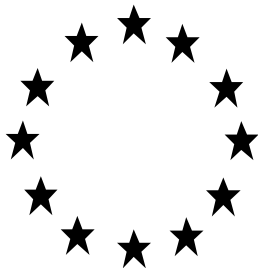
Directive 98/8/EC concerning the placing biocidal products on the market

Inclusion of active substances in Annex I or IA to Directive 98/8/EC

Assessment Report



Spinosad

Product-type 18 (insecticides, acaricides and products to control other arthropods)

May 27, 2010

Annex I- NL

Spinosad (PT 18)

Assessment report

Finalised in the Standing Committee on Biocidal Products at its meeting on May 27, 2010 in view of its inclusion in Annex I to Directive 98/8/EC

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Procedure followed

This assessment report has been established as a result of the evaluation of Spinosad as product-type 18 (insecticides, acaricides and products to control other arthropods), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market[1], with a view to the possible inclusion of this substance into Annex I or IA to the Directive.

Spinosad (CAS no. 168316-95-8) was notified as an existing active substance, by DOW AGROSCIENCES B.V., hereafter referred to as the applicant, in product-type **18**.

Commission Regulation (EC) No 1451/2007 of 4 November 2003[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, The Netherlands was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for Spinosad as an active substance in Product Type 18 was 30 April 2006, in accordance with Annex V of Regulation (EC) No 1451/2007.

On 27 March 2006 NL competent authorities received a dossier from the applicant. The Rapporteur Member State accepted the dossier as complete for the purpose of the evaluation on 22 May 2006.

On 26 March 2008, the Rapporteur Member State submitted, in accordance with the provisions of Article 14(4) and (6) of Regulation (EC) No 1451/2007, to the Commission and the applicant a copy of the evaluation report, hereafter referred to as the competent authority report. The Commission made the report available to all Member States by electronic means on 9 April 2008. The competent authority report included a recommendation for the inclusion of Spinosad in Annex I to the Directive for product-type **18**.

In accordance with Article 16 of Regulation (EC) No 1451/2007, the Commission made the competent authority report publicly available by electronic means on 9 April 2008. This report did not include such information that was to be treated as confidential in accordance with Article 19 of Directive 98/8/EC.

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the

1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

2 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

Commission. Revisions agreed upon were presented at technical and competent authority meetings and the competent authority report was amended accordingly.

On the basis of the final competent authority report, the Commission proposed the inclusion of Spinosad in Annex I to Directive 98/8/EC and consulted the Standing Committee on Biocidal Product on May 27, 2010.

In accordance with Article 15(4) of Regulation (EC) No 1451/2007, the present assessment report contains the conclusions of the Standing Committee on Biocidal Products, as finalised during its meeting held on May 27, 2010.

1.2. Purpose of the assessment report

This assessment report has been developed and finalised in support of the decision to include Spinosad in Annex I to Directive 98/8/EC for product-type **18**. The aim of the assessment report is to facilitate the authorisation in Member States of individual biocidal products in product-type **18** that contain Spinosad. In their evaluation, Member States shall apply the provisions of Directive 98/8/EC, in particular the provisions of Article 5 as well as the common principles laid down in Annex VI.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report, which is available at the Commission website[3], shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Directive 98/8/EC, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1.3. Overall conclusion in the context of Directive 98/8/EC

The overall conclusion from the evaluation is that it may be expected that there are products containing Spinosad for the product-type **18**, which will fulfil the requirements laid down in Article 5 of Directive 98/8/EC. This conclusion is however subject to:

i. compliance with the particular requirements in the following sections of this assessment report,

ii. the implementation of the provisions of Article 5(1) of Directive 98/8/EC, and

iii. the common principles laid down in Annex VI to Directive 98/8/EC.

Furthermore, these conclusions were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Article 5(1) and of the common principles laid down in Annex VI to Directive 98/8/EC.

3 http://ec.europa.eu/comm/environment/biocides/index.htm

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

Spinosad (ISO, ANSI) is a naturally derived fermentation product containing a mixture of two structurally similar molecules which are both active insecticidally and have been designated spinosyn A and spinosyn D. Spinosyn A and spinosyn D may also be referred to as factor A and factor D.

CAS-No	Spinosad	168316-95-8,
	Spinosyn A	131929-60-7
	Spinosyn D	131929-63-0
EINECS-No.	ELINCS: 434-300-1 (spinosad)	
CIPAC- No	Spinosad	636
	Spinosyn A	none
	Spinosyn D	none

The minimum purity of the technical material is 85% (w/w) spinosad. Spinosad typically contains spinosyn A and spinosyn D in a ratio of 85:15 (w/w) and a range between 95:5 (w/w) and 50:50 (w/w).

The current specification of the active substance spinosad is not set according to the *Guidance for identification and naming of substances in REACH*. This issue was discussed in TMIV08 and it was decided that the current specification can be maintained.

The natural fermentation process for production of the spinosad technical material produces several impurities in the technical material, which are structurally similar to spinosyn A and spinosyn D. Because of their low concentration level and their expected similar (eco)toxicity to spinosyn A and D, these impurities are considered not (eco)toxicologically relevant in the technical material.

Spinosad (minimum purity 85% w/w) is a light-grey white solid with a slightly stale water-like or dusty chalk-like odour. The relative density was determined as 1.1866 at 20 °C. Spinosad decomposes at a temperature above 400 °C and thermal degradation products include carbon dioxide, methyl formate, acetaldehyde, and various sugar fragments of the spinosad molecule. Spinosad is not classified as flammable, autoflammable, explosive or oxidising.

In addition, studies have been conducted on the pure active substances spinosyn A and D. Spinosyn A and D are solids with a paint, fish-, and wax-like odour for A and bitter paint- and aspirin-like odour for D. The melting point ranges from 84.0 to 99.5 °C for A and 161.5 to 170.0 °C for D. The relative density at 20 °C is 1.1244 for A and 1.1686 for D. The vapour pressure is low for both isomers (< 10^{-5} Pa at ambient temperature): $3x10^{-8}$ Pa for spinosyn A and $2x10^{-8}$ Pa for spinosyn D at 25 ^{o}C. The water solubility and the partition coefficient depend

on pH. Spinosyn A is moderately soluble in water (290-235-16 mg/L at pH 5, 7, 9 at 20 °C) while Spinosyn D is slightly soluble in water (28.7-0.33-0.053 mg/L at pH 5, 7, 9 at 20 °C). The partition coefficient log K_{ow} at 20 °C is 2.78-4.01-5.16 at pH 5, 7, 9 for spinosyn A and 3.23-4.53-5.21 for spinosyn D. Log K_{ow} values above 4 at pH 7 or higher indicate that bio-accumulation can occur. Spinosyn A and D are weak bases. The dissociation constant pK_a at 20 °C is 8.10 for protonated spinosyn A and 7.87 for protonated spinosyn D. The surface tension for spinosyn A is 41.5 mN/m.

The methods of analysis of active substance as manufactured and for determination of impurities of toxicological, ecotoxicological or environmental concern or which are present at quantities > 0.1 g/kg in the active substance as manufactured have been validated and shown to be sufficiently specific, linear, accurate and precise, and the methods for analysis in environmental matrices, as appropriate for the assessed uses have been validated and shown to be sufficiently sensitive with respect to the levels of concern.

2.1.2. Intended Uses and Efficacy

Spinosad is an active substance for use in product-type PT 18 (insecticides, acaricides and products to control other arthropods). Spinosad contains a mixture of two structurally similar molecules which are both active.

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against the target organism(s) and the evaluation of the summary data provided in support of the efficacy of the accompanying product, establishes that the product may be expected to be efficacious.

In addition, in order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the intended uses of the substance, as identified during the evaluation process, are listed in Appendix II.

2.1.3. Classification and Labelling

Classification	as in Directive 67/548/EEC
Class of danger	N – Dangerous for the environment 
R phrases	R50/53 – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S phrases	S60 – This material and its container must be disposed of as hazardous waste. S61 – Avoid release to the environment. Refer to special instructions/safety data sheets.

For environmental hazards specific concentration limits are set: C ≥ 2,5 %: N; R50/53 0,25 % ≤ C < 2,5 %: N; R51/53 0,025 % ≤ C < 0,25 %: R52/53

Justification for classification and labelling of spinosad technical

N	Triggered by R50/53
R50/53	Triggered by study results (With the EC50 for algae being ≤ 1 mg/L, the log Pow ≥ 3 and the experimentally determined BCF > 100 L/kg, spinosad should be labelled with R50/R53.
S60	Applies to all dangerous substances and preparations. Recommended for substances and preparations not likely to be used by the general public and where S35 is not assigned.
S61	Applies to substances and preparations dangerous for the environment.

Classification	(EC) No 1272/2008
GHS pictogram 	GHS09
Signal word	Warning
Hazard class and category	Aquatic acute 1 Aquatic chronic 1
Hazard statement	H400 H410
M-factor M=10	

2.2. Summary of the Risk Assessment

2.2.1. Human Health Risk Assessment

2.2.1.1. Hazard identification and effect assessment

Oral absorption of spinosad is rapid, and is assumed to be 50%. For the inhalation route 100% absorption is assumed. Dermal absorption of spinosad is low. For concentrated and diluted product dermal absorption values of respectively 0.1% and 2% are assumed. After oral administration spinosad is widely distributed in the body and rapidly excreted, predominantly in the faeces . It is noted that spinosad is extensively excreted in the bile. Metabolism is probably similar for both spinosyn A and D. The metabolites found in faeces were cysteine and glutathione conjugates. Other metabolites detected in faeces, urine and bile were: the glutathione conjugate of spinosyn A and D, and N-and/or O-demethylated spinosyn A and D with or without glutathione conjugation.

The acute oral, dermal and inhalation toxicity of spinosad is low (oral LD50 >2000 mg/kg bw, dermal LD50 >5000 mg/kg bw, inhalation LC50 >5.18 mg/L). Spinosad is not irritating to the skin and eyes and is not a skin sensitizer in a maximisation test.

The toxicological data base indicates that the critical toxicological endpoint for spinosad is the induction of vacuolation. This effect is observed in various tissues in mice, rats and dogs after oral administration in medium-term and long-term toxicity studies. There is no severe necrosis or organ dysfunction. As a consequence, classification with R48/22 is not necessary. The overall NOAEL for medium-term administration is 4.89 mg/kg bw/d, observed in a 90-day study in dogs. The overall NOAEL for long-term administration is 2.4 mg/kg bw/d, observed in a 2-year study in rats. The toxicity after repeated dermal administration is low, with an overall NOAEL of 1000 mg/kg bw/day. There is no evidence of a genotoxic potential of spinosad, and spinosad is unlikely to pose a carcinogenic risk. In a 2-generation reproductive toxicity study in rats, the NOAELs for parental, developmental and reproductive effects were set at 10 mg/kg bw/d. At the next higher dose level (100 mg/kg bw/day), parental effects noted were a decreased feed consumption and body weight, increased incidences of vaginal bleeding, dystocia and mortality during the lactation phase (females only), increased organ weights and histologic alterations (including vacuolation) in several organs. The developmental effects were decreases in gestation survival, litter size, pup weights and neonatal survival. Reproductive toxicity (dystocia, vaginal bleeding and decreased litter size) was observed in the presence of parental toxicity. The NOAEL for reproductive toxicity was 10 mg/kg bw/day. There is no evidence that spinosad induces developmental/teratogenic effects or neurotoxicity.

Overall NOAEL

The toxicological data base indicates that the critical toxicological endpoint for spinosad is the induction of vacuolation. This effect is observed in various tissues in mice, rats and dogs after oral administration in medium-term and long-term toxicity studies. The overall NOAEL for medium-term administration is 4.89 mg/kg bw/d, observed in a 90-day study in dogs. The overall NOAEL for long-term administration is 2.4 mg/kg bw/d, observed in a 2-year study in rats.

ADI (acceptable daily intake) and ARfD (acute reference dose).

ADI (acceptable daily intake)

No human epidemiological data, volunteer studies or case studies are available which allow the establishment of an acceptable daily intake (ADI) for spinosad. The ADI has therefore to be derived from the results of toxicity studies with experimental animals. The calculation of the ADI is based on the highest dose at which no adverse effect is observed in the most appropriate study in the most sensitive species. Spinosad was tested in several acute, medium-, and long-term toxicity studies in dogs, rats, and mice, providing the basis for the establishment of the ADI. Levels obtained in the neurotoxicity, reproduction, and teratogenicity studies were not critical for determining the overall NOAEL.

The lowest NOAEL (2.4 mg/kg bw/day) was obtained from an 24-month oral toxicity study in rats. This NOAEL is used as a starting point for the establishment of the ADI. Application of a safety factor for inter- and intraspecies differences of 100, results in an ADI of 0.024 mg/kg bw/day.

ARfD (acute reference dose)

Spinosad doesn't induce effects in acute oral toxicity studies at doses of 2000 mg/kgbw/day or higher, doesnot induce acute effects in repeated dose studies, has no embryo, foetus or developmental or teratogenic effects without maternal toxicity and has no effects in the acute oral neurotoxicity study. Although acute exposure scenarios are possible, derivation of an ARfD is not necessary based on the toxicological properties of the substance. Therefore, it can be concluded that there is no concern with regard to the acute oral intake of spinosad by consumers.

Drinking water limit

According to Council Directive 97/57/EC, exposure to spinosad through the drinking water should account for not more than 10% of the ADI. If it is assumed that the average daily consumption of water amounts to 2 liter per person of 60 kilogram, a drinking water limit of ((60x0.024)/10)/2 mg/L, i.e. 0.072 mg/L can be established.

According to Document 8064/VI/79 of the European Commission, the EU drinking water limit for pesticides of 0.1µg/L is applicable for spinosad.

AEL (acceptable exposure level)

SpY® (GF-739) will only be used by the professional farmer in animal housing. SpY® is not intended to be used by non-professionals. The use pattern indicates medium-term exposure of the professional user. Therefore a medium-term AEL is established. The AEL for medium-term exposure is based on the NOAEL of 4.89 mg/kg bw/day from oral the 90-day study in the dog, being the lowest relevant NAEL from medium-term oral toxicity studies. For establishment of an internal AEL according to the method used by the ECCO, a safety factor of 100 is used. For correction of incomplete oral absorption a factor of 0.5 is used. This results in an internal systemic medium-term AEL of 0.024 mg/kg bw/day .

Although a long-term AEL is not used in the risk assessment a long-term AEL is established. The lowest NOAEL (2.4 mg/kg bw/day) was obtained from an 24-month oral toxicity study in rats. A safety factor of 100 is used. For correction of incomplete oral absorption a factor of 0.5 is used. This results in an internal systemic long-term AEL of 0.012 mg/kg bw/day.

Although acute exposure scenarios are possible, derivation of an acute AEL is not necessary based on the toxicological properties of the substance. Therefore, it can be concluded that there is no concern with regard to acute exposure by primary exposure and indirect exposure.

MOE (margin of exposure)

SpY® (GF-739) will only be used by the professional farmer in animal housing. SpY® is not intended to be used by non-professionals. The use pattern indicates medium-term exposure of the professional user. Therefore the MOE will be based on the overall systemic NOAEL for short-term exposure. For reasons explained under the paragraph on the AEL, an oral study is used as starting point.

The MOE for medium-term exposure is based on the NOAEL of 4.89 mg/kg bw/day from oral the 90-day study in the dog, being the lowest relevant NOAEL from short-term oral toxicity studies. For correction of incomplete oral absorption a factor of 0.5 is used. Thus, a NOAELsystemic of 2.4 mg/kg bw/day will be used in the risk evaluation for the professional user.

For the risk assessment of spinosad for the professional user a MOE of ≥ 100 is considered acceptable, on the basis of the standard assessment factors of 100 (10 x 10) for the interspecies and intraspecies variability.

2.2.1.2. Exposure assessment and risk characterisation

Professional users

AEL approach

The medium-term exposure and risk assessment for professional users as a result of the use of spinosad is summarised in Table 1 for the AEL approach.

Table 1. Internal medium-term exposures and risk assessment of spinosad for professional users

Route	Estimated internal exposure (mg as/kg bw.d)		AEL-systemic (mg as/kg bw.d)	Risk-index (% of AEL)	
	without PPE	with PPE		without PPE	with PPE
Scattering					
Inhalation	0.0024	0.00024	0.024	10	1
Dermal	0.0013	0.00022	0.024	5	1
Total	0.0037	0.00046	0.024	15	2
Bait stations and trays					
Inhalation	< 0.0024	< 0.00024	0.024	< 10	< 1
Dermal	< 0.0013	< 0.00022	0.024	< 5	< 1
Total	< 0.0037	< 0.00046	0.024	< 15	< 2
Hang- boards / cards					
Inhalation	< 0.0024	< 0.00024	0.024	< 10	< 1
Dermal	< 0.0013	< 0.00022	0.024	< 5	< 1
Total	< 0.0037	< 0.00046	0.024	< 15	< 2
Spraying					
Inhalation	0.010	0.0010	0.024	42	4
Dermal	0.062	0.0037	0.024	258	15
Total	0.072	0.0048	0.024	300	20
Brushing					
Inhalation	0.0019	0.00019	0.024	8	1

Route	Estimated internal exposure (mg as/kg bw.d)		AEL-systemic (mg as/kg bw.d)	Risk-index (% of AEL)	
	without PPE	with PPE		without PPE	with PPE
Dermal	0.0098	0.00085	0.024	41	3
Total	0.0117	0.00104	0.024	49	4

It can be concluded that adverse health effects for the unprotected professional user due to the spraying application cannot be excluded (risk indices >100). The internal exposure due to the spraying application is to a large extent the result of dermal exposure. If adequate PPE is used no adverse health effects due to spray application are expected. It should further be noted that the professional user will probably apply spinosad intermittently, and not at a daily basis. Therefore, the calculated risks may be considered conservative.

Adverse health effects for the unprotected professional user, due to scattering, brushing or the use of the product on bait stations and trays or hang-boards are not expected.

MOE approach

The medium-term exposure and risk assessment for professional users as a result of the use of spinosad is summarised in Table 2 for the MOE approach.

Table 2. Internal medium-term exposures and risk assessment of spinosad for professional users

Route	Estimated internal exposure (mg as/kg bw.d)		NOAEL-systemic (mg as/kg bw.d)	MOE	
	without PPE	with PPE		without PPE	with PPE
Scattering					
Inhalation	0.0024	0.00024	2.4	1000	10000
Dermal	0.0013	0.00022	2.4	1846	10909
Total	0.0037	0.00046	2.4	649	5217
Bait stations and trays					
Inhalation	< 0.0024	< 0.00024	2.4	>1000	>10000
Dermal	< 0.0013	< 0.00022	2.4	>1846	>10909
Total	< 0.0037	< 0.00046	2.4	>649	>5217
Hang- boards / cards					
Inhalation	< 0.0024	< 0.00024	2.4	>1000	>10000
Dermal	< 0.0013	< 0.00022	2.4	>1846	>10909
Total	< 0.0037	< 0.00046	2.4	>649	>5217
Spraying					
Inhalation	0.010	0.0010	2.4	240	2400
Dermal	0.062	0.0037	2.4	39	649
Total	0.072	0.0048	2.4	33	500
Brushing					
Inhalation	0.0019	0.00019	2.4	1263	12632
Dermal	0.0098	0.00085	2.4	245	2824
Total	0.0117	0.00104	2.4	205	2308

It can be concluded that adverse health effects for the unprotected professional user due to the spraying application cannot be excluded (MOE < 100). The internal exposure due to the spraying application is to a large extent the result of dermal exposure. If adequate PPE is used

no adverse health effects due to spray application are expected. It should further be noted that the professional user will probable apply spinosad intermittently, and not at a daily basis. Therefore, the calculated risks may be considered conservative.

Adverse health effects for the unprotected professional user, due to scattering, brushing or the use of the product on bait stations and trays or hang-boards are not expected.

Non-professional users

SpY® (GF-739) will only be used by the professional farmer in animal housing. SpY® is not intended to be used by non-professionals. Therefore, a risk assessment for the non-professional user is not performed.

Indirect exposure as a result of use

Indirect exposure through contact or accidental oral ingestion of granules

Indirect exposure can occur through contact with a treated area, with subsequent hand-to mouth contact, or through accidental oral ingestion of granules. Both scenarios will mainly concern children.

Thus, as a worst case scenario the risk of indirect exposure is estimated for a child of 3.5 years of age. The use pattern indicates medium-term exposure through hand-to-mouth contact or non-dietary ingestion. Therefore the use of a medium-term AEL or medium-term NOAEL (MOE approach) for the risk assessment is considered appropriate.

AEL approach

The internal exposure and risk assessment of spinosad due to indirect exposure is summarised in Table 3. for the AEL approach.

Table 3. Internal exposures and risk assessment of spinosad due to indirect exposure.

	Estimated internal exposure (mg as/kg bw.d)	AEL-systemic (mg as/kg bw.d)	Risk-index (% of AEL)
Contact with treated area			
Dermal	0.00025	0.024	1
Oral	0.014	0.024	58
Total	0.014	0.024	58
Accidental oral ingestion			
Oral	0.106	0.024	442
Total	0.106	0.024	442

It can be concluded that adverse health effect due to accidental oral ingestion of granules by children cannot be excluded (risk index >100). It must therefore be clearly stated on the product label that the granules should be applied out of reach of children. Furthermore, this

risk of ingestion by children is further reduced by the addition of an aversive agent. Adverse health effects due to contact with a treated area is not expected.

MOE approach

The internal exposure and risk assessment of spinosad due to indirect exposure is summarised in Table 4. for the MOE approach.

Table 4. Internal exposures and risk assessment of spinosad due to indirect exposure.

	Estimated internal exposure (mg as/kg bw.d)	NOAEL-systemic (mg as/kg bw.d)	MOE
Contact with treated area			
Dermal	0.00025	2.4	9600
Oral	0.014	2.4	171
Total	0.014	2.4	171
Non-dietary ingestion			
Oral	0.106	2.4	23
Total	0.106	2.4	23

It can be concluded that adverse health effect due to accidental oral ingestion of granules by children cannot be excluded (MOE < 100). It must therefore be clearly stated on the product label that the granules should be applied of reach of children. Furthermore, this risk of ingestion by children is minimised by the addition of adversive agent. Adverse health effects due to contact with a treated area are not expected.

Human exposure via consumption of spinosad containing food

The product GF-739 will be applied out of reach of food or feed and therefore does not leave a residue in plant commodities for human consumption. Although some authorised national labels state that the bait has to be applied away from where the animals can reach them, no restrictions in use have been indicated in the intended use as agreed upon between RMS and applicant (dated 15 January 2007). This means that livestock can be exposed to spinosad and that humans can be exposed indirectly by consumption of animal products containing spinosad residues.

In TMIV-08 it was decided that the CAR would be amended to indicate that it may be necessary to include the biocide use of spinosad in the MRLs context. The CAR elements on potential residues and MRLs coming from the pesticide dossier will be presented on an informative basis. The dietary risk assessment proposal made by NL will be kept in the CAR, together with a statement that it may need revision at a later stage, following methodological developments.

Therefore, RMS presents the residue part in the CAR as a reasonable worst case approach using basic pesticide data, because the methodology for the setting of MRLs for biocides has

to be developed. The proposed dietary risk assessment can be seen as a basis for refining our methods. Consequently, no MRL proposals are presented in the body of the CAR.

Decisions on food residues and MRLs taking into account the possible use of spinosad as a biocide will have to be made at a later stage. The RMS would like to add a provision that this part of the CAR may need revision when more specific tools will be available.

The European commission has recently made an inventory of existing national MRLs in EU MS for substances used for PPP. This resulted in temporary MRLs (tMRLs), which are listed on Annex III of Regulation (EC) 396/2005.

An acute dietary exposure assessment is not performed, because no ARfD is considered necessary.

The tMRLs were used as input for consumer risk assessment for chronic dietary intake using the EFSA Pesticide Residue Intake (PRIMo) Model rev. 2., in which all national EU diets are incorporated.

When using the tMRLs of spinosad from Regulation (EC) 396/2005, the conversion factor for liver and egg for poultry products and the PRIMo Model, for the Total Mean Daily Intake (TMDI) calculation the ADI is used for 182.8%, maximally, for the NL children (1-6y). Assuming that the STMR values are 50% of the MRL maximally, the refined Estimated Daily Intake (EDI) calculation shows that 91.4% of the ADI is used maximally for the NL children (1-6y). All other national diets use less of the ADI.

If only the use as a biocide is taken into account, the contribution of the tMRLs of animal products (ruminant products, poultry products) alone, the TMDI calculation is 86.9% of the ADI, maximally, for FR toddlers (refinement is not necessary). In all other national diets the tMRLs for animal products alone use less of the ADI.

No risk is currently expected taking into account the use of spinosad as a biocide and/or as a plant protection product.

2.2.2. Environmental Risk Assessment

2.2.2.1. Fate and distribution in the environment

Spinosyn A and D have shown to be hydrolytically stable. Aqueous photolysis studies with spinosyn A and D show that both compounds are susceptible to photolysis. In a ready biodegradation test, neglible degradation of spinosad was observed, classifying spinosad as not readily biodegradable. In an aerobic water-sediment study the distribution of the parent was dominated by sorption. At the end of the experiment (120 days), the major part of the radioactivity was in the sediment, and was mainly extractable. Spinosyn A accounted for 59 % of AR in sediment (max. 68.8 % after 39 d) and 7.2 % of AR in water. Corresponding values for spinosyn D were 51.3 % in sediment (max. 61.7 % after 58 d) and 3.8 % in water. No metabolites > 10 % of AR were found in the water phase, metabolites in sediment were spinosyn B (9 %) and N-demethylated spinosyn D (10 %). Bound residues were 21 and 42 % of AR in the test with spinosyn A and D, respectively. A maximum of 0.3% CO_2 was formed. The geometric means for the $DT_{50,water}$ (dissipation) and the $DT_{50,system}$ at 20 ºC were 19.9 and

145 days, respectively, corresponding to 37 and 270 days at 12 ºC. In an anaerobic water/sediment study Spinosyn A and D dissipated quickly from the water phase. DT_{50} values (20°C) for the whole system were 357 and 661 days for spinosyn A and D, respectively, corresponding to 646 and 1197 days at 12°C. Mineralisation was 0.3% and 1.9% of AR for spinosyn A and D respectively. Bound residue was maximal at the end of the test (364 days) and amounted 16 and 17% of AR for spinosyn A and D respectively.

Soil photolysis was tested under sunlight, in air-dried and moisturised soil. In air-dried soil, spinosyn A was photolysed with a DT_{50} of 74 days; in moisturised soil with a DT_{50} of 13 days. Photolysis of spinosyn D was only tested with air-dried soil; the DT_{50} was 42 days.

In an aerobic biodegradation study, maintained in the dark, both spinosyn A and D are rapidly N-demethylated. The geometric mean DT_{50} for spinosyn A and D was 25 and 37 days, respectively, at 12° C and 47 and 69 days, respectively, when expressed to the average EU outdoor temperature of 12 ºC. The main metabolite of spinosyn A was spinosyn B, which was detected in all available studies, at maximum percentages ranging from 39 to 67% of AR after 28 to 182 days. The main metabolite of spinosyn D was N-demethylated spinosyn D, which was detected in all available studies, at maximum percentages ranging from 28 to 68% of AR after 28 to 237 days. No other metabolites were detected at levels of > 10% of AR. Where possible, DT_{50} values were calculated. DT_{50} (20 °C) values for spinosyn B were 157 (DT_{50} 12° C = 284) and 194 (DT_{50} 12° C = 351) days, and for N-demethylated spinosyn D a DT_{50}(20 °C) value of 531 (DT_{50} 12° C = 962) days was found. Mineralisation was at most 6.3 % after 81 – 91 d for spinosyn A and 1.3 – 8.7 % for spinosyn D, bound residues were 8.1 – 39 % and 12 – 33 % of AR, respectively.

An outdoor field study, using locations in the UK, Italy, Northern and Southern France was carried out. Only the data for the UK soil are considered reliable (DT_{50}: 2.37, 3.51, 2.11 and 3.77 days for spinosyn A, D, B and N-demethylated spinosyn D, respectively).

The arithmetic mean Kp_{soil} of spinosyn A is 137.6 L/kg. In line with the conclusions reached during the pesticide assessment in the framework of Directive 91/414, this value is assumed to be valid for spinosyn D as well. The arithmetic mean Kp_{soil} of spinosyn B is 51.4 L/kg, which is assumed to be valid also for N-demethylated spinosyn D. The Kp_{soil} is used for the calculation of the $PEC_{sed,}$ $PEC_{porewater}$ and $PNEC_{soil}$ which are all based on equilibrium partitioning.

Adsorption studies with radiolabelled spinosyn A and its main metabolite spinosyn B, on a range of five and four soils respectively, showed a correlation of K_F values with clay content. Since sorption of spinosad is related to the clay content of the soil, and not to the organic matter content, a K_{clay} was calculated instead of a K_{oc} by normalising the KF to clay content instead of organic carbon content.

This K_{clay} was then corrected by the ratio between organic carbon and clay content as defined in the leaching model PEARL 3.3.3, to derive a pseudo-K_{om} as estimate of the sorption to organic carbon. This pseudo-K_{om} is thus typical for the standard soils in that leaching model. This method is used to estimate the PEC_{grw} applying PEARL 3.3.3 (see Doc IIB, Section 3.3.2.3), and as a complementary approach to the calculation of pore water concentrations.

Predicted Environmental Concentrations (PEC) for soil, groundwater and surface water were calculated according to the OECD Emissions Scenario Document (ESD) for Insecticides for Stables and Manure Storage Systems (OECD, 2006). The ESD assumes that emission of the

active substance after application in animal housing occurs mainly via manure and waste water (STP). The fractions of the active substance that are emitted to those streams are determined by the type of pest, the type of product, the way of application of the product, and the type of housing and manure storage system.

The ESD distinguishes between 18 types of animal housing or stables. Each type has its own characteristics with respect to size, number of animals and fractions of the active substance that are emitted via manure and/or waste water. All available housing types were included in the present calculations, because it could not be decided beforehand which type would yield the highest PEC in the different compartments. Besides, considering all stable types makes it possible to define restrictive measures per animal or stable type in case a potential risk is identified.

As stated above, part of the active substance will reach the environment via application of manure to agricultural soil. The amount of manure that may be applied to arable soil or grassland is determined by the storage time of the manure and the legal standard on nitrogen. After application of manure to the soil, incorporation is assumed.

The pore water concentration is calculated using equilibrium partitioning. As a first tier approach, the concentration in surface water is calculated from the pore water concentration and assuming a 10-times dilution on entry of run-off water.

In principle, the emission to the STP also leads to emission to surface water and to an indirect emission to soil via the application of sludge. As an approach to calculate the PEC for micro-organisms in the STP, it is assumed that for the scenario with the highest emission to the STP, the total amount discharged will enter the STP in one day. For that scenario, the concentration in the STP was calculated with EUSES 2.0.3.

Based on information of the applicant on the intended uses, the following assumptions were made for the calculations:

1) The product is only applied in animal housings (NOT in manure storage systems)
2) The product is to be used against adult houseflies (*Musca domestica*). Therefore, 'bioctype 1' (insecticide - adulticide, specifically against flies) was used in the calculations.
3) Three application ways were taken into account: spraying, scattering and smearing (painting). The proposed uses in bait stations and on moist hang-boards/cards are not considered to result in emissions to the environment, because the devices can be adequately disposed of.
4) The highest application rate is 500 g product/200 m^2 (scattering) or 500 g product/L with 1 L/200 m^2 (spraying, smearing). The product contains 1% w/w of active substance, resulting in 0.025 g as/m^2 for all types of application.
5) According to the intended uses, the product should be re-applied after 3 to 5 weeks. However, because the product will be used alternating with other products, an application frequency of once every six weeks with a maximum of five applications per year was assumed.
6) For each of the scenarios, it is assumed that manure will be applied to either grassland or arable land.
7) The estimations of PIECsoil for arable and grassland scenarios are based on the nitrogen emission standards of 170 kg $N.ha^{-1}.yr^{-1}$ (TMI-08, March 2008; as was decided following a proposal by COM). Calculation of PIECsoil based on phosphate standards can be

considered for refinement, when a risk is shown for animal categories where the maximal manure gift is regulatory limited by the phosphate standards rather than the nitrogen standards.

8) The arithmetic mean Kp_{soil} of 137.6 L/kg (see Doc IIA, 4.1.2) and a $K_{air\text{-}water}$ of 9.79 x 10^{-9} m^3/m^3 (following Eq. 22, TGD) were used.
9) For an initial assessment, no degradation of the active substance in soil and/or manure and water was assumed, if the risk assessment pointed at a potential risk, Time Weighted Average concentrations are calculated, applying a $DT_{50,field}$.

2.2.2.2. Effects assessment

Aquatic compartment

Based on the lowest NOEC of 0.00062 mg/L (0.62 µg/L) for *Chironomus riparius* with an assessment factor of 10, the $PNEC_{aquatic}$ of spinosad for freshwater systems is 0.062 µg/L.

Applying an assessment factor of 10 to the lowest NOECs for *Daphnia magna* or *Chironomus riparius*, the following $PNEC_{aquatic}$ for spinosad metabolites were derived:

spinosyn B:	0.095 µg/L
N-demethylated spinosyn D:	0.023 µg/L
β-13,14-dihydropseudoaglycone of spinosyn A:	56.7 µg/L
β-13,14-dihydropseudoaglycone of spinosyn D:	6.3 µg/L

Based on the NOEC of 60 µg/kg dw sediment for *Chironomus riparius* with an assessment factor of 100, the $PNEC_{sediment}$ for freshwater sediment is 0.23 µg/kg ww (0.6 µg/kg dw).

No data of spiked sediment tests are available on the toxicity of the metabolites for sediment dwelling organisms. As no metabolites were formed in amounts > 10 % in the sediment phase of water sediment systems, and as the aquatic ecotoxicity data indicate that metabolites are comparable or less toxic than the parent, no $PNEC_{sediment}$ values were derived for the different metabolites.

Marine environment

Emission to the marine environment is not relevant for the currently proposed uses, and it is also not considered likely that any future uses of spinosad as an insecticide in Pt 18 will lead to an emission to the marine environment. Therefore, PNEC-values for the marine environment are not derived.

Sewage treatment plants (STPs)

Based on the EC_{10} of > 100 mg/L for inhibition of the respiration of activated sludge with an assessment factor of 10, the $PNEC_{stp}$ for spinosad is > 10 mg/L.

Air

No data are available to derive a $PNEC_{air}$ for spinosad. Significant exposure of the environment via air is not expected.

Terrestrial compartment

Based on equilibrium partitioning, the $PNEC_{soil,EP}$ for spinosad is 2.27 µg/kg ww soil (2.57 µg/kg dw soil). The $PNEC_{soil,EP}$ for major metabolites spinosyn B and N-demethylated spinosyn D is 1.43 and 0.35 µg/kg ww, respectively (1.62 and 0.40 µg/kg dw).

Non compartment specific effects relevant to the food chain (primary and secondary poisoning)

Birds, primary poisoning

The TGD does not give assessment factors to derive a $PNEC_{oral}$ for acute *primary poisoning*. As a first tier approach a "qualitative" comparison is made, comparing predicted intake with LD_{50} values in line with CA-Nov06-Doc.4.3 (assessment of rodenticides).

For chronic primary poisoning the standard $PNEC_{oral}$ derivation according to the TGD applies. Based on the chronic NOEC of 550 mg/kg feed or 66.2 mg/kg bw.d for *Colinus virginianus* and *Anas platyrhynchos* with an assessment factor of 30, the $PNEC_{oral,bird}$ for primary poisoning is 18.3 mg/kg feed or 2.2 mg/kg bw.d.

Birds, secondary poisoning

Based on the chronic NOEC of 550 mg/kg feed for *Colinus virginianus* and *Anas platyrhynchos* with an assessment factor of 30, the $PNEC_{oral,bird}$ for secondary poisoning is 18.3 mg/kg feed (2.2 mg/kg bw.d).

Mammals, primary poisoning

The TGD does not give assessment factors to derive a $PNEC_{oral}$ for *primary poisoning*. As a first tier approach a "qualitative" comparison is made, comparing the predicted intake with the LD_{50} value of > 2000 mg/kg bw in line with CA-Nov06-Doc.4.3 (assessment of rodenticides).

For chronic primary poisoning the standard $PNEC_{oral}$ derivation according to the TGD applies. Based on the chronic NOEC of 10 mg/kg bw.d for rats with an assessment factor of 30, the $PNEC_{oral,mammal}$ for primary poisoning is 0.33 mg/kg bw.d.

Mammals, secondary poisoning

Based on the chronic NOEC of 100 mg/kg feed for rats with an assessment factor of 30, the $PNEC_{oral,mammal}$ for secondary poisoning is 3.33 mg/kg feed (or 0.33 mg/kg bw.d).

2.2.2.3. PBT assessment

Spinosad should thus be considered as Persistent (sediment) and Toxic, but not as Bioaccumulative and is therefore not classified as PBT. Inclusion in Annex I is not restricted by these criteria.

2.2.2.4. Exposure assessment and risk characterisation

Aquatic Environment (fresh water)

The risk assessment shows that the use of spinosad as an insecticide in stables, according the proposed use pattern for this product, does not pose an unacceptable risk for the aquatic compartment exposed via run-off after manure application to soil.

The $PEC/PNEC_{aquatic}$ for spinosad is < 1 for all proposed uses.

Aquatic Environment (sediment)

The $PEC/PNEC_{sediment}$ for spinosad is < 1 for all proposed uses.

Sewage treatment plants (STPs)

Discharge of stable cleaning water contaminated with manure to the municipal STP is considered for some poultry scenarios. Discharge of manure to the sewer (connected to an

STP) depends on national legislation and more commonly this waste stream will be used for spreading over agricultural soil or as dilution water for manure from the cage system (ESD).

The risk assessment shows that the use of spinosad as an insecticide in poultry housing systems, according the proposed use pattern for this product, does not pose an unacceptable risk for the micro-organisms in the STP.

The $PEC/PNEC_{stp}$ for spinosad is < 1 for all proposed uses.

Assessment of drinking water criterion and persistence in sediment

No specific limit value is established for spinosad, the general limit of 0.1 µg/L for organic pesticides applies. The $PEC/PNEC_{aquatic}$ is < 1. Spinosad does comply with the drinking water criterion.

The dissipation of spinosad from the water phase is mainly determined by sorption to sediment, and the $DT_{50,system}$ may be regarded as a *worst*-case estimate of the $DT_{50,sediment}$. The geometric mean $DT_{50,system}$ is 145 days at 20 °C, which is < 6 months. The $DT_{50,system}$ at 12 °C is 275 days, which is >120 days. Mineralisation was < 5 %, but non-extractable residues were never > 70 %. Based on these data, it should be concluded that spinosad potentially may accumulate in sediment; it does not fulfil the persistence criteria that are laid down in the TNsG on Annex I inclusion, but does fulfil the persistence criterion stated in the TGD.

Air

It is not considered likely that significant volatilisation will occur after use of spinosad. Significant exposure of the environment via air is thus not expected.

Terrestrial environment

For spinosad and the major metabolites spinosyn B and N-demethylated spinosyn D, several combinations of stable and application type and land use lead to $PEC_{soil\ initial}/PNEC_{soil}$ > 1. Based on the 30-days Time Weighted Average concentration in soil, the $TWA\text{-}PEC/PNEC_{soil\ EP}$ is < 1 for spinosad and spinosyn B. As to N-demethylated spinosyn D for 16 of the 18 scenarios the $TWA\text{-}PEC/PNEC_{soil\ EP}$ is < 1. In scenario 3 (Veal calves) and scenario 5 (sows) for the spray application a risk is identified for soil organisms. However the PEC_{soil} drops below the level of the PNEC within 11 days. A chronic risk is not expected.

Non-compartment specific effects relevant to the food chain (primary and secondary poisoning)

primary poisoning of birds and mammals

Qualitative assessment indicates that acute effects for birds and mammals cannot be excluded when assuming a daily feed intake by consumption of granules only. This scenario is however very unrealistic. The LD_{50} is reached only when 150-180 granules are eaten. Therefore acute effects can be excluded after accidental consumption of a few granules.

Quantitative risk assessment is considered relevant considering that the product is applied as scattered granules in stables, and thus spinosad can be available for a long period resulting in long-term direct exposure of birds and mammals. The quantitative risk assessment indicates that the $PNEC_{oral}$ is reached at a daily intake of 0.17-0.20 of a granule for birds and 0.02 – 0.03 of a granule for mammals. Therefore uptake of granules might pose a risk to birds and mammals when this occurs for a longer period of time. In the context of the present assessment it is considered justified to assume that the risk to mammals should mainly be focused on pets. For a proper assessment, information on the chance of accidental uptake of granules and the

potential effects should become available. An additional palatability test, with exposure similar to the proposed use (i.e. scattering of granules together with feed items), may indicate whether the proposed use may lead to adverse effects on birds and mammals (pets). If this information is not delivered, the risks for birds and pets can be minimised by taking the following precautionary measures:

- Upon treatment by scattering of granules, the stables should as much as possible made inaccessible to birds and pets, by closing doors and windows, or by using nettings or similar devices to keep birds and pets outside.
- The granules should not be scattered on places where natural feed is available, i.e. among straw, grains, etc.
- Granules must preferably be placed using specially designed bait boxes, inaccessible to non-target animals.

secondary poisoning

The risk secondary poisoning via the routes *water* ➔ *fish* ➔ *fish eating bird or mammal* and *soil* ➔ *earthworms* ➔ *worm eating bird or mammal* is low, PEC/PNEC ratios are well below 1.

Effects on bees and other non-target arthropods

Exposure of bees is considered negligible, since foraging of bees can be excluded for stables or on manure treated land. Therefore, a risk is not expected. Of the other non-target arthropods species, leaf dwelling species are also not considered relevant. Truly soil inhabiting species, such as springtails, are assumed to be covered in the terrestrial risk assessment. However, soil dwelling species such as beetles, may be exposed to residues of spinosad. Assuming a soil mixing depth of 5 and 20 cm for grassland and arable land, respectively, and a wet bulk density of 1700 kg/m^3, the highest initial PEC_{soil} for spinosad (3.29 µg/kg ww soil for grassland and 3.83 µg/kg ww soil for arable land) are equivalent to 2.79 g/ha and 13 g/ha, respectively. A single direct spray of beetles and their feed at application rates up to 540 g as/ha did not result in significant mortality. Effects were observed after repeated application of 540 g as/ha, but in view of the expected exposure for the proposed uses, a risk is not expected.

Groundwater

The initial PEC_{grw}, calculated by equilibrium partitioning, does not exceed the general limit of 0.1 µg/L for organic pesticides. However it was not required, supplementary the PEC_{grw} was calculated using the groundwater leaching model PEARL 3.3.3, which resulted in concentrations < 0.001 µg/L. The absence of groundwater leaching was confirmed by a lysimeter study. After application of spinosyn A and D with 4 x 216 and 4 x 108 g as/ha per

application, respectively, no spinosyn A and D were detected in any of the leachate samples, nor were any of the major metabolites

Assessment of persistence in soil

Spinosad complies with the persistence criteria of $DT_{90,field}$ < 1 year, $DT_{50,field}$ < 3 months and $DT_{50,lab}$ at 20 °C < 6 months that are laid down in paragraph 85 of Annex VI to the Biocides Directive and in the TNsG on Annex I inclusion.

2.2.3. List of endpoints

In order to facilitate the work of Member States in granting or reviewing authorisations, and to apply adequately the provisions of Article 5(1) of Directive 98/8/EC and the common principles laid down in Annex VI of that Directive, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

3. DECISION

3.1. Background to the Decision

Spinosad has been evaluated as an insecticide against adult houseflies in animal housing.

Laboratory and field studies have demonstrated an excellent degree of efficacy of spinosad against adult *Musca domestica*. A range of application techniques are proposed (scattering on surfaces, by placing in bait stations and trays, by sprinkling on (moist) hang-boards/cards, by spraying, by paint brushing) and both laboratory and field studies show the equivalence of the techniques, thus offering a flexibility in application technique. In all cases the levels of control seen with spinosad fly baits has been at least equivalent to that of the standard products based on methomyl (1% bait) and azamethiphos (1% bait).

Inclusion of spinosad in Annex I is feasible for the human health aspect because several safe uses are identified.

Adverse health effects for the unprotected professional user due to the spraying application cannot be excluded. The internal exposure due to the spraying application is to a large extent the result of dermal exposure. If adequate PPE is used no adverse health effects due to spray application are expected. It should further be noted that the professional user will probably apply spinosad intermittently, and not at a daily basis. Therefore, the calculated risks may be considered conservative.

Adverse health effects for the unprotected professional user, due to scattering, brushing or the use of the product on bait stations and trays or hang-boards are not expected.

Adverse health effect due to non-dietary ingestion of granules by children cannot be excluded. It must therefore be clearly stated on the product label that the granules should be applied out

of reach of children. Furthermore, the addition of an aversive agent to the product will help to reduce oral consumption. Adverse health effects of adults or children due to contact with a treated area are not expected.

An acute or chronic risk from dietary exposure to spinosad residues is not expected for humans.

The environmental risk assessment is performed according to the methods of the TGD and TNsG's. Inclusion of spinosad in Annex I is feasible for the environmental aspect because several safe uses are identified.

No risks of spinosad were identified for surface water, sediment, sewage treatment plants, air, soil and groundwater. Spinosad meets the drinking water criterion and the criteria for persistence in sediment and soil.

PEC/PNEC ratios > 1 were derived for the major soil metabolites spinosyn B and N-demethylated spinsyn D for several combinations of stable and application type, but the Dutch CA considers the risks acceptable in view of the following:

- The risk assessment was based on initial concentrations, without taking degradation into account
- The PEC/PNEC based on the 30-days Time Weighted Average PEC_{soil} is < 1.

Special attention has been paid to the potential risks of direct poisoning of birds and mammals after scattering of granules. On the basis of the available information and applying the currently used methods for risk assessment, a risk cannot be fully excluded. Unless additional information is supplied, the proposed application by scattering of granules cannot be considered as a safe use.

3.2. Decision regarding Inclusion in Annex I

Spinosad with a minimum purity of 850 g/kg, with a ratio of spinosyn A : spinosyn D between 95:5 and 50:50 (w/w) shall be included in Annex I to Directive 98/8/EC as an active substance for use in product-type PT 18 (insecticides, acaricides and products to control other arthropods) without specific provisions.

Not all potential uses have been evaluated at the Community level. It is therefore appropriate that Member States assess those risks to the compartments and populations that have not been representatively addressed in the Community level risk assessment and, when granting product authorisations, ensure that appropriate measures are taken or specific conditions imposed in order to mitigate the identified risks to acceptable levels. In particular, products authorised for professional use by spraying shall be used with appropriate personal protective equipment, unless it can be demonstrated in the application for product authorisation that risks to professional users can be reduced to an acceptable level by others means.

Use of biocidal products containing spinosad and used in animal housing may lead to residues in animals. During authorization of such products, Member States shall verify the need to set new and/or amended existing maximum residue levels (MRLs) according to Regulation (EC)

No 470/2009 and/or Regulation (EC) No 396/2005, and take any appropriate risk mitigation measures ensuring that the applicable MRLs are not exceeded.

3.3. Elements to be taken into account by Member States when authorising products

Elements, which were not mentioned under the specific provisions of the decision but which need be taken into account at product authorisation level:

Identity and physical chemical properties
Related to the biocidal product GF-739:

1) Additional tests are required to evaluate palatability before and after storage of the biocidal product at ambient temperature.
2) Palatability was verified by measurement of the cis-9-tricosene content. It is not clear to the RMS how the minimum specification of 0.04% w/w cis-9-tricosene was set: from analytical batch analysis or from efficacy tests. Efficacy tests are required to show palatability to flies in relation to the cis-9-tricosene content.

Methods of analysis
None.

Efficacy
None.

Classification and Labelling
None.

Human toxicology
Use of biocidal products containing spinosad and used in animal housing may lead to residues in animals. During authorization of such products, a consumer risk assessment may then need to be performed comparing the potential residues of spinosad with the appropriate MRLs.

Related to the biocidal product GF-739:

1) The biocidal product should be applied out of reach of children.
2) The biocidal product shall contain an aversive agent.

Environment
Related to the biocidal product GF-739:

1) On the basis of the available information and applying the currently used methods for risk assessment, a risk for direct poisoning of birds and pets after scattering of granules cannot be fully excluded. Due to this, the proposed application by scattering of granules cannot be considered as a safe use, unless the following precautionary measures are taken:
   i) Upon treatment by scattering of granules, the stables should as much as possible made inaccessible to birds and pets, by closing doors and windows, or by using nettings or similar devices.
   ii) The granules should not be scattered on places where natural feed is available, i.e. among straw, grains, etc.

2) The use should preferably be restricted to application via bait stations and trays, by sprinkling on (moist) hang-boards/cards, by spraying after dilution with water, by paint brushing on surfaces after dilution with water.

3.4. Requirement for further information

It is considered that the evaluation has shown that sufficient data have been provided to verify the outcome and conclusions, and permit the proposal for the inclusion of spinosad for use in product-type PT 18 (insecticides, acaricides and products to control other arthropods) in Annex I to Directive 98/8/EC.

3.5. Updating this Assessment Report

This assessment report may need to be updated periodically in order to take account of scientific developments and results from the examination of any of the information referred to in Articles 7, 10.4 and 14 of Directive 98/8/EC. Such adaptations will be examined and finalised in connection with any amendment of the conditions for the inclusion of spinosad in Annex I to the Directive.

Appendix I: List of endpoints

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

Active substance (ISO Common Name)	spinosad (ISO, ANSI) is a mixture of spinosyn A and spinosyn D. Spinosad typically contains spinosyn A and spinosyn D in a ratio of 85:15 (w/w) and a range between 95:5 (w/w) and 50:50 w/w. The list of endpoints refers to spinosad (not the individual spinosyns) unless specified otherwise
Product-type	PT 18 (insecticides, acaricides and products to control other arthropods)

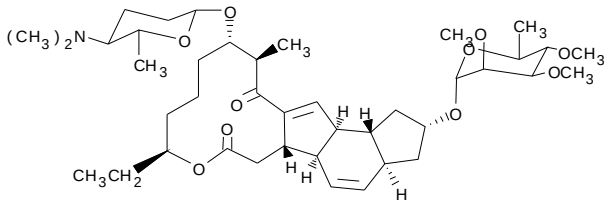
Identity

Chemical name (IUPAC)	**spinosad:** mixture of 50–95% (2*R*,3a*S*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione and 50–5% (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione **spinosyn A:** (2*R*,3a*S*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione **spinosyn D:** (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione
Chemical name (CA)	**spinosad:** (2*R*,3a*S*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-[(6-deoxy-

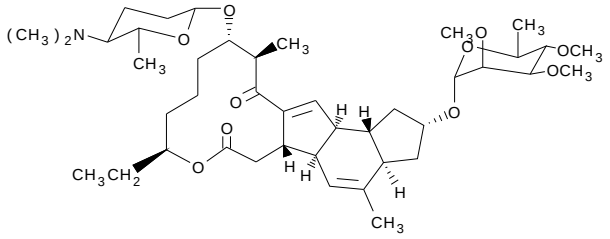
	2,3,4-tri-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-7,15-dione mixture with (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-[(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-7,15-dione **spinosyn A**: (2*R*,3a*S*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-[(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-7,15-dione **spinosyn D**: (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-[(6-deoxy-2,3,4-tri-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-7,15-dione	
CAS No	**spinosad**	168316-95-8
	spinosyn A	131929-60-7
	spinosyn D	131929-63-0
EC No	**spinosad**	434-300-1 (ELINCS)
Other substance No.	**spinosad**	CIPAC no 636
	spinosyn A	none
	spinosyn D	none
Minimum purity of the active substance as manufactured (g/kg or g/l)	85% (w/w) spinosad Spinosad typically contains spinosyn A and spinosyn D in a ratio of 85:15 (w/w) and a range between 95:5 (w/w) and 50:50 (w/w) *	
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	None.	
Molecular formula	**spinosyn A**: $C_{41}H_{65}NO_{10}$ **spinosyn D**: $C_{42}H_{67}NO_{10}$	
Molecular mass	**spinosyn A**: 731.98 **spinosyn D**: 746.00	

Structural formula

spinosyn A



spinosyn D



** The current specification of the active substance spinosad is not set according to the "Guidance for identification and naming of substances in REACH". This issue was discussed in TMIV08 and it was decided that the current specification can be maintained.*

Physical and chemical properties

Melting point (state purity)	**spinosad** not verified **spinosyn A** (98.3% w/w) 84.0 to 99.5 °C **spinosyn D** (98.0% w/w) 161.5 to 170.0 °C
Boiling point (state purity)	Decomposition before boiling (see below)
Temperature of decomposition	**spinosad** (88% w/w A+D) decomposition above 400 °C (92% weight loss) Thermal degradation products included carbon dioxide, methyl formate, acetaldehyde, and various sugar fragments of the spinosad molecule
Appearance (state purity)	**spinosad** (88.0% w/w A+D) light grey-white solid at 23.5 °C Munsell Color System: value N 9.25 and 84.2% reflectance at 23.5 °C slightly stale water-like or dusty chalk-like odour at 23.2 °C **spinosyn A** (90.9% w/w) solid at 23.6 °C Munsell Color System: value 9, hue 2.5Y, chroma 3 at 21.8 °C paint, fish- and wax-like odour at 23.2 °C

	spinosyn D (91.8% w/w) solid at 23.5 °C Munsell Color System: value 9, hue 5Y, chroma 1 at 23.4 °C bitter, paint- and aspirin-like at 23.2 °C
Relative density (state purity)	**spinosad** (88.0% w/w A+D) 1.1866 at 20.2 °C **spinosyn A** (90.9% w/w) 1.1244 at 20.5 °C **spinosyn D** (91.8% w/w) 1.1686 at 20.4 °C
Surface tension	**spinosad** not verified **spinosyn A** (90.9% w/w) 41.5 mN/m **spinosyn D**: not required, because water solubility < 1 mg/L
Vapour pressure (in Pa, state temperature)	**spinosad** not verified **spinosyn A** (99.9% w/w) $3.0x10^{-8}$ Pa at 25 °C **spinosyn D** (> 99% w/w) $2.0x10^{-8}$ Pa at 25 °C
Henry's law constant (Pa m^3 mol^{-1})	**spinosad** not verified **spinosyn A** (99.9% w/w) 1.89×10^{-7} Pa m^3mol^{-1} at 25 °C **spinosyn D** (> 99% w/w) 2.32×10^{-5} Pa m^3mol^{-1} at 25 °C
Solubility in water (g/l or mg/l, state temperature)	**spinosad** not verified **spinosyn A** (98.3% and 99.9% w/w) water solubility at 20 °C pH (unknown): 89.4 mg/L in water pH 5: 290 mg/L in buffer pH 7: 235 mg/L in buffer pH 9: 16 mg/L in buffer **spinosyn D** (99.8% w/w) water solubility at 20 °C pH 8.36: 0.495 mg/l in water pH 5: 28.7 mg/L in buffer pH 7: 0.331 mg/L in buffer pH 9: 0.053 mg/L in buffer
Solubility in organic solvents (in g/l or mg/l, state temperature)	**spinosad** not verified **spinosyn A** (98.3% w/w) at 20 °C:

	dichoromethane: 525 g/L; methanol: 190 g/L; acetone: 168 g/L; acetonitrile: 134 g/L; amyl acetate: 36.9 g/L; hexane: 4.48 g/L; 1-octanol: 9.26 g/L; toluene: 457 g/L; iso-propanol: 39.8 g/L **spinosyn A** (90.9% w/w) at 20 °C: ethyl acetate: 194 g/L; n-heptane: 12.4 g/L; xylene > 250 g/L **spinosyn D** (98.0% w/w) at 20 °C: dichoromethane: 448 g/L; methanol: 2.52 g/L; acetone: 10.1 g/L; acetonitrile: 2.55 g/L; amyl acetate: 23 g/L; hexane: 0.743 g/L; 1-octanol: 1.27g/L; toluene: 152 g/L; iso-propanol: 1.29 g/L **spinosyn D** (91.8% w/w) at 20 °C: ethyl acetate: 19 g/L; n-heptane: 0.3 g/L; xylene: 64 g/L
Stability in organic solvents used in biocidal products including relevant breakdown products	not required, the active substance spinosad as manufactured does not include an organic solvent
Partition coefficient (log P_{OW}) (state temperature)	**spinosad** not verified **spinosyn A** (97% w/w) Log K_{ow} = 3.91 at 23 °C (water) Log K_{ow} = 2.78 at 23 °C (pH 5) Log K_{ow} = 4.01 at 23 °C (pH 7) Log K_{ow} = 5.16 at 23 °C (pH 9) **spinosyn D** (98% w/w) Log K_{ow} = 4.38 at 23 °C (water) Log K_{ow} = 3.23 at 23 °C (pH 5) Log K_{ow} = 4.53 at 23 °C (pH 7) Log K_{ow} = 5.21 at 23 °C (pH 9)
Dissociation constant	**spinosad** not verified **spinosyn A** (97% w/w) is a weak base pK_b of spinosyn A = 5.90 pK_a of N-protonated spinosyn A = 8.10 at 20 °C **spinosyn D** (97% w/w) is a weak base pK_b of spinosyn D = 6.13 pK_a of N-protonated spinosyn D = 7.87 at 20 °C
UV/VIS absorption (max.) (if absorption > 290 nm	**spinosad**

state ε at wavelength)	not verified **spinosyn A** (95.0% w/w) UV spectrum solution in acid methanol ε ($mol^{-1}cm^{-1}$) at 244.2 nm = $1.08x10^5$ ε ($mol^{-1}cm^{-1}$) at 200.2 nm = $5.73x10^4$ solution in basic methanol ε ($mol^{-1}cm^{-1}$) at 244.0 nm = $1.09x10^5$ solution in neat methanol ε ($mol^{-1}cm^{-1}$) at 243.2 nm = $1.10x10^5$ ε ($mol^{-1}cm^{-1}$) at 201.0 nm = $6.77x10^4$ VIS spectrum ε ($mol^{-1}cm^{-1}$) at 290 nm = $2.41\ x10^2$ **spinosyn D** (95.6% w/w) UV spectrum solution in acid methanol ε ($mol^{-1}cm^{-1}$) at 243.8 nm = $1.10x10^5$ ε ($mol^{-1}cm^{-1}$) at 202.8 nm = $9.88x10^4$ solution in basic methanol ε ($mol^{-1}cm^{-1}$) at 243.6 nm = $1.10x10^5$ solution in neat methanol ε ($mol^{-1}cm^{-1}$) at 242.6 nm = $1.10x10^5$ ε ($mol^{-1}cm^{-1}$) at 203.0 nm = $1.08x10^5$ VIS spectrum ε ($mol^{-1}cm^{-1}$) at 290 nm = $1.16x10^2$
Flammability	**spinosad** (88% w/w A+D) Not highly flammable non auto-flammable solid no self-ignition up to a maximum of 400 °C No combustion products are formed below 400 °C.
Explosive properties	**spinosad** (88% w/w A+D) no explosive properties
Oxidative properties	**spinosad** (88% w/w A+D) no oxidizing properties

Classification and proposed labelling

with regard to physical/chemical data	none
with regard to toxicological data	none
with regard to fate and behaviour data	none
with regard to ecotoxicological data	N, R50/R53, S60, S61

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	Two valid HPLC-UV methods.
Impurities in technical active substance (principle of method)	Valid methods are available for analysis of the significant (> 1 g/kg) impurities in the technical

	material.

Analytical methods for residues

Soil (principle of method and LOQ)	The relevant residues for monitoring of soil are spinosyn A, D, B and N-demethyl spinosyn D. Extraction with methanol/5% sodium chloride/1N sodium hydroxide, analysis by LC/MS/MS. LOQ 0.005 mg/kg (spinosyn A, spinosyn D, spinosyn B and N-demethyl spinosyn D individually)
Air (principle of method and LOQ)	Residues relevant for air are spinosyn A and D. Adsorption on TENAX tube, extraction with a solution of methanol/acetonitrile and aqueous ammonium acetate, analysis by LC/MS/MS. LOQ is 0.73 µg/m3 for spinosyn A and spinosyn D, respectively [method GRM 02.18]).
Water (principle of method and LOQ)	Residues relevant for water are spinosyn A and D. Extraction with methyl tert-butyl ether, analysis by LC/MS/MS. LOQ 0.01 µg/L (spinosyn A, spinosyn D, each individually in drinking, surface and groundwater)
Body fluids and tissues (principle of method and LOQ)	not required, since spinosad is not classified as toxic or very toxic.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	not required, since the biocidal product will not be used on any food or feed of plant origin.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	The residue definition for enforcement/monitoring for animal commodities (tissues, milk, eggs) consists of spinosyn A and D. HPLC-UV method GRM 95.03 is valid for the determination of spinosyns A and D in ruminant tissues and milk. Valid range 0.01-10.0 mg/kg for beef fat and cream, and 0.01-1.0 mg/kg for milk, beef liver, lean beef, and beef kidney. LOQ = 0.01 mg/kg Immunoassay method GRM 95.14 is valid for the determination of total spinosad residue in ruminant tissues and milk. Valid range 0.01-0.50 mg/kg for bovine kidney, lean muscle, and whole milk and 0.01- 5.0 mg/kg for bovine liver. LOQ = 0.01 mg/kg. Fat samples were not validated. Method GRM 95.14 is valuable as a screening method to establish the presence of spinosyns. Revised HPLC-UV method GRM 95.15.R1 is valid for the determination of spinosyns A and D in poultry tissues and eggs. Valid range 0.01-1.0 mg/kg for eggs and poultry tissues (liver, meat and meat with overlying skin and associated fat), LOQ = 0.01 mg/kg. Valid range 0.02-2.0 mg/kg for poultry fat, LOQ =0.02 mg/kg.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	rapid; spinosyn A: 60%, spinosyn D: 45% (based on urinary and bile excretion, and tissue residues)
Rate and extent of dermal absorption:	0.1% for the concentrated product 2% for a concentration comparable to the spray liquid
Distribution:	widely distributed (perirenal fat, liver, kidneys, thyroid)
Potential for accumulation:	limited (T½ = 25 - 42 h)
Rate and extent of excretion:	rapid: > 90% in 168 h
Toxicologically significant metabolite(s)	parent compound and metabolites

Acute toxicity

Rat LD_{50} oral	> 2000 mg/kg bw (rat)
Rat LD_{50} dermal	> 5000 mg/kg bw (rabbit)
Rat LC_{50} inhalation	> 5.18 mg/L (rat) (20% of the test substance used in the acute inhalation study at the highest dose was respirable)
Skin irritation	not irritating
Eye irritation	not irritating
Skin sensitization (test method used and result)	not sensitising (M & K)

Repeated dose toxicity

Species/ target / critical effect	Vacuolation in several tissues in various species.
Lowest relevant oral NOAEL / LOAEL	4.89 mg/kg bw/day (50 ppm: 90-d, dogs)
Lowest relevant dermal NOAEL / LOAEL	1000 mg/kg bw/day (21-d, rabbit)
Lowest relevant inhalation NOAEL / LOAEL	≥ 9.5 mg/m^3

Genotoxicity	no genotoxic potential

Carcinogenicity

Species/type of tumour	no carcinogenic potential (mouse, rat)
lowest dose with tumours	-

Reproductive toxicity

Species/ Reproduction target / critical effect	decrease in litter size, survival and body weight at parental toxic levels.
Lowest relevant reproductive NOAEL / LOAEL	10 mg/kg bw/day (rat) for parental, developmental and reproductive toxicity

Species/Developmental target / critical effect	no developmental effects at maternal toxic levels.
Developmental toxicity	
Lowest relevant developmental NOAEL / LOAEL	maternal toxicity: 10 mg/kg bw/day (rabbit) developmental toxicity: > 50 mg/kg bw/day (rabbit)

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	no evidence of neurotoxicity in acute, medium-term and long-term studies
Lowest relevant developmental NOAEL / LOAEL.	-

Other toxicological studies

.....	metabolites spinosyn B and K; acute oral > 2000 mg/kg bw, Ames test negative. Spinosyn D has a lower toxicity than Spinosyn A. Recovery of vacuolation of the thyroid after 22 w, and of the kidneys after 2 w. Genotoxicity studies *in vitro* (Ames, HGPRT, Chrom. Abber.) with leachate samples from lysimeter study were negative.

Medical data

.....	no reports of adverse effects in manufacturing, workers or users

Summary	Value	Study	Safety factor
ADI (if residues in food or feed)	0.024 mg/kg bw/day	24-month rat	100
AEL acute	not necessary (no acute effects) [4]		
AEL medium-term	0.024 mg/kg bw/day	90-day dog	100, 50% correction for oral absorption
AEL long-term	0.012 mg/kg bw/day	24-month rat	100, 50% correction for oral absorption
Drinking water limit	0.1 µg/L		
ARfD (acute reference dose)	not necessary (no acute effects)		

4 : in case of acute exposure, use the medium-term AEL.

Acceptable exposure scenarios (including method of calculation)

Professional users	Adverse health effects for the unprotected professional user due to the spraying application cannot be excluded. Safe use identified for spray application, with PPE. Safe use identified for the following applications; scattering, brushing and the use of the product on bait stations and trays or hang-boards.
Non-professional users	SpY® (GF-739) is not intended to be used by non-professionals
Indirect exposure as a result of use	* Adverse health effect due to non-dietary ingestion of granules by children cannot be excluded. Adverse health effects of adults or children due to contact with a treated area are not expected. * Consumption of animal products containing spinosad residues from biocide use (using tMRLs of spinosad from Regulation (EC) 396/2005: TMDI (all national EU diets): FR toddlers 86.9% of the ADI. All other national diets the tMRLs for animal products use less of the ADI. *Consumption of all products containing spinosad residues from biocide and pesticide (91/414/EC) use (using tMRLs of spinosad from Regulation (EC) 396/2005:EDI (-all national EU diets): NL children (1-6y)91.4% of the ADI. All other national diets use less of the ADI.

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	**spinosyn A** pH 5, 25°C: stable pH 7, 25°C: stable pH 9, 25°C: 9.0% hydrolysed after 30 d, DT_{50} 200 d **spinosyn D** pH 5, 25°C: stable pH 7, 25°C: stable pH 9, 25°C: 5.1% hydrolysed after 30 d, DT_{50} 259 d
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	natural sunlight, 40° northern latitude **spinosyn A** distilled water, pH 7, 25°C: DT_{50} 0.96 d pond water, pH 9.2, 25°C: DT_{50} 0.18 d metabolites (max): A1: 24.9% AR (β isomer of 13,14-dihydro of pseudoaglycone of spinosyn A) A2: 7.3% AR (rearrangement of spinosyn A) A3: 9.4% AR (spinosyn A with an added water molecule)

	spinosyn D distilled water, pH 7, 25°C: DT_{50} 0.84 d pond water, pH 9.2, 25°C: DT_{50} 0.18 d metabolites (max): D1 (≅ A1): 10.2% AR D2: 7.5% AR (could not be interpreted) D3: 6.3% AR (could not be interpreted) D4 (≅ A3): 4.2% AR
Quantum yield of direct phototransformation in water at λ > 290 nm	spinosyn A: 0.019 spinosyn D: 0.021
Readily biodegradable (yes/no)	No
Biodegradation in seawater	-
Degradation in water/sediment (range or median, with n value, with r2 value, state temperature)	$DT_{50,\ water}$: aerobic study, 20°C **spinosyn A**: 16 – 27 d **spinosyn D**: 14 - 26 d geomean $DT_{50,water}$ value: 20 d (37 d, converted to 12°C) anaerobic study, 25°C **spinosyn A**: < 7 d **spinosyn D**: < 7 d microcosm, 20 – 21°C (Indiana, USA) **spinosyn A**: 27 h (1.1 d, n=7, r^2 0.53) **spinosyn D**: 18 h (0.75 d, n=7, r^2 0.51)
	$DT_{50,sediment}$: aerobic study, 20°C: not available anaerobic study, 25°C **spinosyn A**: 267 d (398 d, converted to 20°C, 722 d, converted to 12°C, n=8, r^2 0.92) **spinosyn D**: 539 d (804 d, converted to 20°C, 1457 d, converted to 12°C, n=8, r^2 0.85) microcosm, 20 – 21°C: Concentrations were too low to calculate reliable DT_{50} values.
Non-extractable residues	$DT_{50,whole\ system}$: aerobic study, 20°C **spinosyn A**: 169 - 176 d (315-328 d, converted to 12°C) **spinosyn D**: 103 d (192 d, converted to 12°C) anaerobic study, 25°C **spinosyn A**: 239 d (357 d, converted to 20°C, 646 d, converted to 12°C, n=9, r^2 0.89) **spinosyn D**: 443 d (661 d, converted to 20°C, 1197 d, converted to 12°C, n=9, r^2 0.80) microcosm, 20 – 21°C Concentrations were too low to calculate reliable DT_{50} values.
Distribution in water / sediment systems (active substance)	aerobic study, 20°C **spinosyn A** highest value of 21% of AR after 120 d (end of study)

	spinosyn D highest value of 42% of AR after 120 d (end of study) anaerobic study, 25°C **spinosyn A** highest value of 17% of AR after 364 d (end of study) **spinosyn D** highest value of 16% of AR after 364 d (end of study)
	microcosm dissipation study A mass balance was not established. Supposedly dissipation from the water phase was dominated by sorption to sediment, but concentrations in the sediment remained rather low.
Distribution in water / sediment systems (metabolites)	No degradation products were detected in water or sediment at levels >10% of AR (aerobic). aerobic study, 20°C **spinosyn A** metabolites in sediment (max): spinosyn B 9% AR after 120 d **spinosyn D** metabolites in sediment (max): N-demethylated spinosyn D: 10% AR after 120 d anaerobic study, 25°C **spinosyn A** metabolites in sediment (max): J: 12% AR after 84 d Unknown: 14% AR after 365 d keto-reverse pseudoaglycone A: 14% AR after 365 d **spinosyn D** metabolites in sediment (max): Unknown: 12% AR after 365 d D2: 7.5% AR (could not be interpreted) D3: 6.3% AR (could not be interpreted) D4 (= A3): 4.2% AR

Route and rate of degradation in soil

Mineralization (aerobic)	**spinosyn A** nd – 6.3% of AR after 80 – 91 d **spinosyn D** 1.3 – 8.7% of AR after 84 – 91 d
Laboratory studies (range or median, with number of measurements, with regression coefficient)	$DT_{50,lab}$ (20 °C, aerobic): **spinosyn A** 21 d (n=6, r^2 0.96, test at 25°C, $DT_{50,25°C}$ 14 d, converted assuming a Q_{10} value of 2.2) 11 d (n=5, r^2 0.99, test at 25°C, $DT_{50,25°C}$ 7.1 d, converted assuming a Q_{10} value of 2.2) 24 d (n=3, r^2 1.0) 38 d (n=6, r^2 0.89) 42 d (n=3, r^2 1.0) 29 d (n=3, r^2 1.0) geomean DT_{50} value: 25 d (47d, converted to 12°C)

	spinosyn D 16 d (n=6, r^2 0.97, test at 25°C, $DT_{50,25°C}$ 11 d, converted to 20°C assuming a Q_{10} value of 2.2) 32 d (n=6, r^2 0.72) 63 d (n=6, r^2 0.96) 56 d (n=6, r^2 0.90) 39 d (n=6, r^2 0.86) geomean DT_{50} value: 37 d (69 d, converted to 12°C) **spinosyn B** (degradation product of spinosyn A) Calculated using the highest occurring concentration as start value: 194 d (n=5, r^2 0.73) 157 d (n=6, r^2 0.96) (Tests at 25°C, $DT_{50,25°C}$ 130 and 105 d, converted to 20°C assuming a Q_{10} value of 2.2) geomean DT_{50} value: 170 d (316 d, converted to 12°C) **N-demethylated spinosyn D** (degradation product of spinosyn D) Calculated using the highest occurring concentration as start value: 531 d (n=4, r^2 0.56, test at 25°C, $DT_{50,25°C}$ 356 d, converted to 20°C, 962 d, converted to 12°C, assuming a Q_{10} value of 2.2)
Field studies (state location, range or median with number of measurements)	$DT_{50,field}$: study 1 **spinosyn A** <1 d (Mississippi, USA, average soil temperature at 10 cm depth 28°C) <1 d (California, USA, average soil temperature at 10 cm depth 32°C) The field study is considered representative for southern European regions only, not for the entire European Union. **spinosyn D** not available study 2 UK DT_{50} first order multi-compartment (FOMC) best fit and 0-10 cm. **spinosyn A**: 2.37 d **spinosyn D**: 3.51 d **spinosyn B**: 2.11 d **N-demethylated spinosyn D**: 3.77 d **3)** mini lysimeter dissipation study Location: UK, Letcombe **spinosyn A** 8.4 d **spinosyn D** 9.5 d Due to the uncertainties in the mass balance and the

	unsuitability of the test system the DT_{50} values are considered indicative. N-demethylated spinosyn D varied from 5.7% at t=0 to <LOQ from t=14 days onwards. Spinosyn B was around a value of 3.5% (range <LOQ – 4.4%) at all timepoints. When present above LOQ, the residues were not monotonically decreasing. These data do not warrant an evaluation of the degradation rate of these compounds. Up to 8 individual polar compounds were found, in individual amounts up to 12.4% at t=1 day, 13.2% and 11.0% at 14 days, 11.4% at 31 days and 14.0% at t=62 days. The total maximum amount of polar compounds in the 0-10 cm segment was 58.0% of AR at t=14 days. The high amount of unidentified metabolites needs additional investigation to the identity.
Anaerobic degradation	not available
Soil photolysis	DT_{50}: **spinosyn A** 74 d (air dried soil, n=12, r^2 0.88, test temperature 25°C, natural sunlight, Indianapolis USA, 40° northern latitude) mineralisation: 1.9% of AR after 30 d bound residue: 5.6% of AR after 30 d no major metabolites (>10% of AR) 13 d (moist soil, n=16, r^2 0.97, test temperature 25°C, natural sunlight, Indianapolis USA, 40° northern latitude) mineralisation: 0.34% of AR after 30 d bound residue: 12% of AR after 30 d metabolites: spinosyn B, maximal 15% of AR after 18 days **spinosyn D** 42 d (air dried soil, n=12, r^2 0.90, test temperature 25 °C, natural sunlight, Indianapolis USA, 40° northern latitude) mineralisation: 2.1% of AR after 30 d bound residue: 3.7% of AR after 30 d no major metabolites (>10% of AR)
Non-extractable residues	**spinosyn A** 8.1 – 39% of AR after 80 – 91 d **spinosyn D** 12 – 33% of AR after 84 – 91 d
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	**spinosyn B** (metabolite of spinosyn A) 39 – 67% of AR after 28 – 182 d **N-demethylated spinosyn D** (metabolite of spinosyn D) 28 – 68% of AR after 28 – 237 d
Soil accumulation and plateau concentration	not relevant

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	**spinosyn A** K_F values: 8.5, 5.4, 25, 337, and 312 L/kg (mean 137.6 L/kg) K_F was better correlated with the clay content than with organic matter content of the soil. Corresponding K_{clay} values: 163, 68, 250, 1465, and 975 L/kg (average 584 L/kg) Corresponding K_{OC} values: 2890, 835, 4250, 143225 and 26520 L/kg (average 35024 L/kg) no pH dependence **spinosyn D** not available; it is assumed that spinosyn D has sorption characteristics equal to spinosyn A **spinosyn B** (degradation product of spinosyn A) K_F values: 6.2, 4.3, 17, and 178 L/kg (mean 51.4 L/kg) K_F was better correlated with the clay content than with organic matter content of the soil. Corresponding K_{clay} values: 119, 54, 170, 774 L/kg (average 279 L/kg) Corresponding K_{OC} values: 2108, 665, 2890 and 75650 L/kg (average 20328 L/kg) no pH dependence **N-demethylated spinosyn D** (degradation product of spinosyn D) not available; it is assumed that N-demethylated spinosyn D has sorption characteristics equal to spinosyn B
Column leaching[1]	unaged sand soil, leached for 2 d at 10 cm water/d **spinosyn A** 87% 0 – 5 cm soil layer <1% 5 – 30 cm <1% in the leachate **spinosyn D** 97% 0 – 5 cm soil layer <1% 5 – 30 cm <1% in the leachate

Aged residues leaching[1]	biologically aged for 34 d, sand soil, leached for 2 d at 10 cm water/d **spinosyn A** after ageing, spinosyn A was reduced to 36% of AR, 18% of AR was present as spinosyn B, 21% of AR as unknown metabolites, and 11% as non-extractable residue after leaching, 86% of AR was recovered from the 0 – 5 cm soil layer, 4.3% of AR from the 5 – 30 cm soil layer, and 1.7% of AR in the leachate **spinosyn D** after ageing, spinosyn D was reduced to 31% of AR, 15% of AR was present as N-demethylated spinosyn D, 26% of AR as unknown metabolites, and 0.7% as non-extractable residue after leaching, 84% of AR was recovered from the 0 – 5 cm soil layer, 8.5% of AR from the 5 – 30 cm soil layer, and 1.8% of AR in the leachate photolytically aged for 16 h, sand soil, leached for 2 d at 10 cm water/d **spinosyn A** after ageing, spinosyn A was reduced to 15% of AR, 4.5% of AR was present as spinosyn B, 41% of AR as unknown metabolites, and 13% as non-extractable residue after leaching, 61% of AR was recovered from the 0 – 5 cm soil layer, 18% of AR from the 5 – 30 cm soil layer, and 10% of AR in the leachate **spinosyn D** after ageing (33 days), spinosyn D was reduced to 10% of AR, 1.4% of AR was present as N-demethylated spinosyn D, 53% of AR as unknown metabolites, and 8.1% as non-extractable residue after leaching, 67% of AR was recovered from the 0 – 5 cm soil layer, 13% of AR from the 5 – 30 cm soil layer, and 7.0% of AR in the leachate

Fate and behaviour in air

Direct photolysis in air	not available
Quantum yield of direct photolysis	not available
Photo-oxidative degradation in air	**spinosad** DT_{50}: 1.25 hr (Atkinson calculation; 24 hr day, 0.5 * 10^6 $OH.cm^{-3}$)

	spinosyn A DT_{50}: 20 min (Atkinson calculation; 12 hr day, 1.5 * 10^6 $OH.cm^{-3}$) **spinosyn D** DT_{50}: 19 min (Atkinson calculation ; 12 hr day, 1.5 * 10^6 $OH.cm^{-3}$)
Volatilization	from plant surfaces: **spinosyn A** 1.6% after 24 h **spinosyn D** 0.1% after 24 h from soil: **spinosyn A** -0.1% after 24 h **spinosyn D** -0.4% after 24 h

Monitoring data, if available

Soil (indicate location and type of study)	not available
Surface water (indicate location and type of study)	not available
Ground water (indicate location and type of study)	not available
Air (indicate location and type of study)	not available

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Substance	Time-scale	Endpoint	Toxicity [mg as/L]
Fish				
Cyprinus carpio	Spinosad	acute	LC_{50}	4.5[1]
Oncorhynchus mykiss	Spinosad	chronic	$NOEC_{ELS}$	0.5
Invertebrates				
Daphnia magna	spinosad	acute	EC_{50}	> 1.0
Daphnia magna	spinosyn B	acute	EC_{50}	6.5
Daphnia magna	N-demethylated spinosyn D	acute	EC_{50}	3.8
Daphnia magna	β-13,14-dihydropseudoaglycone of spinosyn A	acute	EC_{50}	> 197
Daphnia magna	β-13,14-dihydropseudoaglycone of spinosyn D	acute	EC_{50}	65.8
Daphnia magna	spinosad	chronic	NOEC	0.0012
Daphnia magna	spinosyn B	chronic	NOEC	0.00095
Daphnia magna	N-demethylated spinosyn D	chronic	NOEC	0.001
Daphnia magna	β-13,14-dihydropseudoaglycone of spinosyn A	chronic	NOEC	1.25
Daphnia magna	β-13,14-dihydropseudoaglycone of spinosyn D	chronic	NOEC	4.85
Algae/diatoms				
Navicula pelliculosa	spinosad	acute	E_rC_{50}	0.079
Navicula pelliculosa	spinosyn B	acute	E_rC_{50}	0.077
Navicula pelliculosa	N-demethylated spinosyn D	acute	E_rC_{50}	0.25
Navicula pelliculosa	β-13,14-dihydropseudoaglycone of spinosyn A	acute	E_rC_{50}	38.8
Navicula pelliculosa	β-13,14-dihydropseudoaglycone of spinosyn D	acute	E_rC_{50}	28
Navicula pelliculosa	spinosad	chronic	NOE_rC	0.036
Navicula pelliculosa	spinosyn B	chronic	NOE_rC	< 0.015
Navicula pelliculosa	N-demethylated spinosyn D	chronic	NOE_rC/ NOE_bC	0.13
Navicula pelliculosa	β-13,14-dihydropseudoaglycone of spinosyn A	chronic	NOE_rC	17.2
Navicula pelliculosa	β-13,14-dihydropseudoaglycone of spinosyn D	chronic	NOE_rC	14
Plants				
Lemna minor	spinosad	chronic	NOE_rC	1.4

Microorganisms				
respiration activated sludge	spinosad	acute	EC_{10}	> 100
Sediment-dwelling organisms				
Chironomus riparius	spinosad	chronic	NOEC	0.00062 mg as/L
Chironomus riparius	spinosad	chronic	NOEC	0.060 µg as/kg dw
Chironomus riparius	spinosyn B	chronic	NOEC	0.0029 mg/L
Chironomus riparius	N-demethylated spinosyn D	chronic	NOEC	0.00023 mg/L
Chironomus riparius	β-13,14-dihydropseudoaglycone of spinosyn A	chronic	NOEC	≥ 0.567 mg/L
Chironomus riparius	β-13,14-dihydropseudoaglycone of spinosyn D	chronic	NOEC	≥ 0.063 mg/L

1: geometric mean of 4.0 and 5.0 mg/L; value differs from LoE 91/414/EEC

Effects on earthworms or other soil non-target organisms (most sensitive species for each group)

Acute toxicity for earthworms (Annex IIIA, point XIII.3.2)	spinosad: LC_{50} > 916 mg/kg dw soil (10 % OM) spinosyn B: LC_{50} > 1000 mg/kg dw soil (10 % OM) N-demethylated spinosyn D: LC_{50} > 1000 mg/kg dw soil (10 % OM)
Reproductive toxicity for earthworms (Annex IIIA, point XIII.3.2)	spinosad: NOEC ≥ 2700 g as/ha ≈ 14.2 mg as/kg dw soil (10 % OM) spinosyn B: NOEC ≥ 3.58 mg/kg dw soil (10 % OM) N-demethylated spinosyn D: ≥ 1.93 mg/kg dw soil (10 % OM)
Reproductive toxicity for springtails	not available
Toxicity to plants	NOEC ≥ 579 g as/ha (2.7 % OM)
Litter bag study	Application of 0.864 kg as/ha followed by a second application one month later of 0.432 kg as/ha had no adverse on the rate of breakdown of straw litter in soil (+1.4% after 7 months when compared to control).

Effects on soil micro-organisms

Nitrogen mineralization	spinosad: no effects > 25 % at 6.3 mg a.i./kg dw soil spinosyn B: no effects > 25 % at 3.58 mg/kg dw soil N-demethylated spinosyn D: no effects > 25 % at 1.93 mg/kg dw soil
Carbon mineralization	no effects > 25 % at 6.3 mg a..i./kg dw soil spinosyn B: no effects > 25 % at 3.58 mg/kg dw soil N-demethylated spinosyn D: no effects > 25 % at 1.93 mg/kg dw soil

Effects on terrestrial vertebrates

Acute toxicity to mammals	LD_{50} > 2000 mg/kg bw
Long-term toxicity to mammals	NOEC 100 mg/kg feed (10 mg/kg bw.d)
Acute toxicity to birds	LD_{50} > 2000 mg/kg bw
Dietary toxicity to birds	LC_{50} > 5156 mg/kg feed (LD_{50} > 1607 mg/kg bw/d) LC_{50} of >5253 mg/kg feed (LD_{50} >1038 mg/kg bw/d)
Reproductive toxicity to birds	NOEC 550 mg/kg feed (NOEC 66.2 mg/kg bw)

Effects on honeybees

Acute oral toxicity	LD_{50} 0.057 µg/bee (spinosad) LD_{50} 0.049 µg as/bee (NAF-85)
Acute contact toxicity	LD_{50} 0.0036 µg/bee (spinosad) LD_{50} 0.050 µg as/bee (NAF-85)
Acute oral toxicity bumblebees	LD_{50} 0.37 µg as/bee (NAF-85)
Acute contact toxicity bumblebees	LD_{50} 17.2 µg/bee (NAF-85)

Field or semi-field tests

Species	Test type	Dose	Parameter	Effect
Apis mellifera	cage treatment before bee activity	0.144 kg as/ha	mortality	no effect
			foraging	small effect (only 1st day after treatment)
			brood development	no effect
Apis mellifera	cage treatment before bee activity	0.540 kg as/ha	mortality	no effect
			foraging	significant effect (several timepoints)
			brood development	indication of effect
Apis mellifera	semi field treatment during bee activity	0.226 kg as/ha	mortality	66% after 1 day (n.s.)
			foraging	48% after 2 days (sign.)
			brood and food store condition	no effects
Apis mellifera	semi field treatment during bee activity	4 x 0.226 kg as/ha	mortality	66% after 1 day (n.s.)
			foraging	66% at day 0, 90% after 2 days, 78% after 3 days (all sign.)
			brood and food store condition	no effects
Bombus terrestris	semi field bee released day after application	0.36 g as/L	mortality	1% after 7 days (n.s.)
			foraging	65% after 2 days, 18% after 4 days, 13% after 6 days (n.s.)
			brood development	27% after 16 days (n.s.)

Effects on other beneficial arthropods

Acute oral toxicity	not applicable
Acute contact toxicity	not applicable

Residual toxicity	*Poecilus cupreus* (14 days test): no significant effect after direct spray of beetles, feed and sand with NAF-85 at 400 g as/ha *Poecilus cupreus* (29 days test): no significant effect after direct spray of beetles, feed and sand with NAF-85 at 540 g as/ha; mortality > 50 % after repeated application of 540 g as/ha.

Bioconcentration

Fish

Bioconcentration factor (BCF)	**spinosyn A** 84 and 114 L/kg **spinosyn D** 100 and 115 L/kg
Depuration time (DT_{50}) (DT_{90})	DT_{50} **spinosyn A** < 5 d **spinosyn D** 2 – 4 d
Level of metabolites (%) in organisms accounting for > 10% of residues	**spinosyn A** spinosyn J **spinosyn D** N-demethylated spinosyn D; spinosyn L; spinosyn O

Earthworms

Bioconcentration factor (BCF)	**spinosyn A** 98 L/kg (estimated with log P_{ow} 3.91 **spinosyn D** 229L/kg (estimated with log P_{ow} 4.38)

Chapter 6: Other End Points

Metabolism in livestock

Animals covered	lactating goat laying hen
Animal residue definition for monitoring	spinosad, sum of spinosyn A and spinosyn D
Animal residue definition for risk assessment	Ruminant milk and tissues: sum of spinosyn A and spinosyn D (no metabolites) Poultry eggs and tissues: sum of spinosyn A, spinosyn D, spinosyn B and N-demethyl spinosyn D
Conversion factor (monitoring to risk assessment)	poultry fat: no conversion factor poultry liver: 2 for spinosyn A

	poultry muscle: 7 for spinosyn D no conversion factor eggs: 1 for spinosyn A 2 for spinosyn D
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes

Appendix II: List of Intended Uses

The intended use presented in the table below is the intended use as agreed upon between RMS and applicant (dated 15 january 2007)

	SpY® (GF-739)
Product description	Granular fly bait product containing 1% w/w of the active substance spinosad The active substance spinosad contains a mixture of 85% spinosyn A and 15% spinosyn D
Organisms to be controlled	Adult Houseflies (*Musca domestica*)
Objects to be protected	Animal housing
Application aim	Control
dosage	1. Scattered on surfaces (e.g. window sills, tops of walls, edges of wa kways, etc.): Application rate: 500 g product/200 m^2 floor space Concentration of a.s. 0.025 g a.s./m^2 2. Placed in bait stations or trays Application rate: 50 g product/bait station; 10 bait stations/200 m^2 floor space. Concentration of a.s. used 0.025 g a.s./m^2 3. Sprinkled onto moistened hang-boards/ cards, Application rate: 100 g product/m^2 of board; 25 boards/200 m^2 floor space using 5 m^2 of boards/200 m^2 floor space. Concentration of a.s. 0.025 g a.s./m^2 4. Diluted in water and sprayed where flies gather. Application rate: 250 g product/0.5 L water; 1 L of diluted product/200 m^2 floor space Concentration of a.s. in diluted form: 5 g a.s./L. (0.025 g a.s./m^2) 5. Diluted with water and painted onto surfaces in areas where flies gather. Application rate: 250 or 500 g product/0.5 L water; 1 L of the 250 g/0.5 L diluted product or 0.5 L of the 500 g/0.5 L diluted product /200 m^2 floor space Concentration of a.s. in diluted form: 5 or 10 g a.s./L. (0.025 g a.s./m^2). Either one of a combination of all application methods can be used at any one time, targeting the areas where flies are known to rest or feed. but total application rate does not exceed 500g product/200 m^2 floor space.
frequency	GF-739 will efficiently manage fly populations for up to six weeks under normal conditions. 1. Scattered on surfaces: Re-apply when granules have become dusty, fouled by dead flies, consumed or removed due to cleaning procedure, or min 3 weeks, max 5 weeks 2. Placed in bait stations or trays, Re-apply when granules have become dusty, fouled by dead flies, consumed or removed due to cleaning procedure, or min 3 weeks, max 5 weeks 3. Sprinkled onto moistened hang-boards/cards Re-apply when granules have become dusty, fouled by dead flies, consumed or removed due to cleaning procedure, or min 3 weeks, max 5 weeks 4. Diluted in water and sprayed.

	Re-apply when treated area has become dusty, fouled by dead flies, consumed or removed due to cleaning procedure, or min 3 weeks, max 5 weeks 5. Diluted with water and painted onto surfaces. Re-apply when treated area has become dusty, fouled by dead flies, consumed or removed due to cleaning procedure, or min 3 weeks, max 5 weeks After a minimum of 3 weeks (max. 5 weeks) the fly control product has to be re-applied. The product (GF-739 or any other product) has to rotate with another product containing a different active substance, to prevent resistance build up (to which *Musca domestica* is particulary prone to). A control scheme could look l ke this: GF-739 for 3 weeks - Product X (maybe a space spray) - GF-739 for 3 weeks - Product Y for 3 weeks (maybe a bait with different active) – GF-739 for 3 weeks - Product Y for 3 weeks - and so on, with GF-739 being used max. 5 times per year. Worst case would be 5 applications of GF-739 / year (but not continuous applications).
season/period for use	Start baiting early before fly population has reached an unacceptable level.
indoors/outdoors	Indoors
Non-professional / professional	Professional use Product is to be used in structures (animal housing). Not for sale to or use by the general public.
Instruction for use	Start baiting early before fly population has reached an unacceptable level. If there is an initial high population use a knockdown space spray to rapidly reduce the fly population. The bait should be placed targeting areas where flies are known or rest and feed by one or a combination of the proposed applications 1. Scattered on surfaces: Scattered evenly in animal housing where flies gather (e.g. window sills, tops of walls, edges of walkways, etc.) 2. Bait stations and trays in areas where flies gather 3. Sprinkled on (moist) hang-boards/cards in areas where flies gather 4. Sprayed with hand held sprayer - diluted in water and sprayed in areas where flies gather 5. Painted: paint brush - diluted in water and painted onto surfaces in areas where flies gather This product should not be used continuously against houseflies in intensive or controlled environment units as this could cause control failure due to insect resistance. If sequential treatments are required, rotate GF-739 with a product having a different active substance and, if necessary, a different control method (such as space sprays). Do not apply more than five treatment regimes of GF-739 per year in the same structure. Rotate to another fly control product between each GF-739 application A control scheme could look l ke this: GF-739 for 3 weeks - Product X (maybe a space treatment) - GF-739 for 3 weeks - Product Y for 3 weeks (maybe a bait with different active) – GF-739 for 3 weeks - Product Y for 3 weeks - and so on, with GF-739 being used max. 5 times per year. Worst case would be 5 applications of GF-739 / year (but not continuous applications).