UNITED NATIONS

PIC

United Nations Environment Programme

Food and Agriculture Organization of the United Nations

Distr.
GENERAL

UNEP/FAO/PIC/INC.10/8
10 April 2003

ORIGINAL: ENGLISH

INTERGOVERNMENTAL NEGOTIATING COMMITTEE FOR AN INTERNATIONAL LEGALLY BINDING INSTRUMENT FOR THE APPLICATION OF THE PRIOR INFORMED CONSENT PROCEDURE FOR CERTAIN HAZARDOUS CHEMICALS AND PESTICIDES IN INTERNATIONAL TRADE
Tenth session
Geneva, 17-21 November 2003
Item 4 (d) of the provisional agenda*

Implementation of the interim prior informed consent procedure: Inclusion of chemicals

INCLUSION OF THE CHEMICAL DNOC AND ITS SALTS AND ADOPTION OF THE DECISION GUIDANCE DOCUMENT

Note by the secretariat

Introduction

1. In paragraph 8 of its resolution on interim arrangements,[1] the Conference of Plenipotentiaries decided that the Intergovernmental Negotiating Committee shall decide, between the date on which the Convention is opened for signature and the date of its entry into force, on the inclusion of any additional chemicals under the interim prior informed consent (PIC) procedure in accordance with the provisions of Articles 5, 6, 7 and 22 of the Convention.

2. Paragraph 5, subparagraph (a) of Article 22 states that amendments to Annex III shall be proposed and adopted according to the procedure laid down in Articles 5 to 9 and paragraph 2 of Article 21. Under paragraph 2 of Article 21, amendments to the Convention shall be adopted at a meeting of the Conference of the Parties and the text of any proposed amendment shall be communicated to the Parties by the Secretariat at least six months before the meeting at which it is proposed for adoption.

* UNEP/FAO/PIC/INC.10/1.

[1] *Final Act of the Conference of Plenipotentiaries on the Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, Rotterdam, Netherlands, 10-11 September 1998* (UNEP/FAO/PIC/CONF/5), annex I, resolution 1.

K0361113 150503

3. At its third session, the Interim Chemical Review Committee reviewed two notifications of final regulatory action from two interim PIC regions to ban or severely restrict the chemical DNOC and, taking into account the criteria set forth in Annex II of the Convention, concluded that the requirements of that Annex had been met. Accordingly, the Interim Chemical Review Committee recommended to the Intergovernmental Negotiating Committee at its ninth session that DNOC should become subject to the interim PIC procedure,[2] noting that it would develop a draft decision guidance document and forward it to the Intergovernmental Negotiating Committee in accordance with Article 7 of the Convention.

4. At its fourth session, the Interim Chemical Review Committee finalized the draft decision guidance document on DNOC and decided to forward it and the Committee's recommendation for inclusion of DNOC in the interim PIC Procedure to the Intergovernmental Negotiating Committee. The revised introduction prepared by the Interim Chemical Review Committee has been included in the draft decision guidance document. The text of the Committee's recommendation, a summary of the deliberations of the Committee, including a rationale for the inclusion of DNOC based on the criteria listed in Annex II of the Convention, and a tabular summary of comments received and how they were addressed, are attached as annex I to the present note. The draft decision guidance document is attached as annex II to the present note.

5. In accordance with decision INC-7/6, which sets out the process for drafting decision guidance documents, and in line with the time frame specified in paragraph 2 of Article 21 of the Convention, the secretariat circulated the present document to all Parties and observers on 14 May 2003.

B. Suggested action by the Committee

6. The Committee may wish to decide to make the chemical DNOC subject to the interim prior informed consent procedure, as defined in paragraph 2 of the resolution on interim arrangements, and to approve the draft decision guidance document.

[2] See UNEP/FAO/PIC/INC.3/19, annexII.

Annex I

DNOC AND ITS SALTS

The Interim Chemical Review Committee,

Noting that at its third session it had reviewed the notifications of final regulatory actions by the European Community and Peru on DNOC and, taking into account the requirements set forth in Annex II of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade, and had come to the conclusion that the requirements of that Annex had been met,

Recalling that, in line with paragraph 6 of Article 5 of the Convention, at its second session it had accordingly recommended to the Intergovernmental Negotiating Committee that DNOC should become subject to the interim prior informed consent procedure and noting (Annex II of its report of its third session (UNEP/FAO/PIC/ICRC.3/19)) that it was to develop a draft decision guidance document and forward it to the Intergovernmental Negotiating Committee in accordance with Article 7 of the Convention,

Recalling also that, in accordance with the operational procedures for the Interim Chemical Review Committee, set forth in decision INC-7/6 of the Intergovernmental Negotiating Committee on the process for drafting decision guidance documents, it had established a group to draft a decision guidance document on DNOC and that this group, upon fulfilling the requirements of the operational procedures and in accordance with paragraph 1 of Article 7 of the Convention, had developed a draft decision guidance document on DNOC (UNEP/FAO/PIC/ICRC.4/12) and had submitted it to the Committee at its fourth session for further action,

Noting that the draft decision guidance document was based on the information specified in Annex I of the Convention, as required by paragraph 1 of Article 7 of the Convention,

Recalling that in accordance with step 7 of the process for drafting decision guidance documents, final documentation forwarded by the Secretariat to all Parties and observers in advance of Intergovernmental Negotiating Committee sessions must include a draft decision guidance document, a recommendation by the Interim Chemical Review Committee for inclusion in the prior informed consent procedure, a summary of the deliberations of the Interim Chemical Review Committee including a rationale for inclusion based on the criteria listed in Annex II to the Convention, and a tabular summary of comments received by the Secretariat and how they had been addressed,

Adopts the following recommendation to the Intergovernmental Negotiating Committee:

The Interim Chemical Review Committee

Recommends, in line with paragraph 6 of Article 5 of the Convention, that the Intergovernmental Negotiating Committee should make DNOC and its salts (such as ammonium salt, potassium salt and sodium salt), subject to the interim prior informed consent procedure;

Chemical	Relevant CAS Number(s)	Category
DNOC and its salts (such as ammonium salt, potassium salt and sodium salt)	534-52-1; 2980-64-5; 5787-96-2; 2312-76-7	Pesticide

Forwards, in line with paragraph 2 of Article 7 of the Convention, this recommendation, together with the draft decision guidance document on DNOC, to the Intergovernmental Negotiating Committee for a decision on the inclusion of DNOC in the interim prior informed consent procedure.

Appendix I

Rationale for the recommendation that DNOC should become subject to the interim prior informed consent procedure (Excerpt from UNEP/FAO/PIC/ICRC.3/19 annex II)

In reviewing the notifications of final regulatory actions by the European Community and Peru together with the supporting documentary information and supplementary information provided by those Parties, the Committee was able to confirm that those actions had been taken in order to protect human health, (particularly as regards operator exposure) and the environment (risks to non-target species). The European Community action stemmed from a risk evaluation based on data that contained some gaps. However, the unaddressed endpoints were not relevant for the evaluation, which concluded that there were concerns about human health and the environment. The action by Peru was based on hazard data supplemented by a study of poisoning incidents in the country. Taken together, that material demonstrated that there had been a risk evaluation that took into account prevailing conditions in that country.

The Committee established that the final regulatory actions had been taken on the basis of risk evaluations and that those evaluations had been based on a review of scientific data. The available documentation demonstrated that the data had been generated in accordance with scientifically recognized methods, that the data reviews had been performed and documented in accordance with generally recognized scientific principles and procedures, and that the final regulatory actions had been based on chemical-specific risk evaluations taking into account the conditions prevailing within the European Community and Peru.

The Committee concluded that the final regulatory actions provided a sufficiently broad basis to merit including DNOC in the interim PIC procedure. It noted that those actions had led to a significant decrease in the quantities and uses of the chemical and the risks for human health and the environment. The Committee also took into account that the considerations underlying the final regulatory actions were not of limited applicability but of broader relevance. On the basis of information from Peru and other available information, the Committee concluded also that there was ongoing international trade in DNOC.

The Committee noted also that concern about intentional misuse of DNOC had not been a reason for the final regulatory actions.

The Committee concluded that the notifications of final regulatory actions by the European Community and Peru met the criteria set out in Annex II to the Convention.

Appendix II

Drafting Group on DNOC

Second-round comments on the draft internal working document for DNOC

POINT		AUTHOR	COMMENT	RESPONSE
Abbreviations				
		Ecuador and Australia	In "Abbreviations which may be used in this document, it does not be enclosed "DT50".	This abbreviation added (page II) since it appears 4 times in the DGD (point 1.8, point 4.1.1, point 4.1.2 (x 2), and point 4.1.5 (x 3).
		Australia	E.C.: European Community	No addition made since no abbreviation used in DGD. The only use was on page 10, now changed to European Community.
			K→k, Kg→Kg, POEM (Prediction → Predictive)	Agreed.
			L→ l	Agreed and consistency applied throughout DGD.
Decision Guidance Document				
1	Identification and uses	Ecuador	On the common name it would be better to write "DNOC and all its salts"	Amended to reflect the guidance provided by INC.9
		Australia	Has the Working Group been provided with sufficient evidence by the E.C. and Peru that the notifications cover other salts in addition to the ammonium salt?	Yes.
		Ecuador	On CAS - No.(s), are the potassium and ammonium salt and what about CAS number (2312-76-7)(The Pesticide Manual, A World Compendium. Twelfth Edition. 2000) for sodium salts ?	Agreed (page 1).
		Australia	Harmonised System Customs Code- Identical codes?	Text amended (page 1).
		Chile	CAS numbers of the salts should be indicated in Annex III	Noted: it will be listed in Annex III as INC 9 advised.
		Ecuador	In use(s) in regulated category after "ovicide", should said as well as "fungicide.	Agreed. (This was not an "intended use" in the E.C. regulation, but it is indicated in the EC documentation (page 6 of the monograph, point 1.4.1.1) that DNOC has a fungicide action).

POINT		AUTHOR	COMMENT	RESPONSE
2.1	Final regulatory action	Ecuador	In 2.1, Final regulatory action, about Peru, the first paragraph, last line, should said "valid for all types of formulations ...."	Language reflects that in Peruvian regulatory action. No change made pending confirmation from Peru (page 2).
2.3	Risk evaluation	Australia	2.3 → 2.2, plus other typographical corrections.	Agreed (page 2).
		Germany	add under point "2.3 Risk evaluation, European Community, Environmental Impact" after the first sentence, that "DNOC is highly toxic to honey bees (LD 50 oral: 2 µg/bee)".	Agreed, subject to reformulation (page 3). Amended and further revised to reflect information contained in the EU monograph that under field condition no significant risks were identified (see point 4.2.3 in the Annex 1). This has also been reflected in point 5.3 of Annex 1.
		Switzerland	Note, last line: … to cover all salts of DNOC.	Agreed (page 3).
3.1	Regulatory measure to reduce exposure	Ecuador	In 3.1, Regulatory measures to reduce exposure, about Peru, in the last line, instead of are prohibited, should said "were prohibited"	Agreed (page 3).
3.3	Alternatives	Ecuador	On page 4, in the second paragraph should said "The European Community and Peru did not provide any specific information on..."	Agreed (page 4).
4	Hazards and risks to human health …	Italy	A correct EU classification is given in the par. 4 of the draft. However in the 28th ATP the R40 phrase is replaced with R68.	Agreed. R 40: possible risks of irreversible effects was renumbered as R 68 after the EC had submitted its notification. Text amended accordingly (page 4).
4.2	Packaging and labelling	Switzerland	- Hazard Class: Cancel UN Subsidary Risks: 8 (See UN Recommendations on the transport of dangerous goods, Model Regulations 2001) - International Maritime dangerous Goods (IMDG) Code: …..(amendment: IMDG, …. …. The Maritime Safety Committee, 30-00, 2000)	Agreed (page 5). Agreed (page 5).

Introduction to the annex				
		Australia	Was this document referenced in either of the notifications from E.C. or Peru? If not, should not be included as this Annex only includes very limited data from sources not referenced by the notifications in support of their final regulatory actions eg WHO first aid information	Noted: The working paper on preparing internal proposals and DGDs states on page 5 in relation to Annex 1 that 'The results of international reviews such as those of WHO/IPCS/JPMR should also be included in this section where available and considered relevant.' In line with the approach taken for monocrotophos a brief comparative summary of the EHC evaluation has been prepared and inserted in Section 2.2.7. The specific references in individual sections of Annex I have been removed and the remaining text checked against the information contained in the monograph on DNOC submitted by the European Commission to ICRC3.
Annex 1: Further information on the substance				
2	**Toxicological properties**			
2.1.3	Absorption, distribution, excretion and metabolism	Australia	Editorial changes	Agreed (page 9-10).
2.2.1	Acute Toxicity	Australia	Editorial changes (dermal)	Agreed (page 10).
2.2.2	Short-term toxicity	Australia	In section 'oral', first sentence: add Charles River before 'rats' In the same section, delete: The NOEL was set at 2.89 mg/kg bw/day. In the same section, add: IPCS, 2000 (ref. ?)	No change made. The strain was not indicated for other species throughout the DGD (page 11). However, we have added F-344 rats in point 2.2.4 and Sprague-Dawley rats in point 2.2.5 because the choice of the strain is important in carcinogenicity and toxicity for reproduction. No change made. Information from EC supporting documentation (page 18 of the EC monograph). No change made. Summary of principal conclusion of EHC is in section 2.2.7.

			Introduce separate sections on dermal and inhalation	Agreed (page 11).
2.2.3	Genotoxicity	Australia	Typo	Agreed (page 11).
2.2.4	Long-term toxicity and carcinogenicity	Australia	Editorial	Agreed (page 12).
		Italy	In par. 2.2.4 is stated "The NOELs for long-term toxicity were set at 0.59 mg/kg bw/day in males on the basis of increased food consumption....". Furthermore in par. 2.2.7 is stated "The calculation of the ADI was carried out from the NOEL in the most sensitive species. From the two-year study in rats, it was established as 0.1 mg/kg bw/day". Please explain this discrepancy.	Inconsistency in text has been corrected
		Australia	Add (ICPS, 2000)	No change made. This study is noted in the EC supporting documentation (section 2.2.7).
2.2.5	Reproduction	Australia	Editorial	Agreed (page 12).
2.2.7	Summary and Overall evaluation	Switzerland	2.2.7 Note … to cover all salts of DNOC.	Agreed (page 12-13).
3	**Toxicological properties**			
3.4	Operator Exp.	Australia	Minor editorial and formatting changes	Agreed (page 14).
3.5	Medical data	Australia	Minor editorial	Agreed, subject to further correction (page 16).
4.1.1	Environmental fate and effects/ soil	Australia	Minor editorial	Agreed (page 16).
4.1.5	Persistence	Australia	Editorial	Agreed (page 17).

4.2	**Ecotoxicity – Effects on non target organisms**			
4.2.1	Terrestrial vertebrates	Italy	In par. 4.2.1 and 5.1 of the Annex 1 an oral rat LD50 of 26 mg/kg bw is used as reference values for mammals risk evaluation. However in par. 2.2.1 the lower limits for the LD50 values are 20 an 16 mg/kg bw for rats and mice respectively. Please explain in the text the reason for that choice even there are not implications in the final risk evaluation.	Point 2.2.1 gives a range of pooled values (20-85 mg/kg) that originate from both notifying countries. During the EC review of the substance, the industry provided several values included in various peer-reviewed handbooks. The reviewing committee asked for primary publications. Among the available original papers, the value of 26 mg/kg was retained as the most reliable to serve as a basis of the EC risk evaluation. Small change made to point 4.2.1 to make it clear that the indicated LD50 value was that retained in the EC risk evaluation. No changes needed to points 2.2.1 and 5.1.
		Australia	Editorial, plus query over LD_0 .	Editorial agreed (page 18). LD50 and LD_0 have been included for pheasants and partridges from the supporting documentation..
4.2.3	Honey Bees & Other arthropods	Australia	Editorial. Use *Brassica napus* instead of 'rape's	Agreed (page 18). Wording at the end of the paragraph has also been modified to take account of change to point 2.3 of DGD.
	Summary	Australia	Typographical correction	Agreed (page 20). Wording also modified to take account of change to point 2.3 of DGD.
Annex 3 – Addresses of designated national authorities				
	EC	Australia	should there be a C entry as well	Changed to "CP" (page 23).
	General	Italy	A general lack of references is observed in the DGD and the Annex 1 drafts. References should be given for tox, eco-tox and phys-chem properties.	No changes made. All the data originate from the supporting documentation of the 2 notifying countries (references included) or from international sources such as EHC 220 (references cited). The drafting of the DGD was performed in line with the guidance document, following the same basic approach as the DGD on monocrotophos.

Annex II

Operation of the interim Prior Informed Consent procedure
for banned or severely restricted chemicals

DecisionGuidance Document

DNOC
(Dinitro-*ortho*-cresol)

Interim Secretariat for the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Introduction

The Rotterdam Convention is a multilateral environmental agreement of which the interim Secretariat is provided jointly by the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization (FAO) of the United Nations. The objective of the Convention is to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals in order to protect human health and the environment from potential harm and to contribute to their environmentally sound use, by facilitating information exchange about their characteristics by providing for a national decision-making process on their import and export and by disseminating these decisions to Parties.

Candidate chemicals for the Rotterdam Convention include those that have been banned or severely restricted by national regulatory actions in two or more Parties in two different regions. Inclusion of a chemical in the Convention is based on regulatory actions taken by Parties that have addressed the risks associated with the chemical by banning or severely restricting it. Other ways might be available to control/reduce such risks. However, inclusion does not imply that all Parties to the Convention have banned or severely restricted this chemical. For each chemical included in the Rotterdam Convention, Parties are requested to make an informed decision whether they consent or not to the future import of the chemical.

In the period before the Convention enters into force the interim PIC procedure is in operation which follows the obligations of the Convention. During this period chemicals are approved for inclusion in the interim PIC procedure by the Intergovernmental Negotiating Committee (INC).

At its XXXX session, held in XXXX on XXXX the Intergovernmental Negotiating Committee adopted the decision guidance document for DNOC with the effect that this chemical became subject to the interim PIC procedure.

The present decision guidance document was communicated to the Designated National Authorities on [xxxx] in accordance with Article 10 paragraph 2 of the Rotterdam Convention.

Purpose of the Decision Guidance Document

For each chemical included in the interim PIC procedure a decision guidance document has been approved by the Intergovernmental Negotiating Committee. Decision guidance documents are sent to all Parties with a request that they provide a decision regarding future import of the chemical.

The decision guidance document is prepared by the Interim Chemical Review Committee (ICRC). The ICRC is a group of government designated experts established in line with Article 18 of the Convention, that evaluates candidate chemicals for possible inclusion in the Convention. The decision guidance document reflects the information provided by two or more Parties in support of the national regulatory actions to ban or severely restrict the chemical. It is not intended as the only source of information on a chemical nor is it updated or revised following its adoption by the Intergovernmental Negotiating Committee.

There may be additional Parties that have taken regulatory actions to ban or severely restrict the chemical as well as others that have not banned or severely restricted it. Such risk evaluations or information on alternative risk mitigation measures submitted by Parties may be found on the Rotterdam Convention web-site.

Under Article 14 of the Convention, Parties can exchange scientific, technical, economic and legal information concerning the chemicals under the scope of the Convention including toxicological, ecotoxicological and safety information. This information may be provided directly to other Parties or through the Secretariat. Information provided to the Secretariat will be posted on the Rotterdam Convention website.

Information on the chemical may also be available from other sources.

Disclaimer

The use of trade names in this document is primarily intended to facilitate the correct identification of the chemical. It is not intended to imply any approval or disapproval of any particular company. As it is not possible to include all trade names presently in use, only a number of commonly used and published trade names have been included in this document.

While the information provided is believed to be accurate according to data available at the time of preparation of this Decision Guidance Document, the Food and Agriculture Organization of the United Nations (FAO) and the United Nations Environment Programme (UNEP) disclaim any responsibility for omissions or any consequences that may flow there from. Neither FAO nor UNEP shall be liable for any injury, loss, damage or prejudice of any kind that may be suffered as a result of importing or prohibiting the import of this chemical.

The designations employed and the presentation of material in this publication do not imply the expression of any opinion whatsoever on the part of FAO or UNEP concerning the legal status of any country, territory, city or area or of its authorities or concerning the delimitation of its frontiers or boundaries

ABBREVIATIONS WHICH MAY BE USED IN THIS DOCUMENT

(N.B. Chemical elements and pesticides are not included in this list)

<	less than
≤	less than or equal to
<<	much less than
>	greater than
≥	greater than or equal to
>>	much greater than
µg	microgram
a.i.	active ingredient
AchE	acetylcholinesterase
ACGIH	American Conference of Governmental Industrial Hygienists
ADI	acceptable daily intake
ADP	adenosine diphosphate
ALT	alanine amino-transferase
AOEL	acceptable operator exposure level
ArfD	acute reference dose
ATP	adenosine triphosphate
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BOEL	biological operator exposure limit
b.p.	boiling point
BSI	British Standards Institution
bw	body weight
^{o}C	Degree Celsius (centigrade)
CA	Chemicals Association
CAS	Chemical Abstract Service
CCPR	Codex Committee on Pesticide Residues
ChE	cholinesterase
CHO	Chinese hamster ovary
d	day
D	dust
DT_{50}	period required for 50% dissipation
EC_{50}	effect concentration, 50% (median effective concentration)
ED_{50}	effect dose, 50% (median effective dose)
EHC	Environmental Health Criteria
ERL	extraneous residue limit
FAO	Food and Agriculture Organization of the United Nations
g	gram
GAP	good agricultural practice
GL	guideline level
h	hour
ha	hectare
IARC	International Agency for Research on Cancer
IC_{50}	inhibition concentration, 50%
ICSC	International Chemical Safety Card
i.m.	intramuscular

ABBREVIATIONS WHICH MAY BE USED IN THIS DOCUMENT

(N.B. Chemical elements and pesticides are not included in this list)

i.p.	intraperitoneal
IPCS	International Programme on Chemical Safety
IPM	integrated pest management
ISO	International Organisation for Standardisation
IRPTC	International Register of Potentially Toxic Chemicals
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues)
k	kilo- (x 1000)
kg	kilogram
K_{oc}	organic carbon/water partition coefficient
K_{ow}	octanol/water partition coefficient
l	litre
LC_{50}	lethal concentration, 50%
LD_{50}	lethal dose, 50%
LD_0	lethal dose, 0%
LD_{100}	lethal dose, 100%
LD_{LO}	lowest lethal dose
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOEL	lowest observed effect level
Log P	logarithm of the octanol/water partition coefficient
m	metre
mg	milligram
ml	millilitre
m.p.	melting point
mPa	millipascal
MRL	maximum residue limit
MTD	maximum tolerated dose
NCI	National Cancer Institute (United States of America)
ng	nanogram
NIOSH	National Institute of Occupational Safety and Health (United States of America)
NOAEL	no-observed-adverse-effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OHS	Occupational Health and Safety
OP	organophosphorus pesticide
p	same as K_{ow}
Pa	pascal
PHI	pre-harvest interval
PIC	Prior Informed Consent
POEM	predictive operator exposure model
POP	Persistent Organic Pollutant
ppm	parts per million

ABBREVIATIONS WHICH MAY BE USED IN THIS DOCUMENT
(N.B. Chemical elements and pesticides are not included in this list)

RfD	reference dose (for chronic oral exposure. Comparable to ADI)
SMR	standardised mortality ratio
STEL	short term exposure limit
TADI	temporary acceptable daily intake
TER	toxicity/exposure ratio
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRL	temporary maximum residue limit
TWA	time weighted average
ULV	ultra low volume
UNEP	United Nations Environment Programme
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VOC	volatile organic compound
WHO	World Health Organisation
wt	weight

Decision guidance document for a banned or severely restricted chemical

DNOC

Published:

1. Identification and uses (see Annex 1)

Common name	**DNOC** (BSI, E-ISO). Throughout this Decision Guidance Document, DNOC means "DNOC and its salts, such as ammonium, potassium and sodium salts".
Chemical name **Other names/ synonyms**	4,6-dinitro-*o*-cresol (IUPAC) 2-methyl-4,6-dinitrophenol (CAS) (Synonyms: 2,4-dinitro-6-methylphenol, 3,5-dinitro-o-cresol, 2,4-dinitro-o-cresol, DNC)
CAS-No.(s)	DNOC, CAS no. 534-52-1 ammonium salt, CAS no. 2980-64-5 potassium salt, CAS no. 5787-96-2 sodium salt, CAS no. 2312-76-7
Harmonised System Customs Code	2908.90 – active ingredient. 3808.10 – formulated product put up as insecticide. 3808.20 – formulated product put up as fungicide. 3808.30 – formulated product put up as herbicide.
Category	Used as a pesticide and as an industrial chemical.
Regulated Category	Pesticide
Use(s) in regulated category	Used as a defoliant in deciduous fruit tree orchards, as a post-emergent herbicide in apple orchards as well as a dessicant for potato haulm. Also used in the winter treatment of orchards as an insecticide, larvicide, and ovicide and fungicide.
Trade names	Antinonin, Bonitol, Dekrysil, Detal, Dinitrol, Dinitrosol, Effusan, Ibertox, K III, K IV, Kapsizole, Lipan, Luxan DNOC Crème 46%, Prokarbol, Supersinox SC, Technolor, Trifanex (130 g DNOC/1), Trifina, Trifocide SC (625 g DNOC ammonium salt/1), Trifocide 50%EC, 2,5 EC, Veraline 10.0% EC *Trade names no longer in use*: Elgetol, Extar-A (Bayer), Nicil, Nitrador, Sandoline, Selinon 615 SC (Bayer), Sinox.
Formulation types	Available as free acid or salts (such as ammonium, potassium or sodium salts) in a variety of formulations**,** such as soluble concentrate (SL), suspension concentrate (SC), emulsifiable (aqueous or oily) concentrate (EC), paste (PA), wettable powder (WP) or cream. The concentration of active ingredient (a.i.) in these formulations ranges from 130 to 560 g/l. It is not known if DNOC is also available in mixtures with other active ingredients.
Uses in other	Industrial use: DNOC is used in the plastics industry as an inhibitor of

categories	polymerisation in styrene and vinyl aromatic compounds. It is also used as an intermediate for synthesis of other fungicides, dyes and pharmaceuticals (IPCS, 2000).
Production	The world-wide annual production of DNOC was approximately 2000 tonnes in the 1950s, all of which was used in agriculture. Currently, of the 600 tonnes or so manufactured annually, 400-500 tonnes are used for industrial purposes and 100-200 tonnes as an agrochemical (IPCS, 2000).
Basic manufacturers	BAYER SA, ELF ATOCHEM AGRI B.V. (The Netherlands). *This is an indicative list of current and former manufacturers of DNOC. It is not intended to be exhaustive.*

2. Reasons for inclusion in the PIC procedure

DNOC and its salts, such as the ammonium, potassium and sodium salts is included in the PIC procedure as a pesticide. It is listed on the basis of the final regulatory actions to ban all agricultural uses of DNOC notified by the European Community and Peru.

No final regulatory actions relating to industrial chemical uses have been reported.

2.1 Final regulatory action: (see Annex 2 for details)

European Community
The authorisations for plant protection products containing DNOC had to be withdrawn by 16 August 1999 in accordance with Commission Decision 1999/164/EC of 17/02/1999 (Official Journal of the European Community L54 of 02/03/1999, p. 21). From the latter date, no authorisations for plant protection products containing DNOC could be granted or renewed.
Reason: Concerns with regard to operator exposure and non-target organisms.

Peru
DNOC was prohibited for registration, import, local formulation, distribution, trade and use (Resolución Jefatural N° 182-2000-AG-SENASA). This prohibition of the pesticidal uses of DNOC entered into force on 9 October 2000 and is valid for formulations as well as for the technical material.
Reason: Concerns with regard to human health and the environment.

2.2 Risk evaluation

European Community
Pursuant to Article 8 (2) of the Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market, DNOC was reviewed to determine whether or not it should be included in Annex I to this Directive (the list of active ingredients that can be used in plant protection products).

In the Member States, DNOC containing pesticides were registered for two main applications, which were considered in the risk evaluation:

Spraying onto fruit trees (apple trees, stone fruits, vine) to control aphids (including eggs), scales, mites, fungi (*e.g. Phomopsis viticola)*, vectors of viruses, other sucking insects, acarids (*e.g. Colomerus vitis*) and other diseases. The intended doses to be used range from 840 to 8400 g of DNOC/ha once a year in orchards and viticulture as a winter spray.

Application as ammonium salt onto potatoes to prevent the development of infectious or viral diseases that could contaminate the tuber. The proposed application rates range from 2500 to 5600 g of DNOC/ha twice a year for the herbicide contact action as a desiccant for potato haulm.

Based on the information available and the proposed conditions of use, it was concluded from the evaluation that DNOC could not fulfil the safety requirements set out in Article 5 (1) (a) and (b) of Council Directive 91/414/EEC. The evaluation identified concerns with regard to the safety of DNOC, in particular with regard to operator exposure and non-target organisms. The main issues are detailed below.

Human Health and Safety
From the toxicological assay results available, the following conclusions on DNOC health hazards were reached: DNOC is very toxic by inhalation, contact with skin and if swallowed. This active ingredient is a potential mutagen and the risk of irreversible effects cannot be excluded. DNOC is also irritating to the skin and may cause sensitisation by skin contact. The risk of serious damage to the eyes has been demonstrated.

No monitoring for operator exposure under normal conditions was performed. Therefore, the United Kingdom Predictive Operator Exposure Model (POEM) and the German model were used to evaluate the exposure for each category of application (orchard trees/potatoes). Toxicological data were missing in a number of key areas, but when using an AOEL (Acceptable Operator Exposure Level) of 0.0034 mg/kg/day, determined on the basis of the available data, exposure levels for an operator wearing gloves were of concern. For further details, see Annex I.

The residues, following an application consistent with good plant protection practices, were studied in order to assess any harmful effects on human or animal health. Considering the intended uses of DNOC, potatoes are the only foodstuffs that are likely to be contaminated. Residue levels in potatoes were lower than the Limit of Detection (LOD) of 0.05 mg/kg, which is identical to the proposed maximum residue limit (MRL). Assuming that the intake is equal to the LOD, consumer dietary exposure (for a standard person) was expected to be close to the temporary ADI of 0.001mg/kg/day that was established (for further details, see Annex I).

On this basis, it was concluded that potential operator exposure levels were of concern and that further data were required for all registered uses. In addition information was needed on the efficiency of gloves in reducing exposure. The potential dietary/consumer exposure from the consumption of treated potatoes was also of concern.

Environmental Impact

From the available data, a high risk to mammals from all the intended uses, a high acute risk to aquatic life at higher application rates and a medium chronic risk to aquatic life were identified. DNOC is not very toxic to earthworms and only higher application rates pose a risk to them. The bioconcentration factor is low (log P < 3). DNOC is highly toxic to honey bees in laboratory conditions (LD_{50} oral: 2 µg/bee)but, has been shown to be only slightly toxic to them under field conditions.

After considering the test data available, it was concluded that DNOC is dangerous for the environment, as it is very toxic to terrestrial and aquatic organisms and may cause long term adverse effects in the environment.

Note: Effects on target organisms and toxicity/ecotoxicity for non-target organisms are due to either the phenolic form of DNOC or the phenolate once absorbed into the organisms. It does not matter from which form or salt the reaction started: in the organism there is rapid equilibration between the phenolic form and phenolate with various counter-ions (that are always present in organisms). The actual mode of action (*i.e*. interference with the energy-producing metabolism in the mitochondriae of the cells) is in general independent of the kind of cation present in the formulated plant protection product. Concerns related to this mode of action were the reason why the final regulatory action was intended to cover all salts of DNOC.

Peru
DNOC was registered in Peru for use as a defoliant in deciduous fruit tree orchards (apple, peach tree, pear and plum trees / vineyard) and as a post-emergent herbicide in apple orchards to control *Chenopodium murale* L. and *Cenchrus echinatus* L.

Based on a study of occupational exposure of farmers using DNOC it was concluded that the risks of continued use were greater than the benefits obtained.

Human Health and Safety
A study conducted in 1992 on the use of DNOC in the valley of Mala revealed that the level in the blood of applicators was significantly higher than in the blood of bystanders. Of the applicators interviewed, 73% admitted that they had suffered the poisoning symptoms explained to them. The following risk factors were observed among populations studied: long hours of exposure to the product, high application dose, short interval between applications, and lack of cleaning after application.

The toxicological hazards identified in the existing scientific data, taken together with the above study of exposure, indicate that the risk to farmers is high.

Environmental Impact
DNOC is toxic to fish and to bees. It is highly phytotoxic.

3. Protective measures that have been applied concerning the chemical

3.1 Regulatory measures to reduce exposure

European Community	From the assessments made, it was concluded DNOC did not satisfy the safety requirements laid down in Directive 91/414/EEC, in particular with regard to acceptable operator exposure and exposure of non-target organisms. As a result, authorisations for all DNOC products had to be withdrawn.
Peru	The registration, local formulation, distribution, trade and use of technical DNOC as well as formulations containing DNOC were prohibited.

3.2 Other measures to reduce exposure

This section should only be completed where a chemical has been subjected to a severe restriction and the notifying countries have allowed continued use of the chemical and associated products.

3.3 Alternatives

DNOC is a broad-spectrum non-systemic insecticide and acaricide with contact and stomach action, contact herbicide and fungicide, used in a wide range of crops. There are a number of alternative methods involving chemical and non-chemical strategies, including alternative technologies available, depending on the individual crop-pest complex under consideration. Countries should consider promoting, as appropriate, integrated pest management (IPM) strategies as a means of reducing or eliminating the use of hazardous pesticides.

The European Community and Peru did not provide any specific information on alternatives to DNOC.

Advice may be available through National IPM focal points, the FAO, agricultural research or development agencies. Where it has been made available by governments, additional information on alternatives to DNOC may be found on the Rotterdam Convention website www.pic.int

It is essential that before a country considers substituting alternative pesticides, it ensures that the use is relevant to its national needs and the anticipated local conditions of use.

3.4 Socio-economic effects

No detailed assessments of socio-economic effects were undertaken by the notifying parties.

4. Hazards and risks to human health and/or the environment

4.1 Hazard Classification

<table>
<tr><td rowspan="11">WHO</td><td>Technical a.i.:</td><td colspan="4">Ib (highly hazardous), classification based on oral toxicity in rats
LD_{50}: 25 mg a.i./kg bw (WHO 2000)</td></tr>
<tr><td>Formulations:</td><td colspan="4"></td></tr>
<tr><td></td><td colspan="2">Oral toxicity</td><td colspan="2">Dermal toxicity</td></tr>
<tr><td></td><td colspan="2">LD_{50} = 25 mg a.i./kg bw</td><td colspan="2">LD_{50} = 200 mg a.i./kg bw</td></tr>
<tr><td></td><td>a.i. (%)</td><td>hazard class</td><td>a.i. (%)</td><td>hazard class</td></tr>
<tr><td>Liquid</td><td>> 10</td><td>Ib</td><td>> 50</td><td>Ib</td></tr>
<tr><td></td><td>> 1</td><td>II</td><td>> 5</td><td>II</td></tr>
<tr><td>Solid</td><td>> 40</td><td>Ib</td><td>> 20</td><td>II</td></tr>
<tr><td></td><td>> 5</td><td>II</td><td>> 5</td><td>III</td></tr>
<tr><td></td><td>> 1</td><td>III</td><td></td><td></td></tr>
<tr><td>European Community</td><td colspan="4">Classification of the active substance is:
Mutagenic category 3; R 4068: possible risks of irreversible effects
T+; R26/27/28: very toxic by inhalation, contact with skin and if swallowed
Xi; R38: irritating to skin, R41: risk of serious damage to eyes
R43: may cause sensitisation by skin contact
R44: risk of explosion if heated under confinement.
N; R 50/53: dangerous for the environment, very toxic to aquatic organisms, may cause long-term effects in the aquatic environment.</td></tr>
<tr><td>US EPA</td><td colspan="4">Category 1 (highly toxic) (EPA 1985)</td></tr>
<tr><td>IARC</td><td colspan="4">Not classified</td></tr>
</table>

4.2 Exposure limits

Food
The Codex Alimentarius has not established any specific Maximum Residue Limits (MRLs) for DNOC.

The FAO/WHO Joint Meeting on Pesticide Residues (JMPR) reviewed DNOC in 1963 and 1965. It has not assessed a specific ADI or acute reference dose (ArfD).

Drinking Water
The WHO has not established a drinking water guideline value for DNOC.

4.3 Packaging and labelling

Hazard Class: The United Nations Committee of Experts on the Transportation of Dangerous Goods classifies DNOC (UN number = 1598) in: Class 6, Division 6.1 (Toxic substances).

Packing:	UN Pack Group: II substances and preparations presenting a serious toxicity risk, formulations containing 50–100% DNOC (LD_{50} (oral, rat) = 25 mg/kg bw). Special provisions: 43 When offered for carriage as pesticides, these substances shall be carried under the relevant pesticide entry (in the case of formulated products) and in accordance with the relevant pesticide provisions.
Limited quantities:	500 g is the maximum quantity per inner packaging authorised for transport of the substance.
Storage:	Separated from strong oxidants, food and feedstuffs.
International Maritime Dangerous Goods (IMDG) Code:	DNOC is classified as a marine pollutant. (amendment: IMCOCIMDG, IMO Dangerous Goods Code, Recommendation prepared by The Maritime Safety Committee, 26-91, 10054, 199130-00, 2000)

For specific guidance on appropriate symbols and label statements regarding formulations of DNOC countries should consult the *FAO Guidelines on Good Labelling Practice for Pesticides (1995)*

4.4 First aid

NOTE: The following advice is based on information available from the World Health Organisation (IPCS 2000) and was correct at the time of publication. This advice is provided for information only and is not intended to supersede any national first aid protocols.

Signs and symptoms of acute DNOC poisoning in humans include yellowish skin tissues and nausea, vomiting, fever, gastric distress, restlessness, sensation of excessive heat, sweating, thirst, deep and rapid respiration, retrosternal pain, mental disorders, tachycardia, pyrexia, cyanosis, collapse and coma. Death is promptly followed by intense *rigor mortis*. A hot environment enhances the intensity of the symptoms and shortens the time before their onset. Acute DNOC poisoning runs a rapid course, and the general rule is either death or recovery within 24–48 h.

First aid personnel should wear nitrile over latex gloves to avoid contamination. Contaminated clothing and contact lenses should be removed as quickly as possible to prevent further absorption. If skin contact occurs, the area should be washed with soap and water. Eyes should be washed for 15–20 minutes with running water or saline solution. In the case of ingestion, if the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical. If the victim is unconscious or convulsing, do NOT give anything by mouth and do NOT induce vomiting. The stomach should be emptied as soon as possible by careful gastric lavage, preferably within one hour of ingestion. In massive overdoses, acute respiratory failure may occur. It is important to keep the airway open and to prevent aspiration if nausea and vomiting occur.

Persons who have been poisoned (accidentally or otherwise) must be transported immediately to a hospital and placed under the surveillance of properly trained medical staff. Where possible show the label of the DNOC container when the patient/affected person is presented for medical attention.

If the substance is formulated with solvent(s), also consult the International Chemical Safety cards (ICSC) of the solvent(s). Carrier solvents used in commercial formulations may affect the toxicity of the active ingredient by altering its extent of absorption from the gastrointestinal tract or through the skin (www.inchem.org).

4.5 Waste management

Regulatory actions to ban a chemical should not result in creation of a stockpile requiring waste disposal. For guidance on how to avoid creating stockpiles of obsolete pesticide stocks the following guidelines are available: FAO Guidelines on Prevention of Accumulation of Obsolete Pesticide Stocks (1995), The Pesticide Storage and Stock Control Manual (1996) and Guidelines for the management of small quantities of unwanted and obsolete pesticides (1999).

The European Community avoided creating stockpiles of DNOC by taking a stepwise approach to the phase-out of permitted uses (See Annex 2). It was considered that the risk was manageable during this phase out period.

In all cases waste should be disposed of in accordance with the provisions of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal (1996), any guidelines thereunder (SBC, 1994) and any other relevant regional agreements.

It should be noted that the disposal/destruction methods recommended in the literature are often not available in, or suitable for, all countries e.g. high temperature incinerators may not be available. Consideration should be given to the use of alternative destruction technologies. Further information on possible approaches may be found in Technical Guidelines for the Disposal of Bulk Quantities of Obsolete Pesticides in Developing Countries (1996).

Annexes

Introduction to Annex I

The information presented in this Annex reflects the conclusions of the two notifying parties: the European Community and Peru. In a general way, information provided by these two parties on the hazards are synthesised and presented together, while the risk assessments, specific to the conditions prevailing in these parties, are presented separately. This information is contained in the documents referenced in the notifications in support of their final regulatory actions banning DNOC. The notification from Peru was first reported in the PIC Circular XIII of June 2001 and the notification from the European Community in PIC Circular XIV of December 2001.

DNOC was the subject of an IPCS Environmental Health Criteria document (Dinitro-ortho-cresol, EHC 220) published in 2000. The conclusions concerning the toxicity of DNOC were not substantially different from that reported here. Section 2.2.7. includes a brief summary of the conclusions of the European Community and IPCS evaluations.

The FAO/WHO Joint Meeting on Pesticide Residue (JMPR) assessed DNOC in 1963 and 1965. These evaluations are outdated and can be regarded as superseded by the reviews of the European Community and the IPCS. Accordingly, they were not included here.

Annex 1 – Further information on the substance

1. Physico-Chemical properties

1.1	**Identity**	DNOC
1.2	**Formula**	$C_7H_6N_2O_5$
1.3	**Chemical name (IUPAC)**	4,6-dinitro-*ortho*-cresol
1.4	**Chemical type**	Dinitrophenol
	Form	Pure DNOC: yellow green crystalline powder
1.5	**Solubility**	In water: 0.213 g/l at pH4, 6.94 g/l at pH7, 33.3 g/l at pH10. At 25°C in toluene: 251 g/l, acetone: 514 g/l, dichloromethane: 503 g/l, ethyl acetate: 338 g/l, hexane: 4.03 g/l, methanol: 58.4 g/l
	Log P	1.78 at pH4, 0.087 at pH7, -1.32 at pH10
1.6	**Vapour pressure**	1.6×10^{-2} Pa at 25 °C
1.7	**Melting point**	85.2 – 89.9 ºC
1.8	**Reactivity**	Hydrolysis: stable in sterile water at all pH after 5 days, $DT_{50} > 1$ year
1.9	**Stability**	Risk of explosion if heated under confinement. Also risk of explosion when dry, which can be reduced by moistening with up to 10 % water. No auto-ignition below 400 °C. DNOC is a pseudo-acid and readily forms water-soluble salts with alkalis. The concentration of DNOC in ionised form increases as the pH increases and at pH ≥ 7, 100 % of DNOC is ionised.
1.10	**Molecular Weight**	198.13

2 Toxicological properties

2.1 General

2.1.1 Mode of action

DNOC is a substituted dinitrophenol compound. It acts mainly as an inhibitor of oxidative phosphorylation at the mitochondrial level, inducing a significant increase in basal metabolism and hyperthermy. The oxidation of carbohydrate forms the main source of energy of the body and the energy is "stored" in the form of compounds containing phosphate (high energy phosphate bonds of adenosine triphosphate or ATP). This compound is then a source of energy to the body. DNOC inhibits the formation of ATP. In the presence of DNOC the oxidative process continues and is even increased, but the energy cannot be converted to a useable form and it is therefore dissipated as heat. In muscle ATP cannot be re-synthesized and is progressively broken down to adenylic acid. The shortage of ATP may lead to muscular paralysis which for critical organs, such as heart and respiratory muscles, includes a blocking of their vital functions and in the case of death by DNOC poisoning, to early rigor mortis.

2.1.2 Symptoms of poisoning

DNOC is extremely toxic for human beings. Symptoms of acute toxicity include abnormal fatigue, excessive sweating, hyperthermia, tachycardia, headache, nausea, loss of appetite, coma and yellow pigmentation of the eye.

Exposures to high levels of DNOC for short periods may cause convulsions, unconsciousness and death. A hot environment enhances the intensity of the symptoms and shortens the time before their onset. Ingestion of DNOC for long periods may cause cataract and dermal eruption.

2.1.3 Absorption, distribution, excretion, and metabolism in mammals

Absorption: The blood concentration is at a maximum 2-4 h after administration by the oral route to rats (1-100 mg/kg bw). Blood concentration maxima are reached 24 h and 48 h after dermal application (18 mg/kg bw, 8 h exposure) to female and male rats respectively. At the peak level, the plasma concentrations represented 2.5 and 5.0-5.8 % of the applied dose of a water-based and an oily DNOC formulation respectively. Percutaneous absorption in rabbits and rats increases with temperature

Distribution and excretion: In general, the concentration of DNOC in the blood is much higher than in other tissues and, over 90% of the DNOC in the blood are found in the plasma. At 24h after a single radiolabelled oral dose to rats at 0.4 mg/kg, 15% of the administered dose was found in the blood, 6.6% in the gastrointestinal tract, 5% in the liver, 1.0% in the kidneys and 28% in the residual carcass. The faeces contained 10.1% of the radioactivity and urine 28.7% with a total recovery at 24 h of 94.4%. More generally, DNOC is excreted in urine as free DNOC and acetylated conjugate 6-ANOC, conjugated as 6-acetamido-4-nitro-o-cresol (6-AcANOC).

Accumulation: The elimination half-life of a single oral dose in rats is 1–1.5 days. Studies in man show that DNOC has a tendency for accumulation with a half life that varies according to the authors from 4 to 7 days.

It is concluded that humans retain DNOC longer than other tested species.

Metabolism: The metabolic routes of DNOC appear to be comparable in rats and rabbits. The main metabolic pathway is the reduction of one of the 2 nitrated substituents of DNOC to form the amino derivatives viz. 6-amino-4-nitro-o-cresol (6-ANOC), and to a lesser extent to 4-amino-6-nitro-o-cresol (4-ANOC). One of the routes of metabolisation is the reduction of one of the 2 nitrated substituents either in position 4 to form the 4-amino derivative product, or in position 6 to form the 6-amino derivative product. Another route leads to the oxidation of the remaining methyl to form 3.5-dinitro-2-hydroxy benzyl alcohol.

2.2 Toxicology Studies

2.2.1 Acute toxicity

Oral

DNOC is very toxic by the oral route, with LD_{50} values ranging from 20 to 85 mg/kg bw for rats, 16-47 mg/kg bw for mice, 50 mg/kg bw for cats, 200 mg/kg bw for sheep and 100 mg/kg bw for goats.
Signs of acute toxicity include hyperactivity, laboured breathing, asphyxial convulsions, coma and death. An increase in environmental temperature enhanced the acute toxicity of DNOC in rats.

Dermal

The acute dermal toxicity of DNOC is solvent-dependent corresponding to low to high toxicity in rats with LD_{50} values ranging from 200 (water) to > 2000 mg/kg (moistened with peanut oil). The LD_{50} is about 1000 mg/kg bw in rabbits

Inhalation

The LC_{50} (aqueous formulation containing 50% DNOC, 4h) is 0.23 mg DNOC/l of air.

Irritation

DNOC is irritating to rabbit's skin and corrosive to rabbit's eyes (tests using New Zealand rabbits).

Sensitisation

DNOC induces skin sensitisation in 100% of guinea pigs tested according to the method of Magnusson and Klingman.

Acute reference dose (ARfD): No ARfD has been reported. .

2.2.2 Short-term toxicity

Oral

A six-week range-finding study was conducted on **rats** fed daily diets containing 0, 5, 13, 32, 80 or 200 mg/kg of 99.5% pure DNOC corresponding to 0, 0.44, 1.17, 2.89, 7.24 and 18.6 mg/kg bw/day. No treatment- related mortality was recorded. No significant effects were observed on food consumption, body temperature and haematology, and no abnormalities were seen at necropsy. However, at the two highest concentrations, the body-weight gain of the females was reduced, a slight, but significant decrease in alanine aminotransferase (ALT) activity was observed and the blood urea level was slightly, but significantly elevated in the females. The NOEL was set at 2.89 mg/kg bw/day.

In a 90-day feeding study, Wistar rats were administered a diet containing DNOC at doses equivalent to 0, 2.5, 5, 10 or 20 mg/kg bw. At the highest dose, 25 % of the rats died and mortality was also observed at 10 mg/kg bw/day. The highest dose was well above the maximum tolerated dose which should be considered to be the next lower dose (10 mg/kg bw). At the two highest doses, body-weight gain was depressed in a dose-related manner; and levels of glucose and urea were increased in both sexes. No histopathological alterations were observed in any groups other than the high dose group. Levels of pyruvates and thyroid hormones T_3 and T_4 levels were decreased at all dose levels. In view of the decreased levels of pyruvate and thyroid hormones at all dose levels a definitive NOEL could not be established. The NOEL would be below the lowest dose level of 2.5 mg/kg bw/day.

A 90-day study was performed on **dogs** receiving 0.17, 0.89 or 4.82 mg/kg bw/day of DNOC in their diet. A limited number of biochemical examinations were performed. No mortalities were recorded. The main effects at the two highest doses were an increase in activity and a decrease in the prothrombin time in the males. A weight increase in the liver in the females was observed at the highest dose only. Food consumption was not changed at any dose level, but there was a reduction in body weight gain in both males and females. This effect is likely related to the mechanism of action of DNOC. The NOEL was set at 0.17 mg/kg bw/day based on the effect observed on body weights at the high concentration.

Dermal, : No information.

Inhalation: No information.

2.2.3 Genotoxicity (including Mutagenicity)

DNOC has been studied in many *in vitro* and *in vivo* systems with contradictory results. The European Community concluded that the available data were inconclusive, but in order to protect human health it decided to classify DNOC as mutagen Category 3.

2.2.4 Long-term toxicity and carcinogenicity

In a two-year study male and female F-344 rats were exposed to DNOC at dietary concentrations of 0, 2.5, 15 or 100 mg of 99.5 % pure DNOC/kg. These concentrations were equivalent to a daily intake of 0.12, 0.75 and 5.03 mg/kg bw in the females and to 0.10, 0.59 and 4.12 mg/kg bw in the males. No significant difference in the mortality rate was observed in the same study between the groups. No clinical signs of adverse effects from the treatment were recorded. In the male rats treated at the highest concentration, food consumption was found to be slightly higher than in the controls (+6%) from week 5 onwards. An increase in food consumption was noted at 0.59 mg/kg bw/day in males from week 84 (+8%). No effect was noted on the body-weight gain of the animals. No significant alterations were recorded in the haematological and biochemical parameters evaluated in the course of the experiment. No carcinogenic effects were demonstrated over the course of the study. The NOELs for carcinogenic effects were set at 5.03 and 4.12 mg/kg bw/day in male and female rats respectively. The NOELs for long-term toxicity were set at 0.59 10 mg/kg bw/day in males on the basis of increased food consumption, (next lowest dose in the same study), and 5.03 mg/kg bw/day in females (highest administered dose).

2.2.5 Effects on reproduction

Reproduction

Developmental effects

In a teratogenic study groups of pregneant Wistar rats were exposed to DNOC equivalent to 0, 1, 5 and 25 mg/kg bw from the 6th to the 15th day of gestation. The high does was maternotoxic and a decrease in food consumption was noted at the high dose. No sign of embryo or foetal toxicity was noted and no particular malformations were observed. A **NOEL** for maternotoxicity was set at 5 mg/kg bw/day. The **NOEL** for fetotoxicity was set at 25 mg/kg/day (the highest dose tested).

Groups of pregnant rabbits received doses of 0, 4.0, 10.0, 25 mg DNOC/kg bw/day by gavage on days 6–18 (inclusive) of gestation. The highest dose was maternotoxic; these dams showed clinical signs of toxicity and produced litters with increased incidence of either external or visceral malformations or skeletal variations. The **NOEL** for teratogenicity was set at 10 mg/kg bw/day.A study was conducted in rabbits by the oral route. At 22 mg/kg bw/day, teratogenic effects of DNOC were evidenced, being hydrocephalia, microcephalia, incomplete ossification of the sternebra and bones of the phalanx. However, this dose is a maternotoxic dose. The teratogenic **NOEL** was set at 10 mg/kg bw/day.

2.2.6 Neurotoxicity/ Delayed neurotoxicity

Neurotoxic effects are not expected given the molecular structure of DNOC and were not observed in subacute and chronic toxicity studies in several animal studies.

2.2.7 Summary and overall evaluation

Note: Effects on target organisms and toxicity/ecotoxicity for non-target organisms are due to either the phenolic form of DNOC or the phenolate once absorbed into the organisms. It does not matter from which form or salt the reaction started: in the organism there is rapid equilibration between the phenolic form and phenolate with various counter-ions (that are always present in organisms). The actual mode of action (*i.e*. interference with the energy-producing metabolism in the mitochondriae of the cells) is in general independent of the kind of cation present in the formulated plant protection product. Concerns related to this mode of action were the reason why its final regulatory action was intended to cover all salts of DNOC.

European Community

Human beings are more likely to accumulate DNOC than other mammals, due to a slower elimination rate.

The oral LD_{50} in rats ranges from 20 to 85 mg/kg bw, thus classifying the active ingredient as very toxic if swallowed according to European Community rules.

The dermal LD_{50} in rats is in the range of 200 to over 2000 mg/kg, depending on the solvent applied, thus classifying DNOC as very toxic by contact with the skin according to European Community rules.

Inhalation LC_{50} values of 0.23 mg/l for a 4 h exposure in rats classify DNOC as very toxic if inhaled according to European Community rules. DNOC is irritating to the skin (New Zealand rabbits), corrosive to the eye (New Zealand rabbits) and is a skin sensitiser in guinea-pigs.

Short-term dietary administration of DNOC for up to 90 days decreased body-weight gain in rats and dogs, usually without significant alteration in food consumption. At high doses the liver was affected. Blood urea levels were also increased at high dosages.

In a long-term dietary feeding study in rats, DNOC did not induce any treatment-related adverse effects at doses of up to 5 mg/kg bw/day. No increase of any type of tumour was observed.

On the basis of all the data available, the mutagenicity of DNOC remains equivocal.

Teratogenic effects were observed only at maternotoxic doses.

No ARfD was established.

The calculation of the ADI was carried out from the NOEL in the most sensitive species. From the two-year study in rats, it was established as 0.1 mg/kg bw/day. Given that in this study no carcinogenic effects were shown and that teratogenic effects were demonstrated at higher doses in rabbits, a safety factor of 100 was used: ADI = 0.1/100 = 0.001 mg/kg/day. The choice of this ADI allows a margin of safety (MOS) of 10,000 with respect to the teratogenic risk as the teratogenic no-effect level by oral administration in rabbits is 10 mg/kg bw/day.

IPCS 2000

The International Programme on Chemical Safety (IPCS) published an Environmental Health Criteria document on Dinitro-ortho-cresol (DNOC) in 2000 (EHC 220).

DNOC is an uncoupler of oxidative phosphorylation and toxic effects observed either in human or in animals result from this mechanism.

Clinical symptoms occur after a relatively short period of exposure. Symptoms include nausea, gastric distress, restlessness, a sensation of heat, excessive sweating, thirst, deep respiration, tachycardia and hyperpyrexia. In severe cases, collapse, coma and death occurred within 24 – 48 h.

The metabolic pathway of DNOC is qualitatively similar across several species. However the rate of DNOC elimination varies substantially across species. Humans retain DNOC longer than other species tested.

In animal studies the oral LD_{50} values, as determined in several species, range from 16 – 100 mg/kg bw.

On the basis of all the data available the mutagenicity of DNOC remains equivocal.

A rat carcinogenicity study did not show any carcinogenic effects. Histopathological examination did not reveal any alteration in any organ that could be attributable to an effect of the treatment with DNOC. No increase in the incidence of any type of tumour was recorded. A **NOEL** of 0.59 mg/kg bw/day. was determined in males on the basis of increased food consumption, and 5.03 mg/kg bw/day in females (highest administered dose).

In a multi-generation reproduction study male and female Sprague-Dawley rats were exposed to 15, 30 and 100 mg DNOC/kg diet throughout maturation, mating, gestation and lactation phases for two successive generations. At the highest dose, during the gestation phase of the F_0 generation there was a significant reduction in mean body weight, and a reduction in food consumption during lactation. In this group the mean litter size and weight at birth were comparable to controls, but were reduced on days 14 and 21 of lactation. The **NOEL** was set at 30 mg/kg diet, equivalent to 1.73 mg/kg bw/day for the F_0 males, 2.24 mg/kg bw/day for the F_0 females, 2.40 mg/kg bw/day for the F_1 males and 2.61 mg/kg bw/day for the F_1 females.

Teratogenicity studies performed in rats and rabbits showed that DNOC induced embryotoxicity and teratogenic effects only at dose levels that were also maternally toxic. In rats the **NOAEL** for teratogenicity and for embryotoxicity was set at 25 mg/kg/bw/day (highest dose tested). In rabbits the **NOAEL** was set at 10 mg/kg/bw/day for foetal effects, on the basis of the malformations observed in the high dose group.

3 Human exposure/Risk evaluation

3.1 Food

European Community

DNOC was registered for application on fruit trees when no fruits and haulm were present. The treatment was carried out in winter 5 to 6 months before harvest. DNOC is not systemic and is rapidly degraded.

Potatoes were treated at 5 kg/ha and only four trials were acceptable (7 days of pre-harvest interval). The residue levels were 0.02 mg/kg or less.

No significant residues of DNOC are expected in potatoes and fruits when plants are treated with DNOC. As DNOC has not been actually detected in treated fruits and potatoes, maximum residue limits (MRLs) were set at the level of 0.05 mg/kg, corresponding to the limit of detection of the residue determination method. Assuming a typical consumer, an adult of 60 kg, and assuming consumption is 328.5 g of potatoes per person per day, the estimated residue intake is 0.00027 mg/kg bw/day or 27% of the ADI.

The maximum residue intake through feed for dairy and beef cattle, pigs and chickens was calculated assuming residues for potatoes at the MRL level (0.05 mg/kg). The theoretical residue intake ranges from 0.0016 mg/animal/day for chickens to 1.8 mg/animal/day for beef cattle.

It was concluded that residues might appear on potatoes and in potato-eating animals, whereas for fruit on fruit trees, the interval between treatment and harvest is great enough to avoid any significant residue.

3.2 Air

DNOC has a low potential to volatilise. Significant exposure of the general population is not expected.

3.3 Water

Not relevant

3.4 Operator Exposure

European Community

In line with internationally accepted practices, the occupational risk evaluation was based on hazard characteristics and worker exposure. There were no measured worker exposure studies for mixing, loading or application of DNOC. Therefore the United Kingdom POEM model was used to estimate exposure for the proposed uses in potatoes and in orchards.

An Acceptable Operator Exposure Level (AOEL) was established based on the NOEL of 0.17 mg/kg bw/day in a 90 day study on dogs and using a 50 fold safety factor:

AOEL = 0.17 mg/kg/day/50 = 0.0034 mg/kg/day

The safety factor was established based on the following considerations:

- The nature of the protocol (limited with regard to biochemical examination) in the 90 day dog study
- The results of the mutagenicity studies were ambiguous
- The lack of a fertility study over two generations and a carcinogenicity study in a second species

Orchard use:
The following parameters were used for the evaluation during the treatment of orchards with a formulation containing 560 g DNOC/l:

- Quantity applied: 8.4 kg of DNOC/ha (highest recommended use)
- Surface treated: 5 ha/day/person (this is a relatively small surface),
- Volume sprayed: 1,500 l/ha (highest recommended use)
- Packaging: jerry can of 10 l with an opening of 49 mm.

Under these conditions, a 70 kg operator without any special protection either during preparation or during spraying is exposed to 0.49 mg/kg/day, taking into account a permeability through the skin of 5%, which is a low estimate. This exposure is of the order of 144 times greater than the AOEL (0.0034 mg/kg/day).

For a 70 kg operator wearing gloves the exposure becomes 0.039 mg/kg/d. This exposure remains 10 times greater than the AOEL.

Potato use:
The following parameters were used in the evaluation of a formulation containing 200 g/l of DNOC ammonium salt used as a desiccant for potatoes haulm:

- Quantity applied: 5 kg/ha/day/person
- Surface treated: 10 hectares/day/person (this is a relatively small surface)
- Volume sprayed: 500 l/ha
- Packaging: jerry can of 20 lL with an opening of 49 mm.

Under these conditions, a 70 kg operator without any special protection either during the preparation of the formulation to be sprayed or during spraying is exposed to 0.401 mg/kg bw/day, taking into account a permeability through the skin of 5%, which is a low estimate. This exposure is of the order of 118 times greater than the AOEL (0.0034 mg/kg/day).

For a 70 kg operator wearing gloves the exposure is 0.073 mg/kg/day. This exposure remains over 20 times greater than the AOEL.

Peru

A study was conducted on the use of DNOC in the valley of Mala. In 1991, 97 farmers exposed to DNOC were examined and 86 in 1992 (within 24 hours, exceptionally 48 hours) after the end of a working day spraying DNOC. The following findings were obtained:

- The levels of DNOC in the blood of the applicators and bystanders were measured, revealing significant statistical differences between the two groups.
- The farmers were unaware of the real risk in using this pesticide and, when they were informed, paid little attention.
- 80% of the target population did not use the protective clothing recommended by WHO while applying the product.
- 73% of the applicators interviewed admitted they had suffered the poisoning symptoms explained to them.
- It was confirmed that DNOC blood levels are eliminated in six to eight weeks.
- The following risk factors were observed among the studied populations: long hours of exposure to the products, high application doses, short intervals between application, lack of cleaning after applications.
- The complaints most frequently suffered by farmers exposed to DNOC were: polydipsia, fatigue, feeling hot, cephalalgia, suffocation, giddiness, blurred vision, diarrhoea, general malaise, nausea and vomiting. However, the farmers considered the situations to be "normal".

Complaints were also received from workers, whose DNOC blood concentration was below the so-called danger level of 10 ppm (NIOSH). At those levels, symptoms, although not specific, can be recognised as part of the symptomatology of DNOC poisoning.

3.5 Medical data

Data from the literature report cases of intoxication resulting from very prolonged exposure in hot weather. The symptoms reported were abnormal fatigue, perspiration, and a sensation of heat and weight loss. The degradation of the general state of the person intoxicated can be quick with tachypnea, tachycardia, and significant important hyperthermia, which may lead to death. One of the important characteristic post-mortem effects is the quick appearance (45 minutes to 1 hour) of *rigor mortis*. In the case of light or moderate exposure, the return back to normal is quick (48 to 72 hours) following exposure, without any after-effects. It should be added that the product is irritating and sensitising to the skin and caustic to the eyes. No treatments, other than symptomatic, can be recommended.

The survey data from Peru confirm that DNOC increases the basal metabolic rate, without proportionally stimulating the cardiovascular system. Effects on the gastrointestinal tract and on the nervous system have also been observed on Peruvian workers exposed to this product.

4 Environmental fate and effects

4.1 Fate

4.1.1 Soil

Mobility: At a low pH, the adsorption of undissociated DNOC to particulate is strong. However, at an environmentally relevant pH DNOC is weakly adsorbed on soil. In a study using three soil types, adsorption was less than 15.4 % after 16 h. Apparent adsorption substantially increased over a longer period but this was likely due to degradation of the compounds. The values of K_{oc} ranged from 53 to 195, for the various soils and concentrations. DNOC is expected to be mobile in soil but, due to rapid degradation, aged residues containing DNOC and its major metabolite (likely 2-methyl-4-nitrophenol) are shown to have a low potential for leaching in soil (leacheates from soil columns were 0.9-5.8 %, mainly as polar metabolites).

The degradation of DNOC in **sterile soil** was not investigated.

The **biodegradation** of DNOC under aerobic conditions in soils is rapid. It was investigated in three types of standard soils over a period of 88 days, at 20 °C, in the dark: at concentrations equivalent to a field application rate of 5 kg DNOC/ha, DT_{50} values were less than 12 days at 20°C and 15 days at 5°C. Degradation proceeds via unidentified polar metabolites. The ring moiety is highly mineralised (>40 %) and bound residues are <40 %. The main non-volatile metabolite was tentatively identified as 2-methyl-4-nitrophenol, which peaks at 14 before decreasing to a low level. Other metabolites remain at low levels.

Degradation under anaerobic conditions and **photodegradation** in soil have not been studied as DNOC is rapidly degraded in the upper soil layer.

4.1.2 Water

DNOC is stable in sterile water at any pH.
The DT_{50} in surface water is 3-5 weeks. The DT_{50} value of photodegradation in aqueous systems might be around 253 hours (10.5 days). Experiments do not provide reliable information on the degradation rate in water/sediment systems.
DNOC is moderately adsorbed on aquatic sediment.

4.1.3 Air

DNOC has a Henry's law constant of 2.46×10^{-7} atm. m^3/mol and therefore will not volatilise from surface water. Due to the low volatility of DNOC, the active substance is not expected to be found in significant amounts in air.

4.1.4 Bioconcentration

Log P < 3. Generally, compounds with Log P < 3 do not bioconcentrate.

4.1.5 Persistence

DNOC is not expected to accumulate in soil as the DT_{50} values for aerobic degradation are less than 12 days at 20°C and 15 days at 5°C. With a DT_{50} of 3-5 week in aerobic surface water, and a photodegradation DT_{50} value of 10.5 d, DNOC is not likely to persist in water systems either.

4.2 Ecotoxicity – Effects on non-target organisms

4.2.1 Terrestrial vertebrates

Mammals

LD_{50} (rat, oral)= 26 mg/kg bw (LD_{50} value retained for the European Community risk evaluation)

Birds

LD_{50} = 8.3 mg/kg (pheasants),
= 15.7 mg/kg (Japanese quail),
= 23 mg/kg (duck),
= 8-25 mg/kg (partridge)
LD_0 = 1.4 mg/kg bw (pheasants)
= 4.4 mg/kg bw. (partridges)
LC_{50} = 637 mg/kg diet (Japanese quail)

Mortality occurs quickly after administration

Concentrations on the treated grain fed to birds equivalent to the field use of 3.5 kg DNOC /ha, had a repellent effect on the birds.

Aquatic Species

Fish

LC_{50} = 6-13 mg/l (carp)
= 0.45 mg/l (96 h, trout)
= 0.95 mg/l (96 h, bluegill)

Aquatic invertebrates

LC_{50} (24 h) = 5.7 mg/l (daphnia)
NOEC (14 d) = 0.6 mg/l (daphnia)

Algae

LC_{50} (96 h) = 6 mg/l

4.2.3 Honey Bees & Other arthropods

Bees: LD_{50} (acute oral) = 2.04 ± 0.25 µg/bee, suggest that DNOC is moderately toxic to honey bees

When bees were exposed in a field experiment to a crop (*Brassica napusrape*) treated at a rate of 5 kg a.i./ha, only 4.8 % mortality was observed, showing that under normal field conditions, the risk to honey bees from DNOC - treated crops is low.

Other arthropods: no data

4.2.4 Earthworms

LC_{50} (7 days) = 17 mg/kg of soil.
LC_{50} (14 days) = 15 mg/kg soil.

4.2.5 Soil micro-organisms

At a concentration of 2.5 mg/kg of soil, DNOC stimulates respiration (formation of CO_2 resulting from decomposition of the organic components of the soil by the microflora).

4.2.6 Terrestrial plants

No data available. May be phytotoxic.

5 Environmental Exposure/Risk Evaluation

5.1 Terrestrial Vertebrates

Mammals and birds

The risk evaluation of the use of DNOC in the European Community was performed taking into account the intended applications notified for authorisation. Application rates of 0.8 to 8.4 kg a.i./ha were considered in vines and orchards and 5.6 kg a.i./ha for potatoes. For calculations, the LD_{50} values of 26 mg/kg bw and 8.3 mg/kg bw were used as reference for the acute toxicity in mammals and in birds respectively.

The Toxicity/Exposure Ratios (TER) were calculated for small and medium-sized grazing or insect eating mammals and birds. These TERs must be greater than the trigger value (10) established in the European Community. All application rates lead to TERs lower than the trigger value, ranging from 0.04 (high rate) to 0.6 (low rate). Therefore, there was evidence of unacceptable risks for all the applications notified for authorisation.

The direct exposure of birds and mammals due to the intended uses of DNOC within the European Community as a desiccant on potatoes and as an insecticide on dormant fruit crop are limited.

5.2 Aquatic Species

Fish/Aquatic invertebrates

The risk evaluation of the use of DNOC in the European Community was performed taking into account application rates of 0.8 to 8.4 kg a.i./ha for orchards and 5.6 kg a.i./ha for potatoes. The exposure levels were calculated for 1 m and 5 m buffer zones respectively. The toxicity data concerning the most sensitive species in each trophic level (see point 4.2.2) were used.

The TERs were calculated for fish, daphnia and algae in acute exposure and for daphnia in chronic exposure . These TERs must be greater than the trigger values (100 for acute and 10 for chronic exposure) established in the European Community.

Almost all the acute TER values were lower than the trigger values even with a 5 metre buffer zone, namely for fish (orchards: at all application rates, potatoes), for daphnia (orchards: at high application rates, potatoes) and algae (orchards: at high application rates, potatoes). The chronic TER values were very close to the trigger value. The results are summarised in the following table.

Application rate (kg a.i./ha)	Crop	Distance (m)	Organism	Time-scale	TER	Trigger Values
8.4	Orchard	5	Fish	Acute	**0.8**	100
8.4	Orchard	5	Daphnia	Acute	**10**	100
8.4	Orchard	5	Algae	Acute	**11**	100
0.8	Orchard	5	Fish	Acute	**8**	100
0.8	Orchard	5	Daphnia	Acute	100	100
0.8	Orchard	5	Algae	Acute	110	100
5.6	Potato	1	Fish	Acute	**6**	100
5.6	Potato	1	Daphnia	Acute	**76**	100
5.6	Potato	1	Algae	Acute	**80**	100
0.8	Orchard	5	Daphnia	Chronic	**11**	10
5.6	Potato	1	Daphnia	Chronic	**8**	10

5.3 Honey bees and other arthropods

Bees: The risk evaluation was performed assuming an acute oral toxicity of 2 µg a.i/bee. Application rates of 0.8 and 8.4 kg a.i/ha for orchards and 5.6 kg a.i./ha for potatoes were considered for the risk evaluation. The hazard quotient (HQ = Application rate/ LD_{50}) in all cases was much higher (400-4200) than the trigger value of 50 and this unacceptable risks thus appeared to have been identified risks that were unacceptable. However, under normal field conditions the risk to honey bees was considered to be low (see point 4.2.3). In addition the use patterns of the plant protection products containing DNOC were not considered to present any significant risk of exposure to honey bees.

Other arthropods: no data

5.4 Earthworms

The risk evaluation was performed in the European Community using the acute toxicity value of LC_{50} (7 days): 17 mg a.i./kg. Only the lowest application rate of 0.8 kg a.i./ha on orchards leads to an acceptable risk to earthworms. With an application rate of 8.4 kg a.i./ha on orchards, even assuming a 50 % interception by grass, the TER value of 1.5 was lower than the trigger value set to 10.

The TER value of 2.3 obtained for an application on potatoes following a single application of 5.6 kg a.i./ha was also lower than the trigger value of 10.

Consequently, the related risks were considered unacceptable.

5.5 Soil micro-organisms

No reliable data were available.

Summary

Although there were a number of deficiencies in the DNOC data package provided to the European Community that prevented a complete evaluation being carried out, it was clear that the data package already available suggested:

- a potential for groundwater contamination,
- for all applications, a high acute risk to birds, and mammals and bees,
- for use in orchards (with a 5 metre buffer zone), a high acute risk to fish, at all application rates, and to daphnia, algae and earthworms at high application rates,
- for use in potatoes, a high acute risk to fish, algae and earthworms,
- for use in orchards and potatoes a medium chronic risk for daphnia.

Annex 2 – Details on final regulatory actions reported

Country Name:	**European Community**

1	**Effective date(s) of entry into force of actions**	The measures laid down by Commission Decision 1999/164/EC of 17/02/1999 had to be put into effect by 16/08/1999 at the latest.
	Reference to the regulatory document	Commission Decision 1999/164/EC of 17/02/1999 concerning the non-inclusion of DNOC in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing the active substance (Official Journal of the European Communities L54 of 02/03/1999, p.21).
2	**Succinct details of the final regulatory action(s)**	DNOC and its salts are not included as an active ingredient in Annex I to Directive 91/414/EEC. It is therefore prohibited to place on the market or to use plant protection products containing DNOC. The authorisations for plant protection products containing DNOC had to be withdrawn by 16/8/1999. From 17/2/1999, no authorisation for plant protection products containing DNOC could be granted or renewed.
3	**Reasons for action**	The Decision followed the review of DNOC and its salts pursuant to Article 8 (2) of the Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. In accordance with that Directive, the Commission initiated a programme of work for the gradual examination of active substances available on the market. DNOC was one of the 90 active substances included in the list of substances covered by the first stage of the work programme. The main notifier (Elf Atochem Agri SA) submitted a dossier, which was reviewed by the Member States and the Commission within the Standing Committee on Plant Health. This review was finalised on 1 December 1998 in the form of a Commission review report for DNOC. From the assessments made, it was concluded that the submitted information had not demonstrated that the safety requirements laid down in Article 5(1)(a) and (b) and 5(2)(b) of Directive 91/414/EEC were met, in particular with regard to operator exposure and non-target organisms.
4	**Basis for inclusion into Annex III**	None of the intended uses were considered to present an acceptable risk as regards operator exposure. Moreover, insufficient data were available to assess consumer exposure to potential residues resulting from use. There were also concerns about high acute toxicity to aquatic and terrestrial organisms.
4.1	**Risk evaluation**	It was concluded that continued use of DNOC and its salts would pose an unacceptably high risk to human health and the environment.
4.2	**Criteria used**	Exposure/effects ratios for occupational use, public health and the environment.

	Relevance to other States and Region	Of special concern to developing countries due to the high risk associated with spraying of DNOC, even when rigorous Good Agricultural Practices (GAP) are employed and protective equipment is used.
5	**Alternatives**	No alternatives are proposed.
6	**Waste management**	Member States were allowed to grant a limited period of grace for disposal, storage, placing on the market and use of existing stocks was provided in accordance with the provisions of Article 4(6) of Directive 91/414/EEC. This period was set at not longer than a maximum of 15 months.
7	**Other**	Authorisations had already been withdrawn by a number of Member States on the basis of DNOC's similarity to other dinitro compounds with known teratogenic potential.

Country Name:	**Peru**

1	**Effective date(s) of entry into force of actions**	9 October 2000
	Reference to the regulatory document	Resolución Jefatural N° 182-2000-AG-SENASA
2	**Succinct details of the final regulatory action(s)**	Prohibition of DNOC for registration, import, local formulation, distribution, trade and use; valid for formulations (including salts) as well as technical material.
3	**Reasons for action**	Based on a study of occupational exposure of farmers using DNOC it was concluded that the risks of continued use were greater than the benefits obtained .
4	**Basis for inclusion into Annex III**	The substantial toxicological hazards identified from existing scientific data, taken together with a study of poisoning incidents in the country, demonstrated a risk under prevailing national conditions. DNOC is toxic to fish and to bees. In addition, it is highly phytotoxic.
4.1	**Risk evaluation**	A study was conducted in 1991-1992 on the use of DNOC in the Valley of Maja where farmers were examined and blood samples taken, 24 hours (exceptionally 48 hours) after a day's work spraying DNOC. Local doctors recorded several complaints from the workers and showed that those spontaneously reporting complaints had higher levels of DNOC in the blood. The levels of DNOC in the blood of applicators and bystanders were significantly different. It took the body 6 to 8 weeks to eliminate DNOC. This study identified concern about human health.
4.2	**Criteria used**	Assessment of impact upon human health
	Relevance to other States and Region	Concerns may apply to the operators from countries with similar agricultural practices.
5	**Alternatives**	The product will be replaced with other products, with lower risk to human and the environment.
6	**Waste management**	No information
7	**Other**	

Annex 3 – Addresses of designated national authorities

European Community

CP Administrator European Commission DG Environment Rue de la Loi, 200 B-1049, Brussels – Belgium *Mr Klaus BEREND*	***Phone*** ***Fax*** ***Telex*** ***e-mail***	+322 299 48 60 +322 295 61 17 klaus.berend@cec.eu.int

PERU

P Directora General de Sanidad Vegetal Servicio Nacional de Sanidad Agraria (SENASA) Dirección General de Sanidad Vegetal Pasaje Zela S/N, Edificio del Ministerio de Trabajo, Piso 10, Lima 11 – PERU *Ing. Alicia De La ROSA BRACHOWICZ*	***Phone*** ***Fax*** ***Telex*** ***e-mail***	+511 433 8048 +511 433 8048 adelarosa@senasa.minag.gob.pe
C Director General Direccción General de Salud Ambiental Ministerio de Salud Las Amapolas 350 Lince Lima –PERU *Mr. Jorge Villena Chavez*	***Phone*** ***Fax*** ***Telex*** ***e-mail***	+511 440 2340/440 0399 +511 440 6562

C Industrial chemicals
CP Pesticides and industrial chemicals
P Pesticides

Annex 4 – References

◆ PART I: FINAL REGULATORY CONTROL ACTION

European Communities

Commission Decision 1999/164/EC of 17/02/1999 concerning the non-inclusion of DNOC in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing the active substance (Official Journal of the European Community L54 of 02/03/1999, p.21) (available at: http://europa.eu.int/eur-lex/pri/en/oj/dat/1999/l_054/l_05419990302en00210022.pdf)

Peru

Resolución Jefatural N° 182-2000-AG-SENASA

◆ Part II: Documentation used for risk evaluation

Review report for the active substance DNOC – Finalised to support European Commission decision concerning the non-inclusion of DNOC as active substance in the Annex I to the Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing this active substance. European Commission – Directorate General for Agriculture DG VI-B.II-1 (7777/VI/98-REV.3, 1.12.1998).

EU Peer review Programme (ECCO) – Full report on DNOC Pesticides Safety Directorate/ECCO Team 5528/ECCO/PSD/97 25.7.97, plus supporting background papers.

Guidance for the setting of **Acceptable Operator Exposure Levels (AOELs).** Commission of the European Communities. Directorate-General for Health and Consumer Protection (7531/VI/95 rev 6, 10.09.2001).

Guidance document on Risk assessment for **Birds and Mammals** under Council Directive 91/414/EEC. European Commission –Directorate-General for Health and Consumer Protection (SANCO/4145/2000, Nov.2001).

Guidance document on **Aquatic Ecotoxicology** within the framework of Directive 91/414/EEC. European Commission –Directorate-General for Health and Consumer Protection (SANCO/3268/2001, Rev. 8, 26.06.2001).

Guidance document on **Terrestrial Ecotoxicology**. European Commission – Directorate-General for Agriculture (2021/VI/98 rev. 7, 08.07.2000).

Guidance document on **Persistence in Soil**. European Commission – Directorate-General for Agriculture (9188/VI/97 rev. 8, 12.07.2000).

Technical Report No. 2001-AG-SENASA-DGSV-DIA, dated 20 September 2001

Report of project on occupational health and rural education (Lima, Peru, 1992, excerpt – table of content and section relevant to DNOC).

FAO/WHO, 1963. Pesticide Residues in Food – 1963 - FAO Meeting Report No. PL/1963/13 (mimeographed); WHO/Food Add./23/1964.

FAO/WHO, 1965. Pesticide Residues in Food – 1965 - Evaluations of the toxicity of pesticide

residues in food. Toxicological and environmental Joint Meeting on Pesticide Residues (JMPR); Report of the second joint meeting of the FAO Committee on Pesticides in Agriculture and the WHO Expert Committee on Pesticide Residues, WHO Geneva WHO/Food Add./27.65, FAO meeting report No. PL/1965/10 (available at: http://www.inchem.org/document/jmpr/jmprmono/v065pr22.htm).

IPCS, 2000. Health and Safety Guide No.220: Dinitro-o-cresol. International Programme on Chemical Safety, IPCS/ World Health Organization, Geneva. (available at: http://www.inchem.org/documents/ehc/ehc/ehc220.htm#_Toc478363972)

Tomlin, Clive 2000. The Pesticide Manual: A World Compendium (12th ed.), British Crop Protection Council, United Kingdom

WHO, 1996. Recommended classification of pesticides by hazard and guidelines to classification 1996-1997. WHO/PCS/96.3. World Health Organization, IPCS, Geneva.

WHO, 1998. Recommended classification of pesticides by hazard and guidelines to classification 1998-1999. WHO/PCS/98.21/Rev.1

WHO, 2000. Recommended classification of pesticides by hazard and guidelines to classification 2000-01. WHO/PCS/01.5. World Health Organization, IPCS, Geneva.

◆ Part III: Relevant guidelines and reference documents

Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and their Disposal 1996.

FAO, 1990. Guidelines for personal protection when working with pesticides in tropical countries. FAO, Rome.

FAO, 1995. Revised guidelines on good labelling practices for pesticides. FAO, Rome.

FAO, 1995. Guidelines on Prevention of Accumulation of Obsolete Pesticide Stocks. FAO, Rome.

FAO, 1996. Technical guidelines on disposal of bulk quantities of obsolete pesticides in developing countries. FAO, Rome.

FAO, 1996. Pesticide Storage and Stock Control Manual. FAO, Rome.

FAO, 1999. Guidelines for the management of small quantities of unwanted and obsolete pesticides, FAO, Rome.
