other routes of exposure

The HSE does not consider it necessary to investigate other routes of exposure for elemental iron. The iron applied via ‘Final Bite ®’ granules will not behave in the environment differently to iron naturally present in the environment.

#### **Outcome of the environmental fate consultation with the Expert Committee on Pesticides (ECP):**

The ECP acknowledged that the HSE assessment represents a weight of evidence approach making the most of standard tools in a qualitative fashion. However, a quantitative assessment requires the application of more appropriate models or tools. Overall, the ECP advised that there are unlikely to be significant levels of exposure in soil, groundwater or surface waters from use of the product compared to natural background levels of iron in the environment. If the active substance is approved, the subsequent UK product assessments should not repeat the same modelling using standard tools. Ideally alternative models should be used. But if this is not possible, then a weight of evidence approach comparing application rates with natural background levels could be employed. HSE should consider placing guidance on the acceptability of the use of the weight of evidence approach on their website.

### 2.9. EFFECTS ON NON-TARGET SPECIES

An incomplete standard toxicity dataset was submitted in support of the risk assessment for non-target species, with literature data and a reasoned case used where toxicity data was lacking. The following is

a summary of the risk assessment conducted. The assessment is based on exposure to iron via the representative product 'Final Bite' which is applied as a granule.

### 2.9.1. Summary of effects on birds and other terrestrial vertebrates

No toxicity test data with birds and iron, or the representative product (Final Bite), were provided. Surrogate endpoints were devised using the lowest amount of iron normally found in avian commercial diets. **An acute toxicity study was submitted using a surrogate product (Slug and Snail Killer).**

Acute and long term toxicity data was available for mammals and iron but not the representative product.

The toxicity data available is summarised in the table below.

Test species	Test substance	Time scale (test type)	Endpoint
Japanese Quail	Slug and Snail Killer (1 % iron)	Acute oral toxicity	LD50 = >2000 mg product/kg bw (equivalent to >19.6 mg a.s./kg bw)
		Acute oral toxicity, extrapolated**	<b>LD50 = 3776 mg product/kg bw (equivalent to 37 mg a.s./kg bw)</b>
n/a	n/a	Reproductive/long term toxicity	NOAEL = 5 mg a.s./kg bw/d*
Rat	Fe0 compared with FeII (carbonyl iron, ferrous sulphate)	Acute oral toxicity	<b>LD50 &gt; 50000 mg Fe/kg bw</b>
Rat	Carbonyl iron	Long-term (90 days)	NOAEL = 35 mg/kg of diet, equivalent to <b>3.2 mg Fe/kg bw/ day</b>
Rat	Carbonyl iron	Long-term (90 days)	NOAEL = 200 mg Fe /kg bw/day
n/a	n/a	Reproductive/long term toxicity	NOAEL = 24 mg Fe/kg bw/d*
n/a	n/a	Reproductive/long term toxicity	NOAEL = 4.5 mg Fe /kg bw/d*

\*calculated based on lowest concentration of iron in a commercial diet expressed in mg a.s./kg diet x 0.1 in line with EFSA guidance (2009).

\*\*In accordance with EFSA guidance (2009), Table 1, an extrapolation factor of 1.888 can be applied to this endpoint (10 animals, zero mortalities)

**Initially**, issues were highlighted regarding the data available. Firstly, the literature data was not drawn from the literature review submitted in support of this application, so there **was** uncertainty that this represents all of the available data regarding iron and toxicity to birds **and mammals**. Secondly, it **was** not possible to compare the iron used in literature data with the agreed specification, so it **was** not clear that they cover the risk from the levels of impurities outlined in the agreed specification. **In response to these concerns, the applicant supplied additional information regarding the literature searches performed and justification regarding the representativeness of the tested material used in the studies, in comparison with the technical specification. This is sufficient to conclude that the tested material is representative of the technical specification and while there are still limitations regarding the transparency of the process used to identify relevant literature, supplementary searches have been performed by HSE to ensure key data are not missed.**



A standard first tier risk assessment for granules was carried out with the data available according to EFSA Guidance for bird and mammal risk assessment (2009). Risk from granules is assessed using the following routes of exposure:

- a) Ingesting granules as a source of food
- b) Ingesting granules as grit (birds only)
- c) Birds may mistake granules for small seed
- d) Birds and mammals may ingest granules when they eat food contaminated with soil
- e) Birds and mammals may consume food contaminated with residues resulting from granular applications.

Of these five routes of exposure, a), b) and e) were not resolved at first tier and required further consideration.

An initial weight of evidence case was submitted to refine the risk assessment citing the following:

- 1) Iron is an essential component of bird and mammal diets
- 2) The blue colouring of the product will repel birds and mammals so it is unlikely to be eaten
- 3) Granules will not be available to birds and mammals in sufficient numbers to cause adverse effects or for long periods of time.
- 4) Consuming slugs and snails that have been poisoned by the representative product is very unlikely

The applicant cited numerous literature sources in support of this reasoned case, however, the data provided was considered insufficient to conclude an acceptable risk.

In response to a request for further information, updated higher tier risk assessments for birds and mammals were provided by the applicant, supported by relevant published literature. The proposed lines of evidence are broadly grouped into the following categories:

- Effects of elemental iron on birds and mammals
- Uptake and regulation of iron
- Potential for exposure of wild birds and mammals to iron via 'Final Bite' granules
- Background exposure of birds and mammals to iron via normal diet

In light of the very low first tier TERs and nature of the information available, no further quantitative risk assessment has been conducted. Instead a qualitative, weight of evidence approach has been followed. The information provided has been reviewed in order to reach a GB conclusion.

For birds, consumption of granules as a food source is considered a more relevant scenario than consumption of granules as grit, given the composition of the granules. Regarding the acute risk to birds, it is demonstrated that it is highly unlikely that relevant bird species would consume sufficient Final Bite granules in an acute feeding scenario to exceed their iron homeostatic regulatory capacity and for this to result in mortality. Additionally, in order to mitigate any risk should seed be spilled, the following label requirement is stipulated:

*'SPe 6: To protect birds / wild mammals remove spillages'*

Overall, it is concluded that it has been clearly established that any mortality is unlikely from acute exposure of birds via consumption of Final Bite granules. The acute risk to mammals was demonstrated to be acceptable based on the first tier risk assessment.

Regarding the long-term/reproductive risk to birds, it is considered unlikely that where granules are scattered across the soil surface, these would be a sufficiently attractive food item that relevant bird



species would consume enough granules across a period of multiple days or weeks that this would overload their ability to regulate their absorption of iron, leading to accumulation of iron in organs, impacting the health and survival of the individual. Therefore, any mortality or reproductive effects are unlikely from exposure of birds to iron via consumption of Final Bite granules. However, due to uncertainty regarding the likelihood of granules being consumed by birds, a confirmatory data requirement is recommended to validate this conclusion. It is proposed to request that the Applicant provides monitoring data investigating whether birds consume Final Bite granules under field conditions. This could be achieved by observing consumption of granules by birds from a specified area where granules have been applied according to the proposed conditions of use. In light of the above risk assessment and since consumption of granules would only need to be monitored for a short time period, this study would not be expected to result in harm to wild vertebrates.

Regarding the long-term/reproductive risk to mammals, it is unlikely that where granules are scattered across the soil surface, these would be a sufficiently attractive food item that relevant mammal species (e.g. wood mouse) would consume enough granules across a period of multiple days or weeks that this would overload their ability to regulate their absorption of iron, thus leading to accumulation of iron in organs, impacting the health and survival of the individual. While, there is still some uncertainty associated with this conclusion given the limited data on granule consumption, the high reproductive output of wood mice means that populations would be able to quickly recover following any impact as a result of exposure to elemental iron. Therefore, it is sufficiently established that there will be no long-term repercussions for abundance and diversity of small mammals.

While exposure of birds and mammals via consumption of poisoned molluscs cannot be categorically excluded, behavioural information demonstrates that exposed molluscs rapidly retreat below the soil surface (or to other hidden locations) after consuming granules containing elemental iron. Therefore, molluscs containing elevated iron levels are unlikely to be a potential food item that is available to scavenging birds or mammals.

Risks via drinking water and secondary poisoning are low.

Overall, it is concluded that the representative uses of elemental iron in Final Bite granules will not result in unacceptable impacts to birds and mammals. However, confirmatory data investigating granule consumption by birds under field conditions is recommended to support this conclusion.

## 2.9.2. Summary of effects on aquatic organisms

The following toxicity data is available and considered reliable for use in the risk assessment for aquatic organisms.

Reference	Author	Species	Substance	Endpoint	Value (mg a.s./L)
10.2.1/2	████████ 2018	<i>D. magna</i>	Final Bite-040226 (1 % Iron)	48 h EC50	>0.5345 (mm)
10.2.1/4	████████ 2018	<i>D. subspicatus</i>	Final Bite-040226 (1 % Iron)	72 h ErC50	>0.529 (mm)
				72 h NOErC	0.529 (mm)

No reliable data was available for the representative product or the active substance and fish. This would normally be considered a data gap, especially for the purposes of hazard classification, however as discussed below it is considered that fish, like other water dwelling organisms, are capable of metabolising the additional iron in surface water from the proposed uses of Final Bite with no toxic symptoms. In the interest of reducing vertebrate testing it is acceptable to waive the data requirement for fish toxicity in this case.

UK Fate and Behaviour evaluators considered Drainflow of the active substance to be the only route of exposure for the aquatic compartment. As discussed in the Fate and Behaviour section above, use of

elemental iron formulated as 'Final Bite' according to the proposed GAP is not considered to add significantly to the amount of iron already bio-available to aquatic organisms in either the surface water or the sediment. The available toxicity data (covering algae and aquatic plants) shows that no adverse effects occur at the highest tested concentration (0.529 mg a.s./L mean measured). Overall, an acceptable risk to the aquatic compartment is concluded.

### **2.9.3. Summary of effects on arthropods**

#### **Bees**

No toxicity data was submitted for bees with the active substance or the representative formulation. Regulation EU No 283-2013 specifies that toxicity data is required when bees are likely to be exposed. The representative product is formulated as a ready to use granular bait applied to the ground to reach the target species, and is therefore not available for bees foraging on flowers. The routes of exposure to bees are therefore limited to dust drift and potentially contaminated pollen/nectar via systemic absorption of the active substance by flowering plants.

In the case of dust drift there is no guidance currently available to assess the risk from this route of exposure. There is also evidence that the risk of dust-drift exposure will be low - as shown in Vol 3CP 2.8.5/01, the representative product was found to be almost dust-free (optical dust factor 1.33).

Plants have been shown to be capable of regulating the uptake of iron from the soil which has high background levels of iron. The background levels are unlikely to be significantly increased by application of the representative formulation. UK Fate and Behaviour evaluators concluded background levels ranging from 2000-50 000 mg iron/kg soil, and a maximum PEC<sub>soil</sub> from the proposed uses of elemental iron to be 12.8 mg/kg. Pollen is also highly nutrient dense with levels of iron as high as 2872.89 mg/kg found in *Helianthus annuus* (common sunflower); the same study showed that unifloral bee pollen from the same plant species contained only 27.42 mg iron/kg, a reduction which was thought to be due to dilution of the flower pollen by honeybee saliva. Honeybee pollen collected from European countries can contain up to 136.1 mg iron/kg pollen. It is considered that the use of elemental iron according to the proposed GAP will not significantly increase the level of iron normally available to bees.

Overall, an acceptable risk to bees was concluded in absence of toxicity data on the basis of negligible exposure.

#### **Other Non-target Arthropods**

Three toxicity studies on soil-dwelling non-target arthropod species were submitted. The toxicity endpoints are summarised in the table below.

## Summary of endpoints for non-target arthropods

Test species – Life stage	Test substance	Time scale (test type)	Endpoint product/ha (kg)	Endpoint (pellets/m <sup>2</sup> ) <sup>4</sup>	Data point Author, year
<i>Aleochara bilineata</i>	Final Bite - 0402206	75 days Laboratory test <sup>1)</sup>	Reproduction: ER <sub>50</sub> > 100 kg product/ha NOER = 100 kg product/ha (1210 g a.s./ha) <sup>3</sup>	Reproduction: ER <sub>50</sub> > <b>737 pellets/m<sup>2</sup></b> NOER = 737 pellets/m <sup>2</sup>	CP 10.3.2.2/01. [REDACTED] 2018
<i>Poecilus cupreus</i>	Final Bite - 0402206	14 days Laboratory test	Survival & feeding: L/ER <sub>50</sub> > 100 kg product/ha NOER = 100 kg product/ha (1210 g a.s./ha) <sup>3</sup>	Survival & feeding: L/ER <sub>50</sub> > <b>743 pellets m<sup>2</sup></b> NOER = 743 pellets m <sup>2</sup>	CP 10.3.2.2/02. [REDACTED] 2018
<i>Pardosa</i> sp.	Final Bite - 0402206	14 days Laboratory test <sup>2)</sup>	Survival & feeding: L/ER <sub>50</sub> > 96.7 kg product/ha NOER = 96.7 kg product/ha (1170.07 g a.s./ha) <sup>3</sup>	Survival & feeding: L/ER <sub>50</sub> > <b>722 pellets m<sup>2</sup></b> NOER = 722 pellets m <sup>2</sup>	CP 10.3.2.2/03. [REDACTED] 2018

<sup>1)</sup> Test item applied whole to the surface of the test area, rather than mixed in.

<sup>2)</sup> Test specimens collected in late April and early May.

<sup>3)</sup> Toxicity endpoint converted to active substance using tested weight for weight percentage content of the test item, i.e. 1.21 %.

<sup>4)</sup> Toxicity endpoints calculated based on reported arena area and number of pellets applied to each test arena.

The standard risk assessment scheme for non target arthropods as proposed under ESCORT II guidance covers the off-field and in-field risk from use of the product. The representative product is formulated as a ready to use granular bait applied to the ground to reach the target species, therefore the potential exposure to standard foliar dwelling species is considered negligible and no data is provided for *T. pyri* and *A. rhopalosiphi*. The risk to the off-field environment is considered to be limited to dust drift. There is no guidance currently available to assess the risk from this route of exposure. There is also evidence that the risk of dust-drift exposure will be low - as shown in Vol 3CP 2.8.5/01, the representative product was found to be almost dust-free (optical dust factor 1.33). Overall, the off-field exposure is considered to be negligible and the risk assessment will focus on the in-field environment, in particular soil-dwelling species.

The risk assessment was based on the scheme outlined in ESCORT II guidance but compares the requested application rate to the rate used in the studies in terms of pellets/m<sup>2</sup>. This more accurately reflects the conditions of the studies conducted. The risk assessment is based on the formulated product alone; the amount of iron already available to soil based non-target arthropods is not thought to be significantly increased by use of the product according to the GAP.

The toxicity data with the formulated product indicates no adverse effects at 722-743 pellets/m<sup>2</sup> which exceeds, with a large margin of safety, the maximum possible number of pellets per m<sup>2</sup> following 6 applications (360 pellets/m<sup>2</sup>). Therefore the risk from the intact pellet is considered to be acceptable.

Another potential route of exposure is from ‘hotspots’ of the product in the immediate vicinity of the partially broken-down pellet. There is also the possibility of consuming prey contaminated with the product. Without a dedicated granule-based toxic reference item, the ability of the test systems used in this application to demonstrate the toxicity of the representative product is uncertain. It is uncertain if the data available covers the risk from ‘hotspots’ of the partially broken down product.

However, data is available with the soil dwelling macroorganisms *H. aculeifer* and *F.candida* (see Section B.9.7, below) where the formulation was ground up and mixed homogenously into the soil. According to SANCO/10329/2002 rev 2 final (Guidance Document on Terrestrial Ecotoxicology), page 24:

*“The standard approach is not appropriate for...plant protection products such as granules, seed treatments and pellets. In these cases it is recommended that studies are conducted with Hypoaspis aculeifer or Folsomia candida as proposed by EPPO (2002a). If deemed appropriate, studies with Aleochara sp. might be conducted, e.g. at tier 2.”*

It is therefore possible to follow the SANCO guidance document and use data with *H. aculeifer* and *F. candida* as first-tier surrogates for soil dwelling non-target arthropods.

As demonstrated in section 2.9.4 of this document, the risk of the formulated product to the above species when used according to the proposed GAP is low. The TER values for *H. aculeifer* and *F. candida* were 48.48 and 18.04, respectively, exceeding the long term trigger value of 5 for these species with a margin of safety. This margin of safety is considered to mitigate the uncertainty involved with extrapolating between these species and the larger soil dwelling arthropods tested with the intact pellet only.

Overall the risk of ‘hotspots’ of the broken down product to soil-dwelling non-target arthropods is considered addressed and a low risk is concluded.

#### 2.9.4. Summary of effects on non-target soil meso- and macrofauna

Toxicity data were submitted for earthworms and soil macro-organisms. The data is summarised in the table below.

Test species	Time scale	Test material	Endpoint *	Data point Author, year
<i>Eisenia fetida</i>	Long-term 8 w	Final Bite – 0402206 1)	NOEC <sub>weight</sub> = 1050 mg product/kg dw soil <b>NOEC<sub>repro</sub> = 100 mg product/kg dw soil</b> LOEC <sub>repro</sub> = 180 mg product/kg dw soil EC <sub>10</sub> = 147.1 mg product/kg dw soil EC <sub>20</sub> = 188.6 mg product/kg dw soil EC <sub>50</sub> = 303.7 mg product/kg dw soil	CP 10.4.1.1/01. ██████ 2018a

Test species	Time scale	Test material	Endpoint *	Data point Author, year
<i>Eisenia andrei</i>	Long-term 8 w	Final Bite – 0402206 2)	$NOEC_{mortality} = 959 \text{ pellets/m}^2$ $LOEC_{mortality} = 1391 \text{ pellets/m}^2$ $LC_{10} = 1109 \text{ pellets/m}^2$ $LC_{20} = 1667 \text{ pellets/m}^2$ $LC_{50} = 3633 \text{ pellets/m}^2$ $NOEC_{weight} = 662 \text{ pellets/m}^2$ $LOEC_{weight} = 959 \text{ pellets/m}^2$ $NOEC_{repro} = <662 \text{ pellets/m}^2$ $LOEC_{repro} = 662 \text{ pellets/m}^2 \text{ dw soil}$ $EC_{10} = \text{n.d.}$ $EC_{20} = 460 \text{ pellets/m}^2$ $EC_{50} = 743 \text{ pellets/m}^2$	CP 10.4.1.1/02. [REDACTED] 2018b
<i>Folsomia candida</i>	Long-term 28 d	Final Bite – 0402206 1)	$NOEC_{mortality} = 4500 \text{ mg product /kg soil}$ $LOEC_{mortality} > 4500 \text{ mg product /kg soil}$ $NOEC_{reproduction} = 1476 \text{ mg product /kg soil}$ $LOEC_{reproduction} = 2140 \text{ mg product /kg soil}$ $EC_{10 \text{ repro}} = 1154.8 \text{ mg product /kg dw soil}$ $EC_{20 \text{ repro}} = 2143.4 \text{ mg product /kg dw soil}$ $EC_{50 \text{ repro}} > 4500 \text{ mg product /kg dw soil}$	CP 10.4.2/01. [REDACTED] 2018c
<i>Hypoaspis aculeifer</i>	Long-term 14 d	Final Bite – 0402206 1)	$NOEC_{mortality} = 4500 \text{ mg product /kg soil}$ $LOEC_{mortality} > 4500 \text{ mg product /kg soil}$ $NOEC_{reproduction} = 3103 \text{ mg product /kg soil}$ $LOEC_{reproduction} = 4500 \text{ mg product /kg soil}$ $EC_{10} = \text{n.d.}$	CP 10.4.2/02. [REDACTED] 2018d

Elemental iron is a naturally occurring element in soil (UK Fate and Behaviour specialists estimate background levels of 2000-50000 mg/kg soil), indicating that the element is present in all soils. The calculated  $PEC_{soil, accumulation}$  is 12.8 mg a.s./kg based on the proposed use of the product accumulating over a 20 year period. This PEC, resulting from the worst case use of the product is significantly lower than the background levels; therefore, no quantitative risk assessment for exposure to the active substance has been carried out. The risk is instead assessed in terms of the formulated product. Data from the available literature indicates that the [REDACTED] increases the toxicity of ferrous active substances to earthworms, which is reflected in the results for the formulation.

The first tier risk assessment for the formulation indicated an acceptable risk to soil macro-organisms (represented by *F. candida* and *H. aculeifer*) however there was a demonstrable risk to earthworms, with a TER value of 1.56 for *E. fetida*.

The applicant submitted a field study ([REDACTED] 2019) which indicated no adverse effects on earthworms at 6x 8 kg product/ha over the course of a year. Initially a number of shortcomings were identified with this study, including low abundance of anecic earthworms, dry conditions during the study and different method of application for the reference item. In response to concerns over use of this study in the GB risk assessment, an additional literature review and supporting information were provided. This focused on the following areas:

- What are typical UK numbers of the anecic species *L. terrestris* and *A. longa*, and how do these compare with the field study by [REDACTED] (2019)?
- What are the ideal growth conditions for the anecic species *L. terrestris* and *A. longa*, and how do these compare with the field study by [REDACTED] (2019)?

- Do foraging anecic earthworms encounter and consume slug pellets and are they affected by iron-containing slug pellets? Do the results of [REDACTED] (2019) indicate any such effects?

The new literature data provides some reassurance that anecic worms had the potential to come into contact with granules and hence be exposed in the study, therefore helping to reduce uncertainties in one of the areas identified as problematic. Data on growth conditions and abundance suggests the anecic numbers in the study are not atypical and this helps with the read across point between times of year. The reference item data for this study, and the extended literature, indicate that the anecic earthworms are potentially being exposed to the test item. The issue remains that the statistical power of the study to detect effects in *L. terrestris* was low at the key timepoints after exposure, hence there is uncertainty that the formulation does not impact this species in the short-medium term.

Data on another anecic species (*A. Longa*) and the data on anecic species in total suggests that where it can be adequately assessed, anecic species populations aren't impacted at all by the formulation. Therefore *L. terrestris* would have to be significantly more sensitive to the formulation for there to be a concern over the impact on this species. There is limited information on this latter point, but there is nothing to indicate that *L. terrestris* would suffer statistically significant effects of ferric test items at the requested field rates. On balance, there is sufficient evidence to conclude an acceptable risk to earthworms for the proposed use of the representative product

#### 2.9.5. Summary of effects on soil nitrogen transformation

No data with iron or the representative product 'Final Bite' were submitted. Data with the surrogate formulation 'Slug and snail killer' was submitted instead.

Test type	Time scale	Test material	Endpoint	Data point Author, year
Nitrogen transformation	28 days	Slug & Snail Killer	-6.5% effect at up and including 333.5 mg product/kg of soil dry weight after 28 days <25% deviation from control by the study end	CP 10.5/01. [REDACTED] 2008

Elemental iron is a naturally occurring element in soil (UK Fate and Behaviour specialists estimate background levels of 2000-50000 mg/kg soil), indicating that the element is present in all soils. The calculated  $PEC_{\text{soil, accumulation}}$  is 12.8 mg a.s./kg based on the proposed use of the product accumulating over a 20 year period. This PEC, resulting from the worst case use of the product is significantly lower than the background levels; therefore, no quantitative risk assessment for exposure to the active substance has been carried out.

The  $PEC_{\text{soil}}$  of the formulation is calculated as 64 mg product/kg soil. This is exceeded by the endpoint above (<25 % effects at 333.5 mg product/kg soil) with a high margin of safety. Overall the risk from soil micro-organisms can be considered acceptable.

#### 2.9.6. Summary of effects on terrestrial non-target higher plants

No toxicity data for non-target plants was submitted.

The risk to non-target plants has been assessed in line with the SANCO Terrestrial Guidance document (2002), with further reference to the data requirements as stipulated under Regulation EU 283/2013. In



the case of elemental iron, the representative product Final Bite is formulated as a ready-to-use bait granule, applied to the soil around the target crops by spreading. The risk of exposure to off-crop non-target plants is therefore considered to be minimal, limited to dust drift. No guidance is currently available to assess the risk from this method of exposure, though with an optical dust factor of 1.33 (See Vol 3CP 2.8.5/01 of this dossier), it is considered that the representative product produces low levels of dust.

Even allowing for exposure, elemental iron is a naturally occurring element in soil (UK Fate and Behaviour specialists estimate background levels of 2000-50000 mg/kg soil) and used as a nutrient in plants. No unacceptable effects are to be expected after application of Final Bite according to the proposed GAP, which has a maximum soil PEC of 12.8 mg/kg, which will not add significantly to the background levels of iron. Hence, germination and growth is unlikely to be impacted. This is corroborated by the efficacy trials data (see Section 6 of this dossier) which indicate no phytotoxicity in cereals, oilseed rape, cabbage and lettuce treated with Final Bite®.

Overall, considering the predicted exposure is low compared to background levels, low observed phytotoxicity in field efficacy trials, and the high naturally occurring nature of the active substance, the risk to off-crop non-target terrestrial plants from the proposed uses of elemental iron is concluded to be acceptable.

### **2.9.7. Summary of effects on other terrestrial organisms (flora and fauna)**

Data with the formulation ‘Slug and snail killer’ has been provided for soil carbon transformation, acute fish toxicity, acute aquatic invertebrate toxicity and algal toxicity. However, in the case of soil carbon transformation this is no longer a data requirement and so the data is included for additional information only. The toxicity studies with aquatic organisms did not analyse for concentrations of the test item so cannot be considered reliable and are included for additional information only.

For further details of these studies please refer to Vol 3CP B9.

### **2.9.8. Summary of effects on biological methods for sewage treatment**

Iron is a naturally occurring element and the amount of iron added to the soil is several orders of magnitude smaller than the natural content commonly found in soils. UK Environmental Fate and Behaviour specialists estimate background levels 2000-50 000 mg Fe/kg soil, and the worst-case PECsoil(accumulation) from the requested GAP for elemental iron is estimated to be 12.8 mg a.s./kg soil. Therefore the amount of iron that sewage treatment plants are naturally exposed to will not be significantly increased by application of elemental iron according to the requested GAP. On this basis no data is required or requested and an acceptable risk to sewage treatment processes is concluded.

### **2.9.9. Summary of product exposure and risk assessment**

A safe use can be concluded for elemental iron, subject to the provision of confirmatory data monitoring the consumption of Final Bite granules by birds.

## **2.10. CLASSIFICATION AND LABELLING**

Elemental iron is not classified for effects on human health.

The relative insolubility of elemental iron means that the toxicity of this active substance to aquatic invertebrates and algae technically qualifies for the highest degree of acute classification, with acute mean measured endpoints equivalent to >0.5 mg a.s./L. However as discussed above, iron occurs

naturally in the aquatic environment but is not usually bioavailable to aquatic organisms, which is reflected in the results of the first tier aquatic studies available, with no effects being noted but a low mean measured endpoint being derived. Overall, the low solubility of this active substance means that it is mostly unavailable to aquatic organisms and so represents a low hazard. The data gap noted for reliable acute fish toxicity data can be waived for the purposes of classification for the same reason i.e. its insoluble nature means that it will largely be unavailable to fish. Overall, no environmental classification is proposed for Elemental iron.

Proposed classification according to Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures

<b>CLP Annex I ref</b>	<b>Hazard class</b>	<b>Proposed classification</b>	<b>Proposed SCLs and/or M-factors</b>	<b>Current classification <sup>1)</sup></b>	<b>Reason for no classification <sup>2)</sup></b>
2.1.	Explosives	None	Not relevant	None	
2.2.	Flammable gases	None	Not relevant	None	
2.3.	Flammable aerosols	None	Not relevant	None	
2.4.	Oxidising gases	None	Not relevant	None	
2.5.	Gases under pressure	None	Not relevant	None	
2.6.	Flammable liquids	None	Not relevant	None	
2.7.	Flammable solids	None	Not relevant	None	
2.8.	Self-reactive substances and mixtures	None	Not relevant	None	
2.9.	Pyrophoric liquids	None	Not relevant	None	
2.10.	Pyrophoric solids	None	Not relevant	None	
2.11.	Self-heating substances and mixtures	None	Not relevant	None	
2.12.	Substances and mixtures which in contact with water emit flammable gases	None	Not relevant	None	
2.13.	Oxidising liquids	None	Not relevant	None	
2.14.	Oxidising solids	None	Not relevant	None	
2.15.	Organic peroxides	None	Not relevant	None	
2.16.	Substance and mixtures corrosive to metals	None	Not relevant	None	
3.1.	Acute toxicity - oral	None	Not relevant	None	
	Acute toxicity - dermal	None	Not relevant	None	
	Acute toxicity - inhalation	None	Not relevant	None	Conclusive but not sufficient for classification
3.2.	Skin corrosion / irritation	None	Not relevant	None	
3.3.	Serious eye damage / eye irritation	None	Not relevant	None	



CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification <sup>1)</sup>	Reason for no classification <sup>2)</sup>
3.4.	Respiratory sensitisation	None	Not relevant	None	
3.4.	Skin sensitisation	None	Not relevant	None	
3.5.	Germ cell mutagenicity	None	Not relevant	None	
3.6.	Carcinogenicity	None	Not relevant	None	
3.7.	Reproductive toxicity	None	Not relevant	None	
3.8.	Specific target organ toxicity –single exposure	None	Not relevant	None	
3.9.	Specific target organ toxicity – repeated exposure	None	Not relevant	None	
3.10.	Aspiration hazard	None	Not relevant	None	
4.1.	Hazardous to the aquatic environment	None	Not relevant	None	
5.1.	Hazardous to the ozone layer				

<sup>1)</sup>Including specific concentration limits (SCLs) and M-factors

<sup>2)</sup>Data lacking, inconclusive, or conclusive but not sufficient for classification

**Labelling:**     Signal word:  
                       Hazard statements:  
                       Precautionary statements:

**Proposed notes assigned to an entry:**

Notes in accordance with CLP Regulation, Annex VI, Section 1.1.3

## **2.11. RELEVANCE OF METABOLITES IN GROUNDWATER**

Elemental iron is a metal and so cannot degrade to form metabolites. The predicted environmental concentrations of iron ( $\text{Fe}^0$ ) or its two oxidation states ( $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ ) in groundwater are not unusual compared to measured background concentrations of iron naturally present in groundwater (Section 2.8.6.2). Furthermore, drinking water treatment plants already use various processes to remove iron from abstracted water to ensure safe levels for human health. Therefore, the HSE considers it acceptable to not perform an assessment of the relevance of metabolites in groundwater.

## **2.12. CONSIDERATION OF ISOMERIC COMPOSITION IN THE RISK ASSESSMENT**

### **2.12.1. Identity and physical chemical properties**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a consideration of isometric composition is not required.

### **2.12.2. Methods of analysis**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a

consideration of isometric composition is not required.

#### **2.12.3. Mammalian toxicity**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a consideration of isometric composition is not required.

#### **2.12.4. Operator, Worker, Bystander and Resident exposure**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a consideration of isometric composition is not required.

#### **2.12.5. Residues and Consumer risk assessment**

Considering the role of iron as essential plant nutrients, the immobility of iron as well as its natural occurrence in soil, monitoring of residues originating from soil application of elemental iron is not necessary. Therefore, no residue definition is given. Relevant residues of elementary iron in food of plant and animal origin, in exceedance of natural background, are not expected to occur. Therefore, a consumer risk assessment is not considered necessary.

An application to list iron in Annex IV of Regulation (EC) No 396/2005, has been made with this submission.

#### **2.12.6. Environmental fate**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a consideration of isometric composition is not required.

#### **2.12.7. Ecotoxicology**

The active substance is an elemental metal and does not exist as a racemic mixture. Therefore, a consideration of isometric composition is not required.

### **2.13. RESIDUE DEFINITIONS**

#### **2.13.1. Definition of residues for exposure/risk assessment**

**Food of plant origin:** N/A

**Food of animal origin:** N/A

**Soil:** Elemental iron ( $\text{Fe}^0$ ), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )

**Groundwater:** Elemental iron ( $\text{Fe}^0$ ), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )

**Surface water:** Elemental iron ( $\text{Fe}^0$ ), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )

**Sediment:** Elemental iron ( $\text{Fe}^0$ ), ferrous iron ( $\text{Fe}^{2+}$ ), ferric iron ( $\text{Fe}^{3+}$ )

**Air:** N/A

**2.13.2. Definition of residues for monitoring**

**Food of plant origin:** N/A

**Food of animal origin:** N/A

**Soil:** N/A Elemental iron and its two oxidation states are naturally occurring compounds

**Groundwater:** N/A Elemental iron and its two oxidation states are naturally occurring compounds

**Surface water:** N/A Elemental iron and its two oxidation states are naturally occurring compounds

**Sediment:** N/A Elemental iron and its two oxidation states are naturally occurring compounds

**Air:** N/A Elemental iron and its two oxidation states are naturally occurring compounds

## **Level 3**

### **Elemental iron**

### 3. PROPOSED DECISION WITH RESPECT TO THE APPLICATION

#### 3.1. BACKGROUND TO THE PROPOSED DECISION

##### 3.1.1. Proposal on acceptability against the decision making criteria – Article 4 and annex II of regulation (EC) No 1107/2009

<b>3.1.1.1. Article 4</b>			
		Yes	No
i)	It is considered that Article 4 of Regulation (EC) No 1107/2009 is complied with. Specifically HSE considers that authorisation is expected to be possible for at least one plant protection product containing the active substance for at least one of the representative uses.	X	It is considered that Article 4 of Regulation (EC) No. 1107/2009 is <b>not now</b> complied with for elemental iron for use as a molluscicide on edible and non edible crops (protected and outdoors) and amenity vegetation (see Volume 1, Level 1, Table 1.4.1 for details of the representative uses considered).  <b>The UK does not consider that the risk to birds and mammals or earthworms for the representative product has been adequately addressed and no safe use can be concluded.</b>
<b>3.1.1.2. Submission of further information</b>			
		Yes	No
i)	It is considered that a complete dossier has been submitted		X
ii)	It is considered that in the absence of a full dossier the active substance may be approved even though certain information is still to be submitted because: (a) the data requirements have been amended or refined after the submission of the dossier; or (b) the information is considered to be confirmatory in nature, as required to increase confidence in the decision.	X	<b>Refer to Ecotoxicology section below for further details</b> <b>Additional confirmatory data is required to monitor the consumption of Final Bite granules by birds. See Section 3.1.4.9.</b>
<b>3.1.1.3. Restrictions on approval</b>			
		Yes	No
	It is considered that in line with Article 6 of Regulation (EC) No 1107/2009 approval should be subject to conditions and restrictions.	X	(a) the minimum degree of purity of the active substance;  Minimum purity 989 g/Kg

			<p><i>(b) the nature and maximum content of certain impurities;</i></p> <p>The following impurities identified in technical elemental iron are considered to be of toxicological or ecotoxicological relevance:</p> <p>Arsenic: Maximum 0.03 g/Kg  Mercury: Maximum 0.0001 g/Kg  Lead: Maximum 0.003 g/Kg  Cadmium: Maximum 0.001 g/Kg  Nickel: Maximum 0.2 g/Kg</p> <p><i>(c) restrictions arising from the evaluation of the information referred to in Article 8 of (EC) no. 1107/2009 taking account of the agricultural, plant health and environmental, including climatic, conditions in question;</i></p> <p>None</p> <p><i>(d) type of preparation;</i></p> <p>Not applicable</p> <p><i>(e) manner and conditions of application;</i></p> <p>Protective clothing (coveralls), protective gloves and face protection (faceshield) when handling the product.</p> <p><i>(f) submission of further confirmatory information to the Competent Authority, where new requirements are established during the evaluation process or as a result of new scientific and technical knowledge;</i></p> <p>Monitoring data to investigate whether birds consume 'Final Bite' granules under field conditions.</p>
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				<p><i>(g) designation of categories of users, such as professional and non-professional;</i></p> <p>Not applicable</p> <p><i>(h) designation of areas where the use of plant protection products, including soil treatment products, containing the active substance may not be authorised or where the use may be authorised under specific conditions;</i></p> <p>Not applicable</p> <p><i>(i) the need to impose risk mitigation measures and monitoring after use;</i></p> <p>Not applicable</p> <p><i>(j) any other particular conditions that result from the evaluation of information made available in the context of Regulation (EC) no. 1107/2009.</i></p> <p>Not applicable</p>
<b>3.1.1.4. Criteria for the approval of an active substance</b>				
<b>Dossier</b>				
		Yes	No	
	It is considered the dossier contains the information needed to establish, where relevant, Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD).	X		An ADI and AOEL have been established, with an ARfD not considered necessary .
	It is considered that the dossier contains the information necessary to carry out a risk assessment and for enforcement purposes (relevant for substances for which one or more representative uses	X		

	includes use on feed or food crops or leads indirectly to residues in food or feed). In particular it is considered that the dossier: (a) permits any residue of concern to be defined; (b) reliably predicts the residues in food and feed, including succeeding crops (c) reliably predicts, where relevant, the corresponding residue level reflecting the effects of processing and/or mixing; (d) permits a maximum residue level to be defined and to be determined by appropriate methods in general use for the commodity and, where appropriate, for products of animal origin where the commodity or parts of it is fed to animals; (e) permits, where relevant, concentration or dilution factors due to processing and/or mixing to be defined.			
	It is considered that the dossier submitted is sufficient to permit, where relevant, an estimate of the fate and distribution of the active substance in the environment, and its impact on non-target species.	X	X	This applies to all the representative uses/use scenarios/products
<b>Efficacy</b>				
		Yes	No	
	It is considered that it has been established for one or more representative uses that the plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use is sufficiently effective.	X		The information provided was sufficient to meet the efficacy requirements for approval of the active substance. The representative product demonstrated control of relevant slug species in a range of crops. At product authorisation it will be important that the rates and claims and resistance management are in line with and appropriate to their conditions.
<b>Relevance of metabolites</b>				
		Yes	No	
	It is considered that the documentation submitted is sufficient to permit the establishment of the toxicological, ecotoxicological or environmental relevance of metabolites.	X		
<b>Composition</b>				



	Yes	No	
It is considered that the specification defines the minimum degree of purity, the identity and maximum content of impurities and, where relevant, of isomers/diastereo-isomers and additives, and the content of impurities of toxicological, ecotoxicological or environmental concern within acceptable limits.	X		The specification includes the minimum purity of iron and the maximum content of 5 relevant impurities: cadmium, nickel, arsenic, lead and mercury.
It is considered that the specification is in compliance with the relevant Food and Agriculture Organisation specification, where such specification exists.			There is not currently an FAO specification for iron.
It is considered for reasons of protection of human or animal health or the environment, stricter specifications than that provided for by the FAO specification should be adopted			There is not currently an FAO specification for iron.
<b>Methods of analysis</b>			
	Yes	No	
It is considered that the methods of analysis of the active substance, safener or synergist as manufactured and of determination of impurities of toxicological, ecotoxicological or environmental concern or which are present in quantities greater than 1 g/kg in the active substance, safener or synergist as manufactured, have been validated and shown to be sufficiently specific, correctly calibrated, accurate and precise.	X		Sufficient information has been provided to support approval of the active substance.
It is considered that the methods of residue analysis for the active substance and relevant metabolites in plant, animal and environmental matrices and drinking water, as appropriate, shall have been validated and shown to be sufficiently sensitive with respect to the levels of concern.	X		Sufficient information has been provided to support the validity of methods for residue analysis where appropriate.
It is confirmed that the evaluation has been carried out in accordance with the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation (EC) no. 1107/2009.	X		
<b>Impact on human health</b>			
<b>Impact on human health - ADI, AOEL, ARfD</b>			
	Yes	No	
It is confirmed that (where relevant) an ADI, AOEL and ARfD can be established with an appropriate safety margin of at least	X		An ADI of 0.8 mg/kg bw/d as previously recommended by EFSA during the EU assessments of iron sulphate (FeSO <sub>4</sub> ; DAR UK 2008, EFSA

	100 taking into account the type and severity of effects and the vulnerability of specific groups of the population.			conclusion 2012), ferric phosphate (FePO <sub>4</sub> RAR, DE 2013, EFSA conclusion 2015) and ferric pyrophosphate (Fe <sub>4</sub> (P <sub>2</sub> O <sub>7</sub> ) <sub>3</sub> DAR PL, EFSA conclusion 2020) can be applied to elemental iron. No ARfD is required. A systemic AOEL can be derived on the same basis as rationale by which the ADI has been established.
<b>Impact on human health – proposed genotoxicity classification</b>				
		Yes	No	
	It is considered that, on the basis of assessment of higher tier genotoxicity testing carried out in accordance with the data requirements and other available data and information, including a review of the scientific literature, reviewed by the Authority, <b>the substance SHOULD BE classified or proposed for classification</b> , in accordance with the provisions of Regulation (EC) No 1272/2008, <b>as mutagen category 1A or 1B.</b>		X	See Section 2.6.4 A read-across from the more soluble forms of iron has been performed. The EU reviews for both iron sulphate and ferric phosphate conclude that on a range of <i>in vitro</i> and <i>in vivo</i> data, neither substance is considered mutagenic. The same conclusion applies to elemental iron
<b>Impact on human health – proposed carcinogenicity classification</b>				
		Yes	No	
i)	It is considered that, on the basis of assessment of the carcinogenicity testing carried out in accordance with the data requirements for the active substances, safener or synergist and other available data and information, including a review of the scientific literature, reviewed by the Authority, <b>the substance SHOULD BE classified or proposed for classification</b> , in accordance with the provisions of Regulation (EC) No 1272/2008, <b>as carcinogen category 1A or 1B.</b>		X	See Section 2.6.5.  There is no convincing evidence of either chronic toxicity or carcinogenicity from the long-term use of elemental iron in the literature review and epidemiological data provided by the applicant.
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default			Not applicable

	value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			
<b>Impact on human health – proposed reproductive toxicity classification</b>				
		Yes	No	
i)	It is considered that, on the basis of assessment of the reproductive toxicity testing carried out in accordance with the data requirements for the active substances, safeners or synergists and other available data and information, including a review of the scientific literature, reviewed by the Authority, <b>the substance SHOULD BE classified or proposed for classification</b> , in accordance with the provisions of Regulation (EC) No 1272/2008, <b>as toxic for reproduction category 1A or 1B.</b>		X	See Section 2.6.6  There is no evidence of reproductive or developmental toxicity in the applicant's literature review and based on the routine supplementation during pregnancy, HSE conclude that no hazard has been identified with regard to this endpoint.
ii)	Linked to above classification proposal. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			Not applicable
<b>Impact on human health – proposed endocrine disrupting properties classification</b>				
		Yes	No	
i)	It is considered that <b>the substance SHOULD BE classified or proposed for classification</b> in accordance with the provisions of Regulation (EC) No 1272/2008, <b>as carcinogenic category 2 and toxic for reproduction category 2 and on that basis shall be considered to have endocrine disrupting properties</b>		X	There is no evidence of carcinogenicity or reproductive toxicity as a result of this assessment. Additionally, this assessment finds Elemental Iron satisfies low risk criteria
ii)	It is considered that <b>the substance SHOULD BE classified or proposed for classification</b> in accordance with the provisions of Regulation (EC) No 1272/2008, <b>as toxic for reproduction category 2 and</b> in addition HSE considers the substance <b>has toxic</b>		X	This assessment finds no evidence of endocrine disrupting properties for Elemental Iron. This active substance also satisfies low risk criteria.

	<b>effects on the endocrine organs and on that basis shall be considered to have endocrine disrupting properties</b>			
iii)	Linked to either i) or ii) immediately above. It is considered that exposure of humans to the active substance, safener or synergist in a plant protection product, under realistic proposed conditions of use, is negligible, that is, the product is used in closed systems or in other conditions excluding contact with humans and where residues of the active substance, safener or synergist concerned on food and feed do not exceed the default value set in accordance with Article 18(1)(b) of Regulation (EC) No 396/2005.			Not applicable
<b>Fate and behaviour in the environment</b>				
<b>Persistent organic pollutant (POP)</b>				
		Yes	No	
	It is considered that the active substance <b>FULFILLS</b> the criteria of a persistent organic pollutant (POP) as laid out in Regulation (EC) no. 1107/2009 Annex II Section 3.7.1.		X	It is not necessary to assess elemental iron as an inorganic substance against criteria for classification as a POP.
<b>Persistent, bioaccumulative and toxic substance (PBT)</b>				
		Yes	No	
	It is considered that the active substance <b>FULFILLS</b> the criteria of a persistent, bioaccumulative and toxic (PBT) substance as laid out in Regulation (EC) no. 1107/2009 Annex II Section 3.7.2.		X	Consideration as a PBT substance is not required for inorganic substances such as elemental metals.
<b>Very persistent and very bioaccumulative substance (vPvB).</b>				
		Yes	No	
	It is considered that the active substance <b>FULFILLS</b> the criteria of a very persistent and very bioaccumulative substance (vPvB) as laid out in Regulation (EC) no. 1107/2009 Annex II Section 3.7.3.		X	Consideration as a vPvB substance is not required for inorganic substances such as elemental metals.



Ecotoxicology		Yes	No	
	It is considered that the risk assessment demonstrates risks to be acceptable in accordance with the criteria laid down in the uniform principles for evaluation and authorisation of plant protection products referred to in Article 29(6) under realistic proposed conditions of use of a plant protection product containing the active substance, safener or synergist. HSE is content that the assessment takes into account the severity of effects, the uncertainty of the data, and the number of organism groups which the active substance, safener or synergist is expected to affect adversely by the intended use.	X	X	<p>No safe use can be concluded. Please see Section 2. The main areas of concern are:</p> <p><b>General</b> Data sourced from available literature not drawn from literature review; therefore it is not certain if the data provided is representative of all of the available data for the toxicity of iron for non-target organisms.</p> <p>Unable to compare specification of iron used in toxicity studies with agreed specification in volume 4.</p> <p><b>Birds and Mammals</b> Insufficient evidence to conclude an acceptable risk from consuming pellets as food, grit or by consuming poisoned target organisms.</p> <p><b>Earthworms</b> Potential risk identified at first tier not resolved by higher tier data.</p> <p>A safe use has been identified, subject to confirmatory data for birds. It has been demonstrated that use of Final Bite granules will not result in unacceptable impacts to non-target organisms.</p>
	It is considered that, on the basis of the assessment of Community or internationally agreed test guidelines, the substance <b>HAS</b> endocrine disrupting properties that may cause adverse effects on non-target organisms.		X	Assessment finds no evidence of endocrine disrupting properties for elemental Iron.
	<p>Linked to the consideration of the endocrine properties immediately above.</p> <p>It is considered that the exposure of non-target organisms to the active substance in a plant protection product under realistic proposed conditions of use is negligible.</p>	X	X	<p>Exposure to non target organisms is possible for all proposed uses. This applies to all the representative uses/use scenarios/products</p>

	<p>It is considered that it is established following an appropriate risk assessment on the basis of Community or internationally agreed test guidelines, that the use under the proposed conditions of use of plant protection products containing this active substance, safener or synergist:</p> <ul style="list-style-type: none"> <li>— will result in a negligible exposure of honeybees, or</li> <li>— has no unacceptable acute or chronic effects on colony survival and development, taking into account effects on honeybee larvae and honeybee behaviour.</li> </ul>	X		<p>The active substance is intended for use as a granular bait, therefore bees will only be exposed by either dust drift or contaminated pollen. The product is not expected to generate any significant amounts of dust, but no risk assessment scheme is possible for this route of exposure in any case. The amount of iron added to the soil by use of the product according to the GAP is not significant compared to the general background levels of iron, therefore bees are not expected to be exposed to more than the usual amount of iron in pollen as a result of using the product.</p>
<b>Residue definition</b>				
		Yes	No	
	<p>It is considered that, where relevant, a residue definition can be established for the purposes of risk assessment and for enforcement purposes.</p>		X	<p>Residue definitions for risk assessment and monitoring are not considered necessary.</p> <p>Considering the role of iron as essential plant nutrients, the immobility of iron as well as its natural occurrence in soil, monitoring of residues originating from soil directed applications of elemental iron is not necessary. Relevant residues of elementary iron in food of plant and animal origin, in exceedance of natural background, are not expected to occur. Therefore, a consumer risk assessment is not considered necessary.</p> <p>See Level 2 for further details.</p>
<b>Fate and behaviour concerning groundwater</b>				
		Yes	No	
	<p>It is considered that it has been established for one or more representative uses, that consequently after application of the plant protection product consistent with realistic conditions on use, the predicted concentration of the active substance or of metabolites, degradation or reaction products in groundwater complies with the respective criteria of the uniform principles for</p>	X		<p>A groundwater exposure assessment was performed for the two oxidation states of elemental iron, Fe<sup>2+</sup> and Fe<sup>3+</sup> ions. Due to worst-case parameters selected for high solubility and mobility, the maximum 80<sup>th</sup> percentile PEC<sub>GW</sub> value for Fe<sup>2+</sup> ions was 567 µg/L. All PEC<sub>GW</sub> values for Fe<sup>2+</sup> ions were significantly greater than 100 µg/L for all application scenarios and timings. Although the PEC<sub>GW</sub> values for Fe<sup>2+</sup> ions greatly exceed the drinking water parametric value of 0.1 µg/L for</p>

	evaluation and authorisation of plant protection products referred to in Article 29(6) of Regulation (EC) no. 1107/2009.		<p>pesticides and in many cases exceed the drinking water standard for iron of 200 µg/L (Drinking Water Inspectorate, 2017), none are unusual compared to background levels of iron present in groundwater which can vary between &lt;10 and &gt;10,000 µg/L. DAR volume 3CA section B.8.2.3.1 describes the processes used by water treatment plants for removal of iron from abstracted water. These processes are adequate to remove any iron from groundwater resulting from the use of 'Final Bite ®', which will be minimal compared to background levels in the environment. The HSE considers it acceptable to not perform a full groundwater relevance assessment for elemental iron.</p> <p>The HSE notes that the FOCUS groundwater models are not suitable to accurately describe the environmental behaviour of metal compounds or ions. The <math>PEC_{GW}</math> values, assuming all iron is either in the ferric form (<math>Fe^{3+}</math>) or in the ferrous form (<math>Fe^{2+}</math>) provide a worst case risk envelope. Actual environmental exposure would be much lower than the <math>PEC_{GW}</math> values generated using the ferrous iron assumption but may be higher than those generated using the ferric iron assumption. <b>Therefore the <math>PEC_{GW}</math> values presented here should not be relied upon in the risk assessment and are for reference only.</b></p> <p>This applies to all the representative uses/use scenarios/products</p>
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**3.1.2. Proposal – Candidate for substitution**

Candidate for substitution			
		Yes	No
	It is considered that the active substance shall be approved as a candidate for substitution		X
		Not applicable	



## 3.1.3. Proposal – Low risk active substance

Low-risk active substances			
	Yes	No	
<p>It is considered that the active substance <b>shall be considered of low risk</b>.</p> <p>In particular it is considered that the substance <b>should NOT be classified or proposed for classification</b> in accordance with Regulation (EC) No 1272/2008 as at least one of the following:</p> <ul style="list-style-type: none"> <li>— carcinogenic,</li> <li>— mutagenic,</li> <li>— toxic to reproduction,</li> <li>— sensitising chemicals,</li> <li>— very toxic or toxic,</li> <li>— explosive,</li> <li>— corrosive.</li> </ul> <p>In addition it is considered that <b>the substance is NOT</b>:</p> <ul style="list-style-type: none"> <li>— persistent (half-life in soil more than 60 days),</li> <li>— has a bioconcentration factor higher than 100,</li> <li>— is deemed to be an endocrine disrupter, or</li> <li>— has neurotoxic or immunotoxic effects.</li> </ul>	X	<del>X</del>	<p>Please refer to Ecotoxicology section above and in Section 2. There are potential risks to the following groups that are not resolved with the data available:</p> <ul style="list-style-type: none"> <li>— Birds and mammals</li> <li>— Earthworms</li> </ul>

## 3.1.4. List of studies to be generated, still ongoing or available but not assessed

Data gap	Relevance in relation to representative use(s)	Study status		
		No confirmation that study available or on-going.	Study on-going and anticipated date of completion	Study available but not assessed
3.1.4.1. Identity of the active substance or formulation				
3.1.4.2. Physical and chemical properties of the active substance and physical, chemical and technical properties of the formulation				
Data must be provided showing satisfactory chemical and physical properties for the product and their retention after ambient storage for two years in the commercial packaging.	All uses		Study ongoing	Study available (Adama Ref: 000109319)
3.1.4.3. Data on uses and efficacy				
3.1.4.4. Data on handling, storage, transport, packaging and labelling				
3.1.4.5. Methods of analysis				
Additional data to support the validity of the analytical methods for the determination of	All uses		Study ongoing	Study available

<p>the relevant impurities in the formulation is required. The methods used for the determination of the relevant impurities (lead, mercury, arsenic, cadmium, nickel) in the technical material may be suitable for the determination of these impurities in the formulation. However, there may be interference from the additional components present in the formulation. Additionally, the methods will require validation to lower levels; the levels of relevant impurities which may be present in the formulation will be much lower than the specification limits in the technical material, given the content of active substance in the formulation (1 % w/w).</p> <p>To ensure the technical material in the formulation complies with the specification, an initial determination of the relevant impurities in the formulation is required, using a method validated to an appropriate level in accordance with SANCO 3030/99 rev. 5.</p>				<p>Method validation: Mercury, Lead and Arsenic (Ref: 000104199)</p>
<p>Additional validation data is required to support the validity of the analytical methods and specification limits proposed for the relevant impurities: mercury, cadmium and nickel.</p> <p>Mercury: As mercury is a relevant impurity, the analytical method for the determination of mercury in the technical material should be validated to a level at least 20% below the technical specification limit. Additional</p>	All uses		Study ongoing	<p>Studies available method validation:</p> <p>Nickel: (Ref: 000107174)</p> <p>Cadmium: (Ref: 000107176)</p> <p>Mercury: (Ref: 000104703)</p>

<p>method validation data (linearity) is required to support the proposed specification limit of max. 0.0001 g/kg.</p> <p>Cadmium and Nickel: Cadmium and Nickel have been identified as relevant impurities during the evaluation. As these are considered relevant impurities, the analytical method for the determination of their content in the technical material should be fully validated in accordance with SANCO/3030/99 rev. 5. Additional method validation data to support the validity of the ICP-OES method used to determine the content of cadmium and nickel in the technical material is required. It should be noted that the analytical method for the determination of these relevant impurities in the technical material should be validated to a level at least 20% below the technical specification limit. It should also be noted that for impurities included in the specification, the identity of the impurity must be confirmed in the technical material.</p>				
<b>3.1.4.6. Toxicology and metabolism</b>				
<b>3.1.4.7. Residue data</b>				
<b>3.1.4.8. Environmental fate and behaviour</b>				

3.1.4.9. <i>Ecotoxicology</i>				
<p>Additional information is required to confirm the outcome of the bird risk assessment. Monitoring data should be provided to further determine whether birds consume Final Bite pellets under field conditions. This requires observing consumption of granules by birds from a specified area where granules have been applied according to the proposed conditions of use.</p> <p>In light of the risk assessment conducted and since consumption of granules only needs to be monitored for a short time period, this study would not be expected to result in harm to wild vertebrates.</p>	All uses	X		

### 3.1.5. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) No 546/2011, and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

Area of the risk assessment that could not be finalised on the basis of the available data	Relevance in relation to representative use(s)
Risk to Terrestrial Vertebrates (birds and mammals) None	All uses
Risk to Earthworms	All uses

### 3.1.6. Critical areas of concern

An issue is listed as a critical area of concern:

(a) where the substance does not satisfy the criteria set out in points 3.6.3, 3.6.4, 3.6.5 or 3.8.2 of Annex II of Regulation (EC) No 1107/2009 and the applicant has not provided detailed evidence that the active substance is necessary to control a serious danger to plant health which cannot be contained by other available means including non-chemical methods, taking into account risk mitigation measures to ensure that exposure of humans and the environment is minimised, or

(b) where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles, as laid out in Commission Regulation (EU) 546/2011, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.



An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

Critical area of concern identified	Relevance in relation to representative use(s)
Risk to Terrestrial Vertebrates (birds and mammals) None	All uses
Risk to Earthworms	All uses

### 3.1.7. Overview table of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in 3.3.1, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

The material tested in the toxicological studies has been demonstrated to be representative of the technical specification.

Representative use		All edible and non edible crops
Operator risk	Risk identified	
	Assessment not finalised	
Worker risk	Risk identified	
	Assessment not finalised	
Bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	
Risk to wild non target terrestrial vertebrates	Risk identified	
	Assessment not finalised	
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	
	Assessment not finalised	
Risk to aquatic organisms	Risk identified	
	Assessment not finalised	
Groundwater exposure active substance	Legal parametric value breached	
	Assessment not finalised	
Groundwater exposure metabolites	Legal parametric value breached	
	Parametric value of 10µg/L <sup>(a)</sup> breached	
	Assessment not finalised	
Comments/Remarks		

The superscript numbers in this table relate to the numbered points indicated within chapter 3.1.5 and 3.1.6. Where there is no superscript number, see level 2 for more explanation.

(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

### 3.1.8. Area(s) where expert consultation is considered necessary

The Expert Committee on Pesticides (ECP) were consulted on the following parts of the assessment report:

Area(s) where expert consultation is considered necessary	Justification
Human Health	Read-across from soluble forms of iron salts to address the data requirements for elemental iron:

	<p>As discussed in the introduction to the DAR Volume 3 CA B6, some potential hazards (especially in relation to repeated dose toxicity at the port of entry) of elemental iron particles have been addressed by the submission of published literature on iron powders. However, for endpoints on which information on elemental iron was not available, the EU assessments of iron salts, iron sulphate (FeSO<sub>4</sub>; DAR UK 2008, EFSA conclusion 2012) and ferric phosphate (FePO<sub>4</sub> RAR, DE 2013, EFSA conclusion 2015) have been used to bridge to the toxicity potential of elemental iron. Iron sulphate and ferric phosphate are approved in the EU for use as pesticidal active substances.</p> <p>Can the ECP members provide advice as to whether or not the read-across for most endpoints from the data on the ferrous and ferric salts (soluble forms) of iron is appropriate to address the data requirements for elemental iron?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CA B6.</p>
Human Health	<p>Impurities in the technical specification:</p> <p>Relevant impurities have been discussed in the DAR Volume 4 (Section C.1.2.40). In addition to the impurities which were detected in the specification, a range of theoretical impurities were also identified by HSE. Of these, arsenic and nickel were not detected in the 5-batch analyses but are proposed to be included as toxicologically relevant impurities since both are hazardous via non-thresholded modes of action.</p> <p>Can the ECP members provide advice as to whether or not the inclusion of these impurities in the technical specification is appropriate?</p> <p>The opinion of the ECP was sought. The DAR Volume 4 was not added to following ECP advice on this.</p>
Human Health	<p>Derivation of AOEC reference value:</p> <p>In a published sub-acute inhalation study in rats described in the DAR Volume 3 CA B6 (B.6.3.3), effects on sensitive biomarkers of pulmonary toxicity were seen, including pulmonary inflammation, impaired particle clearance, deficits in macrophage function, particle-loaded macrophage aggregation at bifurcations of the lower respiratory tract, and adverse histopathology (hypertrophy and cellular proliferation). These findings were noted from 50 mg/m<sup>3</sup>. At 250 mg/m<sup>3</sup>, there was an increase in severity of several of the findings (notably in the grade and persistence of adverse histopathology and inflammation), accompanied by translocation of particulate matter to tracheobronchial lymph nodes. Hence in addition to overwhelming the normal clearance mechanisms (mucociliary escalator towards oral elimination via the GIT), it appears there is some potential for particle retention within the respiratory system following exposure to high load dust burdens of insoluble elemental iron. The LOAEC was established at 50 mg/m<sup>3</sup>, leading to a NOAEC at 5 mg/m<sup>3</sup>.</p> <p>In view of these data, can the ECP members provide advice as to whether or not an AOEC can be reliably established from this published study?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CA B6.</p>
Human Health	<p>Dermal absorption of elemental iron from the representative formulation 'Final Bite'</p> <p>The dermal absorption of the representative product is described in the DAR Volume 3 CP B6. Rigid adherence to the EFSA 2017 guidance on dermal absorption leads to the representative formulation being categorised as an in-use dilution (since the content of elemental iron is just 1% w/w in Final Bite, a ready-to-use bait 'RB' formulation), and results in a default dermal absorption of 70%. The applicant considers this to be excessively precautionary, likening the pellet formulation as being closer to a solid formulation concentrate rather than a dilute preparation. They also view the database supporting the EFSA 2017 guidance default values as being particularly lacking in</p>



	<p>examples of solid RB formulation-specific data. HSE presented an assessment of the physicochemical and physiological properties of elemental iron in the Volume 3 CP B6, highlighting the following points: the large dust-free particle size, the extremely poor solubility of iron and the tight homeostatic controls in place that mean passive penetration of the zerovalent or ionic forms of iron are not expected.</p> <p>Regarding the use of the 50% oral absorption value as a surrogate dermal absorption value, HSE rejected this option as sufficient information is available to indicate that the oral absorption of elemental iron is likely to be lower and systemic exposure to iron is actively controlled. HSE also notes that a value of 10% has been agreed in the EU for ferric and ferrous forms of iron.</p> <p>Can the ECP members provide advice as to whether or not a dermal absorption estimate of 10% is appropriate for elemental iron in Final Bite?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B6.</p>								
Fate and Behaviour in the Environment	<p>The standard environmental fate models used in the risk assessment are typically designed to assess organic compounds. As such, evaluating an elemental metal using these models is problematic. We have used conservative or default parameters in the absence of measured data. Are there any appropriate refinements that could be made?</p> <p>For example, the plant uptake factor was set to 0, however it is well documented that iron is an essential nutrient taken up by plants. The advice of the ECP is sought, should this worst-case value be retained in the absence of appropriate data or could a case be made for using 0.5?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B8.</p>								
Fate and Behaviour in the Environment	<p>The groundwater and drainflow assessments both take into consideration the total conversion of Fe0 to Fe2+ ions as a worst-case conservative approach. This represents an unlikely scenario of the pellets applied during extreme and prolonged flood events. Furthermore, in such a case, the naturally occurring iron present in the soil would reduce and become more mobile. The amount of iron applied via the pellets would be minimal compared to this.</p> <p>The advice of the ECP is sought on whether for the associated product assessment and for any future product assessments, could the PEC calculations for groundwater and drainflow be waived, or should this worst-case approach be maintained?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B8.</p>								
Ecotoxicology – Effects on Non-Target Species	<p>Terrestrial Vertebrates (birds and mammals):</p> <p>No toxicity test data with birds and iron, or the representative product (Final Bite), were provided. Surrogate endpoints were devised by the Applicant using the lowest amount of iron normally found in avian commercial diets. An acute toxicity study was submitted using a surrogate product (Slug and Snail Killer) but it was not possible to compare the iron used in this product with the agreed specification.</p> <p>Acute and long-term/reproductive toxicity data were available for mammals and iron but not the representative product.</p> <p>The toxicity data available are summarised in the table below.</p> <table><tr><th>Test species</th><th>Test substance</th><th>Time scale (test type)</th><th>Endpoint</th></tr><tr><td>Japanese Quail</td><td>Slug and Snail Killer (1 % iron)</td><td>Acute oral toxicity</td><td>LD50 = &gt;2000 mg product/kg bw (equivalent to &gt;19.6 mg a.s./kg bw)</td></tr></table>	Test species	Test substance	Time scale (test type)	Endpoint	Japanese Quail	Slug and Snail Killer (1 % iron)	Acute oral toxicity	LD50 = >2000 mg product/kg bw (equivalent to >19.6 mg a.s./kg bw)
Test species	Test substance	Time scale (test type)	Endpoint						
Japanese Quail	Slug and Snail Killer (1 % iron)	Acute oral toxicity	LD50 = >2000 mg product/kg bw (equivalent to >19.6 mg a.s./kg bw)						

		Acute oral toxicity, extrapolated**	<b>LD50 = 3776 mg product/kg bw (equivalent to 37 mg a.s./kg bw)</b>
n/a	n/a	Reproductive/long term toxicity	<b>NOAEL = 5 mg a.s./kg bw/d*</b>
Rat	Fe0 compared with FeII (carbonyl iron, ferrous sulphate)	Acute oral toxicity	<b>LD50 &gt; 50 g Fe/kg bw</b>
Rat	Carbonyl iron	Long-term (90 days)	NOAEL = 35 mg/kg of diet, equivalent to <b>3.2 mg Fe/kg bw/ day</b>
Rat	Carbonyl iron	Long-term (90 days)	NOAEL = 200 mg Fe /kg bw/day
n/a	n/a	Reproductive/long term toxicity	NOAEL = 24 mg Fe/kg bw/d*
n/a	n/a	Reproductive/long term toxicity	NOAEL = 4.5 mg Fe /kg bw/d*

\*calculated based on lowest concentration of iron in a commercial diet expressed in mg a.s./kg diet x 0.1 in line with EFSA guidance (2009).

\*\*In accordance with EFSA guidance (2009), Table 1, an extrapolation factor of 1.888 can be applied to this endpoint (10 animals, zero mortalities)

Numerous issues were highlighted regarding the data available. Firstly, the literature data was not drawn from the systematic literature review submitted in support of this application, so there is uncertainty that this represents the relevant available data regarding iron and toxicity to birds. Secondly, it is not possible to compare the iron used in literature data with the agreed specification, so it is not clear that they cover the risk from the levels of impurities outlined in the agreed specification. Thirdly, in the case of the surrogate long-term/reproductive endpoint for birds, no assessment of long-term/reproductive effects has been carried out, and there is uncertainty inherent in extrapolating toxicity data from domesticated species to wild birds. Data drawn from the literature indicates that iron storage disease can occur in birds that are not adapted to a high-iron diet (see page 16 of Volume 3CP B9, page 11-12 Volume 3CA B9).

These issues aside, a standard first tier risk assessment for granules was carried out by HSE with the data available according to EFSA Guidance for bird and mammal risk assessment (2009) , which indicates that the risk from granules is assessed using the following routes of exposure:

- Ingesting granules as a source of food
- Ingesting granules as grit (birds only)
- Birds may mistake granules for small seed
- Birds and mammals may ingest granules when they eat food contaminated with soil
- Birds and mammals may consume food contaminated with residues resulting from granular applications.

Of these five routes of exposure, a), b) and e) were not resolved at first tier.

A weight of evidence case was submitted to refine the risk assessment citing the following:

- Iron is an essential component of bird and mammal diets
- The blue colouring of the product will repel birds and mammals so it is unlikely to be eaten
- Granules will not be available to birds and mammals in sufficient numbers to cause adverse effects or for long periods of time.
- Consuming slugs and snails that have been poisoned by the representative product is very unlikely

	<p>The applicant cited numerous literature sources in support of this reasoned case, however as discussed above it is uncertain that the data provided represents the relevant data available regarding the toxicity of iron to birds and mammals. The applicant has provided more information on the sourcing of this data at Appendix A. That aside, the data provided was considered to not be sufficient to conclude an acceptable risk, as outlined below.</p> <p>The advice of the ECP is sought on the use by the Applicant of published data not taken from the 10-year systematic literature search.</p> <p><b>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B9.</b></p>
Ecotoxicology – Effects on Non-Target Species	<p>While iron is an essential component of bird and mammal diets, it is usually at a low concentration – for example, 240 mg iron/kg diet – while the representative product contains 10000 mg iron/kg. It has been found in birds that are not evolved to eat a diet rich in iron that iron storage disease can develop. In the long-term toxicity study with rats and iron, iron deposition was noted in all but the control treatment group (35 mg iron/kg diet). There is uncertainty in using data on the likely concentrations in feed as surrogate toxicity endpoints, especially noting that the concentrations are not relevant to predicted exposure concentrations and the need to extrapolate from commercial diets and domesticated birds to wild birds. Overall, this argument should be used with caution as it is reliant on there being low exposure and should not be the basis for the assumption of low risk.</p> <p>The argument that the blue colouring of the pellets will repel birds and mammals is based on very limited trials data which did not consider feeding pressure present in field conditions. Therefore, it cannot yet be concluded that birds and mammals will not use the granules as a source of food.</p> <p>No data have been submitted to support the assertion that the granules will not be available to birds and mammals for a long period of time. Furthermore, the risk assessment indicates that only a small number of pellets need to be consumed to exceed the acute and long-term/reproductive regulatory dose.</p> <p>The data submitted in support of the risk assessment from consuming poisoned slugs and snails was based on Corvids (Crows, Rooks etc) and no data were presented to show that these are the key focal species for this particular route of exposure. No data were submitted regarding other species of birds that may consume either slug or snails and as a result, there is insufficient evidence to conclude on the risk from this route of exposure</p> <p>The UK does not consider the risk to birds and mammals from outdoor use of the representative product to have been adequately addressed.</p> <p>The advice of the ECP is sought regarding HSE's approach to assessing the risk from the use of iron formulated as a slug pellet to birds and mammals, and in particular the application and interpretation of the EFSA (2009) guidance</p> <p><b>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B9.</b></p>
Ecotoxicology – Effects on Non-Target Species	<p>Non-target Arthropods other than bees (NTA):</p> <p>Three toxicity studies on soil-dwelling non-target arthropod species were submitted. The toxicity endpoints are summarised in the table below.</p> <p><b>Summary of endpoints for non-target arthropods</b></p>

Test species – Life stage	Test substance	Time scale (test type)	Endpoint (kg product/ha)	Endpoint (pellets/m <sup>2</sup> ) <sup>4</sup>	Data point Author, year
<i>Aleochara bilineata</i>	Final Bite - 0402206	75 days Laboratory test <sup>1)</sup>	Reproduction: ER <sub>50</sub> > 100 kg product/ha NOER = 100 kg product/ha (1210 g a.s./ha) <sup>3</sup>	Reproduction: ER <sub>50</sub> > 737 pellets/m <sup>2</sup> NOER = 737 pellets/m <sup>2</sup>	CP 10.3.2.2/01. [REDACTED] 2018
<i>Poecilus cupreus</i>	Final Bite - 0402206	14 days Laboratory test	Survival & feeding: L/ER <sub>50</sub> > 100 kg product/ha NOER = 100 kg product/ha (1210 g a.s./ha) <sup>3</sup>	Survival & feeding: L/ER <sub>50</sub> > 743 pellets m <sup>2</sup> NOER = 743 pellets m <sup>2</sup>	CP 10.3.2.2/02. [REDACTED] 2018
<i>Pardosa</i> sp.	Final Bite - 0402206	14 days Laboratory test <sup>2)</sup>	Survival & feeding: L/ER <sub>50</sub> > 96.7 kg product/ha NOER = 96.7 kg product/ha (1170.07 g a.s./ha) <sup>3</sup>	Survival & feeding: L/ER <sub>50</sub> > 722 pellets m <sup>2</sup> NOER = 722 pellets m <sup>2</sup>	CP 10.3.2.2/03. [REDACTED] 2018

1) Test item applied whole to the surface of the test area, rather than mixed in.  
2) Test specimens collected in late April and early May.  
3) Toxicity endpoint converted to active substance using tested weight for weight percentage content of the test item, i.e. 1.21 %.  
4) Toxicity endpoints calculated based on reported arena area and number of pellets applied to each test arena.

There are currently two pieces of guidance regarding how to assess the risk to non-target arthropods from a pellet formulation, ESCORT and SANCO. The two approaches and associated outcomes are outlined below.

The standard risk assessment scheme for non-target arthropods as proposed under ESCORT II guidance covers the off-field and in-field risk from use of the product. The representative product is formulated as a ready to use granular bait applied to the ground to reach the target species, therefore the potential exposure to standard foliar dwelling species is considered negligible and no data are required for *T. pyri* and *A. rhopalosiphi*.

The risk to the off-field environment is considered to be limited to dust drift. There is no guidance currently available to assess the risk from this route of exposure. There is also evidence that the risk of dust-drift exposure will be low - as shown in Volume 3CP 2.8.5/01, the representative product was found to be almost dust-free (optical dust factor 1.33). Overall, the off-field exposure is considered to be negligible, and as a result, the risk assessment focused on the in-field environment, and in particular soil-dwelling non-target arthropod species.

The risk assessment was based on the scheme outlined in ESCORT II guidance however it was amended in order to compare the requested application rate to the rate used in the studies in terms of pellets/m<sup>2</sup>. This more accurately reflects the conditions of the studies conducted. The risk assessment is based on the formulated product alone; the amount of iron already available to soil based non-target arthropods is not thought to be significantly increased by use of the product according to the GAP.

The toxicity data with the formulated product indicates no adverse effects at 722-743 pellets/m<sup>2</sup> which exceeds, with a large margin of safety, the maximum possible number of pellets per m<sup>2</sup> following 6 applications (360 pellets/m<sup>2</sup>). Therefore, the risk from the intact pellet is considered to be acceptable.

	<p>Another potential route of exposure is from ‘hotspots’ of the product in the immediate vicinity of the partially broken-down pellet. In the absence of data on the risk from broken-down pellets, this route of exposure remains uncertain.</p> <p>According to the SANCO terrestrial guidance document, the risk to non-target arthropods from granular products can be addressed by considering the risk assessment for soil macro-organisms (as represented by <i>F. candida</i> and <i>H. aculeifer</i>) as a first tier, with non-target arthropod data submitted as a second tier if concern is raised. The toxicity studies with ‘Final Bite’ and <i>F. candida</i> and <i>H. aculeifer</i> used pulverised product homogeneously mixed into the test substrate, which was considered to represent more realistically the broken-down product, albeit homogeneously distributed rather than concentrated in ‘hotspots’. This data indicated an acceptable risk at first tier, meaning that according to SANCO, the risk is acceptable and no further data or consideration is required. On this basis it is concluded that the risk to soil NTA is acceptable, based on extrapolation from the soil macro-invertebrate assessment.</p> <p>On the basis of the above, it is considered by HSE that the risk to NTA from the partially broken-down product will be acceptable, noting the uncertainty in this extrapolation from soil macro-organisms to soil-based NTAs.</p> <p>What is the ECP’s view regarding HSE’s interpretation of the available guidance regarding assessing the risk to non-target arthropods from the use of iron formulated as a slug pellet? In particular views on HSE’s interpretation on the inconsistencies in the available guidance and the need to consider the risk from whole and broken-down pellets as well as background levels of iron are requested?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B9.</p>
Ecotoxicology – Effects on Non-Target Species	<p>Earthworm Field Study:</p> <p>Based on first tier toxicity studies with the intact pellet, and the ground up pellet mixed homogeneously into the soil, potential risks were identified at first tier (TER &lt;5) for earthworms.</p> <p>To attempt to resolve this risk the applicant submitted a field study. The field study was conducted to ISO-11628-3 and was well reported. No statistically significant effects on earthworm abundance or biomass were observed in the ‘Final Bite’-treated plots. Statistically significant effects were observed in the case of the reference item (carbendazim spray), indicating sensitivity of the test design with regard to spray applications.</p> <p>HSE raised several uncertainties with this study which meant that it was not sufficiently representative of the proposed uses of Elemental Iron (in the formulation ‘Final Bite’). These uncertainties were discussed further following comments and a position paper from the applicant – please see Appendices B and C for full details.</p> <p>The uncertainties can be summarised as follows. The application of the test item took place during April-June (a relatively dry period of the year). The application timing is not in line with the majority of slug bait applications which will take place during the latter part of the year when it is wetter. As a result, key earthworm species which could be directly exposed to the test item were not abundant or active in sufficient numbers to indicate effects of the test item. In addition, the dry conditions may have reduced the amount of test item bioavailable to the earthworms. There was also uncertainty regarding the suitability of the reference item used in the test, which was applied as a spray. It is therefore not possible to determine if the test is optimised for testing effects of granular based formulations.</p>

	<p>Therefore, the first-tier risk to earthworms remains to be resolved; with the available data no safe use can be concluded for this group.</p> <p>The ECP has previously raised concerns regarding the use of earthworm field studies conducted to ISO 11628-3 and whilst HSE has noted these concerns, this guideline is routinely used to determine potential effects on earthworms under field conditions. For Iron, a study was conducted to this guideline and whilst it was conducted to a satisfactory standard, HSE has raised concerns regarding its representativeness in terms of weather conditions.</p> <p>The ECP's view is requested as to whether HSE's interpretation is scientifically valid; in particular whether the rainfall was representative of the proposed use, whether or not the spray reference item results can be used to indicate sensitivity to granular formulations, and hence whether the study was sufficiently robust?</p> <p>The opinion of the ECP was sought. Details of revision in-light of ECP advice can be found in the DAR Volume 3 CP B9.</p>
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### 3.2. PROPOSED DECISION

It is proposed that:

**Elemental iron can be approved as a low risk substance under the Retained Regulation (EC) No 1107/2009**

It is considered that it should be specified that conditions of use shall include risk mitigation measures, where appropriate.

The following impurities identified in technical elemental iron are considered to be of toxicological or ecotoxicological relevance:

Arsenic: Maximum 0.03 g/Kg

Mercury: Maximum 0.0001 g/Kg

Lead: Maximum 0.003 g/Kg

Cadmium: Maximum 0.001 g/Kg

Nickel: Maximum 0.2 g/Kg

#### **Further information to confirm the approval of the substance**

It is proposed that the competent authority concerned shall request the submission of confirmatory information:

- (a) where new data requirements are established during the evaluation process, or
- (b) as a result of new scientific and technical knowledge, or
- (c) to increase confidence in the decision.
  - 1) Monitoring data to investigate whether birds consume Final Bite granules under field conditions (see Level 3.1.4.9).

#### **Additional considerations**

##### **1. The GB Competent Authorities may request submission of information to support authorisation of a product, as regards:**

- 1) Data must be provided showing satisfactory chemical and physical properties for the product and their retention after ambient storage for two years in the commercial packaging (see Level 3.1.4.2).
- 2) Additional data to support the validity of the analytical methods for the determination of the relevant impurities in the formulation is required (see Level 3.1.4.5).
- 3) Additional validation data is required to support the validity of the analytical methods and specification limits proposed for the relevant impurities: mercury, cadmium and nickel (see Level 3.1.4.5).

##### **2. The GB Competent Authorities may request submission of information for the renewal of the active substance, as regards:**

None

### 3.3. RATIONALE FOR THE CONDITIONS AND RESTRICTIONS TO BE ASSOCIATED WITH THE APPROVAL OR AUTHORISATION(S), AS APPROPRIATE

#### 3.3.1 Particular conditions proposed to be taken into account to manage the risks identified

Proposed condition/risk mitigation measure	Relevance in relation to representative use(s)
<p>PPE requirement due to classification of product:</p> <ul style="list-style-type: none"> <li>Protective clothing (coveralls), protective gloves and face protection (faceshield) when handling the product.</li> </ul>	All proposed uses

### 3.4. APPENDICES

#### 3.4.1. Guidance documents used in this assessment

##### Identity, Physical chemical properties, method of analysis

- Specification: Guidance document on the assessment of the equivalence of technical materials of substances regulated under regulation (EC) No 1107/2009 – Working document, SANCO/10597/2003 – rev. 10.1 (13/7/12)
- Guidance Document For The Generation And Evaluation Of Data On The Physical, Chemical And Technical Properties Of Plant Protection Products Under Regulation (EC) No. 1107/2009 Of The EU Parliament And Council On Placing Plant Protection Products On The Market
- Technical Material and Preparations: Guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 – Working document, SANCO/3030/99 rev. 4 and rev. 5. (European Commission – Directorate General Health and Consumer Protection).
- Residues: Guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (part A, Section 4) and Annex III (part A, Section 5) of Directive 91/414 – Working Document, SANCO/3029/99 rev.4 (11/07/00). (European Commission – Directorate General Health and Consumer Protection).
- Guidance document on pesticide residue analytical methods, SANCO/825/00 rev. 8.1 (16/11/2010). (European Commission – Directorate General Health and Consumer Protection).



**Human health**

- EFSA guidance on the Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092)
- Specification: Guidance document on the assessment of the equivalence of technical materials of substances regulated under regulation (EC) No 1107/2009 – Working document, SANCO/10597/2003 – rev. 10.1 (13/7/12)
- ECHA document agreed upon at the Biocidal Products Committee (BPC)-31 on interpreting the definition of relevant impurities (June 2019)
- Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009 (EFSA/ECHA, 2018). EFSA Journal, Vol 16, Issue 6, June 2018, e05311
- EFSA2017, EFSA 2017a: EFSA guidance on dermal absorption 2017, e04873
- European Food Safety Authority (2014). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products, EFSA Journal 2014;12(10):3874.

**Residues**

- EFSA guidance on the Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA Journal 2011;9(2):2092)

**Environmental fate and behaviour**

- FOCUS (kinetics), 2014. Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. v1.1, 18 December 2014.
- FOCUS (groundwater), 2014. Generic Guidance for Tier 1 FOCUS Ground Water Assessments. v2.2, May 2014.
- FOCUS (surface water), 2015. Generic guidance for FOCUS surface water Scenarios. v1.4, May 2015.
- EFSA Guidance on tiered risk assessments for PPPs for aquatic organisms in edge of field surface waters – EFSA Journal 2013, 11 (7): 3290.
- ECHA (2017) guidance on Information Requirements and Chemical Safety Assessment – PBT/vPvB assessment (v 3.0)

**Ecotoxicology**

- Birds & Mammals:

EFSA (2009). Guidance document on risk assessment for birds and mammals. EFSA Journal 2009;7(12):1438

- Aquatic Organisms:  
EFSA (2013). Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290
- Bees/Soil organisms/Non-target plants:  
SANCO/10329/2002 (rev 2 final). Guidance document on terrestrial ecotoxicology under council directive 91/414/EEC.
- Non-target arthropods:  
ESCORT 2 (Candolfi *et al.*, 2001). Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods.
- Endocrine disruption:  
ECHA/EFSA/JRC guidance for the identification of endocrine disruptors in the context of Regulations (EU) 528/2012 and (EC) No 1107/2009 (EFSA Journal 2018;16(6):5311)

#### **Efficacy:**

- SANCO/10054/2013 (2013) Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products

### **3.5. REFERENCE LIST**

- WHO – Iron in drinking water, background document for development of WHO Guidelines for Drinking water Quality (2003)
- WHO - Evaluation of certain food additives and contaminants (27<sup>th</sup> report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696, 1983, and corrigenda
- WHO recommendations on antenatal care for a positive pregnancy outcome (WHO, 2016)
- EFSA conclusions : Iron sulphate (2012), ferric phosphate (2015), ferric pyrophosphate (2020)