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EU-Beurteilungsbericht Sulfosulfuron

Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen Band D 40

Review Report Sulfosulfuron
Legal Regulations of the European Union
for Plant Protection Products and their Active Substances
Volume D 40

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Vorwort

Für neue Wirkstoffe werden die EU-Mitgliedstaaten in den Richtlinien zur Aufnahme der Wirkstoffe in Anhang I verpflichtet, den nach Abschluss aller Prüfungen erstellten Beurteilungsbericht (Review Report) mit allen Anlagen (mit Ausnahme von vertraulichen Informationen im Sinne von Artikel 14 der Richtlinie 91/414/EWG) allen Interessierten zur Verfügung zu stellen oder auf besonderen Antrag zugänglich zu machen. Für alte Wirkstoffe ergibt sich diese Verpflichtung für die Mitgliedstaaten bereits aus Artikel 7 Absatz 6 Unterabsatz 2 der Verordnung (EWG) Nr. 3600/92.

Die Mitgliedstaaten und die Europäische Kommission haben vereinbart, dass die Beurteilungsberichte, einschließlich der zum Teil sehr umfangreichen Hintergrunddokumente, vorzugsweise beim berichterstattenden Mitgliedstaat angefordert oder eingesehen werden sollen.

Die Biologische Bundesanstalt stellt die Beurteilungsberichte als Berichte aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft als Band D in der Reihe "Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen" über den Saphir Verlag gegen Erstattung der Unkosten zur Verfügung. Das vorliegende 40. Heft dieser Reihe (Band D 40) enthält nicht die Hintergrunddokumente A, B und C des Beurteilungsberichtes. Diese können bei Bedarf bei der BBA eingesehen oder für die Wirkstoffe, für die Deutschland Berichterstatter ist, ebenfalls beim Saphir Verlag gegen Erstattung der Unkosten bezogen werden. Für Sulfosulfuron war Irland Berichterstatter.

In der Reihe "Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen" sind bisher erschienen:

Heft	**Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen**
35/97	Band A: Richtlinie 91/414/EWG und diesbezügliche Protokolle (3. Auflage, Stand: 01. November 1997) *wird zur Zeit bearbeitet*
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	Band C: *wird zur Zeit bearbeitet*

Preface

According to the Directives for the inclusion of active substances in Annex I with regard to new active substances, EU-Member States are obliged to keep available or make available on special request the review report which is prepared after completion of all evaluations including its appendices (excluding confidential information, in accordance with article 14 of Directive 91/414/EEC) to all interested parties. For existing active substance this obligation for Member States already arises from article 7 (6) subparagraph 2 of Regulation (EEC) No 3600/92.

Member States and the European Commission agreed that requests of review reports including their background documents which are partly very voluminous, shall preferably be addressed to the Rapporteur Member State.

The Federal Biological Research Centre makes available review reports as reports from the Federal Biological Research Centre for Agriculture and Forestry, Volume D of the series "Legal Regulations of the European Union for Plant Protection Products and their Active Substances" via Saphir Verlag against reimbursement of expenses. The present 40th report belonging to this series (Volume D 40) does not include background documents A, B and C of the review report. If the need arises, their inspection at the BBA is possible or they may be also obtained from Saphir Verlag against reimbursement of expenses, however, only for active substances with Germany as Rapporteur Member State. For sulfosulfuron Ireland acted as Rapporteur Member State.

In the series Legal Regulations of the European Union for Plant Protection Products and their Active Substances the following Reports have been published:

Report	**Legal Regulations of the European Union for Plant Protection Products and their Active Substances**
35/97	Volume A: Directive 91/414/EEC and respective Protocols (3rd Edition, date: 1 November 1997) *in progress*
68/2000	Volume B: Regulations and Protocols regarding the Evaluation of Active Substances (4th Edition, date: 1 July 2000) *in progress*
	Volume C: *in progress*

RICHTLINIE 2002/48/EG DER KOMMISSION

vom 30. Mai 2002

zur Änderung der Richtlinie 91/414/EWG des Rates und zur Aufnahme der Wirkstoffe Iprovalicarb, Prosulfuron und Sulfosulfuron

DIE KOMMISSION DER EUROPÄISCHEN GEMEINSCHAFTEN —

gestützt auf den Vertrag zur Gründung der Europäischen Gemeinschaft,

gestützt auf die Richtlinie 91/414/EWG des Rates vom 15. Juli 1991 über das Inverkehrbringen von Pflanzenschutzmitteln [1], zuletzt geändert durch die Richtlinie 2002/37/EG der Kommission [2], insbesondere auf Artikel 6 Absatz 1,

in Erwägung nachstehender Gründe:

(1) Die Behörden Irlands haben am 30. März 1998 gemäß Artikel 6 Absatz 2 der Richtlinie 91/414/EWG von der Bayer AG einen Antrag auf Aufnahme des Wirkstoffs Iprovalicarb in Anhang I der Richtlinie erhalten. Mit der Entscheidung 98/512/EG der Kommission [3] wurde bestätigt, dass die Unterlagen „vollständig" sind und somit grundsätzlich die Anforderungen der Anhänge II und III der Richtlinie 91/414/EWG hinsichtlich der Daten und Informationen erfüllen.

(2) Die Behörden Frankreichs haben am 14. Mai 1995 von Novartis — jetzt Syngenta — einen ähnlichen Antrag für Prosulfuron erhalten. Dieser Antrag wurde mit der Entscheidung 97/137/EG der Kommission [4] für vollständig erklärt.

(3) Die Behörden Irlands haben am 24. April 1997 von Monsanto einen ähnlichen Antrag für Sulfosulfuron erhalten. Dieser Antrag wurde mit der Entscheidung 97/865/EG der Kommission [5] für vollständig erklärt.

(4) Die Auswirkungen dieser drei Wirkstoffe auf die menschliche Gesundheit und auf die Umwelt wurden gemäß Artikel 6 Absätze 2 und 4 der Richtlinie 91/414/EWG für die von dem jeweiligen Antragsteller vorgeschlagenen Anwendungen geprüft. Die benannten Bericht erstattenden Mitgliedstaaten haben der Kommission jeweils am 4. November 1999 (Iprovalicarb), 18. Januar 1999 (Prosulfuron) und am 2. April 1998 (Sulfosulfuron) einen Entwurf des Bewertungsberichts über die Wirkstoffe übermittelt.

(5) Die Entwürfe der Bewertungsberichte wurden von den Mitgliedstaaten und der Kommission im Rahmen des Ständigen Ausschusses für die Lebensmittelkette und Tiergesundheit geprüft. Diese Prüfungen wurden am 26. Februar 2002 in Form der Beurteilungsberichte der Kommission für Iprovalicarb, Prosulfuron und Sulfosulfuron abgeschlossen.

(6) Die Unterlagen und die aus den Prüfungen hervorgegangenen Informationen wurden dem Wissenschaftlichen Ausschuss Pflanzen vorgelegt. In Bezug auf Iprovalicarb wurde der Ausschuss gebeten, das Risiko des Metaboliten PMPA für Regenwürmer und die mögliche Bedeutung für den Menschen von Tumoren bei Ratten nach lebenslänglicher Exposition bei hohen Dosen zu kommentieren. In zwei Stellungnahmen [6] [7] verwies der Ausschuss auf die Notwendigkeit weiterer Daten über Regenwürmer, die bereitgestellt und bewertet wurden. Der Ausschuss kam zu dem Schluss, das hinsichtlich der Wirkungen bei Ratten ausreichende Sicherheitsmargen bestehen, um den Schutz von Verbrauchern und Anwendern zu gewährleisten. Die Anmerkungen des Wissenschaftlichen Ausschusses wurden bei der Erstellung dieser Richtlinie und des betreffenden Beurteilungsberichts berücksichtigt.

(7) In Bezug auf Prosulfuron wurde der Ausschuss gebeten, zu dem Risiko von zwei Abbauprodukten des Wirkstoffes für Sedimentlebewesen und zu bei Versuchstieren festgestellten möglichen hormonstörenden Wirkungen Stellung zu nehmen. In seiner Stellungnahme [8] ist der Ausschuss zu dem Schluss gekommen, dass bestimmte uterine und mamilläre Veränderungen, die bei Ratten nach lebenslanger Exposition festgestellt wurden, für die Risikobewertung von Prosulfuron für den Menschen im Rahmen der vorgesehenen Anwendungen des Wirkstoffs nicht relevant sind. Darüber hinaus wies der Ausschuss darauf hin, dass die Risiken der beiden Abbauprodukte für Sedimentlebewesen noch nicht ausreichend bewertet worden sind und bei Sediment-Wasser-Versuchen beträchtliche Mengen anderer persistenter Metaboliten gebildet werden, die anscheinend auch noch nicht bewertet worden sind. Die ausstehenden Informationen und Bewertungen wurden daraufhin übermittelt und die Anmerkungen des Wissenschaftlichen Ausschusses bei der Erstellung der Richtlinie und des entsprechenden Beurteilungsberichts berücksichtigt.

[1] ABl. L 230 vom 19.8.1991, S. 1.
[2] ABl. L 117 vom 4.5.2002, S. 10.
[3] ABl. L 228 vom 15.8.1998, S. 35.
[4] ABl. L 52 vom 22.2.1997, S. 20.
[5] ABl. L 351 vom 23.12.1997, S. 67.

[6] Stellungnahme des Wissenschaftlichen Ausschusses Pflanzen hinsichtlich der Bewertung von Iprovalicarb im Zusammenhang mit der Richtlinie 91/414/EWG über das Inverkehrbringen von Pflanzenschutzmitteln (verabschiedet am 21. März 2001).
[7] Stellungnahme des Wissenschaftlichen Ausschusses Pflanzen zu einer zusätzlichen Frage der Kommission über die Bewertung von Iprovalicarb (SZX 0722) im Zusammenhang mit der Richtlinie 91/414/EWG (verabschiedet am 28. November 2001).
[8] Stellungnahme des Wissenschaftlichen Ausschusses Pflanzen hinsichtlich der Aufnahme von Prosulfuron (CGA 152005) in Anhang I der Richtlinie 91/414/EWG über das Inverkehrbringen von Pflanzenschutzmitteln (SCP/PROSULF/002-endg. vom 21. Juni 2001).

(8) In Bezug auf Sulfosulfuron wurde der Ausschuss um eine Stellungnahme zu dem Auftreten von Blasentumoren bei der 18-monatigen Studie an Mäusen und zu der Möglichkeit der Festlegung einer akuten Referenzdosis für Sulfosulfuron sowie um Bestätigung gebeten, dass eine subletale Studie an Regenwürmern auch bei Persistenz der Bodenmetaboliten unnötig ist. In seiner Stellungnahme [1] vertrat der Ausschuss die Auffassung, dass die bei Mäusen festgestellten krankhaften Veränderungen nicht auf ein Krebsrisiko beim Menschen hindeuten und hielt es nicht für notwendig, eine akute Referenzdosis festzulegen. Darüber hinaus kam er zu dem Schluss, dass keine langfristigen erheblichen Risiken für Regenwürmer zu erwarten sind. Der Ausschuss hob die Notwendigkeit hervor, die möglichen Umweltauswirkungen von drei nicht identifizierten Metaboliten zu untersuchen. Diese Informationen wurden anschließend bereitgestellt und die geforderten Bewertungen durchgeführt.

(9) Die Untersuchungen haben ergeben, dass davon ausgegangen werden kann, dass die betreffenden Wirkstoffe enthaltende Pflanzenschutzmittel im Allgemeinen die Anforderungen gemäß Artikel 5 Absatz 1 Buchstaben a) und b) und Absatz 3 der Richtlinie 91/414/EWG erfüllen, insbesondere hinsichtlich der geprüften und in den Beurteilungsberichten der Kommission behandelten Anwendungen. Daher sollten die betreffenden Wirkstoffe in Anhang I aufgenommen werden, damit Pflanzenschutzmittel mit den betreffenden Wirkstoffen in allen Mitgliedstaaten gemäß den Bestimmungen der Richtlinie zugelassen werden können.

(10) Der Beurteilungsbericht ist erforderlich für die ordnungsgemäße Umsetzung bestimmter Abschnitte der in der Richtlinie 91/414/EWG festgelegten einheitlichen Grundsätze durch die Mitgliedstaaten. Es ist daher vorzuschreiben, dass die Mitgliedstaaten den endgültigen Beurteilungsbericht (mit Ausnahme von vertraulichen Informationen) allen Interessierten zur Einsicht zur Verfügung stellen oder zugänglich machen.

(11) Nach der Aufnahme ist den Mitgliedstaaten eine angemessene Frist einzuräumen, um die Bestimmungen der Richtlinie 91/414/EWG über Pflanzenschutzmittel, die Iprovalicarb, Prosulfuron oder Sulfosulfuron enthalten, umzusetzen und insbesondere bereits bestehende vorläufige Zulassungen zu überprüfen und spätestens mit Ablauf der Frist diese Zulassungen in endgültige Zulassungen umzuwandeln, sie zu ändern oder sie gemäß der Richtlinie 91/414/EWG zu widerrufen.

(12) Die Richtlinie 91/414/EWG ist daher entsprechend zu ändern

(13) Die in dieser Richtlinie vorgesehenen Maßnahmen entsprechen der Stellungnahme des Ständigen Ausschusses für die Lebensmittelkette und Tiergesundheit —

[1] Stellungnahme des Wissenschaftlichen Ausschusses Pflanzen hinsichtlich der Bewertung von MON 37500 (Sulfosulfuron) im Zusammenhang mit der Richtlinie 91/414/EWG über das Inverkehrbringen von Pflanzenschutzmitteln. (SCP/SULFO/002-endg. vom 11. Dezember 2000).

HAT FOLGENDE RICHTLINIE ERLASSEN:

Artikel 1

Anhang I der Richtlinie 91/414/EWG wird gemäß dem Anhang der vorliegenden Richtlinie geändert.

Artikel 2

Die Mitgliedstaaten stellen die Beurteilungsberichte für Iprovalicarb, Prosulfuron und Sulfosulfuron (mit Ausnahme von vertraulichen Informationen im Sinne des Artikels 14 der Richtlinie) allen Interessierten zur Einsicht zur Verfügung oder machen diese gegebenenfalls auf besonderen Antrag zugänglich.

Artikel 3

Die Mitgliedstaaten erlassen und veröffentlichen bis spätestens 31. Dezember 2002 die erforderlichen Rechts- und Verwaltungsvorschriften, um dieser Richtlinie nachzukommen. Sie unterrichten die Kommission unverzüglich davon.

Sie wenden diese Vorschriften ab 1. Januar 2003 an.

Bei Erlass dieser Vorschriften nehmen die Mitgliedstaaten in den Vorschriften selbst oder durch einen Hinweis bei der amtlichen Veröffentlichung auf diese Richtlinie Bezug. Die Mitgliedstaaten regeln die Einzelheiten dieser Bezugnahme.

Artikel 4

(1) Die Mitgliedstaaten müssen die Zulassung für jedes Pflanzenschutzmittel, welches Iprovalicarb, Prosulfuron oder Sulfosulfuron enthält, überprüfen, um sicherzustellen, dass die Bedingungen, die in Anhang I der Richtlinie 91/414/EWG für diese Wirkstoffe festgelegt sind, erfüllt werden. Falls erforderlich, müssen sie die Zulassung gemäß der Richtlinie vor dem 31. Dezember 2002 ändern oder widerrufen.

(2) Die Mitgliedstaaten müssen bei jedem Pflanzenschutzmittel, das Iprovalicarb, Prosulfuron oder Sulfosulfuron als einzigen oder als einen von mehreren in Anhang I der Richtlinie 91/414/EWG vom 1. Juli 2002 aufgeführten Wirkstoffen enthält, in Übereinstimmung mit den allgemeinen Grundsätzen in Anhang VI der Richtlinie 91/414/EWG aufgrund von Unterlagen, welche die entsprechenden Erfordernisse in Anhang III erfüllen, das Mittel neu bewerten. Von dieser Bewertung ausgehend, müssen sie entscheiden, ob das Mittel die in Artikel 4 Abatz 1 Buchstaben b), c), d) und e) der Richtlinie 91/414/EWG festgelegten Bedingungen erfüllt. Falls erforderlich, und spätestens bis zum 31. Dezember 2003, sollten sie die Zulassungen für jedes dieser Pflanzenschutzmittel ändern oder widerrufen.

Artikel 5

Diese Richtlinie tritt am 1. Juli 2002 in Kraft.

Artikel 6

Diese Richtlinie ist an alle Mitgliedstaaten gerichtet.

Brüssel, den 30. Mai 2002

Für die Kommission
David BYRNE
Mitglied der Kommission

ANHANG

In Anhang I werden der Tabelle folgende Einträge angefügt:

Nr.	Gebräuchliche Bezeichnung, Kennnummern	IUPAC-Bezeichnung	Reinheit (1)	Inkrafttreten	Aufnahme befristet bis	Besondere Bedingungen
„30	Iprovalicarb CAS-Nr. 140923-17-7 CICAP-Nr. 620	(2-Methyl-1-[1-(4-methylphenyl)ethylcarbonyl]-propyl)-Carbamidsäureisopropylester	950 g/kg (vorläufige Angabe)	1. Juli 2002	30. Juni 2011	Nur Anwendungen als Fungizid dürfen zugelassen werden. Bei der Anwendung der einheitlichen Grundsätze gemäß Anhang VI sind die Schlussfolgerungen des vom Ständigen Ausschuss für die Lebensmittelkette und Tiergesundheit am 26. Februar 2002 abgeschlossenen Prüfungsberichts über Iprovalicarb und insbesondere dessen Anlagen I und II zu berücksichtigen. Bei dieser Gesamtbewertung — muss die Spezifikation des technischen Materials als gewerbsmäßig hergestellt bestätigt und durch geeignete analytische Daten untermauert werden. Das für das Toxizitätsdossier verwendete Versurchsmaterial sollte mit dieser Spezifikation des technischen Materials verglichen und überprüft werden; — müssen die Mitgliedstaaten dem Schutz der Anwender besondere Aufmerksamkeit widmen.
31	Prosulfuron CAS-Nr. 94125-34-5 CIPAC-Nr. 579	1-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]-urea	950 g/kg	1. Juli 2002	30. Juni 2011	Nur Anwendungen als Herbizid dürfen zugelassen werden. Bei der Anwendung der einheitlichen Grundsätze gemäß Anhang VI sind die Schlussfolgerungen des vom Ständigen Ausschuss für die Lebensmittelkette und Tiergesundheit am 26. Februar 2002 abgeschlossenen Prüfungsberichts über Prosulfuron und insbesondere dessen Anlagen I und II zu berücksichtigen. Bei dieser Gesamtbewertung müssen die Mitgliedstaaten — das Risiko für Wasserpflanzen sorgfältig prüfen, wenn der Wirkstoff neben Oberflächengewässern ausgebracht wird. Gegebenfalls sollten Maßnahmen zur Risikobegrenzung getroffen werden; — dem Grundwasserschutz besondere Aufmerksamkeit widmen, wenn der Wirkstoff in Regionen mit empfindlichen Böden und/oder Klimabedingungen ausgebracht wird, und gegebenenfalls Maßnahmen zur Risikobegrenzung ergreifen.

Nr.	Gebräuchliche Bezeichnung, Kennnummern	IUPAC-Bezeichnung	Reinheit (1)	Inkrafttreten	Aufnahme befristet bis	Besondere Bedingungen
32	Sulfosulfuron CAS-Nr. 141776-32-1 CICAP-Nr. 601	1-(4,6-dimethoxypyrimidin-2-yl)-3-[(2-ethan-sulfonyl-imidazo[1,2-*a*]pyridine)sulfonyl]urea	980 g/kg	1. Juli 2002	30. Juni 2011	Nur Anwendungen als Herbizid dürfen zugelassen werden. Bei der Anwendung der einheitlichen Grundsätze gemäß Anhang VI sind die Schlussfolgerungen des vom Ständigen Ausschuss für die Lebensmittelkette und Tiergesundheit am 26. Februar 2002 abgeschlossenen Prüfungsberichts über Sulfosulforon und insbesondere dessen Anlagen I und II zu berücksichtigen. Bei dieser Gesamtbewertung müssen die Mitgliedstaaten — dem Schutz von Wasserpflanzen und Algen besondere Aufmerksamkeit widmen und gegebenenfalls Maßnahmen zur Risikobegrenzung ergreifen; — dem Grundwasserschutz besondere Aufmerksamkeit widmen, wenn der Wirkstoff in Regionen mit empfindlichen Böden und/oder Klimabedingungen ausgebracht wird.

(1) Weitere Einzelheiten hinsichtlich der Identität und Spezifikation des Wirkstoffs sind dem Beurteilungsbericht zu entnehmen."

COMMISSION DIRECTIVE 2002/48/EC

of 30 May 2002

amending Council Directive 91/414/EEC to include iprovalicarb, prosulfuron and sulfosulfuron as active substances

THE COMMISSION OF THE EUROPEAN COMMUNITIES,

Having regard to the Treaty establishing the European Community,

Having regard to Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market [1], as last amended by Commission Directive 2002/37/EC [2], and in particular Article 6(1) thereof,

Whereas:

(1) In accordance with Article 6(2) of Directive 91/414/EEC, Ireland received on 30 March 1998 an application from Bayer AG for the inclusion of the active substance iprovalicarb in Annex I to the Directive. By Commission Decision 98/512/EC [3] it was confirmed that the dossier was 'complete' in the sense that it could be considered as satisfying, in principle, the data and information requirements laid down in Annexes II and III to Directive 91/414/EEC.

(2) France received a similar application on 14 May 1995 from Novartis, now Syngenta, concerning prosulfuron. This application was declared complete by Commission Decision 97/137/EC [4].

(3) Ireland received a similar application on 24 April 1997 from Monsanto concerning sulfosulfuron. This application was declared complete by Commission Decision 97/865/EC [5].

(4) For these three active substances, the effects on human health and the environment have been assessed, in accordance with Article 6(2) and (4) of Directive 91/414/EEC, for the uses proposed by the applicant. The nominated rapporteur Member States submitted draft assessment reports concerning the substances to the Commission on 4 November 1999 (iprovalicarb), 18 January 1999 (prosulfuron), and 2 April 1998 (sulfosulfuron), respectively.

(5) The draft assessment reports have been reviewed by the Member States and the Commission within the Standing Committee on the Food Chain and Animal Health. The reviews were finalised on 26 February 2002 in the format of the Commission review reports for iprovalicarb, prosulfuron and sulfosulfuron.

(6) The dossier and the information from each of the reviews were submitted to the Scientific Committee for Plants. As regards iprovalicarb, the Committee was asked to comment on the acceptability of the risk of metabolite PMPA on earthworms and on the relevance to humans of tumours which were observed in rats after lifetime exposure to high doses. In two opinions [6] [7], the Committee identified the need for further data on earthworms, which were subsequently provided and assessed, and concluded that concerning the effects observed in rats sufficient safety margins exist to ensure protection of consumers and operators. The observations of the Scientific Committee were taken into consideration in formulating this Directive and the relevant review report.

(7) With respect to prosulfuron, the Committee was asked to comment on the acceptability of the risk of two breakdown products of the active substance to sediment dwelling organisms and on possible hormonal disruption effects observed in test animals. In its opinion [8] the Committee concluded that certain uterine and mammary changes, which were observed in rats after lifetime exposure are not considered relevant for human risk assessment of prosulfuron in the context of its intended uses. The Committee further commented that risks of the two breakdown products to sediment-dwelling species were not yet adequately assessed and noted that other persistent metabolites are formed in significant quantities in sediment-water tests which also did not appear to have been assessed. The pending information and assessments were subsequently provided and the observations of the Scientific Committee were taken into consideration in formulating this Directive and the relevant review report.

[1] OJ L 230, 19.8.1991, p. 1.
[2] OJ L 117, 4.5.2002, p. 10.
[3] OJ L 228, 15.8.1998, p. 35.
[4] OJ L 52, 22.2.1997, p. 20.
[5] OJ L 351, 23.12.1997, p. 67.

[6] Opinion of the Scientific Committee on Plants on the evaluation of iprovalicarb in the context of Directive 91/414/EEC concerning the placing of plant protection products on the market (adopted 21 March 2001).
[7] Opinion of the Scientific Committee on Plants on an additional question from the Commission on the evaluation of iprovalicarb (SZX 0722) in the context of Directive 91/414/EEC (adopted 28 November 2001).
[8] Opinion of the Scientific Committee on Plants regarding the inclusion of prosulfuron (CGA 152005) in Annex I to Directive 91/414/EEC concerning the placing of plant protection products on the market SCP/PROSULF/002-Final 21 June 2001.

(8) With respect to sulfosulfuron the Committee was asked for its opinion on the occurrence of bladder tumours in the 18 months mouse study; to consider whether it would be appropriate to establish an acute reference dose for sulfosulfuron; to confirm that a sub-lethal study for earthworms is unnecessary, notwithstanding the persistence of the soil metabolites. In its opinion [1] the Committee considered that the lesions observed in mice do not predict a carcinogenic hazard to humans and saw no need to establish an acute reference dose. It was further concluded that no significant long term risks to earthworms are likely to arise. The Committee further highlighted the need to assess the potential environmental impact of three unidentified metabolites. This information was subsequently provided and the requested assessments were made.

(9) It has appeared from the various examinations made that plant protection products containing the active substances concerned may be expected to satisfy, in general, the requirements laid down in Article 5(1)(a) and (b) and Article 5(3) of Directive 91/414/EEC, in particular with regard to the uses which were examined and detailed in the Commission review reports. It is therefore appropriate to include these active substances in Annex I, in order to ensure that in all Member States the authorisations of plant protection products containing the active substances concerned, can be granted in accordance with the provisions of the said Directive.

(10) The Commission review report is required for the proper implementation by the Member States, of several sections of the uniform principles laid down in Directive 91/414/EEC. It is, therefore, appropriate to provide that the finalised review reports, except for confidential information, should be kept available or made available by the Member States for consultation by any interested parties.

(11) After inclusion, Member States should be allowed a reasonable period to implement the provisions of Directive 91/414/EEC as regards plant protection products containing iprovalicarb, prosulfuron or sulfosulfuron and in particular to review existing provisional authorisations and, by the end of this period at the latest, to transform those authorisations into full authorisations, to amend them or to withdraw them in accordance with the provisions of Directive 91/414/EEC.

(12) It is therefore appropriate to amend Directive 91/414/EEC accordingly.

(13) The measures provided for in this Directive are in accordance with the opinion of the Standing Committee on the Food Chain and Animal Health,

[1] Opinion of the Scientific Committee on Plants regarding the evaluation of MON 37500 (sulfosulfuron) in the context of Directive 91/414/EEC concerning the placing of plant protection products on the market (SCP/SULFO/002-final dated 11 December 2000).

HAS ADOPTED THIS DIRECTIVE:

Article 1

Annex I to Directive 91/414/EEC is amended as set out in the Annex to this Directive.

Article 2

Member States shall keep available the review reports for iprovalicarb, prosulfuron, and sulfosulfuron, except for confidential information within the meaning of Article 14 of Directive 91/414/EEC, for consultation by any interested parties or shall make it available to them on specific request.

Article 3

Member States shall adopt and publish by 31 December 2002 at the latest the laws, regulations and administrative provisions necessary to comply with this Directive. They shall forthwith inform the Commission thereof.

They shall apply those provisions from 1 January 2003.

When Member States adopt those provisions, they shall contain a reference to this Directive or shall be accompanied by such a reference on the occasion of their official publication. Member States shall determine how such reference is to be made.

Article 4

1. Member States shall review the authorisation for each plant protection product containing iprovalicarb, prosulfuron, or sulfosulfuron, to ensure that the conditions relating to these active substances set out in Annex I to Directive 91/414/EEC are complied with. Where necessary, they shall amend or withdraw the authorisation in accordance with Directive 91/414/EEC before 31 December 2002.

2. Member States shall, for each authorised plant protection product containing iprovalicarb, prosulfuron, or sulfosulfuron, as either the only active substance or as one of several active substances, all of which were listed in Annex I to Directive 91/414/EEC by 1 July 2002, re-evaluate the product in accordance with the uniform principles provided for in Annex VI to Directive 91/414/EEC, on the basis of a dossier satisfying the requirements of Annex III thereto. On the basis of that evaluation, they shall determine whether the product satisfies the conditions set out in Article 4(1)(b), (c), (d) and (e) of Directive 91/414/EEC. Where necessary and by 31 December 2003 at the latest, they shall amend or withdraw the authorisation for each such plant protection product.

Article 5

This Directive shall enter into force on 1 July 2002.

Article 6

This Directive is addressed to the Member States.

Done at Brussels, 30 May 2002.

For the Commission
David BYRNE
Member of the Commission

ANNEX

In Annex I the following rows are added to the end of the Table:

No	Common name, identification numbers	IUPAC Name	Purity (1)	Entry into force	Expiration of inclusion	Specific provisions
'30	Iprovalicarb CAS No 140923-17-7 CICAP No 620	{2-Methyl-1-[1-(4-methylphenyl)ethylcarbonyl] propyl}-carbamic acid isopropylester	950 g/kg (provisional specification)	1 July 2002	30 June 2011	Only uses as fungicide may be authorised. For the implementation of the uniform principles of Annex VI, the conclusions of the review report on iprovalicarb, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 26 February 2002 shall be taken into account. In this overall assessment: — the specification of the technical material as commercially manufactured must be confirmed and supported by apporpriate analytical data. The test material used in the toxicity dossier should be compared and verified against this specification of the technical material, — Member States must pay particular attention to the protection of operators.
31	Prosulfuron CAS No 94125-34-5 CICAP No 579	1-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-3-[2-(3,3,3-trifluoropropyl)-phenylsulfonyl]-urea	950 g/kg	1 Juli 2002	30 June 2011	Only uses as herbicide may be authorised. For the implementation of the uniform principles of Annex VI, the conclusions of the review report on prosulfuron, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 26 February 2002 shall be taken into account. In this overall assessment Member States: — must carefully consider the risk to aquatic plants if the active substance is applied adjacent to surface waters. Risk mitigation measures should be applied where appropriate, — must pay particular attention to the protection of groundwater, when the active substance is applied in regions with vulnerable soil and/or climate conditions. Risk mitigation measures should be applied where appropriate.

No	Common name, identification numbers	IUPAC Name	Purity (1)	Entry into force	Expiration of inclusion	Specific provisions
32	Sulfosulfuron CAS No 141776-32-1 CICAP No 601	1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-ethanesulfonyl-imidazo[1,2-*a*]pyridine) sulfonyl]urea	980 g/kg	1 July 2002	30 June 2011	Only uses as a herbicide may be authorised. For the implementation of the uniform principles of Annex VI, the conclusions of the review report on sulforsulfuron, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 26 February 2002 shall be taken into account. In this overall assessment: — Member States must pay particular attention to the protection of aquatic plants and algae. Where apporpriate, risk mitigation measures should be applied, — Member States must pay particular attention to the protection of the groundwater, when the active substance is applied in regions with vulnerable soil and/or climatic conditons.

(1) Further details on identity and specification of active substances are provided in the review report.'

EUROPEAN COMMISSION
DIRECTORATE-GENERAL HEALTH & CONSUMER PROTECTION

Directorate E - Public, animal and plant health
Unit E1 Legislation relating to crop products and animal nutrition

Sulfosulfuron

7459/VI/98-FINAL

2 July 2002

COMMISSION WORKING DOCUMENT - DOES NOT NECESSARILY REPRESENT THE VIEWS OF THE COMMISSION SERVICES

Review report for the active substance sulfosulfuron

Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 26 February 2002 in view of the inclusion of sulfosulfuron in Annex I of Directive 91/414/EEC.

1. Procedure followed for the evaluation process

This review report has been established as a result of the evaluation of the new active substance sulfosulfuron, made in the context of the work provided for in Articles 5 and 6 of Directive 91/414/EEC concerning the placing of plant protection products on the market, with a view to the possible inclusion of this substance in Annex I to the Directive.

In accordance with the provisions of Article 6(2) of Directive 91/414/EEC, the Irish authorities received on 24 April 1997 an application from Monsanto, hereafter referred to as the applicant, for the inclusion of the active substance sulfosulfuron in Annex I to the Directive. Irish authorities indicated to the Commission on 3 July 1997 the results of a first examination of the completeness of the dossier, with regard to the data and information requirements provided for in Annex II and, for at least one plant protection product containing the active substance concerned, in Annex III to the Directive. Subsequently, and in accordance with the requirements of Article 6(2), a dossier on sulfosulfuron was distributed to the Member States and the Commission.

The Commission referred the dossier to the Standing Committee on Plant Health in the meeting of the working group 'legislation' thereof on 11 July 1997 during which the Member States confirmed the receipt of the dossier.

In accordance with the provisions of Article 6(3), which requires the confirmation at Community level that the dossier is to be considered as satisfying, in principle, the data and information requirements provided for in Annex II and, for at least one plant protection product containing the active substance concerned, in Annex III to the Directive and in accordance with the procedure laid down in Article 20 of the Directive, the Commission confirmed in its Decision 97/865[1] of 17 October 1997 that these requirements were satisfied.

[1] OJ No L351, 23.12.1997, p.67.

Within the framework of that decision and with a view to the further organisation of the works related to the detailed examination of the dossier provided for in Article 6(2) and (4) of Directive 91/414/EEC, it was agreed between the Member States and the Commission that Ireland would, as rapporteur Member State, carry out the detailed examination of the dossier and report the conclusions of its examination accompanied by any recommendations on the inclusion or non-inclusion and any conditions relating thereto, to the Commission as soon as possible and at the latest within a period of one year.

Ireland submitted to the Commission on 2 April 1998 the report of its detailed scientific examination, hereafter referred to as the draft assessment report, including, as required, a recommendation concerning the possible inclusion of sulfosulfuron in Annex I to the Directive.

On receipt of the draft assessment report, the Commission forwarded it for consultation to all the Member States on 14 April 1998 as well as to Monsanto being the sole applicant on 23 April 1998.

The Commission organised further an intensive consultation of specialised scientific experts from a representative number of Member States, to review the draft assessment report and the comments received thereon (peer review), in particular on each of the following disciplines :

- identity and physical /chemical properties ;
- fate and behaviour in the environment ;
- ecotoxicology ;
- mammalian toxicology ;
- residues and analytical methods ;
- regulatory questions.

The meetings for this consultation were organised on behalf of the Commission by the Pesticide Safety Directorate (PSD) in York, United Kingdom, from September 1998 to January 1999.

The report of the peer review (i.e. full report) was circulated, for further consultation, to Member States and the sole applicant on 10 March 1999.

The dossier, draft assessment report including an addendum and the peer review report (i.e. full report) including in particular an outline of the remaining technical questions, were referred to the Standing Committee on Plant Health, and specialised working groups of this Committee, for final examination, with participation of experts from the 15 Member States. This final examination took place from September 1999 to February 2002, and was finalised in the meeting of the Standing Committee on the Food Chain and Animal Health on 26 February 2002.

The present review report contains the conclusions of this final examination; given the importance of the draft assessment report, the peer review report (i.e. full report), the comments and clarifications submitted after the peer review and the Addendum to Annex B (dated March 2000) as basic information for the final examination process, these documents are considered respectively as background documents A, B and C to this review report and are part of it.

These documents were also submitted to the Scientific Committee on Plants. The Committee was asked for its opinion on the occurrence of bladder tumours in the 18 months mouse study; to consider whether it would be appropriate to establish an acute reference dose for

sulfosulfuron; to confirm that a sub-lethal study for earthworms is unnecessary, notwithstanding the persistence of the soil metabolites. In its opinion[2] the Committee considered that the lesions observed in mice do not predict a carcinogenic hazard to humans and saw no need to establish an acute reference dose. It was further concluded that no significant long term risks to earthworms are likely to arise. The Committee further highlighted the need to assess the potential environmental impact of three unidentified metabolites. This information was subsequently provided and the requested assessments were made.

2. Purposes of this review report

This review report, including the background documents and appendices thereto, have been developed and finalised in support of the Directive 2002/48/EC concerning the inclusion of sulfosulfuron in Annex I to Directive 91/414/EEC[3], and to assist the Member States in decisions on individual plant protection products containing Sulfosulfuron they have to take in accordance with the provisions of that Directive, and in particular the provisions of article 4(1) and the uniform principles laid down in Annex VI.

This review report provides also for the evaluation required under Section A.2.(b) of the above mentioned uniform principles, as well as under several specific sections of part B of these principles. In these sections it is provided that Member States, in evaluating applications and granting authorisations, shall take into account the information concerning the active substance in Annex II of the directive, submitted for the purpose of inclusion of the active substance in Annex I, as well as the result of the evaluation of those data.

In parallel with the provisions of Article 7(6) of Regulation 3600/92 for existing active substances, the Commission and the Member States will keep available or make available this review report for consultation by any interested parties or will make it available to them on their specific request. Moreover the Commission will send a copy of this review report (not including the background documents) to the applicant.

The information in this review report is, at least partly, based on information, which is confidential and/or protected under the provisions of Directive 91/414/EEC. It is therefore recommended that this review report would not be accepted to support any registration outside the context of Directive 91/414/EEC, e.g. in third countries, for which the applicant has not demonstrated possession of regulatory access to the information on which this review report is based.

3. Overall conclusion in the context of Directive 91/414/EEC

The overall conclusion from the evaluation is that it may be expected that plant protection products containing Sulfosulfuron will fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC. This conclusion is however subject to compliance with the particular requirements in sections 4, 5, 6 and 7 of this report, as well as to the implementation of the provisions of Article 4(1) and the uniform principles laid down in Annex VI of Directive

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[2] Opinion of the Scientific Committee on Plants regarding the evaluation of MON 37500 (sulfosulfuron) in the context of Council Directive 91/414/EEC concerning the placing of plant protection products on the market. SCP/SULFO/002-final dated 11 December 2000.

[3] OJ L148, 06.06.2002, p.19

91/414/EEC, for each Sulfosulfuron containing plant protection product for which Member States will grant or review the authorisation.

Furthermore, these conclusions were reached within the framework of the following uses which were proposed and supported by the sole submitter:

- herbicide for use in springtime against couch grass, *Bromus spp.* and certain broad-leaved weeds in winter wheat.

Broadening the use pattern beyond those described above will require an evaluation at Member State level in order to establish whether the proposed extensions of use can satisfy the requirements of Article 4(1) and of the uniform principles laid down in Annex VI of Directive 91/414/EEC.

4. Specific conclusions highlighted in this evaluation

4.1 Residues of sulfosulfuron in foodstuffs

The review has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice are non-detectable and consequently have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI) for a 60 kg adult is < 0.1 % of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994).

These low intake values reflect the current limited use pattern for this active substance.

4.2 Exposure of operators, workers and bystanders

The review has identified acceptable exposure scenarios for operators, workers and bystanders, which require, however, confirmation for each plant protection product in accordance with the relevant sections of the above mentioned uniform principles.

4.3 Fate in the environment

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment, as provided for in Article 4 (1) (b) (iv) and (v) of Directive 91/414/EEC, provided that certain conditions are taken into account as detailed in section 7 of this report.

4.3 Ecotoxicology

The review has also concluded that under the proposed and supported conditions of use there are no unacceptable effects, as provided for in Article 4 (1) (b) (iv) and (v) of Directive 91/414/EEC, provided that certain conditions are taken into account as detailed in section 7 of this report.

5. Identity and Physical/chemical properties

The main identity and the physical/chemical properties of sulfosulfuron are given in Appendix I.

The active substance shall have a minimum purity of 980 g/kg technical product.

The review has established that for the active substance notified by the applicant (Monsanto), none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.

6. Endpoints and related information

In order to facilitate Member States, in granting or reviewing authorisations, to apply adequately the provisions of Article 4(1) of Directive 91/414/EEC and the uniform principles laid down in Annex VI of that Directive, the most important endpoints as identified during the evaluation process are listed in Appendix II.

7. Particular conditions to be taken into account on short term basis by Member States in relation to the granting of authorisations of plant protection products containing sulfosulfuron

On the basis of the proposed and supported uses, the following particular issues have been identified as requiring particular and short term (within 12 months at the latest) attention from the Member States, in the framework of any authorisations to be granted, varied or withdrawn, as appropriate:

- Leaching to groundwater: Particular attention should be given to the potential for groundwater contamination, when the active substance is applied in regions with vulnerable soil (e.g. soils with high pH values) and/or climatic conditions.

- Aquatic organisms: Member States must consider carefully the risk to aquatic plants and algae if this active substance is applied near to surface waters. The exposure input from drain flow with respect to local conditions should also be considered. Where appropriate, risk mitigation measures (e.g. buffer zones) should be applied.

8. List of studies to be generated

No further studies were identified which were considered at this stage, and under the current inclusion conditions necessary in relation to the inclusion of sulfosulfuron in Annex I. However, some endpoints may require the generation or submission of additional studies to be submitted to the Member States in order to ensure authorisations for use under certain conditions. This may be the case, in particular, to demonstrate the safety of groundwater resources and aquatic ecosystems.

9. Information on studies with claimed data protection

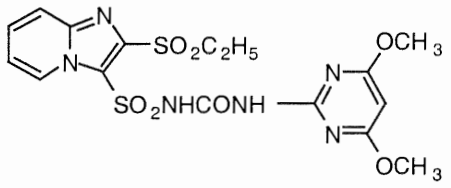
For information of any interested parties, Appendix III gives information about the studies for which the applicant has claimed data protection and which are not present in the original dossier and are not mentioned in the draft assessment report or in the addendum to the draft assessment report. This information is only given to facilitate the operation of the provisions of Article 13 of Directive 91/414/EEC in the Member States. It is based on the best information available to the Commission services at the time this review report was prepared; but it does not prejudice any rights or obligations of Member States or operators with regard to its uses in the implementation of the provisions of Article 13 of the Directive 91/414/EEC nor does it commit the Commission.

10. Updating of this review report

The technical information in this report may require periodic updating to take account of technical and scientific developments as well as of the results of the examination of any information referred to the Commission in the framework of Articles 7, 10 or 11 of Directive 91/414/EEC. Such adaptations will be examined and finalised in the Standing Committee on the Food Chain and Animal Health, in connection with any amendment of the inclusion conditions for sulfosulfuron in Annex I of the Directive.

APPENDIX I

Identity, physical and chemical properties

Common name (ISO)	Sulfosulfuron
Chemical name (IUPAC)	1-(4,6-dimethoxypyrimidin-2-yl)-3-[(2-ethanesulfonyl-imidazo[1,2-*a*]pyridine) sulfonyl]urea
Chemical name (CA)	1 N-[[(4,6,-dimethoxy-2-pyriimidinyl)amino]=carbonyl] - 2-(ethylsulfonyl) imidazo[1,2,a]pyridine-3-sulfonamide
CIPAC No	601
CAS No	141776-32-1
EEC No	None.
FAO SPECIFICATION	None.
Minimum purity	980 g/kg
Molecular formula	$C_{16}H_{18}N_6O_7S_2$
Molecular mass	470.49
Structural formula	

Melting point	201.1 - 201.7 °C (purity 99 %)
Boiling point	Not relevant.
Appearance	White powder, munsell colour N 9.5/90% R (purity 98.9 %)
Relative density	1.5185 g/cm^3 (purity 99.5 %)
Vapour pressure	3.05 ·10^{-8} Pa at 20 °C [by extrapolation]
Henry's law constant	8.15 ·10^{-7} Pa·m^3·mol^{-1} [pH 5] 8.83 ·10^{-9} Pa·m^3·mol^{-1} [pH 7] 2.97 ·10^{-8} Pa·m^3·mol^{-1} [pH 9]
Solubility in water	At 20 °C: pH 5 : 17.6 ± 2.71 mg/l pH 7 : 1626.8 ± 39.8 mg/l pH 9 : 482.44 ± 8.35 mg/l
Solubility in organic solvents	At 20 °C: heptane: < 0.001 g/l xylene: 0.16 g/l 1,2 dichloromethane: 4.35 g/l methanol: 0.33 g/l acetone: 0.71 g/l ethyl acetate: 1.01 g/l
Partition co-efficient (log P_{OW})	pH 5: 0.73 pH 7: -0.77 pH 9: -1.44
Hydrolytic stability (DT_{50})	At 25 °C: pH 4: 7 d pH 5: 48 d pH 7: 168 d pH 9: 156 d
Dissociation constant	pKa = 3.51 at 20 °C in the range pH 1.1 - 6.98.
Quantum yield of direct photo-transformation in water at ε >290 nm	Quantum yield calculated to be Φ = 1.81 x 10^{-3}
Flammability	Sulfosulfuron is not flammable.
Explosive properties	Sulfosulfuron is not explosive.
UV/VIS absorption (max.)	λ max = 208 nm. The molecule's absorption spectrum extends to 320nm. ε = 4169 at λ = 300nm and ε = 2188 at λ = 312nm.
Photostability in water (DT_{50})	At pH 7 in aqueous sterile buffered water $t_{1/2}$ was determined to range from 1.6 – 2.1 days natural sunlight.

APPENDIX II

END POINTS AND RELATED INFORMATION

SULFOSULFURON

1 Toxicology and metabolism

Absorption, distribution, excretion and metabolism in mammals

Rate and extent of absorption:	90% of low dose; 35 - 40% of high dose.
Distribution:	All tissues.
Potential for accumulation:	Nil.
Rate and extent of excretion:	Rapid: >80% and >90% within 24 and 48 hours post-dose, respectively. The major route was urinary at the low dose (77-87%) and via the faeces at the high dose (55 - 63%).
Toxicologically significant compounds:	Mainly parent.
Metabolism in animals:	Up to 88 % of dose excreted as parent. Demethylation and pyrimidine ring hydroxylation occur to a limited extent (cleavage of the sulfuronylurea bond is very limited).

Acute toxicity

Rat LD_{50} oral:	> 5000 mg/kg bw
Rat LD_{50} dermal:	> 5000 mg/kg bw
Rat LC_{50} inhalation:	> 3.0 mg/l
Skin irritation:	Non-irritant.
Eye irritation:	Moderately irritant.
Skin sensitization (test method used and result):	Non-sensitising (Magnusson & Kligman).

Short term toxicity

Target / critical effect:	Urinary tract (kidneys, bladder, ureters)
Lowest relevant oral NOAEL / NOEL:	100 mg/kg bw/d (90-d, dog study)
Lowest relevant dermal NOAEL /NOEL:	1000 mg/kg bw/d (28-d, rat study)
Lowest relevant inhalation NOAEL / NOEL:	Not required.

Genotoxicity

Ames (*S. typh.*)	negative.
HGPRT (CHO)	negative.

CA (CHL)	positive (-S9).
CA (human lymphocytes)	negative.
Mouse micronucleus	negative

Long term toxicity and carcinogenicity

Target / critical effect:	Urinary tract (kidneys, bladder, ureters)
Lowest relevant NOAEL:	24.4 – 30.4 mg/kg bw/d (NOEL; rat study)
Carcinogenicity:	Rat: Transitional cell carcinoma (1 incidence), papilloma (1 incidence) in females at 214 mg/kg bw/day, NOEL = 24.4 – 30.4 mg/kg bw/day. Mice: Increased incidence of mesenchymal tumours in males at > 3000 ppm (394 mg/kg bw/day). NOEL = 700 ppm (93 mg/kg bw/day).

Reproductive toxicity

Target / critical effect – Reproduction:	Body weight effects and urinary system pathology.
Lowest relevant reproductive NOAEL / NOEL:	1312 – 1598 mg/kg bw/day. Syst. NOEL = 312 –378 mg/kg bw/day
Target / critical effect – Developmental toxicity:	Rat: None seen. Rabbit: None seen.
Lowest relevant developmental NOAEL / NOEL:	Rat: > 1000 mg/kg bw/day. Rabbit: > 1000 mg/kg bw/day.

Delayed neurotoxicity

Acute neurotoxicity: NOEL > 2000 mg/kg.
Subchronic neurotoxicity: NOEL 1211 – 1467 mg/kg bw/day.

Other toxicological studies

None.

Medical data

None.

Summary

	Value	Study	Safety factor
ADI:	0.24 mg/kg bw/d	rat, 2-year feeding study	100
AOEL systemic:	short term: 1.00 mg/kg bw/day	dog: 90-day and 1 year	100
AOEL inhalation:	Not relevant.		
AOEL dermal:			
ARfD (acute reference dose):	Not allocated in view of low acute toxicity		

Dermal absorption	The default value of 10% is chosen

2 Fate and behaviour in the environment

2.1 Fate and behaviour in soil

Route of degradation

Aerobic:

Mineralization after 100 days:	1.6% (2.2% at 225d) Im^{14}C 8.1% (13% at 225d) Pd^{14}C
Non-extractable residues after 100 days:	14% (41% at 225d) Im^{14}C 15% (33% at 225d) Pd^{14}C
Relevant metabolites above 10 % of applied active substance: name and/or code % of applied rate (range and maximum)	Sulphonamide 2.2-9.1% (15% at 225d) Im^{14}C Desmethyl 1.0-28.0% (19% at 225d) Im^{14}C 0.9-29.0% (19% at 225d) Pd^{14}C Aminopyrimidine 0.9-3.4% (1.8% at 225d) Pd^{14}C

Supplemental studies

Anaerobic:

Not required.

Soil photolysis:

DT_{50} sunlight	46 d Im^{14}C	51 d Pd^{14}C
DT_{50} darkness	55 d Im^{14}C	117 d Pd^{14}C
Sulphonamide	22.6%	-
Aminopyrimidine	-	24.9%

Remarks:

None.

Rate of degradation

Laboratory studies

	Method of calculation: Pseudo first order kinetics (for Speyer 2.2 and UK soils) Gustafson & Holden 1990 (for US Soils).
DT_{50}lab (20 °C, aerobic):	*Sulfosulfuron*: Speyer 2.2 soil: 51-54 d (n=2); mean = 53 days; r^2 =0.996/0.988 UK soils: 92-226 d (n=4), mean = 176 days r^2 =0.972/0.994 US soils (25 °C): 31-37 d (n=4); mean = 33 days US soils (25°C): 74-88d (n=4); mean = 78 days *Desmethyl*: 132 – 188 days *Aminopyrimidine*: 138 – 147 days *Sulfonamide*: 113 – 156 days

DT_{90}lab (20 °C, aerobic):	Speyer 2.2 soil: 170-181 d (n=2); mean = 176 days; r^2 =0.996/0.988 UK soils: 306-750 d (n=4); mean = 584 days; r^2 =0.972/0.994 US soils (25 °C): 206-262 d (n=4); mean=239 d
DT_{50}lab (10 °C, aerobic):	UK soil: >365 d (n=8)
DT_{50}lab (20 °C, anaerobic):	Not required.

Field studies (country or region)	Method of calculation: Pseudo First order kinetics Timme, Frehse & Laska 1992; Gustafson & Holden 1990.
DT_{50f} from soil dissipation studies:	Belgium/France/Germany/UK: 11-47 d (n=5); mean = 24d; median = 25d. Canada/Saskatchewan/Alberta: 13-52 d (n=2); mean = 33d.
DT_{90f} from soil dissipation studies:	Belgium/France/Germany/UK: 131-358 d (n=11); mean = 261d; median = 276d. Canada/Saskatchewan/Alberta: 370-1190d (n=2); mean = 780 d.
Soil accumulation studies:	No data presented because there is no evidence of accumulation in field studies at recommended use rate.
Soil residue studies:	Sulfosulfuron residues: <0.0005-0.0007 mg/kg after one year (0–20 cm) Sulphonamide/Desmethyl residues: <0.0005-0.0013 mg/kg after one year (0-20 cm) Aminopyrimidine residues: Canadian soils (0-15 cm) 0.009 mg/kg after one year [bare soil treated with 136 g as/ha]; US soils (0-15 cm): 0.006 mg/kg after one year [bare soil treated with 70 g as/ha]

Remarks: e.g. effect of soil pH on degradation rate	None.

Adsorption/desorption

K_f / K_{OC}:	Sulfosulfuron 5.3 – 89.0 (n=5); mean = 33; median = 25. Sulphonamide 60.9 – 260.5 (n=4) mean = 163. Desmethyl 36.7 – 116.0 (n=4) mean = 74. Aminopyrimidine 259.9 – 8279.9 (n=4) mean = 2495. Sulfosulfuron 0.08 – 0.71 (n=5);

K_d:

mean = 0.36; median = 0.23. Sulphonamide 0.52 – 2.07(n=4) mean = 1.25. Desmethyl 0.32 – 0.73 (n=4) mean = 0.54. Aminopyrimidine 2.32 – 165.6 (n=4) mean = 47.4.

pH dependence:

Sulfosulfuron adsorption increases with decreasing soil pH.

Mobility

Laboratory studies:

Column leaching:

Not required.

Aged residue leaching:

	Column leachate	Soil section (0-5 cm)
Applied radioactivity	30 – 39 %	47 – 49 %
Sulfosulfuron	25 – 39 %	19 – 23 %
Sulphonamide	< 2%	< 1%
Desmethyl	*c.*2%	*c.*1%
Sulphonic acid	< 2%	< 1%
Aminopyrimidine	< 2%	< 1%
Unknown	*c.*3%	< 1%

Field studies:

Lysimeter/Field leaching studies

3-year field lysimeter study. Single and successive treatment, in springtime, at 1.5 times recommended rate (30 g as/Ha). Precipitation c.1000 mm/year. Leachate recovery c.8% AR. Sulfosulfuron and twelve radioactive fractions detected in leachate.

Radioactive leachate fractions detected (µg/l)

Application	Single	Successive
Fraction	Yearly Mean	Yearly Mean
Sulfosulfuron	nd - <0.01	0.01 - 0.03
M1 parent equiv.	nd - <0.01	nd - 0.02
M2 parent equiv.	0.02	0.03 - 0.06
M3 parent equiv.	nd - 0.01	0.02 - 0.06
M5*	0.01 - 0.04	0.01 - 0.06
M6*	<0.01 - 0.01	<0.01 - 0.08
M7 (Guanidine)*	0.03 - 0.10	0.02 - 0.10
M8*	<0.01 - 0.04	0.02 - 0.16
M4, M9, M10, M11 & M12	≤0.01	≤0.01

* recalculated on molar basis

The M8 component was unusual in that four successive untypical recordings in year 2 from Sept. to Nov. comprising 0.63, 0.47, 0.26 and 0.22 µg/l respectively were mainly responsible for the highest yearly mean of 0.20 µg/l in the leachate. These may be outlier values

Remarks: None.

2.2 Fate and behaviour in water

Abiotic degradation

Hydrolytic degradation:

	pH4	pH5	pH7	pH9
DT_{50} (days) (25 °C)	7	48	168	156
Relevant metabolites:				
Im^{14}C Sulphonamide	93%	34%	13%	15%
Pd^{14}C Aminopyrimidine	93%	31%	12%	15%

Photolytic degradation:

	Im^{14}C	Pd^{14}C
pH 7.0 Buffer (25 °C)		
DT_{50} (hours)	36.3	33.0

Relevant metabolites:

	Im^{14}C	Pd^{14}C
Aminopyrimidine	-	28.31 %
Sulfamic Acid	-	20.95 %
N-hydroxy Urea	-	14.98 %
Sulphone	28.34 %	-
Sulphonic Acid	14.59 %	-
Oxamic Acid	15.62 %	-

Biological degradation

Readily biodegradable: Not required.

Water/sediment study:	
DT_{50} water:	16.1 - 19.5 d
DT_{90} water:	83.9 - 101.8 d
DT_{50} whole system:	19.8 - 32.2 d
DT_{90} whole system:	103.5 - 107.0 d
Mineralisation after 100 days	< 1.3%
Non-extractable residues after 100 days	56%
Distribution in water / sediment systems (active substance)	11.3 – 11.8% (100 d)
Distribution in water / sediment systems (metabolites)	Desmethyl 12.9 – 14.0% (30 d) Sulphonamide 5.3 – 6.1% (100 d) Aminopyrimidine 1.4 – 1.7% (30/60 d) Unidentified 10.8 – 14.1% (14 d)
Accumulation in water and/or sediment:	None.

Degradation in the saturated zone	Not required. Residues not expected to reach this zone.
Remarks:	None.

2.3 Fate and behaviour in air

Volatility

Vapour pressure:	$3.05 \cdot 10^{-8}$ Pa at 20 °C
Henry's law constant:	$8.15 \cdot 10^{-7}$ Pa·m^3·mol^{-1} [pH 5] $8.83 \cdot 10^{-9}$ Pa·m^3·mol^{-1} [pH 7] $2.97 \cdot 10^{-8}$ Pa·m^3·mol^{-1} [pH 9]

Photolytic degradation

Direct photolysis in air:	Not required.
Photochemical oxidative degradation in air DT_{50}:	0.606 hours (calculated by Atkinson method)
Volatilisation:	Not required.
Remarks:	None.

3 Ecotoxicology

Terrestrial Vertebrates

Acute toxicity to mammals:	Rat: Oral LD_{50} >5000 mg as/kg bw
Acute toxicity to birds:	B. Quail/M. Duck LD_{50} >2250 mg as/kg bw
Dietary toxicity to birds:	B. Quail/M. Duck LC_{50} >5310 mg as/kg diet
Reproductive toxicity to birds:	Mallard Duck NOEC 250 mg as/kg diet
Short term oral toxicity to mammals:	Rat: NOEL 370 mg as/kg bw/day

Aquatic Organisms

Acute toxicity fish:	LC50 (96 h) >91 mg/l
Long term toxicity fish:	NOEC (87 d) = 100 mg/l
Bioaccumulation fish:	No fish bioconcentration study presented. Log Pow (Sulfosulfuron): < 1 (pH5-9)
Acute toxicity invertebrate:	LC50 (48 h) >96 mg/l
Chronic toxicity invertebrate:	NOEC (21 d) = 102 mg/l
Acute toxicity algae:	EC50 (72 h) = 0.221 mg/l
Chronic toxicity sediment dwelling organism:	Not required.
Acute toxicity aquatic plants:	IC50 (14 day) = 0.96 µg/l

Honeybees

Acute oral toxicity:	48 Hour Oral LD_{50} > 30 µg as/bee
Acute contact toxicity:	48 Hour Dermal LD_{50} > 25 µg as/bee

Other arthropod species

TEST SPECIES	
B. tetracolum	Mortality (adult): 0% Effect (0.0303 kg as/ha; Mon 37588)
Pardosa spp.	Food consumption (adult): 0% Effect (0.0303 kg as/ha; Mon 37588)
Typhlodromus pyri	Mortality (pronymph): Effect < 30% (0.0297 kg as/ha; Mon 37588)
Aphidius	Fecundity (adult): Effect ≈ 7% (0.0297 kg as/ha; Mon 37588)

Earthworms

Acute toxicity:	14 Day LC_{50} > 848 mg as/kg soil
Reproductive toxicity:	56 day NOEC ≥ 0.13 mg as/kg soil

Soil micro-organisms

Nitrogen mineralization:	2 soil types treated with 1.5 and 5.76 times recommended field rate, and assessed over a 100 day period. No significant adverse effect on mineral nitrogen level at the low rate in either sandy loam or loamy sand soil or at the five fold rate in the sandy loam soil. In the loamy sand soil at five fold rate a transient effect on soil NO_3 – N levels (31.3%) was observed with subsequent recovery to normal levels.
Carbon mineralization:	Biomass activity was measured in terms of carbon dioxide production. In sandy loam soils, no significant adverse effect on soil respiration was observed. In the loamy sand soil some temporary effects (< 25%) were evident after 14/28 days at higher rates with recovery to normal levels subsequently.

APPENDIX III

SULFOSULFURON

List of studies which were submitted during the evaluation process and were not cited in the draft assessment report (March 1998) or the Addendum to the draft assessment report (March 2000):

Annex point/ reference number	**Author(s)**	**Year**	**Title** **Source (where different from company)** **Company, Report No.** **GLP or GEP status (where relevant)** **Published or not**
IIA, 7.1.3.3	Mahon, S.J., Miller, M.J., Spirlet, M.	2001	Relevance of Leachate Metabolites [M5, M6, M7 (Guanidine) and M8] from the Sulfosulfuron Lysimeter Study Monsanto Un-published

SUMMARY REPORT OF THE MEETING OF THE STANDING COMMITTEE ON THE FOOD CHAIN AND ANIMAL HEALTH HELD ON 26 FEBRUARY 2002 IN BRUXELLES

President : G. Del Bino
All Member States were present.

1 **Examination of a draft Commission Directive concerning the inclusion of Sulfosulfuron in Annex 1 to Council Directive 91/414/EEC** (SANCO/1525/00 rev 4; Review Report 7459/VI/98-rev. 11).

The following declarations were made:

Commission: At the adoption of the Uniform Principles by Council in 1997, the Council and Commission agreed to the following declaration:

"The Council and the Commission note that application of this Directive is without prejudice to the legislation in force concerning the protection of workers. The Council and the Commission state that this principle will be unequivocally clarified in Directive 91/414/EEC on the occasion of the first amendment of that Directive. The Commission intends to submit a proposal for such amendment within one year from the date of notification of this Directive."

The Commission can for its part confirm its agreement with this declaration (subject to adequate adaptation of the deadline in the declaration).

The Commission presented the draft Directive.

Vote : unanimous favourable opinion

The substance is a new active substance used as herbicide.

The measures on which the Committee has given its opinion are subject to the appropriate procedures for formal adoption by the Commission.

A CHECCHI LANG
Director

EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate C - Scientific Opinions
C3 - Management of scientific committees II; scientific co-operation and networks

SCIENTIFIC COMMITTEE ON PLANTS

SCP/SULFO/002-Final
11 December 2000

OPINION OF THE SCIENTIFIC COMMITTEE ON PLANTS ON THE EVALUATION OF SULFOSULFURON IN THE CONTEXT OF COUNCIL DIRECTIVE 91/414/EEC FOR PLACING PLANT PROTECTION PRODUCTS ON THE MARKET

(Opinion adopted by the Scientific Committee on Plants on 30 November 2000)

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1. TITLE

OPINION OF THE SCIENTIFIC COMMITTEE ON PLANTS ON THE EVALUATION OF SULFOSULFURON IN THE CONTEXT OF COUNCIL DIRECTIVE 91/414/EEC FOR PLACING PLANT PROTECTION PRODUCTS ON THE MARKET.
(Opinion adopted by the Scientific Committee on Plants on 30 November 2000)

2. TERMS OF REFERENCE

The Scientific Committee on Plants (SCP) is requested to respond to the following questions in the context of the Commission's work on the implementation of Council Directive 91/414/EEC concerning the placing of plant protection products on the market.

1) Can the Committee give its opinion on the occurrence of bladder tumours in the 18 months mouse study?

2) Can the SCP consider whether it would be appropriate to establish an acute reference dose (ARfD) for sulfosulfuron?

3) Can the SCP confirm that a sub-lethal study for earthworms is unnecessary, notwithstanding the persistence of the soil metabolites?

In addition the SCP expressed an opinion on two specific issues of concern identified in the course of the evaluation.

4) The relevance of three unidentified metabolites "M5", "M6" and "M8".

5) The assessment of a risk for sensitive aquatic plants.

3. BACKGROUND

Sulfosulfuron is a new active substance in the context of Directive 91/414/EEC[1]. The draft Commission Directive for inclusion of this substance in Annex I to Directive 91/414/EEC concerning the placing of plant protection products on the market was submitted to the Committee for opinion. The Committee had been supplied with a draft evaluation report (monograph) prepared by the Rapporteur Member State (Ireland) on the basis of a dossier submitted by the notifier (Monsanto), a review report prepared by the Commission and the Recommendations of the ECCO[2] Peer Review Programme.

Sulfosulfuron is a member of the herbicide family of the sulfonylureas. It is intended for use as spring post-emergence treatment in wheat to control a number of grass weeds as well as various broad-leaved weeds. The supported rate of use is 20 g a.s./ha. Sulfosulfuron acts by contact and residual action.

[1] OJ N° L 230 of 19. 8.1991, p. 1.
[2] European Community Co-ordination.

4. OPINION

4.1 Question 1

"Can the Committee give its opinion on the occurrence of bladder tumours in the 18 months mouse study?"

Opinion of the Commitee

The Committee concluded that as sulfosulfuron did not show genotoxic potential, the increased frequency of submucosal bladder lesions/tumours observed in treated mice in association with urinary calculi was produced by a non-genotoxic mechanism that is not fully characterised. The lesions/tumours of microscopic size that were observed in mice were of mesenchymal origin, were benign, and were of a kind that may occur naturally in mice of certain strains. Such lesions/tumours are not known to occur in humans. The Committee considered that these lesions/tumours do not predict carcinogenic hazard to humans.

Scientific background on which the opinion is based

4.1.2 Assessment of the data

The Committee took note of the responses of the notifier to its requests for further information. The notifier's responses included the following: (a) histopathologic details of the submucosal lesions/tumours of the mouse urinary bladder; (b) documentation that these lesions also occur in untreated mice of certain genetic lineages; and (c) an hypothesis regarding the role of urinary calculi and chronic obstructive uropathy in their development.

Sulfosulfuron has been adequately tested for its potential genotoxicity and was not genotoxic *in vivo*. Chromosome aberration induction was demonstrated *in vitro* in Chinese hamster lung fibroblast cultures at cytotoxic concentrations and at the limit of compound solubility. In contrast, negative results were obtained in human lymphocyte cultures. The Chinese hamster *in vitro* positive result was not considered relevant to intact animals (including humans) as the cytotoxic concentrations could not be achieved *in vivo*.

Sulfosulfuron produced bladder calculi in both rats and mice. Sulfosulfuron caused urinary calculi and urothelial hyperplasia in rats to which were administered diets containing 5,000 and 20,000 ppm sulfosulfuron but only 1 benign and 1 malignant epithelial bladder tumour were observed, both in females of the 5,000 ppm group[3]. These tumours were plausibly related to the presence of urinary calculi.

Sulfosulfuron also caused urinary calculi and urothelial hyperplasia in treated mice, but no epithelial tumours were observed. Sulfosulfuron increased the incidence of only an unusual submucosal lesion/tumour of the urinary bladder in mice. Such lesions/tumours occurred mostly at the higher dose (7000 ppm) and mostly in males, but one such tumour did occur in an untreated female mouse. The submucosal lesions/tumours in mice were invariably microscopic in size, were of mesenchymal origin, and were histologically benign. The pathogenesis of these rare lesions/tumours is not well established. While a hypothesis has been presented that contraction and distension of the murine urinary bladder consequent to chronic or intermittent obstruction of the urinary tract by calculi may play a mechanical role in the development of these lesions/tumours, this

[3] In the oral study in rats, the concentrations tested were of 0, 50, 500, 5,000 and 20,000 ppm.

is not well validated. There is no clear evidence that the presence of calculi in the urinary bladder is causally related to the increased incidence of mesenchymal lesions/tumours in treated mice over controls. Bladder calculi and other persistent foreign bodies are known to be associated with epithelial neoplasms of the urinary bladder in rodents, especially rats, but a causal association with any other kind of true neoplasm in the urinary bladder in rodents is not established. There are some indications that urinary calculi are associated with a slightly increased risk of epithelial neoplasms of the urinary tract in humans. However, mesenchymal lesions/tumours of the kind seen in mice do not occur in humans.

4.1.2 Conclusion

The Committee concluded, on the basis of previously supplied information and the notifier's responses including additional data, that:

- Sulfosulfuron did not show genotoxic potential *in vivo*;

- Sulfosulfuron caused urinary calculi and urothelial hyperplasia in rats at doses of 5,000 and 20,000 ppm but treatment was associated with only 1 benign and 1 malignant epithelial bladder tumour, both in low-dose females. These were plausibly related to the presence of calculi;

- Sulfosulfuron also caused urinary calculi and urothelial hyperplasia in treated mice, but increased the incidence of only an unusual submucosal lesion/tumour of the urinary bladder, mostly at the highest dose (7,000 ppm). The submucosal lesions/tumours observed in mice after chronic treatment were invariably microscopic in size, were of mesenchymal origin, and were histologically benign and of a kind that may occur naturally in mice of certain strains. Such lesions/tumours do not occur in humans;

- There is no clear evidence that the presence of calculi in the urinary bladder is causally related to the increased incidence of mesenchymal lesions/tumours in treated mice over controls;

- Bladder calculi are known to be associated with epithelial neoplasms of the urinary bladder in rodents, especially rats, and are associated with increased risk of cancer of the urinary tract in humans, but a causal association with any other kind of true neoplasm in the urinary bladder either in rodents or in humans is not established;

- The submucosal lesions/tumours in mice treated with sulfosulfuron do not predict a cancer hazard to humans.

4.2 Question 2

"Can the Scientific Committee on Plants consider whether it would be appropriate to establish an acute reference dose (ARfD) for sulfosulfuron?"

Opinion of the Committee:

The Committee concludes that it is not necessary to establish an acute reference dose for sulfosulfuron. The acute toxicity of sulfosulforon is low, and repeated dose studies did not identify relevant toxic endpoints.

Scientific background on which the opinion is based

4.2.1 General consideration on ARfD setting

The toxicological information provided by the Annex II to Directive 91/414/EEC represents the basis for deriving the ARfD. The FAO/WHO 1997 consultation defined acute reference dose as: "*An estimate of the amount of substance in food or drinking water, expressed on a body-weight basis, that can be ingested over a short period of time, usually during one meal or one day, without appreciable risk to the consumer on the basis of all the known facts at the time of evaluation. It is usually expressed in milligrams of the chemical per kilogram body weight.*"[4]

The SCP has concluded that the setting of ARfD should be considered for all plant protection products, though in many instances it will be unnecessary to set one. If a plant protection product is not acutely toxic and an ARfD is considered unnecessary, the reasons supporting this conclusion must be described in detail. Furthermore, the SCP also indicated that the entire toxicity database should be considered in determining the most appropriate species and end-point for deriving an ARfD. The critical end-point should be one relevant to a single exposure in humans.

4.2.2 Chemical and toxicological properties of sulfosulfuron

Sulfosulfuron is a sulphonylurea herbicide with a high water-solubility. It is readily absorbed from the gastrointestinal tract after single administration of a low dose while at high doses the absorbed proportion of the dose decreases in rats. At low single oral doses most of the compound is excreted in the urine whereas at high oral doses (1000 mg/kg) excretion in the faeces predominate excretion in the urine being less important suggesting less complete absorption from the gastrointestinal tract.

The acute toxicity of sulfosulfuron is low both orally and dermally in rats; in both cases the LD_{50} value exceed 5000 mg/kg. In short-term inhalation studies a concentration of 3 mg/l did not induce any observable acute toxicity. The compound does not turn out not to be a primary skin irritant or a dermal sensitizer in studies with rabbits. In a 28-day oral toxicity study the NOAEL[5] for males was 186 and for females 987 mg/kg/day. The toxic end points, transient body-weight loss, a single ocular opacity, and induction of palmitoyl CoA are not relevant for setting an ARfD. In another 28-day study with rats, a NOAEL of 136 mg/kg/day for males and of 154 mg/kg/day for females was based on a decrease in thromboplastin time and a slight kidney effect. In an oral 90-day dose-finding study in dogs a NOAEL of 100 mg/kg/day was established for females and of 300 mg/kg/day in males due to increased thyroid and heart weights. The NOAEL defined on a decrease in serum alkaline phosphatase level in a 90-day oral feeding mouse study was 7000 ppm (350 mg/kg/day). These findings are irrelevant for setting an ARfD for sulfosulfuron.

Sulfosulfuron induced in a 90-day oral feeding study in dogs urolithiasis in males sacrificed *in extremis*. These findings were considered secondary to urinary calculi found in high-dose groups of dogs both in males and females. Similar changes occurred in a one-year feeding study with dogs both in females and males with NOAELs of 100 mg/kg/day for both genders.

Sulfosulfuron is not genotoxic in tests exploring both gene mutations and chromosomal aberrations *in vivo*. Positive *in vitro* results in Chinese hamster were not considered relevant in intact animals or man.

[4] See Opinion of the SCP on the general criteria for setting acute reference doses for plant protection products. http://europa.eu.int/comm/food/fs/sc/scp/out02_ppp_en.html

[5] No observed adverse effect level.

In a chronic two-year feeding study in rats, there was increased mortality among the exposed high-dose rats (20 000 ppm, i.e. 1000 mg/kg/day). This was most likely a result of formation of renal calculi and related abnormalities present in the kidney, ureters, and urinary bladder. Body weights were decreased in the high-dose groups (5000 or 20 000 ppm, 250 or 1000 mg/kg/day), and blood urea nitrogen (BUN) was elevated in the high dose groups. There was one benign and one malignant epithelial bladder tumour in the 5000 ppm dose, but such tumours did not occur at the high-dose group (20 000 ppm). The NOEL[6] for tumorigenicity was 500 ppm in rats.

Sulfosulforon also caused urinary calculi and urothelial hyperplasia in treated mice, but no epithelial tumours occurred. Sulfosulforon increased the incidence of only an unusual submucosal lesion/tumour of the urinary bladder in mice. These tumours occurred mostly at the higher dose (7000 ppm) and mostly in males, but one such tumour occurred in an untreated female mouse. Bladder calculi and other persistent foreign bodies are known to be associated with epithelial neoplasms of the urinary bladder in rodents, especially in rats, but a causal association with any other kind of true neoplasm in the urinary bladder in rodents has not been established. In a long-term mouse study, BUN was also elevated both in the male and female mice in the high-dose group (7000 ppm).

In reproductive studies in rats the NOEL was 5000 ppm (312-378 mg/kg/day). Weight was reduced at the high dose, but reproductive parameters were not adversely affected. In a developmental toxicity study with rabbits, no maternal toxicity or toxic effects in pups were noted up to a dose of 1000 mg/kg/day of sulfosulfuron from days 7-19 of gestation. The NOEL was 1000 mg/kg/day.

In additional studies exploring acute (single dose) or subchronic (14 weeks) neurotoxicity, no signs of behavioural alterations or morphological changes in peripheral nerves were observed.

In supervised field trials according to good agricultural practices, residues of sulfosulfuron were below 0.01 mg/kg cereal grain. This would mean a potential short-term dietary intake (assuming large portion consumption data for the most sensitive population, i.e. young children) of less than 0.0005 mg/kg body-weight.

4.2.3 Conclusion:

The SCP concluded that it is not necessary to establish an acute reference dose for sulfosulfuron because acute toxicity is low and repeated dose studies did not identify relevant toxic endpoints.

4.3 Question 3

Can the SCP confirm that a sub-lethal study for earthworms is unnecessary, notwithstanding the persistence of the soil metabolites?

Opinion of the Committee:

A newly submitted sub-lethal study for earthworms allowed the SCP to conclude that no significant long term risks to earthworms are likely to arise from use of sulfosulfuron at the recommended treatment rate (20 g a.s./ha, once per year), despite the persistence of metabolites in the soil.

Scientific background on which the opinion is based

4.3.1 Fate

[6] No observed effect level.

The persistence of the parent compound varies considerably with soil type and conditions, with estimates of the field DT_{50}[7] in European studies varying from 11-47 days (DT_{90}[8] 131-358 days), and estimates of field DT_{50} in US studies varying from 13-52 days (DT_{90} 370-1190 days). The major routes of degradation of sulfosulfuron in soil are through: (a) cleavage of the sulfonyl-urea bond leading to the formation of aminopyrimidine and sulphonamide and (b) oxidative demethylation of sulfosulfuron to form desmethyl. Sulphonomide was reported at a maximum of 15% (after 225 days, the duration of the study) and 53% (after 360 days, the duration of the study) of applied radioactivity in EU and US soils respectively. Desmethyl was reported at a maximum of 29% applied radioactivity after 100 days in EU soils, but was consistently < 5% applied radioactivity in US soils. Aminopyrimidine was recorded at a maximum of 10.6 % applied radioactivity (after 100 days, the duration of the study) and 39.4% (after 272 days) in EU and US soils respectively.

The steady-state concentrations of the parent and its metabolites have been estimated by evaluators assuming a 50% crop interception and an annual application rate of 20 g a.s./ha[9]. Based on the expected peak concentrations in soil and extreme estimates of DT_{50} values, it has been estimated that the parent compound will reach a steady state of approximately 3.5 µg/kg after 5 years; sulfonomide will reach a steady state of approximately 4.7 µg/kg after 8 years; desmethyl will reach a steady state of approximately 5.1 µg/kg after 9 years, while aminopyrimidine will reach a steady state of approximately 5.9 µg / kg after 12 years.

4.3.2 Ecotoxicity

Originally, only the results of a 14-day earthworm (*Eisenia fetida*) study were submitted. In this study, earthworms were exposed to sulfosulfuron at a test concentration of 1000 mg a.s./kg dry soil (mean measured concentration 848 mg a.s./kg) for 14 days. Despite the unrealistically high test concentration (maximum initial PEC[10] for worst case exposure to bare soil 0.0267 mg/kg soil in 0-5cm), no significant effects on earthworm mortality, appearance, behaviour or body weight were observed over the exposure period.

Annex II criteria propose that an extended test for sub-lethal effects of earthworms is required if the field DT_{90} is above 365 days, independent of the number of times it is applied. Furthermore, metabolites, which reach a concentration greater than 10% of the dose applied should also be tested for long-term sublethal effects, unless they are formed so rapidly that potential effects are covered by the available earthworm tests for the parent compound. Given these recommendations, a further sub-lethal study was appropriate[11]. Indeed, one was about to be called for by the SCP.

In the recently submitted sub-lethal study, adult earthworms (*Eisenia fetida*) were exposed to two concentrations of sulfosulfuron in artificial soils at rates equivalent to 1x and 5x times the maximum proposed application of 20 g a.s./ha, i.e. 0.026 and 0.13 mg a.s./kg dry soil. After 28 days exposure the adult worms were counted and weighed. After a further 28 days the soil was examined for juveniles and cocoons. No mortalities were observed in the study, and the body weights of earthworms did not differ significantly from the controls. Similarly, the number of juveniles produced by the end of the study did not differ significantly (5.5 to 14.2 per adult worm in control replicates, 4.7 to 13.4 per adult in 5x treatment replicates).

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[7] Period required for 50 % dissipation.
[8] Period required for 90 % dissipation.
[9] see UK questions Doc. SCP/SULFO/022, and RMS Addendum to the Annex B of the Monograph.
[10] Predicted environmental concentration.
[11] See Opinion of the Scientific Committee on Plants regarding the draft guidance document on relevant metabolites

Given the data provided in the two separate studies, it is highly unlikely that a single use of sulfosulfuron at the recommended application rate will pose a significant risk to earthworms. However, to address the possible effects of the parent compound and its metabolites accumulated over several seasons, it is necessary to consider the steady-state concentrations. If we treat the NOEC[12] of > 0.13 mg as/kg for the parent as toxicity endpoints for all metabolites, and assume the steady state concentrations previously calculated, then the minimum possible estimate of the long-term TER[13] for the main metabolites is 22. Given that this estimated figure is well above the standard trigger value, the SCP is of the opinion that no significant long-term risks to earthworms are likely to arise from the use of sulfosulfuron at the recommended rate.

4.4 Relevance of unidentified metabolites [M5, M6 and M8]

The Committee has noticed that three unidentified metabolites ("M5", "M6" and "M8") were detected in the leachate of a sandy soil lysimeter at annual average concentrations of 0.1 µg/l.

Opinion of the Committee:

The SCP notes that the three metabolites ("M5", "M6" and "M8") have not been chemically identified and therefore the non necessity for further testing should be scientifically assessed.

Scientific background on which the opinion is based:

The Committee has noticed that three unidentified metabolites ("M5", "M6" and "M8") were detected in the leachate of a sandy soil lysimeter at annual average concentrations of 0.1 µg/l (parent equivalent) or higher (after two treatments of the soil with sulfosulfuron rates of 30 g/ha). The metabolites were not identified in the soil degradation study.

The SCP agrees with the Rapporteur Member State that it is unlikely that the concentration of the metabolites will exceed 0.1µg/l when the a.s. is applied in spring at a rate of 20g/ha. However, the SCP notes that these metabolites have not been chemically identified and therefore the need for further testing should be scientifically assessed (see Opinion of the Scientific Committee on Plants regarding the draft guidance document on relevant metabolites).

4.4 Drain flow calculation

The Committee has noticed that drain flow calculations for a UK clay loam soil with a leaching model that includes preferential flow (MACRO[14]), have indicated risk for sensitive aquatic plants in surface water.

Opinion of the Committee:

This risk does not appear to have been addressed by the Rapporteur Member State.

[12] No observed effect concentration.
[13] Toxicity exposure ration.
[14] Simulation model of plant protection product fate (Jarvis, 1991) see FOCUS report "Soil persistence models and EU registration", http://europa.eu.int/comm/food/fs/ph_ps/pro/wrkdoc/focus/soil_en.pdf

5. REFERENCES

1. IARC. IARC monograph vol. 73, 1999 Capen et *al* 1999, IARC

2. Opinion of the Scientific Committee on Plants regarding the draft guidance document on relevant metabolites (Document SANCO/221/2000-rev2) adopted on 30 November 2000. http://europa.eu.int/comm/food/fs/sc/scp/outcome_ppp_en.html

6. DOCUMENTS MADE AVAILABLE TO THE COMMITTEE

1. Evaluation of sulfosulfuron in the context of Council Directive 91/414/EEC concerning the placing of plant protection products on the market: Terms of Reference (Doc. SCP/SULFO/001-rev.1), submitted by DG SANCO, 3 April 2000.

2. Sulfosulfuron: Evaluation table 7458/VI/98-rev.8 (Doc. SCP/SULFO/003-rev.1), submitted by DG SANCO, 3 April 2000.

3. "Spontaneous neoplastic lesions in the CRL/CD-1®Mouse" P. L. Lang, Charles River laboratories, March 1995, (Doc. SCP/SULFO/004), submitted by Monsanto, 5 January 2000.

4. "Expert report on renal hispathologic changes in a mouse study with MON 37500 (sulfosulfuron)", G.C. Hard, August 1999, (Doc. SCP/SULFO/005), submitted by Monsanto, 16 January 2000.

5. Sulfosulfuron: Danish comments (Doc. SCP/SULFO/006), submitted by DG SANCO, 31 January 2000.

6. Sulfosulfuron: Appendix III: Listing of end points (Doc. SCP/SULFO/007), submitted by DG SANCO, 3 April 2000.

7. Sulfosulfuron: German comments (Doc. SCP/SULFO/009), submitted by DG SANCO, 3 April 2000.

8. Sulfosulfuron: Appendix I and Appendix II (Doc. SCP/SULFO/010), submitted by DG SANCO, 4 April 2000.

9. Sulfosulfuron: question from the SCP to the notifier regarding the evaluation of sulfosulfuron (Doc. SCP/SULFO/011), submitted by the SCP, 23 May 2000.

10. Preliminary response from the notifier to the question raised by the SCP (Doc. SCP/SULFO/012), submitted by Monsanto, 26 May 2000.

11. Sulfosulfuron: Draft review report 7459/VI/98-rev.1 (Doc. SCP/SULFO/013), submitted by DG SANCO, 31 May 2000.

12. Sulfosulfuron: Danish comments (Doc. SCP/SULFO/014), submitted by DG SANCO, 9 June 2000.

13. Sulfosulfuron: Comments from France (Doc. SCP/SULFO/015), submitted by DG SANCO, 9 June 2000.

14. Sulfosulfuron: Danish comments (Doc. SCP/SULFO/016), submitted by DG SANCO, 9 June 2000.

15. Sulfosulfuron: Response from RMS to Danish comments [Doc. SCP/SULFO/006], (Doc. SCP/SULFO/017), submitted by DG SANCO, 9 June 2000.

16. Sulfosulfuron: Volume 3 Addendum to Annex B to the Draft report and proposed decision (Doc. SCP/SULFO/019), submitted by DG SANCO, 23 June 2000.

17. Sulfosulfuron: Dutch assessment of the lysimeter study (Doc. SCP/SULFO/021), submitted by DG SANCO 24 July 2000.

18. Sulfosulfuron: UK questions on sulfosulfuron to the SCP (Doc. SCP/SULFO/022), submitted by DG SANCO, 24 July 2000.

19. Further response from the notifier to questions (SCP/SULFO/011) raised by the SCP (Doc. SCP/SULFO/023), submitted by Monsanto, 23 August 2000.

20. RMS response to the Dutch comments [SCP/SULFO/021] on the lysimeter study (Doc. SCP/SULFO/025), submitted by DG SANCO, 26 September 2000.

20. European Commission: Peer review programme: Sulfosulfuron, monograph prepared by Ireland, March 1998 (Volumes 1 to 4).

7 ACKNOWLEDGEMENTS

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Carcinogenicity WG: Prof. Maroni (Chairman) and Committee members: Dr. Delcour-Firquet, Dr. Meyer, Dr. Moretto, Prof. Savolainen, Prof. Silva Fernandes, Dr. Speijers and invited experts: Prof. Galli, Prof. Parry, Dr. Rice, Prof. Schulte-Hermann and Dr. Wester.

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Berichte aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft erscheinen seit 1995 in zwangloser Folge.

Heft 96, 2002: Liste der zugelassenen Pflanzenschutzmittel (Stand: 1. Januar 2002). Bearbeitet von Andreas Spinti, 74 S.

Heft 97, 2002: EU-Beurteilungsbericht 2,4-D. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 27. Bearbeitet von Dr. Martina Erdtmann-Vourliotis und Susanne Schaper, getr. Zählung.

Heft 98, 2002: NEPTUN 2000 – Erhebung von Daten zum tatsächlichen Einsatz chemischer Pflanzenschutzmittel im Ackerbau Deutschlands. Dr. Dietmar Roßberg, Dr. Volkmar Gutsche, Dr. Siegfried Enzian und Dr. Mario Wick, 27 S., Anhang.

Heft 99, 2002: EU-Beurteilungsbericht Thifensulfuron-methyl. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 28. Bearbeitet von Dr. Martina Erdtmann-Vourliotis und Susanne Schaper, getr. Zählung.

Heft 100, 2002: EU-Beurteilungsbericht Flupyrsulfuron-methyl. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 29. Bearbeitet von Dr. Henning Bruno und Susanne Schaper, getr. Zählung.

Heft 101, 2002: EU-Beurteilungsbericht *Paecilomyces fumosoroseus*. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 30. Bearbeitet von Dr. Martina Erdtmann-Vourliotis, Dr. Axel Wilkening und Susanne Schaper, getr. Zählung.

Heft 102, 2002: EU-Beurteilungsbericht Isoproturon. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 31. Bearbeitet von Dr. Henning Bruno und Susanne Schaper, getr. Zählung.

Heft 103, 2002: Zuständigkeiten bei der Prüfung und Zulassung von Pflanzenschutzmitteln und bei der EU-Wirkstoffprüfung. Stand: Februar 2002. Bearbeitet von Edelgard Adam, 58 S.

Heft 104, 2002: Pflanzenschutz im ökologischen Landbau – Probleme und Lösungsansätze. Sechstes Fachgespräch am 26. Juni 2001 in Braunschweig. Abwehr von Wühlmausschäden im ökologischen Landbau. Bearbeitet von Dr. Hans-Joachim Pelz, 109 S.

Heft 105, 2002: EU-Beurteilungsbericht Acibenzolar-S-methyl. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 32. Bearbeitet von Herbert Köpp und Susanne Schaper, getr. Zählung.

Heft 106, 2002: EU-Beurteilungsbericht Eisen(III)phosphat. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 33. Bearbeitet von Dr. Martina Erdtmann-Vourliotis, Dr. Axel Wilkening und Susanne Schaper, getr. Zählung.

Heft 107, 2002: EU-Beurteilungsbericht Ethofumesat. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 34. Bearbeitet von Dr. Martina Erdtmann-Vourliotis und Susanne Schaper, getr. Zählung.

Heft 108, 2002: EU-Beurteilungsbericht Cyclanilide. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 35. Bearbeitet von Dr. Henning Bruno und Susanne Schaper, getr. Zählung.

Heft 109, 2002: Alternativen zum Einsatz von kupferhaltigen Präparaten im Apfelanbau. Ergebnisse einer Literaturrecherche. Bearbeitet von Dr. Beate Golba in Zusammenarbeit mit dem Institut für Pflanzenschutz im Obstbau der Biologischen Bundesanstalt für Land- und Forstwirtschaft, 67 S.

Heft 110, 2002: Bewertungskonzept zum Nahtransport von Pflanzenschutzmitteln infolge Exposition über den Luftpfad (Abtrift, Verflüchtigung und Deposition). Dr. Reinhard Winkler, Dr. Rainer Binner, Dr. Dietmar Gottschild, Dr. Wolfgang Koch und Dr. Johannes Siebers, 19 S.

Heft 111, 2002: EU-Beurteilungsbericht Iprovalicarb. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 36. Bearbeitet von Herbert Köpp und Susanne Schaper, getr. Zählung.

Heft 112, 2002: EU-Beurteilungsbericht Prosulfuron. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 37. Bearbeitet von Dr. Henning Bruno und Susanne Schaper, getr. Zählung.

Heft 113, 2002: EU-Beurteilungsbericht Pymetrozin. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 38. Bearbeitet von Dr. Martina Erdtmann-Vourliotis, Dr. Axel Wilkening und Susanne Schaper, getr. Zählung.

Heft 114, 2002: EU-Beurteilungsbericht Pyraflufen-ethyl. Rechtliche Regelungen der Europäischen Union zu Pflanzenschutzmitteln und deren Wirkstoffen. Band D 39. Bearbeitet von Dr. Henning Bruno und Susanne Schaper, getr. Zählung.