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Ihr Zeichen/Ihre Nachricht vom	Mein Zeichen/Meine Nachricht vom	Durchwahl	Datum
	AP-WAL 004362-00/00	2 99-34 55	10. März 00

EU-Wirkstoffprüfung nach Verordnung (EWG) Nr. 3600/92 zur Aufnahme der Wirkstoffe Glyphosat/Glyphosat-trimesium in Anhang I der Richtlinie 91/414/EWG

Sehr geehrter

anbei übersende ich Ihnen zwei Addenda zu der Monographie zu den Wirkstoffen Glyphosat/Glyphosat-trimesium.

Ein Addendum betrifft Volume 3 und geht Ihnen parallel per Email zur elektronischen Verteilung via CIRCA zu. Das andere Addendum betrifft Volume 4 der Monographie und beinhaltet eine Zusammenfassung der Verunreinigungsprofile von Glyphosat von unterschiedlichen Herstellern. Beide Addenda wurden auch den Mitgliedstaaten übermittelt.

Mit freundlichen Grüßen

Anlagen

Addendum to the

Monograph - Volume 3

of 11 December 1998

Glyphosate

Glyphosate-trimesium

14 January 2000

Rapporteur Member State: Germany

Part A

Glyphosate

Contents

B.5 Toxicology and metabolism

B.5.5 Long-term toxicity and carcinogenicity

Scientific opinion of the Rapporteur on the publication "A Case-Control Study of Non-Hodgkin Lymphoma and Exposure to Pesticides" (1999) by Lennart Hardell and Mikael Eriksson (Cancer, 85,1353-1360)

An epidemiological case-control study on possible etiological factors of Non-Hodgkin lymphoma (NHL) was performed in the mid nineties in some northern and central regions of Sweden. Among other chemicals, glyphosate was also identified as a potential source of concern because the incidence of NHL was higher in people exposed to this herbicide. Since the results of this study are debated in the public in some countries, the Rapporteur was asked by the ECCO meeting to provide a scientific assessment of the published data and conclusions drawn. The scope of this comment is restricted to those parts of the publication dealing with a possible impact of glyphosate. Results and conclusions regarding other pesticides will not be addressed.

As shown in the monograph, there is no indication of a cancerogenic potential neither of glyphosate nor of glyphosate-trimesium. This statement is based on the negative outcome of all available long-term studies in rats and mice as well as on lacking evidence of cancerogenicity in humans coming from the long-lasting experience at least with the widely used herbicide glyphosate. Glyphosate-trimesium was introduced few years ago only, however, there is also no information available that would point to oncogenic effects. Furthermore, both compounds are devoid of a mutagenic potential.

In contrast, the study by Hardell and Eriksson (1999) suggests a possible link between an exposure to glyphosate and NHL occurrence. However, the actual data do not sufficiently support this hypothesis for the following reasons:

- The assumption is mainly based on an odds ratio of 2.3 (confidence interval ranging from 0.4 to 13) upon univariate analysis when the number of people suffering from NHL with exposure to glyphosate is simply compared to the number of exposed people in the control group. This value would indicate a 2.3 times higher risk for exposed persons to develop NHL. However, it must be stressed that the absolute number of subjects with exposure to this herbicide was very small in either group. Actually, 4 out of 404 NHL patients (cases) responding to the questionnaire reported an exposure to glyphosate in the past. In contrast, 3 out of 741 compliant people from the control group indicated contact with this compound. Time, duration and rate of the exposure were not reported.
  It seems at least rather equivocal whether a valid evaluation can be made on such a limited database. The study authors themselves also mention this problem since they deny the possibility to draw definite conclusions from the multivariate analysis revealing an odds ratio of even 5.8 (confidence interval: 0.6 – 54) "due to the low numbers of exposed subjects in some of the categories".
- Mixed exposure to perhaps many industrial and agricultural chemicals is likely and also indicated by summing up the numbers of exposed people in the case group.
- Ageing is an important factor in tumor development. No information on the age of the few people exposed to glyphosate is available from the publication. However, a mean age of 65 for both the case and the control group appears rather high for detecting a

possible link between neoplasia and exposure to chemicals since it is just within the range of live years with a high spontaneous tumor rate.

- Hardell and Eriksson suspect immunosupression by certain chemicals to be a mechanism behind NHL development enhancing proliferation of oncogenic viruses. This may be true although the etiological role of such viruses may be different in various parts of the world. However, there is a large body of toxicological information on glyphosate but no indication of immunotoxic properties.

Beside their epidemiological data, the study authors report that some *in vitro* mutagenicity and one cancerogenicity study would have revealed evidence of genotoxic or oncogenic effects. So far these studies are available to the Rapporteur, the conclusions of Hardell and Eriksson cannot be confirmed.

The cited long-term study in mice 1986) did not provide evidence of cancerogenicity. The study is described in detail in the monograph on glyphosate-trimesium (volume 3) since this was the test material but not glyphosate.
Positive findings in mouse lymphoma tests and in an SCE assay were taken as evidence for gene mutations and chromosome aberrations. The test material in the cited mouse lymphoma assays was apparently also glyphosate-trimesium instead of glyphosate. These studies were not submitted to the Rapporteur but a more recent, GLP-like study of this type using the trimesium salt was reviewed for purposes of monograph preparation and failed to indicate any mutagenic effect (Cross, 1988, see monograph). The outcome of the SCE assay (Vigfusson and Vyse, 1980) is equivocal and was discussed in detail in an addendum to the monograph on glyphosate addressing possible cytotoxic and mutagenic effects. Furthermore, this study does not comply with current standards. Again, the test material was not glyphosate but, this time, the preparation Roundup. So, there are also clear deficiencies in reporting and evaluating toxicological studies.

B.5.6 List of essential studies (toxicology) for which the main notifiers have claimed data protection

LIST OF STUDIES FOR WHICH THE MAIN SUBMITTER HAS CLAIMED DATA PROTECTION AND WHICH DURING THE RE-EVALUATION PROCESS WERE CONSIDERED AS ESSENTIAL FOR THE EVALUATION WITH A VIEW TO ANNEX I INCLUSION: **GLYPHOSATE**

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.1		1992	(14C)-glyphosate: Absorption and distribution in the rat - prcliminary study. REPORT NO. 6365-676/1 ! 5.1/05 GLP, unpublished TOX95-52358	Y	CHE
AIIA-5.1		1992	(14C)-glyphosate: Absorption, distribution, metabolism and excretion in the rat. REPORT NO. 7006-676/2 ! 5.1/06 GLP, unpublished TOX95-52359	Y	CHE
AIIA-5.2.1		1989	Glyphosate technical: Acute oral toxicity (limit) test in rats. IRI PROJ. NO. 243268 ! 5.2.1/01 GLP, unpublished TOX95-52319	Y	CHE
AIIA-5.2.1		1991	Assessment of acute oral toxicity of "Glyphosate technical" to mice. LAB. NO.: 12321 ! 5.2.1/02 GLP, unpublished TOX95-52320	Y	CHE
AIIA-5.2.1		1994	Glyphosate premix: Acute oral toxicity (limit test) in the rat. PROJ. NO. 545/37 ! 5.2.1/04 GLP, unpublished TOX95-52322	Y	CHE
AIIA-5.2.3		1988	Acute inhalation study of Mon-8750 technical. PROJ. NO. EHL 87147 ! 5.2.3/04 GLP, unpublished TOX95-52332	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.2.3		1994	Glyphosate premix: Acute inhalation toxicity study four-hour exposure (nose only) in the rat. PROJ. NO. 545/39 ! 5.2.3/03 GLP, unpublished TOX95-52331	Y	CHE
AIIA-5.2.3		1989	Glyphosate technical: Acute inhalation toxicity study in rats (limit test). IRI PROJ. NO. 642062 ! 5.2.3/01 GLP, unpublished TOX95-52329	Y	CHE
AIIA-5.2.4		1987	Primary dermal irritation study of Mon 8722 in New Zealand white rabbits. FDRL STUDY NO. 9307A ! 5.2.4/05 GLP, unpublished TOX95-52337	Y	MOD
AIIA-5.2.4		1987	Primary dermal irritation study of Mon-8750 in New Zealand white rabbits. FDRL STUDY NO. 9308A ! 5.2.4/04 GLP, unpublished TOX95-52336	Y	MOD
AIIA-5.2.4		1989	Glyphosate technical: Primary skin irritation test in rabbits. IRI PROJ. NO. 243268 ! 5.2.4/01 GLP, unpublished TOX95-52333	Y	CHE
AIIA-5.2.4		1994	Glyphosate premix: Acute dermal irritation test in the rabbit. PROJ. NO. 545/40 ! 5.2.4/03 GLP, unpublished TOX95-52335	Y	CHE
AIIA-5.2.5		1987	Primary eye irritation of Mon-8750 to New Zealand white rabbits. FDRL STUDY NO. 9308A ! 5.2.5/04 GLP, unpublished TOX95-52341	Y	MOD
AIIA-5.2.5		1987	Primary eye irritation of Mon 8722 in New Zealand white rabbits. FDRL STUDY NO. 9307A ! 5.2.5/05 GLP, unpublished TOX95-52342	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.2.5		1989	Glyphosate technical: Primary eye irritation test in rabbits. IRI PROJ. NO. 243268 ! 5.2.5/01 GLP, unpublished TOX95-52338	Y	CHE
AIIA-5.2.5		1994	Glyphosate premix: Acute eye irritation test in the rabbit. PROJ. NO. 545/41 ! 5.2.5/03 GLP, unpublished TOX95-52340	Y	CHE
AIIA-5.2.5		1996	Primary eye irritation study in rabbits. 2981-96 GLP, unpublished TOX1999-881	Y	MOD
AIIA-5.2.6		1984	A closed-patch repeated insult dermal sensitization study in guinea pigs (modified Buehler method). PROJ. NO. 4989-84 ! 5.2.6/02 not GLP, unpublished TOX95-52344	Y	MOD
AIIA-5.2.6		1988	A closed-patch repeated insult dermal sensitization study in guinea pigs (Buehler method). PROJ. NO. BD-87-218/4470-87 ! 5.2.6/04 GLP, unpublished TOX95-52346	Y	MOD
AIIA-5.2.6		1992	Dermal sensitization study in guinea pigs with Mon 8722 - modified Buehler design- (EPA-OECD-EEC-MAFF). SLS STUDY NO. 3044.299 ! 5.2.6/05 GLP, unpublished TOX95-52347	Y	MOD
AIIA-5.2.6		1989	Glyphosate technical: Magnusson-Kligman maximisation test in guinea pigs. IRI PROJ. NO. 243268 ! 5.2.6/01 GLP, unpublished TOX95-52343	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.2.6		1994	Glyphosate premix: Magnusson & Kligman maximisation study in the guinea pig. PROJ. NO. 545/42 ! 5.2.6/03 GLP, unpublished TOX95-52345	Y	CHE
AIIA-5.3.1		1989	Glyphosate: 4 week dietary toxicity study in rats. IRI PROJ. NO. 437462 ! 5.3.1/04 GLP, unpublished TOX95-52351	Y	CHE
AIIA-5.3.1		1989	Glyphosate: Oral maximum tolerated dose study in dogs. IRI PROJ. NO. 640683 ! 5.3.1/05 GLP, unpublished TOX95-52352	Y	CHE
AIIA-5.3.2		1991	Glyphosate: 13 week dietary toxicity study in rats. IRI PROJ. NO. 437876 ! 5.3.2/05 GLP, unpublished TOX95-52364	Y	CHE
AIIA-5.3.2		1991	Glyphosate: 13 week dietary toxicity study in mice. IRI PROJ. NO. 437918 ! 5.3.2/04 GLP, unpublished TOX95-52363	Y	CHE
AIIA-5.3.3		1993	Glyphosate: 3 week toxicity study in rats with dermal administration. IRI PROJ. NO. 450881 ! 5.3.3/02 GLP, unpublished TOX95-52367	Y	CHE
AIIA-5.4.1	Jensen, J.C.	1991	Mutagenicity test: Ames salmonella assay with glyphosate, batch 206-JaK-25-1. LAB. NO. 12323 ! 5.4.1/04 GLP, unpublished TOX95-52371	Y	CHE
AIIA-5.4.1	Jensen, J.C.	1991	Mutagenicity test: In vitro mammalian cell gene mutation test with glyphosate, batch 206-JaK-25-1. LAB. NO. 12325 ! 5.4.1/05 GLP, unpublished TOX95-52372	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.4.1	Kier, L.D., Stegeman, S.D., Costello, J.G. and Schermes, S.	1992	Ames/salmonella mutagenicity assay of MON 2139 (Roundup herbicide formulation). EHL 91183 ! ML-91-440 ! MSL-11729 not GLP, unpublished TOX1999-239	Y	MOD
AIIA-5.4.1	Stegeman, S.D. and Li, A.P.	1990	Ames/salmonella mutagenicity assay of MON 0818. EHL 89178 ! ML-89-461 ! MSL-10625 not GLP, unpublished TOX1999-241	Y	MOD
AIIA-5.4.1	Vargas, A.A.T.	1996	The salmonella typhimurium reverse mutation by Glifos. G.1.1 - 050 / 96 GLP, unpublished TOX1999-884	Y	MOD
AIIA-5.4.2		1991	Mutagenicity test: Micronucleus test with glyphosate, batch 206-JaK-25-1. LAB. NO. 12324 ! 5.4.2/01 GLP, unpublished TOX95-52374	Y	CHE
AIIA-5.4.2		1992	Mouse micronucleus study of Roundup herbicide formulation. EHL 91200/91204 ! MSL-11771 not GLP, unpublished TOX1999-242	Y	MOD
AIIA-5.4.2		1997	Mouse micronucleus screening assay of MON 0818. EHL 89182 ! ML-89-463 not GLP, unpublished TOX1999-240	Y	MOD
AIIA-5.4.2		1996	A micronucleus study in mice for the product glifos. G1206096 ! G.1.2 - 60/96 not GLP, unpublished TOX1999-253	Y	MOD
AIIA-5.4.2		1996	A micronucleus study in mice for the Glifos. G.1.2 - 060 / 96 GLP, unpublished TOX1999-882	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.4.2		1996	A micronucleus study in mice for the product Glifos. G.1.2 - 60 / 96 GLP, unpublished TOX1999-883	Y	MOD
AIIA-5.5		1991	Glyphosate: 104 week combined chronic feeding/oncogenicity study in rats with 52 week interim kill (results after 52 weeks). IRI PROJ. NO. 438623 ! 5.5/02 GLP, unpublished TOX95-52380	Y	CHE
AIIA-5.5		1993	Glyphosate: 104 week dietary carcinogenicity study in mice. IRI PROJ. NO. 438618 ! 5.5/04 GLP, unpublished TOX95-52382	Y	CHE
AIIA-5.5		1990	Glyphosate: 52 week oral toxicity study in dogs. IRI PROJ. NO. 642675 ! 5.5/05 GLP, unpublished TOX95-52384	Y	CHE
AIIA-5.5		1990	Chronic study of glyphosate administered in feed to albino rats. PROJ. MSL-10495 ! STUDY 87122 ! 5.5/01 GLP, unpublished TOX95-52379	Y	MOD
AIIA-5.6.1		1991	Dietary range finding study of glyphosate in pregnant rats and their juvenile offspring. CHV 42/90619 ! 5.6.1/03 GLP, unpublished TOX95-52388	Y	CHE
AIIA-5.6.1		1992	The effect of dietary administration of glyphosate on reproductive function of two generations in the rat. CHV 47/911129 ! 5.6.1/04 GLP, unpublished TOX95-52389	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.6.1		1990	Two generation reproduction feeding study with glyphosate in Sprague-Dawley rats. PROJ. NO. MSL-10387 ! 5.6.1/02 GLP, unpublished TOX95-52387	Y	MOD
AIIA-5.6.2		1991	The effect of glyphosate on pregnancy of the rabbit (incorporates preliminary investigations). CHV 45 & 39 & 40/901303 ! 5.6.2/02 GLP, unpublished TOX95-52391	Y	CHE
AIIA-5.6.2		1991	The effect of glyphosate on pregnancy of the rat (incorporates preliminary investigation). CHV 43 & 41/90716 ! 5.6.2/04 GLP, unpublished TOX95-52393	Y	CHE
AIIA-5.6.2		1980	Teratology study in rabbits. 401-056 ! IR-79-018 ! 5.6.2/01 not GLP, unpublished TOX95-52390	Y	MOD
AIIA-5.6.2		1980	Teratology study in rats. 401-054 ! IR-79-016 ! 5.6.2/03 not GLP, unpublished TOX95-52392	Y	MOD
AIIA-5.8.1	Bakke, J.P.	1991	Evaluation of the potential of AMPA to induce unscheduled DNA synthesis in the in vitro hepatocyte DNA repair assay using the male F-344 rat. STUDY NO. 2495-V01-91 ! 5.8.1/15 GLP, unpublished TOX95-52409	Y	MOD
AIIA-5.8.1		1992	AMPA: Acute oral toxicity (limit) test in rats. IRI PROJ. NO. 552409 ! 5.8.1/02 GLP, unpublished TOX95-52395	Y	CHE
AIIA-5.8.1		1992	AMPA: Magnusson-Kligman maximisation test in guinea pigs. IRI PROJ. NO. 552409 ! 5.8.1/06 GLP, unpublished TOX95-52397	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.8.1		1992	AMPA: Acute dermal toxicity (limit) test in rats. IRI PROJ. NO. 552409 ! 5.8.1/03 GLP, unpublished TOX95-52396	Y	CHE
AIIA-5.8.1		1979	90-day subacute rat toxicity study. 401-050 ! IRD-78-174 ! 5.8.1/10 not GLP, unpublished TOX95-52401	Y	MOD
AIIA-5.8.1		1992	AMPA: Teratogenicity study in rats. IRI PROJ. NO. 490421 ! 5.8.1/21 GLP, unpublished TOX95-52416	Y	CHE
AIIA-5.8.1		1993	AMPA: 4 week dose range finding study in rats with administration by gavage. IRI PROJ. NO. 450860 ! 5.8.1/09 GLP, unpublished TOX95-52400	Y	CHE
AIIA-5.8.1		1991	A developmental toxicity study of AMPA in rats. PROJ. NO. WIL-50159 ! 5.8.1/20 not GLP, unpublished TOX95-52414	Y	MOD
AIIA-5.8.1		1991	A dose range-finding developmental toxicity study of AMPA in rats. PROJ. NO. WIL-50146 ! 5.8.1/20 GLP, unpublished TOX95-52415	Y	MOD
AIIA-5.8.1		1991	Assessment of acute oral toxicity of (N-methyl-N-phosphonomethyl)glycine to rats. LAB. NO. 12837 ! 5.8.1/07 GLP, unpublished TOX95-52398	Y	CHE
AIIA-5.8.1	Jensen, J.C.	1993	Mutagenicity test: Ames salmonella test with AMPA, batch 286-JRJ-73-4. LAB. NO. 13269 ! 5.8.1/16 GLP, unpublished TOX95-52410	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.8.1	Jensen, J.C.	1993	Mutagenicity test: In vitro mammalian cell gene mutation test performed with mouse lymphoma cells (L5178Y). Test compound: AMPA, batch 286-JRJ-73-4. LAB. NO. 13270 ! 5.8.1/17 GLP, unpublished TOX95-52411	Y	CHE
AIIA-5.8.1		1993	Mutagenicity test: Micronucleus test with AMPA, batch 286-JRJ-73-4. LAB. NO. 13268 ! 5.8.1/18 GLP, unpublished TOX95-52412	Y	CHE
AIIA-5.8.1		1993	Mouse micronucleus study of AMPA. PROJ. NO. EHL-90170/ML-90-404 ! 5.8.1/19 GLP, unpublished TOX95-52413	Y	MOD
AIIA-5.8.1	Lauer, R., Blount, L.M. and Kramer, R.M.	1979	Analysis of animal feed diets in the aminomethylphosphonic acid (AMPA) 90-day subacute rat toxicity study, performed at International Research and Development Corporation. REPORT NO. MSL-0682 ! 5.8.1/10 not GLP, unpublished TOX95-52402	Y	MOD
AIIA-5.8.1		1991	One month study of AMPA administered by capsule to beagle dogs. PROJ. NO. ML-90-186/EHL 90074 ! 5.8.1/12 GLP, unpublished TOX95-52404	Y	MOD
AIIA-5.8.1		1993	AMPA: 13 week toxicity study in rats with administration by gavage. IRI PROJ. NO. 450876 ! 5.8.1/11 GLP, unpublished TOX95-52403	Y	CHE
AIIA-5.8.1		1991	90-day oral (capsule) toxicity study in dogs with AMPA. PROJ. NO. WIL-50173 ! 5.8.1/13 GLP, unpublished TOX95-52406	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.8.2		1987	The subacute toxicity of the isopropylamine salt of glyphosate (Mon-0139) in female cattle. STUDY NO. 82002 ! 5.8.2/08 GLP, unpublished TOX95-52424	Y	MOD
AIIA-5.8.2		1987	The acute oral toxicity of the isopropylamine salt of glyphosate (Mon-0139) in female goats. STUDY NO. 80007 ! 5.8.2/07 GLP, unpublished TOX95-52423	Y	MOD
AIIA-5.8.2		1987	The acute toxicity of glyphosate in female goats. STUDY NO. 80006 ! 5.8.2/06 GLP, unpublished TOX95-52422	Y	MOD
AIIA-5.8.2		1992	Ammonium salt of glyphosate (Mon-8750): General pharmacological study. STUDY: IET 90-0149/ET-92-15 ! 5.8.2/05 GLP, unpublished TOX95-52421	Y	MOD
AIIA-5.9		1987	In vitro adsorption of glyphosate to various adsorbents (cholestylamine, activated charcoal and kayexalete). 5.9/03 not GLP, unpublished TOX95-52427	Y	MOD
AIIIA-7.1.1		1991	Acute oral toxicity study in rats. Test material: Mon 52276. PROJ. NO. 6097-91 ! 7.1.1/01 GLP, unpublished TOX95-52438	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-7.1.1		1992	Acute oral toxicity study in rats with Mon 44068 (EPA-OECD-EEC). SLS STUDY NO. 3044.219 ! 7.1.1/01 GLP, unpublished TOX95-52434	Y	MOD
AIIIA-7.1.2		1991	Acute dermal toxicity study in rats. Test Material: Mon 52276. PROJ. NO. 6098-91 ! 7.1.2/01 GLP, unpublished TOX95-52439	Y	MOD
AIIIA-7.1.2		1991	Acute dermal toxicity study in rats with Mon 44068 (EPA-OECD-EEC-MAFF). SLS STUDY NO. 3044.220 ! 7.1.2/01 GLP, unpublished TOX95-52435	Y	MOD
AIIIA-7.1.4		1991	Primary dermal irritation study in rabbits. Test Material: Mon 52276. PROJ. NO. 6099-91 ! 7.1.4/01 GLP, unpublished TOX95-52440	Y	MOD
AIIIA-7.1.4; AIIIA-7.1.5		1991	Combined eye and skin irritation study in rabbits with Mon 44068 (EPA-OECD-EEC). SLS STUDY 3044.157A ! 7.1.4/01, 7.1.5/01 not GLP, unpublished TOX95-52436	Y	MOD
AIIIA-7.1.4; AIIIA-7.1.5		1991	Combined eye and skin irritation study in rabbits with Mon 44068 (EPA-OECD-EEC). SLS STUDY 3044.157A ! 7.1.4/01, 7.1.5/01 not GLP, unpublished TOX95-52436	Y	MOD
AIIIA-7.1.5		1992	Primary eye irritation study in rabbits. Test Material: Mon 52276. PROJ. NO. 5999-91 ! 7.1.5/01 GLP, unpublished TOX95-52441	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-7.1.6		1992	Closed-patch repeated insult dermal sensitization study in guinea pigs (Buehler method). Test Material: Mon 52276. PROJ. NO. 6100-91 ! 7.1.6/01 GLP, unpublished TOX95-52442	Y	MOD
AIIIA-7.1.6		1992	Dermal sensitization study in guinea pigs with Mon 44068 - modified Buehler design - (EPA-OECD-EEC-MAFF). SLS STUDY NO. 3044.221 ! 7.1.6/01 GLP, unpublished TOX95-52437	Y	MOD

Codes of owner

CHE: Cheminova P.O. Box 9
FSG: Feinchemie Schwebda GmbH
MOD: Monsanto SA

B.8 Ecotoxicology

B.8.9 Effects on other non-target organisms (flora and fauna) believed to be at risk (Annex IIA 8.6)

K. Fletcher and B. Freedman (1995)

In laboratory studies effects of glyphosate on decomposition of several litter substrates were tested. Three substrates were used: foliage of *Acer rubrum*, foliage of *Picea glauca* and forest floor (composed of litter, duff and humus). For testing 6 concentrations (0, 1, 10,100, 1000, 5000 and 10000 ppm) were chosen.
Glyphosat had toxic thresholds at which they reduced decomposition of plant foliage and forest floor substrate but the thresholds were > 50 times higher than residue concentrations that occur in the field after silvicultural herbicide treatment.

H. Eijsackers (1995)

Laboratory tests (effects by direct contact) were carried out with glyphosate (Roundup). Glass dishes, containing a substrate of moist, compaced sandy soil, were sprayed in a Potter tower with 1 % and 4 % (1.49 and 5.96 ml/m²) glyphosate. Observations on numbers of organisms of specific soil fauna species (sprintails, isopoda and carabids) were made daily until the last specimen had died; then, from individual survival periods, mean longevity was calculated.
The data showed a slight but non-significant decrease, with 5.96 ml/m² glyphosate.

Laboratory tests (effects on litter consumption) were carried out. Litter fragmentation have been sampling in the field and offering it in the laboratory to groups of soil organisms.
For field experiments, litter in nylon bags or cloth boxes was buried in the litter.
In both experiments changes in litter fragmentation through spraying of glyphosate were observed but it is difficult to evaluate effects of this herbicide on litter breakdown.

At present, glyphosate does not seem to be very toxic for the soil fauna although adverse effects have been observed in studies with some representatives of the soil fauna (Acarina (Gamasidae) and Isopoda).

Conclusion
In the presented studies glyphosate had no or only slight effects on litter decomposition at concentrations that occur in the environment after treatment. In general glyphosate is not very toxic to soil fauna.
Because of the rapid degradation of glyphosate to metabolite AMPA and the long duration of some presented experience from 5 to18 month (H. Eijsackers (1985) and L. B. Holtby and S.J. Baillie (1989)), these studies also addressed the effects of AMPA on leaf litter decomposition.

B.8.10 List of essential studies (ecotoxicology) for which the main notifiers have claimed data protection

LIST OF STUDIES FOR WHICH THE MAIN SUBMITTER HAS CLAIMED DATA PROTECTION AND WHICH DURING THE RE-EVALUATION PROCESS WERE CONSIDERED AS ESSENTIAL FOR THE EVALUATION WITH A VIEW TO ANNEX I INCLUSION: **GLYPHOSATE**

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.1.1		1991	AMPA: An acute oral toxicity study with the northern bobwhite. 139-277 ! WL 90-397 GLP, unpublished AVS95-00222	Y	CHE
AIIA-8.1.1		1992	Glyphosate technical: Acute oral toxicity (LD50) to the mallard duck (Anas platyrhynchos). CHV 49/91843 GLP, unpublished AVS94-00229	Y	MOD
AIIA-8.1.1		1991	Glyphosate technical: Acute oral toxicity (LD50) to the bobwhite quail. CHV 48/91266 GLP, unpublished AVS94-00230	Y	MOD
AIIA-8.1.2		1991	AMPA: A dietary LC50 study with the mallard. WL-90-399 ! 139-276 GLP, unpublished AVS95-00221	Y	CHE
AIIA-8.1.2		1991	AMPA: A dietary LC50 study with the northern bobwhite. 139-275 ! WL-90-398 GLP, unpublished AVS95-00220	Y	CHE
AIIA-8.2.1		1990	Glyphosate technical: 96-hour acute toxicity study (LC50) in the rainbow trout. 271631 GLP, unpublished WAT95-00011	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.2.1		1991	Glyphosate Technical: 96-hour acute toxicity study (LC50) in the Bluegill sunfish. 271642 (RCC NR.) not GLP, unpublished WAT94-00012	Y	CHE
AIIA-8.2.2		1990	Glyphosate technical: 21-DAY PROLONGED TOXICITY STUDY IN THE RAINBOW TROUT UNDER FLOW-THROUGH CONDITIONS. 271620 (RCC NR.) not GLP, unpublished WAT94-00015	Y	CHE
AIIA-8.2.3	Burgess, D.	1991	Acute toxicity of AMPA to Daphnia magna. AB-90-401 GLP, unpublished WAT94-01163	Y	MOD
AIIA-8.2.4	Wüthrich, V.	1990	48-hour acute toxicity of glyphosate technical to Daphnia magna. 272968 GLP, unpublished WAT95-00006	Y	CHE
AIIA-8.2.5	Wüthrich, V.	1990	Influence of glyphosate on the reproduction of Daphnia magna. 250795 not GLP, unpublished WAT95-00733	Y	CHE
AIIA-8.2.6	Thun, S.	1993	Algae growth inhibition test Test article: "Glyphosate isopropylamine salt". 80-91-2328-01-93 GLP, unpublished WAT93-00002	Y	FSG
AIIA-8.2.6	Wüthrich, V	1990	Acute toxicity of glyphosate to Scenedesmus subspicatus. 250773 GLP, unpublished WAT95-00002	Y	CHE

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.3.1	Kock	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00067	Y	FSG
AIIA-8.3.1	Schulz	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00065	Y	FSG
AIIA-8.3.1	Warnke U.	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00066	Y	FSG
AIIA-8.3.2	Halsall, N.	1990	An evaluation of the toxicitity (PMG 360) glyphosate to the linyphiid spider Meioneta rurestris. CHEM-90-2 GLP, unpublished ANA96-00077	Y	CHE
AIIA-8.3.2	Halsall, N.	1990	An evaluation of the toxicity (PMG 360) glyphosate to the carabid beetle Trechus quadristriatus. CHEM-90-1 GLP, unpublished ANA96-00072	Y	CHE
AIIA-8.3.2	Halsall, N.	1991	A semi-field evaluation of the toxicity of the herbicide Glyphosate 360 to the linyphiid spider. CHEM-91-1 GLP, unpublished ANA96-00073	Y	CHE
AIIA-8.4.1	Klenner, D. and Bathelt, A.	1995	Acute toxicity of glyphosate to Eisenia fetida - laboratory test. RL502 GLP, unpublished ARW96-00093	Y	FSG

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.4.1	Wüthrich, V.	1990	Acute toxicity (LC50) of glyphosate to earthworms. 250784 not GLP, unpublished ARW96-00099	Y	CHE
AIIA-8.5; AIIIA-10.7.1	Maas, G.	1990	Determination of the activity of soil microflora following guide- line part VI. 1-1 (2 annexes). 111/90 GLP, unpublished BMF95-00095	Y	CHE
AIIIA-10.1.1		1991	MON 52276: A dietary LC50 study with the Northern bobwhite. WI 139-304 ! WL-91-271 GLP, unpublished AVS94-00116	Y	MOD
AIIIA-10.1.1		1991	MON 44068: A dietary LC50 study with the Northern bobwhite. WI 139-301 ! WL-91-268 GLP, unpublished AVS94-00004	Y	MOD
AIIIA-10.1.1		1991	MON 52276: A dietary LC50 study with the mallard. WI 139-305 ! WL-91-270 GLP, unpublished AVS94-00115	Y	MOD
AIIIA-10.1.1		1991	MON 44068: A dietary LC50 study with the mallard. WI 139-302 ! WL-91-267 GLP, unpublished AVS94-00003	Y	MOD
AIIIA-10.2.1		1992	Acute Toxicity to Common Carp, Cyprinus carpio, Under Flow- Through Test Conditions. TO-91-298 GLP, unpublished WAT94-00020	Y	MOD
AIIIA-10.2.1		1992	Acute Toxicity to the Common Carp, Cyprinus carpio, Under Flow-Through Test Conditions. TO-91-297 not GLP, unpublished WAT95-00717	Y	MOD

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-10.2.1		1992	MON 44068: Acute toxicity to rainbow trout, Oncorhynchus mykiss, under flow-through test conditions. TO-91-294 not GLP, unpublished WAT95-00718	Y	MOD
AIIIA-10.2.1	Lintott, D.R.	1992	MON 44068: Acute toxicity to the water flea, Daphnia magna, under flow-through test conditions. TO-91-293 not GLP, unpublished WAT95-00719	Y	MOD
AIIIA-10.2.1	Lintott, D.R.	1992	Acute Toxicity to the Water Flea, Daphnia magna, Under Flow- Through Test Conditions. TO-91-295 GLP, unpublished WAT94-00021	Y	MOD
AIIIA-10.2.1		1992	Acute Toxicity To Rainbow Trout, Oncorhynchus mykiss, Under Flow- Through Test Conditions. TO-91-296 GLP, unpublished WAT94-00019	Y	MOD
AIIIA-10.2.1	Neven, B.	1991	Alga, Growth Inhibition Test Effect of MON 52276 on the Growth of Selenastrum capricornutum. LI-91-389 not GLP, unpublished WAT94-00022	Y	MOD
AIIIA-10.2.1	Neven, B.	1992	Alga, growth inhibition test. Effect of MON 44068 on the growth of Selenastrum capricornutum. LI-90-477 not GLP, unpublished WAT95-00720	Y	MOD
AIIIA-10.2.1		1991	Acute toxicity in rainbow trout (Salmo gairdneri). Test article: Taifun 360. 80-91-0130-04-91 GLP, unpublished WAT95-00550	Y	FSG

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-10.2.1	Thun, S.	1991	Final report on the algae growth inhibition test. Test article: Taifun 360. 80-91-0130-01-91 GLP, unpublished WAT95-00553	Y	FSG
AIIIA-10.2.4	Thun, S.	1991	21 d reproduction test in Daphnia magna Test article: Taifun 360. 80-91-0130-02-91 GLP, unpublished WAT95-00552	Y	FSG
AIIIA-10.2.4		1991	Prolonged toxicity test in rainbow trout (Salmo gairdneri). Test article: Taifun 360. 80-91-0130-05-91 GLP, unpublished WAT95-00551	Y	FSG
AIIIA-10.4	Hoxter, K.A., Smith, G.J.	1992	MON 52276: An acute contact toxicity study with the honey bee. . WL-92-233 not GLP, unpublished BIE1999-33	Y	CHE
AIIIA-10.4	Hoxter, K.A., Smith, G.J.	1992	MON 52276: A dietary LC50 toxicity study with the honey bee. . WL-92-232 not GLP, unpublished BIE1999-32	Y	CHE
AIIIA-10.4.1	Kock	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00070	Y	FSG
AIIIA-10.4.1	Schulz	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00069	Y	FSG

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-10.4.1	Warnke, U.	1991	Testing on bee toxicity for the registation procedure, laboratory test, test substance: Taifun 360. not GLP, unpublished BIE96-00068	Y	FSG
AIIIA-10.5.1	Kleiner, R.	1995	Testing toxicity to beneficial arthropods Spider - Pardosa spp. 95 10 48 053 GLP, unpublished ANA98-00029	Y	MOD
AIIIA-10.5.1	Kleiner, R.	1995	Testing toxicity to beneficial arthropods Cereal aphid parasitoid - Aphidius rhopalosiphi (DESTEFANI-PEREZ) Imagines. 95 10 48 054 GLP, unpublished ANA98-00030	Y	MOD
AIIIA-10.5.1	Kleiner, R.	1995	Testing toxicity to beneficial arthropods Predacious mite - Typhlodromus pyri (SCHEUTEN). 95 10 48 056 GLP, unpublished ANA98-00031	Y	MOD
AIIIA-10.6.1.1	Hoxter, K. A. and Lynn, S. P.	1992	MON 44068: An acute toxicity study with the earthworm in an artificial soil substrate. WL-91-269 GLP, unpublished ARW96-00098	Y	MOD
AIIIA-10.6.1.1	Hoxter, K. A. and Smith, G. J.	1992	MON 52276: An acute toxicity study with the earthworm in an artificial soil substrate. 139-306 GLP, unpublished ARW93-00016	Y	MOD

Codes of owner

CHE: Cheminova P.O. Box 9
FSG: Feinchemie Schwebda GmbH
MOD: Monsanto SA

Part B

Glyphosate-trimesium

Contents

B.4 Methods of analysis

B.4.3 Analytical methods (residue) for soil, water and air (Annex IIA 4.2.2-IIA 4.2.4; Annex IIIA 5.2.2-Annex IIIA 5.2.4)

B.4.3.1 Water (including drinking water) (Annex IIA 4.2.3; Annex IIIA, 5.2.3

According to the method 49291/01 (Bolygo, 1999) residues of the TMS-cation can be determined by head space gas chromatography using FP-detection.
After removing interfering impurities from the water samples by solid phase extraction, residues of TMS-cation are concentrated on cation exchange resin. Any residues of TMS-cation are converted to DMS by dealkylation with KOH in the presence of $SnCl_2$.
For validation data see table B-4.3-1.

Table B-4.3-1: Validation data for analytical methods for the determination of residues in water

Reference	Matrix	Fortification level [µg/l]	Recovery rate [%] mean	range	RSD [%]	n
Bolygo	**TMS-cation**					
1999	river	0.1*	78	75-84	4.7	5
(49291/01)		1.0	80	69-83	7.9	5
	ground	0.1*	92	77-100	9.8	5
		1.0	74	66-78	6.5	5
	sea	0.1	71	65-79	7.5	5
		1.0*	81	71-91	10.5	5
	drinking	0.1*	77	72-83	5.4	5
		1.0	83	82-86	1.8	5

* limit of quantification

Reference:

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-4.2.3	Bolygo, E.	1999	Analytical Method for the Determination of Residues of Trimethylsulfonium Ions in Water Technical Letter 49291/01 unpublished MET2000-39	Y	ZNC

B.5 Toxicology and metabolism

B.5.2 Acute toxicity - Clarification of dose levels used in toxicity studies and resulting changes in health effects assessment

Background

As described in the monograph, the herbicidal compound glyphosate-trimesium consists of two moieties, i.e., the phosphonomethylglycine (PMG) anion and the trimethylsulfonium (TMS) cation. The anionic moiety has the same chemical structure like glyphosate acid (N-phosphonomethylglycine, usually described by the technical term "glyphosate") with the only exception that one hydrogen atom is lacking resulting in a negative load (see volume 1 of the monograph on glyphosate/glyphosate-trimesium).

For application in plant protection, glyposate acid is usually also formulated as a salt (i.e. isopropylamine, ammonium, or monosodium salt). However, with the exception of acute toxicity testing, most toxicological studies available have been performed with glyphosate acid being the test material. These studies are extensively reported and evaluated in the monograph on glyphosate.

In contrast, the trimesium salt was tested in a full range of toxicological studies. It is clearly stated under section B.2 in the monograph that the test material actually was technical glyphosate-trimesium, i.e. an aqueous solution of this salt. The content of active ingredient in the technical test material varied between 19% and >60% in the different toxicological experiments with the remaining portion being water. The only manufacturer of plant protection products containing this salt, i.e. ZENECA, did not provide toxicity studies with glyphosate acid or the PMG anion being the test material alone.

Due to this high degree of variability in a.i. content, the ECCO meeting (ECCO 78) expressed serious concern about the dose levels actually reached in the toxicological studies and also asked for adjusting the dose levels in terms of glyphosate acid equivalents to facilitate direct comparison. On request, the notifier performed a data re-evaluation resulting in the correction of some dosages used in acute toxicity testing. Based on the notifiers recent submissions, this addendum was compiled by the Rapporteur for clarification. For practical reasons, correction for a.i. content and calculation of glyphosate acid equivalents are adressed separately.

1. Correction of dose levels in toxicological studies for a.i. content in the test material

With the only exception of some acute studies and a subacute dermal one, intended (nominal) and actually achieved dose levels were corrected for a.i. content in the studies submitted for EC reevaluation purposes. However, it was not always adressed in each of the study reports that such a correction had been performed. Nontheless, the Rapporteurs scientific assessment of the toxicological studies as presented in the monograph was based on the general assumption that all dose levels refer to glyphosate-trimesium a.i. and this approach has been essentially confirmed by the notifier now. This becomes apparent when the tables submitted by the notifier for clarification are considered (see Annex I). These tables clearly indicate that it was necessary to administer higher doses of the technical test material to achieve the nominal dose levels of glyphosate-trimesium a.i. in short term tests, chronic and reproduction/teratogenicity studies. Thus, it is not necessary to change the respective sections of the monograph. Accordingly, the basis for establishing the ADI and AOEL for glyphosate-trimesium will remain the same.

In contrast, a correction for actual a.i. concentration had not been made by the notifier with respect to the oral and dermal acute toxicity studies when the original reports and the overall dossier were submitted. This failure will result in some changes in the acute and short term toxicity part of the monograph and might also affect classification and labeling.
Tables 1 and 2 below summarize the outcome of acute and short term toxicity studies as reported in the monograph but also contain the corrected values as submitted by the notifier on request now. Only studies which are considered acceptable and relevant for risk assessment and classification/labeling are included.

Table 1: Glyphosate-trimesium: Acute toxicity studies

Route/Species/ Purity of test material (a.i. content*)	LD50/LC50 according to the monograph	LD50/LC50 with regard to technical test material	LD50/LC50 corrected for a.i. content	Reference
Rat, oral; purity 62%	LD50 = 748 mg/kg bw (m), 755 mg/kg bw (f)	LD50 = 748 mg/kg bw (m), 755 mg/kg bw (f)	LD50 = 464 mg/kg bw (m), 468 mg/kg bw (f)	1982
Rabbit, dermal; purity 62%	LD50 > 2000 mg/kg bw	LD50 > 2000 mg/kg bw	**LD50 > 1240 mg/kg bw**	1982
Rat, inhalation; purity 57.6%	LC50 > 6.2 mg/l**	LC50 > 9.03 mg/l	LC50 > 5.1 mg/l	1988

* the remaining percentage being water
** In contrast to the table included in the monograph, according to the ECCO meeting recommendations, the relevant analytical concentration (i.e., 5.1 mg/l) should be used rather than the particulate.

Table 2: Glyphosate-trimesium: Short term toxicity studies

Study	**Dose levels [mg/kg bw/d]**	**NOEL (NOAEL) [mg/kg bw/d] according to the monograph**	**NOEL (NOAEL) [mg/kg bw/d] with regard to technical test material**	**NOEL (NOAEL) [mg/kg bw/d] with regard to glyphosate trimesium salt (i.e., corrected for a.i. content)**	**Reference**
Dog, 28 d, oral	0-600 (range) mg/kg/d	Range finding study	0-3125 (range) mg/kg/d	Range finding study	et al., 1983
Rat, 90 d, oral	approx. 0-7-16-36-88 (0-150-350-800-2000 ppm)	40 mg/kg/d (800 ppm)	208.3 mg/kg/d	40 mg/kg/d (800 ppm)	and 1987
Dog, 90 d, oral	0-2-10-50	10 mg/kg/d	52.1 mg/kg/d	10	and 1987
Dog, 90 d, oral	0-10-25-50	25 mg/kg/d	42.1 mg/kg/d	25	1993
Dog, 1 yr, oral	0-2-10-50	10 mg/kg/d	17.8 mg/kg/d	10	nd 1987
Rabbit, 21 d, dermal	0-10-100-1000	1000 mg/kg/d (systemic)	1000 mg/kg/d	573 (systemic)	1988

Discussion and conclusion:
Correction for a.i. content resulted in changes to the acute oral and dermal LD50 values as given in the monograph. In the inhalation study, correction had been considered before already. With regard to short term toxicity testing, changes to be made were confined to the dermal subacute study in rabbits.

The corrected data confirm the moderate acute oral toxicity of the glyposate trimesium salt. Following correction, toxicity appears even more pronounced since not only the oral LD50 but also doses causing adverse effects are much lower than assumed before. This assumption is further supported by an acute neurotoxicity study in rats 1993) which was made available on request recently, too. In this study, marked systemic toxicity was observed following a single oral dose of 300 mg/kg bw whereas the next lower dose of 100 mg/kg bw may be considered a NOEL. However, the current classification and labeling (R 22, Xn) for acute oral toxicity is still considered appropriate. Likewise, the proposed ARfD of 0.25 mg/kg bw should not be changed.
After correction for a.i. content, it becomes obvious that the limit dose of 2000 mg/kg bw had not been reached in the acute dermal study. For formal reasons, a need for classification and labeling for acute dermal toxicity could be assumed. However, this is not considered appropriate since dermal absorption of glyphosate-trimesium is < 1%. No signs of toxicity were observed in this experiment when the compound was applied to intact skin. A direct comparison of oral and dermal toxicity results in the conclusion that the expected dermal LD50 would be well above the limit dose of 2000 mg/kg bw.

The corrected NOEL in the dermal 21-day study in rabbits does not alter health assessment of short term effects.

2. CALCULATION OF GLYPHOSATE ACID EQUIVALENTS AND ITS TOXICOLOGICAL RELEVANCE

On request, the notifier performed a re-calculation of dosages applied in toxicological studies with glyphosate-trimesium in terms of glyphosate acid equivalents. The outcome of these calculations is summarised in tables 3-6 for acute, short term, long term and reproduction/teratogenicity studies, respectively. Afterwards it is discussed whether these acid equivalents may be used in toxicological risk assessment for either glyphosate or glyphosate-trimesium.

Table 3: Glyphosate-trimesium: Acute toxicity studies

Route/Species	LD50/LC50 according to the monograph	LD50/LC50 with regard to technical test material	LD50/LC50 with regard to glyphosate-trimesium salt	LD50/LC50 with regard to glyphosate acid equivalents	Reference
Rat, oral	748 mg/kg bw (m) 755 mg/kg bw (f)	748 mg/kg bw (m) 755 mg/kg bw (f)	464 mg/kg bw (m) 468 mg/kg bw (f)	318 mg/kg bw (m) 321 mg/kg bw (f)	1982
Rabbit, dermal	> 2000 mg/kg bw	> 2000 mg/kg bw	> 1240 mg/kg bw	> 849 mg/kg bw	1982
Rat, inhalation	> 5.1 mg/l*	> 9.03 mg/l	> 5.1 mg/l	> 3.5 mg/l	1988

* In contrast to the table included in the monograph, according to the ECCO meeting recommendations, analytical concentration should be used rather than particulate concentration (6.2 mg/l).

Table 4: Glyphosate-trimesium: Short-term toxicity studies

Study	**Dose levels [mg/kg bw/d]**	**NOEL (NOAEL) [mg/kg bw/d] according to the monograph**	**NOEL (NOAEL) [mg/kg bw/d] with regard to technical test material**	**NOEL (NOAEL) [mg/kg bw/d] with regard to glyphosate trimesium salt**	**NOEL (NOAEL) [mg/kg bw/d] with regard to glyphosate acid equi-valents**	**Reference**
Dog, 28 d, oral	0-600 (range) mg/kg/d	Range finding study	Range finding study	Range finding study	Range finding study	et al., 1983
Rat, 90 d, oral	approx. 0-7-16-36-88 (0-150-350-800-2000 ppm)	40 (800 ppm)	208.3	40 (800 ppm)	27.4	and 1987
Dog, 90 d, oral	0-2-10-50	10	52.1	10	6.9	and 1987
Dog, 90 d, oral	0-10-25-50	25	42.1	25	17.1	1993
Dog, 1 yr, oral	0-2-10-50	10	17.8	10	6.9	d 1987
Rabbit, 21 d, dermal	0-10-100-1000	1000 (systemic)	1000	573 (systemic)	392	1988

Table 5: Glyphosate-trimesium: Long-term studies

Study	**Dose levels [ppm]**	**NOEL (NOAEL) according to the monograph**	**NOEL (NOAEL) [mg/kg bw/d] with regard to technical test material**	**NOEL (NOAEL) with regard to glyphosate trimesium salt**	**NOEL (NOAEL) [mg/kg bw/d] with regard to glyphosate acid equi-valents**	**Reference**
2 yr, oral, CD-rat	0-100-500-1000	21.2 mg/kg bw/d (m); 27 mg/kg bw/d (f) [500 ppm]	37.7 (m); 48.0 (f)	21.2 mg/kg bw/d (m); 27 mg/kg bw/d (f) [500 ppm]	14.5 (m); 18.5 (f)	and 1987
2 yr, oral, CD-1-mouse	0-100-1000-8000	118 mg/kg bw/d (m); 159 mg/kg bw/d (f) [1000 ppm]	210 (m); 282.9 (f)	118 mg/kg bw/d (m); 159 mg/kg bw/d (f) [1000 ppm]	80.8 (m); 108.9 (f)	and 1986

Table 6: Glyphosate-trimesium: Reproduction and teratogenicity studies

Study	**Dose levels**	**NOEL (NOAEL) according to the monograph**	**NOEL (NOAEL) with regard to technical test material**	**NOEL (NOAEL) with regard to glyphosate trimesium salt**	**NOEL (NOAEL) with regard to glypho-sate acid equivalents**	**Reference**
Multigeneration, CD rat	0-150-800-2000 ppm	7.5 mg/kg bw/d [150 ppm]	39.1 mg/kg bw/d	7.5 mg/kg bw/d [150 ppm]	5.1 mg/kg bw/d	and 1984
Teratogenicity, CD rat	0-30-100-333 mg/kg bw/d	100 mg/kg bw/d	520.8 mg/kg bw/d	100 mg/kg bw/d	68.5 mg/kg bw/	nd 1982
Teratogenicity, NZW rabbit	0-10-40-100 mg/kg bw/d	40 mg/kg bw/d	71.2 mg/kg bw/d	40 mg/kg bw/d	27.4 mg/kg bw/d	d 1983

Discussion and conclusion:

Acute toxicity data indicate a higher oral toxicity of glyphosate trimesium salt as compared to glyphosate. This can be readily demonstrated by introducing the glyphosate-trimesium study into the table compiling data obtained upon acute oral toxicity testing of glyphosate (acid) in rats (table 7). The original table is contained in the acute toxicity section of the monograph on glyphosate.

Likewise, glyphosate-trimesium also exhibited a markedly higher acute oral toxicity when compared to the other glyphosate salts (see monograph).

A comparison of NOELs and LOELs for subacute/subchronic toxicity as well as for reproduction/developmental toxicity also suggests a somewhat higher toxicity of glyphosate-trimesium as compared to glyphosate acid.

Table 7: Acute oral toxicity of glyphosate acid and glyphosate-trimesium (following adjustment for a.i. content) in rats

Strain	Test material/ purity	Vehicle	Number of animals/dose level(s) (mg/kg bw)	LD50 (mg/kg bw)	Results	Reference (Notifier)
Sprague-Dawley	Acid, 97.6 %	cotton seed oil	5/sex/2000	> 2000 (limit test)	Slightly congested lungs, splenomegaly, liver: centrilobular congestion	[redacted] 1995 (Sanachem)
Sprague-Dawley	Acid, 95 %	arachis oil	5/sex/2000	> 2000 (limit test)	No findings	[redacted] 1994 (Herbex)
Wistar	Acid, 97.2 %	water	5/sex/5000	> 5000 (limit test)	m: heart weights↓	[redacted] 1994 (Alkaloida)
Sprague-Dawley	Acid, 95 %	CMC	5/sex/5000	> 5000 (limit test)	Piloerection, subdued behaviour, hunched appearance	[redacted] & 1994 (Sinon)
Sprague-Dawley	Acid, >97 %	water	5/sex/2000	> 2000 (limit test)	No findings	[redacted] 1992 (Barclay)
Wistar	Acid, 96.8 %	peanut oil	5/sex/2500 5/sex/5000 5/sex/7500	> 7500 (estimated)	Mortality at 7500 mg/kg bw (2m, 2f); lethargy, ataxia, dyspnoea, weight loss	[redacted] 1991 (Feinchemie)
CD	Acid, 98.1 %	1 % CMC	5/sex/3000 5/sex/5000 5/sex/8000	> 8000	Decreased activity, abnormal gait and/or limb position from 5000 mg/kg bw onwards	[redacted] 1990 (Agrichem)
Sprague-Dawley	Acid, 98.6 %	0.5 % CMC	5/sex/5000	> 5000 (limit test)	Piloerection, re-duced activity, ataxia (males only)	[redacted] & 1989 (Monsanto/ Cheminova)
Haffkine	Acid, 95 %	not stated	5/sex/5000	> 5000 (limit test)	Slight ataxia (at 5000 mg/kg bw)	[redacted] 1983* (Barclay; Luxan)
Sprague-Dawley	Trimesium salt, dosages adjusted for 100%	none	10/sex/dose in the range of 310-558 (m) and 341-558 (f)	464 (m), 468 (f)	Mortality from 341 mg/kg bw onwards; depression, prostration, ptosis, tremor, ataxia, piloerection, chromodacryorrhea, slow and shallow respiration	[redacted] 1982 (Zeneca)

* study considered supplementary only

Thus, the toxicological profile of glyphosate acid and related salts (isopropylamine, ammonium, sodium) is different from that of glyphosate trimesium salt, in particular with regard to acute effects. There are different possible reasons for these differences. Comparing oral absorption data from the toxicokinetic studies, it becomes obvious that absorption rate of the PMG anion from the gastro-intestinal tract when administered together with the TMS cation markedly exceeds that of glyphosate acid. Thus, one could assume that the trimesium cation may enhance absorption of the glyphosate anion. However, this would not sufficiently explain the large difference in acute oral toxicity. Assuming a 30% oral absorption rate for

glyphosate acid, a dose of 5000 mg/kg bw would result in a systemic exposure of 1500 mg/kg bw. However, with glyphosate acid or the other salts, adverse effects were lacking or at least less apparent than following ingestion of much lower doses of glyphosate-trimesium. Therefore, it is more likely that the markedly higher toxicity of the trimesium salt is either due to intrinsic properties of the trimesium moiety or to a true synergistic effect. It might be of scientific interest to distinguish, however, for consumers and operators health protection, the mechanism behind is not so relevant since the trimesium salt of glyphosate is manufactured and intended for use as one complex compound rather than a formulation.

The conclusion can be drawn that toxicity of glyphosate-trimesium is mediated primarily by the trimesium moiety although the mode of action is not clear yet. Therefore,

- **it is not appropriate to use toxicological data obtained with glyphosate-trimesium for purposes of health evaluation of glyphosate or other salts not containing this moiety.**
- **it is not appropriate to use the calculation of glyphosate acid equivalents for risk assessment purposes with regard to glyphosate-trimesium.**

B.5.15 List of essential studies (toxicology) for which the main notifiers have claimed data protection

LIST OF STUDIES FOR WHICH THE MAIN SUBMITTER HAS CLAIMED DATA PROTECTION AND WHICH DURING THE RE-EVALUATION PROCESS WERE CONSIDERED AS ESSENTIAL FOR THE EVALUATION WITH A VIEW TO ANNEX I INCLUSION: **GLYPHOSATE-TRIMESIUM**

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.1		1988	ICIA-0224: Metabolism study in rats. T-12906 ! C2.7/05 GLP, unpublished TOX95-00013	Y	ZNC
AIIA-5.1		1988	The disposition of (14C)-cation TMS+ ICIA 0224 in the rat. IRI PRO.NO.137755 ! C2.7/04 ! CTL/C/2114 GLP, unpublished TOX95-00015	Y	ZNC
AIIA-5.1		1988	The disposition of (14C)-anion CAP ICIA 0224 in the rat. IRI PRO.NO.137708 ! C2.7/03 ! CTL/C/2115 GLP, unpublished TOX95-00014	Y	ZNC
AIIA-5.1		1985	Metabolism, tissue residue and balance studies of orally administered (Methyl 14C)trimethylsulfonium carboxymethylamino-methylphosphonate (SC-0224) in rats. REP. NO. PMS-148 ! C2.7/02 ! CTL/C/2526 not GLP, unpublished TOX95-00016	Y	ZNC
AIIA-5.1		1987	Metabolism, balance and tissue distribution of orally administered (Phosphonomethyl-13C, 14C)SC-0224 in rats. PMS-147;MRC-87-01 ! C2.7/01 ! CTL/C/2527 not GLP, unpublished TOX95-00017	Y	ZNC
AIIA-5.2.3		1988	ICIA 0224: 4-hour acute inhalation toxicity study in the rat. REPORT NO.: CTL/P/2254 (REVISED) GLP, unpublished TOX95-00019	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.2.6	and	1995	Glyphosate trimesium: Skin sensitisation to the guinea pig. REPORT NO.: CTL/P/4723 GLP, unpublished TOX98-50385	Y	ZNC
AIIA-5.2.6		1994	Glyphosate trimesium: Skin sensitisation to the guinea pig. REPORT NO.: CTL/P/4339 GLP, unpublished TOX95-00020	Y	ZNC
AIIA-5.3.1		1983	28 day range-finding study with SC-0224 in beagle dogs. T-11001 ! C2.2/01 GLP, unpublished TOX95-00021	Y	ZNC
AIIA-5.3.2		1987	Three month subchronic oral toxicity study with SC-0224 in beagle dogs. T-11002 ! C2.3/02 GLP, unpublished TOX95-00022	Y	ZNC
AIIA-5.3.2		1987	3-month dietary toxicity study with SC-0224 in rats. T-10888 ! C2.3/01 GLP, unpublished TOX95-00023	Y	ZNC
AIIA-5.3.2		1987	One-year chronic oral toxicity study with SC-0224 in beagle dogs. REPORT NO.: T-11075 ! C2.4/01 GLP, unpublished TOX95-00034	Y	ZNC
AIIA-5.3.2		1993	Glyphosate trimesium: 90 day oral toxicity study in dogs. REPORT NO.: CTL/P/3962 ! C2.3/03 GLP, unpublished TOX95-00024	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.3.3		1988	21-day dermal toxicity study with SC-0224 concentrate in rabbits. T-13038 ! HLA 6142-107 ! C2.2/02 GLP, unpublished TOX95-00025	Y	ZNC
AIIA-5.4.1	Callander, R.D.	1990	ICIA0224 - An evaluation of mutagenic potential using S. typhimurium and E. coli. REPORT NO.: CTL/P/3129 ! C2.6/10 GLP, unpublished TOX95-00027	Y	ZNC
AIIA-5.4.1	Callander, R.D.	1988	ICIA 0224 - An evaluation of mutagenic potential using S. typhimurium and E. coli. REPORT NO.: CTL/P/2203 ! C2.6/08 GLP, unpublished TOX95-00026	Y	ZNC
AIIA-5.4.1	Cross, M.F.	1988	ICIA 0224: Assessment of mutagenic potential using L5178Y mouse lymphoma cells. REPORT NO.: CTL/P/2228 ! C2.6/07 GLP, unpublished TOX95-00028	Y	ZNC
AIIA-5.4.1	Majeska, J.B.	1982	SC-0224 (Lot no. 7646-0901) Mutagenicity evaluation in Salmonella typhimurium. REPORT NO.: T-11070 GLP, unpublished TOX95-00029	Y	ZNC
AIIA-5.4.1	Majeska, J.B.	1985	SC-0224 (Lot no. JHC 8865-20-1) Mutagenicity evaluation in Chinese hamster ovary cytogenetic assay. REPORT NO.: T-12663 ! C2.6/03 GLP, unpublished TOX95-00030	Y	ZNC
AIIA-5.4.2		1990	ICIA0224: Assessment for the induction of unscheduled DNA synthesis in rat hepatocytes in vivo. REPORT NO.: CTL/P/2789 ! C2.6/09 GLP, unpublished TOX95-00031	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.4.2		1986	SC-0224 - Mutagenicity evaluation in bone marrow micronucleus. REPORT NO.: T-12689 ! C2.6/04 GLP, unpublished TOX95-00033	Y	ZNC
AIIA-5.4.2		1982	SC-0224 - Mutagenicity evaluation in bone marrow cytogenetic analysis in rats. REPORT NO.: T-10884 GLP, unpublished TOX95-00032	Y	ZNC
AIIA-5.5		1986	2-year chronic toxicity and oncogenicity dietary study with SC-0224 in mice. REPORT NO.: T-11813 ! C2.4/04 GLP, unpublished TOX95-00035	Y	ZNC
AIIA-5.5		1987	Two year chronic toxicity and oncogenicity dietary study with SC-0224 in rats. REPORT NO.: T-11082 ! C2.4/02 GLP, unpublished TOX95-00037	Y	ZNC
AIIA-5.6.1		1984	SC-0224: Two-generation reproduction study in rats. REPORT NO.: T-11051 ! C2.5/03 GLP, unpublished TOX95-00039	Y	ZNC
AIIA-5.6.2		1982	A teratology study in CD rats with SC-0224. REPORT NO.: T-11050 GLP, unpublished TOX95-00040	Y	ZNC
AIIA-5.6.2		1983	A teratology study in New Zealand white rabbits with SC-0224. REPORT NO.: T-11052 ! C2.5/02 GLP, unpublished TOX95-00041	Y	ZNC
AIIA-5.7		1993	Glyphosate trimesium: Acute neurotoxicity study in rats. CTL/P/3813 GLP, unpublished TOX1999-1123	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-5.7		1989	Acute delayed neurotoxicity of ICIA-0224. REPORT NO.: T-12324 ! C2.8/02 GLP, unpublished TOX95-00042	Y	ZNC
AIIA-5.8.1		1988	Aminomethyl phosphonic acid - an evaluation of mutagenic potential using S. typhimurium and E. coli. REPORT NO.: CTL/P/2206 ! C4.6/01 GLP, unpublished TOX95-00043	Y	ZNC
AIIA-5.8.1		1988	Aminomethyl phosphonic acid: Acute oral toxicity to the rat. REPORT NO.: CTL/P/2266 ! C4.1/10 GLP, unpublished TOX95-00044	Y	ZNC
AIIIA-7.1.1; AIIIA-7.1.2; AIIIA-7.1.4; AIIIA-7.1.5		1987	Acute toxicity tests for SC-0224 4LC-E (Lot # JHC 10190-50-1). T-12589 GLP, unpublished TOX95-00050	Y	ZNC
AIIIA-7.1.6		1987	Dermal sensitization test with SC-0224 4LC-E. T-12588 ! C3.1/14 GLP, unpublished TOX95-00051	Y	ZNC
AIIIA-7.2	Anonym	1999	Operator exposure assessment according to german and UK POEM models. not GLP, unpublished TOX1999-1122	Y	ZNC
AIIIA-7.2	Chester, G., Dick, J., Loftus (CTL), N.J. and Woollen, B.H.	1989	Fluazifop-p-butyl: Dermal exposure of, and absorption by, workers using tractor sprayers in the Netherlands. REPORT SERIES TMF 3487 ! C5.5/06 not GLP, unpublished TOX95-00052	Y	ZNC
AIIIA-7.2	Ward, R.J. and Scott, R.C.	1991	Fluazifop-p-butyl: In vitro absorption from a 125g/l EC formulation trough human epidermis. REPORT NO.: CTL/P/3494 ! C5.2/26 GLP, unpublished TOX95-00053	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-7.3		1995	The dermal absorption of [14C]-anion glyphosate trimesium in rats. 154723 ! 10732 ! CTL/C/2992 GLP, unpublished TOX1999-1120	Y	ZNC
AIIIA-7.3	Ward, R.	1994	ICIA0224: In vitro absorption from a 480g/l SL formulation through human epidermis. REPORT NO.: CTL/P/4345 ! C5.2/01 GLP, unpublished TOX95-00054	Y	ZNC
AIIIA-7.3	Ward, R.J. and Thornton, H.Y.	1995	Glyphosate-trimesium: In vitro absorption from a 480 g/l SL formulation through rat skin. CTL/P/4574 GLP, unpublished TOX1999-1121	Y	ZNC

Codes of owner

ZNC: Zeneca Agro GmbH

B.6 Residues

B.6.13 Estimates of potential and actual dietary exposure through diet and other means

Table B.6.13-1: National estimate of short term intake (NESTI) - adults

Active substance: **Glyphosate-Trimesium**
ARfD (mg/kg bw): **0.25**

Food portion sizes of UK adults aged 16 to 64 years (97.5th percentile)

Food	Portion Size	Unit Weight	Proc. Factor	Variab. Factor	MRL (mg/kg)	Intake (mg/kg) bw	Amount of ARfD (%)
1. FRUITS AND TREE NUTS							
(i) Citrus fruit and citrus juice							
Grapefruit	212.0	160.0	1.0	10.0	0.50	0.01141227	**4.56**
Mandarins	158.0	100.0	1.0	10.0	0.50	0.00713267	**2.85**
Oranges, fruits	262.0	160.0	1.0	10.0	0.50	0.01141227	**4.56**
Oranges, juice	500.0		1.0	1.0	0.50	0.00356633	**1.43**
(v) Berries and small fruit							
a) Table and wine grapes							
Table grapes	190.0		1.0	5.0	0.50	0.00677603	**2.71**

Table B.6.13- 2: National estimate of short term intake (NESTI) - toddlers

Active substance: **Glyphosate-Trimesium**
ARfD (mg/kg bw): **0.25**

Food portion sizes of UK toddlers aged 1.5 to 4.5 years (97.5th percentile)

Food	Portion Size	Unit Weight	Proc. Factor	Variab. Factor	MRL (mg/kg)	Intake (mg/kg) bw	Amount of ARfD (%)
1. FRUITS AND TREE NUTS							
(i) Citrus fruit and citrus juice							
Grapefruit	183.0	160.0	1.0	10.0	0.50	0.05517241	**22.07**
Mandarins	176.0	100.0	1.0	10.0	0.50	0.03448276	**13.79**
Oranges, fruits	181.0	160.0	1.0	10.0	0.50	0.05517241	**22.07**
Oranges, juice	504.0		1.0	1.0	0.50	0.01737931	**6.95**
(v) Berries and small fruit							
a) Table and wine grapes							
Table grapes	158.0		1.0	5.0	0.50	0.02724138	**10.90**

B.8 Ecotoxicology

B.8.9 Effects on other non-target organisms (flora and fauna) believed to be at risk (Annex IIA 8.6)

K. Fletcher and B. Freedman (1995)

In laboratory studies effects of glyphosate on decomposition of several litter substrates were tested. Three substrates were used: foliage of *Acer rubrum*, foliage of *Picea glauca* and forest floor (composed of litter, duff and humus). For testing 6 concentrations (0, 1, 10,100, 1000, 5000 and 10000 ppm) were chosen.
Glyphosat had toxic thresholds at which they reduced decomposition of plant foliage and forest floor substrate but the thresholds were > 50 times higher than residue concentrations that occur in the field after silvicultural herbicide treatment.

H. Eijsackers (1995)

Laboratory tests (effects by direct contact) were carried out with glyphosate (Roundup). Glass dishes, containing a substrate of moist, compaced sandy soil, were sprayed in a Potter tower with 1 % and 4 % (1.49 and 5.96 ml/m²) glyphosate. Observations on numbers of organisms of specific soil fauna species (sprintails, isopoda and carabids) were made daily until the last specimen had died; then, from individual survival periods, mean longevity was calculated.
The data showed a slight but non-significant decrease, with 5.96 ml/m² glyphosate.

Laboratory tests (effects on litter consumption) were carried out. Litter fragmentation have been sampling in the field and offering it in the laboratory to groups of soil organisms.
For field experiments, litter in nylon bags or cloth boxes was buried in the litter.
In both experiments changes in litter fragmentation through spraying of glyphosate were observed but it is difficult to evaluate effects of this herbicide on litter breakdown.

At present, glyphosate does not seem to be very toxic for the soil fauna although adverse effects have been observed in studies with some representatives of the soil fauna (Acarina (Gamasidae) and Isopoda).

Conclusion
In the presented studies glyphosate had no or only slight effects on litter decomposition at concentrations that occur in the environment after treatment. In general glyphosate is not very toxic to soil fauna.
Because of the rapid degradation of glyphosate to metabolite AMPA and the long duration of some presented experience from 5 to18 month (H. Eijsackers (1985) and L. B. Holtby and S.J. Baillie (1989)), these studies also addessed the effects of AMPA on leaf litter decomposition.

B.8.11 List of essential studies (ecotoxicology) for which the main notifiers have claimed data protection

LIST OF STUDIES FOR WHICH THE MAIN SUBMITTER HAS CLAIMED DATA PROTECTION AND WHICH DURING THE RE-EVALUATION PROCESS WERE CONSIDERED AS ESSENTIAL FOR THE EVALUATION WITH A VIEW TO ANNEX I INCLUSION: **GLYPHOSATE-TRIMESIUM**

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.1.1		1982	Acute oral toxicity study with SC-0224 technical in mallard ducks. BLAL 82 DD 13 ! T-11147 ! not GLP, unpublished AVS93-00035	Y	ZNC
AIIA-8.1.1		1988	The acute oral toxicity of ICIA0224 to the bobwhite quail. ISN 177/881062 GLP, unpublished AVS93-00038	Y	ZNC
AIIA-8.1.2		1982	8-day dietary LC50 study with R-50224 technical in bobwhite quail. BLAL 82 QC 16 ! T-11146 not GLP, unpublished AVS93-00037	Y	ZNC
AIIA-8.1.2		1982	8-day dietary LC50 study with R-50224 technical in mallard ducklings. BLAL 82 DC 16 ! T-11145 not GLP, unpublished AVS93-00036	Y	ZNC
AIIA-8.1.3		1990	ICIA0224: A one-generation reproduction study with the mallard (Anas platyrhynchos). 123-151 GLP, unpublished AVS93-00040	Y	ZNC
AIIA-8.1.3		1990	ICIA0224: A one-generation reproduction study with the bobwhite quail (Colinus virginianus). 123-150 GLP, unpublished AVS93-00039	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.2.1		1982	Acute toxicity of R-50224 to Rainbow trout (Salmo gairdneri). #BW-82-4-1153 not GLP, unpublished WAT94-01534	Y	ZNC
AIIA-8.2.1		1988	ICIA0224: Determination of acute toxicity to mirror carp Cyprinus carpio. BL/B/3397 not GLP, unpublished WAT94-01535	Y	ZNC
AIIA-8.2.2	, and	1991	GLYPHOSATE TRIMESIUM: The 21 day LC50 to rainbow trout (Oncorhynchus mykiss). BL4178/B GLP, unpublished WAT94-01537	Y	ZNC
AIIA-8.2.2.2		1988	Early life stage toxicity of SC-0224 technical to Rainbow trout (Salmo gairdneri) in a Flow-Through System. #35819 not GLP, unpublished WAT94-01536	Y	ZNC
AIIA-8.2.4	Anonym	1993	AMPA: Acute toxicity to Daphnia magna. BL5061/B GLP, unpublished WAT94-00500	Y	ZNC
AIIA-8.2.4	Spare, W.C., Gottfried, G.J. and Dillon, F.	1983	The acute toxicity of R-50224 technical to Daphnia magna Strauß. 82-E-11150 GLP, unpublished WAT94-01538	Y	ZNC
AIIA-8.2.5	Forbis, A.D.	1987	Chronic toxicity of 14C-SC-0224 to Daphnia magna under flow- through test conditions. #35820 GLP, unpublished WAT94-01539	Y	ZNC
AIIA-8.2.6	Smyth, D.V. and Tapp, J.F.	1988	ICIA0224: Determination of toxicity to the green alga Selenastrum capricornutum. FT54/88 GLP, unpublished WAT94-01540	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIA-8.2.8	Smyth, D.V., Kent, S.J. and Shillabeer, N.	1997	Glyphosate-Trimesium: Toxicity to duckweed (Lemna gibba). BL5965/B not GLP, unpublished WAT98-00232	Y	ZNC
AIIA-8.3.1	Collins, I.G., Jackson, D. and Brown, R.A.	1988	ICIA0224 Acute Contact and Oral Toxicity to Honey Bees (Apis mellifera) of an SL formulation. RJ0670B GLP, unpublished BIE95-00079	Y	ZNC
AIIA-8.3.2	Canning, L., Lloyd, E.J. and Lewis, G.B.	1992	GLYPHOSAT-TRIMESIUM - Investigation of the Toxicity of a 400 g/l SL Formulation to the Carabid Beetle Pterostichus melanarius and a Lycosid Spider. RJ 1066B GLP, unpublished ANA95-00206	Y	ZNC
AIIA-8.3.2	Turner, C. R.	1995	The effects of Glyphosat-Trimesium on the predatory mite Typhlodromus pyri. REPORT NO: 95.02 GLP, unpublished ANA95-00225	Y	ZNC
AIIA-8.4.1	Coulson, J. M., Dowdeswell, C. S., Yearsdon, H. A. and Edwards, P. J.	1989	ICIAO224: Investigation of the toxicity to the earthworm Eisenia fetida. RJ0709B ! 88JH342 GLP, unpublished ARW95-00014	Y	ZNC
AIIA-8.5	Lewis, F.J., Aze, C.J. and Castle, D.L.	1989	ICIA0224 : Study of Effects on Microbial Activities in soil. RJ 0747B GLP, unpublished BMF95-00003	Y	ZNC
AIIIA-10.2.4	Larkin, J.; Spare, W.C.; Gottfried, G.J. and Dillon, F.	1984	The Acute Toxicity of SC-0224 (20 % a.i.) to the Mayfly (Stenonem pudium). 35290093 not GLP, unpublished WAT98-00438	Y	ZNC

Annex point/ reference number	Author(s)	Year	Title source (where different from company) report no. GLP or GEP status (where relevant), published or not BBA registration number	Data protection claimed Y/N	Owner
AIIIA-10.4.1	Collins, I.G., Jackson, D. and Brown, R.A.	1988	ICIA0224 Acute Contact and Oral Toxicity to Honey Bees (Apis mellifera) of an SL formulation. GLP, unpublished BIE95-00080	Y	ZNC
AIIIA-10.5	Canning, L., Lloyd, E.J. and Lewis, G.B.	1992	GLYPHOSAT-TRIMESIUM - Investigation of the Toxicity of a 400 g/l SL Formulation to the Carabid Beetle Pterostichus melanarius and a Lycosid Spider. RJ 1066B GLP, unpublished ANA95-00207	Y	ZNC

Codes of owner

ZNC: Zeneca Agro GmbH