cerexagri
ARKEMA GROUP

3. Time schedule

The experimental phases of the study were carried out in 1997 in Study DL 97-006 (under provisions of GLP), in 1998 and 1999 in Study DL 98-044 (not under GLP) and finished January, 2002 in Study DL 01-067 (under GLP). Study completion date is defined to be the date of signing by the Study Director of the GLP Compliance Statement and Authentication Statement.

4. Results

4.1 Introduction

Ethylenethiourea (ETU) is a relatively stable decomposition product and metabolite of ethylenebis(dithiocarbamates) (maneb, mancozeb, metiram and zineb) and it has been considered as a compound under suspicion of being carcinogenic.
To have validated and international recognised analyses on pesticides the worldwide organisation of CIPAC, in cooperation with FAO/WHO and ASTM, organises the development and institution of analytical methodology for Pesticides.
Therefore in connection with CIPAC methods have been developed to determine the ETU content in EBDC's.
These methods involved paper chromatography and liquid chromatography (HPLC).
The first edition was made by the Dithiocarbamates Panel of PAC-GB, chaired by A. Stevenson of Robinson Brothers Ltd. This method was revised in 1995.
All these methods used methanol as extraction solvent because this solvent gave the best yield of ETU.
At the CIPAC symposium of 1998 in London, UK, Dr. Daniel F. Clarke of Central Science Laboratories in York, U.K. gave a presentation on repeated serial extraction of EBDC with methanol. He found that with the 2nd extraction the relative yield was 200 % and with the 5th the yield was 250 %. His conclusion was that ETU is generated during extraction with methanol. With this information structural investigations for a more appropriate, selective solvent should be used to dissolve only the actual ETU content. Dr. Clarke suggested using water as extraction solvent.

4.2 Different extraction solvents

At Cerexagri (Elf Atochem Agri at that time) bad experiences were obtained with water as extraction solvent, therefore a study was started to improve the methodology.
Several solvents were studied in which ETU dissolves very well.
Maneb TC was used to test with as this compound showed results with relatively high ETU concentrations. Tested were next to methanol, water, ethanol, acetone, acetonitrile and aqueous solutions of compounds that were expected to prevent decomposition of maneb (0.05 mol cysteine (pH6.5)/l), reducing agents (0.01 mol sodium sulphite/l and 0.05 mol ascorbic acid (pH 7)/l) and EBDC solubility suppressor (0.05 mol zinc sulphate/l). All solvents showed the same effect, the longer the extraction time the higher yield of ETU.
Obviously EBDC without extractable ETU does not exist.
As a check on dissolution rate solid ETU was dissolved in the same amount of solvents at the same dissolution (extraction) time at a concentration equivalent to 10 g/kg:
for every solvent (water and the above mentioned organic solvents) a 100 % recovery was achieved.
However the variation in amount of ETU found in maneb was astonishing: the amount of ETU found was dependent on the concerned solvent and without correlation to the solubility of ETU in the concerned solvent.

For instance the amount of ETU found after 5 minutes of extraction with methanol was 0.99 g/kg while with acetone only 0.20 g/kg was found. After 1 hr of extraction these values where respectively 1.48 and 0.35 g/kg. Compared to the total amount of ETU that is able to dissolve in 5 min stirring in methanol or in acetone equivalent (respectively 349 g/kg and 191 g/kg sample) the conclusion is that all present actual ETU in the sample should have been dissolved in the first 5 minutes. Also the difference in initial ETU contents for both solvents and the difference in results between 5 min extraction in methanol and 1 hr extraction in acetone show that most of the amount of ETU found is related to the decomposition of maneb in methanol and not actually present in the product.

Water and aqueous solutions of the investigated agents appeared to show even more ETU than pure organic solvents. In the same investigation we have proven that maneb decomposition took place in the different solvents through the generation of increasing amounts of other decomposition products of EBDCs sulphur and DIDT.
The author, P.C. Diepenhorst, Head Analytical Development of then Elf Atochem Agri, had the opportunity to present the results of this study at the CIPAC symposium of 1999 in Budapest, Hungary. It was clearly demonstrated to the attendances that most of the ETU found was generated almost immediately after contact with the solvent ("instantly") and depending on the solvent used.
The program of the CIPAC Symposium 1999, a graph of extractions (presented in Budapest) and the main conclusions drawn can be found in Appendix A.
Discussions were held with a.o. Dr. Allen Hill of Central Science Laboratories in York and Chairman then of the PAC-UK panel, what should be done: assessment of the actual amount of ETU in the sample material or the potential of the product to generate ETU under certain conditions. As for registration purposes the actual ETU content is important some suggestions, done by Dr Hill, were tested in our setup but no improvement of the extraction method was reached.

In the discussions between Dr. Schreuder of the Dutch CTB and Dr. Hill with Dr. Gillespie and Dr. Dewhurst of the PSD these small amounts of ETU in the product were defined to be not of interest anymore because ETU was considered not as dangerous as it was supposed before. Find a Copy of that email discussion attached in Appendix B.

The methodology has been sustained on the CIPAC method so "instantly" generating ETU and we have adapted our method so that the same ETU contents are found with the CIPAC method.
The lower concern and the less interest for ETU has to do with new insights leading to the declassification of ETU by the IARC (International Agency for Research on Cancer) in September 2001 from group 2B to group 3 as not classifiable as to its carcinogenicity to humans. See Appendix C.
The study of the validation (DL 01-067) has been done with the knowledge of that time stage because of the lower toxicological impact and extraction efficiency in water or methanol did not matter anymore.

4.3 Waterdispersible granules formulations (WG)

For WG formulations of EBDCs which are designed for aqueous dispersion the extraction efficiency for ETU in methanol cannot be demonstrated because the unavoidable need of water to disperse the granules. In methanol no dispersion takes place. However water cannot be used because of the continuous formation of more ETU

than present in the product! Therefore a reference mixture has been composed of the formulation agents and ETU at 0.5 g/kg in inert kaolin clay and granulated.
These reference granules have been tested with extraction of water to assess the exact content of ETU. The granules of the reference sample have been milled in a mortar and extracted with methanol.
These tests and results have been reported in Report DL 01-067: obviously the importance of these tests has not been recognised by the PSD, because the lack of detailed scientific backgrounds of the matter in the report.

For that same reason, generation of ETU "instantly" due to extraction, standard addition is not an option for the extraction efficiency. The way to add the standard amount of ETU to the sample amount in the assessment could be done by weighing or by addition of a solution of ETU in solvent. Addition of the standard by weighing can only be done accurately enough as multiple amounts of the expected 0.5 g/kg in the sample. However than the range of the method is too large for the small amount to be assessed.
But when the standard addition is done by adding as a solution the right concentration level can be reached but not the extraction efficiency because the added ETU has already been dissolved.
Also for accuracy the same problem plays a role. Therefore we prefer extraction with an internal standard solution so we can manage the duration of the manipulations and extraction more easily.

The methodology Cerexagri applies is with internal standardization and not external standardisation: the linearity of detection of ETU and the Internal standard has been given in Report DL 97-006. The regression lines (copied from Report DL 97-006) are added as Appendix D.
Therefore no calibration line is used because the linearity for these compounds has been proven but calibration is checked in duplicate before and after duplicate analysis (see calculation sheets in Report DL 01-067). Important is the stability of the calibration solutions: stable for more than a month (Report DL 97-006). It has been demonstrated that the stability of the samples extracts is bad so the method is designed in such a way that measurement on HPLC is done directly after filtration of the solid material. The longer waiting time used the higher ETU content is measured.

AMENDMENTS TO THE STUDY PLAN

Not applicable.

DEVIATIONS FROM THE STUDY PLAN

Not applicable.

CONCLUSION AND DISCUSSION

The present CIPAC methodology of assessment of the ETU content in EBDCs does not measure the actual ETU content in the sample but also the amount of ETU formed within 15 minutes of stirring with methanol. The result of the measurement is depending on extraction time and the kind of solvent used. This phenomenon has been reported to CIPAC by various investigators.
The actual ETU content in the EBDCs is probably significantly lower than the results obtained from the used methodology.

The formation of ETU during extraction by decomposition of the EBDC is the reason why the accuracy of the methodology and the extraction efficiency cannot be established by standard addition because EBDCs that will not generate ETU on extraction do not exist.

The necessity to obtain a better method for the determination of the actual ETU in EBDCs has been doubted in CIPAC discussions as the potential danger of the compound ETU has been downgraded and the interest for the impurity has been minimized in a more or less public expert discussion within CIPAC and between British Registration authorities.

The used methodology is a measure to characterize the quality of an EBDC, but the actual ETU content has to be considered always lower than the result of the analysis.

There are no known circumstances that could have adversely influenced the results of the study.

ARCHIVING

All report forms, data sheets and a copy of the final report are kept in the GLP archives of Cerexagri B.V., Tankhoofd 10, 3196 KE VONDELINGENPLAAT/Rt, The Netherlands for a period of ten years after completion of the study. At the end of this period, the decision will be made on continuation for another decade of storage or disposal of the data.

REFERENCES

SOP DLA-010.6 Version 4 "Ethylenethiourea (ETU) by HPLC in WG formulations of ethylenebis(dithiocarbamates)"
Final Report DL 97-006 Validation in Mancozeb 80 WP of the analytical method DLA-010.4 "Ethylenethiourea (ETU) by HPLC in TC, TK and WP formulations of ethylenebis(dithiocarbamates)"
Final Report DL 01-067 Validation of the SOP DLA-010.6 version 4 (tentative), "Ethylenethiourea (ETU) by HPLC in WG formulations of ethylenebis(dithiocarbamates)"
Presentations made on CIPAC symposia in 1998 in London, United Kingdom and in 1999 in Budapest, Hungary
Correspondence related to ETU determination in EBDCs with members of CIPAC
Classification of ethylenethiourea by I.A.R.C., Vol.: 79 (2001) (page 659)

APPENDICES INDEX

Addendum	:	Endorsement of Compliance with the OECD Principles of GLP
Appendix A	:	Program of the CIPAC symposium 1999 in Budapest, Hungary, Extraction graph and main conclusions of the presentation
Appendix B	:	Copy of Email discussion between Dr R. Schreuder and Dr A. Hill
Appendix C	:	Classification of ETU by IARC
Appendix D	:	Linearity of ETU and internal standard by HPLC (copy of Report DL 97-006)

cerexagri
ADDENDUM

voedsel en waren autoriteit

ENDORSEMENT OF COMPLIANCE

WITH THE OECD PRINCIPLES OF GOOD LABORATORY PRACTICE

Pursuant to the Netherlands GLP Compliance Monitoring Programme and according to Directive 2004/9/EC the conformity with the OECD Principles of GLP was assessed on 10-12 October 2005 at

Cerexagri BV
Development Laboratory
Tankhoofd 10, PO Box 6030
3196 XH Vondelingenplaat/Rotterdam

It is herewith confirmed that the afore-mentioned test facility is currently operating in compliance with the OECD Principles of Good Laboratory Practice in the following area of expertise: Physical and chemical tests.

The Hague, 07 November 2005

Dr Th. Helder
Manager GLP Compliance Monitoring Progam

Food and Consumer Product Safety Authority (VWA)
Prinses Beatrixlaan 2, 2595 AL Den Haag
Postbus 19506, 2500 CM Den Haag, The Netherlands

cerexagri
ARKEMA GROUP

APPENDIX A

Program CIPAC Symposium 1999

CIPAC Symposium

Wednesday, 2nd June 1999
Budapest, Hungary
(Park Hotel Flamenco)

08.15 : **Registration**

09.00 : **Welcome**, L.Bura, Plant Health and Soil Conservation Station, Budapest

Morning Session: Chairman: Dr. M. Galoux, Belgium

09.10 : Dr.M.D.Müller, Swiss Federal Research Station, Switzerland
Fate and Modelling of Pesticide Residues in a Lake System using Laboratory and Field Data

09.35 : Dr.H.R.Buser, Swiss Federal Research Station, Switzerland
Monitoring of Pesticide Residues in Swiss Lakes using High-Resolution Gas Chromatography-Mass Spectrometry

10.00 : Coffee/tea Break

10.30 : Dr. M.J.Tandy, Zeneca Agrochemicals, UK
The Role of Electrophoretic Separations in Agrochemical Characterisation-three years on

11.10 : D. Clarke, Central Science Laboratory, UK
The Monitoring of Active Ingredient in Pesticide Formulations for Regulation by Gas Chromatography

11.40 : Dr. S.C.Michaelidou, Ministry of Health-General Laboratory, Cyprus
Pesticide Application and Impacts on Surface Waters in Cyprus: Development of a New System for Effective Control, Management and Prevention

12.05 : V.D.Chmil, Institute of Ecohygine and Toxicology, Ukraine
Molecular Connectivity Indices and Retention of Pesticides in Thin-Layer Chromatography

12.30 : Lunch

14.00 : **Poster session**

1. Dr.A.Hourdakis, Benaki Phytopathological Institute, Greece
An HPLC method for the determination of mixtures of aminotriazole, simazine and atrazine in WP and GR formulations
2. S.Velea, Pesticide Research Institute, Romania
Sonication versus Soxhlet: a comparative study for extraction of Lenacil residues from soils
3. L.Preda, Pesticide Research Institute, Romania
On-line precolumn HPLC- a simplified method for determination of residual level of imazethapyr in soil samples

cerexagri
ARKEMA GROUP

APPENDIX A

Program CIPAC Symposium 1999

4. M.Cojocar, Oltchim S.A., Romania
HPLC method for active ingredient determination of aryloxyalkanoic herbicides
5. T.Iurașcu, Central Laboratory for Phytosanitary Quarantine, Romania
Determination of atrazine from different mixtures by liquid chromatographic method
6. Dr. J.Ferenczi, Plant Health and Soil Conservation Station of Zala County,
Study of pesticide runoff following simulated rainfall
7. Dr. L.Györfi, Budapest Plant Health and Soil Conservation Station, Hungary
Monitoring results of quality control of pesticide formulations in Hungary

Afternoon Session: Chairman: Dr. A.R. Hanks, Purdue University, USA

14.45 : Dr.J.Lantos, Plant Health and Soil Conservation Station of Sz.Sz.B. County
Applicability of Gas Chromatographyc Databases for Qualitative Identification of Active Ingredients of Pesticide Formulations

15.05 : Dr.A.Ramesh, Frederick Institute of Plant Protection and Toxicology, India
Application of Baker' s Yeast Cells for Selective Preconcentration of Herbicides from Environmental Samples and Kinetics and Hydrolysis of Fenamiphos, Fipronil and Trifluralin in Aqueous Buffer Solutions

15.45 : Coffee/tea Break

16.15 : C.Diepenhorst, Elf Atochem Agri, The Netherlands
The Determination of ETU in EBDC's

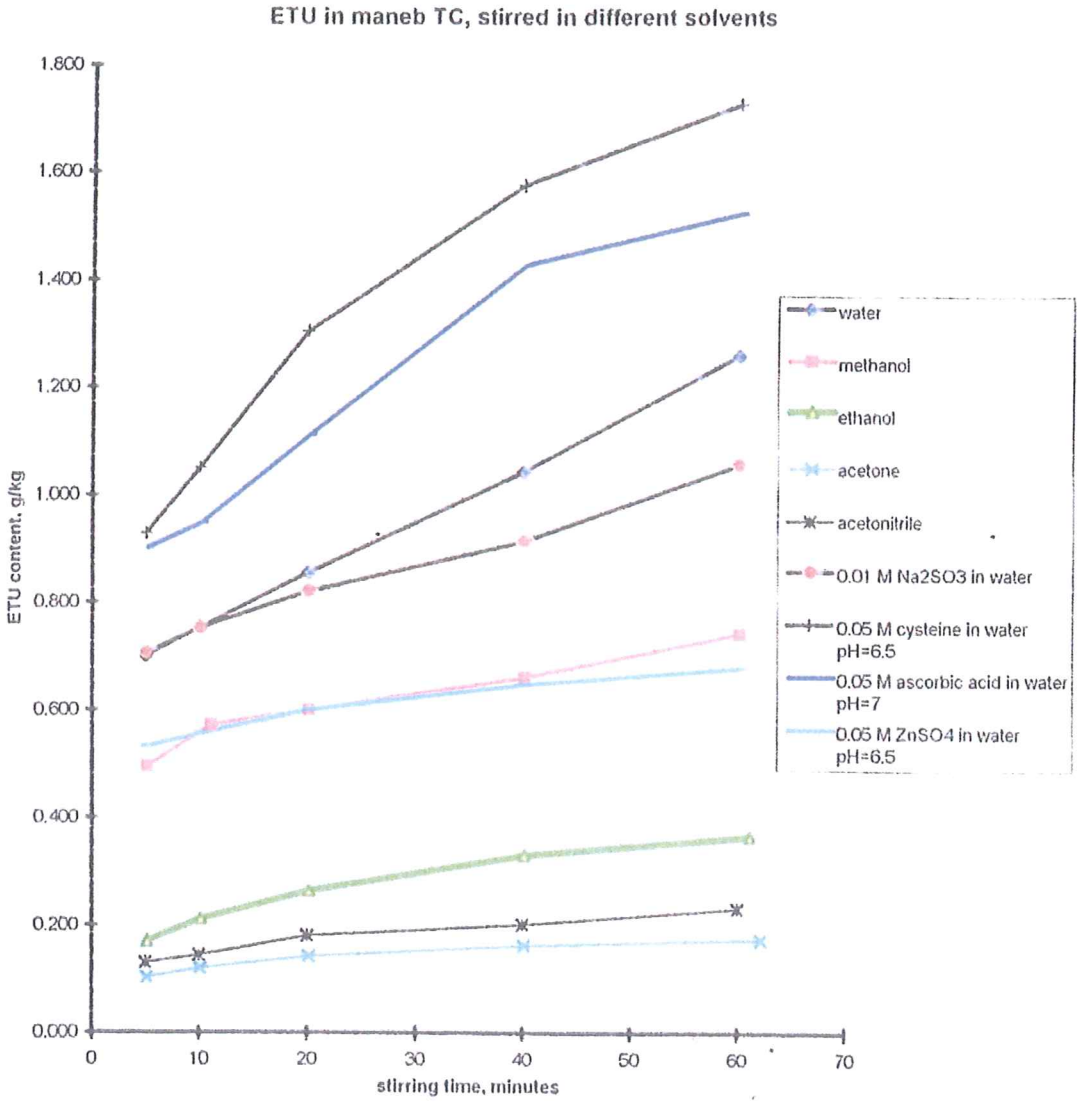
16.40 : General Discussion

16.50 : Summary and Closing

cerexagri
ARKEMA GROUP

APPENDIX A

Extraction graph presentation CIPAC in Budapest 1999



cerexagri
ARKEMA GROUP

APPENDIX A

Main conclusions CIPAC presentation in Budapest 1999

Conclusions

1. **All solvents investigated are capable for dissolving the expected amount of ETU.**

2. **In all solvents increasing amounts of ETU are found at increasing stirring times.
Not only in methanol ETU is generated. Also especially in water and aqueous solutions most of the ETU is found initially and formed on stirring.**

3. **Cysteine and ascorbic acid have no stabilizing affects on Maneb dispersions.**

4 **In water and methanol ETU is found 6-7 times as much as in acetone, acetonitrile and ethanol.
As also more DIDT and sulphur are found in water and methanol while the solubility for these compounds are less compared to acetone acetonitrile and ethanol.**

5. **All indications are that not the actual ETU content is determined but also amount of ETU formed by dissolution of the maneb.**

6. **The ETU formed by degradation is depending on :**

   1 **the solvent used**

   2 **the quality of the maneb**

Copy of Email discussion between Dr R. Schreuder and Dr A. Hill

Peter KOOL
28/07/2000 15:27

To: Carel DIEPENHORST/ROTTERDA/ATO_NL/ATO
cc:
Subject: FW: ETU

---------- Forwarded by Peter KOOL/ROTTERDA/ATO_NL/ATO on 28/07/2000 15:26 ----------

R.H.Schreuder@CTB.Agro.NL on 28/07/2000 15:02:04

To: Peter KOOL/ROTTERDA/ATO_NL/ATO@ATOCHEM
cc:
Subject: FW: ETU

Beste Peter en Carel
Hierbij stuur ik een uitgebreid antwoord van Alan Hill toe op een korte vraag van mij.
Ik heb het nog niet helemaal op een rij maar het lijkt alsof Hill verdere activiteit voor het middel op dit moment van minder belang vindt tov. de vorming in de spuittank.
Wat is jullie mening hierover.
Goed weekend,
groeten,
rudolf Schreuder

-----Oorspronkelijk bericht-----
Van: Alan Hill [mailto:alan.hill@csl.gov.uk]
Verzonden: vrijdag 28 juli 2000 12:27
Aan: Schreuder, R.H.
CC: Gillespie, Jo; Dewhurst, Ian
Onderwerp: Re: ETU

Dear Rudolf,

It's nice to hear from you! The York EPRW was very interesting and successful. I look forward to the possibility of CIPAC/FAO meetings in The Netherlands.

There was discussion of ETU and EBDCs in the FAO meeting but no date was set for review of the specifications. The problem was that without suitable methods, and without clear requirements for the risks to be managed, there was no obvious way forward.

Previously, I discussed ETU in EBDCs with Jo Gillespie and Dr Ian Dewhurst of PSD and I have discussed it again with Ian, today. He remains of the opinion that enough is known of the metabolism and toxicology of the EBDCS and ETU to conclude that unless, perhaps, more than 10-20% was present as ETU, it is unlikely to be a cause for concern, even for regular users. Even 10 or 20% is by no means a certain cut-off, as more than this proportion of ingested/inhaled EBDCs is likely to be converted into ETU in the body.

cerexagri
ARKEMA GROUP

APPENDIX B

Copy of Email discussion between Dr R. Schreuder and Dr A. Hill

If we assume that ETU is the only degradation product (which it isn't), the current FAO tolerances on EBDC content (3-15%) and storage stability (0-10%) therefore seem to be sufficient to manage the ETU risk to users posed by the formulation.

A small percentage of ETU in the dry formulation may therefore be irrelevant but it must also be very important that the EBDCs do not degrade rapidly to ETU when diluted for spraying. There would be no point in knowing that, in the container, a 70% zineb formulation contains 68% m/m and less than 0.5% m/m ETU if, within a few minutes of dilution in the spray tank, it changed to 1% m/m zineb and 25% m/m ETU (i.e. more or less complete conversion). The efficacy would definitely be adversely affected and operator/environmental risks could be increased.

The scenario described is unlikely, of course, but it suggests what we should be doing, or not doing. Unless the EBDC concentration becomes unacceptably affected, the ETU concentration seems unlikely to be of major importance. A formulation found to contain too little EBDC would be rejected. However, the current FAO specifications do not control the rate of degradation in the spray tank and perhaps we should focus on this.

Thus we return to the concept of measurements made on the diluted formulation, which would avoid the enormous problems of determining, and interpreting the data on, ETU in the formulation itself.

In principle, such a measurement could be of either "EBDC lost" or "ETU produced". In the former case, it would only be necessary to produce and validate and extension of the current CIPAC method. In the latter case, a completely new method would have to be produced and validated. In either case it would be necessary to decide upon the water(s), the temperature, the time, the EBDC concentration and the agitation to be used.

On the other hand, if when diluted in water we can be sure that EBDCs can never degrade to the extent that they do not (in effect) meet the FAO specification for EBDC content, there seems no point in pursuing further method development.

So, unless unstabilised EBDC formulations degrade rapidly to ETU after dilution for spraying, efforts (or legal/contractual requirements) to find ways of controlling ETU may be unnecessary.

I would be interested in Peter Kool's response to this, because we must be sure of exactly why ETU is to be controlled before we start collaborative studies.

With kind regards.

Alan.

"Schreuder, R.H." wrote:
>
> Dear Alan,
> Did you succeed already to pick up the normal work after meetings workshops
> etc.

cerexagri
ARKEMA GROUP

APPENDIX B

Copy of Email discussion between Dr R. Schreuder and Dr A. Hill

> How was the congress on methods for residues.
> I will start the discussion with the director of the CTB about the
> possibility to organise the FAO/CIPAC meetings in the Netherlands in
> 2002/2003.
> But now I have a question --- again--- about the ETU.
> I wonder if you discussed the point of the EBDC'specifications,
including
> the ETU content during the last day of the FAO meeting.
>
> This morning I had contact with Peter Kool from Elf-Atochem about this
> impurity. This summer his lab has not the time to work on the
finalisation
> off the method. But he is in favour to continue. Because already so much
> work was done, he would like to finish his work wish a ring trial as soon
as
> the method has been worked out well. Anyhow he will contact again Rohm &
> Haas.
>
> Kind Regards,
> Rudolf
>
> Rudolf H. Schreuder
> CTB - College voor de Toelating van Bestrijdingsmiddelen
> Stadsbrink 5
> 6707 AA Wageningen
> Postbus 217, 6700 AE Wageningen
>
> Tel : 0317 471851
> Fax : 0317 471899
> E-mail : r.h.schreuder@ctb.agro.nl

cerexagri
ARKEMA GROUP

APPENDIX C

Classification of ETU by IARC

ETHYLENETHIOUREA
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 79 (2001) (p. 659)

CAS No.: 96-45-7
Chem. Abstr. Name: 2-Imidazolidinethione

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Ethylenethiourea is used as a vulcanization accelerator in the rubber industry. It is a degradation product of and an impurity in ethylenebisdithiocarbamate fungicides, and field workers may be exposed to ethylenethiourea while applying these fungicides. The general population may be exposed to low concentrations of residues of ethylenethiourea in foods.

5.2 Human carcinogenicity data

The available data were inadequate to evaluate the carcinogenicity of ethylenethiourea to humans.

5.3 Animal carcinogenicity data

Ethylenethiourea was tested for carcinogenicity by oral administration in two studies in three strains of mice, with perinatal exposure in one study. It was also tested in five studies in rats by oral administration, with perinatal exposure in one study. In mice, it produced thyroid follicular-cell tumours and tumours of the liver and anterior pituitary gland. In rats, it consistently produced thyroid follicular-cell adenomas and carcinomas. Ethylenethiourea did not cause neoplasms in one strain of hamsters.

5.4 Other relevant data

Ethylenethiourea caused thyroid gland enlargement (goitre) in rats and mice as a result of diffuse hypertrophy and hyperplasia of thyroid follicular cells. Administration of ethylenethiourea under bioassay conditions that caused predominantly benign follicular-cell tumours resulted in alteration of thyroid hormone homeostasis, including increased secretion of thyroid-stimulating hormone. The underlying mechanism of the changes induced by ethylenethiourea is interference with the functioning of thyroid peroxidase activity. This is considered to be the basis for its tumorigenic activity in experimental animals.

One retrospective study of pregnancy outcomes in women employed in the manufacture of rubber containing ethylenethiourea showed no exposure-related effects. Ethylenethiourea was teratogenic in rats, but not in mice, hamsters or guinea-pigs. The central nervous system was particularly vulnerable in rats. The available data suggest that both toxicokinetics and embryo sensitivity are components of the species-specificity of the teratogenicity of ethylenethiourea. Furthermore, effects on thyroid function do not appear to be involved.

Ethylenethiourea was not genotoxic in appropriate tests in bacteria and cultured mammalian cells or in rodents *in vivo*. Ethylenethiourea induced chromosomal recombination and aneuploidy in yeast and cell transformation in mammalian cells.

cerexagri
ARKEMA GROUP

Classification of ETU by IARC

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of ethylenethiourea.

There is *sufficient evidence* in experimental animals for the carcinogenicity of ethylenethiourea.

Overall evaluation

Ethylenethiourea is *not classifiable as to its carcinogenicity to humans (Group 3)*.

In making its evaluation, the Working Group concluded that ethylenethiourea produces thyroid tumours in mice and rats by a non-genotoxic mechanism, which involves interference with the functioning of thyroid peroxidase resulting in a reduction in circulating thyroid hormone concentrations and increased secretion of thyroid-stimulating hormone. Consequently, ethylenethiourea would not be expected to produce thyroid cancer in humans exposed to concentrations that do not alter thyroid hormone homeostasis.

An additional consideration of the Working Group, based on the lack of genotoxicity of ethylenethiourea, was that the liver tumours and benign pituitary tumours in mice were also produced by a non-genotoxic mechanism.

Evidence from epidemiological studies and from toxicological studies in experimental animals provide compelling evidence that rodents are substantially more sensitive than humans to the development of thyroid tumours in response to thyroid hormone imbalance.

Previous evaluations: Vol. 7 (1974); Suppl. 7 (1987)

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 4,5-Dihydroimidazole-2(3*H*)-thione
- 4,5-Dihydro-2-mercaptoimidazole
- *N,N'*-1,2-ethanediylthiourea
- Ethylenethiocarbamide
- Ethylene thiourea
- 1,3-Ethylenethiourea
- 1,3-Ethylene-2-thiourea
- *N,N'*-Ethylenethiourea
- ETU
- Imidazoline-2-thiol
- Imidazolidinethione
- 2-Imidazoline-2-thiol
- 2-Mercapto-4,5-dihydroimidazole
- Mercaptoimidazoline
- 2-Mercaptoimidazoline
- 2-Mercapto-2-imidazoline
- Tetrahydro-2*H*-imidazole-2-thione
- 2-Thioimidazolidine

Last updated: 25 September 2001

APPENDIX D

cerexagri
ARKEMA GROUP

Linearity of ETU and internal standard by HPLC (copy of Report DL 97-006)

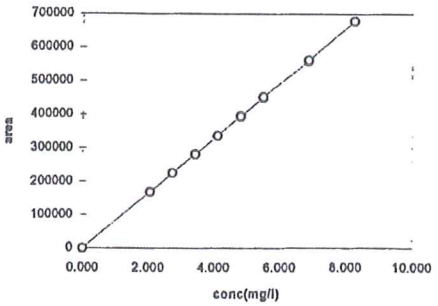
Appendix A

LINEARITY ETU
97-006

M.R.Felperlaan
26/03/97

ETU 57.4

conc mg/l	area	conc calc mg/l
0.000	0	0.000
0.000	0	0.000
2.064	169529	2.069
2.064	168240	2.054
2.752	225600	2.754
2.752	225897	2.757
3.441	281595	3.437
3.441	280487	3.424
4.129	336601	4.108
4.129	336862	4.112
4.817	396444	4.839
4.817	394167	4.811
5.505	450482	5.498
5.505	452954	5.529
6.881	558723	6.820
6.881	561753	6.857
8.257	677934	8.275
8.257	678616	8.283
corr.coeff.	0.999984	0.999984
slope	81928.19	1
intercept	-302.4054	-0.00369



LINEARITY TrMTU
97-006

M.R.Felperlaan
26/02/97

TrimTU 103.7

conc mg/l	area	conc calc mg/l
0.000	0	0.000
0.000	0	0.000
3.729	261108	3.733
3.729	261609	3.740
4.973	346585	4.955
4.973	349036	4.990
6.216	430652	6.157
6.216	433673	6.200
7.459	515268	7.366
7.459	517406	7.397
8.702	606845	8.676
8.702	606593	8.701
9.945	693641	9.916
9.945	696013	9.950
12.432	864470	12.359
12.432	861640	12.318
14.918	1050181	15.014
14.918	1045528	14.947
corr.coeff.	0.999939	0.999939
slope	69948.55	1
intercept	-1278.717	-0.01828