HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

Gelet op artikel 69 en artikel 71, eerste lid, eerste lid Verordening (EG) Nr. 1107/2009 (hierna te noemen:Verordening 1107/2009) juncto artikel 39 Wet gewasbeschermingsmiddelen en biociden (hierna te noemen: Wgb);

Overwegende dat:

- *het College voor de toelating van gewasbeschermingsmiddelen en biociden (hierna te noemen: het College) op grond van artikel 4 Wet gewasbeschermingsmiddelen en biociden (hierna te noemenr: Wgb) is aangewezen als de bevoegde autoriteit voor Nederland als bedoeld in artikel 75 Verordening 1107/2009;*
- *artikel 39 Wgb het College de bevoegdheid geeft om het op de markt brengen of het gebruik van een toegelaten gewasbeschermingsmiddel tijdelijk te beperken of te verbieden, indien er duidelijke aanwijzingen bestaan dat het gewasbeschermingsmiddel een ernstig risico inhoudt voor de gezondheid van mens en dier of voor het milieu;*
- *gebleken is dat er aanwijzingen zijn dat het gebruik van gewasbeschermingsmiddelen, gebaseerd op de werkzame stof metam-natrium waarschijnlijk een ernstig risico inhoudt voor de gezondheid van de mens;*
- *dit bevestigd is doordat er zich in Nederland de afgelopen jaren een aantal incidenten met metam-natrium houdende gewasbeschermingsmiddelen hebben voorgedaan, waarbij er sterke aanwijzingen zijn dat bij omwonenden acute effecten zijn geweest, ondanks het feit dat volgens rapportage van de NVWA conform de wettelijke voorschriften zou zijn toegepast;*
- *het College naar aanleiding van bovenstaande op 28 mei 2014 heeft besloten, onder toepassing van artikel 39 Wgb en artikel 71 Verordening 1107/2009, de 3 betreffende gewasbeschermingsmiddelen te schorsen zonder hierbij een respijitperiode toe te kennen (bijlage I);*
- *de toelatinghouders van deze middelen na het nemen van dit besluit aanvullende gegevens hebben verstrekt waaruit blijkt dat de risico's voor omwonenden kunnen worden bestreden met mitigerende maatregelen;*
- *deze aanvullende gegevens uit oogpunt van proportionaliteit vragen om een wijziging van het op 28 mei jongstleden genomen besluit,*

BESLUIT HET COLLEGE als volgt

1. Wijziging noodmaatregel

Het College besluit om, onder toepassing van artikel 39 Wgb en artikel 71 Verordening (EG) 1107/2009, de schorsing, en derhalve het verbod op gebruik, van de gewasbeschermingsmiddelen:

- Monam (toelatingsnummer 6443 N)
- Monam Cleanstart (toelatingsnummer 6321 N)
- Nemasol (toelatingsnummer 9635 N)

op te heffen en te vervangen door de verplichting de volgende gebruiksvoorschriften na te leven:

- Er mag een maximale oppervlakte van 1 hectare behandeld worden, met minimaal 150 meter afstand tussen behandelde velden.
- Dek de behandelde grond direct na toepassing af met VIF (Virtually Impermeable Film) folie gedurende een periode van ten minste 14 dagen.
- Een bufferzone van ten minste 150 meter moet toegepast worden tussen de te behandelen velden en de kadastrale grens van woningen en overige verblijfsplaatsen waar mensen langere tijd verblijven, zoals scholen, winkels, bedrijven en kantoren.
- Het middel dient op ten minste 20 cm diepte ingebracht te worden.

Deze gebruiksvoorwaarden gelden aanvullend op de wettelijke gebruiksvoorschriften van de genoemde middelen en blijven verplicht totdat een communautaire maatregel als bedoeld in artikel 71, derde lid Verordening (EG) 1107/2009 is vastgesteld.

2. Geen respijtperiode

Aangezien dit besluit zijn grondslag vindt in artikel 71 Verordening (EG) 1107/2009, kan van het toekennen van een respijtperiode als bedoeld in artikel 46 van Verordening (EG) 1107/2009 geen sprake zijn. Een respijttermijn wordt derhalve niet toegekend.

3. Motivering

Metam-natrium is de werkzame stof van een aantal grondontsmettingsmiddelen en is een fumigant die werkt doordat het in de bodem wordt omzet in het gasvormige MITC. Er zijn in Nederland drie middelen toegelaten (een moedertoelating, met twee afgeleiden), die voornamelijk worden ingezet om nematoden (aaltjes) in de grond te bestrijden.

Sommige van deze nematodensoorten zijn in de EU als quarantaine-organismen aangemerkt, die op grond van Europese regelgeving door lidstaten bestreden moeten worden.

Uit de risicobeoordeling van de noodmaatregel van 28 mei 2014 blijkt (bijlage I) dat het gebruik van de onderhavige gewasbeschermingsmiddelen op basis van metam-natrium waarschijnlijk een ernstig risico inhoudt voor de gezondheid van de mens, aangezien bij gebruik volgens de huidige toelating de blootstelling zodanig is dat voor omwonenden concentraties te verwachten zijn die aanzienlijk boven de humane norm liggen. Bij een dergelijk gebruik wordt de vastgestelde veiligheidsnorm voor omwonenden en met name omwonende kinderen, zo blijkt uit de voor het stofdossier aangeleverde veldstudies, met een factor 10 overschreden.

Mede gezien de tekst van preambule nr. 8 van de Verordening 1107/2009 heeft het College dit als een potentieel ernstig risico als bedoeld in artikel 71 Verordening 1107/2009 gekwalificeerd. Daar een lidstaat voorlopige beschermende noodmaatregelen kan nemen indien het de Europese Commissie officieel in kennis stelt van de noodzaak daartoe, er (nog) geen noodmaatregel is genomen door de Commissie en er duidelijke aanwijzingen zijn dat de huidige toelatingsvoorschriften geen goede bescherming bieden voor kwetsbare groepen, zoals kinderen, heeft het College op 28 mei 2014 besloten tot een schorsing van de genoemde middelen. Dit besluit is tevens op 28 mei 2014 bekend gemaakt.

Na dit besluit hebben de toelatingshouders aanvullende gegevens aangeleverd. Aan de hand van deze nieuwe gegevens heeft het College opnieuw een risicobeoordeling uitgevoerd (bijlage II). Uit deze risicobeoordeling blijkt dat, op basis van de aangeleverde gegevens, maatregelen kunnen worden geïdentificeerd waarmee de risico's voor omwonenden kunnen worden bestreden. Zonder de geïdentificeerde maatregelen kunnen effecten zoals hierboven beschreven niet worden uitgesloten. Zowel de risicobeoordeling als deze resultaten zijn afgestemd met België de zonale Rapporterende Lidstaat met betrekking tot de genoemde middelen..

Daar noodmaatregelen op basis van artikel 71 Verordening 1107/2009 juncto 39 Wgb proportioneel dienen te zijn, wordt de bij besluit van 28 mei 2014 vastgestelde schorsing en het verbod op gebruik van de toelating van de genoemde middelen opgeheven. Deze schorsing wordt vervangen door de verplichting de gebruiksvoorschriften, zoals gesteld onder punt 1 van dit besluit, na te leven bij het gebruik van de genoemde middelen.

Degene wiens belang rechtstreeks bij dit besluit is betrokken kan gelet op artikel 4 van Bijlage 2 bij de Algemene wet bestuursrecht en artikel 7:1, eerste lid, van de Algemene wet bestuursrecht, binnen zes weken na de dag waarop dit besluit bekend is gemaakt een bezwaarschrift indienen bij: het College voor de toelating van gewasbeschermingsmiddelen en biociden (Ctgb), Postbus 217, 6700 AE WAGENINGEN. Het Ctgb heeft niet de mogelijkheid van het elektronisch indienen van een bezwaarschrift opengesteld.

Wageningen, 19 augustus 2014

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN,

ir. J.F. de Leeuw
Voorzitter

Bijlage I – Besluit 28 mei 2014

HET COLLEGE VOOR DE TOELATING VAN GEWASBESCHERMINGSMIDDELEN EN BIOCIDEN

Gelet op artikel 69 en artikel 71, eerste lid, eerste lid Verordening (EG) Nr. 1107/2009 juncto artikel 39 Wet gewasbeschermingsmiddelen en biociden (hierna te noemen: Wgb);

Overwegende dat:

- *het Ctgb (verder: het College) op grond van artikel 4 Wet gewasbeschermingsmiddelen en biociden (verder: Wgb) is aangewezen als de bevoegde autoriteit voor Nederland als bedoeld in artikel 75 Verordening (EG) 1107/2009*
- *artikel 39 Wgb het College de bevoegdheid geeft om het op de markt brengen of het gebruik van een toegelaten gewasbeschermingsmiddel tijdelijk te beperken of te verbieden, indien er duidelijke aanwijzingen bestaan dat het gewasbeschermingsmiddel een ernstig risico inhoudt voor de gezondheid van mens en dier of voor het milieu*
- *de noodzakelijke beperkingen voor de kortst mogelijke duur gesteld dienen te worden*
- *het College de toelatinghouders van de metam-natrium houdende gewasbeschermingsmiddelen:*
- Monam (toelatingsnummer 6443 N)
- Monam Cleanstart (toelatingsnummer 6321 N)
- Nemasol (toelatingsnummer 9635 N),

  heeft bericht dat het op grond van artikel 44 Verordening (EG) 1107/2009 aanleiding heeft gezien om de betreffende toelatingen opnieuw te bekijken omdat er sterke aanwijzingen bestaan dat niet langer wordt voldaan aan de toelatingseisen
- *het College de toelatinghouders de mogelijkheid heeft geboden om opmerkingen te formuleren of nadere gegevens te verstrekken in verband met het voornemen van het Ctgb om de toelatingen in te trekken of te wijzigen*

- *tevens gebleken is dat er aanwijzingen zijn dat het gebruik van gewasbeschermingsmiddelen, gebaseerd op de werkzame stof metam natrium waarschijnlijk een ernstig risico inhouden voor de gezondheid van de mens, die of milieu*
- *dit bevestigd is doordat er zich in Nederland de afgelopen jaren een aantal incidenten met metam-natrium houdende gewasbeschermingsmiddelen hebben voorgedaan, waarbij er sterke aanwijzingen zijn dat bij omwonenden acute effecten zijn geweest, ondanks het feit dat volgens rapportage van de NVWA conform de wettelijke voorschriften zou zijn toegepast*
- *de betreffende toelatinghouders bij het Ctgb geen melding hebben gedaan van informatie over mogelijke schadelijke of onaanvaardbare effecten als bedoeld in artikel 56 Gewasbeschermingsverordening*
- *de risico's op basis van de beschikbare gegevens niet voldoende kunnen worden bestreden met passende en adequate maatregelen om een veilig gebruik te kunnen garanderen en de toelatingsvoorschriften mitsdien geen goede bescherming garanderen*
- *het ministerie van Economische Zaken derhalve, mede namens College de Europese Commissie derhalve heeft verzocht om noodmaatregelen te nemen om het gebruik en/of de verkoop van de betrokken gewasbeschermingsmiddelen te beperken of te verbieden*
- *het Ctgb van mening is dat de bevoegdheid om in de lopende toelating in te grijpen op basis van artikel 44 Verordening (EG) 1107/2009, in dit geval onvoldoende soelaas biedt omdat op grond van het Ctgb ten dienste staande informatie duidelijk is geworden dat deze gewasbeschermingsmiddelen op korte termijn in Nederland toegepast gaan worden terwijl op basis van de beschikbare gegevens geen maatregelen kunnen worden bepaald die tot veilig gebruik zullen leiden,*

BESLUIT

1. Schorsing toelatingen en verbod gebruik

Het College besluit om, onder toepassing van artikel 39 Wgb en artikel 71 Verordening (EG) 1107/2009, de toelating van de gewasbeschermingsmiddelen

- Monam (toelatingsnummer 6443 N)
- Monam Cleanstart (toelatingsnummer 6321 N)
- Nemasol (toelatingsnummer 9635 N)

te schorsen, en het gebruik ervan derhalve tijdelijk te verbieden met ingang van inwerkingtreding van dit besluit. De schorsing en het verbod gelden totdat een communautaire maatregel als bedoeld in artikel 71, derde lid Verordening (EG) 1107/2009 is vastgesteld.

2. Geen respijtperiode

Aangezien dit besluit zijn grondslag vindt in artikel 71 Verordening (EG) 1107/2009, kan van het toekennen van een respijtperiode als bedoeld in artikel 46 van Verordening (EG) 1107/2009 geen sprake zijn. Een respijttermijn wordt derhalve niet toegekend.

2. Motivering

Metam-natrium is de werkzame stof van een aantal grondontsmettingsmiddelen. Metam-natrium is een fumigant die werkt doordat het in de bodem wordt omzet in de gasvormige vorm MITC. Er zijn in Nederland drie middelen toegelaten (een moedertoelating, met twee afgeleiden), die voornamelijk worden ingezet om nematoden (aaltjes) in de grond te bestrijden.

Sommige van deze nematodensoorten zijn in de EU als quarantaine-organismen aangemerkt, die op grond van Europese regelgeving door lidstaten bestreden moeten worden.

Zoals uit het onderstaande en bijlage I bij dit besluit blijkt, is het duidelijk dat het gebruik van de onderhavige gewasbeschermingsmiddelen op basis van metam-natrium waarschijnlijk een ernstig risico inhoudt voor de gezondheid van de mens, aangezien bij gebruik volgens de huidige toelating de blootstelling zodanig is dat voor omwonenden concentraties te verwachten zijn die aanzienlijk boven de humane norm liggen. De vastgestelde veiligheidsnorm wordt voor omwonenden en met name omwonende kinderen, zo blijkt uit de voor het stofdossier aangeleverde veldstudies, met een factor 10 overschreden.

De geleverde veldstudies geven een zeer wisselend beeld mbt de luchtconcentraties en in de belangrijkste studie, met de hoogste piekconcentratie is een veel lagere dosering gebruikt (300 l/ha) dan de maximaal toegelaten dosering (750 L/ha).

Het is derhalve niet uit te sluiten, dat in de praktijk omwonenden kunnen worden blootgesteld aan hogere luchtconcentraties dan waar de risicobeoordeling in bijlage I vanuit gaat. Dit sluit aan bij de acute oogklachten en ademhalingsproblemen van omwonenden; vanuit het stofdossier waren deze klachten niet te verwachten bij de gemeten luchtconcentraties. Bovendien blijkt uit eerdere incidenten in Nederland dat ook onder bijzondere omstandigheden, zoals windstil of mistig weer, de concentraties tot zodanige hoogte kunnen oplopen dat omwonenden acute oogklachten en ademhalingsproblemen rapporteren. Onder deze bijzondere omstandigheden kan kennelijk niet worden uitgesloten dat de concentratie MITC waar omwonenden mee in aanraking kunnen komen, de humane norm zodanig wordt overschreden dat er een geenszins als denkbeeldig te verwaarlozen mogelijkheid bestaat dat daadwerkelijk gezondheidsschade optreedt.

In de humane norm zit een veiligheidsfactor van 100. In de risicobeoordeling in bijlage I is een overschrijding van 10 berekend, zodat de afstand tot de veilige norm nog maar 10 is. Gezien de onzekerheden en variatie in de gemeten luchtconcentraties, en de in de praktijk veelal hogere doseringen, geeft deze factor 10 onvoldoende bescherming, met name aan gevoelige groepen zoals kinderen met luchtwegproblemen (astma etc).

Mede gezien de tekst van preambule nr. 8 van de Gewasbeschermingsverordening kwalificeert het Ctgb kwalificeert deze mogelijkheid als een potentieel ernstig risico als bedoeld in artikel 71 Gewasbeschermingsverordening.

Het College stelt daarnaast vast dat het bepaalde in artikel 71 Gewasbeschermingsverordening met zich meebrengt dat een lidstaat voorlopige beschermende noodmaatregelen kan nemen indien het de Europese Commissie officieel in kennis stelt van de noodzaak daartoe, er (nog) geen noodmaatregel is genomen door de Commissie en er duidelijke aanwijzingen zijn dat de toelatingsvoorschriften geen goede bescherming bieden voor kwetsbare groepen, zoals kinderen.

Uit het voorgaande komt tevens naar voren dat, waar er aanwijzingen zijn dat er een geenszins als denkbeeldig te verwaarlozen mogelijkheid bestaat dat zich onder praktijkomstandigheden daadwerkelijk risico's voor kinderen voor kunnen doen, een afweging tussen (enerzijds) het belang bij de mogelijkheid om de betreffende middelen te verkopen en te gebruiken en (anderzijds) het belang dat kinderen gevrijwaard worden van mogelijke schadelijke effecten op de gezondheid, het laatstgenoemde belang dient te prevaleren.

Wageningen, 28 mei 2014

HET COLLEGE VOOR DE TOELATING VAN
GEWASBESCHERMINGSMIDDELEN EN
BIOCIDEN,

ir. J.F. de Leeuw
voorzitter

Bijlage - Risicobeoordeling

Monam cleanstart voor omwonenden - bufferzone
ASPECT BEOORDELING GEWASBESCHERMING TOXICOLOGIE

Naar aanleiding van de signalen omtrent MITC is er een herbeoordeling uitgevoerd voor omwonenden. Voor de operator, omstander en werker is geen herbeoordeling gedaan.

1. Mammalian toxicology

List of Endpoints
Metam sodium is an existing active substance that is approved for inclusion in Annex I. The final List of Endpoints presented below is taken from the EFSA Scientific Report on Metam (2011); 9(9) 2334. Where relevant, some additional remarks/information are given in italics.

The representative formulated product for the evaluation was "Metam sodium 510 g/L", soluble concentrate (SL), registered under different trade names in Europe. Metam sodium acts as fumigant through rapid degradation to methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

Impact on Human and Animal Health
Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1) metam and MITC

Rate and extent of oral absorption ‡	85 % (based on urinary (50%) and expired air (35%) excretion within 48 h)
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	Slight potential for accumulation in thyroid
Rate and extent of excretion ‡	Rapid and extensive (app. 85 %) within 48 h, mainly via urine (50 %) within 24 h, 4 % via faeces, 35 % via expired air
Metabolism in animals ‡	Extensive degradation of metam into MITC which is further conjugated with GSH or decomposes into MIC, COS and CO_2. Another important metabolic pathway is formation of CS_2 which is related to acidic conditions of stomach
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites: Methylisothiocyanate (MITC) , methylisocyanate (MIC), COS, CS_2
Toxicologically relevant compounds ‡ (environment)	Methylisothiocyanate (MITC), methylisocyanate (MIC), COS, CS_2

Acute toxicity (Annex IIA, point 5.2) metam sodium

Rat LD_{50} oral ‡	896 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	**-**
Rat LC_{50} inhalation ‡	2.54 mg/L air /4h (whole body)	**R20**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	Non-irritant	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Acute toxicity (Annex IIA, point 5.2) MITC

Rat LD_{50} oral ‡	147 mg/kg bw	**R25**
Rat LD_{50} dermal ‡	1290 mg/kg bw	**R21**
Rat LC_{50} inhalation ‡	0.54 mg/L air /4h (whole body)	**R23** **R37**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	No study required	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Short term toxicity (Annex IIA, point 5.3) metam sodium

Target / critical effect ‡	Nasal cavity (rat), urinary bladder(mice), liver(dog)	
Relevant oral NOAEL ‡	1-year dog: 0.1 mg/kg bw/day 90-day rat: 0.5 mg/kg bw/day 90-day mice: 0.8 mg/kg bw/day	**R48/ 22**
Relevant dermal NOAEL ‡	21-day, rabbit: 31.2 mg/kg bw/day	
Relevant inhalation NOAEL ‡	90-day rat: 6.5 mg/m^3 corresponding to 1.75 mg/kg bw/d	

Short term toxicity (Annex IIA, point 5.3) MITC

Target / critical effect ‡	Nasal cavity (rat), liver (dog)	
Relevant oral NOAEL ‡	90-day, dog 0.04 mg/kg bw/day	
Relevant dermal NOAEL ‡	No data - not required	
Relevant inhalation NOAEL ‡	28-day rat : 5 mg/m^3 (1.35 mg/kg bw/d)	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Metam and MITC are unlikely to be genotoxic[1)]	

[1)] *Based on a negative Ames test, an equivocal HGPRT assay in CHO cells, one positive and one equivocal* in vitro *chromosomal aberration test in human lymphocytes, a negative UDS test in hepatocytes, a negative* in vivo *Micronucleus test in mice, and a negative* in vivo *chromosomal aberration test in Chinese hamsters.*

Long term toxicity and carcinogenicity (Annex IIA, point 5.5) metam sodium

Target/critical effect ‡	Nasal cavity (rat) urinary bladder (mice)	
Relevant NOAEL ‡	1.5 mg/kg bw/day; 2-year, rat 1.9 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	Angiosarcomas in mice	**R40**

Long term toxicity and carcinogenicity (Annex IIA, point 5.5) MITC

Target/critical effect ‡	Changes in some WBC parameters	
Relevant NOAEL ‡	0.44 mg/kg bw/day; 2-year, rat 3.3 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	MITC is unlikely to pose a risk to humans	

Reproductive toxicity (Annex IIA, point 5.6) metam sodium

Reproduction toxicity

Reproduction target / critical effect ‡	Decreased pup and litter weight at the parental toxic dose in the rat	
Relevant parental NOAEL ‡	0.03 mg/L (4 mg/kg bw/day)	
Relevant reproductive NOAEL ‡	>0.1 mg/L (12 mg/kg bw/day)	
Relevant offspring NOAEL ‡	0.03 mg/L(4 mg/kg bw/day)	

Developmental toxicity

Developmental target / critical effect ‡	Increased incidence of variations and retardations at maternally toxic dose in rats; decreased number live foetuses and increased incidence of dead implants at maternal toxic doses in rabbits	**R63**
Relevant maternal NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 5 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Reproductive toxicity (Annex IIA, point 5.6) MITC

Reproduction toxicity

Reproduction target / critical effect ‡	Reproduction parameters not significantly altered	
Relevant parental NOAEL ‡	0.7 mg/kg bw/day	

Relevant reproductive NOAEL ‡	>3.6 mg/kg bw/day	
Relevant offspring NOAEL ‡	>3.6 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Decreased fetal weight at maternal toxic doses in rabbits	
Relevant maternal NOAEL ‡	Rat: 3 mg/kg bw/day Rabbit: 3 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7) metam sodium

Acute neurotoxicity ‡	NOAEL> 1500 mg/kg bw	
Repeated neurotoxicity ‡	NOAEL = 14.7 mg/kg bw/d	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No studies performed
Studies performed on metabolites or impurities ‡	No further studies performed

Medical data ‡ (Annex IIA, point 5.9) metam sodium

No medical surveillance data for manufacturing plant personnel was found for metam sodium.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage study	100
ADI MITC	0.004 mg/kg bw/day	dog, 90-d drinking water study	100
AOEL ‡ metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage	100
AOEL MITC	0.004 mg/kg bw/day	dog, 90-d drinking water study	100
ARfD ‡ metam sodium	0.1 mg/kg bw	rat, overall developmental toxicity	100
ARfD MITC	0.03 mg/kg bw	rat, developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	Concentrate: 1%; 12%: for the dilution ‡ Rat in vivo and comparative in vitro (human/rat skin)

‡ Endpoint identified by the EU-Commission as relevant for Member States when applying the Uniform Principles.

Local effects

Metam sodium produces local effects after single exposure (corrosive for skin). For the operator these local effects are covered in the risk assessment/management by means of assignment of R-and S-phrases. Furthermore, irritant dermatitis is reported among workers cleaning up a spill of metam sodium in California in 1991 and persistent respiratory health effects occurred after a metam sodium spill in California in 1994 (see DAR section 6.9.3). MITC also produces local effects (irritation of upper airways) after single and repeated exposure. For bystanders/resident no personal protective equipment can be assigned to cover the local effects. This has therefore, been taken into account in the risk assessment.

Data requirements active substance
No additional data requirements are identified.

1.1 Toxicity of the formulated product (IIIA 7.1)

Metam sodium is only available as an aqueous solution containing about 510 g/L a.i. and the product is equivalent to the technical active substance as manufactured. Therefore, all acute toxicity studies were conducted with aqueous metam sodium (or potassium) solutions as manufactured and are described in Annex II, point B.6.2 (DAR, section 6.14).

It was agreed that for operators applying metam sodium, the relevant assessment is for MITC (EFSA Scientific Report on Metam (2011); 9(9) 2334). Also for workers, bystanders and residents, the relevant assessment is considered to be for MITC.

Acute toxicity (Annex IIA, point 5.2) metam sodium

Rat LD_{50} oral ‡	896 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	**-**
Rat LC_{50} inhalation ‡	2.54 mg/L air /4h (whole body)	**R20**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	Non-irritant	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Acute toxicity (Annex IIA, point 5.2) MITC

Rat LD_{50} oral ‡	147 mg/kg bw	**R25**
Rat LD_{50} dermal ‡	1290 mg/kg bw	**R21**
Rat LC_{50} inhalation ‡	0.54 mg/L air /4h (whole body)	**R23** **R37**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	No study required	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

1.1.1 Data requirements formulated product

No additional data requirements are identified.

1.2 Dermal absorption (IIIA 7.3)

See List of Endpoints. The formulation Monam Cleanstart is identical to the tested formulation. For the risk assessment, dermal absorption values of 1% for the concentrate.

1.3 Available toxicological data relating to non-active substances (IIIA 7.4)

See 4.1. Metam sodium is only available as an aqueous solution containing about 510 g/L a.i. and the product is equivalent to the technical active substance as manufactured.

1.4 Exposure/risk assessments

Overview of the intended uses
Monam Cleanstart is a SC (suspension concentrate) formulation and contains 510 g/L metam sodium. Application of Metam sodium is carried out by a soil-injection technique using tractor-mounted equipment. The intended uses are listed under Appendix 1 (GAP).

1.4.1 Operator exposure/risk

Calculation of the EU-AOEL / Tolerable Limit Value (TLV)
For metam sodium no TLV has been set. The AOEL will be used for the risk assessment.Since the formulation is applied up to two times during the period July - October, a semi-chronic exposure duration is applicable for the operator (including contract workers). A semi-chronic AOEL is therefore derived. The semi-chronic EU-AOEL of MITC is 0.004 mg/kg bw/day (= 0.28 mg/day for a 70 kg operator), based on the NOAEL of 0.4 mg/kg bw/day in a 90-d drinking water study with dogs and a safety factor of 100 is used for the risk assessment (see List of Endpoints).

Because metam sodium is almost instantly hydrolysed to MITC, it was agreed in the PRAPeR meeting of experts 54 (subgroup1) held in Parma in July 2008 that the operator, worker and bystander risk assessment should be performed for MITC (EFSA Scientific Report on Metam (2011); 9(9): 2334).

Exposure measurements / estimations
No appropriate exposure models are available to calculate exposure during mixing, loading and application to the volatile MITC that is formed rapidly after application of Monam Cleanstart when metam sodium enters into contact with soil, as is also confirmed by the DAR (section B.6.15.1).

Mixing
Since the formulation Monam Cleanstart is used without dilution, exposure during mixing will not occur since no mixing is necessary.

Loading
In the Dutch operating instructions, the following directions for use are prescribed:
"Wear suitable dermal protective clothing, gloves with long shafts and rubber boots during all activities during which skin contact with the formulation may occur, including the soil disinfection and the first cultivation activities after application of the formulation. Take off all contaminated clothing. Immediately rinse off gloves and boots that may have been in contact with the formulation with plenty of water. Store gloves outside the cabin. Wear a full face mask with B2-P3 filter, ideally with proflow blower, during the preparation of the equipment, during trouble shooting and the internal cleaning of the equipment."

Because of the loading procedure can be considered as 'closed system' and full personal protective equipment should be used, the exposure during loading is considered negligible.

Application
In the updated DAR Re-submission of May 2011, 4 exposure studies were included in which metam sodium was applied by soil injection (2 studies), soil fumigation (1 study) or drip-irrigation (1 study). The soil injection and fumigation applications were open field studies, while the drip-irrigation study was a greenhouse/tunnel study.

For Monam Cleanstart, the open field soil injection studies were the relevant studies. A brief summary of the studies is included:

Study 1: Mulder et al. 1994
Metam-sodium (510 g/L) was applied onto 15 different parcels at 12 different field locations in the Netherlands during soil decontamination of industrial potato land. Tractor-drawn equipment was used with 12 parcels treated with spade injector and 3 parcels treated with cultivator injection equipment, respectively. In order to avoid exposure during turning at the headlands all injection equipments used were fitted with an anti-drip systems, i.e. anti-drip caps or blow-through system. Irrespective of the injection equipment used all tractors were fitted with one to two flat driven rollers for sealing of the soil. Application rate of Monam was 300 L/ha.
The MITC exposure study performed after soil injection application of Metam-sodium under representative field conditions demonstrated that in some situations there was exceeding of the inhalation AOEL of MITC. Appropriate respiratory protection is recommended for the operator during the whole process.

Note Ctgb: *no bystander/resident exposure was measured.*

Study 2: De Rooij et al. 1993
Metam-sodium (BASF monam, Aamonam, Shell-NMC and Luxan monam (Metam-sodium 510 g/L) was applied for soil decontamination purposes onto 11 representative bulb parcels at an application rate ranging from 420 L/ha to 700 L/ha. All parcels were treated using specialized equipment, i.e. cultivator injectors that inject Metam-sodium into the soil at a depth of about 18 – 20 cm. Immediately after injection, one or two flat rollers one of which was a driven roller to ensure that the soil was well compressed and sealed compressed the soil. In all cases, the injection activities started on the downwind side of the parcel thereby reducing additional exposure because of emission of MITC form parcels that were already treated. The MITC exposure studies demonstrated that after soil injection application of Metam-sodium on eleven representative fields under representative conditions the AOEL of MITC was

exceeded in most of the field parcels treated when RPE was absent. Overall, it can be concluded that under these experimental conditions, operator exposure to MITC is below AOEL only with special protective equipment.

Note CTGB: *No bystander/resident exposure was measured.*

Study 3: Links et al. 2006
In this study, metam sodium was applied at 300L/ha with a tractor mounted Rumptstad shear injector to approximately 5 Ha (application rate according to label 300L/Ha). The machine featured a working width of 3 m. Metam sodium was loaded in the tank (capacity 500 L) that was located at the front of the tractor. Via a flexible pressure tubing metam sodium was transported under pressure to the spray valves below the plough. The Rumptstad injected metam sodium in the soil at a depth of 15-20 cm, and worked the soil with a roto-tiller. After injection the soil was flattened with a roller that was part of the application equipment. Besides operator exposure, the degradation products of metam sodium were determined after application in a field at different locations, from the edge of the field (location 1-8) to a maximum distance of 225 meters (location 9-16).

Findings: MIC, CS_2 and methylamine were not detected around the treated field; all values were below the limit of detection.

Potential exposure of the operator to MITC was 76.51µg/m^3 which represents 0.00956 mg/kg bw/d. The stationary air measurement inside the tractor during these tasks was 70.33µg/m^3 which is equivalent to 0.00879 mg/kg bw/d and outside the tractor the concentration MITC were 0.107 mg/m^3 representing 0.0134 mg/kg bw/d.

Air concentrations of MITC around the field ranged from the limit of detection (0.042 µg/m^3) to a maximum value of 35.97 µg/m^3 with a geometric mean of 0.87 µg/m^3 (GM calculated with 100% LOD for concentrations <LOD, n=96). The 95th percentile was 13.22 µg/m^3 and the 75th percentile 6.41 µg/m^3. No direct relation could be found between the time expired after application (with a maximum of 3 days) and the MITC air concentrations at the different locations, although the first measurements over 4 hours was at almost every location the highest. Wind direction, on the other hand, seems to be important with the highest concentrations occurring downwind.

Substance	**Experimental conditions**	**MITC Concentration (µg/m^3)**
Location 1: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 2: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 3: 10 samples	Field boundary, downwind	4.47 – 23.71
Location 4: 10 samples	Field boundary, downwind, measure during whole study duration	0.07-1.82
Location 5	Field boundary, downwind	Pump defect, no valid measurement.
Location 6: 10 samples	Field boundary, downwind, measure during whole study duration	4.77-24.35
Location 7: 10 samples	Field boundary, downwind, measure during whole study duration	4.21-13.31
Location 8: 10 samples	Field boundary, measure during whole study duration	0.042-6.85
Location 9: 2 samples	100 m of field, upwind	0.08
Location 10: 1 sample	100 m of field, upwind	0.09
Location 11: 1 sample	100 m of field, upwind	0.04
Location 12: 9 samples	100 m of field, downwind, measure during whole study duration	0.66-3.62

Substance	Experimental conditions	MITC Concentration (µg/m³)
Location 13: 10 samples	100 m of field, downwind, measure during whole study duration	2.10-13.19
Location 14 : 10 samples	100 m of field, downwind, measure during whole study duration	0.042-35.96
Location 15: 1 sample	200 m of field, upwind	0.1
Location 16: 1 sample	200 m of field, upwind	0.09
Geometric mean		**0.87**
Minimum – maximum:		**0.042 -35.97**

De metingen t.b.v. de operator blootstelling vonden plaats op het raam en boven een wiel van een trekker; de hoogte waarop gemeten is voor de bystanders (langs het veld), is echter niet gespecificeerd in de samenvatting in de DAR. De meting duur om het veld is 4 dagen lang (voor operator 3 dagen). Er is veel variatie in wanneer er pieken van MITC gemeten worden. Toch wordt wel gemeld dat het meeste gemeten wordt de eerste 4 uur na toepassing.

Note CTGB: *The dose used in the study 300 L/ha is below the intended use 750 L/ha.*
No specific resident exposure is calculated in the DAR. Therefore, a resident exposure assessment is carried out using the "bystander" exposure values from the study in the DAR. These values are also representative for residents as they were taken either directly besides or further from the field.

Table 1: Resident exposure estimate to MITC after application of Monam Cleanstart based on the results from the study Link et al. 2006

	Exposure level	***Peak value***	***GM***	***75th***	***95th***
Adult					
Maximum value	***air level (µg/m³) [1]***	*35.97*	*0.87*	*6.41*	*13.22*
	exposure (µg/kg bw/d) [2]	*8.27*	*0.2001*	*1.4743*	*3.0406*
	% [3] AOEL	***207***	***5.0***	***36.9***	***76.0***
Child					
Maximum value	***air level (µg/m³) [1]***	*35.97*	0.87	6.41	13.22
	exposure (µg/kg bw/d) [4]	*38.49*	0.9309	6.8587	14.15
	% [3] AOEL	***962***	***23.3***	***171***	***354***

[1]: maximum air concentration; [2] : taking into account a respiration rate of 0.23 m³/day/kg, and a 24 h breathing period, default b.w.=60 kg, in the absence of RPE. [3]: AOEL (MITC) =0.004 mg/kg b.w./d
[4] : taking into account a respiration rate of 1.07 m³/day/kg, and a 24 h breathing period, default b.w.=10 kg (default in EFSA OPEX calculator), in the absence of RPE.

Only with the use of the geometric mean does the resident exposure not exceed the AOEL. However, the acceptability of the GM can be questioned since this represent the mean of both the downwind and upwind situation. A 75th percentile is considered to be more appropriate. It is worth noting that the acute reference dose of 30 µg/kg bw/d for MITC is exceeded for children when using the peak exposure value.

Based on the assessment, it can be concluded that adverse health effects cannot be excluded for residents living near fields treated with Monam Cleanstart.
In the study an application rate of 300 L/ha was used, while the current application rate for Monam cleanstart is 750 L/ha, a factor of 2.5 higher. It can therefore be expected that the actual exposure level are higher than those measured in this study.

Study 4: Saeed et al. 2000
This study was conducted in four fallow fields intended to be grown with potatoes. Methyl isothiocyanate air concentrations were measured above these fields following application of metam-sodium (345 g a.i/kg) either through injection using a ground rig (fields 1 and 2) or by chemigation using the center-pivot irrigation systems (fields 3 and 4). Both methods are used commercially in Wisconsin for the application of the fumigant and are claimed to be equally effective. Solutions of metam-sodium (345g a.i. /kg) were injected in the soil at a rate of 480litre/ha (166 kg/ ha) in fields one and two using a ground applicator

with knives or shanks spaced 15cm apart. The knives were pulled through the soil at a depth of 25cm and the fumigant was released from ports behind each shank at depths of 5, 15 and 25cm. A soil compactor was connected to each rig to compact the soil over the furrow made by the injection shanks. In fields three and four the fumigant solution at a rate of 480 liter/ha was mixed with 169m^3/ha of irrigation water through a metering pump that was connected to the center-pivot irrigation system. Immediately following fumigant application to each of the four fields, equipment for measuring MITC air concentration, temperature and wind speed was installed and measurements were started. The focus of this study was to estimate the loss of MITC by volatilization when metam-sodium was applied through either chemigation or injection to arable fields. Methyl isothiocyanate is the principal product of the transformation and constitutes about 90% of the total amount of metam-sodium applied to soils.

On most sampling occasions, higher MITC emissions were observed in chemigated than in injected fields. The highest MITC concentrations were 11.2 and 7.4µg/m^3 recorded 10cm above the ground 6-8h following application and the lowest concentrations were 0.7 and 0.2 µg/m^3 observed at 200cm 30 and 35h after application above chemigated and fumigated fields, respectively. Volatilization losses measured by trapping vaporized MITC indicated that in all treated fields, regardless of application method, average MITC air concentrations were highest in the first 8h following application and decreased thereafter. It was found that use of a soil compactor following fumigant injection into the soil had a substantial effect in reducing MITC emissions (Saeed and Rouse, unpublished data). Thus, manipulation of soil surface to reduce MITC loss by volatilization could serve as an approach to environmentally acceptable disease control practices.

Field/time after application (h)	**MITC air concentration (µg/m^3)**		
	200 cm	**100 cm**	**10cm**
Injected field 1: 166 kg/ha (480L)			
5.3	1.1	1.2	1.3
11.4	1.3	1.4	1.6
29.4	0.9	1.0	1.1
78	0.7	0.8	0.9
Mean:	1.0	1.1	1.22
Injected field 2: 166 kg/ha (480L)			
4	0.4	0.9	7.0
6	0.9	1.3	7.4
11	0.4	0.5	5.9
27.5	0.3	1.0	1.0
29.5	0.5	1.6	1.6
34.5	0.2	0.4	0.4
Mean:	0.45	0.95	3.88
Chemigated field 3: 166 kg/ha (480L) diluted in 169m^3 water/ha			
3	1.6	2.0	3.5
6	0.9	1.3	2.8
8.4	2.0	3.0	11.2
10	1.2	1.3	4.0
14	0.7	0.8	1.7
Mean:	1.28	1.7	4.64
Chemigated field 4: 166 kg/ha (480L) diluted in 169m^3 water/ha			
6.3	4.6	5.9	7.1
10.3	1.2	2.1	3.2
14.3	2.9	2.9	4.8
18.3	4.6	6.4	6.5
22.3	2.0	2.3	2.8
26.3	1.4	1.7	1.8
30.3	0.7	0.8	1.3
Mean:	2.5	3.15	3.9

The mean exposure was the highest at 10 cm ranging between 1.22 to 4.64 µg/m^3. The highest peak exposure was measured also measured at 10 cm above ground with 11.2 µg/m^3.

Note CTGB: *Residential exposure is calculated using the exposure levels shown in the table above. Separate exposure estimates are made for the injected fields and het chemigated field. To estimate the exposure for children the air concentration at both 10cm and 100 cm is used. For adults only the 100 cm air concentration is used.*

Table 2: Resident exposure estimate to MITC after application of Monam Cleanstart based on the results from the study Saeed et al. 2000

	Exposure level	***Peak value***	***Mean***	***Peak value***	***Mean***
		Injected field		***Chemigated field***	
Adult (100 cm air concentration)					
Maximum value	***air level (µg/m³) [1]***	*1.6*	*1.1*	*6.4*	*3.15*
	exposure (µg/kg bw/d) [2]	*0.368*	*0.253*	*1.472*	*0.7245*
	% [3] AOEL	***9.2***	***6.325***	***36.8***	***18.1***
Child (100 cm air concentration)					
Maximum value	***air level (µg/m³) [1]***	*1.6*	*1.1*	*6.4*	*3.15*
	exposure (µg/kg bw/d) [4]	*1.712*	*1.177*	*6.848*	*3.3705*
	% [3] AOEL	***42.8***	***29.4***	***171***	***84.3***
Child (10 cm air concentration)					
Maximum value	***air level (µg/m³) [1]***	*7.4*	*3.88*	*11.2*	*4.64*
	exposure (µg/kg bw/d) [4]	*7.918*	*4.1516*	*11.984*	*4.9648*
	% [3] AOEL	***198***	***104***	***300***	***124***

[1]: maximum air concentration;
[2] : taking into account a respiration rate of 0.23 m^3/day/kg, and a 24 h breathing period, default b.w.=60 kg, in the absence of RPE.
[3]: AOEL (MITC) =0.004 mg/kg b.w./d
[4] : taking into account a respiration rate of 1.07 m^3/day/kg , and a 24 h breathing period, default b.w.=10 kg (default in EFSA OPEX calculator), in the absence of RPE.

The estimated resident exposure is exceeded for children for both application methods. Therefore, adverse health effects cannot be excluded for residents living near fields treated with Monam Cleanstart.

It is noted that the application rate used in the study (480 L/ha) is below the current application rate of Monam Cleanstart (700 L/ha) so actual exposure level are expected to be even higher.

Study 5: Van den Berg, F. 1993

Behaviour of Metam sodium and MITC in soil as well as the emission of MITC in the air was described by a computer simulation model and results compared with measured figures after soil injection application of Metam sodium into the soil of two selected fields in the Netherlands (field A near Valtermond and field B near Eeserveen).

For both fields, Metam sodium was applied at an application rate of 300 L/ha (510 g Metam sodium/L) and injected at a depth of approx. 18 cm using a horizontal blade injector with spray nozzles below the blades and subsequent compression of the soil with a roller. The treated area comprised 5.9 ha for both fields.

Both the computed as well as the measured MITC concentrations in the air demonstrated that a bystander walking at the downwind side of a fumigated field (distance 0 – 214 m) approx. 1 to 9 days after treatment is exposed to MITC concentrations amounts to 14 µg/m^3. The measurements were taken at 1.5 meters above ground. The study lasted 7-9 days, with a total of 4 – 5 measurements.

Note CTGB: *Based on the maximum computed MITC level of 14 µg/m^3 an internal exposure value of 3.22 µg/kg bw is calculated for adults (**80.5%** of the AOEL) and 14.98 µg/ kg bw for children (**374.5%** of the AOEL). Based on the maximum measured exposure concentration of 3.1 µg/kg bw an estimated internal exposure is calculated of 0.713 µg/kg bw (**17.8%** of the AOEL) and 3.317 µg/kg bw (**83%** of the AOEL) for adults and children, respectively. It should be noted the application rate used in the study (300 L/ha) was below the current application rate of Monam Cleanstart (700 L/ha). Therefore, it can be expected that the actual exposure level will be higher.*

Study 6: Schepel en Dijksterhuis 2003

Bystanders might also be present during breaking of the seal after soil fumigation with Metam-sodium or when the plastic film is opened to prepare the soil for planting. In such a case, bystanders might be exposed to remainders of the volatile compound MITC, which is released from the soil due to the breaking of the seal or opening of plastic film coverage. The MITC concentrations in air after breaking of seal or opening/removing of a plastic film coverage before planting can be estimated from the measurements at the edge of the field during and after breaking the seal (experimental protocol detailed under point B.6.15.4.2.1). The maximum air concentration of 8.8834 µg/m^3 was found 50 m downwind in the time period 0-2 h after breaking the seal 14 days after fumigation with Metam sodium at an application rate of 300 L/ha.

Note CTGB: *Based on the maximum computed MITC level of 8.8 µg/m^3 an internal exposure value of 2.02 µg/kg bw is calculated for adults (**50.6%** of the AOEL) and 9.42 µg/kg bw for children (**235%** of the AOEL). Based on the assessment, it can be concluded that adverse health effects cannot be excluded for residents near field treated with Monam Cleanstart.*

It should be noted the application rate used in the study (300 L/ha) was below the current application rate of Monam Cleanstart (700 L/ha). Therefore, it can be expected that the actual exposure level will be even higher.

Local effects:
The highest air concentration surrounding the field in all studies was 35.97 µg/m^3. MITC can induce local effects, such as eye irritation, skin irritation and respiratory irritation. However, these effects were observed in rats at higher concentrations than the levels found in the exposure studies.

Overall summary of the resident exposure assessment

Six field exposure studies are available. Of these six, four included measurements of air concentrations that could be used for bystander/resident exposure assessment. Overall, based on the risk assessment using these exposure studies it is concluded that **adverse health effects cannot be excluded** for children living near fields treated with Monam Cleanstart.

Reactie onderbouwing etiketwijziging Monam

<u>Voorgestelde risk mitigation measurements:</u>

Op perceelszijden grenzend aan percelen met een woon- of verblijfsbestemming, een bufferzone van 7,5 meter aanhouden (gemeten vanaf de kadastrale grens).

Reactie Ctgb: De aanvrager stelt een bufferzone van 7.5 m voor. Hiervoor verwijzen ze naar het nog in te dienen dossier voor de herregistratie van Monam en deze bufferzone zou berekend zijn met een bufferzone calculator. In de onderbouwing wordt kort aangegeven dat deze bufferzone calculator gebaseerd is op diverse studies waarbij de concentratie in de lucht in de omgeving is gemeten. Het is echter niet duidelijke onder welke condities deze studies zijn uitgevoerd (middel, werkzame stof, vluchtigheid, application rate, toepassingsmethode, locaties waar gemeten is, etc.). Het is daarom onduidelijk in hoeverre deze gegevens geschikt zijn voor het gebruik van metam-natrium in de Nederlandse situatie. Aangezien we hier te weinig informatie over hebben zullen we uitgaan van de informatie van de blootstellingstudies in de DAR van metam.

In de DAR is er 1 studie waarbij op verschillende afstanden van het veld gemeten is (0, 100 en 200 m) in Nederland. In deze studie werd de hoogste concentratie MITC gemeten op 100 meter afstand van het veld (zie onderstaande tabel). Over het geheel gezien lijkt er weinig verschil te zijn in de concentratie MITC aan de rand van het veld (downwind) en op 100 m afstand (downwind). Op basis van deze experimentele gegevens blijkt dat een bufferzone van 7.5 m dus geen verlaging van de blootstelling zal veroorzaken.

Substance	**Experimental conditions**	**MITC Concentration ($\mu g/m^3$)**
Location 1: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 2: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 3: 10 samples	Field boundary, downwind	4.47 – 23.71
Location 4: 10 samples	Field boundary, downwind, measure during whole study duration	0.07-1.82
Location 5	Field boundary, downwind	Pump defect, no valid measurement.
Location 6: 10 samples	Field boundary, downwind, measure during whole study duration	4.77-24.35
Location 7: 10 samples	Field boundary, downwind, measure during whole study duration	4.21-13.31
Location 8: 10 samples	Field boundary, measure during whole study duration	0.042-6.85
Location 9: 2 samples	100 m of field, upwind	0.08
Location 10: 1 sample	100 m of field, upwind	0.09
Location 11: 1 sample	100 m of field, upwind	0.04
Location 12: 9 samples	100 m of field, downwind, measure during whole study duration	0.66-3.62
Location 13: 10 samples	100 m of field, downwind, measure during whole study duration	2.10-13.19
Location 14 : 10 samples	100 m of field, downwind, measure during whole study duration	0.042-**35.96**
Location 15: 1 sample	200 m of field, upwind	0.1
Location 16: 1 sample	200 m of field, upwind	0.09

Substance	Experimental conditions	MITC Concentration ($\mu g/m^3$)
Geometric mean		0.87
Minimum – maximum:		0.042 -35.97

Van de 200 m afstand zijn alleen upwind metingen aanwezig. Er kan dus geen indicatie gegeven worden welke afstand nodig is voor een geschikte bufferzone.

De toepassing uitstellen indien de volgende weersomstandigheden, binnen 48 uur na toepassing, voorspeld worden:
- mist;
- temperatuursinversie;
- windstil weer.

Reactie Ctgb: Dit advies is in de praktijk moeilijk uitvoerbaar en te handhaven. Kan er 48 uur van te voren voorspeld worden dat de weeromstandigheden zo blijven?

Voorkom stuiven door op stuifgevoelige gronden aanvullende maatregelen te nemen zoals b.v. toepassen van papiercellulose.

Reactie Ctgb: Op basis van de omschrijving in de DAR lijkt dat in de meeste veldstudies de grond niet afgedekt is met folie maar alleen met “roller” gesloten is. Afdekking met bijv. papiercellulose zou de blootstelling mogelijk kunnen verlagen, maar hier zijn geen gegevens over.

Overige punten:

Moet schaarinjectie verplicht worden gesteld?

Reactie Ctgb: Hier valt weinig over zeggen. In de DAR staat 1 studie waar 2 verschillende toepassingsmethodes met elkaar vergeleken worden (injectie in veld 1 en 2 en irrigatie systeem in veld 3 en 4). Gemiddeld lijkt de injectietoepassing tot iets lagere blootstelling te leiden. Echter, op 10 cm hoogte is er eigenlijk geen verschil tussen veld 2 en veld 4 (zie tabel hieronder). Schaarinjectie zou een mogelijke verlaging kunnen geven van de blootstelling, maar op basis van de weinige gegevens die er zijn kan dit niet geconcludeerd worden.

Field/time after application (h)	MITC air concentration ($\mu g/m^3$)		
	200 cm	100 cm	10 cm
Injected field 1: 166 kg/ha (480L)			
5.3	1.1	1.2	1.3
11.4	1.3	1.4	1.6
29.4	0.9	1.0	1.1
78	0.7	0.8	0.9
Mean:	1.0	1.1	1.22
Injected field 2: 166 kg/ha (480L)			
4	0.4	0.9	7.0
6	0.9	1.3	7.4
11	0.4	0.5	5.9
27.5	0.3	1.0	1.0
29.5	0.5	1.6	1.6
34.5	0.2	0.4	0.4
Mean:	0.45	0.95	3.88
Chemigated field 3: 166 kg/ha (480 L) diluted in 169m^3 water/ha			
3	1.6	2.0	3.5
6	0.9	1.3	2.8
8.4	2.0	3.0	11.2
10	1.2	1.3	4.0
14	0.7	0.8	1.7
Mean:	1.28	1.7	4.64

Field/time after application (h)	MITC air concentration (µg/m^3)		
	200 cm	**100 cm**	**10 cm**
Chemigated field 4: 166 kg/ha (480 L) diluted in 169m^3 water/ha			
6.3	4.6	5.9	7.1
10.3	1.2	2.1	3.2
14.3	2.9	2.9	4.8
18.3	4.6	6.4	6.5
22.3	2.0	2.3	2.8
26.3	1.4	1.7	1.8
30.3	0.7	0.8	1.3
Mean:	2.5	3.15	3.9

Moet een maximale dosering van 300 L/ha verplicht worden gesteld?

Reactie Ctgb: In de DAR zijn verschillende doseringen gebruikt in de blootstellingstudies (300 – 700 L/ha). In de studie die voor omwonenden de meest relevante informatie levert is 300 L/ha gebruikt. Daarom lijkt een maximale toepassing van 300 L/ha geschikt.

Verder moet echter ook gespecificeerd worden hoe diep het middel geïnjecteerd moet worden. In de studies in de DAR is het middel 15-25 cm diep ingebracht. Op het huidige gebruiksvoorschrift staat 10 cm.

Risicobeoordeling besluit 28 mei 2014

Monam cleanstart voor omwonenden - bufferzone
ASPECT BEOORDELING GEWASBESCHERMING TOXICOLOGIE

Naar aanleiding van de signalen omtrent MITC is er een herbeoordeling uitgevoerd voor omwonenden. Voor de operator, omstander en werker is geen herbeoordeling gedaan.

1. Mammalian toxicology

List of Endpoints
Metam sodium is an existing active substance that is approved for inclusion in Annex I. The final List of Endpoints presented below is taken from the EFSA Scientific Report on Metam (2011); 9(9) 2334. Where relevant, some additional remarks/information are given in italics.

The representative formulated product for the evaluation was “Metam sodium 510 g/L”, soluble concentrate (SL), registered under different trade names in Europe. Metam sodium acts as fumigant through rapid degradation to methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1) metam and MITC

Rate and extent of oral absorption ‡	85 % (based on urinary (50%) and expired air (35%) excretion within 48 h)
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	Slight potential for accumulation in thyroid
Rate and extent of excretion ‡	Rapid and extensive (app. 85 %) within 48 h, mainly via urine (50 %) within 24 h, 4 % via faeces, 35 % via expired air
Metabolism in animals ‡	Extensive degradation of metam into MITC which is further conjugated with GSH or decomposes into MIC, COS and CO_2. Another important metabolic pathway is formation of CS_2 which is related to acidic conditions of stomach
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites: Methylisothiocyanate (MITC) , methylisocyanate (MIC), COS, CS_2
Toxicologically relevant compounds ‡ (environment)	Methylisothiocyanate (MITC), methylisocyanate (MIC), COS, CS_2

Acute toxicity (Annex IIA, point 5.2) metam sodium

Rat LD_{50} oral ‡	896 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	**-**
Rat LC_{50} inhalation ‡	2.54 mg/L air /4h (whole body)	**R20**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	Non-irritant	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Acute toxicity (Annex IIA, point 5.2) MITC

Rat LD_{50} oral ‡	147 mg/kg bw	**R25**
Rat LD_{50} dermal ‡	1290 mg/kg bw	**R21**
Rat LC_{50} inhalation ‡	0.54 mg/L air /4h (whole body)	**R23** **R37**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	No study required	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Short term toxicity (Annex IIA, point 5.3) metam sodium

Target / critical effect ‡	Nasal cavity (rat), urinary bladder(mice), liver(dog)	
Relevant oral NOAEL ‡	1-year dog: 0.1 mg/kg bw/day 90-day rat: 0.5 mg/kg bw/day 90-day mice: 0.8 mg/kg bw/day	**R48/ 22**
Relevant dermal NOAEL ‡	21-day, rabbit: 31.2 mg/kg bw/day	
Relevant inhalation NOAEL ‡	90-day rat: 6.5 mg/m^3 corresponding to 1.75 mg/kg bw/d	

Short term toxicity (Annex IIA, point 5.3) MITC

Target / critical effect ‡	Nasal cavity (rat), liver (dog)	
Relevant oral NOAEL ‡	90-day, dog 0.04 mg/kg bw/day	
Relevant dermal NOAEL ‡	No data - not required	
Relevant inhalation NOAEL ‡	28-day rat : 5 mg/m^3 (1.35 mg/kg bw/d)	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Metam and MITC are unlikely to be genotoxic[1)]	

[1)] *Based on a negative Ames test, an equivocal HGPRT assay in CHO cells, one positive and one equivocal* in vitro *chromosomal aberration test in human lymphocytes, a negative UDS test in hepatocytes, a negative* in vivo *Micronucleus test in mice, and a negative* in vivo *chromosomal aberration test in Chinese hamsters.*

Long term toxicity and carcinogenicity (Annex IIA, point 5.5) metam sodium

Target/critical effect ‡	Nasal cavity (rat) urinary bladder (mice)	
Relevant NOAEL ‡	1.5 mg/kg bw/day; 2-year, rat 1.9 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	Angiosarcomas in mice	**R40**

Long term toxicity and carcinogenicity (Annex IIA, point 5.5) MITC

Target/critical effect ‡	Changes in some WBC parameters	
Relevant NOAEL ‡	0.44 mg/kg bw/day; 2-year, rat 3.3 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	MITC is unlikely to pose a risk to humans	

Reproductive toxicity (Annex IIA, point 5.6) metam sodium

Reproduction toxicity

Reproduction target / critical effect ‡	Decreased pup and litter weight at the parental toxic dose in the rat	
Relevant parental NOAEL ‡	0.03 mg/L (4 mg/kg bw/day)	
Relevant reproductive NOAEL ‡	>0.1 mg/L (12 mg/kg bw/day)	
Relevant offspring NOAEL ‡	0.03 mg/L(4 mg/kg bw/day)	

Developmental toxicity

Developmental target / critical effect ‡	Increased incidence of variations and retardations at maternally toxic dose in rats; decreased number live foetuses and increased incidence of dead implants at maternal toxic doses in rabbits	**R63**
Relevant maternal NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 5 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Reproductive toxicity (Annex IIA, point 5.6) MITC

Reproduction toxicity

Reproduction target / critical effect ‡	Reproduction parameters not significantly altered	
Relevant parental NOAEL ‡	0.7 mg/kg bw/day	

Relevant reproductive NOAEL ‡	>3.6 mg/kg bw/day	
Relevant offspring NOAEL ‡	>3.6 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Decreased fetal weight at maternal toxic doses in rabbits	
Relevant maternal NOAEL ‡	Rat: 3 mg/kg bw/day Rabbit: 3 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7) metam sodium

Acute neurotoxicity ‡	NOAEL> 1500 mg/kg bw	
Repeated neurotoxicity ‡	NOAEL = 14.7 mg/kg bw/d	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No studies performed
Studies performed on metabolites or impurities ‡	No further studies performed

Medical data ‡ (Annex IIA, point 5.9) metam sodium

	No medical surveillance data for manufacturing plant personnel was found for metam sodium.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage study	100
ADI MITC	0.004 mg/kg bw/day	dog, 90-d drinking water study	100
AOEL ‡ metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage	100
AOEL MITC	0.004 mg/kg bw/day	dog, 90-d drinking water study	100
ARfD ‡ metam sodium	0.1 mg/kg bw	rat, overall developmental toxicity	100
ARfD MITC	0.03 mg/kg bw	rat, developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	Concentrate: 1%; 12%: for the dilution ‡ Rat in vivo and comparative in vitro (human/rat skin)

‡ Endpoint identified by the EU-Commission as relevant for Member States when applying the Uniform Principles.

Local effects

Metam sodium produces local effects after single exposure (corrosive for skin). For the operator these local effects are covered in the risk assessment/management by means of assignment of R-and S-phrases. Furthermore, irritant dermatitis is reported among workers cleaning up a spill of metam sodium in California in 1991 and persistent respiratory health effects occurred after a metam sodium spill in California in 1994 (see DAR section 6.9.3). MITC also produces local effects (irritation of upper airways) after single and repeated exposure. For bystanders/resident no personal protective equipment can be assigned to cover the local effects. This has therefore, been taken into account in the risk assessment.

Data requirements active substance
No additional data requirements are identified.

1.1 Toxicity of the formulated product (IIIA 7.1)

Metam sodium is only available as an aqueous solution containing about 510 g/L a.i. and the product is equivalent to the technical active substance as manufactured. Therefore, all acute toxicity studies were conducted with aqueous metam sodium (or potassium) solutions as manufactured and are described in Annex II, point B.6.2 (DAR, section 6.14).

It was agreed that for operators applying metam sodium, the relevant assessment is for MITC (EFSA Scientific Report on Metam (2011); 9(9) 2334). Also for workers, bystanders and residents, the relevant assessment is considered to be for MITC.

Acute toxicity (Annex IIA, point 5.2) metam sodium

Rat LD_{50} oral ‡	896 mg/kg bw	**R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	**-**
Rat LC_{50} inhalation ‡	2.54 mg/L air /4h (whole body)	**R20**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	Non-irritant	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

Acute toxicity (Annex IIA, point 5.2) MITC

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Rat LD_{50} dermal ‡	1290 mg/kg bw	**R21**
Rat LC_{50} inhalation ‡	0.54 mg/L air /4h (whole body)	**R23** **R37**
Skin irritation ‡	Corrosive	**R34**
Eye irritation ‡	No study required	**-**
Skin sensitisation ‡	Sensitising (M & K)	**R43**

1.1.1 Data requirements formulated product

No additional data requirements are identified.

1.2 Dermal absorption (IIIA 7.3)

See List of Endpoints. The formulation Monam Cleanstart is identical to the tested formulation. For the risk assessment, dermal absorption values of 1% for the concentrate.

1.3 Available toxicological data relating to non-active substances (IIIA 7.4)

See 4.1. Metam sodium is only available as an aqueous solution containing about 510 g/L a.i. and the product is equivalent to the technical active substance as manufactured.

1.4 Exposure/risk assessments

Overview of the intended uses
Monam Cleanstart is a SC (suspension concentrate) formulation and contains 510 g/L metam sodium. Application of Metam sodium is carried out by a soil-injection technique using tractor-mounted equipment. The intended uses are listed under Appendix 1 (GAP).

1.4.1 Operator exposure/risk

Calculation of the EU-AOEL / Tolerable Limit Value (TLV)
For metam sodium no TLV has been set. The AOEL will be used for the risk assessment.Since the formulation is applied up to two times during the period July - October, a semi-chronic exposure duration is applicable for the operator (including contract workers). A semi-chronic AOEL is therefore derived. The semi-chronic EU-AOEL of MITC is 0.004 mg/kg bw/day (= 0.28 mg/day for a 70 kg operator), based on the NOAEL of 0.4 mg/kg bw/day in a 90-d drinking water study with dogs and a safety factor of 100 is used for the risk assessment (see List of Endpoints).

Because metam sodium is almost instantly hydrolysed to MITC, it was agreed in the PRAPeR meeting of experts 54 (subgroup1) held in Parma in July 2008 that the operator, worker and bystander risk assessment should be performed for MITC (EFSA Scientific Report on Metam (2011); 9(9): 2334).

Exposure measurements / estimations
No appropriate exposure models are available to calculate exposure during mixing, loading and application to the volatile MITC that is formed rapidly after application of Monam Cleanstart when metam sodium enters into contact with soil, as is also confirmed by the DAR (section B.6.15.1).

Mixing
Since the formulation Monam Cleanstart is used without dilution, exposure during mixing will not occur since no mixing is necessary.

Loading
In the Dutch operating instructions, the following directions for use are prescribed:
"Wear suitable dermal protective clothing, gloves with long shafts and rubber boots during all activities during which skin contact with the formulation may occur, including the soil disinfection and the first cultivation activities after application of the formulation. Take off all contaminated clothing. Immediately rinse off gloves and boots that may have been in contact with the formulation with plenty of water. Store gloves outside the cabin. Wear a full face mask with B2-P3 filter, ideally with proflow blower, during the preparation of the equipment, during trouble shooting and the internal cleaning of the equipment."

Because of the loading procedure can be considered as 'closed system' and full personal protective equipment should be used, the exposure during loading is considered negligible.

Application
In the updated DAR Re-submission of May 2011, 4 exposure studies were included in which metam sodium was applied by soil injection (2 studies), soil fumigation (1 study) or drip-irrigation (1 study). The soil injection and fumigation applications were open field studies, while the drip-irrigation study was a greenhouse/tunnel study.

For Monam Cleanstart, the open field soil injection studies were the relevant studies. A brief summary of the studies is included:

Study 1: Mulder et al. 1994
Metam-sodium (510 g/L) was applied onto 15 different parcels at 12 different field locations in the Netherlands during soil decontamination of industrial potato land. Tractor-drawn equipment was used with 12 parcels treated with spade injector and 3 parcels treated with cultivator injection equipment, respectively. In order to avoid exposure during turning at the headlands all injection equipments used were fitted with an anti-drip systems, i.e. anti-drip caps or blow-through system. Irrespective of the injection equipment used all tractors were fitted with one to two flat driven rollers for sealing of the soil. Application rate of Monam was 300 L/ha.
The MITC exposure study performed after soil injection application of Metam-sodium under representative field conditions demonstrated that in some situations there was exceeding of the inhalation AOEL of MITC. Appropriate respiratory protection is recommended for the operator during the whole process.

Note Ctgb: *no bystander/resident exposure was measured.*

Study 2: De Rooij et al. 1993
Metam-sodium (BASF monam, Aamonam, Shell-NMC and Luxan monam (Metam-sodium 510 g/L) was applied for soil decontamination purposes onto 11 representative bulb parcels at an application rate ranging from 420 L/ha to 700 L/ha. All parcels were treated using specialized equipment, i.e. cultivator injectors that inject Metam-sodium into the soil at a depth of about 18 – 20 cm. Immediately after injection, one or two flat rollers one of which was a driven roller to ensure that the soil was well compressed and sealed compressed the soil. In all cases, the injection activities started on the downwind side of the parcel thereby reducing additional exposure because of emission of MITC form parcels that were already treated. The MITC exposure studies demonstrated that after soil injection application of Metam-sodium on eleven representative fields under representative conditions the AOEL of MITC was

exceeded in most of the field parcels treated when RPE was absent. Overall, it can be concluded that under these experimental conditions, operator exposure to MITC is below AOEL only with special protective equipment.

Note CTGB: *No bystander/resident exposure was measured.*

Study 3: Links et al. 2006
In this study, metam sodium was applied at 300L/ha with a tractor mounted Rumptstad shear injector to approximately 5 Ha (application rate according to label 300L/Ha). The machine featured a working width of 3 m. Metam sodium was loaded in the tank (capacity 500 L) that was located at the front of the tractor. Via a flexible pressure tubing metam sodium was transported under pressure to the spray valves below the plough. The Rumptstad injected metam sodium in the soil at a depth of 15-20 cm, and worked the soil with a roto-tiller. After injection the soil was flattened with a roller that was part of the application equipment. Besides operator exposure, the degradation products of metam sodium were determined after application in a field at different locations, from the edge of the field (location 1-8) to a maximum distance of 225 meters (location 9-16).

Findings: MIC, CS_2 and methylamine were not detected around the treated field; all values were below the limit of detection.

Potential exposure of the operator to MITC was 76.51µg/m^3 which represents 0.00956 mg/kg bw/d. The stationary air measurement inside the tractor during these tasks was 70.33µg/m^3 which is equivalent to 0.00879 mg/kg bw/d and outside the tractor the concentration MITC were 0.107 mg/m^3 representing 0.0134 mg/kg bw/d.

Air concentrations of MITC around the field ranged from the limit of detection (0.042 µg/m^3) to a maximum value of 35.97 µg/m^3 with a geometric mean of 0.87 µg/m^3 (GM calculated with 100% LOD for concentrations <LOD, n=96). The 95th percentile was 13.22 µg/m^3 and the 75th percentile 6.41 µg/m^3. No direct relation could be found between the time expired after application (with a maximum of 3 days) and the MITC air concentrations at the different locations, although the first measurements over 4 hours was at almost every location the highest. Wind direction, on the other hand, seems to be important with the highest concentrations occurring downwind.

Substance	**Experimental conditions**	**MITC Concentration (µg/m^3)**
Location 1: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 2: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 3: 10 samples	Field boundary, downwind	4.47 – 23.71
Location 4: 10 samples	Field boundary, downwind, measure during whole study duration	0.07-1.82
Location 5	Field boundary, downwind	Pump defect, no valid measurement.
Location 6: 10 samples	Field boundary, downwind, measure during whole study duration	4.77-24.35
Location 7: 10 samples	Field boundary, downwind, measure during whole study duration	4.21-13.31
Location 8: 10 samples	Field boundary, measure during whole study duration	0.042-6.85
Location 9: 2 samples	100 m of field, upwind	0.08
Location 10: 1 sample	100 m of field, upwind	0.09
Location 11: 1 sample	100 m of field, upwind	0.04
Location 12: 9 samples	100 m of field, downwind, measure during whole study duration	0.66-3.62

Substance	Experimental conditions	MITC Concentration (µg/m³)
Location 13: 10 samples	100 m of field, downwind, measure during whole study duration	2.10-13.19
Location 14 : 10 samples	100 m of field, downwind, measure during whole study duration	0.042-35.96
Location 15: 1 sample	200 m of field, upwind	0.1
Location 16: 1 sample	200 m of field, upwind	0.09
Geometric mean		**0.87**
Minimum – maximum:		**0.042 -35.97**

De metingen t.b.v. de operator blootstelling vonden plaats op het raam en boven een wiel van een trekker; de hoogte waarop gemeten is voor de bystanders (langs het veld), is echter niet gespecificeerd in de samenvatting in de DAR. De meting duur om het veld is 4 dagen lang (voor operator 3 dagen). Er is veel variatie in wanneer er pieken van MITC gemeten worden. Toch wordt wel gemeld dat het meeste gemeten wordt de eerste 4 uur na toepassing.

Note CTGB: *The dose used in the study 300 L/ha is below the intended use 750 L/ha.*
No specific resident exposure is calculated in the DAR. Therefore, a resident exposure assessment is carried out using the "bystander" exposure values from the study in the DAR. These values are also representative for residents as they were taken either directly besides or further from the field.

Table 1: Resident exposure estimate to MITC after application of Monam Cleanstart based on the results from the study Link et al. 2006

	Exposure level	*Peak value*	*GM*	*75th*	*95th*
Adult					
Maximum value	***air level (µg/m³)*** [1]	*35.97*	*0.87*	*6.41*	*13.22*
	exposure (µg/kg bw/d) [2]	*8.27*	*0.2001*	*1.4743*	*3.0406*
	% [3] ***AOEL***	***207***	***5.0***	***36.9***	***76.0***
Child					
Maximum value	***air level (µg/m³)*** [1]	*35.97*	0.87	6.41	13.22
	exposure (µg/kg bw/d) [4]	*38.49*	0.9309	6.8587	14.15
	% [3] ***AOEL***	***962***	***23.3***	***171***	***354***

[1]: maximum air concentration; [2] : taking into account a respiration rate of 0.23 m³/day/kg, and a 24 h breathing period, default b.w.=60 kg, in the absence of RPE. [3]: AOEL (MITC) =0.004 mg/kg b.w./d
[4] : taking into account a respiration rate of 1.07 m³/day/kg, and a 24 h breathing period, default b.w.=10 kg (default in EFSA OPEX calculator), in the absence of RPE.

Only with the use of the geometric mean does the resident exposure not exceed the AOEL. However, the acceptability of the GM can be questioned since this represent the mean of both the downwind and upwind situation. A 75th percentile is considered to be more appropriate. It is worth noting that the acute reference dose of 30 µg/kg bw/d for MITC is exceeded for children when using the peak exposure value.

Based on the assessment, it can be concluded that adverse health effects cannot be excluded for residents living near fields treated with Monam Cleanstart.
In the study an application rate of 300 L/ha was used, while the current application rate for Monam cleanstart is 750 L/ha, a factor of 2.5 higher. It can therefore be expected that the actual exposure level are higher than those measured in this study.

Study 4: Saeed et al. 2000

This study was conducted in four fallow fields intended to be grown with potatoes. Methyl isothiocyanate air concentrations were measured above these fields following application of metam-sodium (345 g a.i/kg) either through injection using a ground rig (fields 1 and 2) or by chemigation using the center-pivot irrigation systems (fields 3 and 4). Both methods are used commercially in Wisconsin for the application of the fumigant and are claimed to be equally effective. Solutions of metam-sodium (345g a.i. /kg) were injected in the soil at a rate of 480litre/ha (166 kg/ ha) in fields one and two using a ground applicator with knives or shanks spaced 15cm apart. The knives were pulled through the soil at a depth of 25cm and the fumigant was released from ports behind each shank at depths of 5, 15 and 25cm. A soil compactor was connected to each rig to compact the soil over the furrow made by the injection shanks. In fields three and four the fumigant solution at a rate of 480 liter/ha was mixed with 169m^3/ha of irrigation water through a metering pump that was connected to the center-pivot irrigation system. Immediately following fumigant application to each of the four fields, equipment for measuring MITC air concentration, temperature and wind speed was installed and measurements were started. The focus of this study was to estimate the loss of MITC by volatilization when metam-sodium was applied through either chemigation or injection to arable fields. Methyl isothiocyanate is the principal product of the transformation and constitutes about 90% of the total amount of metam-sodium applied to soils.

On most sampling occasions, higher MITC emissions were observed in chemigated than in injected fields. The highest MITC concentrations were 11.2 and 7.4µg/m^3 recorded 10cm above the ground 6-8h following application and the lowest concentrations were 0.7 and 0.2 µg/m^3 observed at 200cm 30 and 35h after application above chemigated and fumigated fields, respectively. Volatilization losses measured by trapping vaporized MITC indicated that in all treated fields, regardless of application method, average MITC air concentrations were highest in the first 8h following application and decreased thereafter. It was found that use of a soil compactor following fumigant injection into the soil had a substantial effect in reducing MITC emissions (Saeed and Rouse, unpublished data). Thus, manipulation of soil surface to reduce MITC loss by volatilization could serve as an approach to environmentally acceptable disease control practices.

Field/time after application (h)	**MITC air concentration (µg/m^3)**		
	200 cm	**100 cm**	**10cm**
Injected field 1: 166 kg/ha (480L)			
5.3	1.1	1.2	1.3
11.4	1.3	1.4	1.6
29.4	0.9	1.0	1.1
78	0.7	0.8	0.9
Mean:	1.0	1.1	1.22
Injected field 2: 166 kg/ha (480L)			
4	0.4	0.9	7.0
6	0.9	1.3	7.4
11	0.4	0.5	5.9
27.5	0.3	1.0	1.0
29.5	0.5	1.6	1.6
34.5	0.2	0.4	0.4
Mean:	0.45	0.95	3.88
Chemigated field 3: 166 kg/ha (480L) diluted in 169m^3 water/ha			
3	1.6	2.0	3.5
6	0.9	1.3	2.8
8.4	2.0	3.0	11.2
10	1.2	1.3	4.0
14	0.7	0.8	1.7
Mean:	1.28	1.7	4.64
Chemigated field 4: 166 kg/ha (480L) diluted in 169m^3 water/ha			
6.3	4.6	5.9	7.1
10.3	1.2	2.1	3.2
14.3	2.9	2.9	4.8
18.3	4.6	6.4	6.5
22.3	2.0	2.3	2.8
26.3	1.4	1.7	1.8
30.3	0.7	0.8	1.3
Mean:	2.5	3.15	3.9

The mean exposure was the highest at 10 cm ranging between 1.22 to 4.64 µg/m^3. The highest peak exposure was measured also measured at 10 cm above ground with 11.2 µg/m^3.

Note CTGB: *Residential exposure is calculated using the exposure levels shown in the table above. Separate exposure estimates are made for the injected fields and het chemigated field. To estimate the exposure for children the air concentration at both 10cm and 100 cm is used. For adults only the 100 cm air concentration is used.*

Table 2: Resident exposure estimate to MITC after application of Monam Cleanstart based on the results from the study Saeed et al. 2000

	Exposure level	***Peak value***	***Mean***	***Peak value***	***Mean***
		Injected field		***Chemigated field***	
Adult (100 cm air concentration)					
Maximum value	***air level (µg/m³)*** [1]	*1.6*	*1.1*	*6.4*	*3.15*
	exposure (µg/kg bw/d) [2]	*0.368*	*0.253*	*1.472*	*0.7245*
	% [3] ***AOEL***	***9.2***	***6.325***	***36.8***	***18.1***
Child (100 cm air concentration)					
Maximum value	***air level (µg/m³)*** [1]	*1.6*	*1.1*	*6.4*	*3.15*
	exposure (µg/kg bw/d) [4]	*1.712*	*1.177*	*6.848*	*3.3705*
	% [3] ***AOEL***	***42.8***	***29.4***	***171***	***84.3***
Child (10 cm air concentration)					
Maximum value	***air level (µg/m³)*** [1]	*7.4*	*3.88*	*11.2*	*4.64*
	exposure (µg/kg bw/d) [4]	*7.918*	*4.1516*	*11.984*	*4.9648*
	% [3] ***AOEL***	***198***	***104***	***300***	***124***

[1]: maximum air concentration;
[2] : taking into account a respiration rate of 0.23 m^3/day/kg, and a 24 h breathing period, default b.w.=60 kg, in the absence of RPE.
[3]: AOEL (MITC) =0.004 mg/kg b.w./d
[4] : taking into account a respiration rate of 1.07 m^3/day/kg , and a 24 h breathing period, default b.w.=10 kg (default in EFSA OPEX calculator), in the absence of RPE.

The estimated resident exposure is exceeded for children for both application methods. Therefore, adverse health effects cannot be excluded for residents living near fields treated with Monam Cleanstart.

It is noted that the application rate used in the study (480 L/ha) is below the current application rate of Monam Cleanstart (700 L/ha) so actual exposure level are expected to be even higher.

Study 5: Van den Berg, F. 1993

Behaviour of Metam sodium and MITC in soil as well as the emission of MITC in the air was described by a computer simulation model and results compared with measured figures after soil injection application of Metam sodium into the soil of two selected fields in the Netherlands (field A near Valtermond and field B near Eeserveen).

For both fields, Metam sodium was applied at an application rate of 300 L/ha (510 g Metam sodium/L) and injected at a depth of approx. 18 cm using a horizontal blade injector with spray nozzles below the blades and subsequent compression of the soil with a roller. The treated area comprised 5.9 ha for both fields.

Both the computed as well as the measured MITC concentrations in the air demonstrated that a bystander walking at the downwind side of a fumigated field (distance 0 – 214 m) approx. 1 to 9 days after treatment is exposed to MITC concentrations amounts to 14 µg/m³. The measurements were taken at 1.5 meters above ground. The study lasted 7-9 days, with a total of 4 – 5 measurements.

Note CTGB: *Based on the maximum computed MITC level of 14 µg/m³ an internal exposure value of 3.22 µg/kg bw is calculated for adults (**80.5%** of the AOEL) and 14.98 µg/ kg bw for children (**374.5%** of the AOEL). Based on the maximum measured exposure concentration of 3.1 µg/kg bw an estimated internal exposure is calculated of 0.713 µg/kg bw (**17.8%** of the AOEL) and 3.317 µg/kg bw (**83%** of the AOEL) for adults and children, respectively. It should be noted the application rate used in the study (300 L/ha) was below the current application rate of Monam Cleanstart (700 L/ha). Therefore, it can be expected that the actual exposure level will be higher.*

Study 6: Schepel en Dijksterhuis 2003

Bystanders might also be present during breaking of the seal after soil fumigation with Metam-sodium or when the plastic film is opened to prepare the soil for planting. In such a case, bystanders might be exposed to remainders of the volatile compound MITC, which is released from the soil due to the breaking of the seal or opening of plastic film coverage. The MITC concentrations in air after breaking of seal or opening/removing of a plastic film coverage before planting can be estimated from the measurements at the edge of the field during and after breaking the seal (experimental protocol detailed under point B.6.15.4.2.1). The maximum air concentration of 8.8834 µg/m^3 was found 50 m downwind in the time period 0-2 h after breaking the seal 14 days after fumigation with Metam sodium at an application rate of 300 L/ha.

Note CTGB: *Based on the maximum computed MITC level of 8.8 µg/m^3 an internal exposure value of 2.02 µg/kg bw is calculated for adults (**50.6%** of the AOEL) and 9.42 µg/kg bw for children (**235%** of the AOEL). Based on the assessment, it can be concluded that adverse health effects cannot be excluded for residents near field treated with Monam Cleanstart.*

It should be noted the application rate used in the study (300 L/ha) was below the current application rate of Monam Cleanstart (700 L/ha). Therefore, it can be expected that the actual exposure level will be even higher.

Local effects:
The highest air concentration surrounding the field in all studies was 35.97 µg/m^3. MITC can induce local effects, such as eye irritation, skin irritation and respiratory irritation. However, these effects were observed in rats at higher concentrations than the levels found in the exposure studies.

Overall summary of the resident exposure assessment

Six field exposure studies are available. Of these six, four included measurements of air concentrations that could be used for bystander/resident exposure assessment. Overall, based on the risk assessment using these exposure studies it is concluded that **adverse health effects cannot be excluded** for children living near fields treated with Monam Cleanstart.

Reactie onderbouwing etiketwijziging Monam

<u>Voorgestelde risk mitigation measurements:</u>

Op perceelszijden grenzend aan percelen met een woon- of verblijfsbestemming, een bufferzone van 7,5 meter aanhouden (gemeten vanaf de kadastrale grens).

Reactie Ctgb: De aanvrager stelt een bufferzone van 7.5 m voor. Hiervoor verwijzen ze naar het nog in te dienen dossier voor de herregistratie van Monam en deze bufferzone zou berekend zijn met een bufferzone calculator. In de onderbouwing wordt kort aangegeven dat deze bufferzone calculator gebaseerd is op diverse studies waarbij de concentratie in de lucht in de omgeving is gemeten. Het is echter niet duidelijke onder welke condities deze studies zijn uitgevoerd (middel, werkzame stof, vluchtigheid, application rate, toepassingsmethode, locaties waar gemeten is, etc.). Het is daarom onduidelijk in hoeverre deze gegevens geschikt zijn voor het gebruik van metam-natrium in de Nederlandse situatie. Aangezien we hier te weinig informatie over hebben zullen we uitgaan van de informatie van de blootstellingstudies in de DAR van metam.

In de DAR is er 1 studie waarbij op verschillende afstanden van het veld gemeten is (0, 100 en 200 m) in Nederland. In deze studie werd de hoogste concentratie MITC gemeten op 100 meter afstand van het veld (zie onderstaande tabel). Over het geheel gezien lijkt er weinig verschil te zijn in de concentratie MITC aan de rand van het veld (downwind) en op 100 m afstand (downwind). Op basis van deze experimentele gegevens blijkt dat een bufferzone van 7.5 m dus geen verlaging van de blootstelling zal veroorzaken.

Substance	**Experimental conditions**	**MITC Concentration ($\mu g/m^3$)**
Location 1: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 2: 10 samples	Field boundary, upwind, measure during whole study duration	<0.042
Location 3: 10 samples	Field boundary, downwind	4.47 – 23.71
Location 4: 10 samples	Field boundary, downwind, measure during whole study duration	0.07-1.82
Location 5	Field boundary, downwind	Pump defect, no valid measurement.
Location 6: 10 samples	Field boundary, downwind, measure during whole study duration	4.77-24.35
Location 7: 10 samples	Field boundary, downwind, measure during whole study duration	4.21-13.31
Location 8: 10 samples	Field boundary, measure during whole study duration	0.042-6.85
Location 9: 2 samples	100 m of field, upwind	0.08
Location 10: 1 sample	100 m of field, upwind	0.09
Location 11: 1 sample	100 m of field, upwind	0.04
Location 12: 9 samples	100 m of field, downwind, measure during whole study duration	0.66-3.62
Location 13: 10 samples	100 m of field, downwind, measure during whole study duration	2.10-13.19
Location 14 : 10 samples	100 m of field, downwind, measure during whole study duration	0.042-**35.96**
Location 15: 1 sample	200 m of field, upwind	0.1
Location 16: 1 sample	200 m of field, upwind	0.09

Substance	Experimental conditions	MITC Concentration ($\mu g/m^3$)
Geometric mean		0.87
Minimum – maximum:		0.042 -35.97

Van de 200 m afstand zijn alleen upwind metingen aanwezig. Er kan dus geen indicatie gegeven worden welke afstand nodig is voor een geschikte bufferzone.

De toepassing uitstellen indien de volgende weersomstandigheden, binnen 48 uur na toepassing, voorspeld worden:
- mist;
- temperatuursinversie;
- windstil weer.

Reactie Ctgb: Dit advies is in de praktijk moeilijk uitvoerbaar en te handhaven. Kan er 48 uur van te voren voorspeld worden dat de weeromstandigheden zo blijven?

Voorkom stuiven door op stuifgevoelige gronden aanvullende maatregelen te nemen zoals b.v. toepassen van papiercellulose.

Reactie Ctgb: Op basis van de omschrijving in de DAR lijkt dat in de meeste veldstudies de grond niet afgedekt is met folie maar alleen met “roller” gesloten is. Afdekking met bijv. papiercellulose zou de blootstelling mogelijk kunnen verlagen, maar hier zijn geen gegevens over.

Overige punten:

Moet schaarinjectie verplicht worden gesteld?

Reactie Ctgb: Hier valt weinig over zeggen. In de DAR staat 1 studie waar 2 verschillende toepassingsmethodes met elkaar vergeleken worden (injectie in veld 1 en 2 en irrigatie systeem in veld 3 en 4). Gemiddeld lijkt de injectietoepassing tot iets lagere blootstelling te leiden. Echter, op 10 cm hoogte is er eigenlijk geen verschil tussen veld 2 en veld 4 (zie tabel hieronder). Schaarinjectie zou een mogelijke verlaging kunnen geven van de blootstelling, maar op basis van de weinige gegevens die er zijn kan dit niet geconcludeerd worden.

Field/time after application (h)	MITC air concentration ($\mu g/m^3$)		
	200 cm	100 cm	10 cm
Injected field 1: 166 kg/ha (480L)			
5.3	1.1	1.2	1.3
11.4	1.3	1.4	1.6
29.4	0.9	1.0	1.1
78	0.7	0.8	0.9
Mean:	1.0	1.1	1.22
Injected field 2: 166 kg/ha (480L)			
4	0.4	0.9	7.0
6	0.9	1.3	7.4
11	0.4	0.5	5.9
27.5	0.3	1.0	1.0
29.5	0.5	1.6	1.6
34.5	0.2	0.4	0.4
Mean:	0.45	0.95	3.88
Chemigated field 3: 166 kg/ha (480 L) diluted in 169m^3 water/ha			
3	1.6	2.0	3.5
6	0.9	1.3	2.8
8.4	2.0	3.0	11.2
10	1.2	1.3	4.0
14	0.7	0.8	1.7
Mean:	1.28	1.7	4.64

Field/time after application (h)	MITC air concentration (μg/m^3)		
	200 cm	**100 cm**	**10 cm**
Chemigated field 4: 166 kg/ha (480 L) diluted in 169m^3 water/ha			
6.3	4.6	5.9	7.1
10.3	1.2	2.1	3.2
14.3	2.9	2.9	4.8
18.3	4.6	6.4	6.5
22.3	2.0	2.3	2.8
26.3	1.4	1.7	1.8
30.3	0.7	0.8	1.3
Mean:	2.5	3.15	3.9

Moet een maximale dosering van 300 L/ha verplicht worden gesteld?

Reactie Ctgb: In de DAR zijn verschillende doseringen gebruikt in de blootstellingstudies (300 – 700 L/ha). In de studie die voor omwonenden de meest relevante informatie levert is 300 L/ha gebruikt. Daarom lijkt een maximale toepassing van 300 L/ha geschikt.

Verder moet echter ook gespecificeerd worden hoe diep het middel geïnjecteerd moet worden. In de studies in de DAR is het middel 15-25 cm diep ingebracht. Op het huidige gebruiksvoorschrift staat 10 cm.

Bijlage II - Resident Exposure

<table>
<tr>
<td>Comments:
IIIA 7.4</td>
<td>Only the resident exposure part of section 7.4 was evaluated at this time.

In the core dRR resident exposure was only assessed for adults living near fields treated with Nemasol. No resident exposure assessment was provided for children.

The applicant therefore provided a resident exposure assessment for children in the NL national addendum on which the applicant concludes that there is no risk for residents (assessment as submitted by applicant is shown below the commenting box). The assessment is however not agreed with by NL and also appears to deviate substantially from the core assessment in term of both the exposure level used (value from the Links 2006 study) and in reference value (AOEL) used. Overall it is noted that this evaluation should have been included in the core and not in a NL national addendum as it does not concern national specific requirements.

The resident exposure as provided by the applicant was reassessed as indicated below. This evaluation was carried out by Ctgb in collaboration with the RMS (Belgium).

AOEL:
In the NL addendum the applicant uses an AOEL based on a 4-week rat inhalation study.

The proposed alternative AOEL is not agreed with by NL:
▪ In the EU assessment of metam the agreed AOEL of 0.004 mg/day based on the 90-day dog study was also agreed for the bystander/resident assessment. The reference values used for the active substance evaluation should not be deviated from for the product assessment as changes in reference values should be addressed at EU/Commission level.

The point of the different reference value was discussed with the RMS in July 2014. The RMS agreed with the position of NL that changes in reference values should be addressed via the Commission/EFSA and cannot be done for a specific product authorisation.

It is noted that in the core assessment the EU agreed AOEL based on the 90-day dog study was used and not the proposed AOEL of 0.0135 mg/kg bw/d as used in the NL addendum.

Exposure values:
For the exposure values from the Links et al. 2006 study the applicant deviates from the core assessment and uses the 75th percentile instead of the time weighted average as used in the core. This was not accepted by Ctgb for the following reasons:
▪ In the core a time weighted average of 11.8 m^3 was used. Since exposure values from exposure studies are not nationally specific these values should not differ. Although it is noted that the exact calculation of the time weight average is unclear to Ctgb.
▪ MITC levels are highly dependent on several climate and geographical conditions a.o.:
    o Soil type: A study by Simpson et al. 2010 showed that MITC volatilization is highly dependent on soil texture with loamy soil resulting in higher volatilisation than sandy soil as indicated in the figure below.</td>
</tr>
</table>

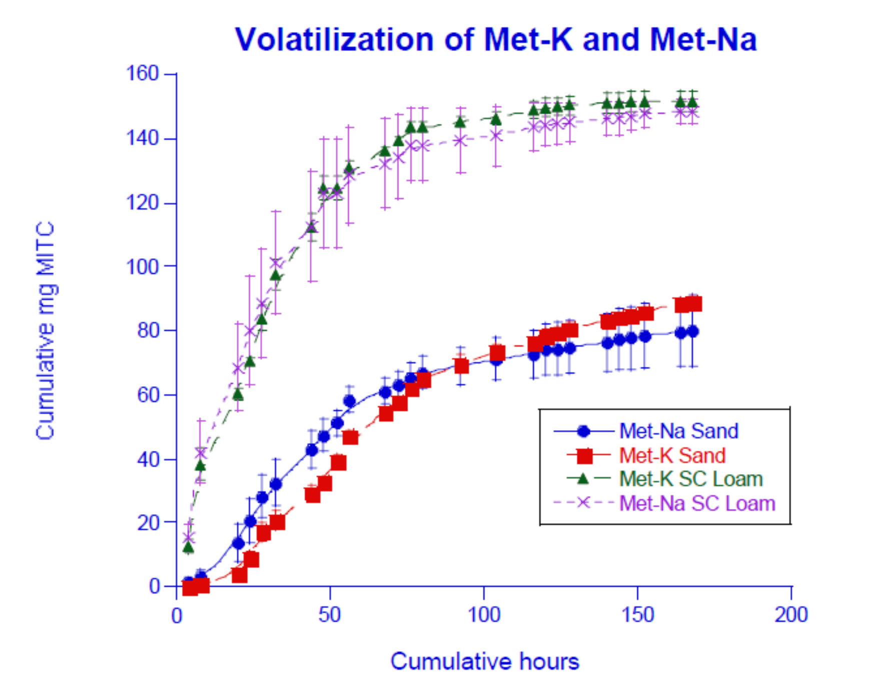

Figure 1. Cumulative volatilization of MITC by MS and MK in sandy soil vs. sandy clay loam.

- Soil moisture can significantly influence MITC volatilisation with a higher moisture content resulting in lower volatilisation as indicated in the figure below (Zheng et al. 2006).

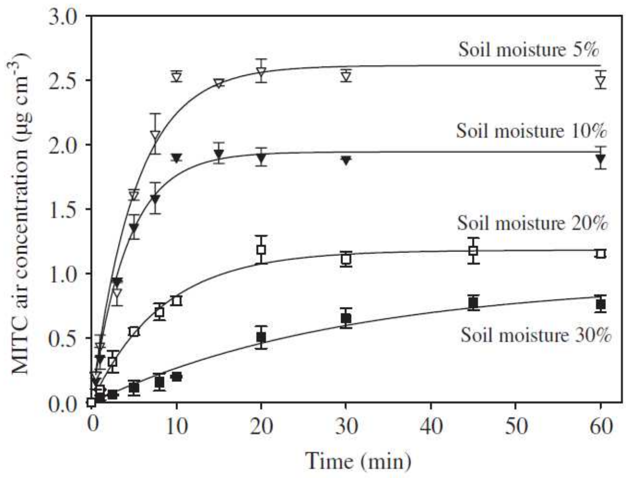

Fig. 2. The effect of soil moisture on the formation and volatilization of MITC produced from the decomposition of metam sodium (0.5 mmol kg^{-1}) in Arlington sandy loam at 21 °C. Data points are the mean of triplicate samples; error bars indicate the standard error.

- A relative high number of the individual measured air concentrations exceed the AOEL. In the most harsh estimate (EFSA model, children), and only taking into account the downwind measurements (thus disregarding the upwind data), about 73% of the samples are ≥100% of the AOEL. In this calculation, the results per location are integrated over the whole time-lapse, i.e. the 4-day continual measurement post-treatment (55 measurement points for the total of the reported 96 points in the Links study). It was also noted that using the input parameters from the EFSA Guidance all measurements at downwind locations directly bordering the field exceed the AOEL (see Appendix 4).

The study by Links et al. 2006 only show values after a single application in a single field. In the study of Links, it is not explicitly reported which was the soil composition/texture neither the water content. In the meteorological data, one deduces that the weather was moderate (about 8-18°C) with a relative air humidity of about 71-90%, wind S-SW, light to gentle breeze, indicating that the application was performed according to the GAP. The ambient air values are considered relevant for the practical cases of application.

Based on the above considerations a higher percentile than the 75th percentile could be chosen. The RMS also acknowledged that in a single study, the final choice of a relevant percentile remains speculative, and that a higher %ile could be chosen. However, the choice of a percentile, as described in the EFSA guidance relies on a comparison of a data subset with a parametrical value, which we do not have.

Regardless of the percentile used, the risk assessment (see below) shows that using the default values for body weight and breathing rate from the draft EFSA OPEX guidance lead to an exceedance of the AOEL with both the 75th and 95th percentile.

Risk assessment:

The tables below show the resident exposure assessment applying the agreed EU AOEL of 0.004 mg/kg bw/day and for the Links et al. 2006 study using the 75th as proposed by the applicant as well as the 95th percentile exposure values, the maximum value and the time weighted average exposure value as used in the core.

No default values for body weight or breathing rate are yet accepted at EU level nor in the Netherlands at national level. Therefore, for the default values for body weight and breathing rates the default values as described by Martin et al. (2008) are used. In addition, the default values from the EFSA OPEX guidance are used. Although it is recognized that this guidance is still a draft it is expected to become the EU agreed OPEX model in the near future. It is unlikely that the default values as defined in the current draft guidance will be changed in the final accepted guidance.

The main difference between the two sets of default values is that the default values from Martin et al. 2008 appear to be related to children from 2 to 5 years old (with a body weight of 16.15 kg and breathing rate of 8.31 m^3/day) while the EFSA OPEX takes children from 1 to 3 years old (with a body weight of 10 kg and breathing rate of 10.7 m^3/day) into account as worst case.

Table IIIA 7.4-3: Measurements of resident exposure to MITC and exposure assessment using the German BfR bystander and resident (adult and child) body weights and breathing rates (Martin et al. 2008)

Exposure to MITC	Resident exposure to MITC		Experimental conditions
	µg/m^3	**in µg/kg bw/day* & % AOEL**	
Soil injection – open field application			
Links *et al.*, 2006 Adult assessment	6.56	1.81 45%	75th percentile of data (n=95) taken within 100 m of the field
Links *et al.*, 2006 Child assessment		3.30 83%	
Links *et al.*, 2006 Adult assessment	13.22	3.65 91%	95th percentile of data all data points

Links *et al.*, 2006 Child assessment		**6.65** **166%**	
Links *et al.*, 2006 Adult assessment	36	**9.94** **249%**	Maximum air concentration
Links *et al.*, 2006 Child assessment		**18.11** **453%**	
Links *et al.*, 2006 Adult assessment	11.8	3.26 81%	Time weighted value taken over 1535 minutes
Links *et al.*, 2006 Child assessment		**5.94** **148%**	
Van den Berg, 1993 Adult assessment	3.1	0.86 21%	Maximum air concentration measured within 2 days of treatment. *(it is noted that in the DAR the RMS concluded this study to be less robust)*
Van den Berg, 1993 Child assessment		1.56 39%	
Soil injection – soil cultivation after application / breaking of seal			
Schepel and Dijksterhuis, 2003 Adult assessment	0.619	0.17 4%	24 hour TWA value which includes the maximum concentration measured during cultivation (8.88 µg MITC/m^3)
Schepel and Dijksterhuis, 2003 Child assessment		0.31 7%	

* Compared to the systemic AOEL of 0.004 mg/kg bw/day

Table IIIA 7.4-4: Measurements of resident exposure to MITC and exposure assessment using the EFSA (draft) guidance for resident (adult and child) body weights and breathing rates

Exposure to MITC	Resident exposure to MITC		Experimental conditions
	µg/m^3	in µg/kg bw/day* & % AOEL	
Soil injection – open field application			
Links *et al.*, 2006 Adult assessment	6.56	1.51 38%	75th percentile of data (n=95) taken within 100 m of the field
Links *et al.*, 2006 Child assessment		**7.02** **175%**	
Links *et al.*, 2006 Adult assessment	13.22	3.04 76%	95th percentile of data all data points
Links *et al.*, 2006 Child assessment		**14.15** **354%**	
Links *et al.*, 2006 Adult assessment	36	**8.28** **207%**	Maximum air concentration
Links *et al.*, 2006 Child assessment		**38.52** **963%**	
Links *et al.*, 2006	11.8	2.71	Time weighted value taken

Adult assessment		68%	over 1535 minutes
Links *et al.*, 2006 Child assessment		**12.63** **316%**	
Van den Berg, 1993 Adult assessment	3.1	0.71 18%	Maximum air concentration measured within 2 days of treatment. *(it is noted that in the DAR the RMS concluded this study to be less robust)*
Van den Berg, 1993 Child assessment		3.32 83%	
Soil injection – soil cultivation after application / breaking of seal			
Schepel and Dijksterhuis, 2003 Adult assessment	0.619	0.14 4%	24 hour TWA value which includes the maximum concentration measured during cultivation (8.88 µg MITC/m^3)
Schepel and Dijksterhuis, 2003 Child assessment		0.66 16%	

* Compared to the systemic AOEL of 0.004 mg/kg bw/day

Using the German default values for breathing rate and body weight (Martin et al. 2008) the AOEL is exceeded for children using the 95th percentile, the maximum value and the time weighted average taken over 1535 minutes from the Links et al. 2006 study. For adults the AOEL is only exceeded when the maximum exposure value used is.

Using the EFSA defaults the AOEL is exceeded for children based on the 75th percentile, 95th percentile, maximum air concentration and time weighted value taken over 1535 minutes from the Links et al. 2006 study. For adults again only the maximum exposure value results in a exposure estimate above the AOEL.

Risk mitigation

The following combination of risk mitigation measures are proposed by Ctgb to reduce exposure.

- A maximum treatment area of 1 ha with a minimum distance of 150 meters between individual treated plots.
- A bufferzone of at least 150 meters should be applied as the minimum distance between treated plots and residential and public buildings.
- Apply a Virtually Impermeable Film (VIF) cover directly after treatment for at least 14 days.
- The product should be incorporated into the soil at at least 20 cm.

A justification for the proposed risk mitigation measures is included below:

<u>Bufferzone</u>

To determine whether a bufferzone could be set that would allow a safe use of metam sodium for residents a re-evaluation was first carried out of the Links et al. 2006 study (see Appendix 4). However, it was concluded that based on the available data no reliable bufferzone could be set. The main reason no reliable bufferzone could be set is that only a limited number of individual measurement points at different distances from the field were available. Moreover, these different points were all in different directions. As a consequence the main effect that could be observed was the influence of wind directions on air concentrations.

The applicant provided two additional studies performed where metam sodium (511 g/L SL formulation) was applied via a single drip irrigation application (661 kg a.s./ha and 547 kg as/ha) under barrier film in a plastic tunnel in France and under barrier film in a greenhouse in Spain. The studies are evaluated in Appendix 5.

Although the studies concern a different type of application than the ground incorporation which is the intended use for Nemasol in the Netherlands, the exposure values found at 5 meters surrounding the plastic tunnels and greenhouse are in the range of and even slightly higher to the exposure values

	found in the Links et al. 2006 study. Therefore, it is proposed to use the greenhouse studies to get an indication of a possible bufferzone for the field application. In both studies the MITC concentration rapidly decreased in the first 50 meters from the field. Based on the study in France a bufferzone of 50 meters could be derived as the average concentration in each location nor the GM or the 75th percentile lead to an exceedance of the AOEL. Based on the study in Spain a similar bufferzone could be derived although it is noted that in one location (West) higher concentrations were found up to 80 meters. Overall it is concluded that the studies show that MITC air concentration decrease with increasing distances from the field. However, this does not completely mitigate the concern regarding the exposure values found in the Links et al. study as relatively high exposure values were also found throughout the study at a greater distance from the field. Moreover, the two exposure studies Wiseman et al. 2014a en 2014b took place in a plastic tunnel or greenhouse and the product was applied under barrier film. In addition, in the study performed in France (Wiseman 2014a) the particle size distribution of the soil showed that the soil consisted of 84% sand, 8% silt and 8% clay with a 10.2% moisture. In the study in Spain (Wiseman 2014b) the soil consisted of 93% sand, 2% silt, and 5% clay with a moisture content of 3%. As indicated previously the type of soil can influence MITC volatilization with loam soil showing higher volatilization than sandy soil. It should also be kept in mind that the total applied area is far much smaller in greenhouses (about 2700m² in the French GH and 6200m² in the Spanish GH) than in full-field (5ha=50000m²). Therefore, the RMS proposed to consider a safe use on the basis of a comparable exposure study (Thouvenin 2012a), with another MITC-generating substance Dazomet (dRR under evaluation), in a one-ha large GH, with tarping, resulting in a conservative bufferzone of 150m. If this would be extrapolable for a full-field situation with the same dose, area and tarping, the same restrictions could be proposed for a full-field situation. Although the evaluation was not finalised at the time of the present assessment, these conditions could be proposed by precaution, pending final assessment. If such a read-across would be acceptable, RMS would then propose to adopt a harmonised approach for all MITC-generating substances so far. The dazomet dossier was not submitted in the Netherlands. However, Ctgb agrees with the RMS to adopt a harmonised approach for MITC-generating substances. Therefore, a worst-case bufferzone of 150 m is proposed. <u>Area size</u> Since in the dazomet studies a safe use was only covered for the treatment of maximally one hectare, a restriction for a maximum treatment area of 1 ha. is also proposed. A 150 meter distance should be applied between treated area’s to prevent accumulation of MITC. <u>Plastic cover</u> Public literature studies indicate that the use of plastic (polyethylene film and virtually impermeable film) can reduce volatilization of MITC (Ou et al. 2006). It has been shown that virtually impermeable film (VIF) is a better barrier to reduce volatilization than polyethylene film. The table below shows the volatilization rates of MITC from the surface beds after application of 323 kg metam sodium /ha.

Table 1. Average volatilization rates of MITC from the surface of field beds after application of metam sodium by broadcast, double drip tape delivery, or single drip tape delivery systems

Application	Cover	Flux rate (g ha^{-1} min^{-1}) (time after completion of metam sodium application [hours]) 0.3	20	44	*n*
Broadcast	Bare	106.7 ± 91.0	0	0	4
Broadcast	PE	58.5 ± 37.3	1.7 ± 3.3 (5)	0	8
Broadcast	VIF	0	0	0	8
Drip, two tapes	Bare	29.5 ± 19.8	8.3 ± 5.0	0	6
Drip, two tapes	PE	10.0 ± 7.7 (1)	0	0	6
Drip, two tapes	VIF	0	0	0	6
Drip, one tape	Bare	15.3 ± 17.5 (2)	0	0	6
Drip, one tape	PE	3.5 ± 5.5 (4)	0	0	6
Drip, one tape	VIF	0	0	0	0

The beds were covered with PE, VIF, or no cover. *n* = number of surface air collection pans. Numbers in parentheses indicate number of surface air collection pans that did not have MITC.

Polyethylene covering led to a reduction in volatilization of around 50%. With virtually impermeable film MITC did not volatilize in detectable amounts from the surface.

In a similar public literature study (Papiernik et al. 2004) the use of VIF covering rather than HDPE reduced cumulative emission of MITC by 80%. A study by Goa et al. 2011 indicates that the emission-reduction potential of low-permeability tarps (e.g. VIF) is >90%.

No VIF covering period is mentioned in available literature. Based on the tunnel/greenhouse studies and the decline in MITC air concentrations found over time and after barrier removal a period of 14 days is proposed. This is similar to the results from a study performed with other soil fumigants (chloropicrin and 1,3-dichloropropone) where a tarp covering period of 10 days is recommended (Ajwa et al. 2012, abstract only).

The RMS has stated that they find the use of publically available literature data acceptable. They also noted that in the Dazomet-dossier, limited laboratory test comparing MITC flux after application of the substance on bare soil, covered with VIF (virtually impermeable film, 90% reduction) or TIF (totally impermeable film,99% reduction), also demonstrated efficient mitigation of MITC volatilisation. A cautionous approach is however appropriate, as the cited values pertain 0.5-1d post-application. Further refinement may be useful, to assess the times of break-through and conditions of accelerated break-through, such as high humidity levels, possibly enhancing leakage of MITC through a tarp.

Water seal

An alternative option to the plastic cover is the use of a water seal. The figure below shows the influence of a water seal on MITC volatilization (Nelson et al. 2012) which was determined in a laboratory scale study.

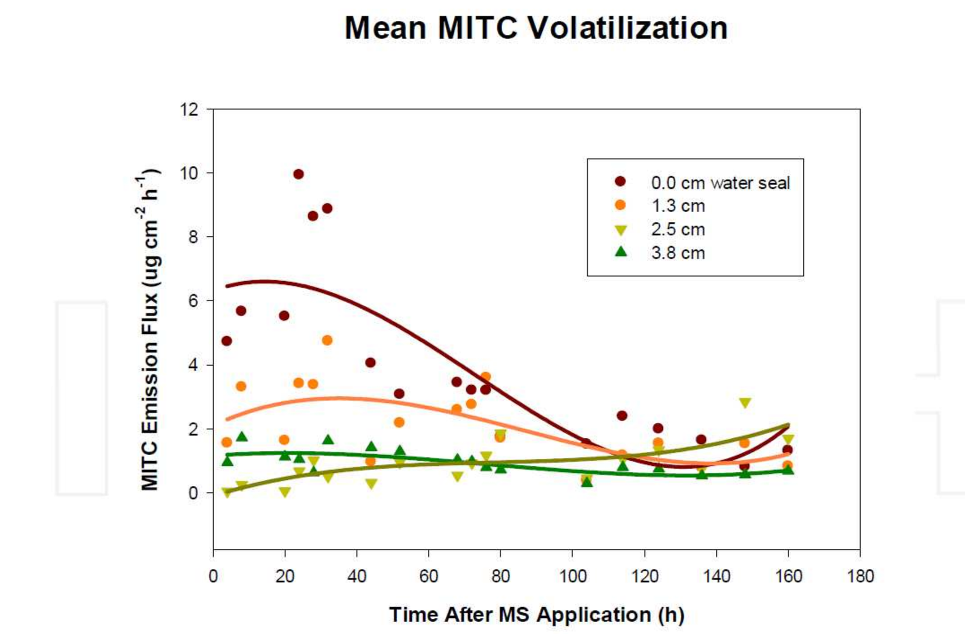

Fig. 5. The mount of MITC volatilized and captured on charcoal filters over time. Data represents mean of three replicates per water seal treatment.

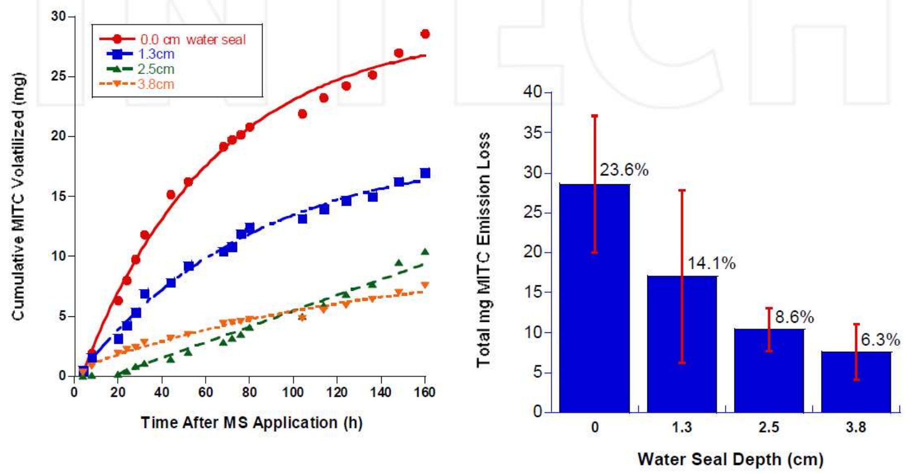

Fig. 6a. Mean MITC emitted from soil columns. Fig. 6b. MITC release ± std error mean.

Fig. 6. Total cumulative MITC evolved from soil columns as captured on charcoal filters.

MITC volatilisation showed a clear decrease as a consequence of the use of a water seal. The lowest amount of MITC flux observed occurred from both the 2.5 cm and 3.8 cm water seal treatment although to a lower extent than VIF covering does. It is noted that in the study it was concluded that on-farm field investigations are needed to back up the laboratory findings to confirm the results. Therefore, the option of VIF covering is preferred over the use of a water seal.

A study by Gao et al. 2011 has also indicated that water seal covering is less efficient in reducing emission from soil fumigants than VIF covering (20-50% versus 90%). In the same study it is also noted that water treatment may reduce efficacy (see table below).

TABLE 1. Emission-reduction potential and cost estimates for surface sealing/treatments to reduce emissions from soil fumigation

Soil-surface treatment	Emission-reduction potential	Cost (excluding fumigant)	Other considerations
Bare soil	Reference level, often > 60% of total applied fumigant emissions	Not estimated for field preparations such as disking and compaction	
HDPE tarp	Up to 50%, depending on soil moisture and temperature	HDPE: $950–$1,100 per acre (materials, ~ $500; glue, $100; application, $350; cutting and removal, $100)	Effective in relatively moist soils
Low-permeability tarps (e.g., VIF)	> 90%, if tarp is installed successfully	VIF: $1,200–$1,600 per acre, assuming material cost is 1.5 to 2 times HDPE, and other costs similar to HDPE	Effective in almost all conditions; unclear time needed for safe tarp removal
Water treatment	20%–50%, depending on water amount and number of applications	< $300 per acre, depending on water price and whether grower owns or rents sprinkler system	May reduce efficacy at surface soil, requiring double treatments in sequence
Chemicals (e.g., thiosulfate)	> 50%	Fumigant-to-thiosulfate active ingredient ratio of 1:1 to 1:2, at $150–$300 per acre	Oversupply of nutrients to soil, post-treatment odor and potential soil-property changes
Composted manure	Inconclusive	Depends on application rate and material costs; commercial composted manure is $15–$30 per ton	Improves soil properties; consider when free or low-cost materials are available

Other

The label currently states that the product should be incorporated in the soil at a depth of at least 10cm. In the available exposure studies in the DAR metam-sodium was incorporated in the soil at depths of at least 20cm. The depth of incorporation into the soil should therefore be changed to at least 20cm.

The RMS has stated that they agree with this point, although it was noted that the use of soil incorporation depth seems to be dependent on the intended use (5cm in tomato, undefined depth during drip irrigation, 25cm in potato,…).

Conclusion

MITC volatilisation is known to be highly dependent on environmental condition such as soil type and moisture of the soil. Based on the available study relevant for resident (Links et al. 2006) no safe use could be concluded for children living near fields treated with Nemasol without the use of further mitigating measures.

The Links study was considered unsuitable to derive risk mitigating measures such as a bufferzone due to a limited number of individual measurement points.

One the one hand, based on two newly submitted tunnel/greenhouse study, a bufferzone of 50 meters could be set.

However,

(i) The data are extracted from studies with an application on 2700-6200m², i.e. 8-19× lower than the field-study (Links et al. 2006, 5 ha). Whereas such a buffer-zone could be acceptable in the case of the greenhouse-studies, it is unclear whether this is extrapolable for an application on a much higher surface.

(ii) Such a measure does also not completely mitigate the concern from the field study (Links et al. 2006) because the two studies use a different type of application, under a barrier film and in sandy soil.

Therefore, further risk mitigating measures are considered necessary. A read-across, taking into account a greenhouse study on a similar MITC-generating compound Dazomet, indicates that a safe use could be considered if a buffer zone of 150m would be imposed around a treated field or greenhouse, and in the presence of a tarp of minimally VIF-standard, or even TIF-standard. In the latter study, an acceptable use was only covered for the treatment of maximally one hectare. As there is some margin of exposure for bystanders in the Metam greenhouse studies overall, it is proposed to fix a limitation for all treated areas, both open field and greenhouse, to one hectare with 150 meters between treated fields.

Finally, it was noted that the incorporation depth of 10 cm currently stated on the label is not supported by the available exposure studies. The product should be incorporated into the soil at at least 20 cm.

Based on the assessment the following combination of risk mitigation measures is proposed to

	reduce exposure. - A maximum treatment area of 1 ha with a minimum distance of 150 meters between individual treated plots. - A bufferzone of at least 150 meters should be applied as the minimum distance between treated plots and residential and public buildings. - Apply a Virtually Impermeable Film (VIF) cover directly after treatment for at least 14 days. - The product should be incorporated into the soil at at least 20 cm.