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Stockholm Convention on Persistent Organic Pollutants

Persistent Organic Pollutants Review Committee
Fourth meeting
Geneva, 13–17 October 2008
Item 7 (a) of the provisional agenda*

Consideration of chemicals newly proposed for inclusion in Annexes A, B or C of the Convention

Additional information on endosulfan

Note by the Secretariat

1. The annex to the present note contains a detailed dossier prepared by the European Community and its member States that are Parties to the Stockholm Convention in support of a proposal from the same source for listing endosulfan in Annexes A, B or C of the Convention pursuant to paragraph 1 of Article 8 of the Convention (UNEP/POPS/POPRC.4/14). The annex is being circulated as submitted and has not been formally edited.

2. At the third meeting of the Committee, the European Community and its member States that are Parties to the Convention submitted a proposal to list endosulfan in Annexes A, B or C of the Convention (UNEP/POPS/POPRC.3/5). The Committee agreed to defer consideration of the proposal to its fourth meeting pending receipt of additional information.

3. The Committee invited members and observers to provide through the Secretariat any further relevant information. The Secretariat received information from the European Community and its member States that are Parties to the Convention, Haiti, United States of America, CropLife International and Pesticide Action Network International. That information is set out in electronic format on a CD-ROM that is available from the Secretariat and can be downloaded from the website of the Stockholm Convention.[1]

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* UNEP/POPS/POPRC.4/1

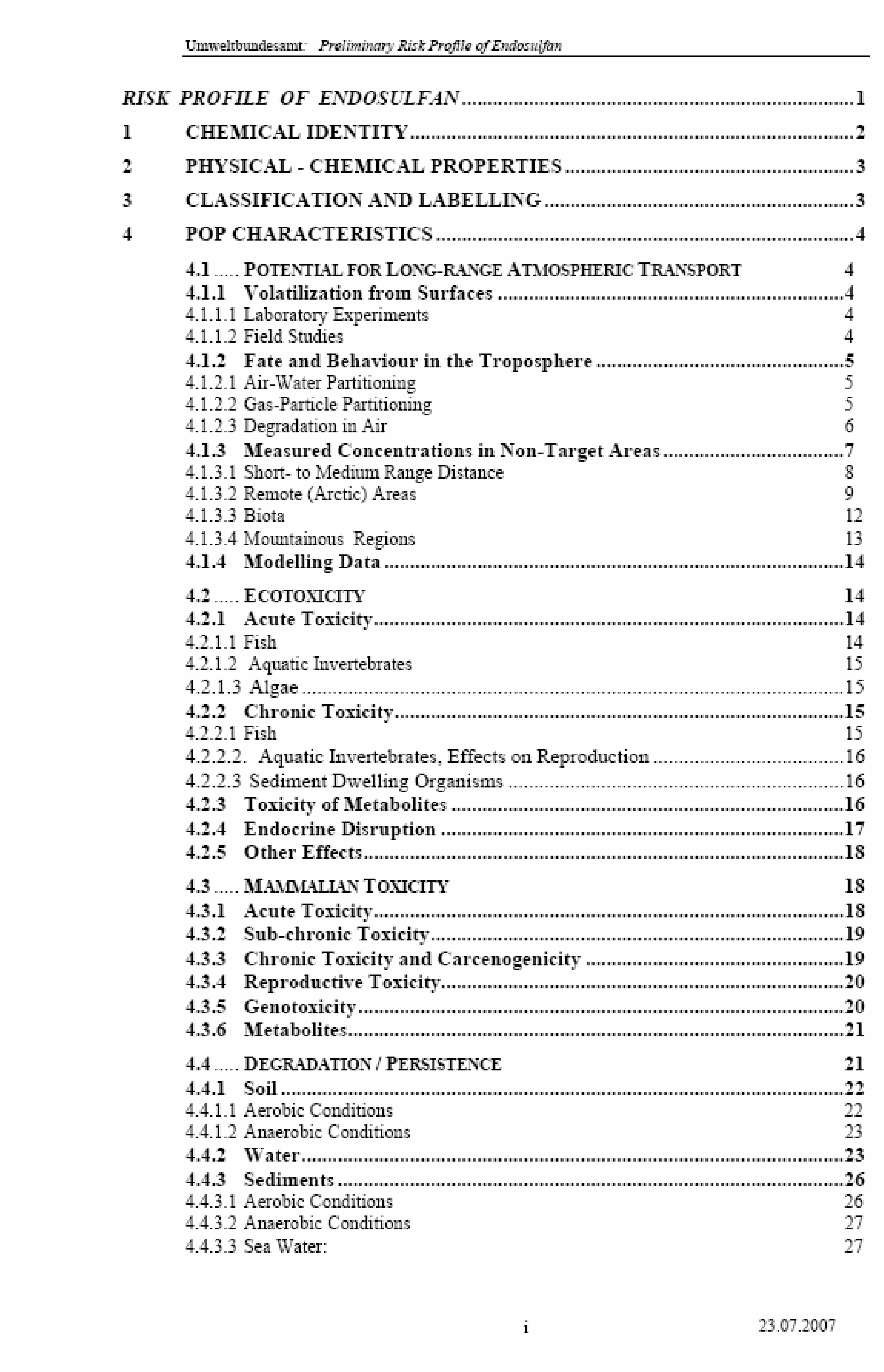
[1] http://chm.pops.int/Convention/tabid/359/Default.aspx

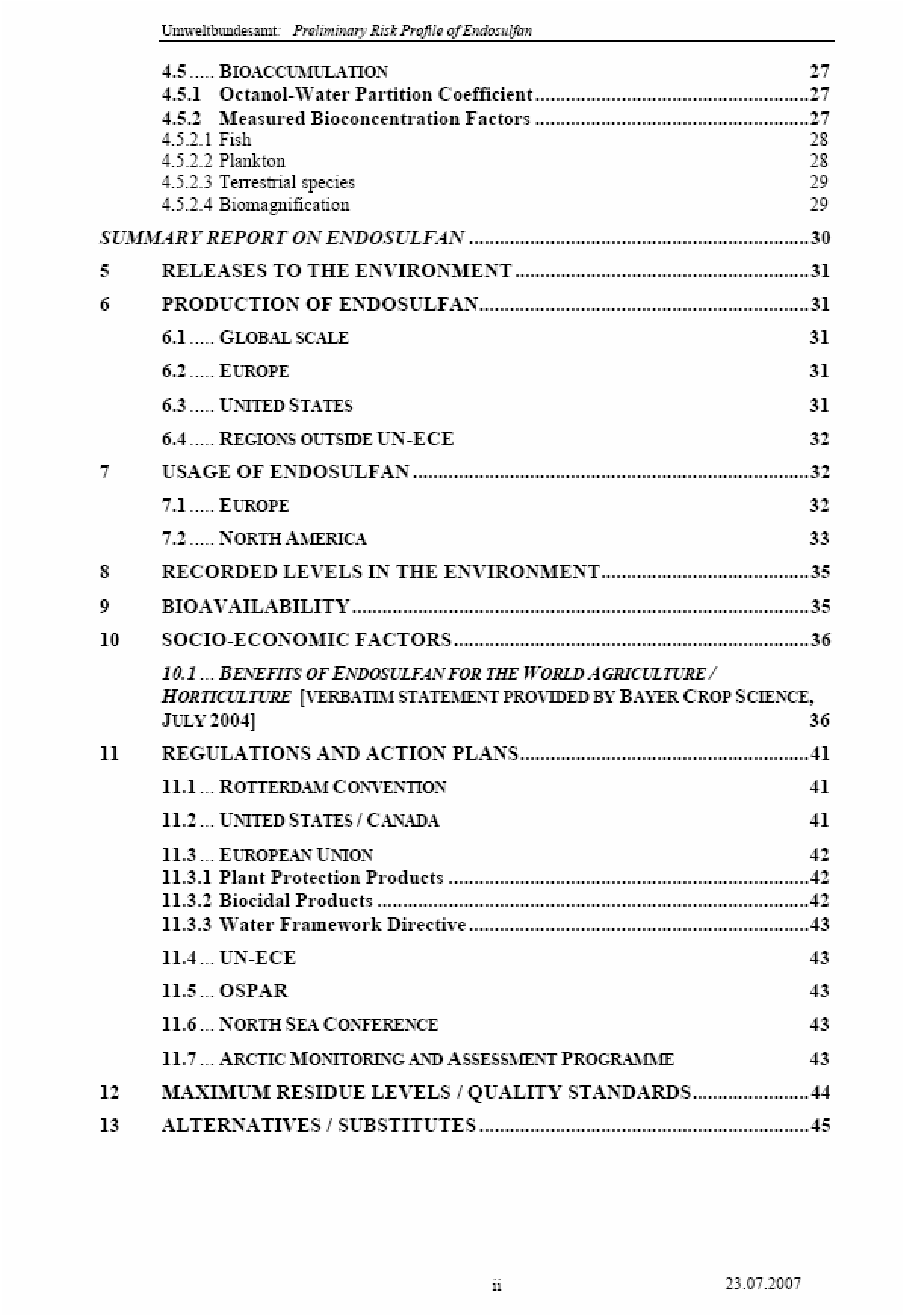
Annex

ENDOSULFAN

Draft Dossier prepared in support of a proposal of endosulfan to be considered
as a candidate for inclusion in the Annexes to the Stockholm Convention

German Federal Environment Agency – Umweltbundesamt, Dessau
February 2007





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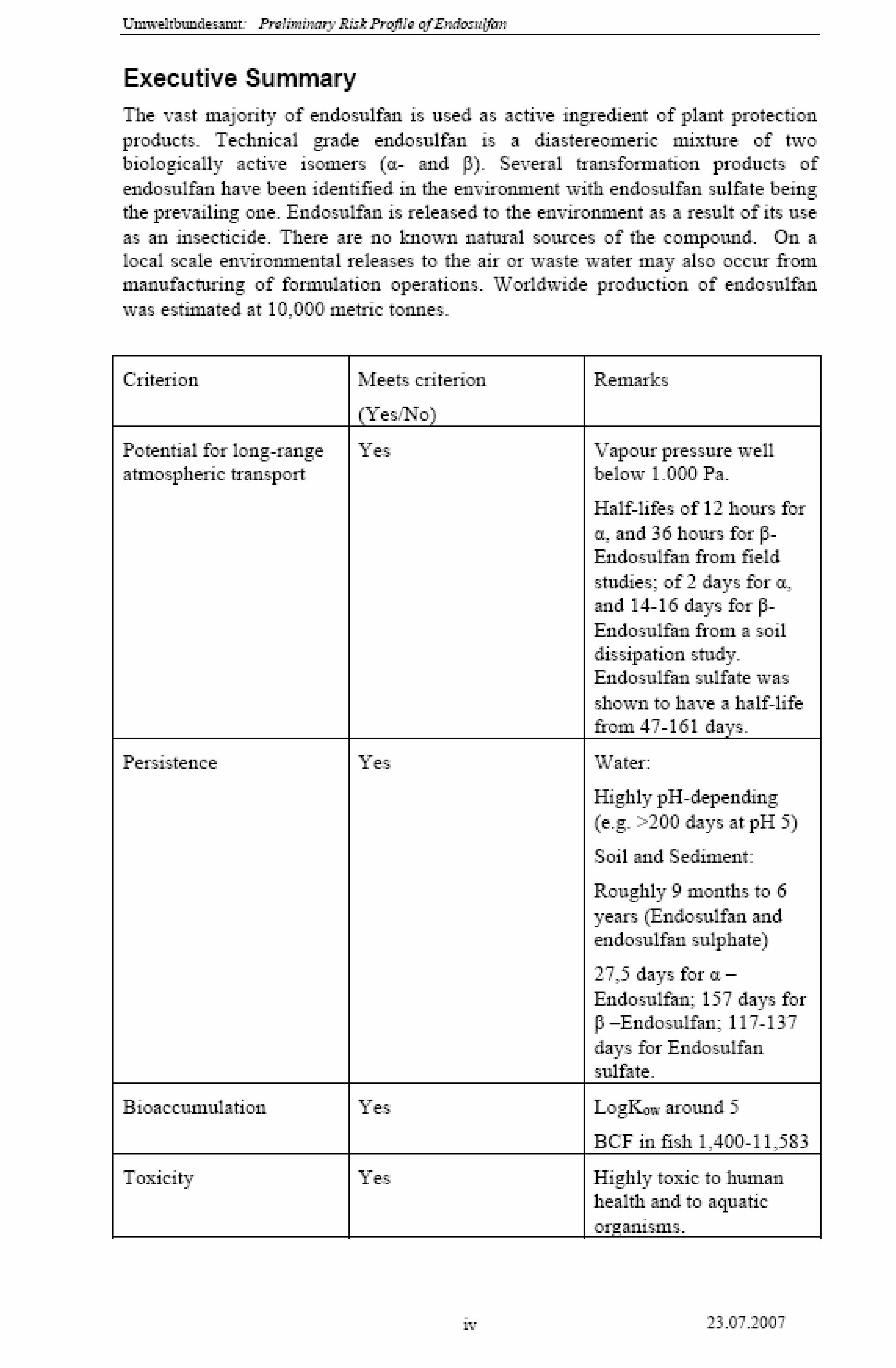

Executive Summary

The vast majority of endosulfan is used as active ingredient of plant protection products. Technical grade endosulfan is a diastereomeric mixture of two biologically active isomers (α- and β). Several transformation products of endosulfan have been identified in the environment with endosulfan sulfate being the prevailing one. Endosulfan is released to the environment as a result of its use as an insecticide. There are no known natural sources of the compound. On a local scale environmental releases to the air or waste water may also occur from manufacturing of formulation operations. Worldwide production of endosulfan was estimated at 10,000 metric tonnes.

Criterion	Meets criterion (Yes/No)	Remarks
Potential for long-range atmospheric transport	Yes	Vapour pressure well below 1.000 Pa. Half-lifes of 12 hours for α, and 36 hours for β-Endosulfan from field studies; of 2 days for α, and 14-16 days for β-Endosulfan from a soil dissipation study. Endosulfan sulfate was shown to have a half-life from 47-161 days.
Persistence	Yes	Water: Highly pH-depending (e.g. >200 days at pH 5) Soil and Sediment: Roughly 9 months to 6 years (Endosulfan and endosulfan sulphate) 27,5 days for α –Endosulfan; 157 days for β –Endosulfan; 117-137 days for Endosulfan sulfate.
Bioaccumulation	Yes	LogK_{ow} around 5 BCF in fish 1,400-11,583
Toxicity	Yes	Highly toxic to human health and to aquatic organisms.

The available data from monitoring studies show clearly contamination of air by Endosulfan. The compound commonly used as an insecticide is highly toxic to human health following acute oral exposure and to the aquatic environment. The most critical part of the assessment concerns the persistence, due to the broad range of data and different quality of the studies. Thus, not all measured data are consistently above the required values. However, the available data support the conclusion that Endolsulfan is persistent in the environment.

Overall, it can be considered that Endosulfan fulfils the criteria for persistence, potential to cause adverse effects, bioaccumulation and potential for long-range environmental transport listed in Annex D of the Stockholm Convention.

INTRODUCTION

Endosulfan is widely used as an agricultural insecticide. It was introduced into the market already back in the mid 1950s but plant production products containing endosulfan are still used in a number of countries worldwide. In scientific literature a huge number of information is available, dealing with (eco)toxicity, environmental fate, residues in food and feedstuff, environmental concentrations, etc. of endosulfan. In addition a number of various reviews were published during the last decade:

In 2002 the US EPA has finished an extensive re-evaluation exercise of endosulfan. The various documents provided for a re-registration eligibility decision (RED) are available on the internet at[i]. For more particulars it is referred to the Environmental Fate and Effects Division (EFED)´s part on environmental risk assessment [ii] and the Health Effects Division (HED)´s part on human health risk assessment [iii].

A comprehensive toxicological profile for endosulfan was published by the U.S. Department of Health and Human Services in 2000 [iv].

Further to EPA´s re-registration eligibility decision of November 2002, endosulfan was re-evaluated in the EU for inclusion on Annex I of Directive 91/414/EEC. It was decided not to include endosulfan in this annex.

In May 2004 a final review of endosulfan was issued by the Australian National registration authority for agricultural and veterinary chemicals [v].

In its decision 1998/2 the Executive Body of the LRTAP Convention set up elements of information to be provided on substances Parties may wish to propose for amendments of annexes I, II or III. The decision lays down that information should be provided on potential for long-range transboundary atmospheric transport of a candidate substances, its toxicity, persistence and bioaccumulation along with indicative values suggesting POP characteristics. Indicative values were provided as a guidance for decision on whether a substance may be of concern warranting further evaluation within the scope of the Protocol.

The numeric indicative values given in Dec.98/2 for POP characteristics appear being straightforward. As no further details on study conditions (temperature) or relevance for particular environmental compartments (e.g. pH value) are provided test results are subject to interpretation of "relevant" environmental conditions.

Supportive information on whether a substance can be considered a POP can be drawn from monitoring data preferably from areas remote of production and application sites. A number of data in Arctic regions have been reported in scientific literature but results remain inconclusive. A recently compiled report

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[i] http://www.epa.gov/oppsrrd1/REDs/endosulfan_red.pdf

[ii] http://www.epa.gov/oppsrrd1/reregistration/endosulfan/finalefed_riskassess.pdf

[iii] http://www.epa.gov/oppsrrd1/reregistration/endosulfan/endosulfan_revisedrisk.PDF

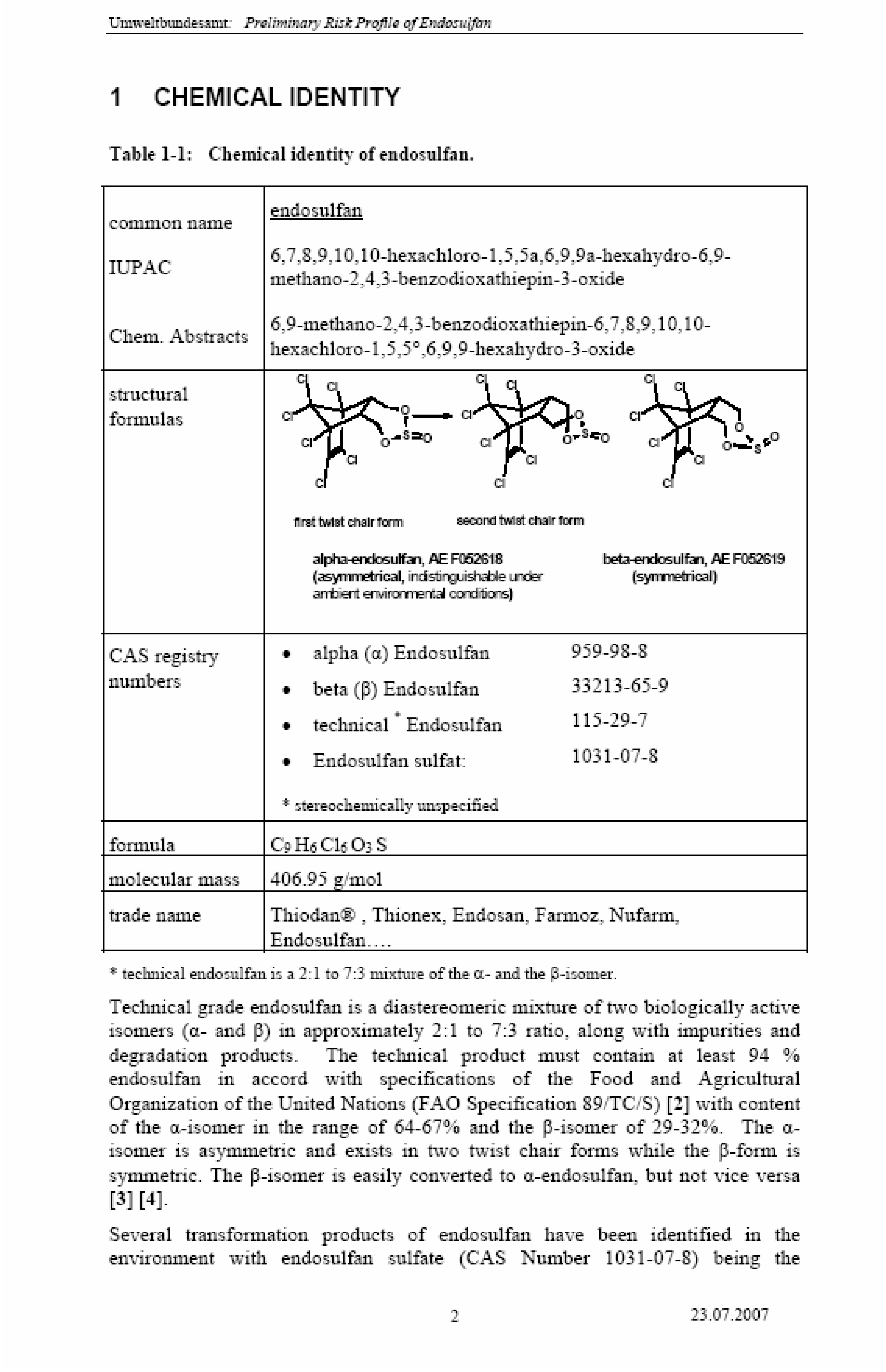
[iv] http://www.atsdr.cdc.gov/toxprofiles/tp41-p.pdf

[v] http://www.nra.gov.au/chemrev/prsendo71.pdf

on such monitoring data of endosulfan in has been released by Bayer CropScience [1]. Furthermore, results from a global monitoring network for POPs published in 2006 revealed that Endosulfan is most abundant and that its use has increased **[189]** **[190]**.

PART I

RISK PROFILE OF ENDOSULFAN



1 CHEMICAL IDENTITY

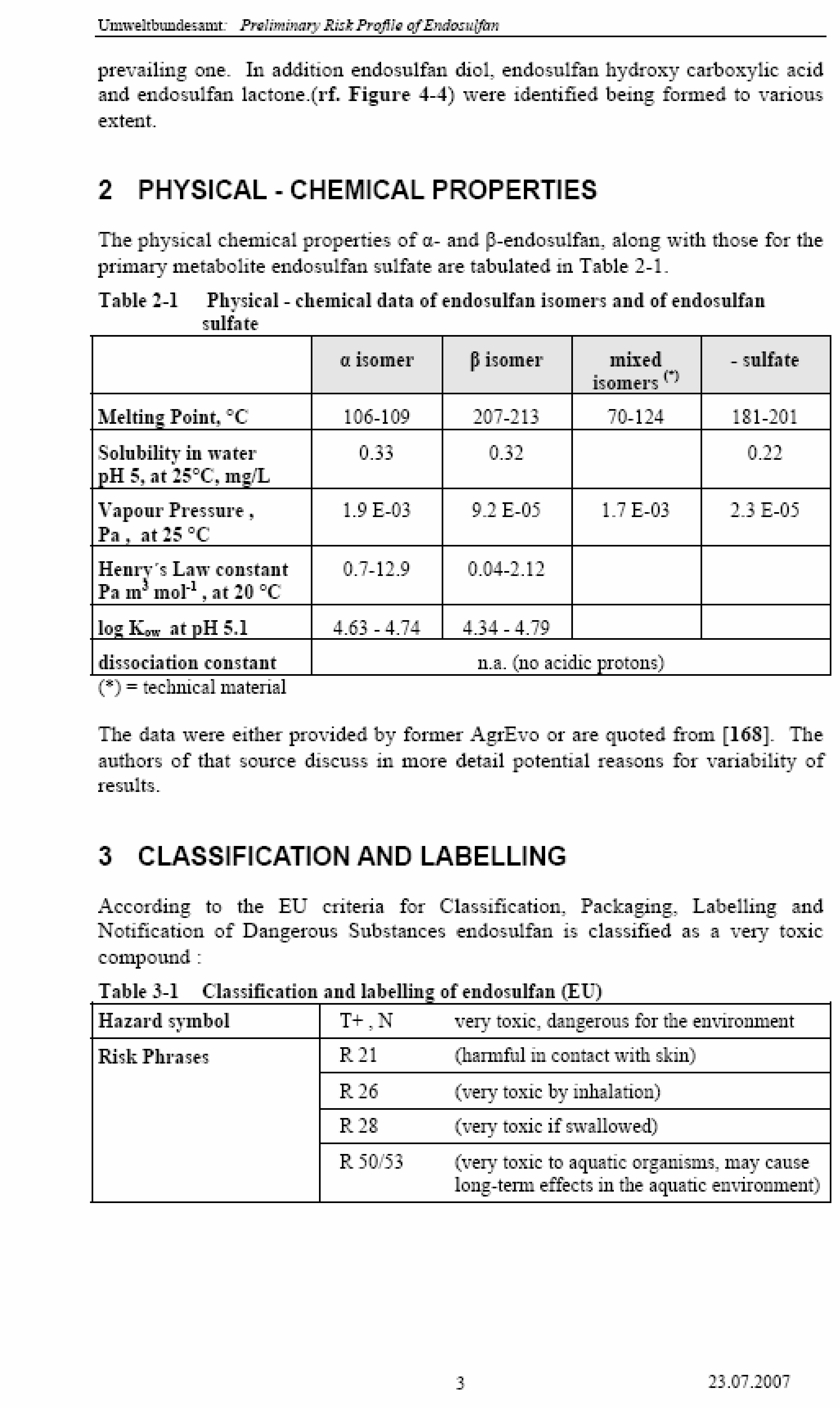
Table 1-1: Chemical identity of endosulfan.

common name	endosulfan
IUPAC	6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide
Chem. Abstracts	6,9-methano-2,4,3-benzodioxathiepin-6,7,8,9,10,10-hexachloro-1,5,5°,6,9,9-hexahydro-3-oxide
structural formulas	first twist chair form second twist chair form alpha-endosulfan, AE F052618 (asymmetrical, indistinguishable under ambient environmental conditions) beta-endosulfan, AE F052619 (symmetrical)
CAS registry numbers	• alpha (α) Endosulfan 959-98-8 • beta (β) Endosulfan 33213-65-9 • technical * Endosulfan 115-29-7 • Endosulfan sulfat: 1031-07-8 * stereochemically unspecified
formula	$C_9H_6Cl_6O_3S$
molecular mass	406.95 g/mol
trade name	Thiodan® , Thionex, Endosan, Farmoz, Nufarm, Endosulfan….

* technical endosulfan is a 2:1 to 7:3 mixture of the α- and the β-isomer.

Technical grade endosulfan is a diastereomeric mixture of two biologically active isomers (α- and β) in approximately 2:1 to 7:3 ratio, along with impurities and degradation products. The technical product must contain at least 94 % endosulfan in accord with specifications of the Food and Agricultural Organization of the United Nations (FAO Specification 89/TC/S) [2] with content of the α-isomer in the range of 64-67% and the β-isomer of 29-32%. The α-isomer is asymmetric and exists in two twist chair forms while the β-form is symmetric. The β-isomer is easily converted to α-endosulfan, but not vice versa [3] [4].

Several transformation products of endosulfan have been identified in the environment with endosulfan sulfate (CAS Number 1031-07-8) being the



prevailing one. In addition endosulfan diol, endosulfan hydroxy carboxylic acid and endosulfan lactone.(**rf. Figure 4-4**) were identified being formed to various extent.

2 PHYSICAL - CHEMICAL PROPERTIES

The physical chemical properties of α- and β-endosulfan, along with those for the primary metabolite endosulfan sulfate are tabulated in Table 2-1.

Table 2-1 Physical - chemical data of endosulfan isomers and of endosulfan sulfate

	α isomer	**β isomer**	**mixed isomers (*)**	**- sulfate**
Melting Point, °C	106-109	207-213	70-124	181-201
Solubility in water pH 5, at 25°C, mg/L	0.33	0.32		0.22
Vapour Pressure , Pa , at 25 °C	1.9 E-03	9.2 E-05	1.7 E-03	2.3 E-05
Henry´s Law constant Pa m^3 mol^{-1} , at 20 °C	0.7-12.9	0.04-2.12		
log K_{ow} at pH 5.1	4.63 - 4.74	4.34 - 4.79		
dissociation constant	n.a. (no acidic protons)			

(*) = technical material

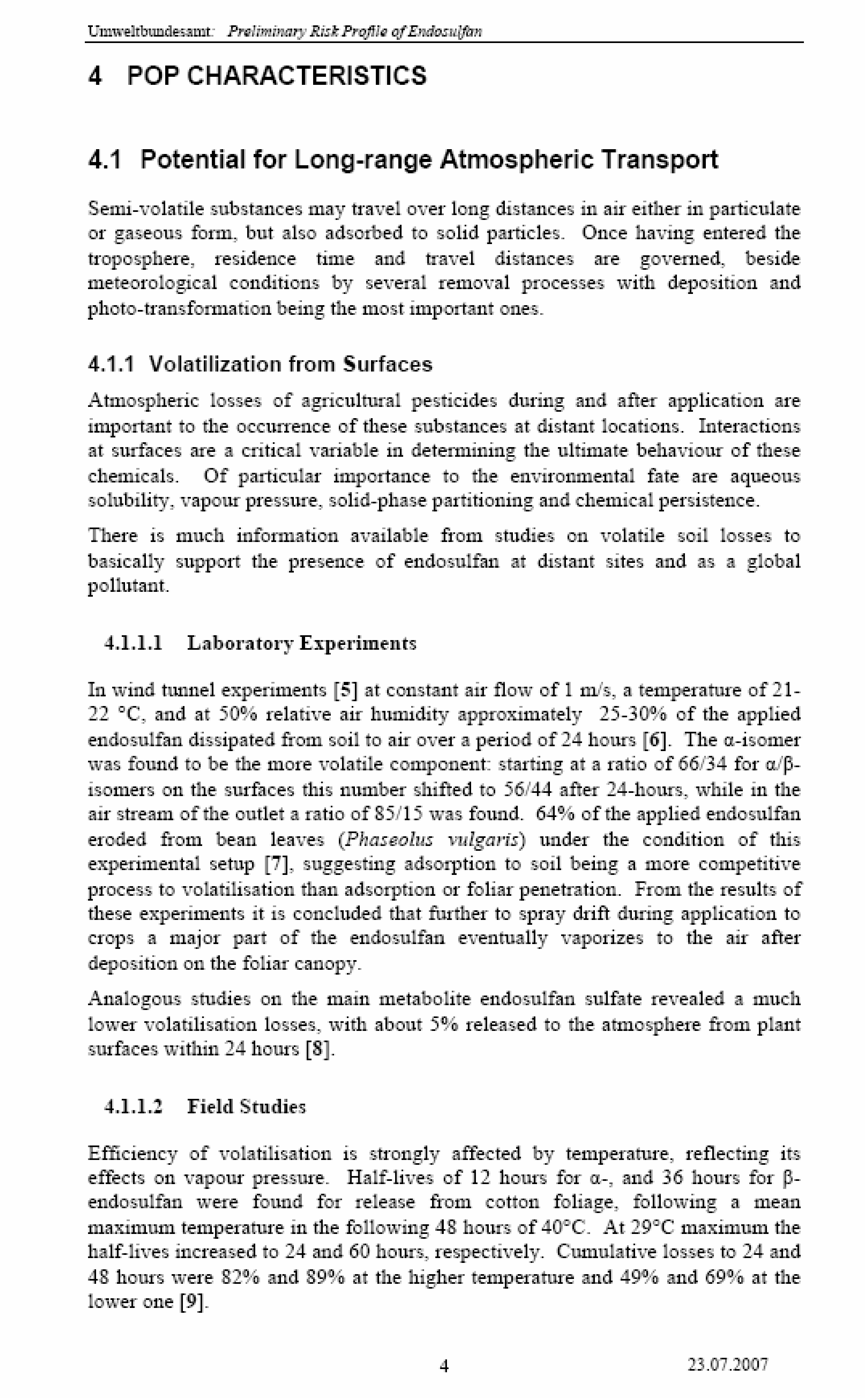
The data were either provided by former AgrEvo or are quoted from [**168**]. The authors of that source discuss in more detail potential reasons for variability of results.

3 CLASSIFICATION AND LABELLING

According to the EU criteria for Classification, Packaging, Labelling and Notification of Dangerous Substances endosulfan is classified as a very toxic compound :

Table 3-1 Classification and labelling of endosulfan (EU)

Hazard symbol	T+ , N	very toxic, dangerous for the environment
Risk Phrases	R 21	(harmful in contact with skin)
	R 26	(very toxic by inhalation)
	R 28	(very toxic if swallowed)
	R 50/53	(very toxic to aquatic organisms, may cause long-term effects in the aquatic environment)



4 POP CHARACTERISTICS

4.1 Potential for Long-range Atmospheric Transport

Semi-volatile substances may travel over long distances in air either in particulate or gaseous form, but also adsorbed to solid particles. Once having entered the troposphere, residence time and travel distances are governed, beside meteorological conditions by several removal processes with deposition and photo-transformation being the most important ones.

4.1.1 Volatilization from Surfaces

Atmospheric losses of agricultural pesticides during and after application are important to the occurrence of these substances at distant locations. Interactions at surfaces are a critical variable in determining the ultimate behaviour of these chemicals. Of particular importance to the environmental fate are aqueous solubility, vapour pressure, solid-phase partitioning and chemical persistence.

There is much information available from studies on volatile soil losses to basically support the presence of endosulfan at distant sites and as a global pollutant.

4.1.1.1 Laboratory Experiments

In wind tunnel experiments [**5**] at constant air flow of 1 m/s, a temperature of 21-22 °C, and at 50% relative air humidity approximately 25-30% of the applied endosulfan dissipated from soil to air over a period of 24 hours [**6**]. The α-isomer was found to be the more volatile component: starting at a ratio of 66/34 for α/β-isomers on the surfaces this number shifted to 56/44 after 24-hours, while in the air stream of the outlet a ratio of 85/15 was found. 64% of the applied endosulfan eroded from bean leaves (*Phaseolus vulgaris*) under the condition of this experimental setup [**7**], suggesting adsorption to soil being a more competitive process to volatilisation than adsorption or foliar penetration. From the results of these experiments it is concluded that further to spray drift during application to crops a major part of the endosulfan eventually vaporizes to the air after deposition on the foliar canopy.

Analogous studies on the main metabolite endosulfan sulfate revealed a much lower volatilisation losses, with about 5% released to the atmosphere from plant surfaces within 24 hours [**8**].

4.1.1.2 Field Studies

Efficiency of volatilisation is strongly affected by temperature, reflecting its effects on vapour pressure. Half-lives of 12 hours for α-, and 36 hours for β-endosulfan were found for release from cotton foliage, following a mean maximum temperature in the following 48 hours of 40°C. At 29°C maximum the half-lives increased to 24 and 60 hours, respectively. Cumulative losses to 24 and 48 hours were 82% and 89% at the higher temperature and 49% and 69% at the lower one [**9**].

Approximately half of the amount of α- and β-endosulfan applied to surface soils in Queensland and New South Wales, Australia, dissipated through volatilisation within 3-5 and 5-8 days, respectively **[10]**. Even heavy rainfalls in the first days after treatment of freshly tilled soil could not prevent a 34.5% volatile flux of α-endosulfan within 20 days **[11]** while for the more water soluble β-isomer these losses were determined to be 14.5% under that specific conditions.

Rapid dissipation losses of endosulfan and endosulfan sulfate were also reported from a field study in Andalusia, Spain **[12]**. Following an application at rate of 840 g/ha a.i. to soil (in July) a DT50 of 1.4 days and a corresponding DT90 of 8.9 days was determined for α-endosulfan. In line with other studies the β-isomer showed being less volatile at a DT50 of 7.5 days and a corresponding DT90 of 36.6 days. In this study endosulfan sulfate reached a maximum soil residue level of 7.5% two weeks post application. Calculated DT50 values for that metabolite were 75.2 days and a DT90 of 249.7 days.

A similar soil dissipation study based on an application rate of 840 g/ha a.i. to bare soil plots (end of June) was performed in Greece in the year 2000 **[13]**. For the α-isomer a DT50 of 2 days was found in that study, while for β endosulfan a DT50 of 14-16 days was determined. Depending on the evaluation method DT50 values ranged from 47 to 161 days for endosulfan sulfate. The maximum concentrations of endosulfan sulfate in soil remained less than 10% of the applied amount parent at any time during the course of the study, but was still present in soil at small amounts after 12 months.

Note: A major drawback from field studies is that no differentiation between fraction of degraded and evaporated substance can be accomplished.

4.1.2 Fate and Behaviour in the Troposphere

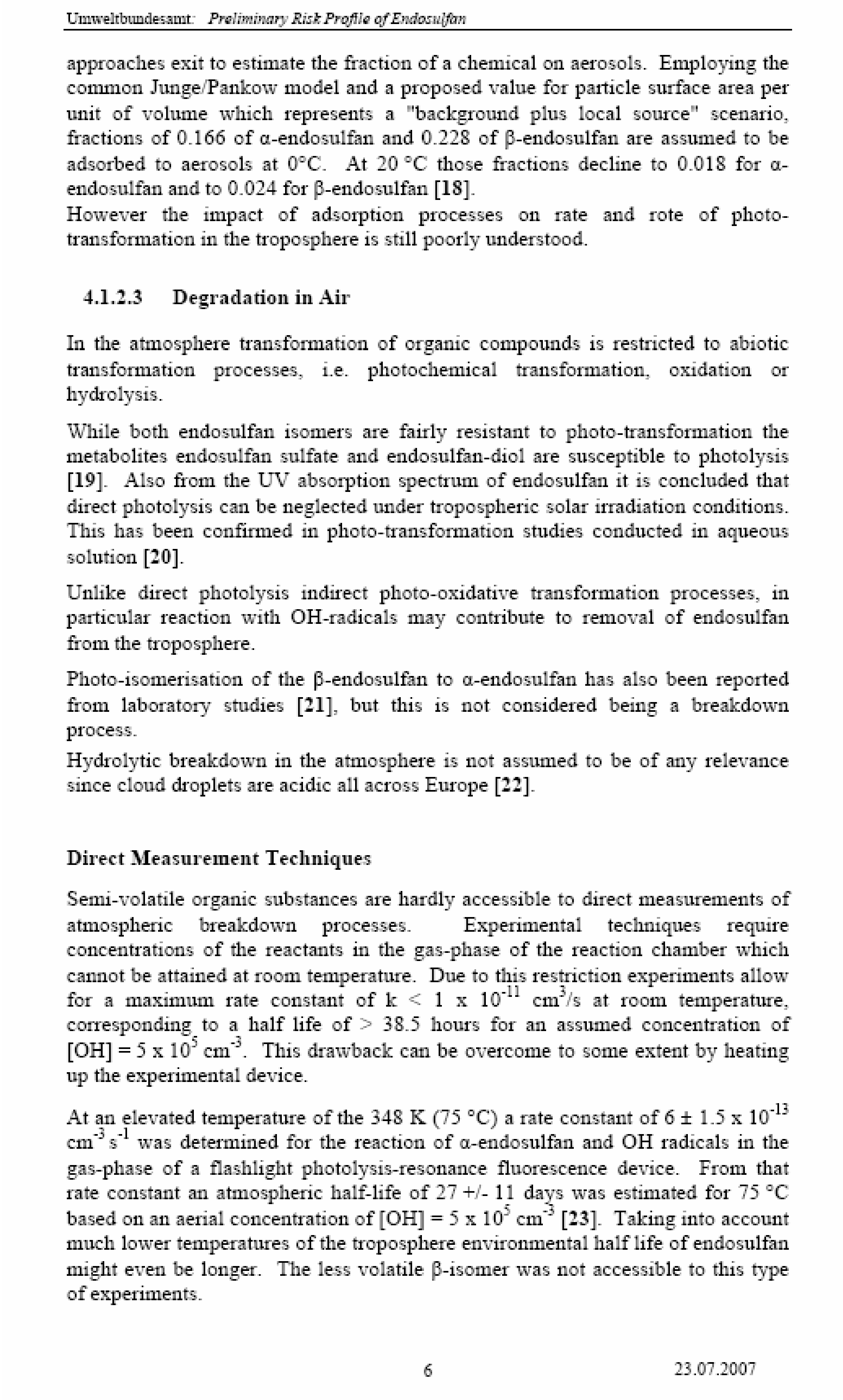
Inter-media exchange processes between gas phase and airborne particulate matter are key for understanding atmospheric transport and transformation, particularly of organic substances of intermediate volatility like endosulfan.

4.1.2.1 Air-Water Partitioning

The Henry's Law constant (H) is a critical property for describing air-water exchange. Employing a wetted wall column technique a value of H = 7.95 Pa m^3 mol^{-1} was determined for α-endosulfan at 25 °C **[14]**. In another study using the same methodology a value of 0.071 Pa m^3 mol^{-1} was determined for α-endosulfan and 0.039 Pa m^3 mol^{-1} for β-endosulfan **[15]**. Estimates of H derived from the liquid-phase vapour pressure of α-endosulfan and its solid-phase solubility, which was corrected by an experimentally determined factor to the liquid phase of ΔS_f = 26.2 J mol^{-1} K^{-1} **[16]** resulted in a value of 1.9 Pa m^3 mol^{-1} **[17]**. This variety of results greatly affects estimates of atmospheric air-water gas exchange processes and thus deposition velocity.

4.1.2.2 Gas-Particle Partitioning

Gas/particle partitioning is an important process that impacts deposition, chemical reactions and long-range transport of semi-volatile compounds. Several model



approaches exit to estimate the fraction of a chemical on aerosols. Employing the common Junge/Pankow model and a proposed value for particle surface area per unit of volume which represents a "background plus local source" scenario, fractions of 0.166 of α-endosulfan and 0.228 of β-endosulfan are assumed to be adsorbed to aerosols at 0°C. At 20 °C those fractions decline to 0.018 for α-endosulfan and to 0.024 for β-endosulfan **[18]**.
However the impact of adsorption processes on rate and rote of photo-transformation in the troposphere is still poorly understood.

4.1.2.3 Degradation in Air

In the atmosphere transformation of organic compounds is restricted to abiotic transformation processes, i.e. photochemical transformation, oxidation or hydrolysis.

While both endosulfan isomers are fairly resistant to photo-transformation the metabolites endosulfan sulfate and endosulfan-diol are susceptible to photolysis **[19]**. Also from the UV absorption spectrum of endosulfan it is concluded that direct photolysis can be neglected under tropospheric solar irradiation conditions. This has been confirmed in photo-transformation studies conducted in aqueous solution **[20]**.

Unlike direct photolysis indirect photo-oxidative transformation processes, in particular reaction with OH-radicals may contribute to removal of endosulfan from the troposphere.

Photo-isomerisation of the β-endosulfan to α-endosulfan has also been reported from laboratory studies **[21]**, but this is not considered being a breakdown process.
Hydrolytic breakdown in the atmosphere is not assumed to be of any relevance since cloud droplets are acidic all across Europe **[22]**.

Direct Measurement Techniques

Semi-volatile organic substances are hardly accessible to direct measurements of atmospheric breakdown processes. Experimental techniques require concentrations of the reactants in the gas-phase of the reaction chamber which cannot be attained at room temperature. Due to this restriction experiments allow for a maximum rate constant of $k < 1 \times 10^{-11}$ cm^3/s at room temperature, corresponding to a half life of > 38.5 hours for an assumed concentration of $[OH] = 5 \times 10^5$ cm^{-3}. This drawback can be overcome to some extent by heating up the experimental device.

At an elevated temperature of the 348 K (75 °C) a rate constant of $6 \pm 1.5 \times 10^{-13}$ cm^{-3} s^{-1} was determined for the reaction of α-endosulfan and OH radicals in the gas-phase of a flashlight photolysis-resonance fluorescence device. From that rate constant an atmospheric half-life of 27 +/- 11 days was estimated for 75 °C based on an aerial concentration of $[OH] = 5 \times 10^5$ cm^{-3} **[23]**. Taking into account much lower temperatures of the troposphere environmental half life of endosulfan might even be longer. The less volatile β-isomer was not accessible to this type of experiments.

Indirect Measurements Techniques

On behalf of gas phase reactions inert solvent-systems (CFC 113) are suggested as a surrogate matrix for simulting atmosphere, in which to measure OH-reactivity of semi-volatile compounds {i}. Rate constants of the test substance are thereby determined by relating the decline of the concentration of the test substance to that of a reference substance of known gas phase OH-reactivity. In such an experiment employing toluene as a reference half-lives of > 2.7 days were found for α-endosulfan [24] and of > 15 days for β-endosulfan [25]. For endosulfan sulfate a half life of 2.7 days in the troposphere at minimum was determined in such a model system as well [26].

QSAR Calculations

Rate constants for gas-phase reactions of semi-volatile compounds can also be estimated from experimentally determined incremental values of more volatile organic compounds [27]. Based on the method of ATKINSON a reaction rate constant of $.8 \times 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1} was estimated for the reaction of endosulfan and OH-radicals, resulting in a corresponding atmospheric half life of 8.5 days [28]. However, the authors of this calculation estimated an uncertainty factor of 10 for that number.

Employing a recent version (v1.91) of the QSAR program model "AOPWIN" a rate of $k = 6.8 \times 10^{-12}$ cm^3 $molec^{-1}$ s^{-1} is derived for the primary transformation of endosulfan with abstraction of aliphatic hydrogen atoms (partial rate of 4.01×10^{12} cm^3 $molec^{-1}$ s^{-1}) and OH-addition to the olefinic bond for (2.8×10^{-12} cm^3 $molec^{-1}$ s^{-1}) being the primary breakdown processes. Assuming an annually and globally averaged OH radical concentration of $[OH] = 5 \times 10^5$ cm^{-3} for the troposphere layer a half-life of 56.5 hours, corresponding to 4.7 [12-h days] is derived for the overall breakdown rate (for details of calculation see Annex I).

It has to be noted however, that disagreement between measured and calculated rate constants is most common for halogen-containing organic substances [29]. The Atkinson method is particularly not recommended for per-halogenated compounds [30], which applies for that moiety of the molecule bearing the double bond. Moreover no steric hindrance from the adjacent chlorine atoms is taken into account for the addition reaction to the olefinic bond.

4.1.3 Measured Concentrations in Non-Target Areas

Reflecting its continued use in North America, endosulfan to data is one of the most abundant and ubiquitous organic chlorine pesticides in the continental atmosphere [31]. Evidence for long range transport of endosulfan and endosulfan sulfate is provided from a number of literature sources reporting concentrations in various environmental media from Arctic regions [32].

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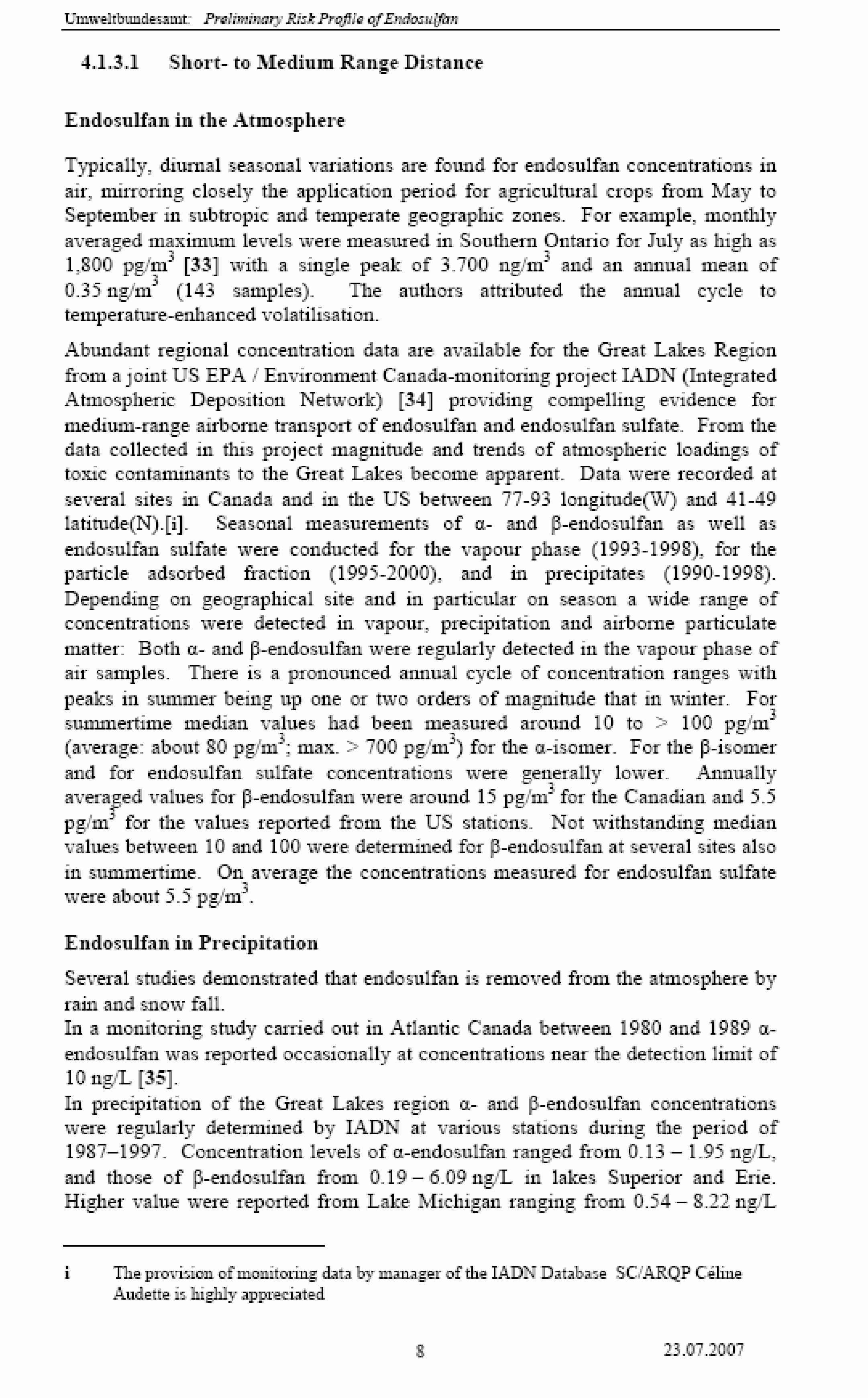
i it is debated whether such data can be transposed to environmental conditions for two reasons: (i) different diffusion-controlled impacts in gas and liquid phase, (ii) suspected "compression effects are suspected to the transition complex of the addition reaction to the double bound".



4.1.3.1 Short- to Medium Range Distance

Endosulfan in the Atmosphere

Typically, diurnal seasonal variations are found for endosulfan concentrations in air, mirroring closely the application period for agricultural crops from May to September in subtropic and temperate geographic zones. For example, monthly averaged maximum levels were measured in Southern Ontario for July as high as 1,800 pg/m^3 [**33**] with a single peak of 3.700 ng/m^3 and an annual mean of 0.35 ng/m^3 (143 samples). The authors attributed the annual cycle to temperature-enhanced volatilisation.

Abundant regional concentration data are available for the Great Lakes Region from a joint US EPA / Environment Canada-monitoring project IADN (Integrated Atmospheric Deposition Network) [**34**] providing compelling evidence for medium-range airborne transport of endosulfan and endosulfan sulfate. From the data collected in this project magnitude and trends of atmospheric loadings of toxic contaminants to the Great Lakes become apparent. Data were recorded at several sites in Canada and in the US between 77-93 longitude(W) and 41-49 latitude(N).[i]. Seasonal measurements of α- and β-endosulfan as well as endosulfan sulfate were conducted for the vapour phase (1993-1998), for the particle adsorbed fraction (1995-2000), and in precipitates (1990-1998). Depending on geographical site and in particular on season a wide range of concentrations were detected in vapour, precipitation and airborne particulate matter: Both α- and β-endosulfan were regularly detected in the vapour phase of air samples. There is a pronounced annual cycle of concentration ranges with peaks in summer being up one or two orders of magnitude that in winter. For summertime median values had been measured around 10 to > 100 pg/m^3 (average: about 80 pg/m^3; max. > 700 pg/m^3) for the α-isomer. For the β-isomer and for endosulfan sulfate concentrations were generally lower. Annually averaged values for β-endosulfan were around 15 pg/m^3 for the Canadian and 5.5 pg/m^3 for the values reported from the US stations. Not withstanding median values between 10 and 100 were determined for β-endosulfan at several sites also in summertime. On average the concentrations measured for endosulfan sulfate were about 5.5 pg/m^3.

Endosulfan in Precipitation

Several studies demonstrated that endosulfan is removed from the atmosphere by rain and snow fall.

In a monitoring study carried out in Atlantic Canada between 1980 and 1989 α-endosulfan was reported occasionally at concentrations near the detection limit of 10 ng/L [**35**].

In precipitation of the Great Lakes region α- and β-endosulfan concentrations were regularly determined by IADN at various stations during the period of 1987–1997. Concentration levels of α-endosulfan ranged from 0.13 – 1.95 ng/L, and those of β-endosulfan from 0.19 – 6.09 ng/L in lakes Superior and Erie. Higher value were reported from Lake Michigan ranging from 0.54 – 8.22 ng/L

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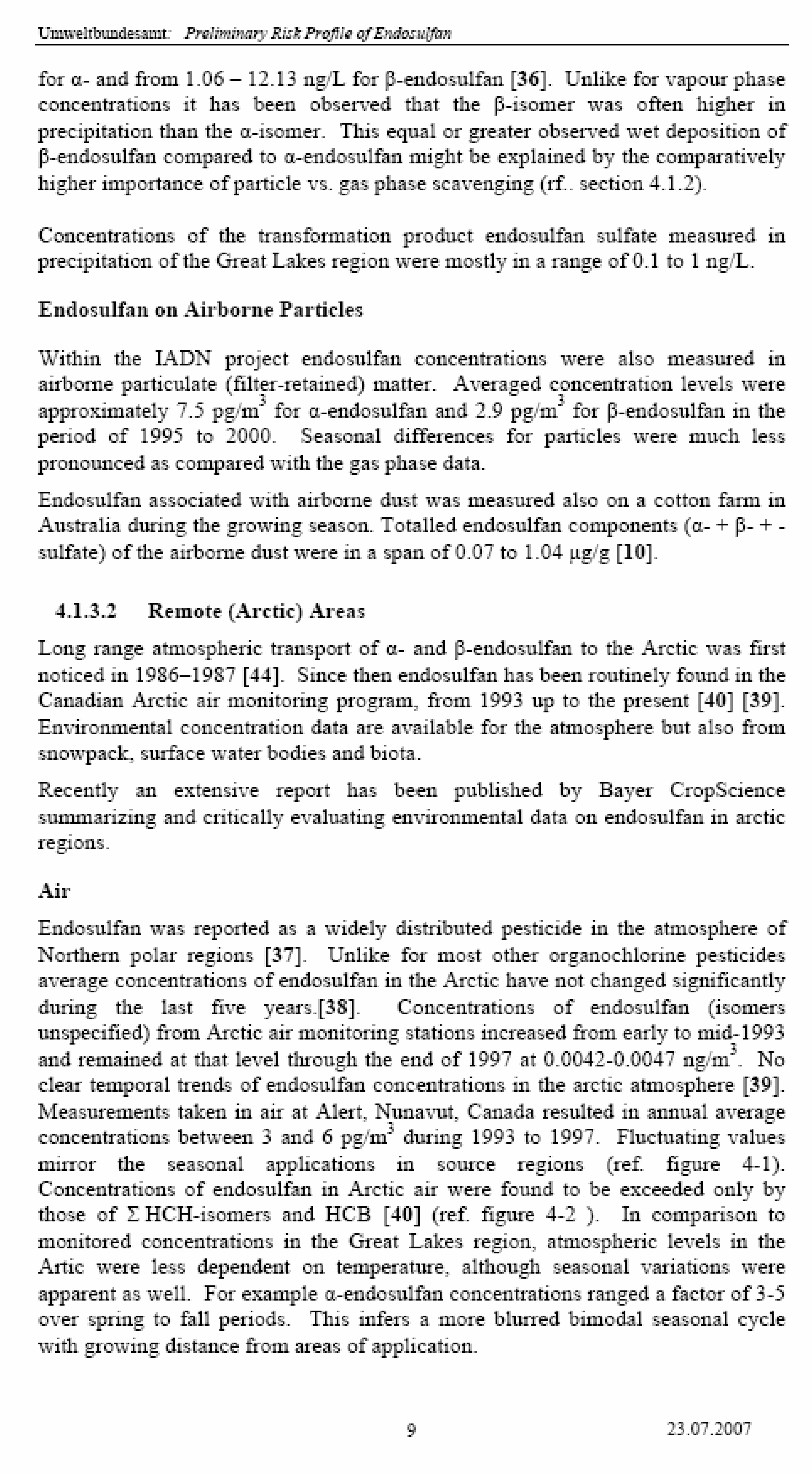
[i] The provision of monitoring data by manager of the IADN Database SC/ARQP Céline Audette is highly appreciated



for α- and from 1.06 – 12.13 ng/L for β-endosulfan **[36]**. Unlike for vapour phase concentrations it has been observed that the β-isomer was often higher in precipitation than the α-isomer. This equal or greater observed wet deposition of β-endosulfan compared to α-endosulfan might be explained by the comparatively higher importance of particle vs. gas phase scavenging (rf.. section 4.1.2).

Concentrations of the transformation product endosulfan sulfate measured in precipitation of the Great Lakes region were mostly in a range of 0.1 to 1 ng/L.

Endosulfan on Airborne Particles

Within the IADN project endosulfan concentrations were also measured in airborne particulate (filter-retained) matter. Averaged concentration levels were approximately 7.5 pg/m^3 for α-endosulfan and 2.9 pg/m^3 for β-endosulfan in the period of 1995 to 2000. Seasonal differences for particles were much less pronounced as compared with the gas phase data.

Endosulfan associated with airborne dust was measured also on a cotton farm in Australia during the growing season. Totalled endosulfan components (α- + β- + -sulfate) of the airborne dust were in a span of 0.07 to 1.04 µg/g **[10]**.

4.1.3.2 Remote (Arctic) Areas

Long range atmospheric transport of α- and β-endosulfan to the Arctic was first noticed in 1986–1987 **[44]**. Since then endosulfan has been routinely found in the Canadian Arctic air monitoring program, from 1993 up to the present **[40]** **[39]**. Environmental concentration data are available for the atmosphere but also from snowpack, surface water bodies and biota.

Recently an extensive report has been published by Bayer CropScience summarizing and critically evaluating environmental data on endosulfan in arctic regions.

Air

Endosulfan was reported as a widely distributed pesticide in the atmosphere of Northern polar regions **[37]**. Unlike for most other organochlorine pesticides average concentrations of endosulfan in the Arctic have not changed significantly during the last five years.**[38]**. Concentrations of endosulfan (isomers unspecified) from Arctic air monitoring stations increased from early to mid-1993 and remained at that level through the end of 1997 at 0.0042-0.0047 ng/m^3. No clear temporal trends of endosulfan concentrations in the arctic atmosphere **[39]**. Measurements taken in air at Alert, Nunavut, Canada resulted in annual average concentrations between 3 and 6 pg/m^3 during 1993 to 1997. Fluctuating values mirror the seasonal applications in source regions (ref. figure 4-1). Concentrations of endosulfan in Arctic air were found to be exceeded only by those of Σ HCH-isomers and HCB **[40]** (ref. figure 4-2). In comparison to monitored concentrations in the Great Lakes region, atmospheric levels in the Artic were less dependent on temperature, although seasonal variations were apparent as well. For example α-endosulfan concentrations ranged a factor of 3-5 over spring to fall periods. This infers a more blurred bimodal seasonal cycle with growing distance from areas of application.

Hung et al. [41] used temperature normalization, multiple linear regression , and digital filtration to analyze the temporal trends of an atmospheric dataset on organochlorine pesticides (OCs) collected at the Canadian high arctic site of Alert, Nunavut. While air concentrations of Lindan and Chlordane showed decreasing trends through the 1990s with halflives of 5.6 and 4.8 years α-endosulfan showed a very slow decline with a halflive of 21 years.

Seasonal variation of concentrations was also reported from Sable Island (240 km east of Nova Scotia at 43°57´N, 60°00´W). In summer aerial endosulfan concentration (α- and β-isomer) were determined between 69 and 159 ng/m^3 while for wintertime values dropped to 1.4-3.0 pg/m^3 (only α -isomer) [42].

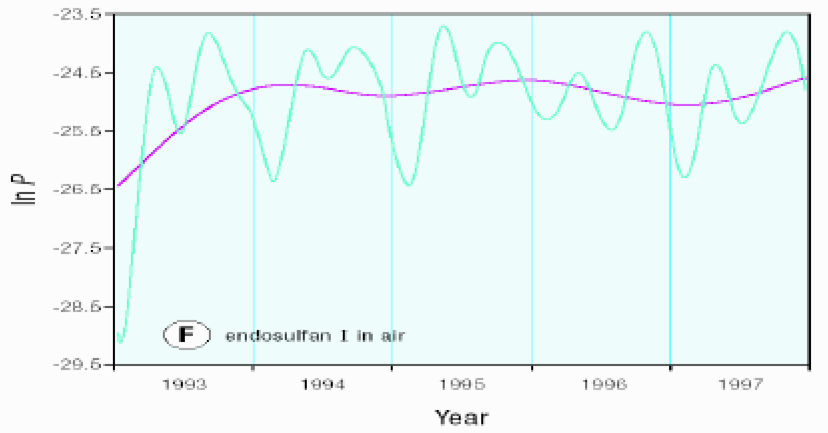


figure 4-1 Trend (purple) and seasonal cycle (blue) of α-endosulfan in air at Alert, Nunavut, Canada (82°30´N, 62°20´W); source [39]

Similar data on α-endosulfan have been reported from Resolute Bay (Cornwallis Island, 75 N lat.) where air concentrations of approximately 4 pg/m^3 have been measured [43] and from air samples taken on an iceberg that calved off the Ward Hunt Ice Shelf on the northern shore of Ellesmere Island (approx. 81°N, 100°W). Mean concentration of α-endosulfan in summer 1986 and 1987 were 7.1 and 3.4 ng/m^3, respectively [44]. Additional evidence for airborne long-range transport is provided by data from Newfoundland showing mean concentrations of 20 pg/m^3 in summer 1977 [45].

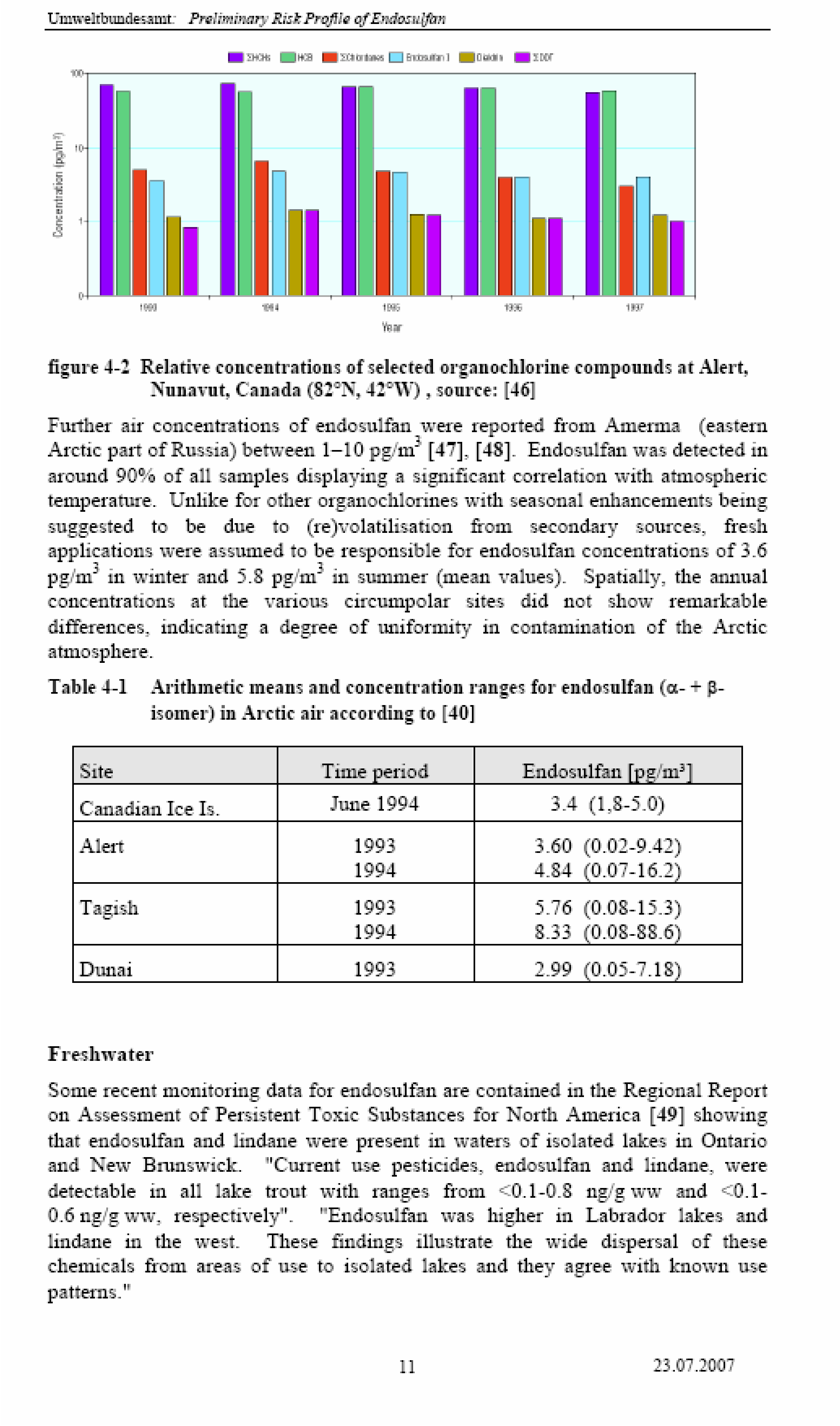


figure 4-2 Relative concentrations of selected organochlorine compounds at Alert, Nunavut, Canada (82°N, 42°W) , source: [46]

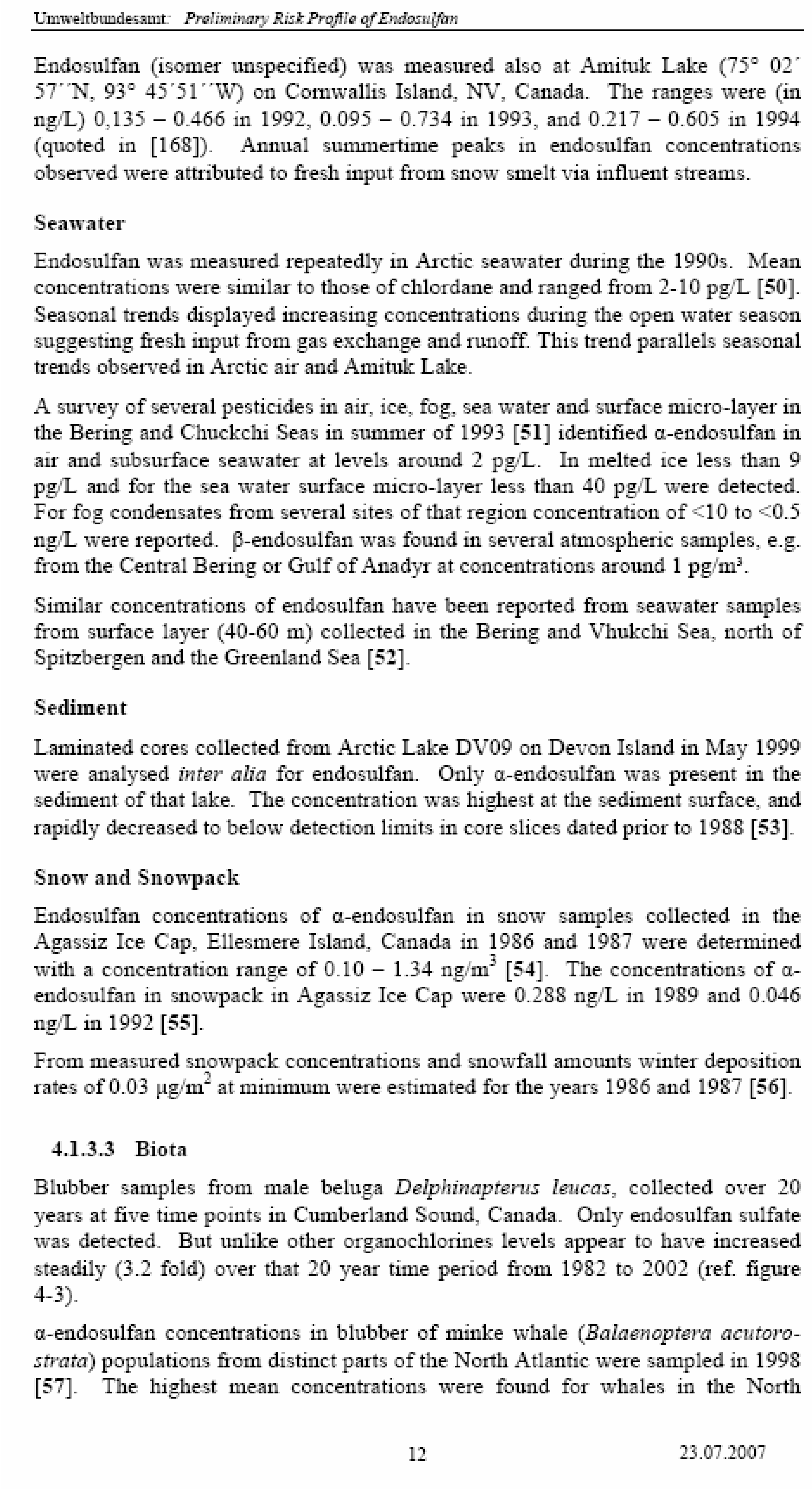
Further air concentrations of endosulfan were reported from Amerma (eastern Arctic part of Russia) between 1–10 pg/m^3 [47], [48]. Endosulfan was detected in around 90% of all samples displaying a significant correlation with atmospheric temperature. Unlike for other organochlorines with seasonal enhancements being suggested to be due to (re)volatilisation from secondary sources, fresh applications were assumed to be responsible for endosulfan concentrations of 3.6 pg/m^3 in winter and 5.8 pg/m^3 in summer (mean values). Spatially, the annual concentrations at the various circumpolar sites did not show remarkable differences, indicating a degree of uniformity in contamination of the Arctic atmosphere.

Table 4-1 Arithmetic means and concentration ranges for endosulfan (α- + β-isomer) in Arctic air according to [40]

Site	Time period	Endosulfan [pg/m³]
Canadian Ice Is.	June 1994	3.4 (1,8-5.0)
Alert	1993 1994	3.60 (0.02-9.42) 4.84 (0.07-16.2)
Tagish	1993 1994	5.76 (0.08-15.3) 8.33 (0.08-88.6)
Dunai	1993	2.99 (0.05-7.18)

Freshwater

Some recent monitoring data for endosulfan are contained in the Regional Report on Assessment of Persistent Toxic Substances for North America [49] showing that endosulfan and lindane were present in waters of isolated lakes in Ontario and New Brunswick. "Current use pesticides, endosulfan and lindane, were detectable in all lake trout with ranges from <0.1-0.8 ng/g ww and <0.1-0.6 ng/g ww, respectively". "Endosulfan was higher in Labrador lakes and lindane in the west. These findings illustrate the wide dispersal of these chemicals from areas of use to isolated lakes and they agree with known use patterns."



Umweltbundesamt: *Preliminary Risk Profile of Endosulfan*

Endosulfan (isomer unspecified) was measured also at Amituk Lake (75° 02´ 57´´N, 93° 45´51´´W) on Cornwallis Island, NV, Canada. The ranges were (in ng/L) 0,135 – 0.466 in 1992, 0.095 – 0.734 in 1993, and 0.217 – 0.605 in 1994 (quoted in [168]). Annual summertime peaks in endosulfan concentrations observed were attributed to fresh input from snow smelt via influent streams.

Seawater

Endosulfan was measured repeatedly in Arctic seawater during the 1990s. Mean concentrations were similar to those of chlordane and ranged from 2-10 pg/L [**50**]. Seasonal trends displayed increasing concentrations during the open water season suggesting fresh input from gas exchange and runoff. This trend parallels seasonal trends observed in Arctic air and Amituk Lake.

A survey of several pesticides in air, ice, fog, sea water and surface micro-layer in the Bering and Chuckchi Seas in summer of 1993 [**51**] identified α-endosulfan in air and subsurface seawater at levels around 2 pg/L. In melted ice less than 9 pg/L and for the sea water surface micro-layer less than 40 pg/L were detected. For fog condensates from several sites of that region concentration of <10 to <0.5 ng/L were reported. β-endosulfan was found in several atmospheric samples, e.g. from the Central Bering or Gulf of Anadyr at concentrations around 1 pg/m³.

Similar concentrations of endosulfan have been reported from seawater samples from surface layer (40-60 m) collected in the Bering and Vhukchi Sea, north of Spitzbergen and the Greenland Sea [**52**].

Sediment

Laminated cores collected from Arctic Lake DV09 on Devon Island in May 1999 were analysed *inter alia* for endosulfan. Only α-endosulfan was present in the sediment of that lake. The concentration was highest at the sediment surface, and rapidly decreased to below detection limits in core slices dated prior to 1988 [**53**].

Snow and Snowpack

Endosulfan concentrations of α-endosulfan in snow samples collected in the Agassiz Ice Cap, Ellesmere Island, Canada in 1986 and 1987 were determined with a concentration range of 0.10 – 1.34 ng/m^3 [**54**]. The concentrations of α-endosulfan in snowpack in Agassiz Ice Cap were 0.288 ng/L in 1989 and 0.046 ng/L in 1992 [**55**].

From measured snowpack concentrations and snowfall amounts winter deposition rates of 0.03 µg/m^2 at minimum were estimated for the years 1986 and 1987 [**56**].

4.1.3.3 Biota

Blubber samples from male beluga *Delphinapterus leucas*, collected over 20 years at five time points in Cumberland Sound, Canada. Only endosulfan sulfate was detected. But unlike other organochlorines levels appear to have increased steadily (3.2 fold) over that 20 year time period from 1982 to 2002 (ref. figure 4-3).

α-endosulfan concentrations in blubber of minke whale (*Balaenoptera acutorostrata*) populations from distinct parts of the North Atlantic were sampled in 1998 [**57**]. The highest mean concentrations were found for whales in the North

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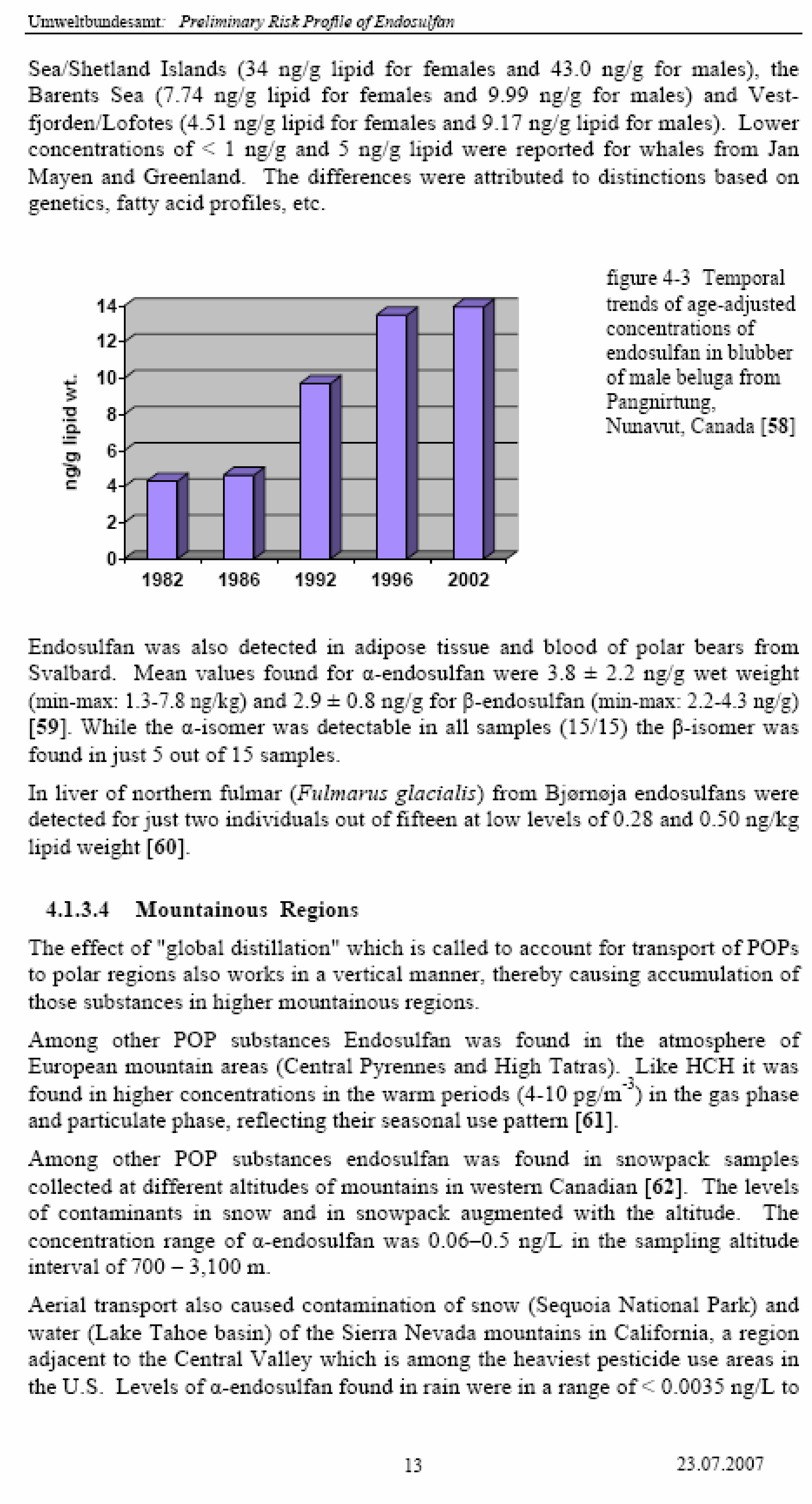


Sea/Shetland Islands (34 ng/g lipid for females and 43.0 ng/g for males), the Barents Sea (7.74 ng/g lipid for females and 9.99 ng/g for males) and Vestfjorden/Lofotes (4.51 ng/g lipid for females and 9.17 ng/g lipid for males). Lower concentrations of < 1 ng/g and 5 ng/g lipid were reported for whales from Jan Mayen and Greenland. The differences were attributed to distinctions based on genetics, fatty acid profiles, etc.

figure 4-3 Temporal trends of age-adjusted concentrations of endosulfan in blubber of male beluga from Pangnirtung, Nunavut, Canada [**58**]

Endosulfan was also detected in adipose tissue and blood of polar bears from Svalbard. Mean values found for α-endosulfan were 3.8 ± 2.2 ng/g wet weight (min-max: 1.3-7.8 ng/kg) and 2.9 ± 0.8 ng/g for β-endosulfan (min-max: 2.2-4.3 ng/g) [**59**]. While the α-isomer was detectable in all samples (15/15) the β-isomer was found in just 5 out of 15 samples.

In liver of northern fulmar (*Fulmarus glacialis*) from Bjørnøja endosulfans were detected for just two individuals out of fifteen at low levels of 0.28 and 0.50 ng/kg lipid weight [**60**].

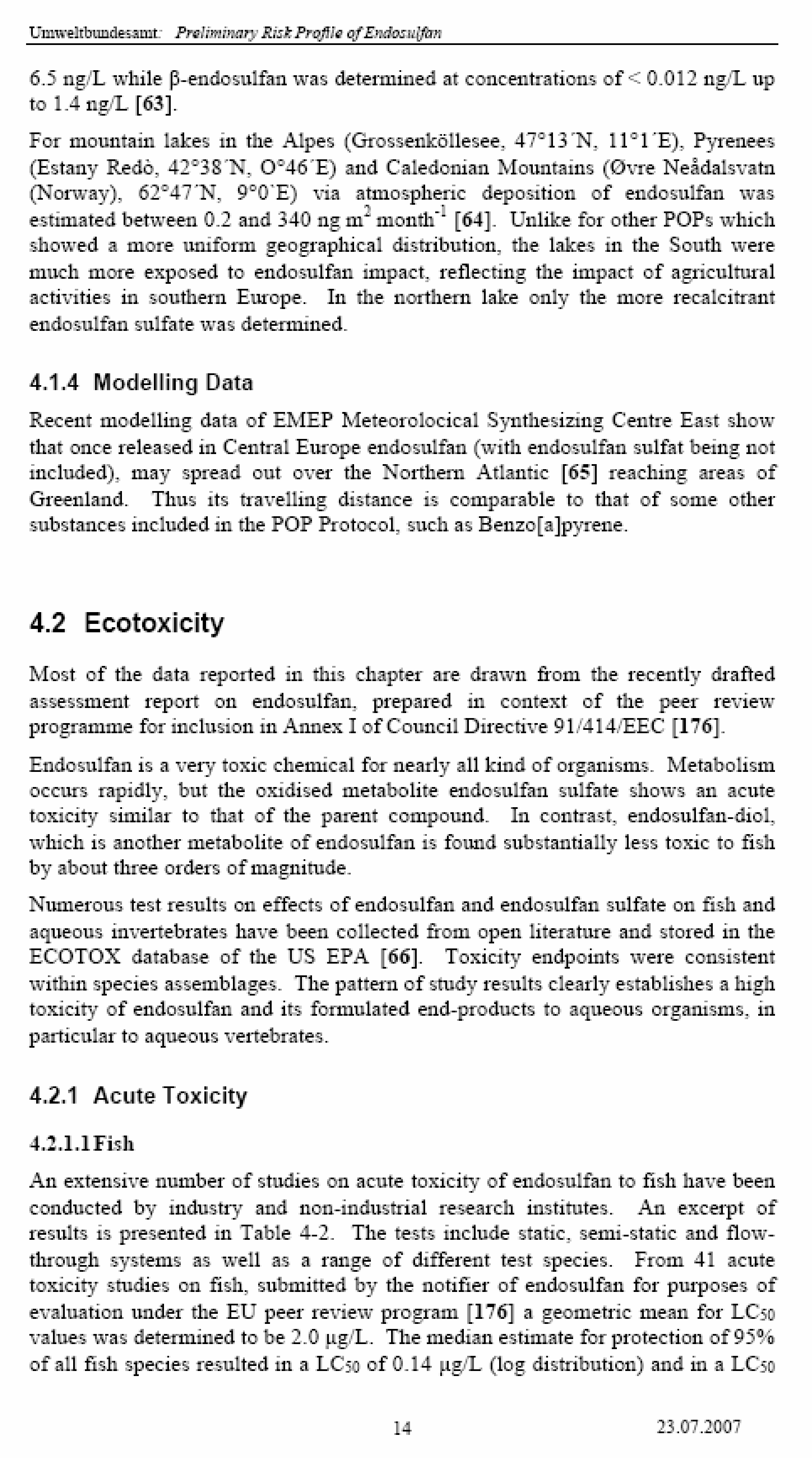
4.1.3.4 Mountainous Regions

The effect of "global distillation" which is called to account for transport of POPs to polar regions also works in a vertical manner, thereby causing accumulation of those substances in higher mountainous regions.

Among other POP substances Endosulfan was found in the atmosphere of European mountain areas (Central Pyrennes and High Tatras). Like HCH it was found in higher concentrations in the warm periods (4-10 pg/m^{-3}) in the gas phase and particulate phase, reflecting their seasonal use pattern [**61**].

Among other POP substances endosulfan was found in snowpack samples collected at different altitudes of mountains in western Canadian [**62**]. The levels of contaminants in snow and in snowpack augmented with the altitude. The concentration range of α-endosulfan was 0.06–0.5 ng/L in the sampling altitude interval of 700 – 3,100 m.

Aerial transport also caused contamination of snow (Sequoia National Park) and water (Lake Tahoe basin) of the Sierra Nevada mountains in California, a region adjacent to the Central Valley which is among the heaviest pesticide use areas in the U.S. Levels of α-endosulfan found in rain were in a range of < 0.0035 ng/L to



6.5 ng/L while β-endosulfan was determined at concentrations of < 0.012 ng/L up to 1.4 ng/L [**63**].

For mountain lakes in the Alpes (Grossenköllesee, 47°13´N, 11°1´E), Pyrenees (Estany Redò, 42°38´N, O°46´E) and Caledonian Mountains (Øvre Neådalsvatn (Norway), 62°47´N, 9°0´E) via atmospheric deposition of endosulfan was estimated between 0.2 and 340 ng m^2 $month^{-1}$ [**64**]. Unlike for other POPs which showed a more uniform geographical distribution, the lakes in the South were much more exposed to endosulfan impact, reflecting the impact of agricultural activities in southern Europe. In the northern lake only the more recalcitrant endosulfan sulfate was determined.

4.1.4 Modelling Data

Recent modelling data of EMEP Meteorolocical Synthesizing Centre East show that once released in Central Europe endosulfan (with endosulfan sulfat being not included), may spread out over the Northern Atlantic [**65**] reaching areas of Greenland. Thus its travelling distance is comparable to that of some other substances included in the POP Protocol, such as Benzo[a]pyrene.

4.2 Ecotoxicity

Most of the data reported in this chapter are drawn from the recently drafted assessment report on endosulfan, prepared in context of the peer review programme for inclusion in Annex I of Council Directive 91/414/EEC [**176**].

Endosulfan is a very toxic chemical for nearly all kind of organisms. Metabolism occurs rapidly, but the oxidised metabolite endosulfan sulfate shows an acute toxicity similar to that of the parent compound. In contrast, endosulfan-diol, which is another metabolite of endosulfan is found substantially less toxic to fish by about three orders of magnitude.

Numerous test results on effects of endosulfan and endosulfan sulfate on fish and aqueous invertebrates have been collected from open literature and stored in the ECOTOX database of the US EPA [**66**]. Toxicity endpoints were consistent within species assemblages. The pattern of study results clearly establishes a high toxicity of endosulfan and its formulated end-products to aqueous organisms, in particular to aqueous vertebrates.

4.2.1 Acute Toxicity

4.2.1.1 Fish

An extensive number of studies on acute toxicity of endosulfan to fish have been conducted by industry and non-industrial research institutes. An excerpt of results is presented in Table 4-2. The tests include static, semi-static and flow-through systems as well as a range of different test species. From 41 acute toxicity studies on fish, submitted by the notifier of endosulfan for purposes of evaluation under the EU peer review program [**176**] a geometric mean for LC_{50} values was determined to be 2.0 µg/L. The median estimate for protection of 95% of all fish species resulted in a LC_{50} of 0.14 µg/L (log distribution) and in a LC_{50}

value of 0.13 µg/L (normal distribution). There are indications from the majority of study results conducted on single isomers that the α-isomer is more toxic than the β-endosulfan **[67]** **[68]**, but the data is not all consistent.

At the lower end of data LC_{50} values for fish are 0.09 µg/L for *Leistomus xanthurus* and 0.1 µg/L for *Morone saxatilis*.

Table 4-2 Some typical study results for acute fish toxicity of endosulfan

study type	species	LC_{50}	Reference
static	rainbow trout	1.6 µg/L	**[69]**
static (12 °C)	rainbow trout	0.9 µg/L	**[70]**
static	rainbow trout	1.6 µg/L	**[71]**
dynamic	rainbow trout	0.3 µg/L	
static	fathead minnow	0.8 µg/L	
dynamic	fathead minnows	1 µg/L	
semi-static	(Channa punctata)	4.5-7.5 µg/L	**[72]**
static	bluegill sunfish	1.8-3.3 µg/L	**[73]**

4.2.1.2 Aquatic Invertebrates

Aquatic invertebrates appear commonly being acutely susceptible to endosulfan concentrations in the order of 100 µg/L, although considerable variation is evident, spanning several orders of magnitude. As an indication an EC_{50} of 150 µg/L over 48 hours on *Daphnia magna* is suggested **[176]**, representing a 90-percentile of a compiled data set on this species.

Short-term LC_{50} for a variety of species of shrimp vary between 0.04 and 17 µg/L. The lowest 96-hour LC_{50} reported for a single crustacean species was reported at 0.04 µg/L for *Penaeus duorarum* [74]. *Crangon septemspinosa* had an LC_{50} value of 0.2 µg/L, whereas the LC_{50} for all other crustaceans in this study were greater than 0.4 µg/L.

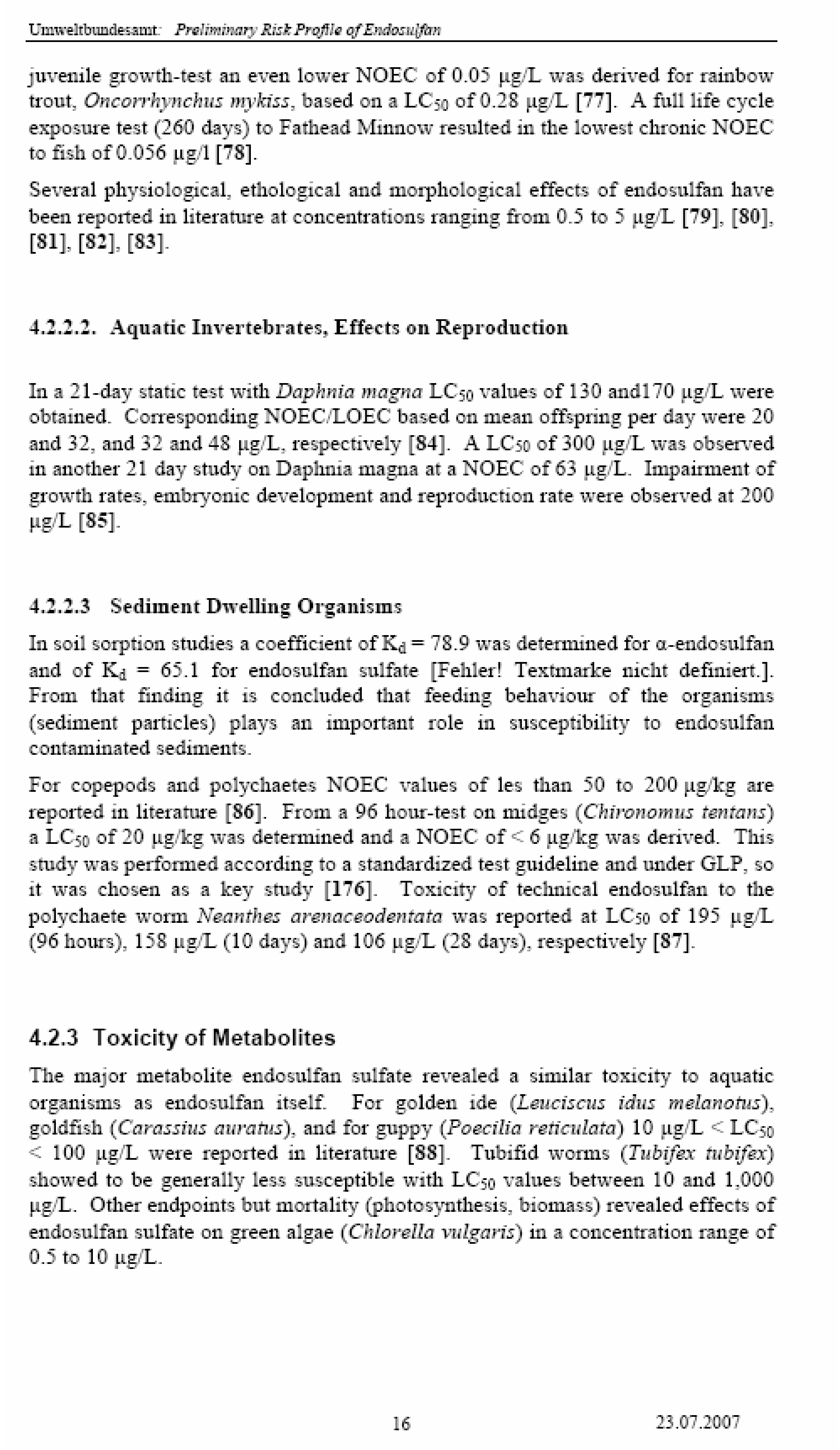
4.2.1.3 Algae

Much less data are available on algae as compared with invertebrates and fish. From 72 hour-tests on the green algae *Scenedesmus subspicatus* a NOEC of 560 µg/L is suggested **[75]**.

4.2.2 Chronic Toxicity

4.2.2.1 Fish

Generally, for chronic toxicity to fish NOECs of 0.05–0.4 µg/L were observed **[178]**. E.g. from a 28-day early-life-stage test on sheepshead minnow, *Cyprinodon variegates* a NOEC of 0.4 µg/L was reported **[76]**. In a 21-day



juvenile growth-test an even lower NOEC of 0.05 µg/L was derived for rainbow trout, *Oncorrhynchus mykiss*, based on a LC_{50} of 0.28 µg/L **[77]**. A full life cycle exposure test (260 days) to Fathead Minnow resulted in the lowest chronic NOEC to fish of 0.056 µg/l **[78]**.

Several physiological, ethological and morphological effects of endosulfan have been reported in literature at concentrations ranging from 0.5 to 5 µg/L **[79]**, **[80]**, **[81]**, **[82]**, **[83]**.

4.2.2.2. Aquatic Invertebrates, Effects on Reproduction

In a 21-day static test with *Daphnia magna* LC_{50} values of 130 and170 µg/L were obtained. Corresponding NOEC/LOEC based on mean offspring per day were 20 and 32, and 32 and 48 µg/L, respectively **[84]**. A LC_{50} of 300 µg/L was observed in another 21 day study on Daphnia magna at a NOEC of 63 µg/L. Impairment of growth rates, embryonic development and reproduction rate were observed at 200 µg/L **[85]**.

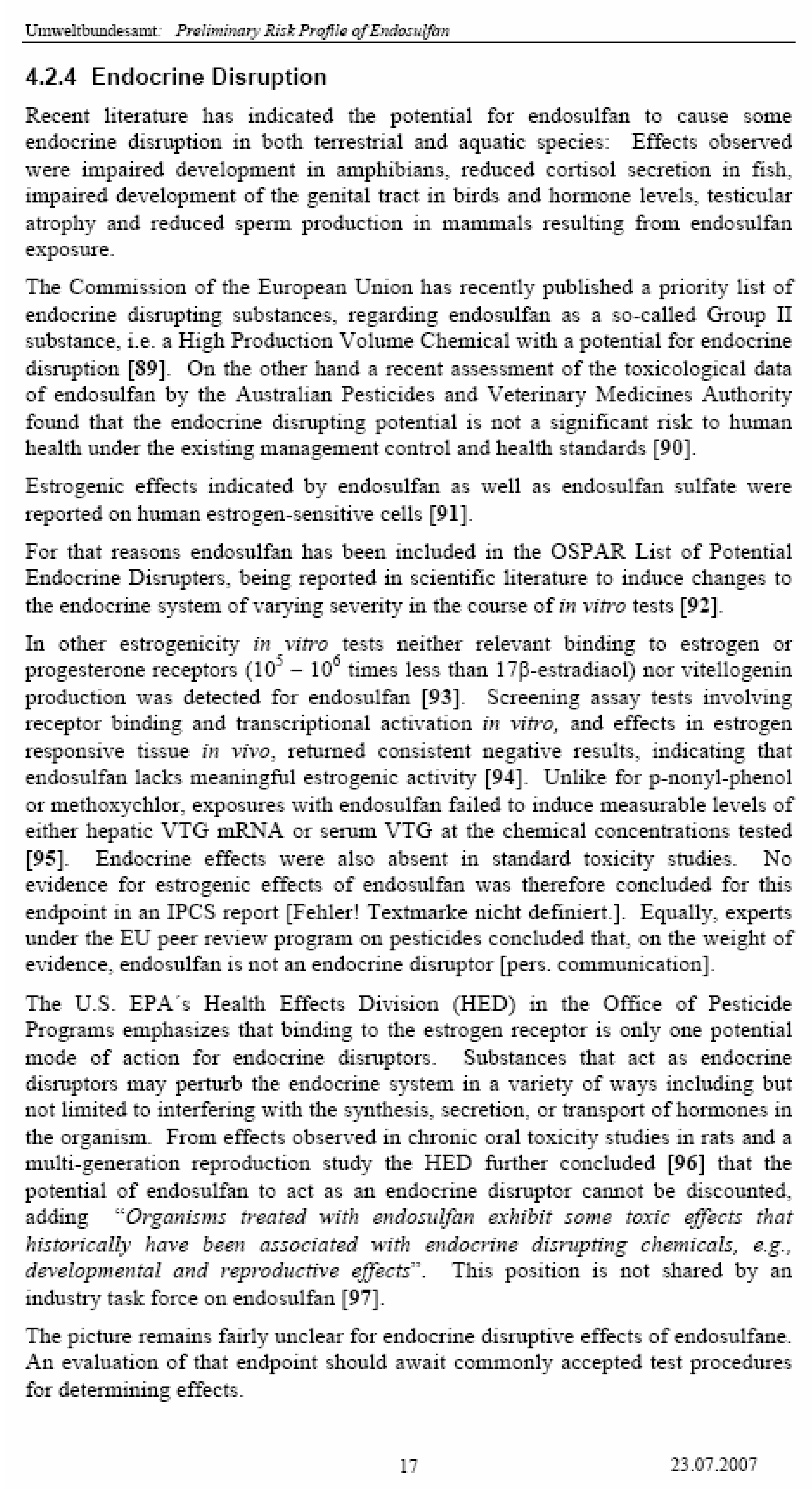
4.2.2.3 Sediment Dwelling Organisms

In soil sorption studies a coefficient of K_d = 78.9 was determined for α-endosulfan and of K_d = 65.1 for endosulfan sulfate [Fehler! Textmarke nicht definiert.]. From that finding it is concluded that feeding behaviour of the organisms (sediment particles) plays an important role in susceptibility to endosulfan contaminated sediments.

For copepods and polychaetes NOEC values of les than 50 to 200 µg/kg are reported in literature **[86]**. From a 96 hour-test on midges (*Chironomus tentans*) a LC_{50} of 20 µg/kg was determined and a NOEC of < 6 µg/kg was derived. This study was performed according to a standardized test guideline and under GLP, so it was chosen as a key study **[176]**. Toxicity of technical endosulfan to the polychaete worm *Neanthes arenaceodentata* was reported at LC_{50} of 195 µg/L (96 hours), 158 µg/L (10 days) and 106 µg/L (28 days), respectively **[87]**.

4.2.3 Toxicity of Metabolites

The major metabolite endosulfan sulfate revealed a similar toxicity to aquatic organisms as endosulfan itself. For golden ide (*Leuciscus idus melanotus*), goldfish (*Carassius auratus*), and for guppy (*Poecilia reticulata*) 10 µg/L < LC_{50} < 100 µg/L were reported in literature **[88]**. Tubifid worms (*Tubifex tubifex*) showed to be generally less susceptible with LC_{50} values between 10 and 1,000 µg/L. Other endpoints but mortality (photosynthesis, biomass) revealed effects of endosulfan sulfate on green algae (*Chlorella vulgaris*) in a concentration range of 0.5 to 10 µg/L.



4.2.4 Endocrine Disruption

Recent literature has indicated the potential for endosulfan to cause some endocrine disruption in both terrestrial and aquatic species: Effects observed were impaired development in amphibians, reduced cortisol secretion in fish, impaired development of the genital tract in birds and hormone levels, testicular atrophy and reduced sperm production in mammals resulting from endosulfan exposure.

The Commission of the European Union has recently published a priority list of endocrine disrupting substances, regarding endosulfan as a so-called Group II substance, i.e. a High Production Volume Chemical with a potential for endocrine disruption [89]. On the other hand a recent assessment of the toxicological data of endosulfan by the Australian Pesticides and Veterinary Medicines Authority found that the endocrine disrupting potential is not a significant risk to human health under the existing management control and health standards [90].

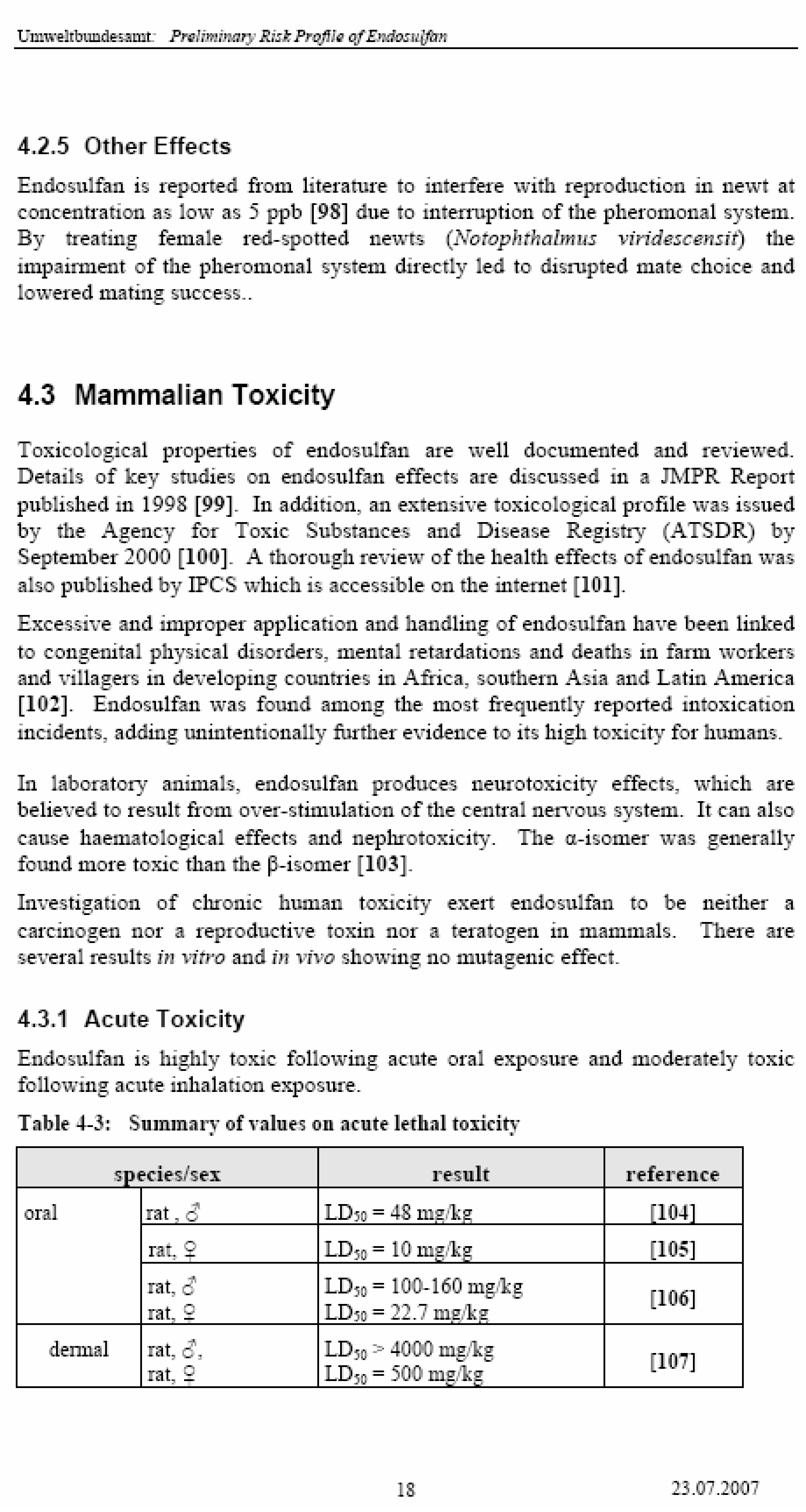
Estrogenic effects indicated by endosulfan as well as endosulfan sulfate were reported on human estrogen-sensitive cells [91].

For that reasons endosulfan has been included in the OSPAR List of Potential Endocrine Disrupters, being reported in scientific literature to induce changes to the endocrine system of varying severity in the course of *in vitro* tests [92].

In other estrogenicity *in vitro* tests neither relevant binding to estrogen or progesterone receptors ($10^5 – 10^6$ times less than 17β-estradiaol) nor vitellogenin production was detected for endosulfan [93]. Screening assay tests involving receptor binding and transcriptional activation *in vitro,* and effects in estrogen responsive tissue *in vivo*, returned consistent negative results, indicating that endosulfan lacks meaningful estrogenic activity [94]. Unlike for p-nonyl-phenol or methoxychlor, exposures with endosulfan failed to induce measurable levels of either hepatic VTG mRNA or serum VTG at the chemical concentrations tested [95]. Endocrine effects were also absent in standard toxicity studies. No evidence for estrogenic effects of endosulfan was therefore concluded for this endpoint in an IPCS report [Fehler! Textmarke nicht definiert.]. Equally, experts under the EU peer review program on pesticides concluded that, on the weight of evidence, endosulfan is not an endocrine disruptor [pers. communication].

The U.S. EPA´s Health Effects Division (HED) in the Office of Pesticide Programs emphasizes that binding to the estrogen receptor is only one potential mode of action for endocrine disruptors. Substances that act as endocrine disruptors may perturb the endocrine system in a variety of ways including but not limited to interfering with the synthesis, secretion, or transport of hormones in the organism. From effects observed in chronic oral toxicity studies in rats and a multi-generation reproduction study the HED further concluded [96] that the potential of endosulfan to act as an endocrine disruptor cannot be discounted, adding "*Organisms treated with endosulfan exhibit some toxic effects that historically have been associated with endocrine disrupting chemicals, e.g., developmental and reproductive effects*". This position is not shared by an industry task force on endosulfan [97].

The picture remains fairly unclear for endocrine disruptive effects of endosulfane. An evaluation of that endpoint should await commonly accepted test procedures for determining effects.



4.2.5 Other Effects

Endosulfan is reported from literature to interfere with reproduction in newt at concentration as low as 5 ppb **[98]** due to interruption of the pheromonal system. By treating female red-spotted newts (*Notophthalmus viridescensit*) the impairment of the pheromonal system directly led to disrupted mate choice and lowered mating success..

4.3 Mammalian Toxicity

Toxicological properties of endosulfan are well documented and reviewed. Details of key studies on endosulfan effects are discussed in a JMPR Report published in 1998 **[99]**. In addition, an extensive toxicological profile was issued by the Agency for Toxic Substances and Disease Registry (ATSDR) by September 2000 **[100]**. A thorough review of the health effects of endosulfan was also published by IPCS which is accessible on the internet **[101]**.

Excessive and improper application and handling of endosulfan have been linked to congenital physical disorders, mental retardations and deaths in farm workers and villagers in developing countries in Africa, southern Asia and Latin America **[102]**. Endosulfan was found among the most frequently reported intoxication incidents, adding unintentionally further evidence to its high toxicity for humans.

In laboratory animals, endosulfan produces neurotoxicity effects, which are believed to result from over-stimulation of the central nervous system. It can also cause haematological effects and nephrotoxicity. The α-isomer was generally found more toxic than the β-isomer **[103]**.

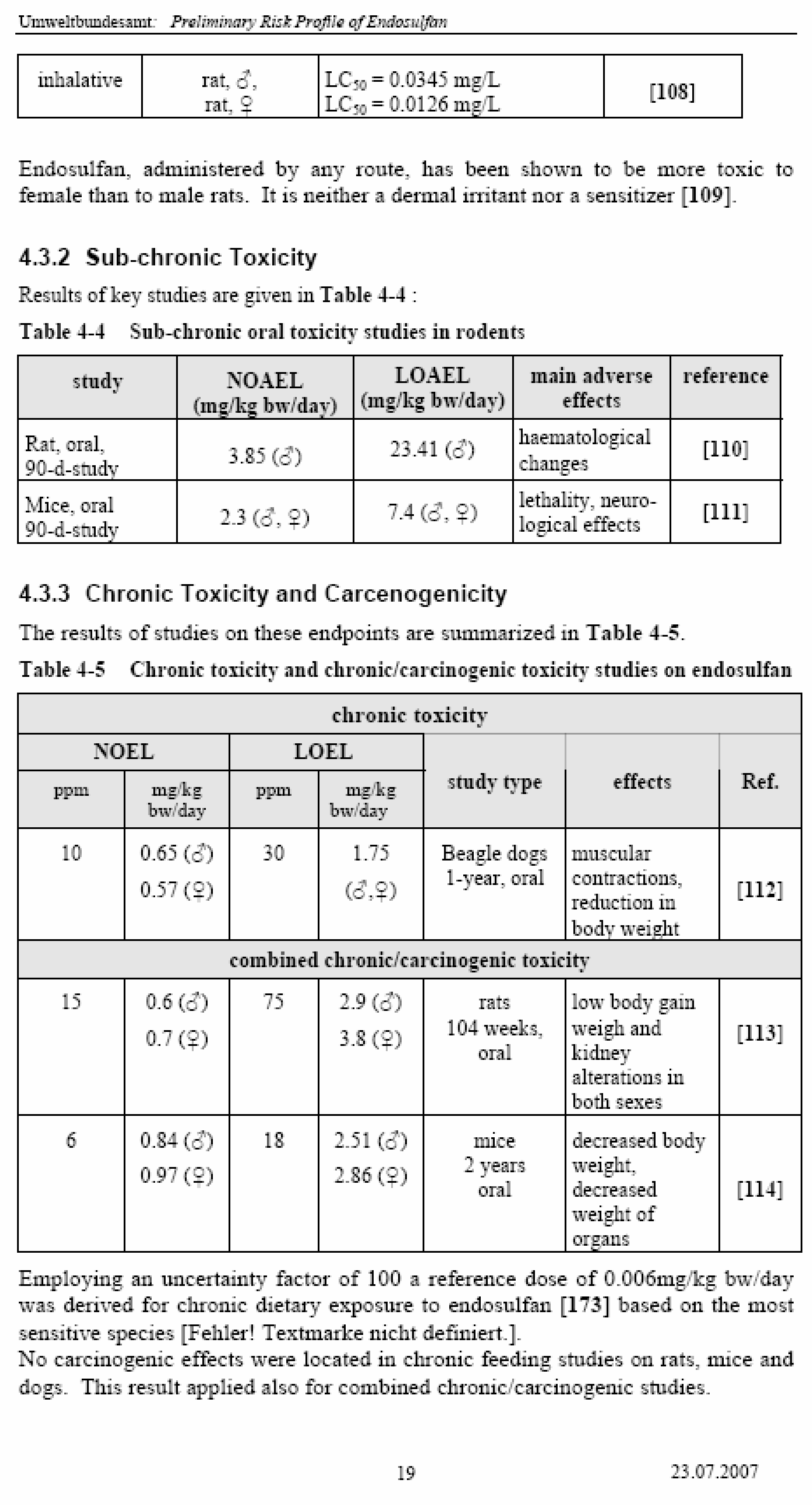
Investigation of chronic human toxicity exert endosulfan to be neither a carcinogen nor a reproductive toxin nor a teratogen in mammals. There are several results *in vitro* and *in vivo* showing no mutagenic effect.

4.3.1 Acute Toxicity

Endosulfan is highly toxic following acute oral exposure and moderately toxic following acute inhalation exposure.

Table 4-3: Summary of values on acute lethal toxicity

species/sex		result	reference
oral	rat , ♂	LD_{50} = 48 mg/kg	[104]
	rat, ♀	LD_{50} = 10 mg/kg	[105]
	rat, ♂ rat, ♀	LD_{50} = 100-160 mg/kg LD_{50} = 22.7 mg/kg	[106]
dermal	rat, ♂, rat, ♀	LD_{50} > 4000 mg/kg LD_{50} = 500 mg/kg	[107]



inhalative	rat, ♂, rat, ♀	LC_{50} = 0.0345 mg/L LC_{50} = 0.0126 mg/L	**[108]**

Endosulfan, administered by any route, has been shown to be more toxic to female than to male rats. It is neither a dermal irritant nor a sensitizer **[109]**.

4.3.2 Sub-chronic Toxicity

Results of key studies are given in **Table 4-4** :

Table 4-4 Sub-chronic oral toxicity studies in rodents

study	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	main adverse effects	reference
Rat, oral, 90-d-study	3.85 (♂)	23.41 (♂)	haematological changes	**[110]**
Mice, oral 90-d-study	2.3 (♂, ♀)	7.4 (♂, ♀)	lethality, neurological effects	**[111]**

4.3.3 Chronic Toxicity and Carcenogenicity

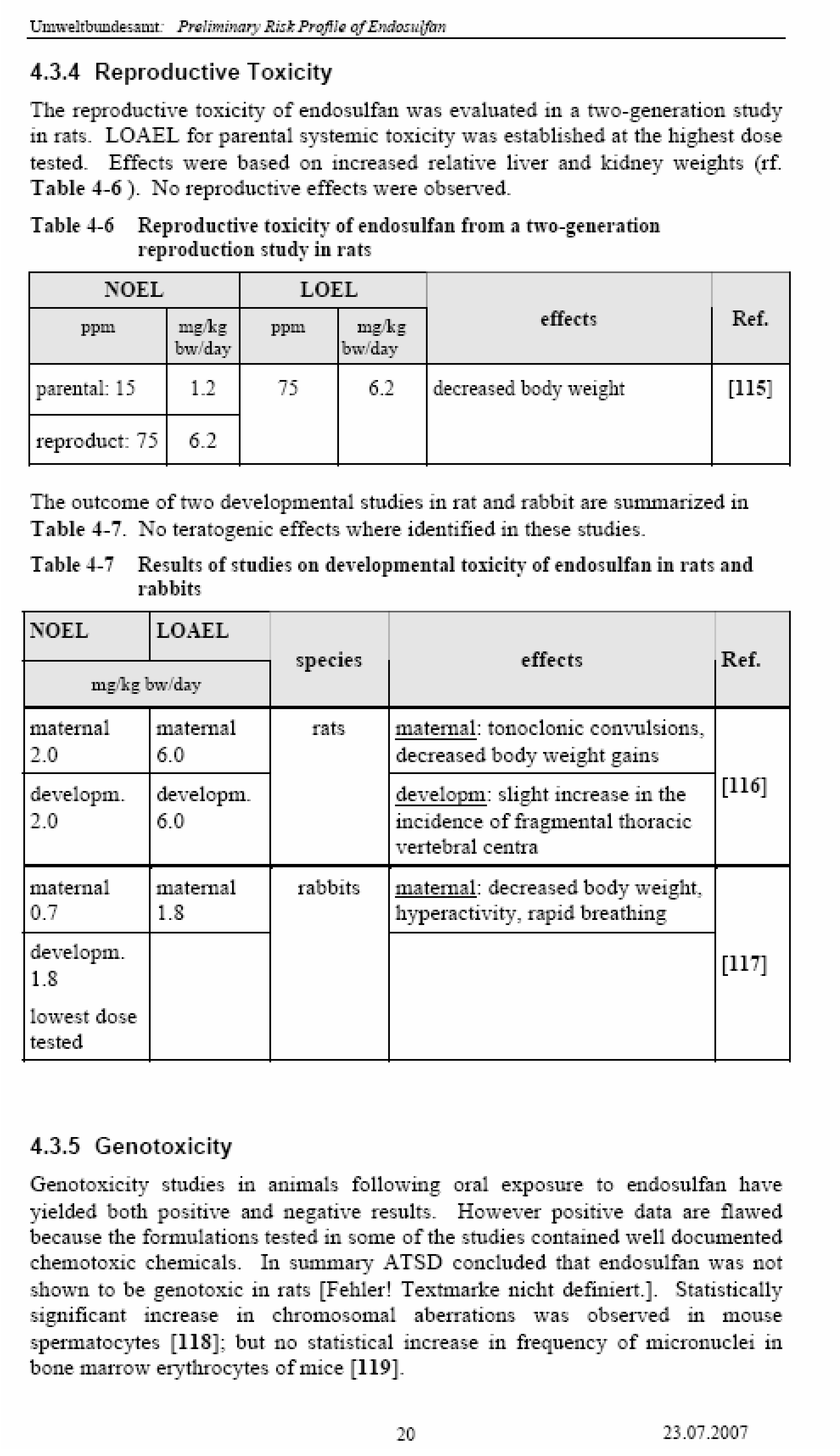
The results of studies on these endpoints are summarized in **Table 4-5**.

Table 4-5 Chronic toxicity and chronic/carcinogenic toxicity studies on endosulfan

chronic toxicity						
NOEL		**LOEL**		**study type**	**effects**	**Ref.**
ppm	mg/kg bw/day	ppm	mg/kg bw/day			
10	0.65 (♂) 0.57 (♀)	30	1.75 (♂,♀)	Beagle dogs 1-year, oral	muscular contractions, reduction in body weight	**[112]**
combined chronic/carcinogenic toxicity						
15	0.6 (♂) 0.7 (♀)	75	2.9 (♂) 3.8 (♀)	rats 104 weeks, oral	low body gain weigh and kidney alterations in both sexes	[113]
6	0.84 (♂) 0.97 (♀)	18	2.51 (♂) 2.86 (♀)	mice 2 years oral	decreased body weight, decreased weight of organs	[114]

Employing an uncertainty factor of 100 a reference dose of 0.006mg/kg bw/day was derived for chronic dietary exposure to endosulfan **[173]** based on the most sensitive species [Fehler! Textmarke nicht definiert.].

No carcinogenic effects were located in chronic feeding studies on rats, mice and dogs. This result applied also for combined chronic/carcinogenic studies.



4.3.4 Reproductive Toxicity

The reproductive toxicity of endosulfan was evaluated in a two-generation study in rats. LOAEL for parental systemic toxicity was established at the highest dose tested. Effects were based on increased relative liver and kidney weights (rf. **Table 4-6**). No reproductive effects were observed.

Table 4-6 Reproductive toxicity of endosulfan from a two-generation reproduction study in rats

NOEL		LOEL		effects	Ref.
ppm	mg/kg bw/day	ppm	mg/kg bw/day		
parental: 15	1.2	75	6.2	decreased body weight	**[115]**
reproduct: 75	6.2				

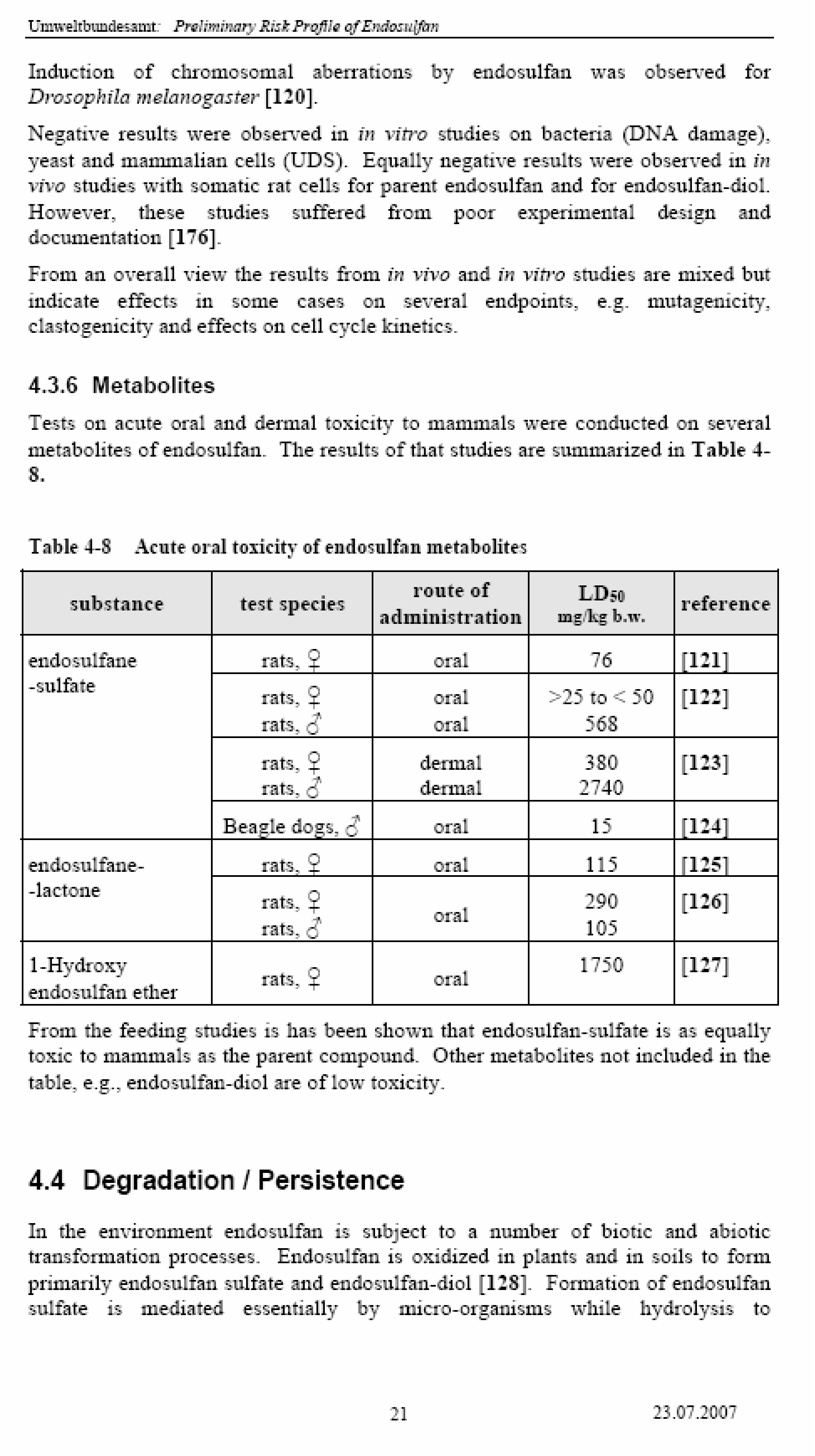
The outcome of two developmental studies in rat and rabbit are summarized in **Table 4-7**. No teratogenic effects where identified in these studies.

Table 4-7 Results of studies on developmental toxicity of endosulfan in rats and rabbits

NOEL	LOAEL	species	effects	Ref.
mg/kg bw/day				
maternal 2.0	maternal 6.0	rats	maternal: tonoclonic convulsions, decreased body weight gains	[116]
developm. 2.0	developm. 6.0		developm: slight increase in the incidence of fragmental thoracic vertebral centra	
maternal 0.7	maternal 1.8	rabbits	maternal: decreased body weight, hyperactivity, rapid breathing	[117]
developm. 1.8 lowest dose tested				

4.3.5 Genotoxicity

Genotoxicity studies in animals following oral exposure to endosulfan have yielded both positive and negative results. However positive data are flawed because the formulations tested in some of the studies contained well documented chemotoxic chemicals. In summary ATSD concluded that endosulfan was not shown to be genotoxic in rats [Fehler! Textmarke nicht definiert.]. Statistically significant increase in chromosomal aberrations was observed in mouse spermatocytes **[118]**; but no statistical increase in frequency of micronuclei in bone marrow erythrocytes of mice **[119]**.



Umweltbundesamt: *Preliminary Risk Profile of Endosulfan*

Induction of chromosomal aberrations by endosulfan was observed for *Drosophila melanogaster* **[120]**.

Negative results were observed in *in vitro* studies on bacteria (DNA damage), yeast and mammalian cells (UDS). Equally negative results were observed in *in vivo* studies with somatic rat cells for parent endosulfan and for endosulfan-diol. However, these studies suffered from poor experimental design and documentation **[176]**.

From an overall view the results from *in vivo* and *in vitro* studies are mixed but indicate effects in some cases on several endpoints, e.g. mutagenicity, clastogenicity and effects on cell cycle kinetics.

4.3.6 Metabolites

Tests on acute oral and dermal toxicity to mammals were conducted on several metabolites of endosulfan. The results of that studies are summarized in **Table 4-8.**

Table 4-8 Acute oral toxicity of endosulfan metabolites

substance	test species	route of administration	LD_{50} mg/kg b.w.	reference
endosulfane -sulfate	rats, ♀	oral	76	**[121]**
	rats, ♀ rats, ♂	oral oral	>25 to < 50 568	**[122]**
	rats, ♀ rats, ♂	dermal dermal	380 2740	**[123]**
	Beagle dogs, ♂	oral	15	**[124]**
endosulfane- -lactone	rats, ♀	oral	115	**[125]**
	rats, ♀ rats, ♂	oral	290 105	**[126]**
1-Hydroxy endosulfan ether	rats, ♀	oral	1750	**[127]**

From the feeding studies is has been shown that endosulfan-sulfate is as equally toxic to mammals as the parent compound. Other metabolites not included in the table, e.g., endosulfan-diol are of low toxicity.

4.4 Degradation / Persistence

In the environment endosulfan is subject to a number of biotic and abiotic transformation processes. Endosulfan is oxidized in plants and in soils to form primarily endosulfan sulfate and endosulfan-diol **[128]**. Formation of endosulfan sulfate is mediated essentially by micro-organisms while hydrolysis to

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endosulfan-diol can be chemical, especially under alkaline conditions and/or microbial. Microbial mineralisation is generally slow.

The β-isomer of endosulfan is more persistent while the α-isomer is more volatile and dissipative. Identified routes of degradation in soil and water are illustrated in figure 4-4.

Given a comparable toxicity of the sulfate metabolite a number of authors make use of the term "endosulfan(sum)" which includes the combined residues of both isomers of the parent and endosulfan sulfate.

4.4.1 Soil

Numerous data are available from soil degradation studies carried out in various soils and under various climatic conditions. Much of them are compiled in the draft EU report on endosulfan **[1769]**. For purposes of this document the results of only some key studies are reported. Degradation in soil resulted in several metabolites with endosulfan sulfate being the major one. Remarkably, none of the identified degradation products were formed from cracking of the norbornene structure or any dechlorination. This may have attributed to the experimental design which did not include addition of fresh soil after certain intervals. At favourable conditions, i.e. repeated addition of fresh soil to incubation flasks containing ^{14}C-ring-labelled endosulfan sulfate releases up to ^{14}CO2 up to 35 % of the added dose were observed (pers, communication by BCS).

Both endosulfan isomers are strongly adsorbed to soil as indicated by K_{oc} values around 10,000 **[141]**. To this end it can be concluded that the different transformation rates are not caused by diverging adsorption strengths. Endosulfan sulfate is adsorbed to a similar extent as the parent compound, while affinity to organic surfaces is less pronounced for the endosulfan-diol, reported at K_{oc} values around 1,000 **[129]**.

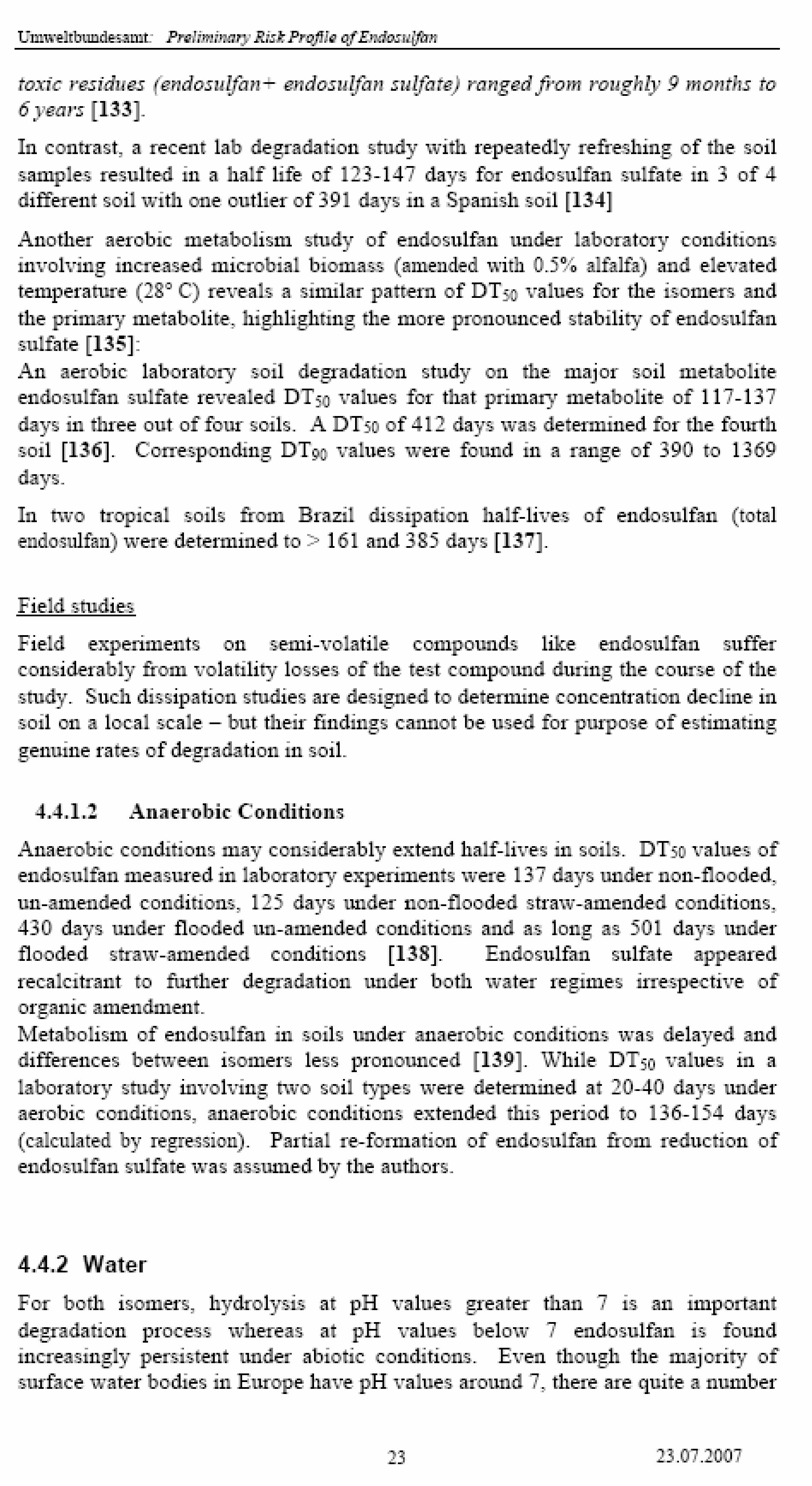
Photolytic degradation of endosulfan on soil surfaces is of no relevance. Half-lives have been reported to be greater than 200 days under simulated **[130]** and natural sunlight conditions **[131]**.

4.4.1.1 Aerobic Conditions

Laboratory studies

In five different soil types DT_{50} values of 12 to 39 days (arithmetic mean: 27.5 days) at corresponding DT_{90} values of 29 to 128 days were determined for the α-isomer under aerobic conditions. The β-isomer proved consistently to be more recalcitrant to enzymatic decomposition. Measured DT_{50} values were spanning from 108 - 264 days (arithmetic mean of 157 days) and DT_{90} values from 357 to 877 days. Encompassing both isomers and the metabolite endosulfan sulfate ("total endosulfan") values of 288 to 2,241 days resulted for DT_{50} **[132]**.

The authors of US EPA´s RED conclude: *Half-lives in acidic to neutral soils range from one to two months for α-endosulfan and from three to nine months for β-endosulfan under aerobic condition. The estimated half-lives for the combined*



toxic residues (endosulfan+ endosulfan sulfate) ranged from roughly 9 months to 6 years **[133]**.

In contrast, a recent lab degradation study with repeatedly refreshing of the soil samples resulted in a half life of 123-147 days for endosulfan sulfate in 3 of 4 different soil with one outlier of 391 days in a Spanish soil **[134]**

Another aerobic metabolism study of endosulfan under laboratory conditions involving increased microbial biomass (amended with 0.5% alfalfa) and elevated temperature (28° C) reveals a similar pattern of DT_{50} values for the isomers and the primary metabolite, highlighting the more pronounced stability of endosulfan sulfate **[135]**:

An aerobic laboratory soil degradation study on the major soil metabolite endosulfan sulfate revealed DT_{50} values for that primary metabolite of 117-137 days in three out of four soils. A DT_{50} of 412 days was determined for the fourth soil **[136]**. Corresponding DT_{90} values were found in a range of 390 to 1369 days.

In two tropical soils from Brazil dissipation half-lives of endosulfan (total endosulfan) were determined to > 161 and 385 days **[137]**.

Field studies

Field experiments on semi-volatile compounds like endosulfan suffer considerably from volatility losses of the test compound during the course of the study. Such dissipation studies are designed to determine concentration decline in soil on a local scale – but their findings cannot be used for purpose of estimating genuine rates of degradation in soil.

4.4.1.2 Anaerobic Conditions

Anaerobic conditions may considerably extend half-lives in soils. DT_{50} values of endosulfan measured in laboratory experiments were 137 days under non-flooded, un-amended conditions, 125 days under non-flooded straw-amended conditions, 430 days under flooded un-amended conditions and as long as 501 days under flooded straw-amended conditions **[138]**. Endosulfan sulfate appeared recalcitrant to further degradation under both water regimes irrespective of organic amendment.

Metabolism of endosulfan in soils under anaerobic conditions was delayed and differences between isomers less pronounced **[139]**. While DT_{50} values in a laboratory study involving two soil types were determined at 20-40 days under aerobic conditions, anaerobic conditions extended this period to 136-154 days (calculated by regression). Partial re-formation of endosulfan from reduction of endosulfan sulfate was assumed by the authors.

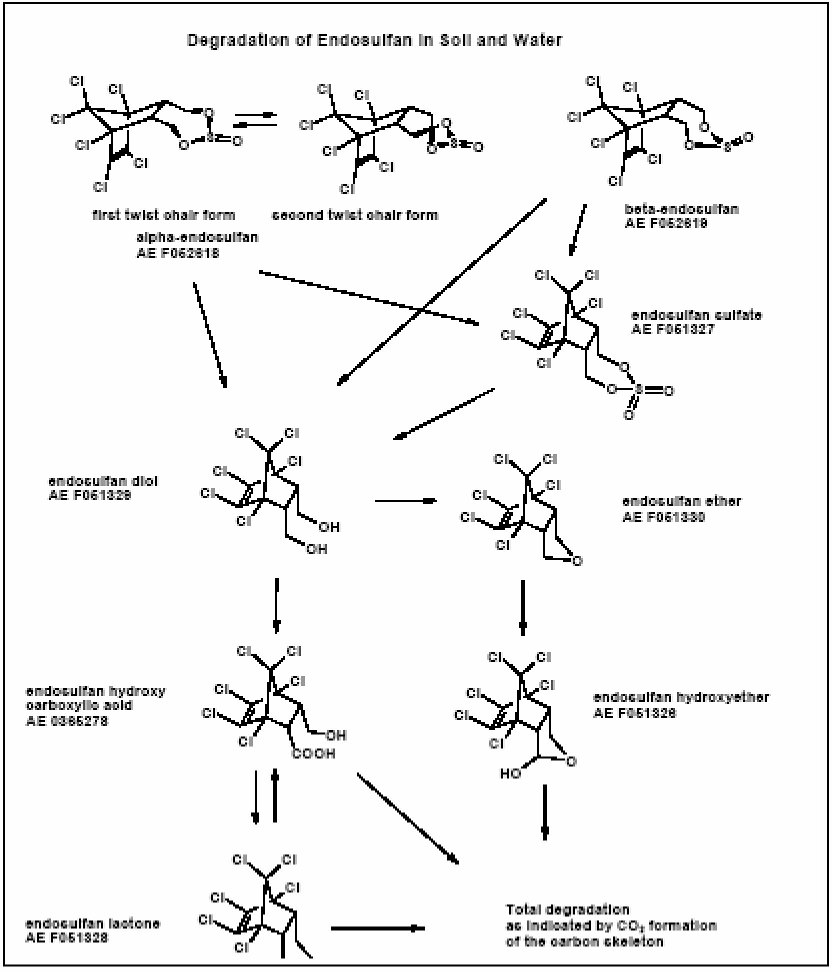
4.4.2 Water

For both isomers, hydrolysis at pH values greater than 7 is an important degradation process whereas at pH values below 7 endosulfan is found increasingly persistent under abiotic conditions. Even though the majority of surface water bodies in Europe have pH values around 7, there are quite a number

of acidic creeks, small rivers and lakes in boreal but also in mountainous European regions [140]. Yet it is this type of habitats being ecologically valuable.

Rain water in Central Europe could, as a consequence of atmospheric carbon dioxide content and naturally occurring trace substances, have an acidity (pH value) of something between 4.6 and 5.6 pH. In fact, the pH value for rain water in Germany lies on average between 4.0 and 4.6 pH [141]. Hydrolysis in the atmosphere is thus an irrelevant breakdown process for endosulfan in the atmosphere and in the headwater of rivers with low buffer capacity.

figure 4-4 Routes of degradation of endosulfan in soil and water (source: Aventis Crop Science, 2002)



Hydrolytic breakdown of endosulfan is enhanced with increasing pH resulting in DT_{50} of 10-20 days at pH 7 and around 0.2 days at pH 9 (at 25 °C) with β-endosulfan degrading somewhat faster than the α-isomer. In alkaline sea water hydrolysis is therefore deemed to be the main degradation process.
{i}

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i Water is an environmental compartment which is of great variety. Although a large majority of freshwater systems has a pH values around 7 there are water bodies of low buffer capacity, particularly in Northern areas, which are acidic, i.e. pH values of 6 or below. On the other side alkalinity of marine waters is depending on salinity. Furthermore, degradation of organic substances in pore water of soils and sediments is impacted by the particular redox potential. Finally, it is of utmost importance if water is considered as an abiotic matrix or a "natural" water body involving microbial activity, suspended organic matter and sediments, as described by water/sediment test systems.
Each out of the test parameters may strongly affect DT_{50} of an organic substances" in water".

Endosulfan-diol was found to be the major hydrolysis product.

Photochemical transformation does not contribute to environmental breakdown in water since endosulfan does not absorb solar radiation of the troposphere (wavelengths > 290 nm). No indication for potential photo-transformation in natural water bodies caused by photo-sensitizing substances (e.g. humic acids) or reactive transient species (e.g. hydroxy or peroxy radicals) could be made available from literature

Table 4-9 Hydrolysis of endosulfan; half-lives (DT_{50}) in days (25 °C), according to [178]

	pH 5	pH 7	pH 9
α- endosulfan	> 200	19	0.25
β- endosulfan	> 200	10.7	0.18

4.4.3 Sediments

Endosulfan entering natural water bodies in gaseous or dissolved phase is assumed to rapidly adsorb to suspended matter. Sedimentation of particles or direct partitioning to sediment causes rapid removal from the water body. More than 75% of the endosulfan in the River Rhine was found to be associated with particulate matter **[142]**. All sediment studies have been performed at pH values greater than 7. Hence hydrolysis may have been an important degradation process beside microbial degradation.

4.4.3.1 Aerobic Conditions

The fate of endosulfan in aerobic water/sediment systems were reported from two studies, each encompassing two systems: In all cases endosulfan was observed to be readily transferred to the sediments. A study involving river water (pH of 7.3) and a gravel pit (pH of 7.8) showed a short residence time of dissolved endosulfan in the water phase, caused by preferential sorption to bottom sediment (K_{oc} values of 10,600 and 13,600 mL/g were determined for α- and β-endosulfan). DT_{50} values of 12 and 10 days respectively were estimated for the parent endosulfan in the entire systems (supernatant water plus sediment), whereas 21 days and 18 days were estimated for “total endosulfan” encompassing endosulfan plus endosulfan sulfate plus endosulfan carboxylic acid **[143]**.

Similar results were obtained from another freshwater/sediment study involving two sediments, a sandy sediment of a carbon content of 0.1% and a clay loam[i] sediment of 3.2% organic carbon **[144]**. Endosulfan readily dissipated from the water phase at a DT_{50} of 0.7 days in the clay loam system and of 1.6 days in the sandy sediment system. DT_{50} of endosulfan for the total system were determined at 3.6 days for the clay loam and 35.1 days for the sand. Notably, the supernatant waters had a pH of 7.8 and 7.9 and kept in a narrow range around pH 8 in the loamy system, but declined to approximately 7 in the sand system. This difference

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[i] according to USDA classification scheme

is expected to be relevant for hydrolysis and may contribute beside differing biomass (61.6 vs. 2.3 mgC/100g) to the differing DT_{50} values in both systems. Beside endosulfan sulfate and endosulfan-diol being early formed metabolites endosulfan hydroxy carboxylic acid was formed as major metabolites in both systems. Formation of $^{14}CO_2$ from the radiolabelled chlorinated moiety of the molecule was insignificant with 0.7 and 1.1% over the study period (120 days), respectively.

4.4.3.2 Anaerobic Conditions

Under “oxygen-limited conditions” half lives > 200 days were estimated for α-endosulfan and >> 200 days for endosulfan sulfate **[145]**. Notably, most sediments have a small aerobic top layer while in deeper layers anaerobic conditions are prevailing.

4.4.3.3 Sea Water:

Sea water is a moderately alkaline medium. Hence swift hydrolysis of endosulfan is expected in this medium: In a seawater/sediment study a half life of 8.3 days was determined for the β-isomer and a half-life of 22 days for the α-isomer **[146]**.

4.5 Bioaccumulation

4.5.1 Octanol-Water Partition Coefficient

From QSAR calculations a n-octanol/water partition coefficient of $\log K_{ow} = 3.5$ is indicated **[147]**.

Employing the HPLC screening method a $\log K_{ow} = 4.65$ for α-endosulfan and a $\log K_{ow} = 4.34$ for β-endosulfan under neutral conditions was estimated **[148]**.

Shake flask tests resulted in higher values of ($\log K_{ow} > 4.7$ ($K_{ow} = 55{,}500$) for the α-isomer and $\log K_{ow} = 4.8$ ($K_{ow} = 61{,}400$) for β-endosulfan at pH of 5.1 and a temperature of 22°C **[149]**. Since measured data are deemed more reliable over estimates a high potential for bioconcentration in fatty tissue is suspected from the measured data.

The K_{ow} of endosulfan sulfate has also been determined by means of HPLC technique **[148]**, resulting in $\log K_{ow} = 3.77$. Notably QSAR calculations of K_{ow} for this metabolite yielded $\log K_{ow} = 3.64$. This value is very close to the measured one but below that estimated for the parent itself by QSAR. It is concluded that endosulfan sulfate is therefore less hydrobic and less bioaccumulative as compared to endosulfan.

4.5.2 Measured Bioconcentration Factors

Reported values for the measured BCF of endosulfan in various aqueous organisms cover a wide range. In some species like oysters and bivalves BCF values as low as < 100 are reported **[150]**, while on the other end studies on freshwater as well as marine fish suggest bioconcentration factors from 1,400X up to 11,000X in whole fish **[151]**, **[152]**, **[153]**, **[154]**, **[155]**.

4.5.2.1 Fish

The BCF value of >11,000 in yellow tetra fish (*Hyphessobrycon bifasciatus)* was based on extrapolated data because steady state was not reached within the course of the study (21 days). A concurring fast elimination of endosulfan from fish (halflife of 1.8 days) concluded from the same study appears to be inconsistent with that finding since this should cause equilibrium to be attained within a period shorter than 21 days. Irrespectively, a BCF of 6,000 is derived from the reported concentration in fish on the 21th day **[154]**. No reduced rates for concentration increase in fish were observed until this time point. A reduced elimination rate of 2.9–5.6 days was reported by the same authors for zebra fish (*Brachydanio rerio*) at a corresponding BCF of 2640 ± 441.

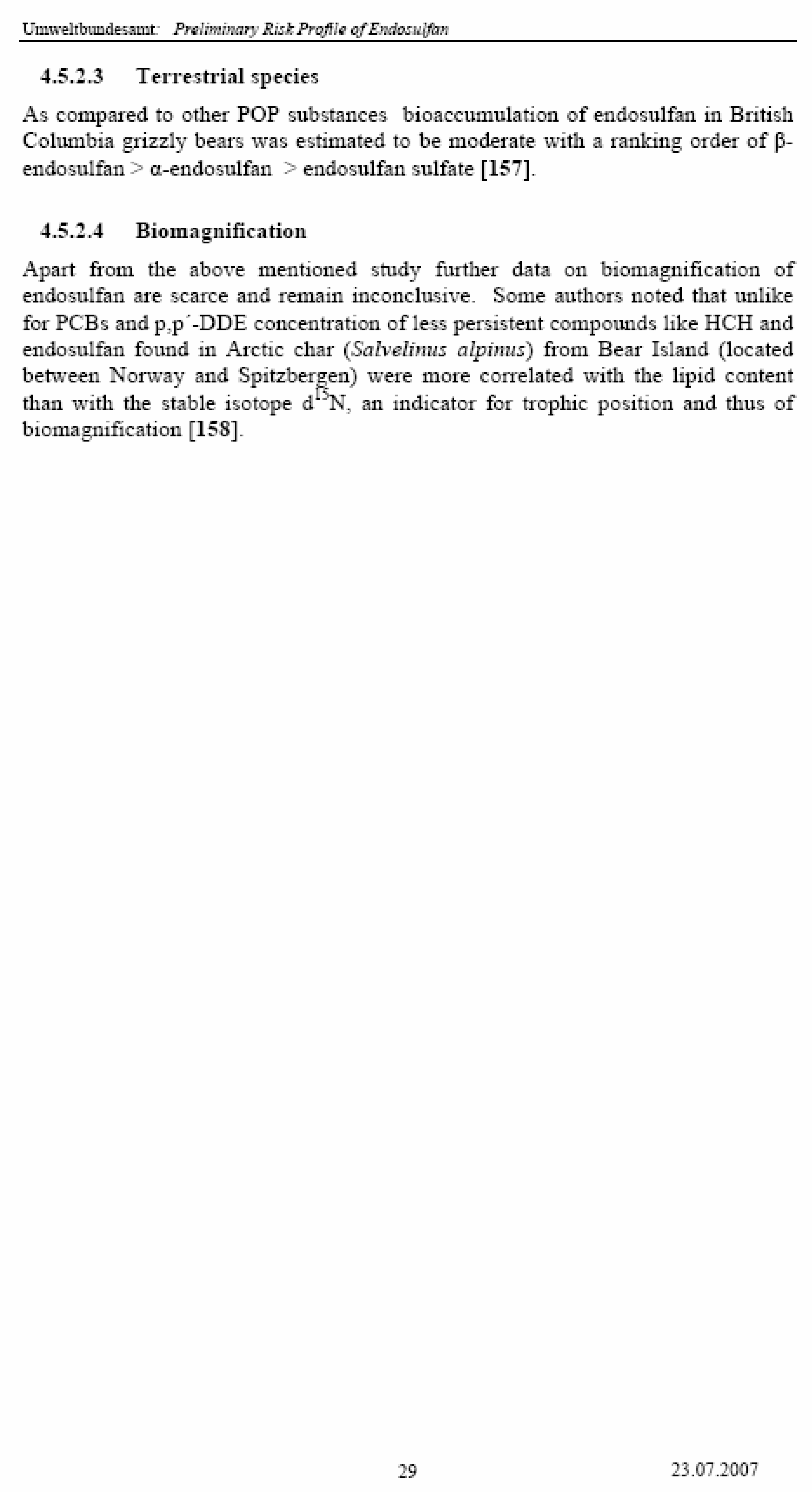
An outdoor microcosm study revealed simulating exposure of fish and aquatic invertebrates to a multiple entry of endosulfan at different dose levels and different entry routes. For total radioactivity (consisting of parent endosulfan and aquatic metabolites) a BCF of approx. 1000 and for endosulfan sulfate a BCF of 2900-4600 was derived **[176]**

Table 4-10 Bioaccumulation data for fish

Test species	conc. in water , µg/L	BCF	$T/2_{\text{depuration}}$ days	Reference
striped mullet	0.035 (α + β)	2429-2755	< 2	**[151]**
zebra fish	0.3 (α)	2,000	2.9	**[1543]**
	0.3 (β)	1,400	5.1	
	sulfate, formed during study *in vivo*		5.9	
yellow tetra fish	0.3 (α + β)	11,583	1.8	**[154]**
	0.2 (α)	10,994	2.0	
	0.1 (β)	9,908	1.74	

4.5.2.2 Plankton

Freshwater green algae (*Pseudokirchneriella subcapitatum*) were found to sequester endosulfan from a surrounding water containing 100 µg/l of the substance at an average BCF of 2,682 after 16 hours. For *Daphnia magna* in a 100 µg/L endosulfan water-only exposure a BCF of 3,278 was reported under such conditions **[156]**. Endosulfan was rapidly accumulated and concentrated from water by neonates of both species. Daphnia magna feeding on contaminated algae in clean water did not accumulate endosulfan suggesting that uptake from the water column is the dominant route for bioaccumulation of endosulfan by zooplankton.



4.5.2.3 Terrestrial species

As compared to other POP substances bioaccumulation of endosulfan in British Columbia grizzly bears was estimated to be moderate with a ranking order of β-endosulfan > α-endosulfan > endosulfan sulfate [**157**].

4.5.2.4 Biomagnification

Apart from the above mentioned study further data on biomagnification of endosulfan are scarce and remain inconclusive. Some authors noted that unlike for PCBs and p,p´-DDE concentration of less persistent compounds like HCH and endosulfan found in Arctic char (*Salvelinus alpinus*) from Bear Island (located between Norway and Spitzbergen) were more correlated with the lipid content than with the stable isotope $d^{15}N$, an indicator for trophic position and thus of biomagnification [**158**].

PART II

SUMMARY REPORT ON ENDOSULFAN

5 RELEASES TO THE ENVIRONMENT

Endosulfan is released to the environment almost exclusively as a result of its use as an insecticide. There are no known natural sources of the compound. On a local scale environmental releases to the air or waste water may also occur from manufacturing of formulation operations. Its deliberate wide dispersive application on large areas, along with its physico-chemical properties makes it prone to spread over large distances as a consequence of post-application evaporation.

6 PRODUCTION OF ENDOSULFAN

Endosulfan is synthesized involving the following steps: Diels-Alder addition of hexachloro-cyclopentadiene and cis-butene-1,4-diol in xylene. Subsequently the adduct is hydrolysed to form the cis-diol or di-alcohol. Reaction of this cis-dol with thionyl chloride forms the final product.

6.1 Global scale

Worldwide production of endosulfan was estimated at 10,000 metric tonnes in 1984 [**159**]. More recent data on production volumes could not be made available. However, current global production is likely to be significantly higher as use remains widespread.

6.2 Europe

Within the European Union there is only one producer, manufacturing endosulfan at one single production site. It is located in Frankfurt-Griesheim (Germany). According to the operating company endosulfan discharges from this plant to water or air meet the legal requirements in Germany and are below the limit of analytical quantification, i.e. less than 0,05 µg/L (information provided by Aventis CropScience, 2002). No relevant emission to the environment is therefore expected from this potential source.

The manufactured volume of endosulfan at this site currently amounts for approximately 4,000 tpa (information from Bayer Crop Science, 2003). A huge majority of this volume is exported for use in tropical and subtropical regions such as Latin America, Carribean and southeast Asia [**160**].

6.3 United States

In 1974 the annual production of endosulfan in the United States was 1,360 tpa. with FMC Corporation being the major manufacturer. Endosulfan has not been produced in the U.S. since 1982 ([**161**] as of 9/2000).

6.4 Regions outside UN-ECE

Besides Germany manufacturing of endosulfan has been reported for Israel, India and South Korea **[162]**. Recently, a production start has been reported for Peoples Republic of China.

7 USAGE OF ENDOSULFAN

The vast majority of endosulfan is used as active ingredient of plant protection products. That means it is deliberately spread over large soil or plant areas.

Formulations of endosulfan include emulsifiable concentrate, wettable powder, ultra-low volume (ULV) liquid, and smoke tablets. It is compatible with many other active ingredients and may be found in formulations with other active ingredients like dimethoate, malathion, methomyl, monocrotophos, pirimicarb, triazophos, fenoprop, parathion, petroleum oils, and oxine-copper. It is not compatible with alkaline materials due to hydrolytic breakdown.

Endosulfan controls a wide range of sucking and chewing insect pests, notably aphids, thrips, beetles, foliar feeding larvae, mites, borers, cutworms, bollworms, bugs, whiteflies, leafhoppers. It is used on non-food crops, such as cotton, tobacco, in forest and on ornamentals but also on food crops, such as vegetables, fruits, corn, cereals, oilseeds, potatoes, tea, coffee, cacao, and soy bean **[163]**. It has also historically been used to control termites and tsetse fly **[164]**].

Non-agricultural use of endosulfan within the European Union endosulfan were only reported by Belgium as an industrial and domestic wood preservative at a consumption of 187 kg per annum until the early 1990s **[165]**. Use of endosulfan for wood preservation was reported for the U.S. in 1999 **[166]** but this use obviously was discontinued.

7.1 Europe

Endosulfan containing products hold authorisation in seven member states of the Community. But use of endosulfan within the EU has seen a steadily decrease for the last years. Almost 90 % of 490 tpa consumed in 1999, were used in Mediterranean parts of the EU.

For purposes of the OSPAR-DYNAMEC process plant protection industry has provided current information on the annual endosulfan consumption volumes in European countries. Figures for the various countries are summarized in table 7-1. According to that information Spain was the main consumer of endosulfan within the European Union, accounting for almost half of the total volume, followed by Italy (about 20%) Greece and France (about 15% each). The tabulated volumes reveal diverging trends for European geographical regions: Whilst endosulfan consumption was seen to continuously decrease in the Northern parts just a slight decline is observed for the Southern countries.

7.2 North America

In the U.S. endosulfan is currently limited to agricultural and commercial uses. Voluntary cancellations for all home and residential applications have been submitted to US EPA [**173**]. Total average annual use of endosulfan is estimated at approximately 626 metric tonnes of active ingredient according to EPA and registrant estimates with the most important crops in terms of sales being cotton (14.2%), cantaloupe (13.2%), tomatoes (12.2%), and potatoes (8.15%) in 2001. Crops with the highest average percent drop treated are squash (40%), eggplant (41%), cantaloupe (31%), sweet potato (31%), broccoli (26%), pears (20%) and pumpkins (20%) [**167**]. As much as 6% is believed to be applied by horticultural nurseries in greenhouses.

The US uses an average annual amount of 626 tons (mean 1990-1999), currently at less than 400 t/a.

Endosulfan usage is also common practise in some Canadian provinces. Ontario used 25 metric tons in 1993 on fruit and vegetable crops alone and Quebec reported application of 55 metric tons per annum [**168**].

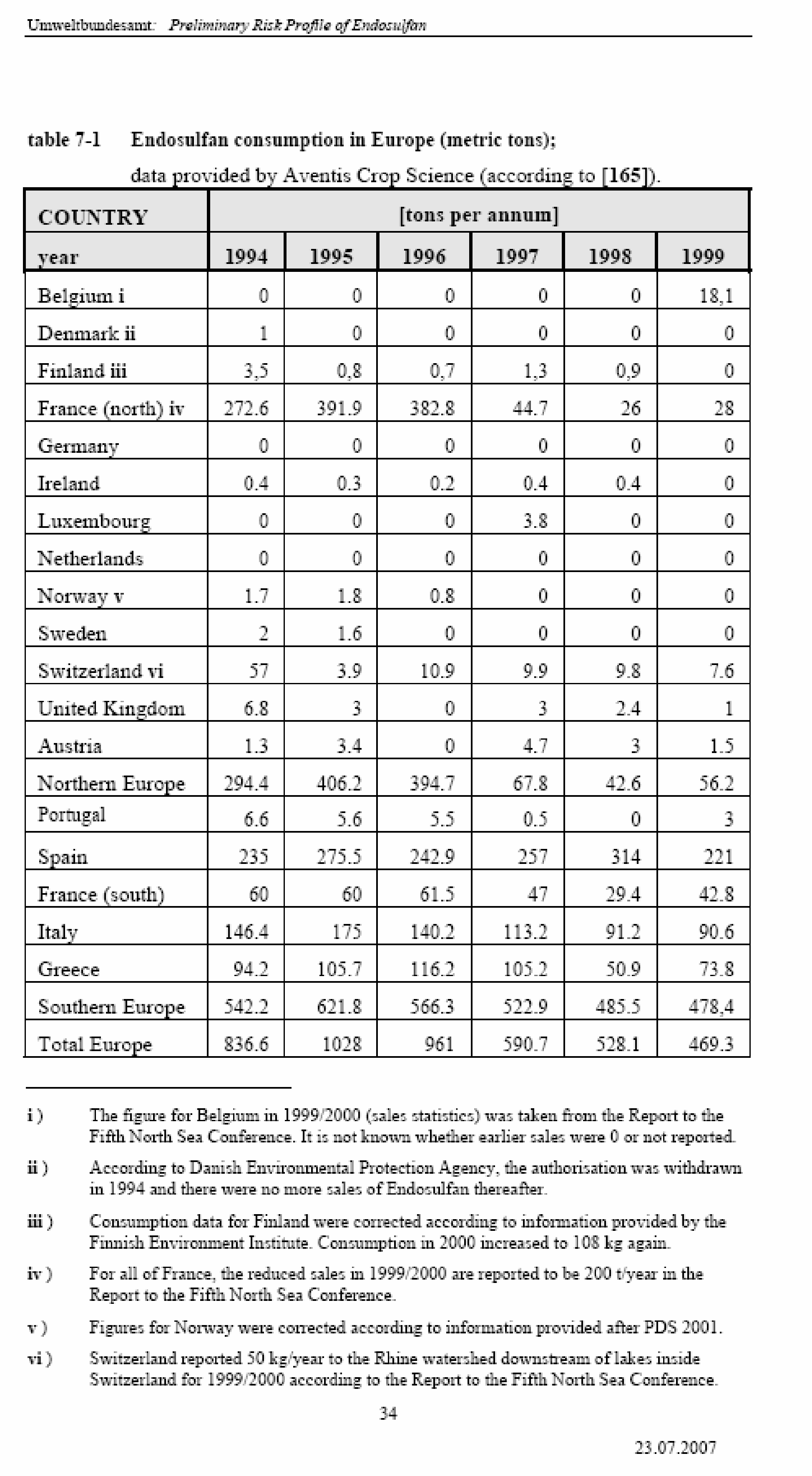


table 7-1 Endosulfan consumption in Europe (metric tons);
data provided by Aventis Crop Science (according to **[165]**).

COUNTRY	[tons per annum]					
year	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Belgium i	0	0	0	0	0	18,1
Denmark ii	1	0	0	0	0	0
Finland iii	3,5	0,8	0,7	1,3	0,9	0
France (north) iv	272.6	391.9	382.8	44.7	26	28
Germany	0	0	0	0	0	0
Ireland	0.4	0.3	0.2	0.4	0.4	0
Luxembourg	0	0	0	3.8	0	0
Netherlands	0	0	0	0	0	0
Norway v	1.7	1.8	0.8	0	0	0
Sweden	2	1.6	0	0	0	0
Switzerland vi	57	3.9	10.9	9.9	9.8	7.6
United Kingdom	6.8	3	0	3	2.4	1
Austria	1.3	3.4	0	4.7	3	1.5
Northern Europe	294.4	406.2	394.7	67.8	42.6	56.2
Portugal	6.6	5.6	5.5	0.5	0	3
Spain	235	275.5	242.9	257	314	221
France (south)	60	60	61.5	47	29.4	42.8
Italy	146.4	175	140.2	113.2	91.2	90.6
Greece	94.2	105.7	116.2	105.2	50.9	73.8
Southern Europe	542.2	621.8	566.3	522.9	485.5	478,4
Total Europe	836.6	1028	961	590.7	528.1	469.3

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i) The figure for Belgium in 1999/2000 (sales statistics) was taken from the Report to the Fifth North Sea Conference. It is not known whether earlier sales were 0 or not reported.

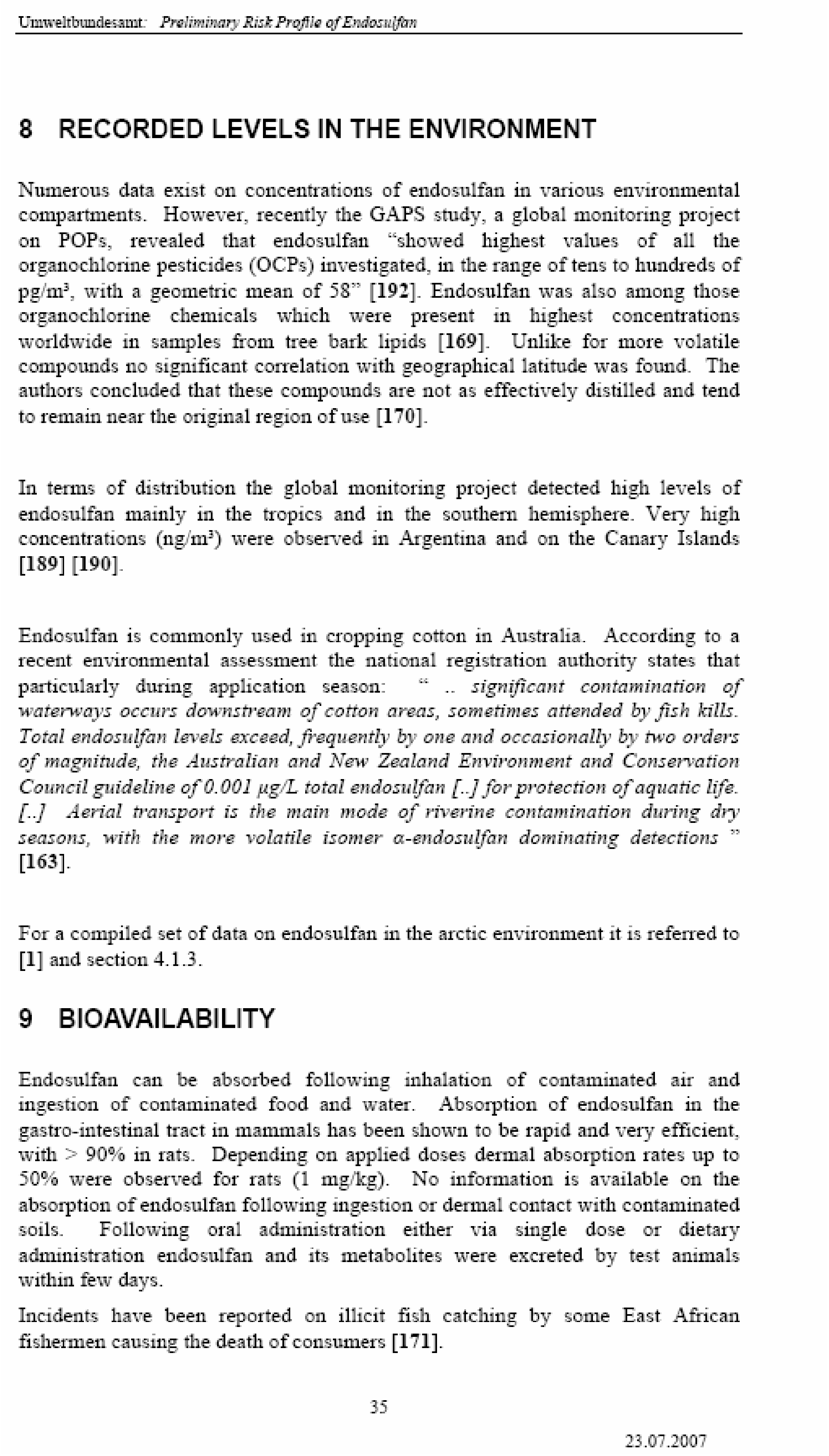
ii) According to Danish Environmental Protection Agency, the authorisation was withdrawn in 1994 and there were no more sales of Endosulfan thereafter.

iii) Consumption data for Finland were corrected according to information provided by the Finnish Environment Institute. Consumption in 2000 increased to 108 kg again.

iv) For all of France, the reduced sales in 1999/2000 are reported to be 200 t/year in the Report to the Fifth North Sea Conference.

v) Figures for Norway were corrected according to information provided after PDS 2001.

vi) Switzerland reported 50 kg/year to the Rhine watershed downstream of lakes inside Switzerland for 1999/2000 according to the Report to the Fifth North Sea Conference.



8 RECORDED LEVELS IN THE ENVIRONMENT

Numerous data exist on concentrations of endosulfan in various environmental compartments. However, recently the GAPS study, a global monitoring project on POPs, revealed that endosulfan "showed highest values of all the organochlorine pesticides (OCPs) investigated, in the range of tens to hundreds of pg/m³, with a geometric mean of 58" **[192]**. Endosulfan was also among those organochlorine chemicals which were present in highest concentrations worldwide in samples from tree bark lipids **[169]**. Unlike for more volatile compounds no significant correlation with geographical latitude was found. The authors concluded that these compounds are not as effectively distilled and tend to remain near the original region of use **[170]**.

In terms of distribution the global monitoring project detected high levels of endosulfan mainly in the tropics and in the southern hemisphere. Very high concentrations (ng/m³) were observed in Argentina and on the Canary Islands **[189]** **[190]**.

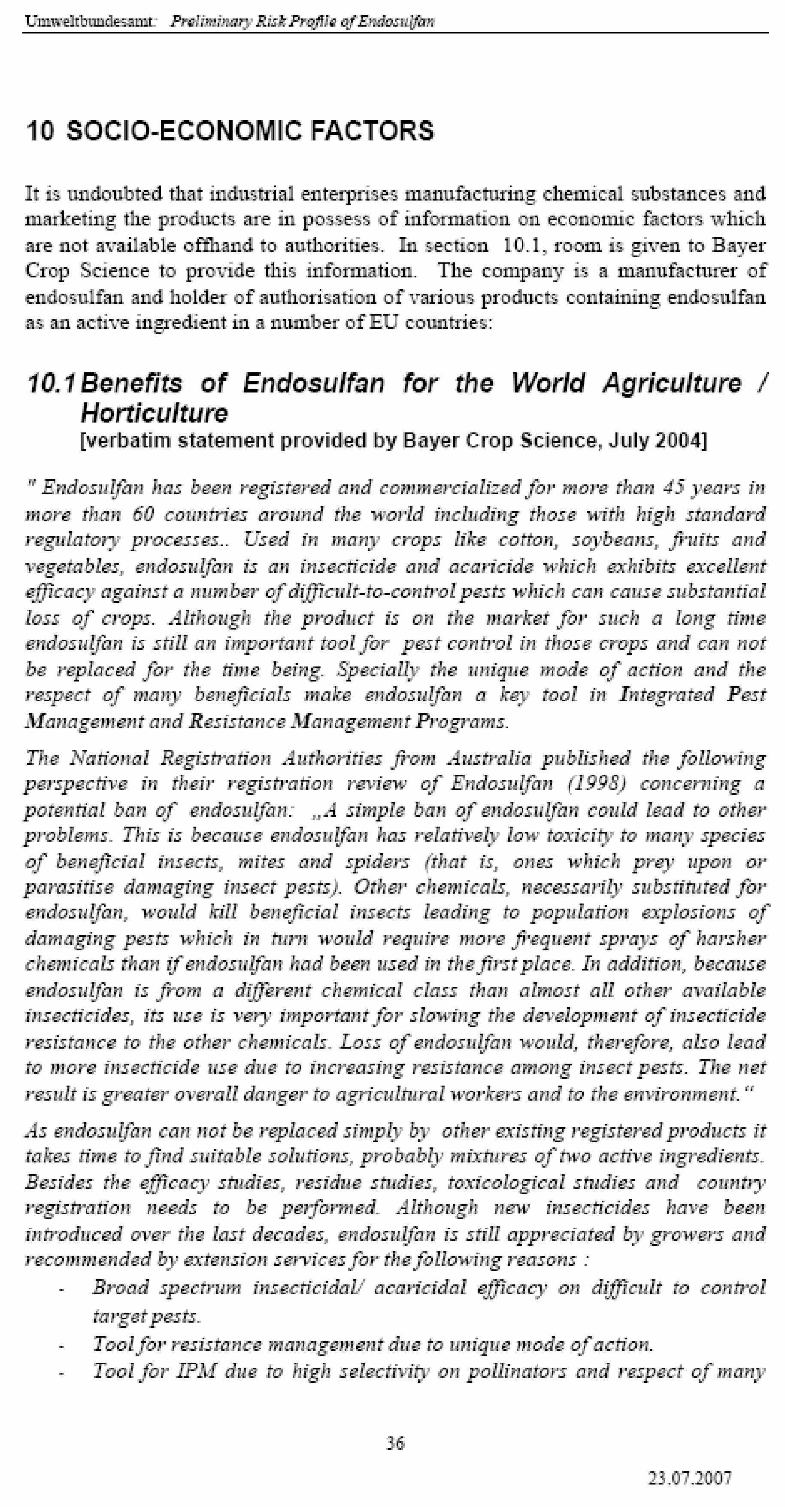
Endosulfan is commonly used in cropping cotton in Australia. According to a recent environmental assessment the national registration authority states that particularly during application season: " .. *significant contamination of waterways occurs downstream of cotton areas, sometimes attended by fish kills. Total endosulfan levels exceed, frequently by one and occasionally by two orders of magnitude, the Australian and New Zealand Environment and Conservation Council guideline of 0.001 µg/L total endosulfan [..] for protection of aquatic life. [..] Aerial transport is the main mode of riverine contamination during dry seasons, with the more volatile isomer α-endosulfan dominating detections* " **[163]**.

For a compiled set of data on endosulfan in the arctic environment it is referred to **[1]** and section 4.1.3.

9 BIOAVAILABILITY

Endosulfan can be absorbed following inhalation of contaminated air and ingestion of contaminated food and water. Absorption of endosulfan in the gastro-intestinal tract in mammals has been shown to be rapid and very efficient, with > 90% in rats. Depending on applied doses dermal absorption rates up to 50% were observed for rats (1 mg/kg). No information is available on the absorption of endosulfan following ingestion or dermal contact with contaminated soils. Following oral administration either via single dose or dietary administration endosulfan and its metabolites were excreted by test animals within few days.

Incidents have been reported on illicit fish catching by some East African fishermen causing the death of consumers **[171]**.



10 SOCIO-ECONOMIC FACTORS

It is undoubted that industrial enterprises manufacturing chemical substances and marketing the products are in possess of information on economic factors which are not available offhand to authorities. In section 10.1, room is given to Bayer Crop Science to provide this information. The company is a manufacturer of endosulfan and holder of authorisation of various products containing endosulfan as an active ingredient in a number of EU countries:

10.1 Benefits of Endosulfan for the World Agriculture / Horticulture

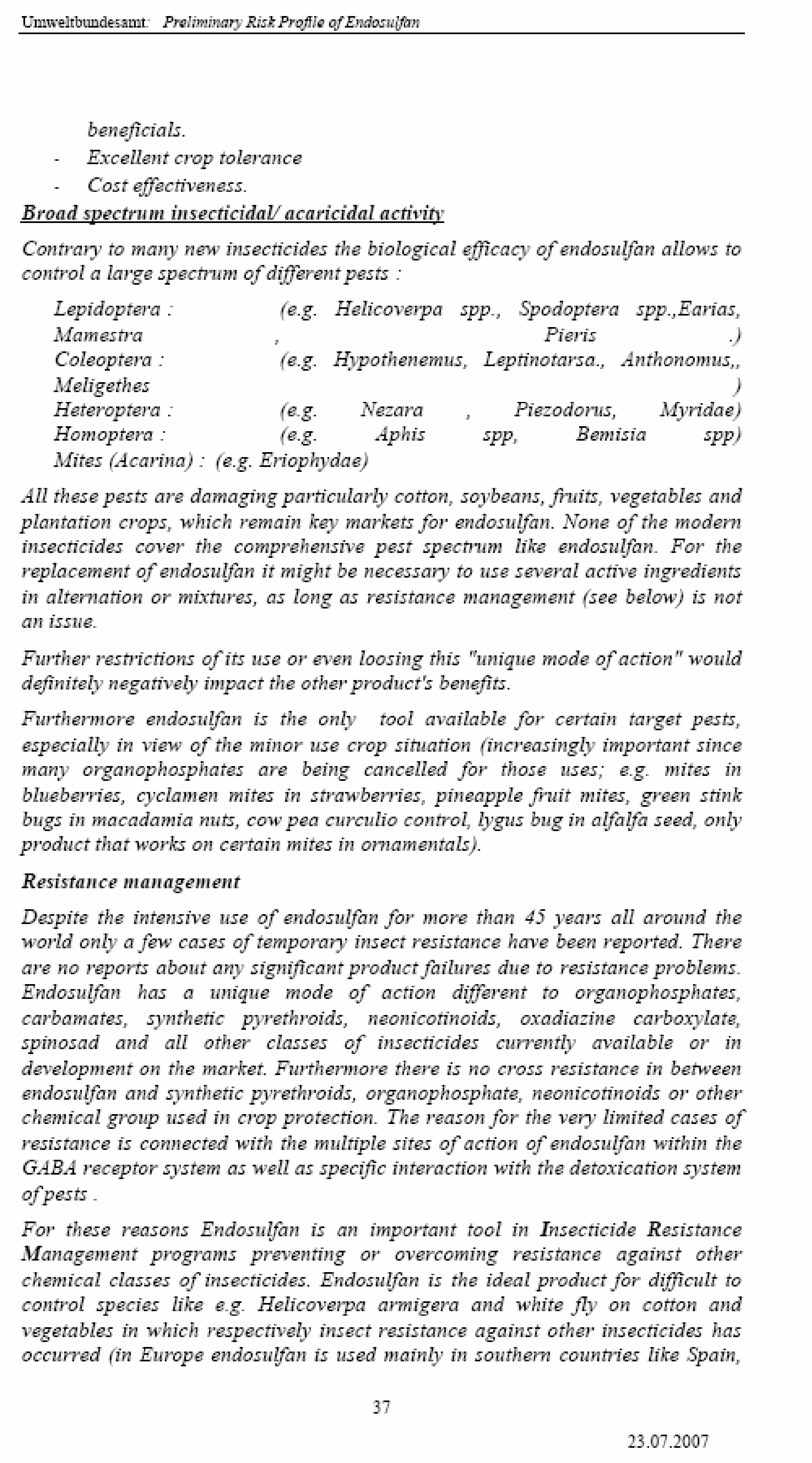
[verbatim statement provided by Bayer Crop Science, July 2004]

" Endosulfan has been registered and commercialized for more than 45 years in more than 60 countries around the world including those with high standard regulatory processes.. Used in many crops like cotton, soybeans, fruits and vegetables, endosulfan is an insecticide and acaricide which exhibits excellent efficacy against a number of difficult-to-control pests which can cause substantial loss of crops. Although the product is on the market for such a long time endosulfan is still an important tool for pest control in those crops and can not be replaced for the time being. Specially the unique mode of action and the respect of many beneficials make endosulfan a key tool in ***I****ntegrated* ***P****est Management and* ***R****esistance* ***M****anagement* ***P****rograms.*

The National Registration Authorities from Australia published the following perspective in their registration review of Endosulfan (1998) concerning a potential ban of endosulfan: „A simple ban of endosulfan could lead to other problems. This is because endosulfan has relatively low toxicity to many species of beneficial insects, mites and spiders (that is, ones which prey upon or parasitise damaging insect pests). Other chemicals, necessarily substituted for endosulfan, would kill beneficial insects leading to population explosions of damaging pests which in turn would require more frequent sprays of harsher chemicals than if endosulfan had been used in the first place. In addition, because endosulfan is from a different chemical class than almost all other available insecticides, its use is very important for slowing the development of insecticide resistance to the other chemicals. Loss of endosulfan would, therefore, also lead to more insecticide use due to increasing resistance among insect pests. The net result is greater overall danger to agricultural workers and to the environment."

As endosulfan can not be replaced simply by other existing registered products it takes time to find suitable solutions, probably mixtures of two active ingredients. Besides the efficacy studies, residue studies, toxicological studies and country registration needs to be performed. Although new insecticides have been introduced over the last decades, endosulfan is still appreciated by growers and recommended by extension services for the following reasons :

- *Broad spectrum insecticidal/ acaricidal efficacy on difficult to control target pests.*
- *Tool for resistance management due to unique mode of action.*
- *Tool for IPM due to high selectivity on pollinators and respect of many*



beneficials.

- *Excellent crop tolerance*
- *Cost effectiveness.*

Broad spectrum insecticidal/ acaricidal activity

Contrary to many new insecticides the biological efficacy of endosulfan allows to control a large spectrum of different pests :

Lepidoptera :	*(e.g. Helicoverpa spp., Spodoptera spp.,Earias, Mamestra , Pieris .)*
Coleoptera :	*(e.g. Hypothenemus, Leptinotarsa., Anthonomus,, Meligethes)*
Heteroptera :	*(e.g. Nezara , Piezodorus, Myridae)*
Homoptera :	*(e.g. Aphis spp, Bemisia spp)*
Mites (Acarina) :	*(e.g. Eriophydae)*

All these pests are damaging particularly cotton, soybeans, fruits, vegetables and plantation crops, which remain key markets for endosulfan. None of the modern insecticides cover the comprehensive pest spectrum like endosulfan. For the replacement of endosulfan it might be necessary to use several active ingredients in alternation or mixtures, as long as resistance management (see below) is not an issue.

Further restrictions of its use or even loosing this "unique mode of action" would definitely negatively impact the other product's benefits.

Furthermore endosulfan is the only tool available for certain target pests, especially in view of the minor use crop situation (increasingly important since many organophosphates are being cancelled for those uses; e.g. mites in blueberries, cyclamen mites in strawberries, pineapple fruit mites, green stink bugs in macadamia nuts, cow pea curculio control, lygus bug in alfalfa seed, only product that works on certain mites in ornamentals).

Resistance management

Despite the intensive use of endosulfan for more than 45 years all around the world only a few cases of temporary insect resistance have been reported. There are no reports about any significant product failures due to resistance problems. Endosulfan has a unique mode of action different to organophosphates, carbamates, synthetic pyrethroids, neonicotinoids, oxadiazine carboxylate, spinosad and all other classes of insecticides currently available or in development on the market. Furthermore there is no cross resistance in between endosulfan and synthetic pyrethroids, organophosphate, neonicotinoids or other chemical group used in crop protection. The reason for the very limited cases of resistance is connected with the multiple sites of action of endosulfan within the GABA receptor system as well as specific interaction with the detoxication system of pests .

*For these reasons Endosulfan is an important tool in **I**nsecticide **R**esistance **M**anagement programs preventing or overcoming resistance against other chemical classes of insecticides. Endosulfan is the ideal product for difficult to control species like e.g. Helicoverpa armigera and white fly on cotton and vegetables in which respectively insect resistance against other insecticides has occurred (in Europe endosulfan is used mainly in southern countries like Spain,*

Greece, Italy Portugal and France, in areas with established pest problems where resistance to insecticides is becoming an increasingly important issue). Theoretically most of the pest can be controlled by other product groups as well like organophosphates and pyrethroids, but the loss of endosulfan would increase the use of these products with the consequence of increasing resistance.

Furthermore it can be expected that due to restricted use of organophosphates in future endosulfan will become even more important within the resistance strategies.

Resistance management examples:

***USA**: cotton in Arizona*

Based on the comments from the Arizona Extension Service and the National Cotton Council that were submitted to EPA in response to the RED, it has been shown that endosulfan has been ranked for the last four years examined in Arizona (1998-2001) either as the number 2 or number 3 most used insecticide in terms of application acres. Endosulfan is used there primarily to control plant bugs (Lygus hesperus) and white flies (Bemisia tabaci). Endosulfan is the only useful insecticide that controls effectively Lygus and Bemisia at the higher recommended rate (1.5 kg/ha) simultaneously. The other available Lygus insecticides cannot control whitefly or the recommended IGRs are effective against Bemisia only. Therefore, endosulfan is a very important tool to have under these circumstances. Endosulfan is also needed as an important rotational synergist at lower rates (0.75 kg/ha) for pyrethroids that are otherwise mixed mainly with organophosphates."

Another case of strong support by farmers is the need for the product in Florida for the control of whiteflies in beans and vegetables, mainly used as a resistance management tool.

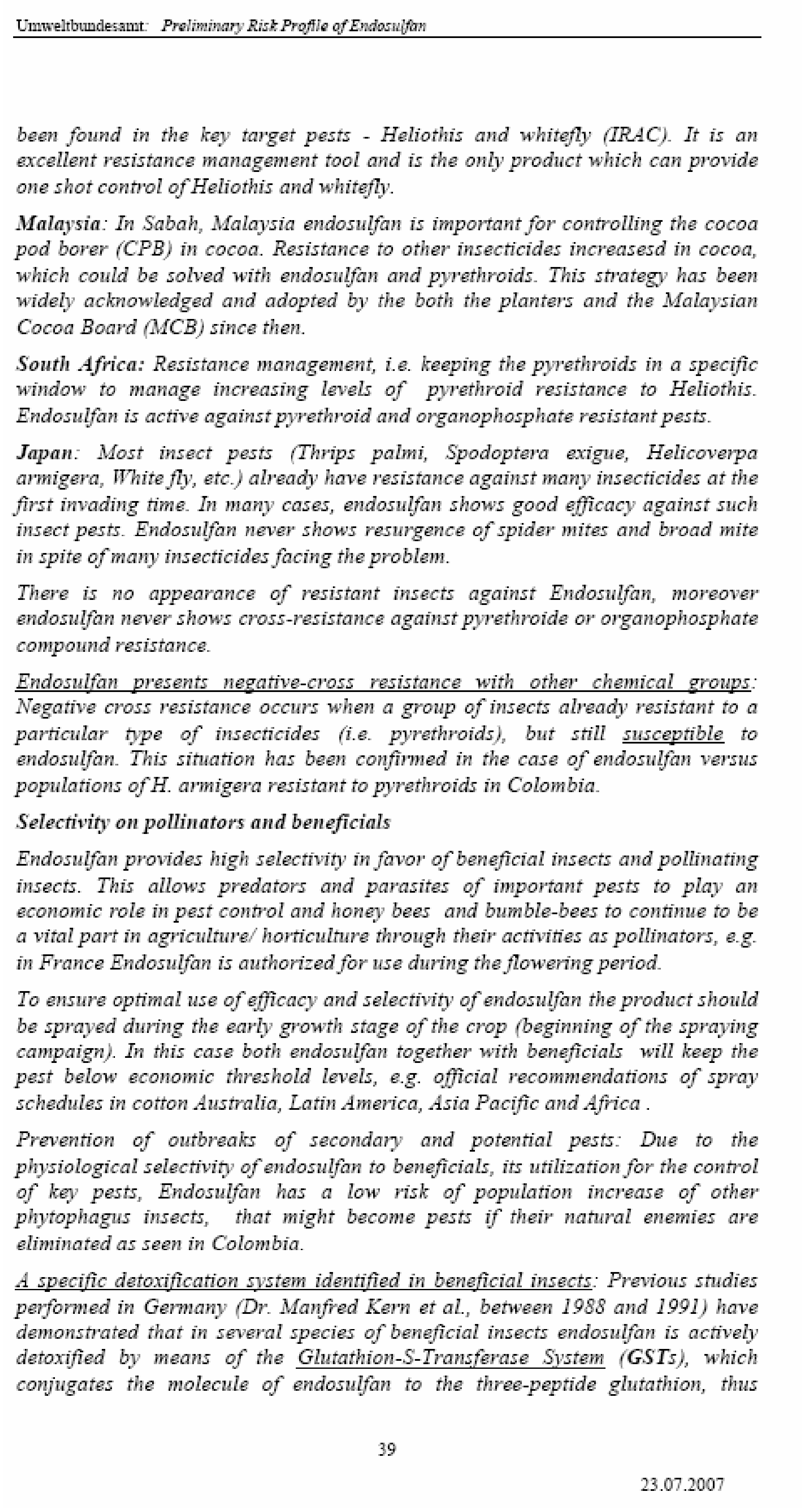
***China**: In Xinjiang area of China, endosulfan has gained a very good reputation as a "soft" insecticide adapted very well to the cotton IPM program for both sucking & chewing insect pests. So, it is unlikely to be replaced by other products in next 5 years despite generic pressure and competition from other products*

Endosulfan is well known as one of best insecticides with unique action and benefit to resistance management of some important insect pests, including cotton bollworm, cotton aphids, tea small green leafhopper and apple aphids and etc. Cotton and tea are two largest markets of endosulfan in China.

***India**: Endosulfan is recommended for use in a number of crops in India including cotton, rice, pulses, plantation crops, fruit crops and vegetables for control of various pests. It is highly recommended in IPM programs and also in Helicoverpa resistance management programs especially in cotton crop.*

Endosulfan is one of the very economic solutions for managing various pests in a number of crops. It is still one of the widely used molecules by farmers in India. It is recommended in the package of practices of almost all Agriculture Universities in India for control of various pests in different crops especially in Integrated Pest Management Programs due to its selectivity and lower toxicity to various beneficial insects.

***Pakistan**: Despite more than 30 year's of use of endosulfan, no resistance has*



been found in the key target pests - Heliothis and whitefly (IRAC). It is an excellent resistance management tool and is the only product which can provide one shot control of Heliothis and whitefly.

***Malaysia**: In Sabah, Malaysia endosulfan is important for controlling the cocoa pod borer (CPB) in cocoa. Resistance to other insecticides increasesd in cocoa, which could be solved with endosulfan and pyrethroids. This strategy has been widely acknowledged and adopted by the both the planters and the Malaysian Cocoa Board (MCB) since then.*

***South Africa:** Resistance management, i.e. keeping the pyrethroids in a specific window to manage increasing levels of pyrethroid resistance to Heliothis. Endosulfan is active against pyrethroid and organophosphate resistant pests.*

***Japan**: Most insect pests (Thrips palmi, Spodoptera exigue, Helicoverpa armigera, White fly, etc.) already have resistance against many insecticides at the first invading time. In many cases, endosulfan shows good efficacy against such insect pests. Endosulfan never shows resurgence of spider mites and broad mite in spite of many insecticides facing the problem.*

There is no appearance of resistant insects against Endosulfan, moreover endosulfan never shows cross-resistance against pyrethroide or organophosphate compound resistance.

Endosulfan presents negative-cross resistance with other chemical groups: Negative cross resistance occurs when a group of insects already resistant to a particular type of insecticides (i.e. pyrethroids), but still susceptible to endosulfan. This situation has been confirmed in the case of endosulfan versus populations of H. armigera resistant to pyrethroids in Colombia.

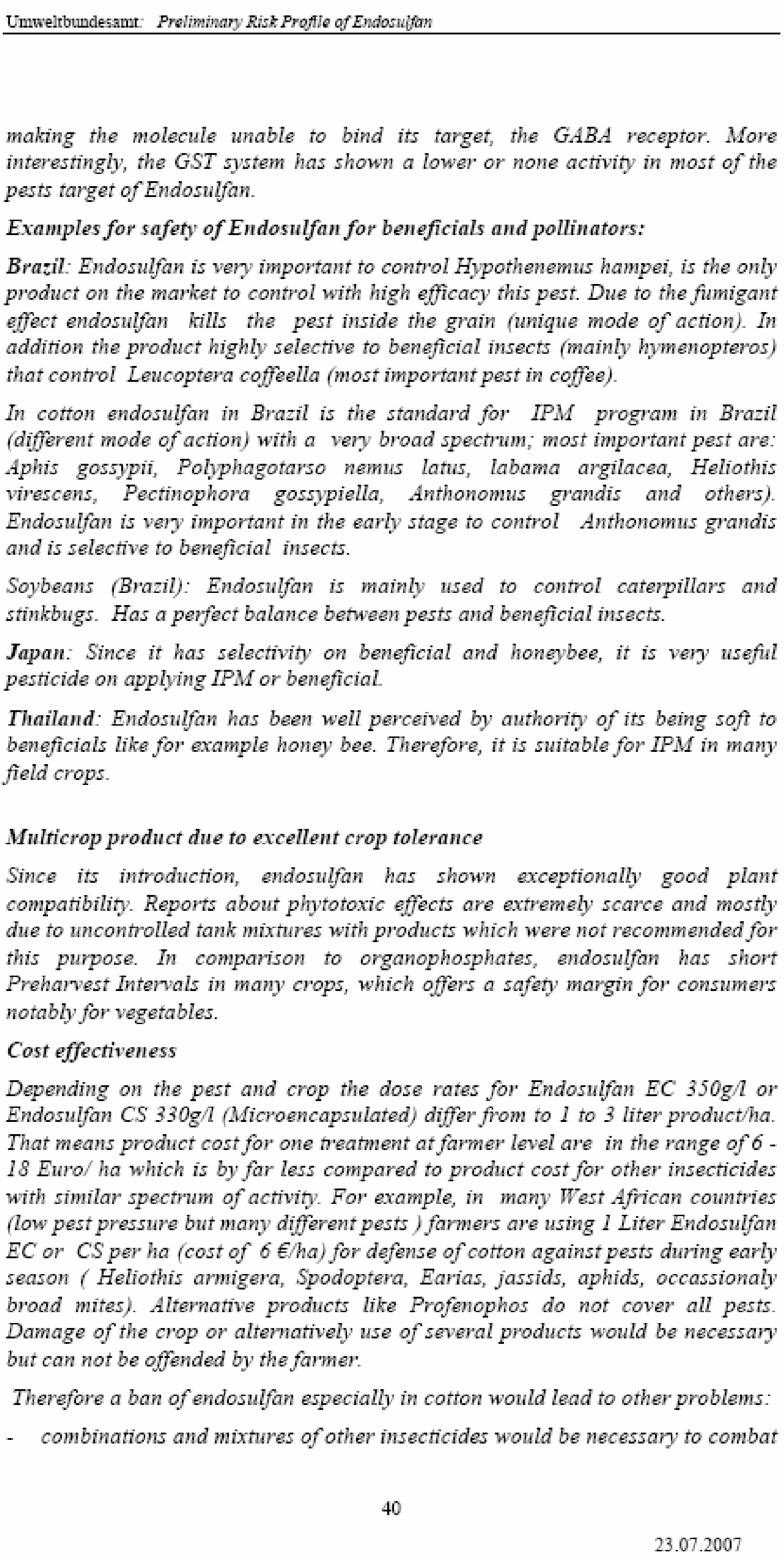
Selectivity on pollinators and beneficials

Endosulfan provides high selectivity in favor of beneficial insects and pollinating insects. This allows predators and parasites of important pests to play an economic role in pest control and honey bees and bumble-bees to continue to be a vital part in agriculture/ horticulture through their activities as pollinators, e.g. in France Endosulfan is authorized for use during the flowering period.

To ensure optimal use of efficacy and selectivity of endosulfan the product should be sprayed during the early growth stage of the crop (beginning of the spraying campaign). In this case both endosulfan together with beneficials will keep the pest below economic threshold levels, e.g. official recommendations of spray schedules in cotton Australia, Latin America, Asia Pacific and Africa .

Prevention of outbreaks of secondary and potential pests: Due to the physiological selectivity of endosulfan to beneficials, its utilization for the control of key pests, Endosulfan has a low risk of population increase of other phytophagus insects, that might become pests if their natural enemies are eliminated as seen in Colombia.

*A specific detoxification system identified in beneficial insects: Previous studies performed in Germany (Dr. Manfred Kern et al., between 1988 and 1991) have demonstrated that in several species of beneficial insects endosulfan is actively detoxified by means of the Glutathion-S-Transferase System (**GSTs**), which conjugates the molecule of endosulfan to the three-peptide glutathion, thus*



making the molecule unable to bind its target, the GABA receptor. More interestingly, the GST system has shown a lower or none activity in most of the pests target of Endosulfan.

Examples for safety of Endosulfan for beneficials and pollinators:

Brazil: *Endosulfan is very important to control Hypothenemus hampei, is the only product on the market to control with high efficacy this pest. Due to the fumigant effect endosulfan kills the pest inside the grain (unique mode of action). In addition the product highly selective to beneficial insects (mainly hymenopteros) that control Leucoptera coffeella (most important pest in coffee).*

In cotton endosulfan in Brazil is the standard for IPM program in Brazil (different mode of action) with a very broad spectrum; most important pest are: Aphis gossypii, Polyphagotarso nemus latus, labama argilacea, Heliothis virescens, Pectinophora gossypiella, Anthonomus grandis and others). Endosulfan is very important in the early stage to control Anthonomus grandis and is selective to beneficial insects.

Soybeans (Brazil): Endosulfan is mainly used to control caterpillars and stinkbugs. Has a perfect balance between pests and beneficial insects.

Japan: *Since it has selectivity on beneficial and honeybee, it is very useful pesticide on applying IPM or beneficial.*

Thailand: *Endosulfan has been well perceived by authority of its being soft to beneficials like for example honey bee. Therefore, it is suitable for IPM in many field crops.*

Multicrop product due to excellent crop tolerance

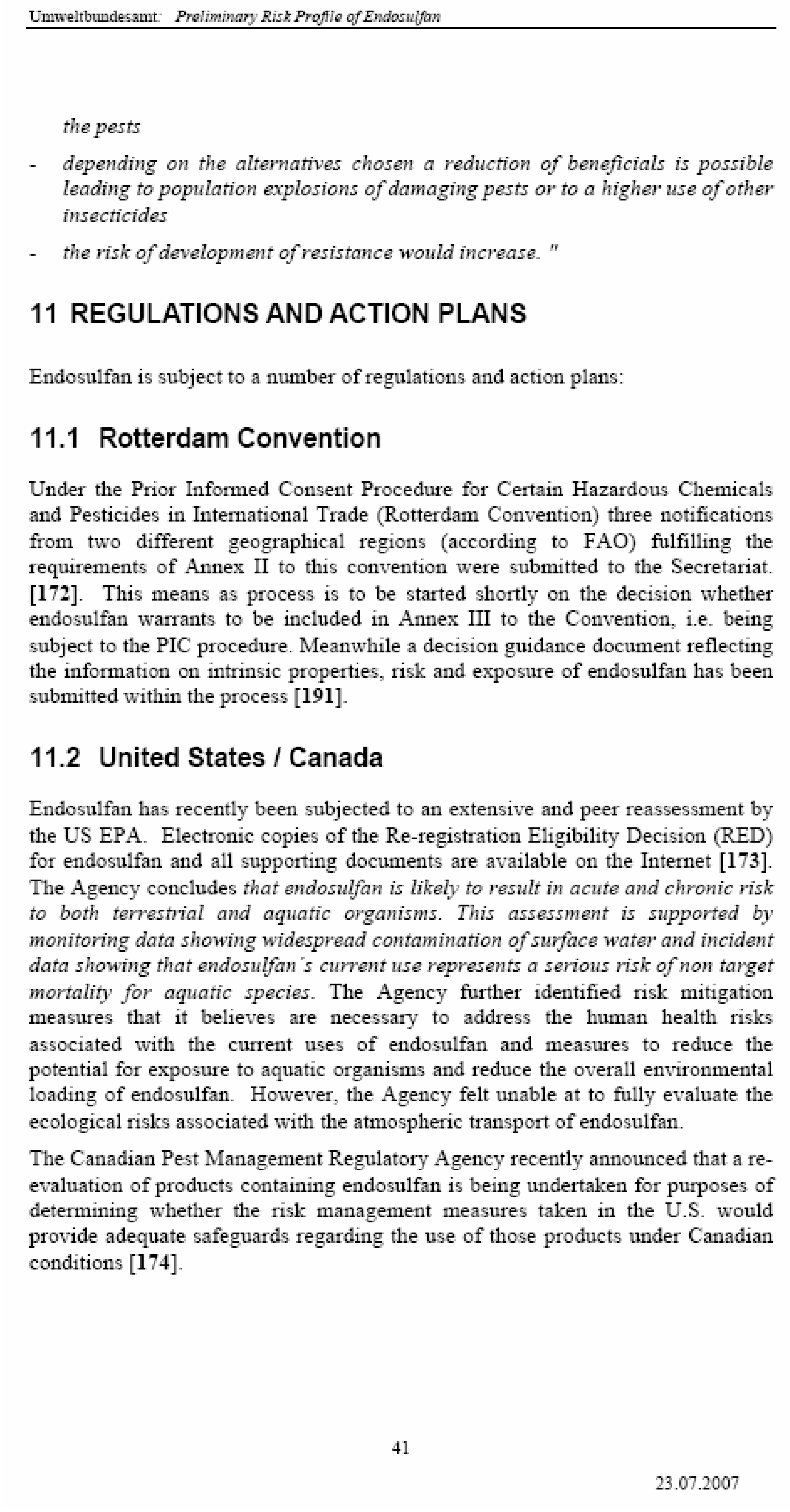
Since its introduction, endosulfan has shown exceptionally good plant compatibility. Reports about phytotoxic effects are extremely scarce and mostly due to uncontrolled tank mixtures with products which were not recommended for this purpose. In comparison to organophosphates, endosulfan has short Preharvest Intervals in many crops, which offers a safety margin for consumers notably for vegetables.

Cost effectiveness

Depending on the pest and crop the dose rates for Endosulfan EC 350g/l or Endosulfan CS 330g/l (Microencapsulated) differ from to 1 to 3 liter product/ha. That means product cost for one treatment at farmer level are in the range of 6 - 18 Euro/ ha which is by far less compared to product cost for other insecticides with similar spectrum of activity. For example, in many West African countries (low pest pressure but many different pests) farmers are using 1 Liter Endosulfan EC or CS per ha (cost of 6 €/ha) for defense of cotton against pests during early season (Heliothis armigera, Spodoptera, Earias, jassids, aphids, occassionaly broad mites). Alternative products like Profenophos do not cover all pests. Damage of the crop or alternatively use of several products would be necessary but can not be offended by the farmer.

Therefore a ban of endosulfan especially in cotton would lead to other problems:

- *combinations and mixtures of other insecticides would be necessary to combat*



the pests

- *depending on the alternatives chosen a reduction of beneficials is possible leading to population explosions of damaging pests or to a higher use of other insecticides*
- *the risk of development of resistance would increase. "*

11 REGULATIONS AND ACTION PLANS

Endosulfan is subject to a number of regulations and action plans:

11.1 Rotterdam Convention

Under the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (Rotterdam Convention) three notifications from two different geographical regions (according to FAO) fulfilling the requirements of Annex II to this convention were submitted to the Secretariat. [172]. This means as process is to be started shortly on the decision whether endosulfan warrants to be included in Annex III to the Convention, i.e. being subject to the PIC procedure. Meanwhile a decision guidance document reflecting the information on intrinsic properties, risk and exposure of endosulfan has been submitted within the process [191].

11.2 United States / Canada

Endosulfan has recently been subjected to an extensive and peer reassessment by the US EPA. Electronic copies of the Re-registration Eligibility Decision (RED) for endosulfan and all supporting documents are available on the Internet [173]. The Agency concludes *that endosulfan is likely to result in acute and chronic risk to both terrestrial and aquatic organisms. This assessment is supported by monitoring data showing widespread contamination of surface water and incident data showing that endosulfan's current use represents a serious risk of non target mortality for aquatic species.* The Agency further identified risk mitigation measures that it believes are necessary to address the human health risks associated with the current uses of endosulfan and measures to reduce the potential for exposure to aquatic organisms and reduce the overall environmental loading of endosulfan. However, the Agency felt unable at to fully evaluate the ecological risks associated with the atmospheric transport of endosulfan.

The Canadian Pest Management Regulatory Agency recently announced that a re-evaluation of products containing endosulfan is being undertaken for purposes of determining whether the risk management measures taken in the U.S. would provide adequate safeguards regarding the use of those products under Canadian conditions [174].

11.3 European Union

11.3.1 Plant Protection Products

Under the Plant Protection Products Directive 91/414/EEC the risks of all existing active substance in plant protection products are being currently evaluated under a peer review programme. The assessment of the safety of the use of endosulfan has been made by the Member States and the Commission with the outcome of that it does not satisfy the minimum safety, and as a consequence, the Commission decision notified hereby proposes not to include endosulfan in the positive Community list (Annex I)[175]. Any uses for which the authorisation is to be withdrawn shall expire not later than 31 December 2007

The non-inclusion Decision provides for some essential uses until 2007 for three southern member states and Poland. The Commission Decision requires member states to ensure that authorisations for plant protection products containing endosulfan are withdrawn with a use-up period of 18 months. Given that this decision stands endosulfan containing products must not be authorized in EU Member States thereafter.

It was decided not to include endosulfan in Annex I to Council Directive 91/414/EEC on grounds of insufficient information available to satisfy the requirements set out in Annex II and Annex III of that Directive **[176]** in particular with regard to

- the environmental fate and ecotoxicology of the substance
- the operator exposure under indoor conditions
- certain data gaps concerning methods of analysis and the route and rate of degradation of the substance in soil and water/sediment systems

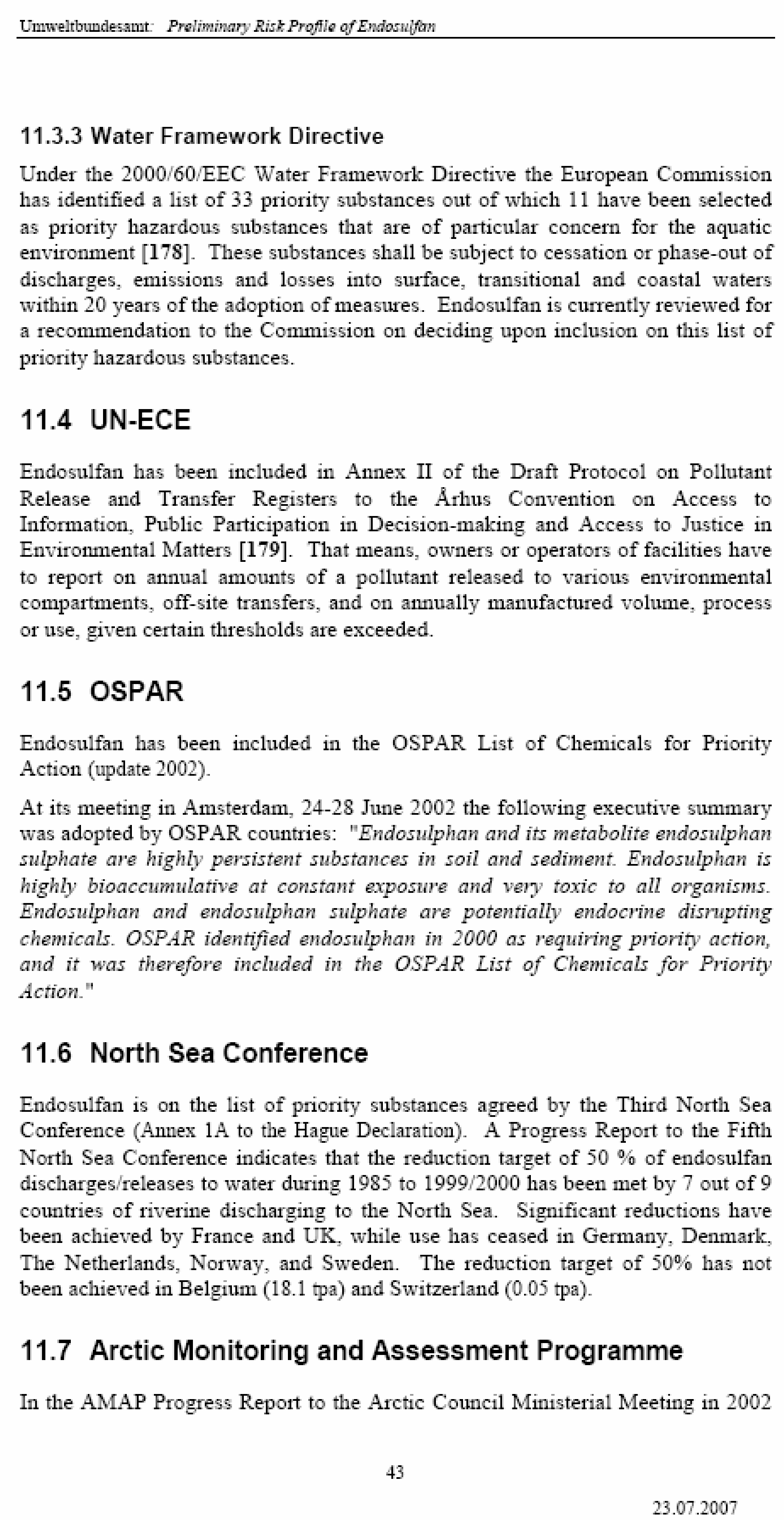
In addition, concerns were identified with regard to

- the fate and behaviour of the substance in the environment, in particular its degradation, persistence, potential of long range transport and potential of bioaccumulation
- its possible impact on non-target organisms
- its possible impact on operators under indoor conditions

Hence no plant protection products containing the active substance concerned is expected to satisfy in general the requirements laid down in Article 5 (1) (a) and (b) of Council Directive 91/414/EEC Directive 91/414. A period of grace may be granted by Member States until end of 2007.

11.3.2 Biocidal Products

Under the EU´s Biocidal Products Directive 98/8/EC **[177]** active ingredients in biocidal products are to be assessed within the next years. Endosulfan was identified but not notified for this exercise. Hence biocidal products containing endosulfan are allowed to be marketed in the EU at present but industry will not support this use category beyond a phasing out period.



11.3.3 Water Framework Directive

Under the 2000/60/EEC Water Framework Directive the European Commission has identified a list of 33 priority substances out of which 11 have been selected as priority hazardous substances that are of particular concern for the aquatic environment [178]. These substances shall be subject to cessation or phase-out of discharges, emissions and losses into surface, transitional and coastal waters within 20 years of the adoption of measures. Endosulfan is currently reviewed for a recommendation to the Commission on deciding upon inclusion on this list of priority hazardous substances.

11.4 UN-ECE

Endosulfan has been included in Annex II of the Draft Protocol on Pollutant Release and Transfer Registers to the Århus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters [179]. That means, owners or operators of facilities have to report on annual amounts of a pollutant released to various environmental compartments, off-site transfers, and on annually manufactured volume, process or use, given certain thresholds are exceeded.

11.5 OSPAR

Endosulfan has been included in the OSPAR List of Chemicals for Priority Action (update 2002).

At its meeting in Amsterdam, 24-28 June 2002 the following executive summary was adopted by OSPAR countries: "*Endosulphan and its metabolite endosulphan sulphate are highly persistent substances in soil and sediment. Endosulphan is highly bioaccumulative at constant exposure and very toxic to all organisms. Endosulphan and endosulphan sulphate are potentially endocrine disrupting chemicals. OSPAR identified endosulphan in 2000 as requiring priority action, and it was therefore included in the OSPAR List of Chemicals for Priority Action.*"

11.6 North Sea Conference

Endosulfan is on the list of priority substances agreed by the Third North Sea Conference (Annex 1A to the Hague Declaration). A Progress Report to the Fifth North Sea Conference indicates that the reduction target of 50 % of endosulfan discharges/releases to water during 1985 to 1999/2000 has been met by 7 out of 9 countries of riverine discharging to the North Sea. Significant reductions have been achieved by France and UK, while use has ceased in Germany, Denmark, The Netherlands, Norway, and Sweden. The reduction target of 50% has not been achieved in Belgium (18.1 tpa) and Switzerland (0.05 tpa).

11.7 Arctic Monitoring and Assessment Programme

In the AMAP Progress Report to the Arctic Council Ministerial Meeting in 2002 it is stated: "*There is evidence that POPs substances other than those included in the LRTAP Protocol and Stockholm Convention may be at or approaching levels in the Arctic that could justify regional and global action. For example […] some current-use pesticides such as endosulfan have been monitored in Arctic air and biota*" **[180]**.

12 MAXIMUM RESIDUE LEVELS / QUALITY STANDARDS

Due to the broad spectrum of crops treated with endosulfan, a great number of individual maximum residue levels (MRL) for crops exist within the European Union´s consumer protection legislation. MRL for maximum levels in and on fruits and vegetables range from 0.05, e.g. berries, cherries, figs, bananas, olives, etc. to 0.1 in nuts , and to 0.5 mg/kg in various citrus crops. A compilation of specific MRLs is posted on the web at **[181]**. Similar MRL have been stipulated in other countries.

Residues of endosulfan are among the most frequently found. For example, in a recent EU coordinated monitoring program on twenty pesticides, residues of endosulfan were found most often (16.9%) **[182]**.

German quality standard for aquatic environment (set to 0,005 µg/L) were found to be exceeded at more than 25% of the sampling sites during 1996 to 1998. On the other hand the EU drinking water limit common for all pesticide active ingredients (set at 0.1 µg/L, irrespective of their (eco)toxicity) was not exceeded in any drinking water sample **[183]**.

For the Directorate for Environmental Protection and the Directorate for Chemicals of The Netherlands the RIVM calculated maximum permissible concentrations for surface water and soil based on direct effects for birds and mammals **[184]**.

Table 12-1 Maximum permissible concentrations (MPC) for Endosulfan for surface water and soil, based on effects on birds and mammals

freshwater [µg/l]	**saltwater** [µg/l]	**aquatic combined** [µg/l]	**soil** [mg/kg]
0,013	0,0004	0,0004	0,05
bird [mg/kg food]	**mammal** [mg/kg food]	**bird/mammal combined** [mg/kg]	
8,1	0,68	0,68	-

The Australian and New Zealand Environment and Conservation Council (ANZECC) has developed guidelines that specify acceptable levels for pesticides in fresh waters and marine waters. For total endosulfan (α- + β-endosulfan + endosulfan-sulfate) a level of 0.01 µg/L has been stipulated **[185]**. For the most recent results of the Central and North West Regions Water Quality Program (cropping season1996/97) this level was exceeded by 63% of the surface water samples.

Maximum residue levels have been set up by FAO/WHO for food products, being in a range of 01 to 2.0 mg/kg **[163]**.

Restriction on the use of endosulfan products were imposed by the Australian Registration Authority for Agricultural and Veterinary Chemicals, caused by exceedings of endosulfan residue limits in beef **[186]**.

Based on recommendations of the WHO **[187]** an acceptable daily intake ADI[i] of 0.006 mg/kg/day was stipulated.

The US EPA Integrated Risk Information System (IRIS) lists an oral reference dose RfD of 0.006 mg/kg/day for endosulfan and endosulfan sulfate **[188]**. No reference concentration (RfC) for chronic inhalation exposure to endosulfan was reported.

13 ALTERNATIVES / SUBSTITUTES

Unlike for other chlorinated hydrocarbon insecticides, which have already been phased out in many countries endosulfan is still widely used.

Existing bans in countries which formerly used endosulfan products demonstrate that substitutes are available to take the place of endosulfan. Hence, there appear to be substitutes for a majority of applications, as illustrated by the decline of endosulfan. Notwithstanding, there are reportedly certain uses where there are no immediately available alternatives (Aventis Crop Science, quoted from **[160]**) Due to the wide variety of crops and pests for which endosulfan is still applied, detailed suggestions of alternatives, including integrated pest management practises for each single crop is beyond the scope of this document. However the agronomic implications and in particular the likely need for viable alternative chemicals will need careful consideration to avoid escalating use of alternatives. Among existing substitutes are organophosphorous pesticides like methamidiphos, phosphomidon and dimethoate, organo-thiophosphates like Oxydemethon-methyl, or pyrethroids, e.g. cyfluthrin, beta cyfluthrin.

It should be noted however that some experts are of the opinion that endosulfan remains vital to insecticide resistance management strategies, offering a control option from a distinct chemical class (rf. section 10.1.) : Endosulfan reacts with the GABA receptor and thus blocking the chlorine channels in the cell membrane, a mode of action different from that of mentioned substitutes.

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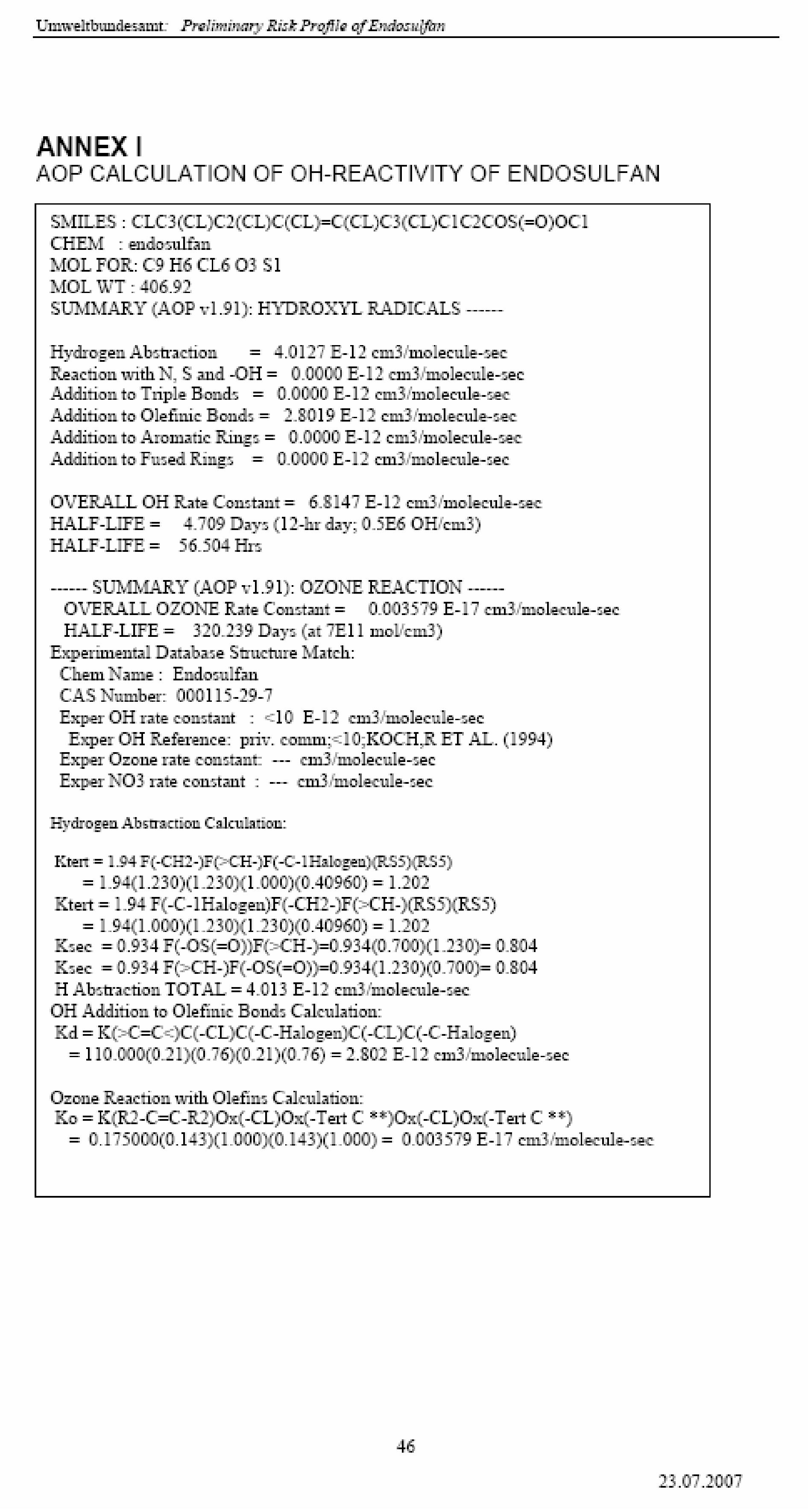
[i] **Acceptable Daily Intake (ADI):** The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects



ANNEX I

AOP CALCULATION OF OH-REACTIVITY OF ENDOSULFAN

```
SMILES : CLC3(CL)C2(CL)C(CL)=C(CL)C3(CL)C1C2COS(=O)OC1
CHEM   : endosulfan
MOL FOR: C9 H6 CL6 O3 S1
MOL WT : 406.92
SUMMARY (AOP v1.91): HYDROXYL RADICALS ------

Hydrogen Abstraction       =  4.0127 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =  0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =  2.8019 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =  0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant =   6.8147 E-12 cm3/molecule-sec
HALF-LIFE =     4.709 Days (12-hr day; 0.5E6 OH/cm3)
HALF-LIFE =    56.504 Hrs

------ SUMMARY (AOP v1.91): OZONE REACTION ------
  OVERALL OZONE Rate Constant =     0.003579 E-17 cm3/molecule-sec
  HALF-LIFE =    320.239 Days (at 7E11 mol/cm3)
Experimental Database Structure Match:
 Chem Name :  Endosulfan
 CAS Number:  000115-29-7
 Exper OH rate constant   :  <10  E-12  cm3/molecule-sec
   Exper OH Reference:  priv. comm;<10;KOCH,R ET AL. (1994)
 Exper Ozone rate constant:  ---  cm3/molecule-sec
 Exper NO3 rate constant  :  ---  cm3/molecule-sec

Hydrogen Abstraction Calculation:

 Ktert = 1.94 F(-CH2-)F(>CH-)F(-C-1Halogen)(RS5)(RS5)
       = 1.94(1.230)(1.230)(1.000)(0.40960) = 1.202
 Ktert = 1.94 F(-C-1Halogen)F(-CH2-)F(>CH-)(RS5)(RS5)
       = 1.94(1.000)(1.230)(1.230)(0.40960) = 1.202
 Ksec  = 0.934 F(-OS(=O))F(>CH-)=0.934(0.700)(1.230)= 0.804
 Ksec  = 0.934 F(>CH-)F(-OS(=O))=0.934(1.230)(0.700)= 0.804
 H Abstraction TOTAL = 4.013 E-12 cm3/molecule-sec
OH Addition to Olefinic Bonds Calculation:
 Kd = K(>C=C<)C(-CL)C(-C-Halogen)C(-CL)C(-C-Halogen)
    = 110.000(0.21)(0.76)(0.21)(0.76) = 2.802 E-12 cm3/molecule-sec

Ozone Reaction with Olefins Calculation:
 Ko = K(R2-C=C-R2)Ox(-CL)Ox(-Tert C **)Ox(-CL)Ox(-Tert C **)
    =  0.175000(0.143)(1.000)(0.143)(1.000) =  0.003579 E-17 cm3/molecule-sec
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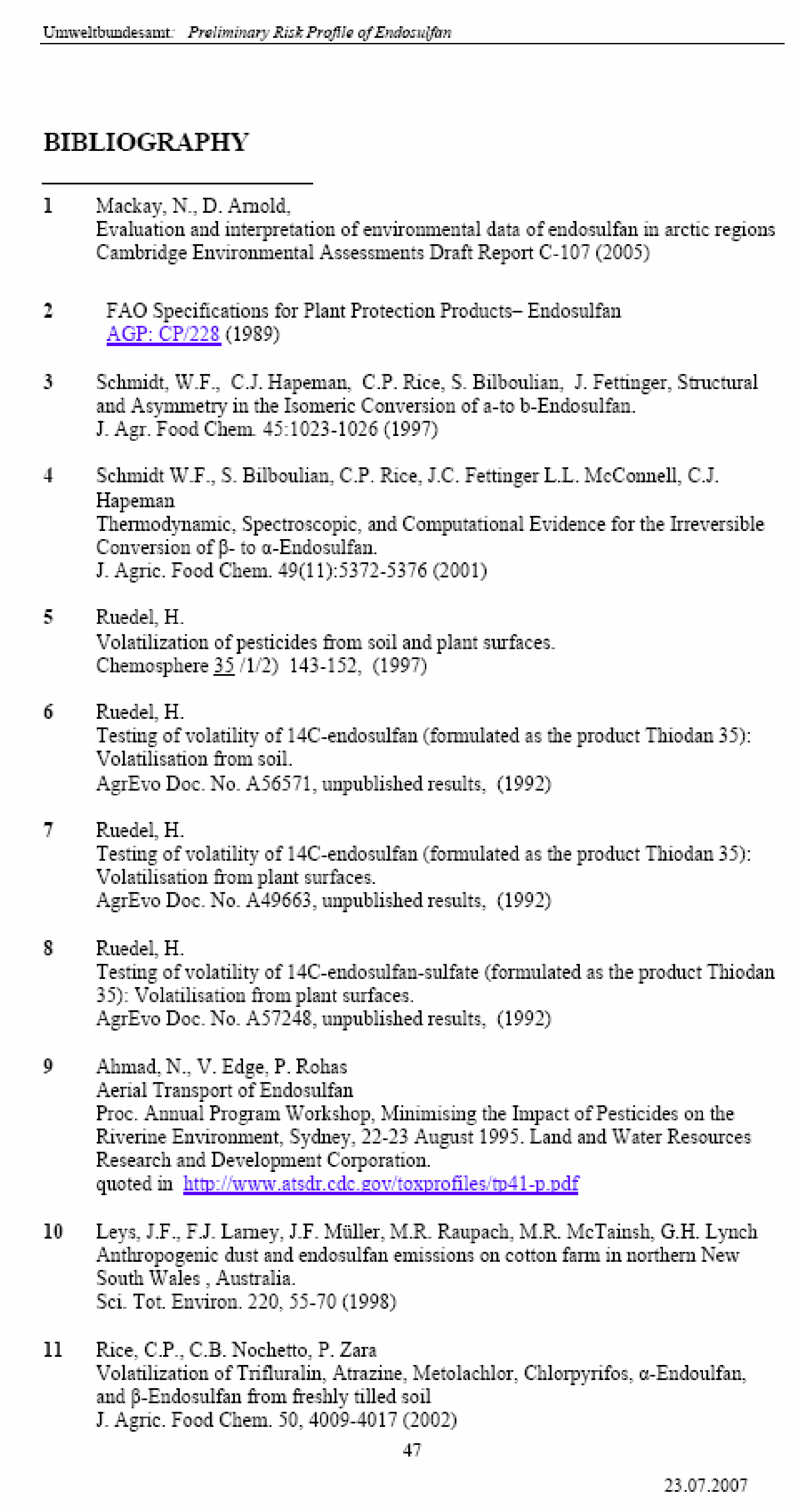

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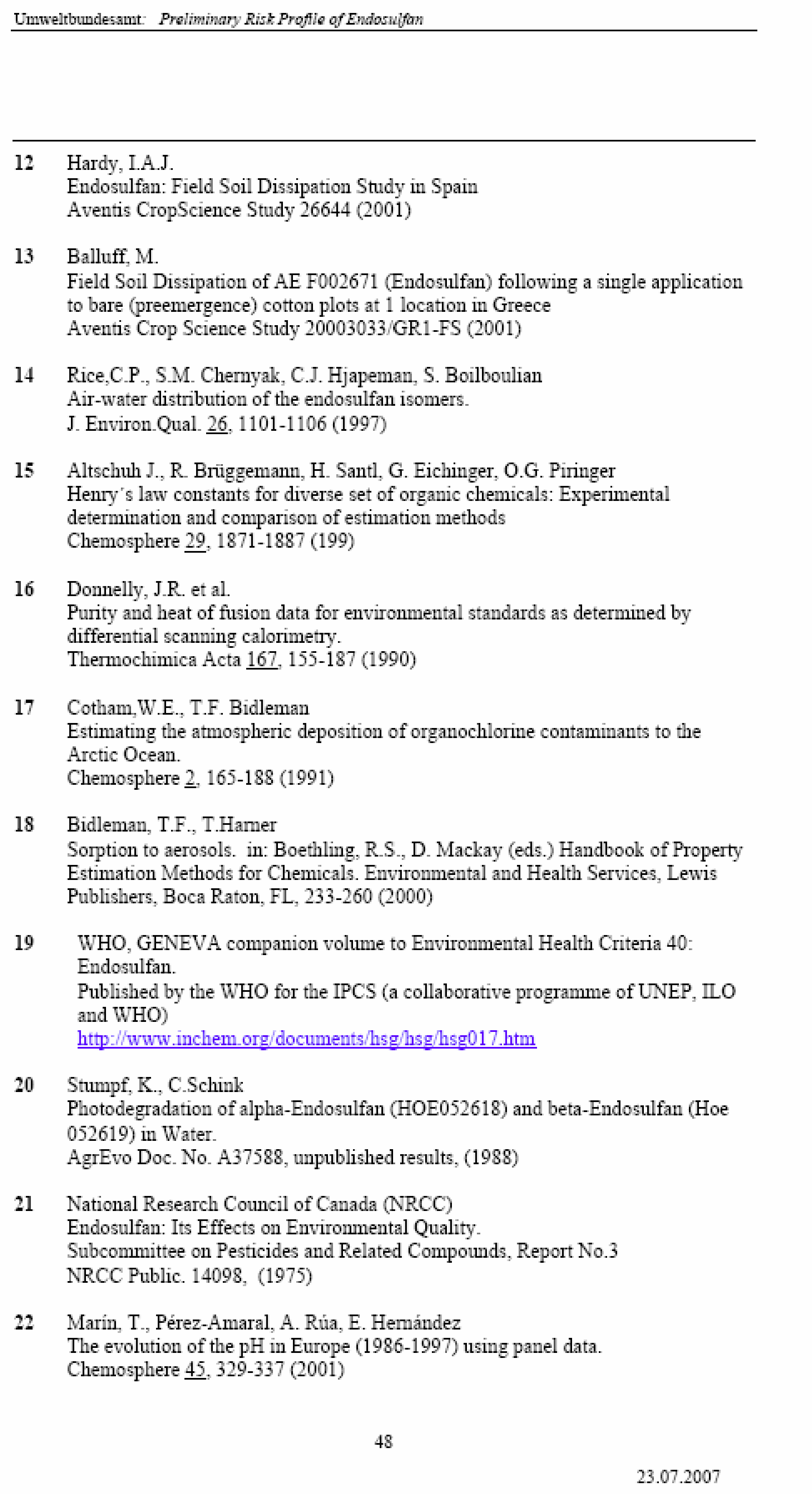

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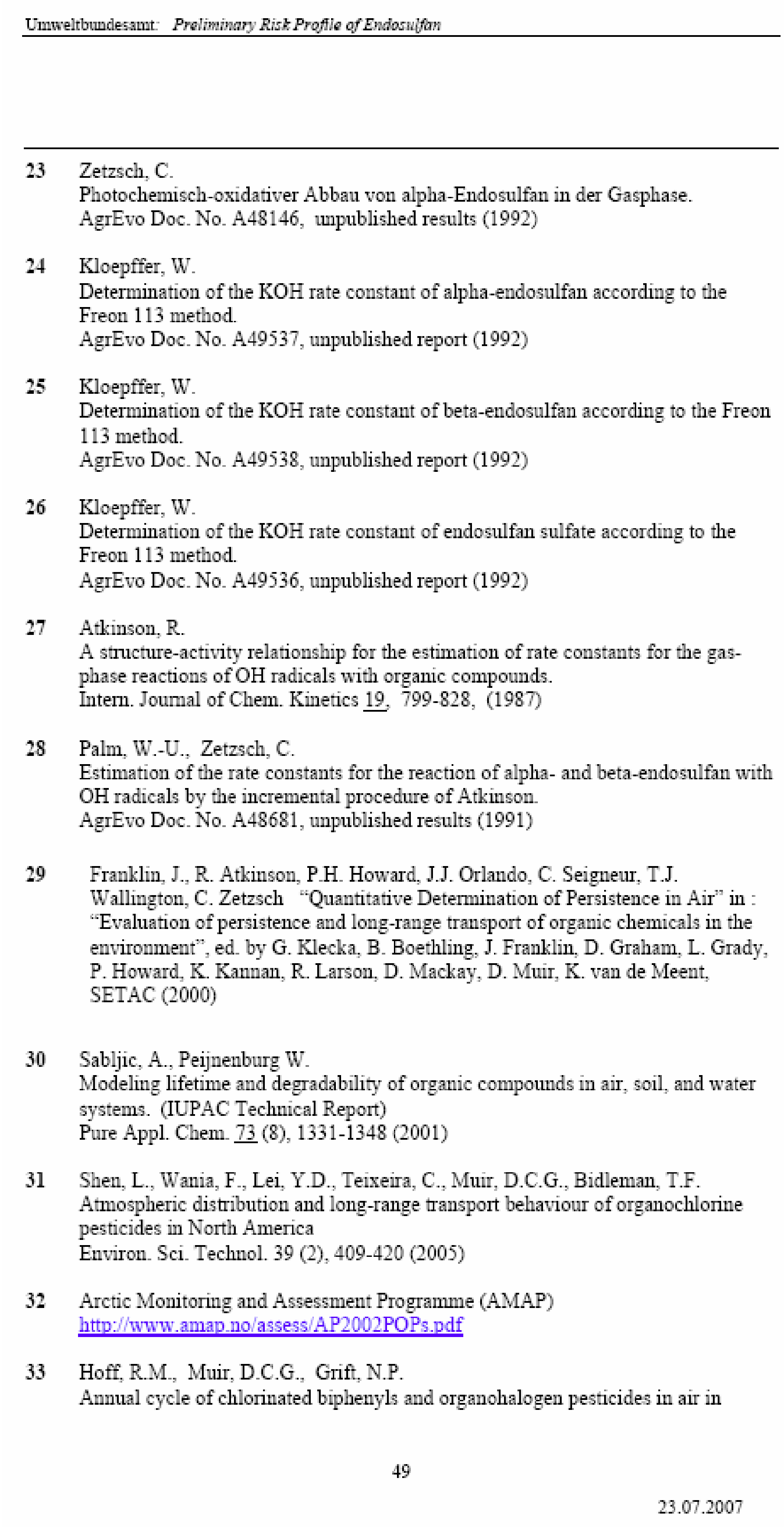

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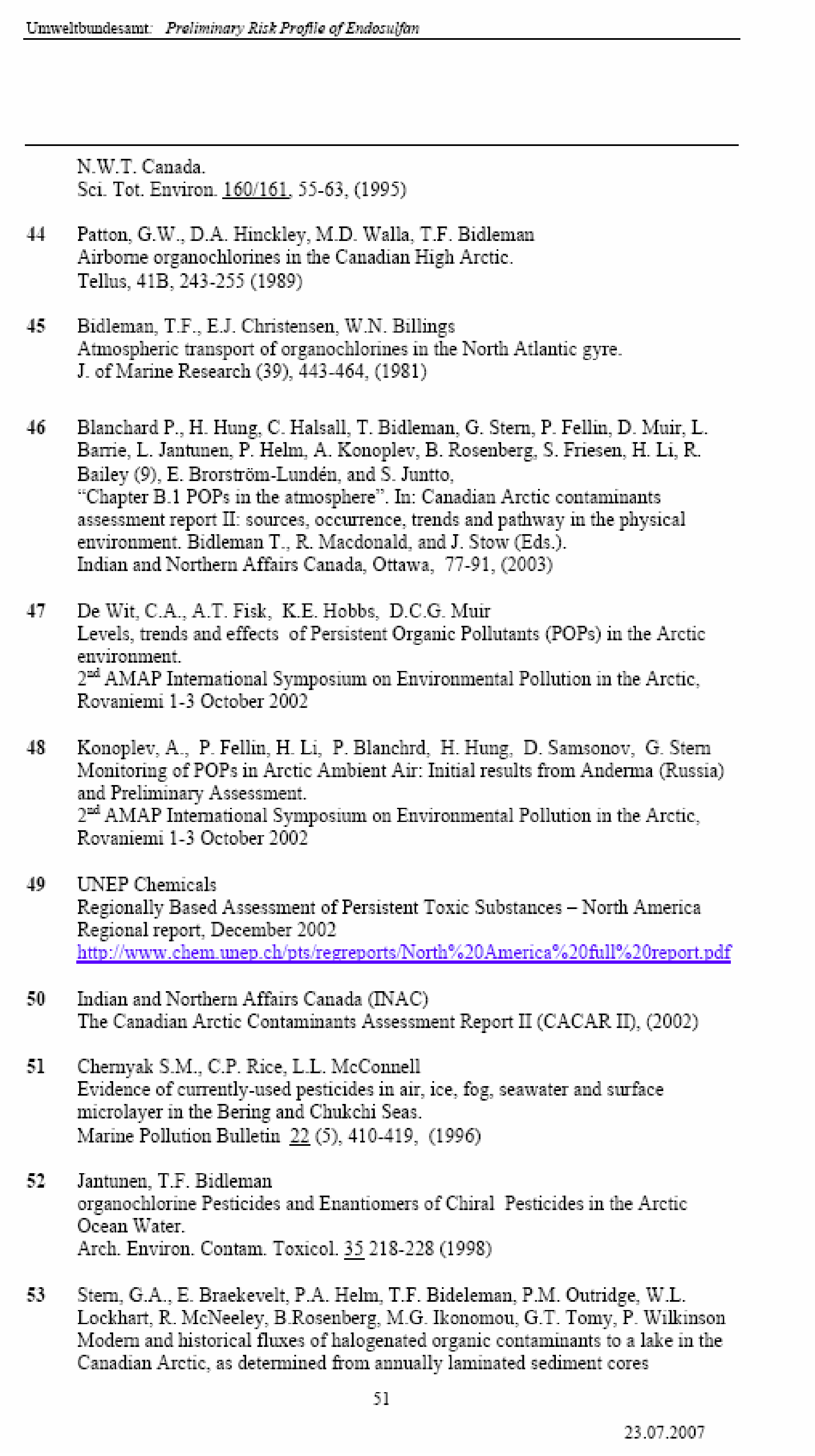

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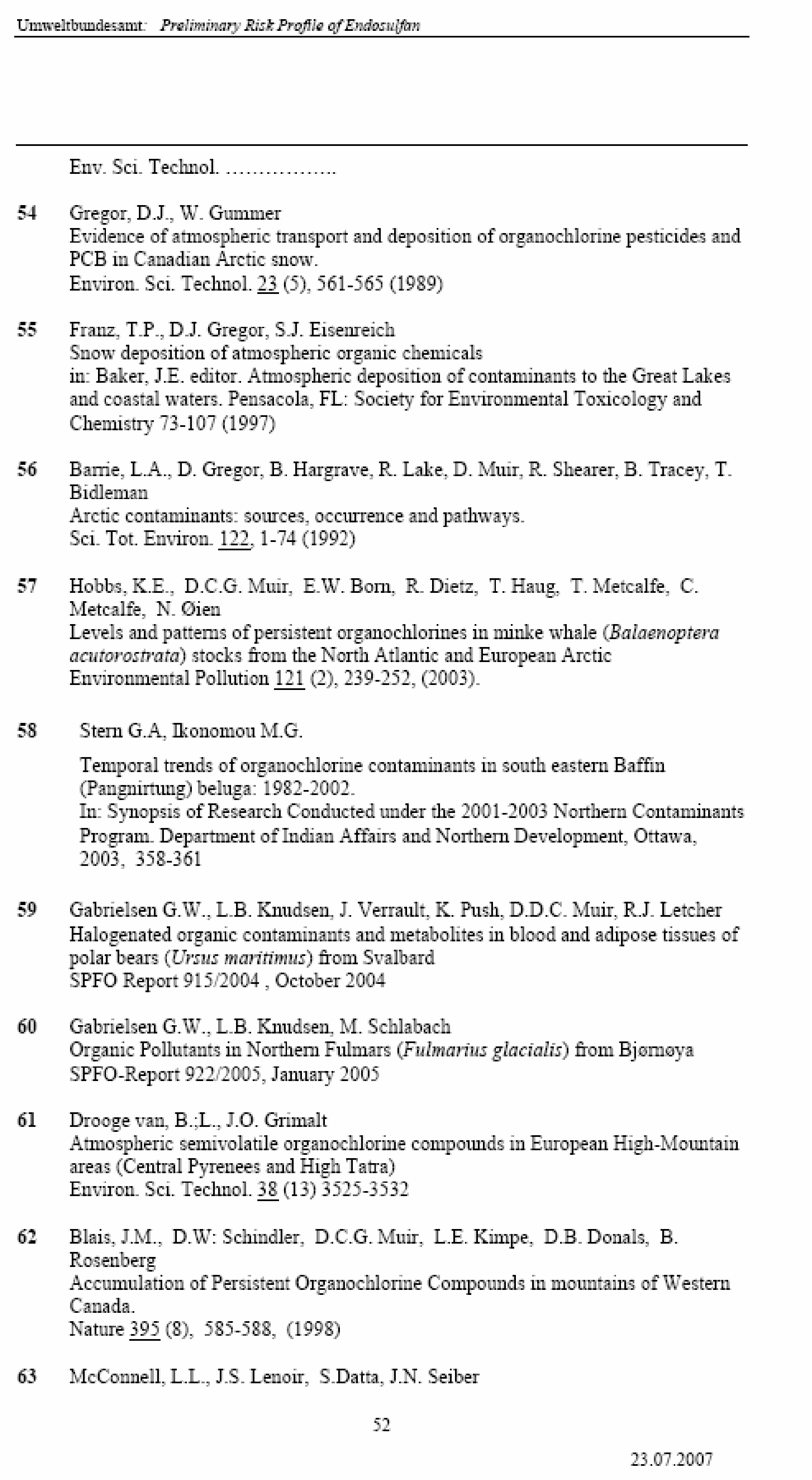

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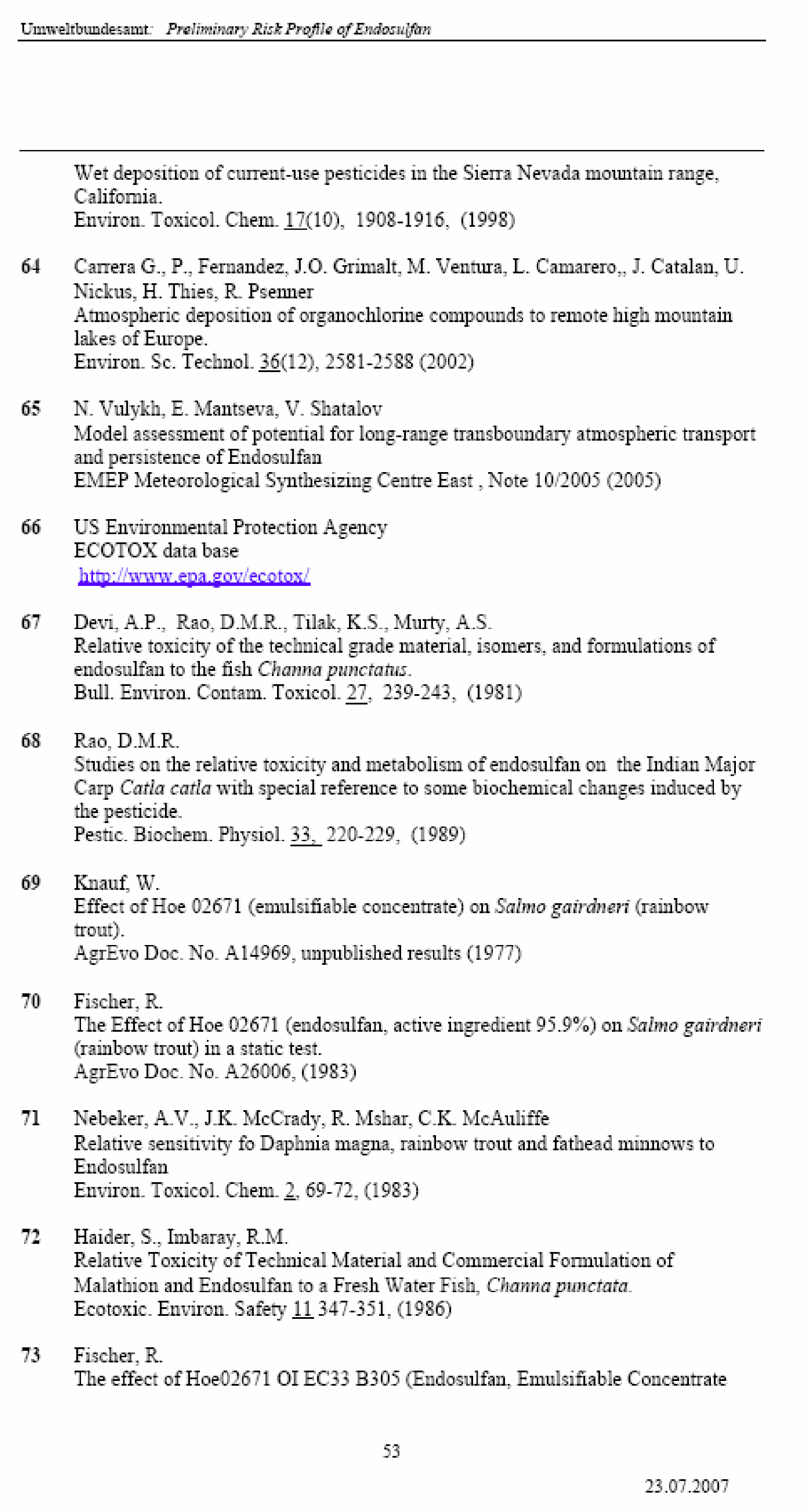

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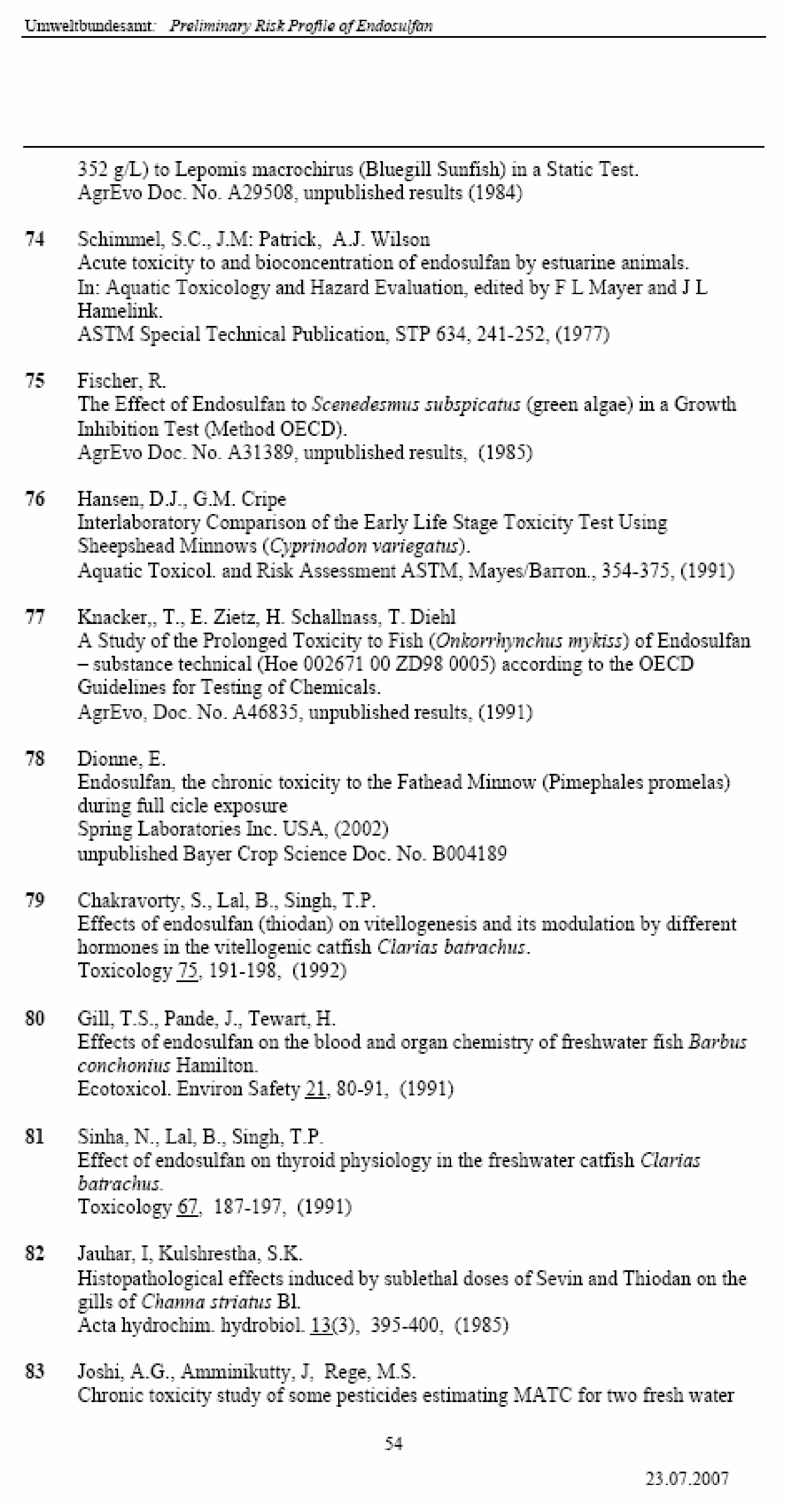

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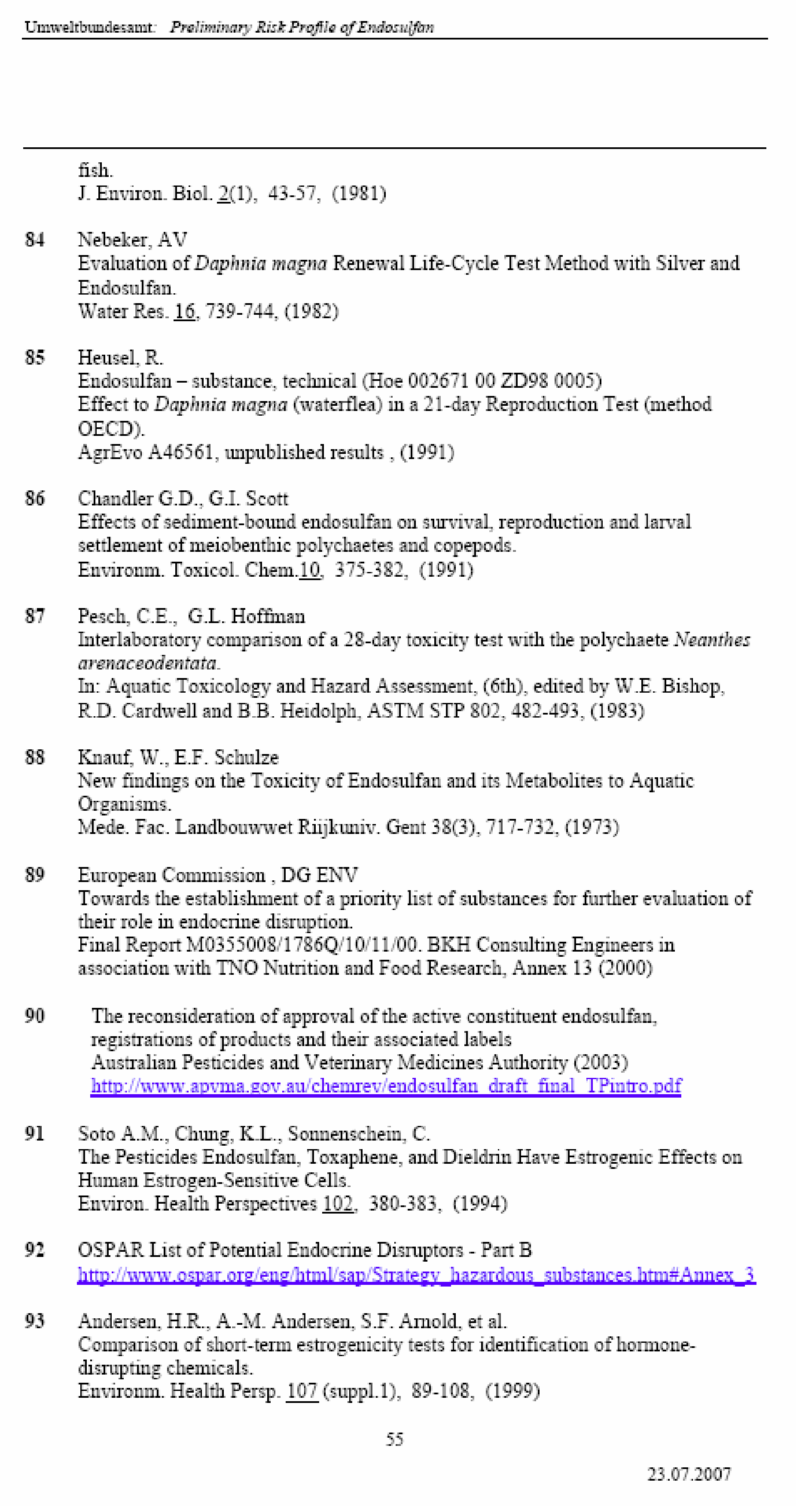

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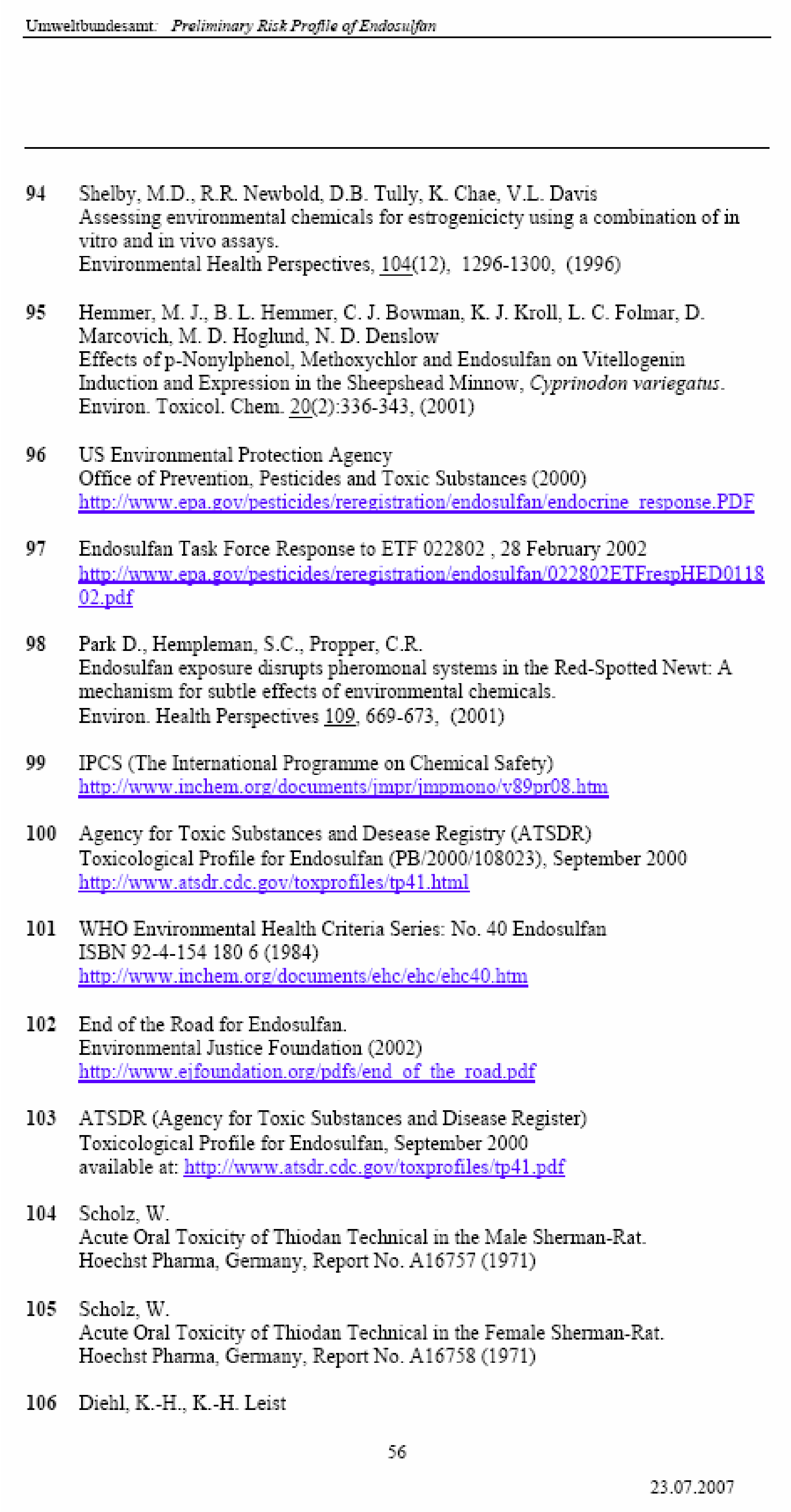

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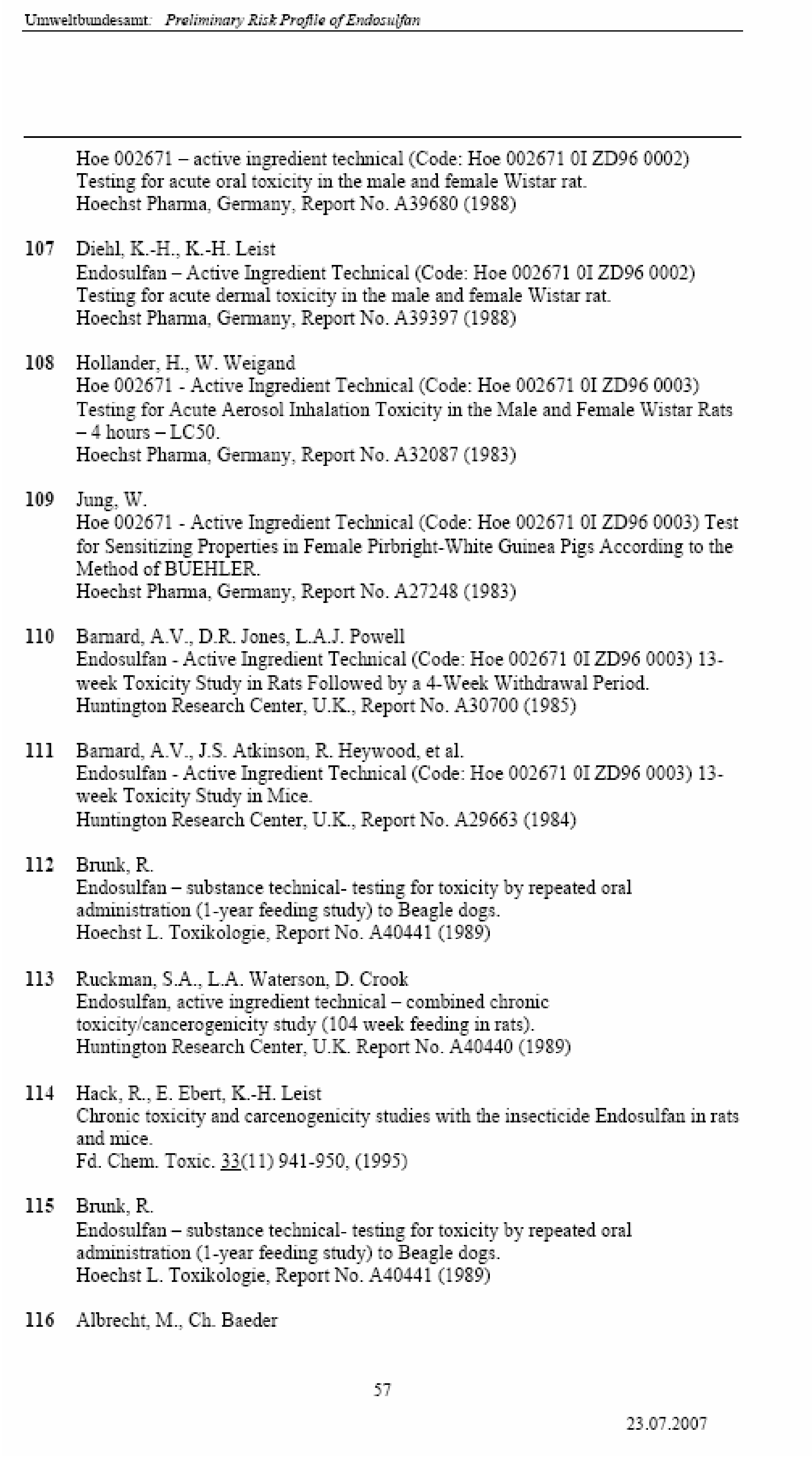

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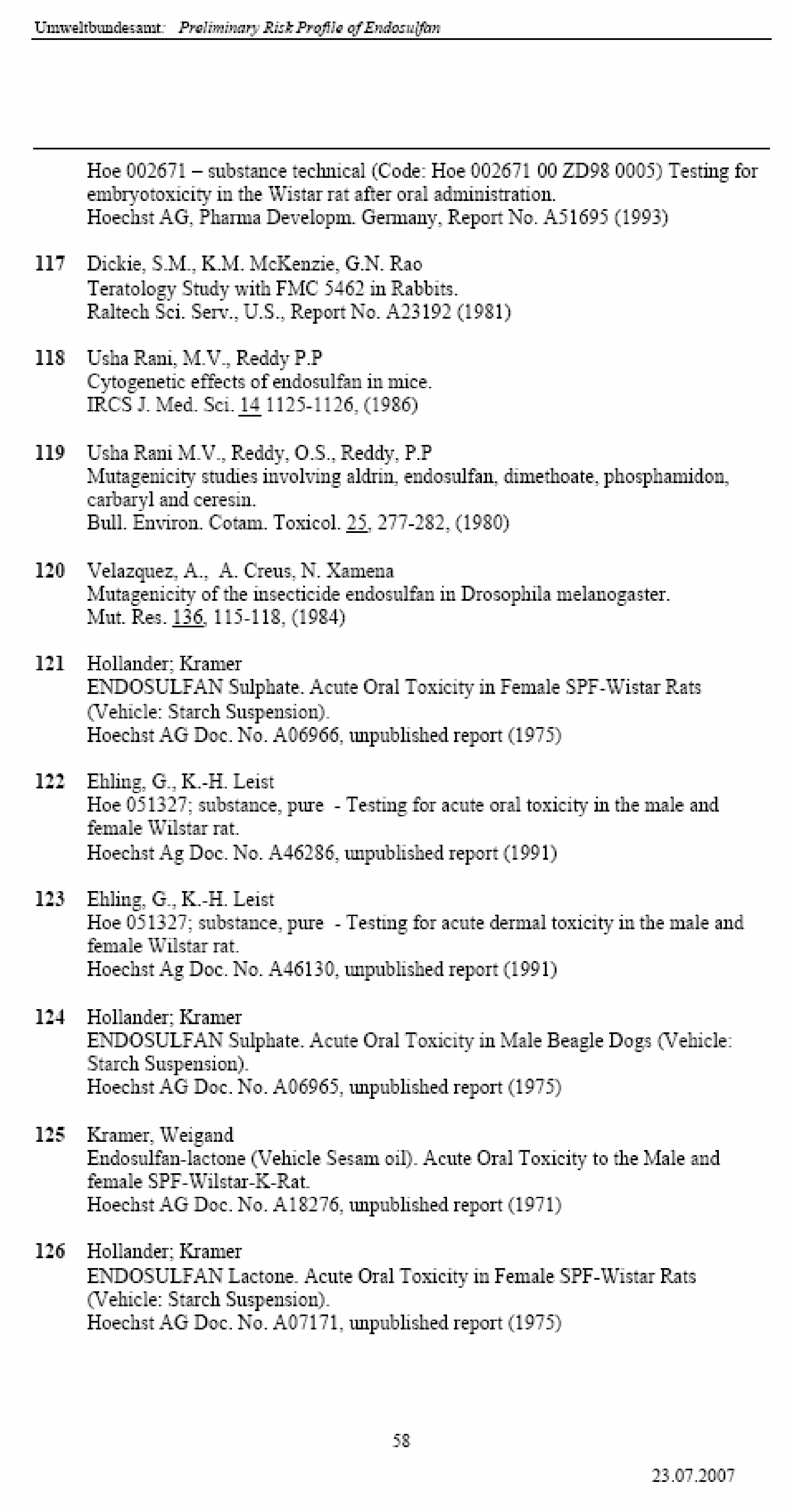

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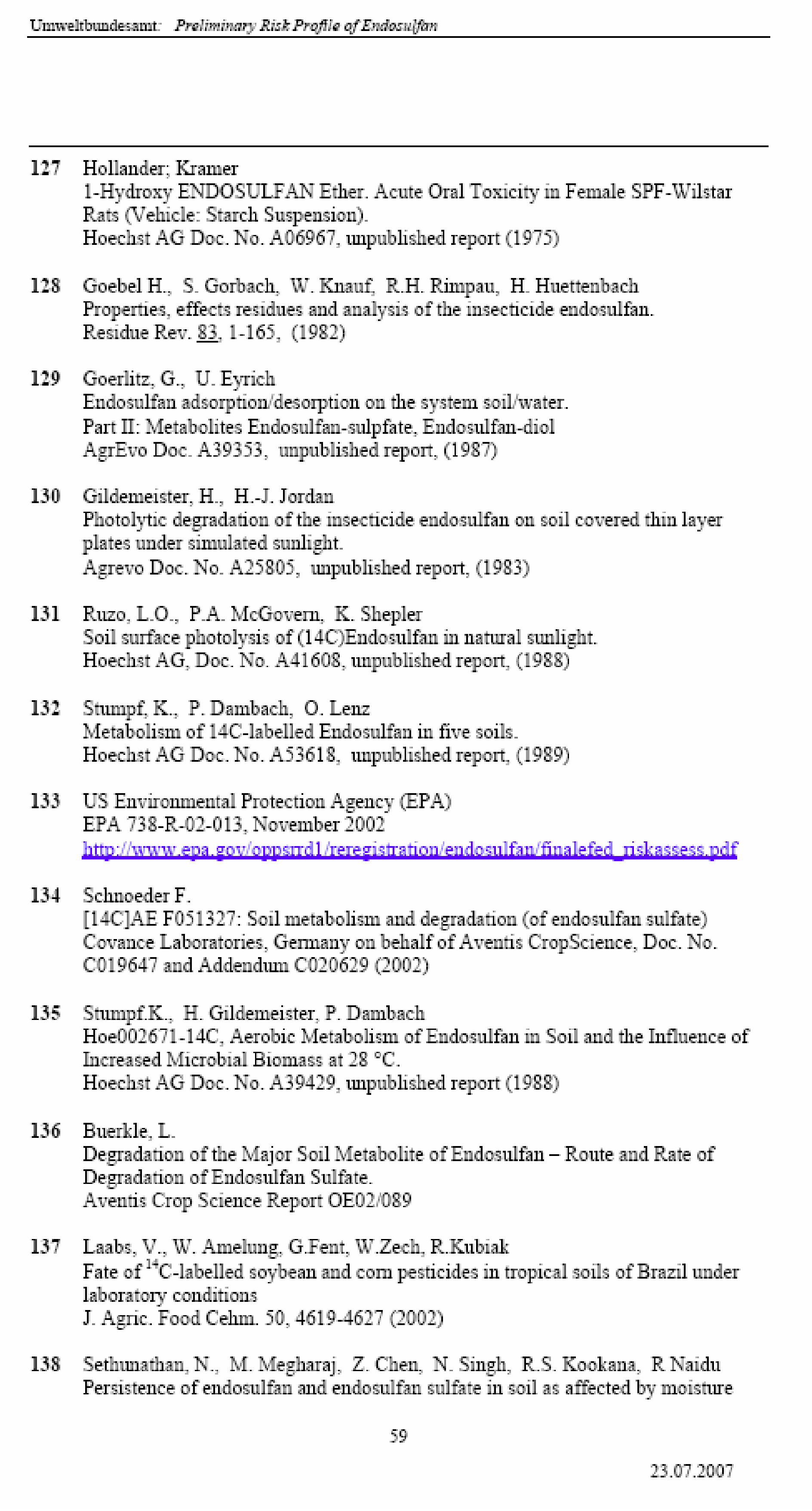

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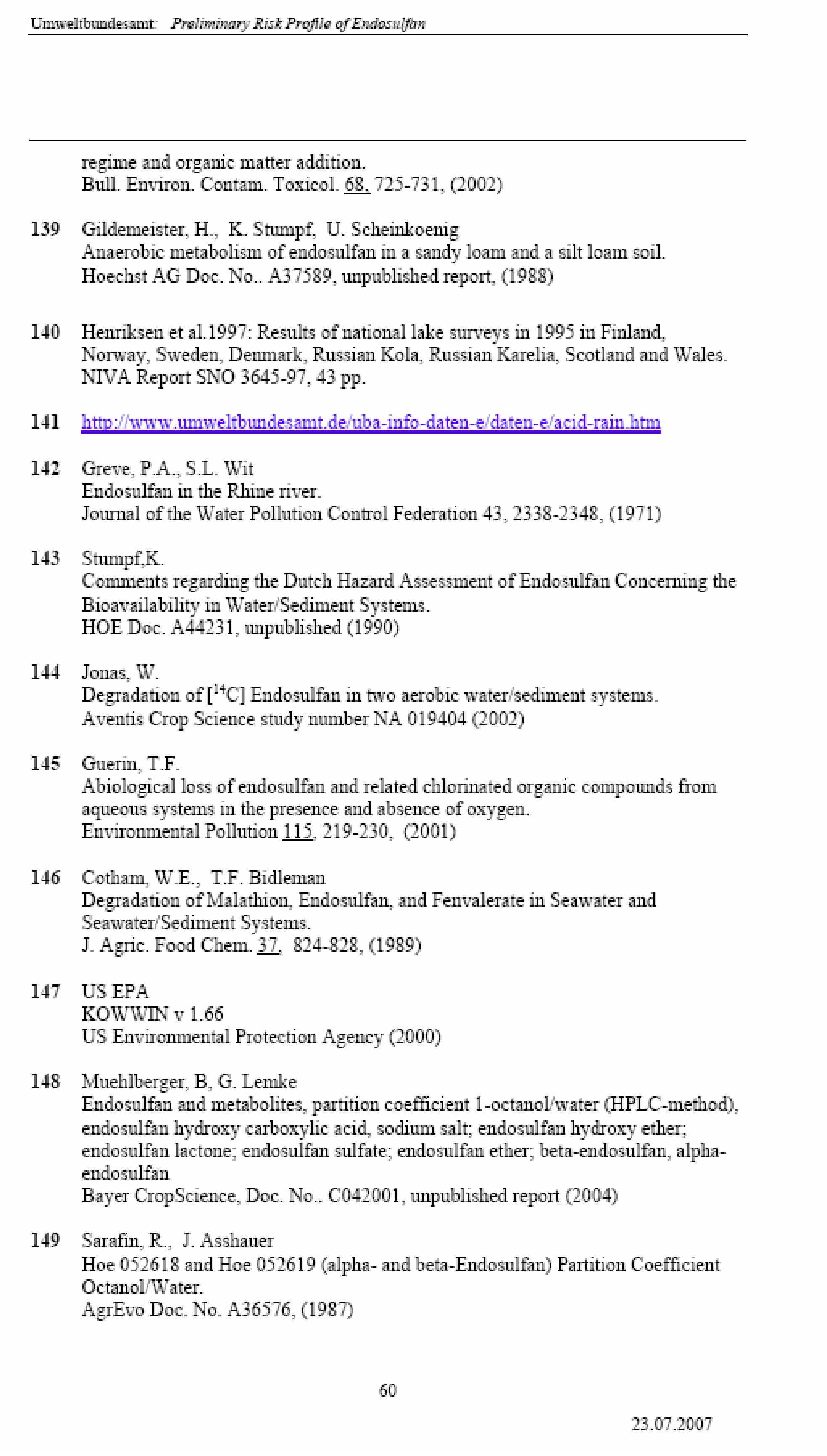

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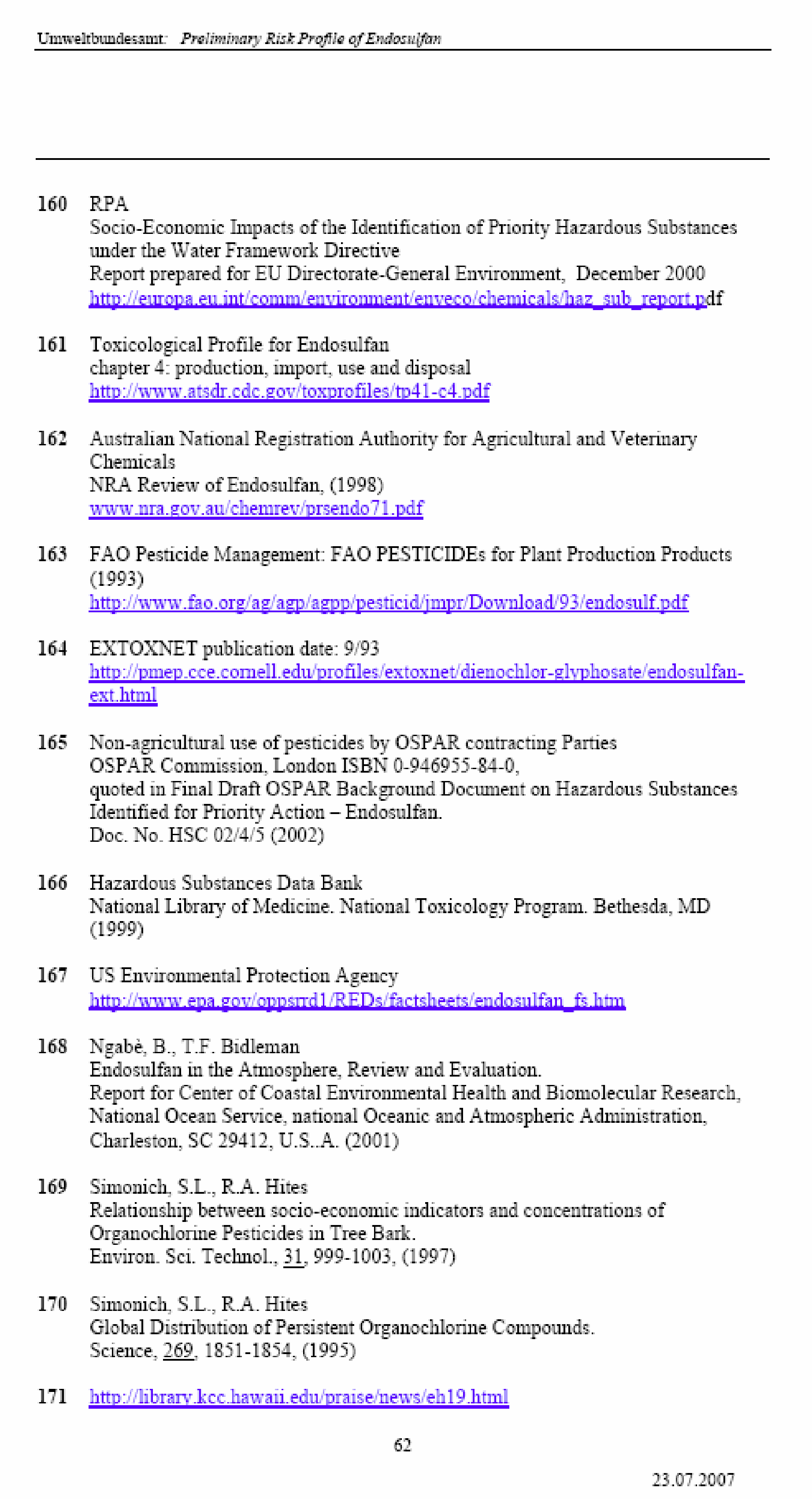

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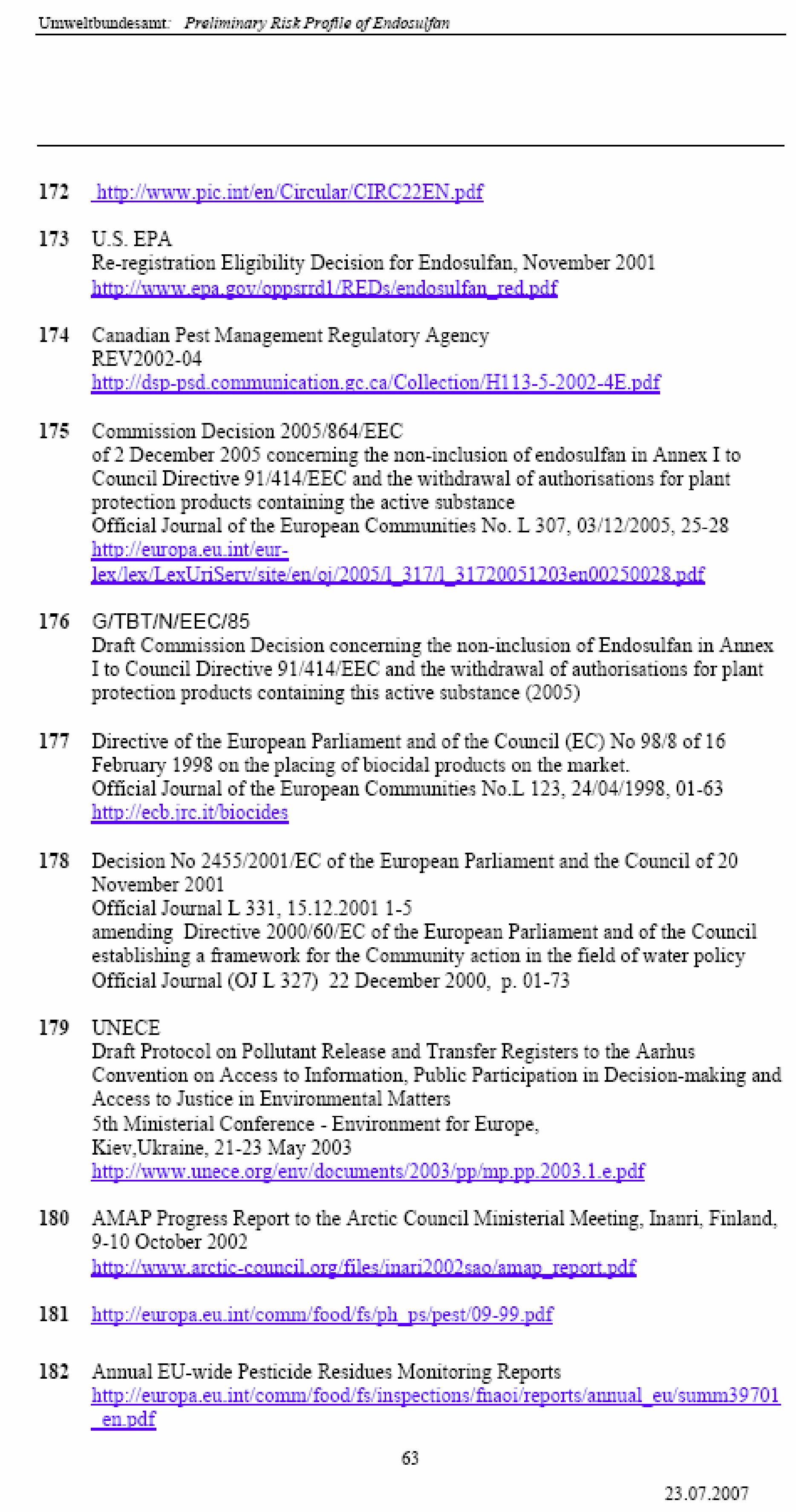

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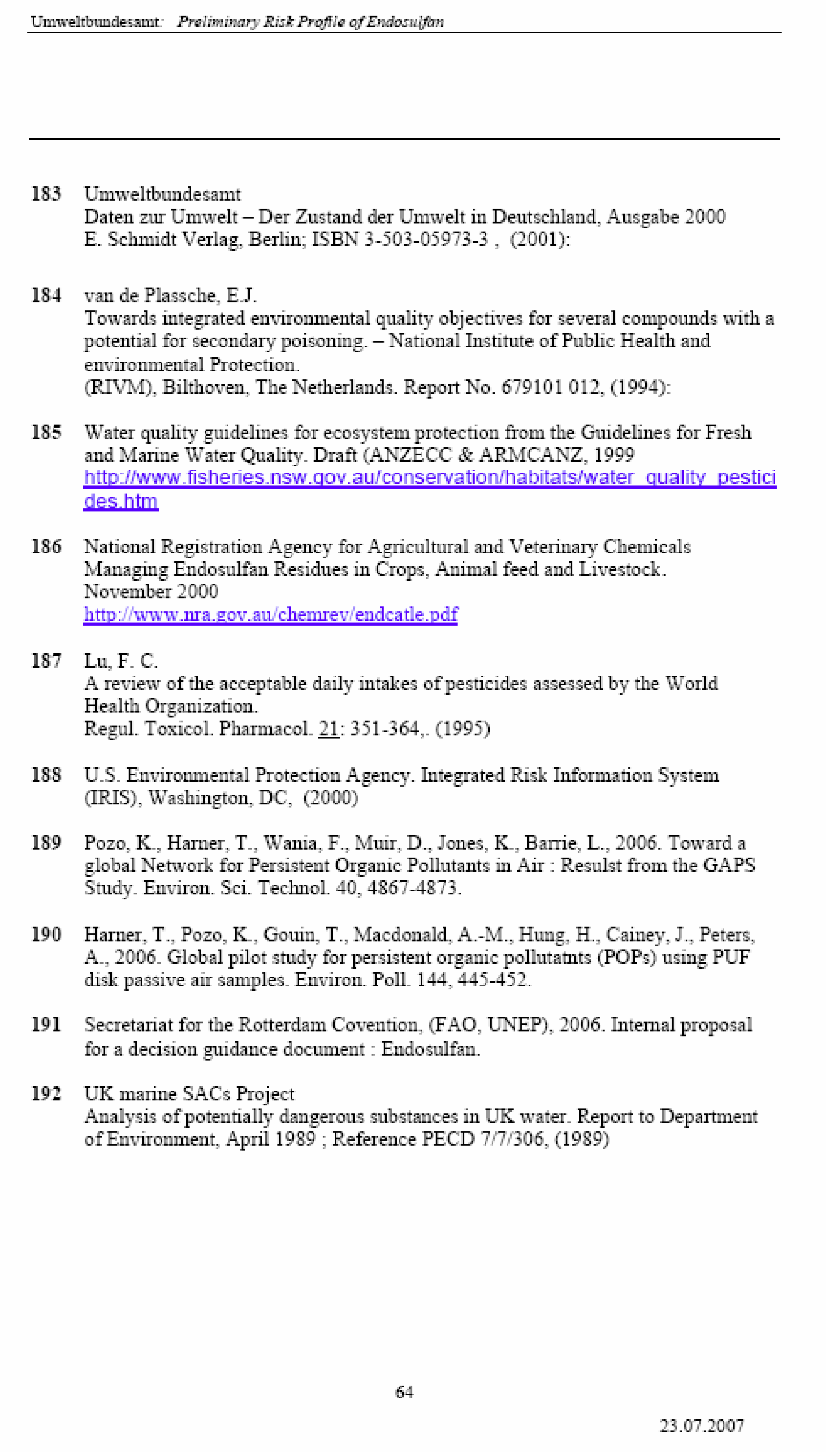

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