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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance ethanol[1]

(Question No EFSA-Q-2008-394)

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SUMMARY

Ethanol is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004,[2] as amended by Regulation (EC) No 1095/2007.[3] This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on ethanol in accordance with the provisions of Article 21(1) of the Regulation (EC) No 2229/2004, which was received by the EFSA on 7 January 2008. The peer review was initiated on 25 February 2008 by dispatching the DAR for consultation of the Member States and the sole notifier Catalytic Generators UK Limited. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by the EFSA to identify the remaining issues. The identified issues as well as further information made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in October 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in December 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative use as an ethene precursor, as proposed by the notifier, which comprises of the use of ethanol in a catalytic generator to produce ethene gas, which is used as a growth regulator for the ripening of bananas. Ethanol would not be applied directly to the plants.

The representative formulated product for the evaluation was 'Ethy-Gen II', a gas generator (GE) containing 90 % (w/w) ethanol.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance ethanol. *EFSA Scientific Report* (2008) 215, 1-48.
[2] OJ L379, 24.12.2004, p.13.
[3] OJ L246, 21.9.2007, p.19.

Considering the applied for use, ethanol cannot be regarded as an active substance, since ethene is in fact the true active substance. A risk assessment for ethene (ethylene) has been presented in a separate DAR.

However, the experts on toxicology decided to discuss the substance according to the agenda. No metabolism or toxicity study was submitted to the rapporteur Member State, therefore all the toxicological information came from the open literature, mainly from the US EPA and the IARC review of 1988. The animal data and published information submitted was of insufficient quality to set NOAELs, although these studies had identified target organs and tissues. Considering the representative use, ethanol does not come into contact with food materials being treated and therefore no ADI or ARfD are needed. With regards to the operator exposure risk assessment, the experts concluded that, in view of the low dermal and inhalation exposure (as a worst case, operator exposure would represent the dermal application of 1.08 ml ethanol/day), compared with other sources of general use (as in cosmetics, medicines, household products), there was no concern over the risk assessment to operators. No exposure is foreseen for workers or bystanders related to ethanol and therefore no AOEL was considered necessary. Accordingly, no data gap was set to define NOAELs (either short term, long term, for reproductive toxicity or from further studies) with ethanol. No classification proposal could be concluded based on the available information, but was not required for the risk assessment.

A data gap was set on the toxicological information of the reaction product, ethene and other breakdown products, for formal reasons, as in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. This information is needed to conclude on the worker risk assessment (operators and bystanders are not considered to be exposed to ethene and other breakdown products). Another data gap was confirmed for information on the nature and levels of impurities as a result of the catalytic generation.

No data or information with regard to residues and consumer exposure were available in the peer review procedure. Under the notified conditions of use the crop will not be exposed to ethanol but to ethene. However ethene and potential other metabolites or reaction products were not subjected to an assessment during the peer review of ethanol. An addendum prepared by the rapporteur Member State on the 'Assessment of available information on the residues of the reaction and degradation products (ethene and ethene oxide)' could not be considered in the meeting of experts due to the restrictions laid down in Commission Regulation (EC) No. 1095/2007. Consequently, no discussion or conclusion on the consumer risk assessment and in terms of a MRL proposals were possible. It is proposed by EFSA to set a data gap with regard to the assessment of the relevant information on the residues of the reaction and degradation products of ethanol.

The evaluation of the environmental fate and behaviour of ethanol in soil and natural surface water systems is not relevant for the representative use as there will be no exposure to these environmental compartments from ethanol. However, it was recognised that there may be the potential of exposure to two metabolites, or reaction products, of ethanol: ethene and ethene

oxide. As these reaction products were not assessed in the DAR for ethanol, but a reference was made to the DAR for ethene, which has not been peer reviewed. A data gap for data and/or information on ethene and ethene oxide was identified.

The risk to non-target organisms from the use of ethanol was considered to be minimal due the lack of exposure. The risk from exposure from the two metabolites, or reaction products, ethene and ethene oxide however needs to be assessed. These reaction products were not assessed in the DAR for ethanol, but a reference was made to the DAR for ethylene, which has not been peer reviewed. A data gap to address the potential risk from ethene and ethene oxide was identified during the peer review.

Key words: ethanol, ethene, ethylene, peer review, risk assessment, pesticide, plant growth regulator

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BACKGROUND

Commission Regulation (EC) No 2229/2004 laying down the detailed rules for the implementation of the fourth stage of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 1112/2002, as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Ethanol is one of the 295 substances of the fourth stage, covered by the amended Regulation (EC) No 2229/2004 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 21(1) of the Regulation (EC) No 2229/2004, the United Kingdom submitted the report of its initial evaluation of the dossier on ethanol, hereafter referred to as the draft assessment report, received by the EFSA on 7 January 2008. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 24(2) of the Regulation (EC) 1095/2007 on 25 February 2008 to the Member States and to the sole notifier Catalytic Generators UK Limited, as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, the EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

A public consultation on the DAR was launched on 8 September 2008 when the DAR became publicly available upon specific request at the EFSA website and the deadline for submission of comments was 19 October 2008. Public comments were received by the EFSA during the consultation period.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in October 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in December 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

In accordance with Article 24c(1) of the amended Regulation (EC) No 2229/2004, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant endpoints for the active substance as well as the formulation is provided in appendix A.

The documentation developed during the peer review was compiled as a peer review report comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (revision 1-1; 17 July 2008),

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1; 18 December 2008).

Given the importance of the draft assessment report including its addendum (compiled version of November 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Ethanol is an aliphatic alcohol.

The representative formulated product for the evaluation was 'Ethy-Gen II', a gas generator (GE) containing 90 % (w/w) ethanol.

The representative use evaluated comprised of the use of ethanol in a catalytic generator to produce ethene gas, which is used as a growth regulator for the ripening of bananas. Ethanol would not be applied directly to the plants.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The identity of the active substance was discussed in the meeting of experts PRAPeR 56 (October 2008). The meeting agreed that for the proposed representative use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true active substance. Ethanol is not applied directly to the crops. A risk assessment for ethene (ethylene) has been presented in a separate DAR. It should be noted that a product similar to the representative formulated product notified here was also included in the ethylene task force dossier. As a consequence of the decision of the PRAPeR expert meeting 56, the discussion of ethanol as an active substance was not continued with regard to physical/chemical properties.

2. Mammalian toxicity

Ethanol was discussed at the PRAPeR expert's meeting on mammalian toxicology (PRAPeR 59) in October 2008 on basis of the draft assessment report (December 2007). In view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the addendum 2 of October 2008 could not be considered in the peer review.

The meeting of experts PRAPeR 56 (see section 1) concluded that for the representative use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true active substance and is already covered by its own risk assessment. However the meeting on toxicology considered that, as ethanol was notified in accordance with the legislation and it was a policy decision to consider ethanol and ethene as separate active substances, it was not for the meeting to comment on policy decisions but only on the risk assessment. Therefore, the meeting agreed to discuss ethanol according to the agenda.

No metabolism or toxicity studies have been submitted or evaluated by the rapporteur Member State; all the information and toxicological data referred came from the published literature, mainly from the US EPA[4] and IARC[5] review of 1988.

[4] US EPA Re-registration Eligibility Document: Aliphatic alcohols, 1995 (EPA RED 1995).

No classification proposal could be concluded. It was recognised that classification was a very difficult and sensitive area, given the widespread general public exposure to ethanol, and it was noted that no classification had been agreed yet from the toxicological point of view at the competent European Authority for Classification and Labelling, but as original studies were missing, no conclusion could be drawn on this issue by the meeting. Given the representative use of ethanol, classification data were not required for the risk assessment.

Consideration was given to the wide use of ethanol in industry, its presence in varying quantities in commonly encountered substances (cosmetics, household products, medicines) and in widely consumed beverages (such as beers, wines and spirits), although the latter was not taken into consideration for the risk assessment.

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

Ethanol is rapidly and extensively absorbed from the gastrointestinal tract by simple diffusion. The rate of absorption is decreased by delayed gastric emptying and by the intestinal content. Distribution throughout the body is rapid. Ethanol is eliminated from the body mainly by metabolism in the liver with minor amounts excreted in urine, via lungs and in sweat.

Ethanol is metabolised by the liver using three basic steps: i) oxidation of ethanol to acetaldehyde, mainly by alcohol dehydrogenase (ADH) or also by catalase and cytochromes P450; ii) conversion of acetaldehyde to acetate by aldehyde dehydrogenase (ALDH) ; iii) acetate is then metabolised to carbon dioxide, fatty acids and water via the citric acid cycle (Krebs cycle).

2.2. Acute toxicity

Ethanol has low acute toxicity either via the oral, dermal or inhalation routes. It is not a skin irritant or a skin sensitiser, but there was some evidence of eye irritating potential. The acute oral administration of ethanol can induce a significant increase in lipid content of rat hepatocytes (steatosis) and hepatomegaly. Following inhalation exposure, the reported clinical signs of toxicity included incoordination, behavioural effects, narcosis and lethality.

2.3. Short-term toxicity

The animal data and published information submitted was of insufficient quality to set NOAELs, although these studies had identified target organs and tissues. The experts agreed that NOAELs could not be set with confidence based on the data submitted by the notifier and discussed the need for it. Considering the representative use of ethanol, no ADI, or ARfD are necessary, as there is no dietary exposure of consumers; the experts concluded that the AOEL was also not needed considering the risk assessment proposed by the rapporteur Member

[5] IARC Monograph on the Evaluation of Carcinogenic Risks to Humans (1988): Alcohol Drinking, Vol. 44 (IARC 1988).

State (see section 2.12 below). Therefore there is no need to establish short term NOAELs for ethanol.

The liver was the major target organ of ethanol following oral administration to rats, characterised by liver enlargement, fatty liver, biochemical and histopathological changes. Fatty change of the renal tubules was also evident at lower doses than the liver findings; in addition, haematological changes on red and white blood cell parameters were reported, as well as irritation effects in the gastrointestinal tract.

2.4. Genotoxicity

Information submitted by the notifier consisted of the review made by IARC in 1988 of experimental studies *in vitro* and *in vivo*. The experts questioned whether there was a valid *in vivo* study in both somatic and germ cells, on which to set a classification as Cat. 2 for mutagenicity. The meeting noted that the limited information provided was of questionable validity and quality to assess the genotoxicity of ethanol, as was the case in section 2.3 above for setting the NOAELs. Therefore based on the data provided, no classification proposal for genotoxicity could be concluded. The meeting agreed to flag up for ECHA[6] to critically consider the genotoxic properties of ethanol. Taking into consideration the representative use of ethanol, these data are not required.

2.5. Long-term toxicity

One published chronic toxicity and carcinogenicity study in rat was submitted to the rapporteur Member State together with the IARC review (1988). The animal data and published information submitted was of insufficient quality to set NOAELs, although these studies had identified target organs and tissues. In the published study (1994), non-neoplastic finding included liver and bile duct injury, inflammation of the pancreas and clitoral gland, hyperplasia in the thyroid and adrenal glands, and peripheral nerve degeneration. There was no evidence of ethanol-induced carcinogenic activity in rats at dose levels of 1 % and 3 % ethanol in a semi-synthetic liquid diet. The IARC review concluded that the evidence for ethanol-induced carcinogenicity in experimental animals was inadequate, but there was sufficient evidence for carcinogenicity of alcoholic beverages in humans. Therefore, the IARC classified alcoholic beverages as carcinogenic to humans.

Again, the meeting concurred that, as for genotoxic properties, there was insufficient information to decide on the carcinogenic properties of ethanol. It was also noted that the major metabolite, acetaldehyde has been classified as a Cat. 3 Carcinogen in Annex I of Directive 67/548/EEC, 19th ATP[7]. Considering the representative use of ethanol, neither chronic NOAELs, nor carcinogenic properties clarification were required.

[6] ECHA: European Chemical Agency

[7] Commission Directive 93/72/EEC of 1 September 1993 adapting to technical progress for the nineteenth time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances

2.6. Reproductive toxicity

There are a vast number of studies in the public domain dealing with the reproductive effects of ethanol administration on experimental animals; again the IARC review was the main source of information given in the DAR.

The weight of evidence approach indicates that ethanol administration at relatively high dose levels induces an extensive number of serious adverse effects on the reproductive organs and tissues of experimental animals. The database submitted does not allow for NOAELs to be set, or for conclusions to be reached on the reproductive properties. Again this should be flagged to ECHA. Considering the representative use, these data were not required.

2.7. Neurotoxicity

No specific neurotoxicity studies were submitted. However, behavioural effects, nerve demyelination and serious developmental effects on the nervous system (including foetal alcohol syndrome – FAS – in monkeys) have been reported in the standard studies. Considering the representative use, further data were not required.

2.8. Further studies

Metabolites

Acetaldehyde

In the DAR, information was given on acetaldehyde, which is the primary metabolite of ethanol in mammals. Acetaldehyde is currently classified as Xn, "Harmful", Carc Cat 3, R40 "Limited evidence of a carcinogenic effect" and as Xi, "Irritant", R36/37, "Irritating to eyes and respiratory system". The genetic and reproductive toxicity of acetaldehyde have been reviewed by IARC (1987). Positive results were observed with acetaldehyde in a series of *in vitro* and *in vivo* studies. Foetal malformations and resorptions were found in rats and foetal malformations were found in mice treated with acetaldehyde.

Reaction and degradation products

Ethene

The rapporteur Member State presented in addendum 2 (October 2008) as assessment of available information on the toxicology of the reaction and degradation products ethene and ethene oxide, which could not be taken into consideration by the meeting in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007. Therefore a data gap was set for formal reasons on toxicological information on ethene and other breakdown products.

Impurities resulting from the catalytic generation of ethene

The meeting was informed that a study is ongoing; the rapporteur Member State had no information on the outcome. The data gap was confirmed for information on the nature and levels of impurities as a result of catalytic generation.

2.9. Medical data

There are numerous and extensive published studies on the effects of ethanol in humans. Ethanol is a central nervous system depressant. Effects of acute ingestion include behavioural and physiological disturbances that can result in coma, convulsions and death. Fatal acute doses for adults appear to be 5-8 g/kg bw and 3 g/kg bw for children.

Adverse changes on the gastrointestinal tract were reported in the mouth, salivary glands, oesophagus and stomach. The effects on the liver include fatty liver, alcoholic hepatitis and fibrosis to irreversible cirrhosis. Other ethanol-induced effects include acute and chronic pancreatitis, effects on the heart ventricles, on the endocrine system (adrenals, thyroid and gonads) and on the immune system in patients with alcoholic liver disease.

Reproductive effects and prenatal toxicity of ethanol in humans is also well-documented, as the 'foetal alcohol syndrome' (FAS) which is characterized by both physical and mental effects upon ethanol consumption during pregnancy.

Epidemiological studies available in the IARC publication (1988) report on the effects of alcoholic (ethanol) beverages. IARC classified alcoholic beverages as carcinogenic to humans (Group 1 on IARC system).

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

There are insufficient data to set reference values for ethanol. The rapporteur Member State did not propose any reference value in the DAR. However, considering the representative use, ethanol does not come into contact with food materials being treated, and therefore no ADI or ARfD were required. The meeting discussed the need to set an AOEL value. Taking into consideration the operator exposure assessment (see section 2.12 below), no AOEL was required. **No ADI, ARfD or AOEL were set.**

2.11. Dermal absorption

No study was submitted and therefore the default value of 100 % for dermal absorption is applicable.

2.12. Exposure to operators, workers and bystanders

Operator exposure

The representative use of ethanol is in a catalytic generator to produce ethene gas for controlling the ripening of bananas. Ethanol is used as a precursor in the production of ethene in specially designed generators. The representative formulation 'Ethy-gen II' is a 90 % ethanol liquid formulation supplied in 0.946 litre containers for use in these catalytic ethene generators. The product is poured in at the top of the generator and the lid replaced before turning on. Control (computerised) is from outside the ripening store, the system being completely closed with no operators present during the application process. The room is

sealed for 24 hours and then ventilated before an operator may re-enter to remove the generator and monitor the progress of the ripening process.

Operator exposure to ethanol is therefore limited to the loading of ethanol into the generator. Typically, two loading operations are needed per room treated and a typical store was considered to have 30 ripening rooms. The UK POEM includes data for hand contamination experienced during mixing and loading (manual pouring with single trip containers). In the unlikely event that a single operator decanted all of these containers on the same day, estimated dermal contamination would be 1.2 ml product (1.08 ml ethanol/day). The experts considered that both dermal and inhalation exposure appear to be low when compared with the exposure resulting from other sources, such as cosmetics, medicine and household products - but excluding alcoholic drinks. Therefore no concern was raised regarding the risk for operators.

It was concluded also that there is no operator exposure to ethene, as persons re-entering the room would then be considered as workers.

Worker exposure

From the representative use explained above, there is no worker exposure to ethanol. Worker exposure is related to ethene, for which no toxicological data were available for the meeting (see section 2.8 above). The experts considered, however, that exposure appears to be negligible in view of the intended use (the room is ventilated through an automated system before re-entry is allowed). Worker exposure to ethene is nevertheless a data gap for formal reasons.

Bystander exposure

As the system involves the exclusion of operatives during the application process, no bystanders will be present.

3. Residues

Ethanol was discussed at the PRAPeR 60 meeting of experts in residues in October 2008.

The representative use of ethanol is in a catalytic generator to produce ethene gas for controlling the ripening of bananas. Direct exposure of the crop to ethanol is therefore not expected. However, under the notified conditions of use the crop will be exposed to ethene but no information on ethene and potential metabolites or reaction products was submitted in the DAR on ethanol. Relevant information on ethene was reported and assessed in the DAR on ethylene (rapporteur Member State UK), which has not been subjected to a peer review. An addendum to the ethanol DAR on the "Assessment of available information on the residues of the reaction and degradation products (ethene and ethene oxide)" was provided by the rapporteur Member State on 6 October 2008. This addendum was not peer reviewed due to restrictions concerning the acceptance of new (newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007.

Moreover, the experts took note that the meeting of experts PRAPeR 56 on physical/chemical properties and methods of analysis concluded that for the applied for representative use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true active substance and is already covered by its own risk assessment in the non-peer reviewed DAR on ethylene. Consequently, no discussion was possible in the PRAPeR 60 meeting. It is proposed by EFSA to set a data gap for the open issues confirmed by PRAPeR 60 with regard to the assessment of the relevant information on the residues of the reaction and degradation products of ethanol.

3.1. Nature and magnitude of residues in plant

No data or information were available in the peer review of ethanol. An addendum submitted by the rapporteur Member State could not be considered in the meeting of experts (for details see section 3 above).

3.2. Nature and magnitude of residues in livestock

Not relevant for the representative use on bananas since bananas are usually not fed to livestock.

3.3. Consumer risk assessment

Due to lack of data a consumer risk assessment could not be conducted for the notified use.

3.4. Proposed MRLs

Due to lack of data the issue of MRLs could not be considered.

4. Environmental fate and behaviour

The PRAPeR 56 meeting of experts on physical/chemical properties (October 2008) concluded that for the applied for representative use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true active substance and is already covered by its own risk assessment. However, ethanol was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 57 in October 2008 on the basis of the information reported in the DAR for ethanol (December 2007).

4.1. Fate and behaviour in soil

For the representative use in catalytic generators to produce ethene gas for controlling the ripening of bananas, exposure of the soil environmental compartment is excluded. Information on the fate and behaviour of ethanol in soil is therefore not required. However, no information on the environmental metabolites, or reaction products of ethanol, ethene and ethene oxide, were submitted in the DAR for ethanol. The relevant information and assessment for these compounds were provided in the DAR (UK as rapporteur Member State)

for ethylene, which has not been peer reviewed. An assessment of the available information on the environmental fate and behaviour of ethene and ethene oxide was provided by the rapporteur Member State in an addendum to the ethanol DAR on 6 October 2008, but was not peer reviewed due to the restrictions laid down in Commission Regulation (EC) No. 1095/2007. Therefore, a data gap for the relevant information and PEC (Predicted Environmental Concentration) soil assessment for ethene and ethene oxide was set by the experts of PRAPeR 57.

Whilst some data were available on the anaerobic biodegradation of ethanol in soil and were summarised on the original DAR, the information was considered to be supplemental.

4.2. Fate and behaviour in water

For the representative use in catalytic generator to produce ethene gas for controlling the ripening of bananas, exposure of the natural surface water environmental compartment is excluded. Information on the fate and behaviour of ethanol in natural water systems is therefore not required. However, no information on the environmental metabolites, or reaction products of ethanol, ethene and ethene oxide were submitted in the DAR for ethanol. The relevant information and assessment for these compounds were provided in the DAR (UK as rapporteur Member State) for ethylene, which has not been peer reviewed. An assessment of the available information on the environmental fate and behaviour of ethene and ethene oxide was provided by the rapporteur Member State in an addendum to the ethanol DAR on 6th October 2008, but was not peer reviewed due to the restrictions laid down in Commission Regulation (EC) No. 1095/2007. Therefore, a data gap for the relevant information and PEC_{sw} (PEC in surface waters) assessment for ethene and ethene oxide was set by the experts of PRAPeR 57.

Some data were available on the ready biodegradability of ethanol and were summarised in the DAR. Whilst the study did not conform to current standards, it was considered providing sufficient information to conclude that ethanol would be expected to pass the ready biodegradability criteria of a modern study.

As there will be no exposure of soil by ethanol from the proposed use, it is considered that there will be no potential for groundwater to be contamination by ethanol.

4.3. Fate and behaviour in air

For the representative use in catalytic generators to produce ethene gas for controlling the ripening of bananas, exposure of the air environmental compartment is excluded. Information on the fate and behaviour of ethanol in air is therefore not required.

5. Ecotoxicology

The meeting of physical/chemical properties experts PRAPeR 56 (October 2008) concluded that for the applied for representative use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true active substance. Nevertheless, ethanol was discussed in the meeting of

ecotoxicology experts PRAPeR 58 in October 2008, on the basis of the DAR (December 2007).

In the overall conclusion of the ethanol DAR, the rapporteur Member State considered that the risk to non-target organisms from the use of ethanol was considered to be minimal due to lack of exposure. There would however, be possible potential exposure from two metabolites, or reaction products, ethene and ethene oxide. The risk from these metabolites was not addressed in the ethanol DAR but a reference was made to the DAR for ethylene, which has not been peer reviewed. During the peer review of ethanol, the notifier was asked to provide relevant information on endpoints and environmental risk assessment for ethene and ethene oxide. The information was provided by the rapporteur Member State in addendum 4 (October 2008) however it was noted, that in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the information provided on ethene and ethene oxide could not be considered in the peer review. Consequently Member State experts agreed on a data gap for the notifier to address the risk to non-target organisms from the degradation products ethene and ethene oxide.

5.1. Risk to terrestrial vertebrates

No data have been submitted on the toxicity of ethanol or any metabolite or reaction product to birds. Data on the toxicity of ethanol to mammals are presented in section 2. As the intended use of ethanol is indoors in a catalytic generator no exposure of birds or mammals from the correct use of ethanol is to be expected. Given that information on the fate and behaviour of the ethanol metabolites ethene and ethene oxide cannot be evaluated at this time, a data gap remains for the notifier to address the risk to birds and mammals from ethene and ethene oxide (see section 5).

5.2. Risk to aquatic organisms

Based on the exposure assessment presented in section 4.2 exposure to aquatic life was considered to be minimal and hence the risk was considered to be low. Acute toxicity data for several fish, invertebrate and algae species were available for classification and labelling purpose. Based on the available data no classification was required for ethanol or the associated formulation. Given that information on the fate and behaviour of the ethanol metabolites ethene and ethene oxide cannot be evaluated at this time, a data gap remains for the notifier to address the risk to aquatic organisms from ethene and ethene oxide (see section 5).

5.3. Risk to bees and other arthropods species

No studies on bees or beneficial arthropods were submitted in the dossier as no exposure was expected from the intended use of ethanol. It was considered, however, that exposure of bees and non-target arthropods to ethene could occur when the curing houses were vented. Given that information on the fate and behaviour of the ethanol metabolites ethene and ethene oxide

cannot be evaluated at this time, a data gap remains for the notifier to address the risk to bees and other arthropods species from ethene and ethene oxide (see section 5).

5.4. Risk to earthworms, other soil organism and soil micro-organisms as well as other fauna and flora

The notifier has stated the earthworms, other soil organism and soil micro-organisms as well as other fauna and flora will not be exposed to ethanol. On the basis of the environmental exposure assessment in the DAR (see section 4.1) it was concluded that exposure would be minimal, therefore the risk to this range of organisms was considered to be low. Given that information on the fate and behaviour of the ethanol metabolites ethene and ethene oxide cannot be evaluated at this time, a data gap remains for the notifier to address the risk to soil organisms and other fauna and flora from ethene and ethene oxide (see section 5).

5.5. Risk to biological methods of sewage treatment

Given the pattern of use of ethanol and it fate and behaviour, it was considered that sewage treatment plants would not be exposed, therefore the risk was considered to be acceptable.

6. Residue definitions

Based on the information available in the DAR for ethanol, a conclusion on the environmental occurring metabolites requiring further assessment by other disciplines could not be finalised (data gap identified by PRAPeR 57 for relevant information on ethene and ethene oxide).

6.1. Food of plant origin

Definition for risk assessment:	no peer reviewed data and information available to conclude.
Definition for monitoring:	no peer reviewed data and information available to conclude.

6.2. Food of animal origin

Definition for risk assessment:	not required for the representative use.
Definition for monitoring:	not required for the representative use.

6.3. Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

The assessed pattern of use precludes exposure of soil, groundwater, natural surface waters and air to ethanol. However, a data gap was set for relevant information on the environmental metabolites, or reaction products, ethanol ethene and ethene oxide.

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Information on the nature and levels of impurities as a result of catalytic generation (relevant for all representative uses evaluated; study ongoing, no submission date proposed by the notifier; see section 2.8).
- Information on the toxicity of the reaction and degradation products ethene and ethene oxide to assess the worker risk assessment (relevant for all representative uses evaluated; data included in the DAR for ethylene, which is not peer reviewed; see section 2.8 and 2.12).
- Relevant information on the residues of the reaction and degradation products of ethanol to conclude the consumer risk assessment (relevant for all representative uses evaluated; information included in the DAR on ethylene and in the addendum 2 to the DAR on ethanol of October 2008, which are however not peer reviewed; data gap proposed by EFSA for the open issues confirmed by the meeting of experts PRAPeR 60; see section 3).
- Relevant information on the environmental fate and PEC values assessment for the reaction and degradation products ethene and ethene oxide (data included in the DAR for ethylene, which is not peer reviewed; assessment of available information on the environmental fate and behaviour of ethene and ethene oxide submitted by the rapporteur Member State on the 6th October 2008, but not peer reviewed; data gap identified by the meeting of experts PRAPeR 57; see section 4).
- A residues definition for the environmental compartments could not be finalised by the peer review (relevant for all representative uses evaluated, see section 6).
- Information on the toxicity of the reaction and degradation products ethene and ethene oxide to assess the risk to non-target organisms (relevant for all representative uses evaluated; data included in the DAR for ethylene, which is not peer reviewed; see section 5.1 to 5.4).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative use as an ethene precursor, as proposed by the notifier, which comprise the use of the ethanol in a catalytic generator to produce ethene gas, which is used as a growth regulator for the ripening of bananas. Ethanol would not be applied directly to the plants.

The representative formulated product for the evaluation was 'Ethy-Gen II', a gas generator (GE) containing 90 % (w/W) ethanol.

Considering the proposed use, ethanol cannot be regarded as an active substance, since it is intended for use in a catalytic generator to produce *in situ* ethene gas, which is in fact the true

active substance. Ethanol is not applied directly to the crops. A risk assessment for ethene (ethylene) has been presented in a separate DAR.

It should be noted that a product similar to the representative formulated product notified here was also included in the ethylene task force dossier.

However, the experts on toxicology decided to discuss the substance according to the agenda. No metabolism or toxicity study was submitted to the rapporteur Member State, therefore all the toxicological information came from the open literature, mainly from the US EPA and the IARC review of 1988. The animal data and published information submitted was of insufficient quality to set NOAELs, although these studies had identified target organs and tissues. Considering the representative use, ethanol does not come into contact with food materials being treated, therefore, no ADI or ARfD are needed. With regards to the operator exposure risk assessment, the experts concluded that, in view of the low dermal and inhalation exposure (as a worst case, operator exposure would represent the dermal application of 1.08 ml ethanol/day), compared with other sources of general use (as in cosmetics, medicines, household products), there was no concern over the risk assessment to operators. No exposure is foreseen for workers or bystanders related to ethanol, therefore no AOEL was also considered necessary. Accordingly, no data gap was set to define NOAELs (either short term, long term, for reproductive toxicity or from further studies) with ethanol. No classification proposal could be concluded based on the available information, but was not required for the risk assessment.

A data gap was set for toxicological information on the reaction products ethene and ethene oxide, for formal reasons, as in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. This information is needed to conclude on the worker risk assessment (operators and bystanders are not considered to be exposed to ethene and other breakdown products). A data gap was also confirmed for information on the nature and levels of impurities as a result of the catalytic ethene generation.

No data or information with regard to residues and consumer exposure were available in the peer review procedure. Under the notified conditions of use the crop will not be exposed to ethanol but to ethene. However ethene and potential other metabolites or reaction products were not subjected to an assessment during the peer review of ethanol. An addendum prepared by the rapporteur Member State on the "Assessment of available information on the residues of the reaction and degradation products (ethene and ethene oxide)" could not be considered in the meeting of experts due to the restrictions laid down in Commission Regulation (EC) No. 1095/2007. Consequently, discussion and conclusion on the consumer risk assessment and in terms of MRL proposals was not possible. It is proposed by EFSA to set a data gap for the open issues confirmed by PRAPeR 60 with regard to the assessment of the relevant information on the residues of the reaction and degradation products of ethanol.

The evaluation of the environmental fate and behaviour of ethanol in soil and natural surface water systems is not relevant for the representative use as there will be no exposure to these

environmental compartments from ethanol. However, it was recognised that there may be the potential of exposure to two metabolites, or reaction products, of ethanol: ethene and ethene oxide. As these reaction products were not assessed in the DAR for ethanol, but a reference was made to the DAR for ethylene, which has not been peer reviewed, a data gap for data and/or information on ethene and ethene oxide was identified.

The risk to non-target organisms from the use of ethanol was considered to be minimal due to the lack of exposure. The risk from exposure from the two metabolites, or reaction products, ethene and ethene oxide however needs to be assessed. These reaction products were not assessed in the DAR for ethanol, but a reference was made to the DAR for ethylene, which has not been peer reviewed. A data gap to address the potential risk from ethene and ethene oxide was identified during the peer review.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

None.

CRITICAL AREAS OF CONCERN

- Ethanol is not considered as active substance.
- Due to lack of data and information on ethene and potential other reaction and breakdown products, a consumer risk assessment could not be conducted.
- The relevant information on the environmental fate and behaviour and PEC assessment of the reaction and degradation products (ethene and ethene oxide) of ethanol were not available for the assessment of ethanol.
- Based on the information available in the DAR for ethanol, a conclusion on the environmental occurring metabolites requiring further assessment by other disciplines (mammalian toxicology and ecotoxicology) could not be finalised.
- The risk to non-target organisms could not been addressed due to lack of data and information on ethene and ethane oxide.

APPENDICES

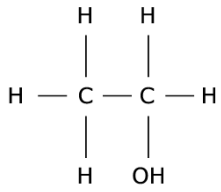
APPENDIX A – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Ethanol no ISO common name exists for this substance
Function (*e.g.* fungicide)	Ethylene precursor/ generator

Rapporteur Member State	UK
Co-rapporteur Member State	N/A

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Ethanol
Chemical name (CA) ‡	Ethanol
CIPAC No ‡	None
CAS No ‡	64-17-5
EC No (EINECS or ELINCS) ‡	200-578-6
FAO Specification (including year of publication) ‡	None Exists
Minimum purity of the active substance as manufactured ‡	Not considered as active substance
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	C_2H_5OH
Molecular mass ‡	46.1 g/mol
Structural formula ‡	

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

Physical and chemical properties (Annex IIA, point 2)

NOTE: Purity rarely available for these data

Melting point (state purity) ‡	-114.9 °C ()
Boiling point (state purity) ‡	78.3 °C ()
Temperature of decomposition (state purity)	No data
Appearance (state purity) ‡	Clear, colourless liquid.
Vapour pressure (state temperature, state purity) ‡	7.87 x 10^{3} Pa at 25 °C (.)
Henry's law constant ‡	5.2 x 10^{-6} atm m^{3} mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	Completely miscible
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 15-25°C Ether, acetone and benzene >10%. Online sources state miscible with aliphatic hydrocarbon, halogenated hydrocarbon and alcohol
Surface tension ‡ (state concentration and temperature, state purity)	22.75 mN/m on contact with vapour
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = -0.31
Dissociation constant (state purity) ‡	pKa_1 = 15.9 at 25°C
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	UV absorption λ: 210 nm A_{max}: 0.5 λ: 220 nm A_{max}: 0.25 λ: 230 nm A_{max}: 0.1 λ: 250 nm A_{max}: 0.03 λ: 270 nm A_{max}: 0.005 UV absorption at >290nm-is considered unlikely as ethanol is commonly used as a solvent in UV-Vis spectroscopy due to its low absorbance.
Flammability ‡ (state purity)	Flash point = 13°C (highly Flammable)
Explosive properties ‡ (state purity)	Not explosive
Oxidising properties ‡ (state purity)	Not oxidising

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

Summary of representative uses evaluated (*name of active substance or the respective variant*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Banana		Ethy-Gen II	I	PGR	GE	90%	Gas	Post harvest	1	N/A					(1)

(1) Ethanol is not considered as active substance.-This use was considered in the ethylene task force dossier

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)

(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha

(m) PHI - minimum pre-harvest interval

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

(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	

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

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	ASTM E-1100
Impurities in technical as (analytical technique)	ASTM E-1100
Plant protection product (analytical technique)	ASTM E-1100

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		None as ethanol does not come into contact with plants.
Food of animal origin		None as ethanol does not come into contact with foodstuffs.
Soil		None as there is no environmental exposure
Water	surface	None as there is no environmental exposure
	drinking/ground	None as there is no environmental exposure
Air		None as there is no environmental exposure
Body Fluids and Tissues		Ethanol and acetaldehyde.

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	None
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	None
Soil (analytical technique and LOQ)	None
Water (analytical technique and LOQ)	None
Air (analytical technique and LOQ)	None

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

Body fluids and tissues (analytical technique and LOQ)	Open: None provided for ethanol, but numerous detection capabilities are available. None provided for ethylene as Notifier states volatility of ethylene means it is unlikely to be found in body tissues/fluids.

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	Ethanol: highly flammable (considered ethylene generator) Ethylene: highly flammable

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

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Extensive and rapid absorption from the GI tract (based on general scientific and medical literature).
Distribution ‡	Rapid and widespread throughout the body (based on general scientific and medical literature).
Potential for accumulation ‡	No potential for accumulation (based on general scientific and medical literature).
Rate and extent of excretion ‡	Rapidly and extensively eliminated (based on general scientific and medical literature).
Metabolism in animals ‡	Ethanol is oxidised to acetaldehyde which is converted to acetate which is metabolised to CO_2, H_20 and fatty acids via the Krebs cycle (based on general scientific and medical literature).
Toxicologically relevant compounds ‡ (animals and plants)	Parent.
Toxicologically relevant compounds ‡ (environment)	Parent.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	>6 g/kg bw	
Rat LD_{50} dermal ‡	>20 g/kg	
Mouse LC_{50} inhalation ‡	39 mg/l air (4-hour exposure)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Limited data indicating irritation	*[8]
Skin sensitisation ‡	Negative (M & K test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver, kidneys and CNS	
Relevant oral NOAEL ‡	Insufficient data – not required	
Relevant dermal NOAEL ‡	No data – not required	
Relevant inhalation NOAEL ‡	No valid data – not required	

[8] *: insufficient data to conclude, ECHA to consider classification

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

Genotoxicity ‡ (Annex IIA, point 5.4)

Insufficient data – not required	*[9]

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

Target/critical effect ‡	Liver, pancreas, endocrine glands and the nervous system	
Relevant NOAEL ‡	Insufficient data – not required	
Carcinogenicity ‡	Insufficient data – not required	*

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Insufficient data- not required	*
Relevant parental NOAEL ‡	Insufficient data- not required	
Relevant reproductive NOAEL ‡	Insufficient data- not required	
Relevant offspring NOAEL ‡	Insufficient data- not required	

Developmental toxicity

Developmental target / critical effect ‡	Insufficient data- not required	*
Relevant maternal NOAEL ‡	Insufficient data- not required	
Relevant developmental NOAEL ‡	Insufficient data- not required	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Insufficient data- not required	
Repeated neurotoxicity ‡	Insufficient data- not required	*
Delayed neurotoxicity ‡	Insufficient data- not required	

Other toxicological studies (Annex IIA, point 5.8)

Studies performed on metabolites or impurities ‡	Acetaldehyde is the primary metabolite of ethanol and it is currently classified by the ECB as a CAT 3 carcinogen (R40) and as an eye and respiratory irritant (R36/37). In addition, it also induces foetal malformations and resorptions. (ECB public database).

[9] *: insufficient data to conclude, ECHA to consider classification

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

Medical data ‡ (Annex IIA, point 5.9)

Human investigations	Ethanol is a CNS depressant. Acute intoxication results behavioural and physiological disturbances that can result in convulsions and death. Repeated exposure induces effects on the GI tract (e.g. mouth, salivary glands, oesophagus and stomach), liver (e.g. fatty liver, alcoholic hepatitis, fibrosis and cirrhosis), pancreas and heart. The fetal alcohol syndrome (FAS) is well-documented and characterized. There is sufficient evidence to relate the occurrence of malignant tumours of the oral cavity, pharynx, larynx, oesophagus and liver to the consumption of alcoholic beverages. IARC classified alcoholic beverages as carcinogenic to humans (Group 1 on IARC system).

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	Insufficient data, could not be established – not required based on the representative use.		
AOEL ‡	Insufficient data, could not be established – not required based on the representative use.		
ARfD ‡	Insufficient data, could not be established – not required based on the representative use.		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Ethy-Gen II containing 90% ethanol)	100% (based on absence of data)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Exposure is estimated as a dermal dose of 1.08 ml ethanol/day. This is not considered to represent a significant risk to human health when compared to volumes encountered in other exposure scenarios. There is no operator exposure to ethylene.
Workers	Ethanol is converted to ethylene gas and other breakdown products and there will be no exposure to ethanol during re-entry activities. Data are required on ethylene and other breakdown products to assess worker exposure
Bystanders	As entry to stores is excluded during application, no bystanders will be present.

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

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance classified (Ethanol)	Not concluded due to insufficient data. ECHA to consider classification

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

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	No data
Rotational crops	No data - Not relevant for notified use
Metabolism in rotational crops similar to metabolism in primary crops?	N/A
Processed commodities	No data
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No data
Plant residue definition for monitoring	None proposed. RMS maintains ethanol is an ethylene generator and ethanol is therefore unlikely to be found in plants. No data on ethylene available in the peer review.
Plant residue definition for risk assessment	None proposed. RMS maintains ethanol is an ethylene generator and ethanol is therefore unlikely to be found in plants. No data on ethylene available in the peer review.
Conversion factor (monitoring to risk assessment)	N/A

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	No data - Not relevant for notified use
Time needed to reach a plateau concentration in milk and eggs	N/A
Animal residue definition for monitoring	N/A
Animal residue definition for risk assessment	N/A
Conversion factor (monitoring to risk assessment)	N/A
Metabolism in rat and ruminant similar (yes/no)	N/A
Fat soluble residue: (yes/no)	No. (ethanol)

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

N/A

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

N/A as no residue data presented

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

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	N/A	N/A	N/A
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	N/A	N/A	N/A
Liver	N/A	N/A	N/A
Kidney	N/A	N/A	N/A
Fat	N/A	N/A	N/A
Milk	N/A		
Eggs		N/A	

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

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Banana	Global Indoor use	No data presented		None	N/A	N/A

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

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

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8) –

Note: none consumer risk assessment conducted

ADI	No data
TMDI (% ADI) according to WHO European diet	No data
TMDI (% ADI) according to national (to be specified) diets	No data
IEDI (WHO European Diet) (% ADI)	No data
NEDI (specify diet) (% ADI)	No data
Factors included in IEDI and NEDI	No data
ARfD	No data
IESTI (% ARfD)	No data
NESTI (% ARfD) according to national (to be specified) large portion consumption data	No data
Factors included in IESTI and NESTI	No data

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
No data	N/A	N/A	N/A	N/A

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

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

..... .	No MRLs proposed for the ethanol (no exposure of the crop to ethanol) Issue not considered for ethylene due to lack of data and information in the peer review

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

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

PLEASE NOTE: Ethanol is a precursor to the production of ethylene, as a result there will be no exposure of the environment to ethanol, hence no data are required and no PEC calculated.

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡ Non-extractable residues after 100 days ‡ Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No data presented. No data required as there will be no exposure to the soil from the proposed use.

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation‡	No reliable data available, not required.
Mineralization after 100 days	No reliable data available, not required.
Non-extractable residues after 100 days	No reliable data available, not required.
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No reliable data available, not required.
Soil photolysis ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data presented. No data required as there will be no exposure to the soil from the proposed use.

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

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

No data presented.
No data required as use is indoors only.

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	No data presented. No data required as there will be no exposure from the proposed use.
Lysimeter/ field leaching studies ‡	No data presented. No data required as there will be no exposure from the proposed use.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	No data presented. No data required as there will be no exposure from the proposed use.
Application data	Not relevant.

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Not relevant		Not relevant	

Metabolite Method of calculation	Data gap identified by PRAPeR 57 for PECs assessment of the reaction and degradation products ethylene and ethylene oxide.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	No data presented. No data required as there will be no exposure from the proposed use.

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

Photolytic degradation of active substance and metabolites above 10 % ‡	No data presented. No data required as there will be no exposure from the proposed use.
Quantum yield of direct phototransformation in water at Σ > 290 nm	No data presented. No data required as there will be no exposure from the proposed use.
Readily biodegradable ‡ (yes/no)	A non-guideline ready biodegradability study was submitted from which it can be concluded that ethanol would be expected to pass the ready biodegradability criteria of a modern study.

Degradation in water / sediment

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent	Not required as there will be no exposure from the proposed use.
Metabolite X Parameters used in FOCUSsw step 1 and 2	Data gap identified by PRAPeR 57 for PECs assessment of the reaction and degradation products ethylene and ethylene oxide.

PEC (ground water) (Annex IIIA, point 9.2.1)

Application rate	Not required as there will be no exposure from the proposed use.

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

As there will be no exposure of soil then there is considered that there will be no potential for groundwater to be contaminated by ethanol.

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

As ethanol will be used indoors and there will be no exposure to the environment, there is not expected to be any exposure of the air compartment.

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

Residues requiring further assessment

Environmental occurring metabolites requiring further assessment by other disciplines (toxicology and ecotoxicology)	Based on the information available in the DAR for ethanol, a conclusion on the environmental occurring metabolites requiring further assessment by other disciplines could not be finalised (data gap identified by PRAPeR 57 for relevant information on ethylene and ethylene oxide).

Monitoring data, if available (Annex IIA, point 7.4)

No data submitted

Points pertinent to the classification and proposed labelling with regard to fate and behaviour

None

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

PLEASE NOTE: Ethanol is a precursor to the production of ethylene, as a result there will be no exposure of the environment to ethanol, hence no data are required and no TER calculated.

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	Endpoint (mg/kg bw/day)	Endpoint (mg/kg feed)
Birds ‡				
Not required as there will be no exposure from the proposed use.				
Mammals ‡				
Not required as there will be no exposure from the proposed use.				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Crop and application rate

Not relevant, as there will be no exposure from the proposed use.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Onchorhynchus mykiss	a.s.	24 hr (static)	Mortality, LC_{50}	11200
Onchorhynchus mykiss	a.s.	96 hour (static)	Mortality, LC_{50}	13200
Pimephales promelas	a.s.	96 hr (static)	Mortality, LC_{50}	13480
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Mortality, EC_{50}	12340
Ceriodaphnia dubia	a.s.	48 h (static)	Mortality, EC_{50}	5012
Culex restuans	a.s.	18 h (static)	Mortality, EC_{50}	22400
Daphnia pulex	a.s.	18 h (static)	Mortality, EC_{50}	15300
Palaemonetes kadlakensis	a.s.	96 h (static)	Mortality, EC_{50}	>250
Palaemonetes kadlakensis	a.s.	18 h (static)	Mortality, EC_{50}	12800

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

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Hyalella azteca	a.s.	18 h (static)	Mortality, EC_{50}	10400
Artemia salina	a.s.	72 h	Mortality, EC_{50}	695
Algae				
Skeletonema	a.s.	120 h (static)	$EC_{50\ total\ cell\ count}$	11619
Chlamydomonas	a.s.	48 h (static)	$EC_{50\ cell\ population}$ Growth rate: E_rC_{50}	2000
Chlorella vulgaris	a.s.	120 h (static)	EC_{50} (chlorophyll production):	>50 (approxima-tion)
Selenastrum capricornutum	a.s.	120 d (static)	EC_{50} (chlorophyll production)	1000 (approxima-tion)
Aquatic higher plants				
No acceptable data				
Microcosm or mesocosm tests				
Not required				

[1] based on nominal ($_{nom}$).

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Not relevant due to proposed use indoors.

Bioconcentration				
	Active substance			
$logP_{O/W}$	1.13			
Bioconcentration factor (BCF)[1] ‡	n.r.			
Annex VI Trigger for the bioconcentration factor	n.r.			
Clearance time (days) (CT_{50})	n.r.			
(CT_{90})	n.r.			
Level and nature of residues (%) in organisms after the 14 day depuration phase	n.r.			

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

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

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	Not required as there will be no exposure from the proposed use.	

[1] for preparations indicate whether endpoint is expressed in units of a.s. or preparation

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Crop and application rate

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	Not required as there will be no exposure from the proposed use.	50
a.s.	oral		50
Preparation	Contact		50
Preparation	oral		50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡		Mortality	Not required as there will be no exposure from the proposed use.
Aphidius rhopalosiphi ‡		Mortality	

[1] for preparations indicate whether endpoint is expressed in units of a.s. or preparation

Crop and application rate

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
	Typhlodromus pyri	Not required as there will be no exposure from the proposed use.			2
	Aphidius rhopalosiphi				2

[1] indicate distance assumed to calculate the drift rate

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	Endpoint
Earthworms			
Not required as there will be no exposure from the proposed use.			

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

Test organism	Test substance	Time scale	Endpoint
Collembola			
Not required as there will be no exposure from the proposed use.			
Soil micro-organisms			
Not required as there will be no exposure from the proposed use.			
Carbon mineralisation			
Not required as there will be no exposure from the proposed use.			

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
Not required as there will be no exposure from the proposed use.					
Other soil macro-organisms					
Soil mite					
Not required as there will be no exposure from the proposed use.					
Collembola					
Not required as there will be no exposure from the proposed use.					

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Not required as there will be no exposure from the proposed use.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	endpoint
Not required as there will be no exposure from the proposed use.	

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Based on the information available in the DAR for ethanol, a conclusion on the ecotoxicological relevant compounds could not be finalised (data gap identified by PRAPeR 58 for relevant information on ethylene and ethylene oxide).
water	
sediment	
groundwater	

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

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	No classification required.

	RMS/peer review proposal
Preparation	No classification is required, only phrase required is: 'Do not contaminate water with the product or its container.'

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

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

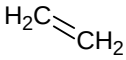
APPENDIX B – LIST OF ABBREVIATIONS

ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
AV	avoidance factor
BCF	bioconcentration factor
bw	body weight
CAS	Chemical Abstract Service
cGAP	critical good agricultural practice
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HQ	hazard quotient
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry

kg	kilogram
K_{foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure

TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TWA	time weighted average
UV	ultraviolet
W/S	water/sediment
WG	water dispersible granule
WHO	World Health Organisation
yr	year

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
Ethene Ethylene	Ethene	
Ethene oxide	Ethene oxide	
Acetaldehyde	Acetaldehyde