

Maisons-Alfort, 21 November 2007

OPINION

of the French Food Safety Agency (Afssa)

on a marketing authorisation application for the thiamethoxam-based insecticide, CRUISER, from the company Syngenta Agro SAS, as part of a mutual recognition procedure

THE DIRECTOR GENERAL

On 20 September 2007, the French Food Safety Agency (Afssa) received an application for the thiamethoxam-based insecticide, Cruiser, submitted by the company Syngenta Agro SAS for a marketing authorisation as part of a mutual recognition procedure.

In accordance with articles L.253, R.253 and subsequent articles of the French Rural Code, Afssa's Opinion on the assessment of this mutual recognition application is required.

After consulting the Scientific Panel "Plant protection products: chemical substances and preparations", which met on 20 November 2007, Afssa issues the following Opinion.

HAVING REGARD TO THE SUBJECT OF THE REQUEST

This Opinion concerns the thiamethoxam-based insecticide Cruiser, intended to treat sweet corn and maize seeds. The applications requested (crops and annual application rates) are specified in Annex 1 (Table 1).

The mutual recognition request refers to the insecticide Cruiser 350 FS, authorised in Germany (authorisation no. 4914-00) on maize and sweet corn to deter frit flies and click beetles. This insecticide has been assessed scientifically by the German authorities and is exactly the same as the Cruiser insecticide (the trade name requested in France).

This Opinion is based on an examination of the assessment report¹, issued by the German competent authority, and on the application made in accordance with the requirements of Directive 91/414/EEC² and the mutual recognition procedure provided for in this Directive.

The Inclusion Directive for thiamethoxam³, and its associated documents⁴, as well as the results of an assessment conducted by the French body⁵ consulted on this application in the previous Opinion have also been taken into account.

The effective application rate of active substance per hectare differs according to sowing density. The applicant submitted additional data in France for a sowing density of 140 000 seeds/ha (or 88.2g a.s.⁶/ha), while the sowing density considered by Germany is 110 000 seeds/ha, corresponding to 69.3 a.s./ha.

Only the doses and applications authorised in Germany are assessed as part of this mutual recognition procedure (Annex 1, Table 2).

¹ The assessment report issued by the German competent authority is a compilation of reports from the BVL (Federal Office for Consumer Protection and Food Safety), the BBA (Federal Centre for Agricultural and Forestry Biological Research), the BfR (Federal Office for the Assessment of Health risks) and the UBA (Federal Environment Agency).

² Directive transposed into French law by the order of 6 September 1994 implementing Decree 94/359 of 5 May 1994 on the control of plant protection products.

³ Commission Directive 2007/6/EC of 14 February 2007 amending Council Directive 91/414/EEC to include metrafenone, *Bacillus subtilis*, spinosad and thiamethoxam as active substances

⁴ European Commission (2006) Review report for the active substance thiamethoxam, SANCO/10390/2002 –rev. Final, 14 July 2006.

⁵ Report of the Toxicity Study Committee of Antiparasitic Products for Agricultural Use and Similar Products (CET ["Com Tox"]) – session of 14 June 2006.

⁶ a.s.: active substance

IDENTITY OF THE FORMULATED PRODUCT

The product, Cruiser, is a suspension concentrate with 350 g/L thiamethoxam (minimum purity 98%), applied to treat seeds.

PHYSICOCHEMICAL PROPERTIES AND ANALYTICAL METHODS

The specifications of the active substance contained in the insecticide Cruiser 350 FS characterise this active substance and comply with regulatory requirements.

The physical and chemical properties of Cruiser 350 FS are described in the German assessment report and the available data confirm that this insecticide is neither explosive, nor combusive, nor self-igniting, and that it is stable in its packaging for at least two years at 20°C.

Regarding the technical properties of Cruiser 350 FS, the available data guarantee that this insecticide is safe to use under the recommended conditions of use.

The methods for analysing the active substance in Cruiser 350 FS and different substrates (plants, soil, water and air) are described in the German assessment report. These methods are considered acceptable.

All of these conclusions apply to the insecticide Cruiser.

TOXICOLOGICAL PROPERTIES

The toxicological data for Cruiser 350 FS described in the German assessment report are as follows:

- LD₅₀⁷ by oral route in rats over 3000 mg/kg bw⁸,
- LD₅₀ by cutaneous route in rats over 4000 mg/kg bw,
- No skin irritant effects in rabbits,
- No eye irritant effects in rabbits,
- No skin sensitisation effects in guinea-pigs.

No toxicity studies by inhalation have been furnished on the insecticide, but in view of the properties of the active substance and co-formulants⁹, no additional study is required. On the basis of these results, it can be considered that Cruiser 350 FS does not present any acute toxic, irritant or sensitising effects.

All of these conclusions apply to the insecticide Cruiser.

OPERATOR AND WORKER EXPOSURE***Estimation of operator exposure***

Germany assessed operator exposure from use of the insecticide Cruiser 350 FS using the SEEDTROPEX model, with an absorption value of 0.02% and an active substance dose of 315 g a.s./100 kg (for a thousand-grain weight (TGW) of 200 g). It estimated that the risk for operators was acceptable only when wearing a coverall and gloves during all seed treatment operations except for packing.

Nonetheless, based on the same skin absorption study, Afssa has adopted a skin absorption value of 0.5% in view of the assessment conducted by the body previously in charge of the application. This value has been used to assess the exposure risk for the insecticide Cruiser in France using the SEEDTROPEX model with a dose of 315 g a.s./100 kg. The risk for operators has been estimated as acceptable only when gloves are worn during all seed treatment

⁷ LD₅₀: the fatal insecticide dose for 50% of a batch of laboratory animals subject to testing after a single administration.

⁸ bw: body weight

⁹ The LC₅₀ by inhalation of thiamethoxam exceeds 3.72 mg/L (maximum concentration obtained). No co-formulants result in a classification of the insecticide for inhalation.

operations except packing, and when breathing protection (P2 level at least) is worn when cleaning. Protective clothing is, however, recommended for all seed treatment operations.

Estimation of worker exposure

Worker (sower) exposure from use of the insecticide Cruiser 350 FS has been assessed using the SEEDTROPEX model, with an absorption value of 0.02% by Germany, who considered that the risk for workers was acceptable.

The SEEDTROPEX model also concludes, on the basis of the skin absorption value of 0.5% adopted by Afssa, that the risk is acceptable.

Although it does not represent the type of sowing machine used for maize, the SEEDTROPEX model was used by default. A monitoring study of sower exposure is requested to confirm the low exposure estimated.

RESIDUES AND CONSUMER EXPOSURE

The residue data provided for this mutual recognition application are described in the German assessment report. They contain data submitted for including thiamethoxam in Annex I of Directive 91/414/EEC, supplemented by data submitted for authorisation of the insecticide Cruiser 350 FS in Germany (five tests used out of the seven available, as the “South” tests are not required by Germany).

In addition to these data, the mutual recognition application submitted in France also contains two residue tests conducted in France in 1998 in the “South” pedo-climatic zone on maize and four new tests on maize conducted in France in 2003 (two “North” tests and two “South” tests). These tests were considered because of their location in the “South” pedo-climatic zone of Europe, which were not required for authorisation in Germany.

Definition of residue

Metabolism studies in maize grown from treated seeds, pears and cucumber subject to foliar treatment, lettuce, potatoes, tobacco and rice subject to soil and foliar treatment as well as in animals (dairy cows and laying hens), studies of plant product transformation processes and studies of residues in the following crops were carried out for the Annex I inclusion of thiamethoxam.

These studies defined the residue in plants and products of animal origin as the sum of thiamethoxam (parent compound) and its metabolite CGA322704 (identical to clothianidin expressed as thiamethoxam equivalent) for the monitoring, control and assessment of consumer risk.

Residue trials

17 residue trials on maize were assessed for the Annex I inclusion of thiamethoxam with the reference insecticide Cruiser 70WG (700 g/kg) for the same good agricultural practices (GAPs) claimed. No pre-harvest interval (PHI) has been set because of the application method (seed treatment).

These 17 trials carried out with the insecticide Cruiser 70WG, as well as five others carried out with the insecticide Cruiser 350 FS according to the GAPs claimed on maize, resulted in Cruiser 350 FS being authorised in Germany.

All of the tests carried out with the insecticide Cruiser 350 FS present residue levels that are below the limit of quantification (LOQ) of 0.04 mg/kg (thiamethoxam equivalent) and compatible with the maximum residue limit (MRL) of 0.05 mg/kg recommended during the European assessment.

The six additional tests to be considered for use in France were conducted according to the same GAPs as recommended for Cruiser 350 FS in Germany. All of the tests carried out with the insecticide Cruiser 350 FS present residue levels that are below the limit of quantification (LOQ) of 0.04 mg/kg (thiamethoxam equivalent) and compatible with the maximum residue limit (MRL) of 0.05 mg/kg recommended during the European assessment.

The residue data provided for this mutual recognition procedure are considered adequate to support use on maize and sweet corn.

Animal feed studies

The animal feed studies conducted for the Annex I inclusion of thiamethoxam cover the risks associated with the use of Cruiser 350 FS on maize crops for animal feed.

All of these conclusions apply to the insecticide Cruiser.

Crop rotations

The crop rotation studies conducted for the Annex I inclusion of thiamethoxam are adequate to conclude that use of the insecticide Cruiser 350 FS does not lead to the presence of active substance residues in following crops. This is because the main metabolites are not extractable from wheat, radish or lettuce. Residues of thiamethoxam and its metabolite, CGA 322704, are less than 0.02 mg/kg on all the rotational crops studied.

All of these conclusions apply to the insecticide Cruiser.

Effects of industrial transformations and home preparations.

Because of the low level of residues in foods that are likely to be consumed by humans, studies on the effects of industrial transformations and home preparations on residue type and level are unnecessary.

Assessing the consumer risk

Based on the Acceptable Daily Intake (ADI¹⁰) of 0.026 mg/kg bw/d for thiamethoxam and in view of all of the residue trials submitted for this mutual recognition, assessment of the consumer risk from use of the insecticide Cruiser 350 FS on maize and sweet corn shows that the theoretical maximum daily intake (TMDI), estimated using the European consumption model (EFSA model), represents, depending on diet, from 4 to 24% of the TDI (0.001 to 0.006 mg/kg bw/d). It can therefore be considered that the insecticide Cruiser on maize does not pose an unacceptable risk for consumers in the event of chronic exposure.

Based on the Acute Reference Dose (ARfD¹¹) of 0.5 mg/kg bw/d for thiamethoxam and in view of all of the residue trials submitted for this mutual recognition, the assessment of consumer exposure from use of the insecticide Cruiser 350 FS on maize and sweet corn shows that the estimate of short-term intake (ESTI), calculated using the European consumption model (EFSA model), is at the most 0.6% of the ARfD (0.0029 mg/kg bw/d) for all diets. Based on this information, it can be considered that Cruiser on maize does not pose an unacceptable risk for consumers in the event of acute exposure.

Maximum Residue Limit

A maximum residue limit (MRL) of 0.05 mg/kg of maize was proposed once thiamethoxam had been included in Annex I of Directive 91/414/EEC.

Pre-Harvest Interval

No pre-harvest interval was set for the inclusion of thiamethoxam in Annex I of Directive 91/414/EEC due to its application as a seed treatment.

FATE AND BEHAVIOUR IN THE ENVIRONMENT

Thiamethoxam breaks down in the soil, mainly releasing the metabolites CGA 322704 (the same as clothianidin), CGA 355190, NOA 459602 and SYN 501406.

¹⁰ The Acceptable Daily Intake (ADI) is the estimation of the amount present in food or drinking water, expressed on the basis of body weight, that can be ingested daily throughout a person's life with no noticeable risk for consumer health.

¹¹ The Acute Reference Dose (ARfD) is the estimated amount of substance present in food or drinking water, expressed on the basis of body weight, that can be ingested over a short period, generally during a meal or a day, with no noticeable risk for consumer health.

The laboratory breakdown rate of thiamethoxam in the soil is from 34 to 276 days (DT50¹² lab). The field dissipation rate ranges from 7 to 172 days (mean DT50_{field} of 52 days). The field dissipation studies conducted by spraying thiamethoxam and the studies conducted with treated seeds indicate similar dissipation rates and kinetics between foliar application and seed treatment. All of the dissipation data are therefore considered for assessment, with no distinction between application method.

The laboratory breakdown rate of CGA 322704 is between 178 and 284 days. The field dissipation rates were discussed between Member States during the Community assessment of the substance. The DT50 values reported in the European conclusions are 57 and 77 days, while the values previously used in France consider DT50s between 22 and 228 days for five types of soil, with a standardised geometric mean of 95 days and a median of 112 days¹³. Because the latter are more similar to Afssa's conclusions for clothianidin, they have been selected for assessing the fate of CGA 322704 in soil. Differences are found, however, between the median DT50 values obtained for CGA 322704, depending on whether it forms from thiamethoxam or is applied directly on soil (clothianidin). These differences are explained by the associated kinetic formation fractions. The kinetic formation fraction DT50 value couple for CGA 322704 as a metabolite correctly describes the values measured, but the value of each one considered separately is uncertain. In particular, a couple combining a smaller kinetic formation fraction and a large DT50 might well correctly describe the values observed and tally better with the conclusions for clothianidin applied as it is. That said, it does not seem likely that these adjustments will modify the risk assessment.

The laboratory breakdown rates for the metabolites CGA 355190, NOA 459602, SYN 501406 and NOA 407475 are the same in the various conclusions.

Thiamethoxam and its metabolites CGA 322704, SYN 501406 and NOA 459602 are not absorbed much into the soil. However, the applicant states that the final values reported in the European conclusions for thiamethoxam are under discussion with the Rapporteur country. This is because these values are the mean of the Koc¹⁴ values and Kfoc¹⁵ values when, although similar, these parameters should not be averaged between themselves, particularly if the adsorption isotherms are not linear (which is the case for thiamethoxam with a 1/n parameter value between 0.80 and 0.93). As a result, only the Kfoc values combined with the corresponding 1/n values should be used to assess the risk of groundwater becoming contaminated (median Kfoc = 36.5 L/kg and median 1/n = 0.87). The conclusions of the French thiamethoxam assessment¹⁶ provide additional information on the metabolite NOA 459602, which does not adsorb after two days in contact with the soil.

The conclusions on the behaviour of the molecule in anaerobic conditions, its accumulation potential, behaviour in water and aquatic systems and behaviour in air are consistent between European and French assessments of the dossier, and are therefore not repeated here.

Calculating predicted environmental concentrations in soil (PEC_{soil})

To determine the PEC in soil, Germany used a dissipation rate that does not correspond with the maximum field DT50 value validated at European level. This calculation has therefore not been selected. Using the rate of 88.2 g/ha and field DT50 validated at European level, the PEC calculation put forward by the applicant covers the conditions of use in Germany. This conservative calculation can be used to estimate the predicted concentration levels of thiamethoxam in soil over time as well as its accumulation potential. These data are necessary for assessing the risks for soil organisms. The PEC thus obtained is not likely to call into question the conclusions of the risk assessment for soil organisms as drawn at European level for this application.

Calculating predicted environmental concentrations in groundwater (PEC_{gw})

¹² DT 50: Time it takes for 50% of the initial quantity of substance to be eliminated.

¹³ Both these values are combined with kinetic formation fractions (ffM) between 0.2 and 0.3.

¹⁴ Koc: soil/solution partition coefficient normalised to organic carbon content

¹⁵ Kfoc: Freundlich adsorption parameter normalised to organic carbon content

¹⁶ Report of the Toxicity Study Committee of Antiparasitic Products for Agricultural Use and Similar Products (CET) – session of 14 June 2006.

The Directive on the inclusion of thiamethoxam in Annex I of Directive 91/414/EEC stipulates *“Member States must pay particular attention to the potential for groundwater contamination, particularly of the active substance and its metabolites NOA 459602, SYN 501 406 and CGA 322704, when the active substance is applied in regions with vulnerable soil and/or climate conditions.”*

Germany’s conclusions are based on two lysimeter studies conducted in Germany and Switzerland. No modelling seems to have been assessed by the German authorities. Germany concludes its risk assessment for groundwater by indicating *“that a hazard for groundwater for the doses recommended for seed treatment can be excluded”*. The German report does, however, state that *“the toxicological relevance of the metabolite NOA 459602”* was due to be assessed.

The location of the lysimeter studies probably explains the fact that Germany considers the results of these studies to be more relevant than the modelling calculations. No explanation is given, however. The possible extrapolation of these results to French agro-pedo-climatic conditions has not been demonstrated, particularly for the main maize cultivation areas down the whole of the west of France from Normandy to the Pyrénées-Atlantiques.

As a result, it is considered that Germany’s conclusions cannot be extrapolated to assess the risk of groundwater contamination in France.

The risk of thiamethoxam and its metabolites transferring to groundwater is assessed by modelling. 47 national scenarios have been developed and adjusted for the PELMO model by the applicant, considering thiamethoxam application on various crops and integrating crop rotations.

Three of these scenarios are specifically based on maize single-crop farming (Aquitaine, Fr323, Midi-Pyrénées Fr263 and Rhône-Alpes Fr329). The application rate considered in these scenarios for maize is 88g a.s./ha.

The impact of modifying the K_{foc} adsorption parameter value of thiamethoxam being discussed with the reporting country on the estimated concentration levels in groundwater has been assessed for the 3 scenarios based on maize single-crop farming (the modelled dose being 88 g/ha). In these conditions, the modelled concentration levels are less than 0.1 µg/L for thiamethoxam and its metabolites CGA322704 and SYN 501406. Those for the metabolite NOA 459602 may exceed 0.1 µg/L.

Moreover, the impact of increasing the frequency of maize cultivation in the crop rotation for other regions (considering a fairly conservative maize re-cropping of every other year) and of modifying the K_{foc} adsorption parameter has also been assessed for some of the scenarios in which maize was cultivated during the crop rotation (Brittany Fr286, Lower-Normandy Fr343, Burgundy Fr260, Centre Fr336, Upper-Normandy Fr343 and Picardy Fr343). In these conditions, the modelled concentration levels are less than 0.1 µg/L for thiamethoxam and its metabolites CGA322704 and SYN 501406, but may exceed 0.1 µg/L for the metabolite NOA 459602.

The toxicological and ecotoxicological relevance of the metabolite NOA 459602 has been assessed using the guidance document Sanco/221/2000 – rev.10-Final¹⁷. A limit of 0.75 µg/L in groundwater was set after examining the information available on this metabolite.

The assessment of predictable concentration levels in groundwater still contains uncertainties over the sensitivity of models to input parameters, as described above. Because the calculated predicted concentration levels in groundwater are similar to the regulatory value of 0.1 µg/L for all these compounds, it is recommended, for the protection of groundwater, that this or any other product containing substances from the same family not be used to treat seeds on more than one in three crops in the rotation. A monitoring programme for groundwater quality will also need to be set up, particularly for groundwater that may be supplied from zones on which seeds have been treated with the insecticide Cruiser. This follow-up will consider thiamethoxam and the metabolites CGA 322704, NOA 459602 and SYN 501406.

¹⁷ Report of the Toxicity Study Committee of Antiparasitic Products for Agricultural Use and Similar Products (CET) – session of 14 June 2006.

Calculating predicted environmental concentrations in surface water (PEC_{sw})

No PEC calculation has been presented by Germany, which considers that applying Cruiser for seed treatment does not pose a risk of surface water contamination.

The applicant submitted an assessment of predicted concentration levels in surface water, adapted to the case where winter cereal follows maize cultivation. These calculations were made on the basis of the “la Jallière” drainage scenario, integrating a simultaneous contamination of thiamethoxam and CGA 322704. They are considered to be acceptable, but have been adapted to take account of maize cultivation only. The concentration levels obtained for thiamethoxam and CGA 322704 are used for assessing the risk for aquatic organisms.

ECOTOXICOLOGICAL DATA**Assessing the risks for birds and mammals*****Risks for birds and grain-eating mammals***

No particular attention is requested for birds and grain-eating animals in the thiamethoxam inclusion Directive. The Tier-1 assessment results highlight a high risk for birds and grain-eating mammals, but no refined assessment has been produced.

According to the German assessment report, the acute, short-term and long-term risks for birds, herbivorous and grain-eating mammals are acceptable. However, the authorisation certificate includes two precautionary phrases:

NT679: “The product is toxic to birds; for this reason, it must be ensured that no seed lies exposed on the soil. Before lifting the sowing machine, it must be stopped in time to stop seed losses after lifting”.

NT467: “Do not let the product, product remains, empty containers or packaging or rinsing liquids contaminate water. This includes indirect runoff in pipes during use in gardens and alleys, as well as rain or wastewater runoff drains”.

To back up the mutual recognition request, the applicant put forward refined assessments, with an update for maize. The assessment indicates high acute risks for grain-eating birds, with TERs¹⁸ less than 1 for three species likely to consume maize grains (starlings, pigeons and pheasants). The number of grains to reach the LD50 is estimated to be 32 for a starling and 320¹⁹ for a pheasant. This amount corresponds to a search surface area of 2.9m² for a starling and 29m² for a pheasant, if the seeds remain on the surface. The assessment indicates high acute risks for grain-eating mammals, with a TER of 1.1 for mice. The number of grains to reach the LD50 is estimated to be 31, which corresponds to a search surface area of 2.8m² if the seeds remain on the surface. As few seeds remain visible on the surface after accurate sowing, the probability of a life-threatening amount of seeds being rapidly ingested is low.

The short-term risks for grain-eating birds are considered to be acceptable, based on this assessment. The long-term exposure of birds and grain-eating mammals is not relevant.

Since this assessment does not cover accidental exposure to piles of lost seeds, however, to protect birds and wild animals it should be recommended that the treated seeds be completely buried in the soil and to verify that that is the case at the end of the rows.

Risks for small birds and herbivorous mammals

The inclusion Directive for thiamethoxam stipulates “*Member States must pay particular attention to the long-term risk to small herbivores if the substance is used for seed treatment*”.

The German assessment report does not contain an assessment of the risks for birds and herbivorous mammals.

¹⁸ The TER is the ratio between the toxicity value (DL50, CL50, NOEL, LOEL) and the estimated exposure, expressed in the same unit. This ratio is compared to a limit defined in Annex VI of Directive 91/414/EEC below which the limit value is not considered to be adequate for the risk to be acceptable.

¹⁹ Calculations revised by Afssa with a PMG of 200 g (200 mg/grain) used to convert the seed density into a dose per hectare, or 0.63 mg a.s./grain.

To back up the mutual recognition request, the applicant put forward a refined assessment. For herbivorous birds, it is based on European toxicity data²⁰ and refers to the thiamethoxam residues measured in treated maize (315 g a.s./100 kg) during the first few weeks of growth of young maize shoots [concentration levels of 69 mg a.s./kg (maximum) and 31.3 mg/a.s./kg (mean), mean dissipation time 50% = 3.33 days (mean)]. The acute TERs are 17, 11 and 19 for larks, partridges and geese. The dietary TERs based on a no-observed-effect-level on survival are higher, at 34, 22 and 39 for larks, partridges and geese. The long-term TERs are 8.2, 5.4 and 9.3 for the same species. Taking account of formation of the metabolite CGA 322704 increases the initial maximum and mean residue levels by 5.4% and 7% respectively. The dissipation rate of the two residues in plantlets is similar. The risks for herbivorous birds are acceptable.

For herbivorous mammals, the acute risks have been assessed using the LD50 of 783 mg a.s./kg bw. The long-term risk for wild vertebrates is assessed using a NOEL²¹ of 46 mg a.s./kg bw/d. The applicant presents a NOAEL²² of 115 mg a.s./kg bw/d (2500 ppm), based on the same study. Given the type and low range of effects at 115 mg a.s./kg bw/d²³, this NOAEL can be accepted for an in-depth assessment.

The assessment also takes account of the thiamethoxam residues measured in treated maize. The acute TERs are 8.2 and 41 for a vole and rabbit and the long-term TERs are 11.5 and 57.5 for the same species. The acute TER of 8.2 for a small herbivorous animal exposed exclusively to the treated food is considered to be an adequate safety margin. Taking account of formation of the metabolite CGA 322704 in plantlets increases the initial maximum and mean residue levels by 5.4% and 7% respectively. The dissipation rate of the two residues in plantlets is similar. The risks for herbivorous mammals are acceptable.

Assessing the risks for aquatic organisms

The inclusion Directive for thiamethoxam stipulates “*Member States must pay particular attention to the protection of aquatic organisms.*” The European assessment’s conclusions mention the possibility of exposure to the metabolite CGA 322704 in surface water. No assessment has been put forward by the Rapporteur Member State for seed treatment.

In Germany, the risk associated with drainage has not been assessed. The German assessment report concludes that there is only a negligible risk for aquatic organisms as they are not exposed for this application method. However, thiamethoxam and CGA 322704 are mobile and can be transferred to surface water. They present very similar ecotoxicological profiles. Their simultaneous presence in surface water from soil drainage needs assessing and considering in the risk evaluation for aquatic organisms.

The in-depth assessment is based on the concept of toxic units and compares the acute and chronic toxicity data of thiamethoxam and the metabolite CGA 322704. A thiamethoxam/CGA 322704 toxicity ratio of 7 has been selected on the basis of all the acute and chronic toxicity data of both substances on aquatic invertebrates.

The PNEC²⁴ selected for assessing risks is the most critical, expressed as CGA322704 equivalent. It is 0.066µg/L. The maximum PEC has been reviewed for the 69.3 g a.s./ha rate and expressed as CGA 322704 equivalent. It is 0.042 µg/L. The resulting PEC/PNEC ratio is less than 1. Note that the PEC/PNEC ratio is more than 1 for an 88.2 g a.s./ha application rate.

The risk associated with the deposit of dust emitted during sowing was also assessed by the applicant. 5 metres from a field, the deposit was measured and corresponds to a rate of 0.475 g a.s./ha (88.2 g a.s./ha x 0.54%), or a concentration of 0.159 µg thiamethoxam/L in a static model system. This concentration, less than the PNEC, indicates an acceptable risk.

Assessing the risks for bees

The thiamethoxam inclusion Directive does not mention any specific precautions to protect bees.

²⁰ NOEL of 29.4 mg a.s./kg bw/d instead of NOEL and NOAEL of 34.9 and 100 mg a.s./kg bw in 2003

²¹ NOEL: No observed effect level

²² NOAEL: No observed adverse effect level

²³ 2 to 6.7% of body weight variation

²⁴ PNEC: predicted no effect concentration (on aquatic organisms)

Regarding the data assessed at European level, thiamethoxam and CGA 322704 are very toxic to bees. Thiamethoxam is systemic and can migrate to pollen and nectar. It hydrolyses into CGA 322704 which is considered to be a relevant residue in plants. This major metabolite can persist and residues in the soil can be mobilised by the crops that follow. A flow of thiamethoxam and CGA 322704 towards the hive cannot be excluded and the hive bees may be exposed (larva, nurse bees, winter bees).

The German assessment is based on plastic tunnel and field tests on various crops. These tests, in accordance with EPPO²⁵ guidelines with rape, sunflower and maize seed treatments, do not show any significant effect on mortality, pollen gathering, population growth, larval growth or bee behaviour.

In a plastic tunnel test, rape treated with increasing doses on seeds (from one to eight times the dose) affects pollen-gathering activity at the highest dose. Up to 202 g a.s./ha, six times the recommended rate, there are no significant effects on survival, pollen gathering, colony growth or larval condition.

Two behavioural studies indicate NOECs of 100 µg/kg²⁶ for the exchange of food (trophallaxis) and 25 µg/kg²⁷ (for return to the hive). At 50 µg/kg²⁸, return to the hive is significantly affected.

The toxicity of thiamethoxam and CGA 322704 by repeated administration for 10 days in adult bees was determined, with a NOEC of 10 µg/kg²⁹ on survival.

Analyses of thiamethoxam and CGA 322704 residues in the different samples taken during the tests show levels that are less than or similar to the limit of quantification of 1 µg/kg in nectar, pollen, hive honey and nectar taken from the crop of pollen-gathering bees. The maximum levels were measured in the pollen of spring rape (3.6 µg/kg), sunflower (3.2 and 2 µg/kg) and maize (3 µg/kg). The residues measured in the pollen of rape treated at 8 times the dose (269 g a.s./ha)³⁰ are 27 µg/kg and 10 µg/kg for thiamethoxam and CGA 322704 respectively. The residues measured in the pollen of rape treated at the recommended dose are 1.8 µg/kg for thiamethoxam and less than 1 µg/kg for CGA 322704.

Germany concludes that there is a negligible risk for bees due to the method of applying the product for seed treatment.

To back up its mutual recognition request, the applicant submitted residue tests on assessing the risk for bees. In the maize pollen gathered by bees, the mean values are 4.81 µg/kg (2005), 2.09 µg/kg (2006) and 3.45 µg/kg (2005 and 2006) for thiamethoxam³¹ and 2.65 µg/kg (2005), 1.37 µg/kg (2006) and 2.01 µg/kg (2005 and 2006) for CGA 322704³².

The risk quotients (Hazard Quotient or HQ) that compare the product doses applied per hectare with the LD50 values measured during the acute toxicity tests have been defined for sprayed products and are therefore irrelevant for the products used to treat soil or seeds.³³ For the products recommended for seed treatment, the Directive stipulates that the bee risk assessment integrates the measured concentrations in pollen and/or nectar as measured during the residue studies.

²⁵ EPPO: European and Mediterranean Plant Protection Organization

²⁶ corresponds to a NOEL of 5 ng thiamethoxam/bee; likewise for CGA 322704, the NOEC of 100 µg/kg corresponds to a NOEL of 2.8 ng CGA 322704/bee.

²⁷ corresponds to a NOEL of 3 ng thiamethoxam/bee; likewise for CGA 322704, the NOEC of 25 µg/kg corresponds to a NOEL of 0.8 ng /bee.

²⁸ corresponds to a NOEL of 5.5 ng thiamethoxam/bee.

²⁹ corresponds to a NOEL of 1.845 ng thiamethoxam/bee/10 d or 1.892 ng /bee/10d.

³⁰ corresponding to 3360 g a.s./q, 0.2 mg a.s./seed and 269 g a.s./ha.

³¹ LOQ of 1 µg thiamethoxam /kg in pollen.

³² LOQ of 1 µg CGA322704 /kg in pollen.

³³ Document Sanco/10329/2002 rev 2final chapter 4.

Data on the residue measured in pollen, reported above, are used to calculate the intake per bee, on the basis of 65 mg pollen consumption for 10 days, 80% of which is maize pollen³⁴. The NOELs used come from prolonged toxicity studies over 10 days and are 0.002 µg/bee for 10 days for thiamethoxam and its metabolite CGA 322704³⁵. Because these NOELs were measured over 10-day periods, they are compared to the mean concentration levels in pollen so as to avoid the overestimation of exposure that would occur if occasional peaks in concentration were taken into account. The NOEL/intake ratios of 0.090 for thiamethoxam and 0.055 for CGA 322704 indicate an acceptable short-term risk for nurse bees. These calculations for pollen-gathering bees consuming pollen are more conservative than those corresponding to other scenarios exposing other categories of pollen-consuming bees.

Analyses of residues in different matrices sampled on winter rape and exposed bees and colonies have also been provided (nine studies). Two crop scenarios were applied (rape treated alone and treated barley followed by treated rape) in three sites. Thiamethoxam was measured in the nectar collected by bees (1.85 µg/kg for the scenario of rape alone, 1.7 µg/kg for the barley-rape scenario)³⁶. The metabolite CGA 322704 was never quantified³⁷. The levels of thiamethoxam residue in pollen are similar to or less than those measured in nectar collected by bees. In nectar collected in the hives, thiamethoxam was only quantified on one site (0.7 µg/kg for two crop scenarios) and the metabolite was never quantified. Thiamethoxam and its metabolite were not quantified in honey, wax³⁸ or royal jelly. The residue levels in the soil during the sowing of winter rape, after barley treated in the spring had been sown (77 g a.s./ha, PEC estimated to be 0.1027 mg thiamethoxam/kg of soil and 0.0316 mg CGA 322704/kg of soil), are 0.003-0.0035 mg of thiamethoxam/kg of soil and 0.002-0.002 mg of CGA 322704/kg of soil³⁹. The scenario selected by the applicant to meet the request for following crops shows that residues in treated rape after treated spring barley are low, and less than the levels assessed in maize pollen.

Lastly, the deposit of dust from sowing at various distances from the sowing line was measured. The estimated exposure via dust at five metres is 0.37 g a.s./ha for a sowing rate of 110 000 seeds/ha. This is less than the NOAEL of 1 g thiamethoxam/ha/per application on flowering phacelia arising from a thiamethoxam dispersible granule formulation.

In conclusion, the short-term risks are considered to be acceptable for adult bees. No effect associated with exposure to the pollen or nectar of treated crops was detected in the plastic-tunnel or field trials. The assessment of long-term risk to a colony is yet to be completed, pending the additional studies under way. Information on the exposure levels through pollen and nectar confirms a low exposure level in a scenario where barley is cultivated in the springtime and rape in the winter.

Pending the results of additional studies, and to reduce exposure via the gathering of pollen or nectar from the treated crop or following crops which are likely to contain residues of thiamethoxam, hives should be moved more than 3km away from the crops cultivated from treated seeds during the flowering period. In addition, plants that might attract bees should not be introduced at a later date in the crop rotation and measures should be applied to limit bee exposure. A follow-up of pilot hives under realistic conditions is also recommended to quantify the potential contamination level in hives and refine the impact and nature of long-term risks.

The risks for other non-target arthropods, soil macro- and micro-organisms and plants adjacent to the treated plot of land are acceptable.

BIOLOGICAL [EFFICACY] DATA

No comparability dossier has been put forward for this mutual recognition procedure.

Effectiveness

³⁴ Approach in accordance with the proposals of the working group "assessment of systemic products in soil or seed treatment" of the International Commission for Plant-Bee Relationships).

³⁵ The NOEL for clothianidin is 0.0029 µg/bee/10d.

³⁶ LOQ of 0.5 µg thiamethoxam/kg in nectar, honey, royal jelly and wax

³⁷ LOQ of 1 µg CGA 322704/kg in nectar, honey, royal jelly and wax

³⁸ 2 detections in 2 plastic tunnels and in a single sub-sample each time (mean of 0.75 µg thiamethoxam/kg)

³⁹ Concentration in a thickness of 0-30 cm of soil

All of the effectiveness tests presented by the applicant show that the insecticide Cruiser 350 FS is of similar effectiveness to the imidacloprid-based reference insecticide for treating maize seeds against click beetles and frit flies, at the recommended dose of 0.09 L formulated product per seed unit (1 unit = 50 000 grains).

All of these conclusions are applicable to the insecticide Cruiser, for applications on maize and sweet corn.

Note that the German assessment report also presents an assessment on the treatment of maize and sweet corn seeds to protect against the Western corn rootworm *Diabrotica virgifera*. This treatment is not applied in France, and its marketing authorisation is incompatible with the status of the quarantine insect *Diabrotica virgifera*, which is subject to organised pest control by the French public services for eradication purposes. It has therefore not been considered for this mutual recognition.

Phytotoxicity

The tests conducted with the insecticide Cruiser FS show that, whatever the variety of maize or sweet corn, no notable phytotoxic effect on population, robustness, yield or colouring or discolouring of maize or sweet corn plants has been observed.

This conclusion is applicable to the insecticide Cruiser.

Impact of treatment on yield and/or quality of plants or plant products

The data provided in the German assessment report on the insecticide Cruiser 350 FS for maize and sweet corn show no notable negative effect on the yield or quality of plants or plant products after this insecticide has been used as recommended to treat seeds.

This conclusion is applicable to the insecticide Cruiser.

Comments on adverse or side effects

The data provided in the German assessment report on the insecticide Cruiser 350 FS for maize and sweet corn show no notable adverse or side effects after this insecticide has been used as recommended to treat seeds.

This conclusion is applicable to the insecticide Cruiser.

However, the applicant has not supplied any tests regarding impact on the germination of seeds from treated maize seed plants. These tests should be conducted once authorisation has been obtained.

Resistance

The risk of insects becoming resistant to thiamethoxam is deemed to be the same as for other neonicotinoids. It is estimated to be less for soil pests (click beetles and frit flies) than for airborne pests (aphids, Colorado potato beetle). The most important resistance risks concern aphids, which are likely to be exposed to neonicotinoids through the treatment of other host plants.

The risk of cross-resistance developing between thiamethoxam and synthetic pyrethroids, carbamates or organophosphates is low because these molecules act in different ways. That said, this risk of cross-resistance developing should not be excluded as regards other neonicotinoids.

Resistance risk management is recommended for all neonicotinoids. In this context, the applicant lists a certain number of recommendations, including not using neonicotinoids for the foliar treatment of crops when the seeds have been treated with these active substances. This recommendation is considered to be sensible and adequate to manage this risk of cross-resistance developing.

CONCLUSIONS AND RECOMMENDATIONS

The French Food Safety Agency estimates that:

- A** The risks for operators, workers and consumers associated with use of the insecticide Cruiser 350 FS, as assessed by the German competent authorities, are acceptable. This conclusion applies to the insecticide Cruiser in the conditions of use specified below. A surveillance study of worker (sower) exposure should nevertheless be put in place to confirm these estimations.

The environmental risks from using the insecticide Cruiser are considered acceptable in the conditions of use specified below. The levels of thiamethoxam and the metabolites CGA 322704, NOA 459602 and SYN 501406 should nevertheless be monitored in groundwater that may be supplied from zones on which seeds have been treated with the insecticide Cruiser, according to a protocol defined in advance with the competent authorities.

The risks for environmental organisms, particularly birds, wild animals and aquatic organisms, associated with use of the insecticide Cruiser are acceptable. For bees, the risk is also considered acceptable. Nevertheless, the assessment of long-term risk to the colony may be completed once the results of additional studies under way become available. Pending these results, the hives should be moved more than 3km away from crops grown from treated seeds during the flowering period. A follow-up of pilot hives under realistic conditions is also recommended, to quantify the potential contamination level in hives and to refine the impact and nature of long-term risks.

- B** The level of effectiveness of Cruiser 350 FS for treating maize and sweet corn seeds against click beetles and frit flies at the recommended dose of 0.09 L f.p/U⁴⁰ in France is satisfactory. This conclusion is applicable to the insecticide Cruiser.

The following should nevertheless be set up:

- post-authorisation trials for seed-bearing maize to assess the impact of seed treatments on the germination of seeds from treated maize;
- post-authorisation monitoring to check that the insecticide remains effective on soil pests over time.

Lastly, to prevent risks of cross-resistance developing, it is recommended not to use insecticides from the neonicotinoid family for foliar treatment in crops where the seeds have been treated with thiamethoxam..

Classification of the insecticide, risk phrases and safety phrases:

N, R50/53 S60 S61

- N : Dangerous for the environment
 R50/53 : Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

 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 sheet

Conditions of use:

- Wear gloves and a protective overall during all seed treatment operations, and respiratory protection (minimum level P2) during cleaning.
- SP1: Do not pollute water with the product or its packaging. [Do not clean the application equipment near surface water. /Avoid contamination via water evacuation systems from farmyards or roads.].
- SPe1: To protect groundwater, do not apply this or any other product containing substances from the same family to treat seeds more than one in three years in the rotation.
- SPe5: To protect birds and wild animals, the treated seeds must be entirely incorporated in the soil; ensure that the treated seeds are also entirely incorporated at the end of rows.

⁴⁰ : formulated product per seed unit. 1 unit = 50 000 grains of seed.

- SPe8: Dangerous to bees. Move hives more than 3km away from crops cultivated from treated seeds during the flowering period. Do not later introduce plants that may attract bees in the crop rotation or apply measures that may limit bee exposure.
- **Maximum sowing density:** 110 000 grains/ha.
- **Interval during which people must not enter the treated plots:** not applicable for seed treatment.
- **Maximum residue limits (MRLs):** refer to European MRLs⁴¹
- **Pre-Harvest Interval (PHI):** no pre-harvest interval has been set because the insecticide is used for seed treatment.

Label:

The draft label complies with the requirements for recommended use. The Table of Use should nevertheless state that:

- this is a seed treatment.
- the recommended rate of use is understood to be of “formulated product”.

In accordance with Directive 2006/8/EC⁴², the label must also state: “Contains 1,2-benzisothiazoline-3-one. Can cause an allergic reaction.”

In view of all the data available, the French Food Safety Agency therefore issues a favourable Opinion for the marketing authorisation of Cruiser within the context of a mutual recognition procedure, for use on maize and sweet corn, to protect against frit flies and click beetles (Annex 1, Table 2), under the aforementioned conditions for labelling and use.

Moreover, in accordance with article R.253-17 of the French Rural Code, Afssa recommends that all marketing authorisation decisions for plant protection products require the holder to provide it annually with accurate statistics on the amount of product marketed in France, which will be useful for any subsequent assessment of this product.

[signed by the Director-General of Afssa]

⁴¹ Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin.

⁴² Commission Directive 2006/8/EC of 23 January 2006 amending, for the purposes of their adaptation to technical progress, Annexes II, III and V of Directive 199/45/EC of the European Parliament and of the Council concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations.

Annex 1

Table 1: List of uses requested in France of the insecticide Cruiser

Uses	Rate of use	Maximum rate of active substance	Maximum number of applications
15551101 - Maize*seed treatment *frit flies	0.09 L f.p /U*	88.2 g a.s./ha **	1
15551103 – Maize*seed treatment *click beetles			
15551104 – Maize*seed treatment *aphids			
15551105 – Maize*seed treatment *leafhoppers			
16661102 - Maize*seed treatment *frit flies			
Sweet corn*seed treatment* click beetles			
Sweet corn*seed treatment* aphids			
Sweet corn*seed treatment* leafhoppers			
15561102 – Sorghum*seed treatment *click beetles			

*f.p /U: formulated product per seed unit. 1 unit = 50 000 grains

** based on a sowing density of 2.8 U/ha (or 140 000 grains/ha).

Table 2: List of uses considered for the mutual recognition procedure and submitted for authorisation in France for the insecticide Cruiser

Uses	Dose for use	Maximum dose of active substance	Maximum number of applications
15551101 - Maize*seed treatment *frit flies	0.09 L f.p /U*	69.3 g a.s./ha **	1
15551103 - Maize*seed treatment *click beetles			
16661102 - Sweet corn*seed treatment*frit flies			
Sweet corn*seed treatment* click beetles			

*f.p /U: formulated product per seed unit. 1 unit = 50 000 grains

** based on a sowing density of 2.2 U/ha (or 110 000 grains/ha).