# TRIFLURALIN

**Dossier prepared in support of a proposal of trifluralin to be considered as a candidate for inclusion in the Annex I to the Protocol to the 1979 Convention on Long-Range Transboundary Air Pollution on Persistent Organic Pollutants (LRTAP Protocol on POPs)**

**European Commission, DG Environment, Brussels**
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## *CONTENTS*

## *EXECUTIVE SUMMARY*

Trifluralin is a synthetic fluorinated dinitroaniline herbicide which is used in the control of annual grasses and broad-leaved weeds in agriculture, horticulture, viticulture, amenity and home gardens. The major crops, on which it is used, are oilseed rape and sunflowers and, to a lesser extent, cotton and cereals. Trifluralin was first registered in 1963 and is marketed in a number of formulations, often combined with other active ingredients. It is currently widely registered for use throughout the world although the registration within the EU will be withdrawn from the autumn of 2007. Given the specific herbicidal uses of trifluralin, it can be expected that all amounts manufactured are ultimately released to the environment.

Trifluralin is persistent although it has a short half-life in water. This short half-life does not represent rapid degradation but rather a transfer to other environmental compartments, mainly sediment. Trifluralin is considered persistent in the water/sediment systems due to the low degree of mineralisation and the formation of high amounts of bound residues. Trifluralin is persistent in soil and is shown to be "not readily biodegradable". Under favourable conditions, photolysis in water is rapid, whereas, hydrolysis appears to be insignificant.

With BCF values in the range 1580-8870 trifluralin is considered to be highly bioaccumulative.

The acute toxicity of trifluralin in animals is low and there are few reports of acute toxicity in humans. It is moderately toxic in short, medium and long duration repeat dose toxicity studies in animals, producing changes in some haematological and blood chemistry parameters and renal damage. Trifluralin is not considered to have genotoxic properties. It has however produced a range of tumours, including renal and urinary tract tumours, liver, thyroid and testicular tumours in rats, although a similar carcinogenic potential was not seen in mice. Trifluralin does not have specific effects on reproductive performance or fertility and there is no convincing evidence to suggest that trifluralin exerts endocrine-modulating effects in the environment.

Trifluralin is very toxic to aquatic organisms, the most sensitive group being fish. Some of the major metabolites formed in water/sediment systems are shown not to be toxic to terrestrial and sediment-living organisms. The major products of photolysis of trifluralin are shown not to be of high acute toxicity towards aquatic organisms. The chronic toxicity of metabolites is not known. Trifluralin is regarded as toxic on the basis of its effects in the aquatic environment.

Trifluralin is rapidly photodegraded in air and significant transport to distant locations via the air is thus not expected. However, trifluralin residues in the atmosphere of remote arctic have been reported, suggesting that it has a potential for long-range transport. Furthermore, transport of sediment particles in ocean currents as well as biotic transport could contribute to long-range environmental transport of trifluralin. Monitoring data in biota from remote areas are not available. Model estimation shows that trifluralin distributes and persists in the environment to the same extent as already listed POPs.

# 1 INTRODUCTION

## 1.1 Chemical identity of the proposed substance

Trifluralin is a synthetic fluorinated dinitroaniline herbicide which is used in the control of annual grasses and broad-leaved weeds in agriculture, horticulture, viticulture, amenity and home gardens. The major crops on which it is used, are oilseed rape and sunflowers and, to a lesser extent, cotton and cereals.

### 1.1.1 Names and registry numbers

**CAS chemical name**

2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl)benzenamine

**Synonyms**

Trifluralin (ISO 1750)
α,α,α-trifluoro-2,6-dinitro-*N*,*N*-dipropyl-*p*-toluidine (IUPAC)
Benzenamine, 2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl)-
2,6-Dinitro-N,N-dipropyl-4-trifluoromethylaniline

**Trade names**

Agriflan; Agriflan 24; Crisalin; Digermin; Eloncolan; Ipersan; Ipifluor; L 36352; Lilly 36,352; Nitran; Nitran K; Olitref; Su Seguro Carpidor; Sinflouran; Synfloran ;TR-10; Trefanocide; Treflan; Treflan EC; Treflan-R; Treficon; Trifloran; Trifluraline; Triflurex; Triflurex 48EC; Trikepin; Trim; Tristar.

In addition, formulations containing trifluralin (alone or together with other active ingredients) are marketed under many different names. These include: Portman Trifluralin; Ardent; Tandril 48; Axit GR; Das-320; Premiere; Alpha Trifluralin 48 EC; Arizona; Blois; O-Tan; Sword; Uranus; Zimbali; Autumn Kite; MAGDELIN; Snitch; Triflur; Trimaran; Digermin; Triplen; Hawk; Reserve; Trilogy.

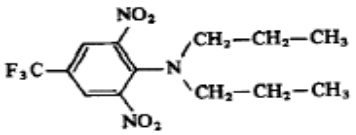
**CAS registry number**

1582-09-8

**Former CAS registry numbers**

39300-53-3; 52627-52-8; 61373-95-3; 71281-30-6; 75635-23-3

### 1.1.2 Structure



**Formula**

$C_{13}H_{16}F_3N_3O_4$

### 1.1.3 Physical and chemical properties

The physical and chemical properties of trifluralin are listed in Table 1.1.

**Table 1.1 Physical and chemical properties of trifluralin.**

| Property | Unit | Value | Reference (1) |
|---|---|---|---|
| Molecular formula | | $C_{13}H_{16}F_3N_3O_4$ | OSPAR (2005) |
| Molecular mass | g/mole | 335.28 | OSPAR (2005) |
| Appearance at normal temperature and pressure | | bright orange crystalline solid | OSPAR (2005) |
| Vapour Pressure | Pa | $9.5 \times 10^{-3}$ Pa at 25°C (100% pur.)<br>$6.1 \times 10^{-3}$ Pa at 25°C (96.8% pur.) | OSPAR (2005) |
| Water solubility | g/L | $1{,}94 \times 10^{-4}$ (unbuffered 100% pur.)<br>pH 7: $2{,}21 * 10^{-4}$ | OSPAR (2005) |
| Melting point | °C | 43.0-47.5 °C | OSPAR (2005) |
| Boiling point | °C | not determined, decomposition | OSPAR (2005) |
| Log $K_{OW}$ | - | 5.27 at 20 °C (100% pur.) | OSPAR (2005) |
| Log $K_{oc}$ | [L/kg] | 4.13 (calc.)<br>3,81–4,13 (meas.)<br>no pH-dependency | OSPAR (2005) |
| Henry's Law Constant | Pa $m^3$/mol | .,19 x $10^{-3}$ (calc.)<br>4.12 x $10^{-3}$ (meas. 20°C) | OSPAR (2005) |
| Atmospheric OH Rate Constant | $cm^3$/molecule-sec | 24.0039 x $10^{-12}$ (2) | EU DAR, (2005) |

(1) The full reference is quoted in the review cited.

(2) Reactivity with OH-radicals atmospheric half-life [d] is given by OSPAR (2005) as 0.22 d. The half life calculated from the figure shown in the table is 0.446 d.

### 1.1.4 Significant impurities

Technical grade trifluralin may be contaminated with N-nitrosodi-n-propylamine and limits are set for an upper level of this contaminant by FAO and the US EPA (IARC 1991).

## 1.2 Data sources

This Draft Risk Profile is mainly based on information from the following review reports:

- EU Draft Assessment Report (DAR) on Trifluralin under EU Council Directive 91/414/EEC. January 2005.

- Conclusion regarding the peer review of the pesticide risk assessment of the active substance trifluralin. EFSA Scientific Report (2005).
- United States Environmental Agency Reregistration Eligibility Decision, trifluralin (1996).
- OSPAR background document on trifluralin. Hazardous Substances Series. OSPAR Commission, 2005.
- Trifluralin in Drinking-water. Background document for development of WHO Guidelines for Drinking-water Quality, 2003.
- PAN reports on Trifluralin.

The above reports were used as the main source of information on this candidate POP chemical. Where the reviews above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list.

A search for recent peer reviewed literature (2005-2007) included a literature search in Toxline, FINDit and ToxCenter (search terms: trifluralin; CAS No.: 1582-09-8). The databases include US EPA "Ecotox" (US EPA, 2006), "NITE" (Japan, National Institute of Technology and Evaluation[1] and Environmental Fate DataBase[2].

In addition, the Arctic Monitoring and Assessment Programme[3] and the UNEP Regionally Based Assessment of Persistent Toxic Substances Global Report[4] were consulted. Most of these gave no further information regarding trifluralin. Information was, however, obtained from the Canadian Artic Contaminants Program (2006).

## 1.3 Regulatory Status of trifluralin

### 1.3.1 National and international risk evaluations, assessments or profiles and labelling information and hazard classifications

The use of trifluralin has been reviewed by the US EPA (United States Environmental Agency Reregistration Eligibility Decision, trifluralin 1996) and by the EU (Draft Assessment Report on Trifluralin under Council Directive 91/414/EEC. January 2005). In addition, trifluralin has been evaluated for carcinogenicity by the International Agency for Research into Cancer, when they concluded that trifluralin was not classifiable as to its carcinogenicity to humans (Group 3) (IARC group 3) (IARC group 3) (IARC, 1991).

Background documents on trifluralin have been prepared by OSPAR (2005) and WHO (WHO Guidelines for Drinking-water Quality, 2003).

In the United Kingdom, trifluralin is a prescribed substance (Red List), where the release into water is prohibited or restricted, under the Environmental Protection (Prescribed Processes and Substances) Regulations of 1991. In addition, controls are imposed over the discharge into the public sewers of trade effluents under the Trade Effluents (Prescribed Processes and Substances) Regulations of 1989 (quoted from OSPAR, 2005).

[1] http://www.safe.nite.go.jp/english/db.html
[2] http://www.syrres.com/esc/efdb.htm
[3] http://www.amap.no/
[4] http://www.chem.unep.ch/pts/gr/Global_Report.pdf

Trifluralin is banned in Norwar and has in Sweden been banned since 1993 because of its properties as non-readily biodegradable, bioaccumulative and toxic to water-living organisms. Trifluralin has been banned in Denmark since 1997, but a derogation for use in seed production was in force from 1999 to 2004 (quoted from OSPAR, 2005; PAN, 2007). Trifluralin is registered to be used in among others Australia, Canada, Finland, Germany, Hungary, India, Japan, New Zealand, Portugal, South Africa, US, Vietnam[5].

#### 1.3.2 Status of the chemical under international conventions

Trifluralin is not listed under Stockholm convention on Persistent Organic Pollutant. Trifluralin is not listed under the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (Rotterdam Convention). WHO does not consider trifluralin as an outdated pesticide.

Trifluralin has been added to the OSPAR (Convention for the Protection of the Marine Environment of the North-East Atlantic) List of Chemicals for Priority Action in 2002 because it is considered to be a PBT substance fulfilling the criteria for Persistence, Bioaccumulation and Toxicity (quoted from EFSA, 2005).

WHO has recommended a guideline value of 20 µg/L (rounded figure) for drinking water, based on an allocation of 10% of the TDI to drinking water (WHO, 2003).

# *2 SUMMARY INFORMATION RELEVANT FOR THE RISK PROFILE*

## 2.1 Sources

### 2.1.1 Production

The production of trifluralin initially involves the reaction of hydrogen fluoride with *p*-chlorotoluene to produce 4-trifluoromethylchlorobenzene. The latter compound is then nitrated to form 2,6-dinitro-4-trifluoromethylchlorobenzene, followed by reaction with di-*N*-propylamine, which replaces the chlorine to form trifluralin (NRC, 1981, IARC, 1991).

Trifluralin was originally produced by Eli Lilly in the USA and first registered in 1963 (NRC, 1981, IARC, 1991).

The US EPA (1996) reports the main producers to be DowElanco (Indiana, USA), Makhteshim-Agan (Israel), Industria Prodotti Chimici S.P.A (I.Pi.Ci.) (Italy), Tri Corporation (Texas, USA) and Albaugh Inc. (Missouri, USA). OSPAR (2005) reports that the active ingredient, trifluralin, is manufactured in only one facility in the European Union in Manerbio in Northern Italy.

Other countries and production sites for trifluralin are Argentina (Atanor), Australia (Nufarm), Brazil (Defensa Industria de Defensivos), China (Zhejiang Dongyang Pesticide Factory), Guatemala (Agrotran SA), Hungary (Budapest Chemical Works), Italy (Dintec Agroquimica, Milan[6]), South Africa (Sanachem, Canelands) and USA (Eli Lilly (Dintec Agroquimica)) (Fluoride Action Network, 2006).

[5] (http://fluoridealert.org/pesticides/trifluralin-page.htm.)

[6] Dintec is an incorporated company formed in 1994 between Dow AgroSciences, B.V., established at Rotterdam, The Netherlands, and I.Pi.Ci. S.p.A. Industria Prodotti Chimici (I.Pi.Ci.), established at Novate, Milan, Italy.

### 2.1.2 Trade and stockpiles

In the USA, trifluralin is available as 94.6–98% active ingredient technical product (US EPA, 1996). It is available as emulsifiable concentrates, granules and liquid formulations (US EPA, 1996). Trifluralin is formulated in combination with other pesticides including alachlor, benefin (benfluralin), bromoxynil octanoate, clomazone, chlorpyrifos, disulfoton, flumetsulam, ioxynil octanoate, imazethapyr, imazaquin, isoproturon, isoxaben, linuron, metribuzin, napropamide, neburon, tebuthiuron, terbutryne, and triallate, trietazine (IARC, 1991, US EPA, 1996).

Trifluralin is registered for use in South Africa, Australia, India, New Zealand, Canada, US (PAN, 2007), Japan and Vietnam (Fluoride Action Network, 2006). Within the EU, trifluralin is authorised in Austria, Belgium, Finland, France, Germany, Greece, Italy, Ireland, Portugal, Spain and the United Kingdom. Trifluralin is currently banned for use in Denmark, Sweden, Norway, Luxembourg and the Netherlands (quoted from OSPAR, 2005). The conclusions of the EU review of trifluralin under Directive 91/414/EEC is that this substance cannot be included in Annex I (i.e. registration cannot be continued) (EC, 2007) because it was not possible to conclude that trifluralin met the safety criteria for inclusion on the basis of the information available. This decision will be published in the Official Journal of the European Communities up to 6 months after the vote in March 2007 (about September 2007) (UK PSD, 2007).

IARC reports annual worldwide production is 20.000–25.000 tonnes (IARC, 1991).

According to the US EPA, 12,500 tonnes of trifluralin are used annually in the US (US EPA, 1996). The use of trifluralin in California in 2005 was over 500 tonnes (PAN, 2007). Approx. 3,200 tonnes active substance trifluralin are annually used in the EU, including Poland, Czech Republic and Hungary. According to industry, sales of active substance remain at a constant level of about 3,200 tonnes/year in Europe (quoted from OSPAR, 2005).

### 2.1.3 Uses

Trifluralin is a herbicide for pre-sowing or pre-emergence treatment of grasses and dicotyledonous weeds at a rate of 1200 g active substance per ha (using 150–500 L/ha). Major crops are oilseed rape and sunflowers and, to a lesser extent, cotton and cereals. There are other minor uses in a wide range of agricultural and horticultural crops. Non-agricultural uses of trifluralin are not known. (quoted from OSPAR, 2005).

Of the approx. 12,500 tonnes of active ingredient annually used on agricultural crops in the USA, 64% is used on soybeans with another 19% used on cotton. The remaining 17% is used on a wide range of crops (US EPA, 1996). Crops with more than 50% of the planted acres receiving an application of trifluralin include green beans, broccoli, tomatoes and cotton. Other crops with more than 20% of the planted acres treated with trifluralin include collards, cabbage, sunflowers, dry beans, cauliflower, okra, soybeans, carrots, flax, Brussels sprouts, asparagus and sweet peppers. For non-food crops, trees and ornamentals appear to be the most significant sites with approx. 75 tonnes of active ingredient used annually. Little use of trifluralin on turf was reported (US EPA, 1996).

### 2.1.4 Releases to the environment

Given the specific herbicidal uses of trifluralin, it can be expected that all amounts manufactured are ultimately released to the environment.

## 2.2 Environmental fate

The partitioning of trifluralin in the environment will be governed by its high log $K_{ow}$ (5.27) and low water solubility (200 µg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic material (living organisms). Under aerobic laboratory conditions trifluralin is medium to highly persistent with half-lives between 81 to 356 d at 22 °C. The degradation under anaerobic conditions was faster than under aerobic conditions. Data indicate that trifluralin is strongly adsorbed to soil and could be classified as immobile. Trifluralin is hydrolytically stable under environmental relevant conditions. Aqueous photolysis may contribute to the environmental degradation of trifluralin, producing TR-6 and TR-15 metabolites (the different metabolites formed are shown in Annex 1). Trifluralin is not readily biodegradable (quoted from EFSA, 2005). Trifluralin is volatile, especially in wet conditions (PAN, 2001). Trifluralin residues in the atmosphere of remote, non-use regions have been reported, suggesting its potential for long-range transport (PAN, 2001).

### 2.2.1 Persistence

#### Hydrolysis

Trifluralin is hydrolytically stable in sterile aqueous buffers between pH 3 and pH 9 at temperatures up to 52 °C. Since < 10% degradation of trifluralin was observed at 50 °C, this is equivalent to an environmental half-life of > 1 year. Therefore, hydrolysis is not expected to be a significant route of dissipation of trifluralin in the environment. (quoted from OSPAR, 2005).

#### Photodegradation in air

The photochemical oxidative degradation half-life of trifluralin in air is rapid (5.3 hours or 0.22 days) using equations of Atkinson and Howard. (quoted from OSPAR, 2005).

#### Photodegradation in water

Trifluralin is rapidly photodegraded in sterile aqueous buffer at pH 7 under artificial sunlight at 25 °C with an estimated first-order $DT_{50}$ of 7 hours. Two significant photolysis products are formed, i.e. TR-6 (up to 50% AR) by the oxidative dealkylation of both N-propyl groups and reduction of one of the nitro groups, and TR-15 (up to 32% AR) by cyclisation to form the benzimidazole and dealkylation of the remaining N-propyl group. Trifluralin rapidly photodegrades in natural water with an estimated $DT_{50}$ value of 1.1 hours. This is likely due to biotic activity and photosensitising compounds found in natural water systems. It should be noted that rapid photolysis in both experiments was seen under conditions that would be expected to facilitate aqueous photolysis, i.e. non-turbid, shallow water with no sediment (quoted from OSPAR, 2005).

#### Photodegradation in soil

Trifluralin degrades with a reported half-life of 41 days when exposed to a light source on sandy loam soil. The half-life of dark control samples of trifluralin was reported to be 66 days. Two degradation products, 2,6-dinitro-N-propyl-4 -trifluoromethylbenzenamine and 2-ethyl-7-nitro-5-trifluoromethylbenzimidazole-3-oxide were identified in the light-exposed samples. (quoted from US EPA, 1996).

### Aerobic biodegradation in water and sediment

Ready biodegradability of trifluralin has been investigated with a Modified Sturm Test. The results show that trifluralin is "not readily biodegradable" under the conditions of this test (GLP study). (quoted from OSPAR, 2005)

A water/sediment study according to the BBA guideline IV 5-1 was conducted under GLP (1993) with two sediments (clayey sand and loamy clay) and associated water samples from the same river for 60 days. Half-life in water for trifluralin was determined in the water/sediment system to be 1-2 days. Half-life in sediment was calculated to be 7-15 days and 6-15 days in the total system. An older study arrived at slightly longer $DT_{50}$ values. Mineralisation of trifluralin is insignificant (< 1% of the total radioactivity, AR). A significant amount of trifluralin remained in the sediment. Furthermore, up to 77% AR was not extractable (bound residues). Potential metabolites are shown in Annex 1. (quoted from OSPAR, 2005).

### Degradation and dissipitation in soil

Trifluralin (incorporated) was steadily degraded in soil under aerobic conditions according to first-order kinetics (non-GLP test according to EPA Subdiv. N 162-1, 1982). The DT50(lab) ranged from 81-179 days (mean 181 days; 22 °C), with faster degradation being seen in the low organic carbon soils. No major metabolites are formed. Non-extractable residue levels increased to 33-54% AR by 364 days and were mostly associated with the humin fraction in the majority of the soils. Some trifluralin volatilisation occurred from soil, but this was < 10% AR over the study period, due to the fact that the substance was mixed into the soil.

An older study (1976; non-GLP; according to BBA Merkblatt No. 37) investigated two Speyer soils under laboratory conditions at 22 °C. DT50 values were 136-356 days. The effect of temperature on the aerobic degradation rate of trifluralin has not been investigated experimentally. However, an estimation of the likely degradation rates at 10°C can be made from the data available at 20 °C (22 °C in reality) using a Q10 factor of 2,2 (cf. FOCUS 2000).

European and US field studies showed that trifluralin dissipates slowly in soil, with DT50(field) and DT90(field) values for the EC formulation ranging from 35-375 days (mean 164 days) and 116-1246 days (mean 544 days), respectively. Trifluralin was incorporated into the soil in these field trials too. Slower degradation in colder climates is supported by comparing dissipation data between the European and US trials, where temperatures in the European trials were generally lower than in the US, and where dissipation was slower.

In trials on the influence of tillage and other crop management measures (e.g. straw incorporation, fertilisation; non-GLP, non-guideline studies) on the dissipation of trifluralin in soil the following statements were made with respect to volatilisation of trifluralin from soil. DT50(field) values were calculated to be between 300 and 350 days at both sites following the initial soil incorporated application. DT50(field) values were estimated to be lower (< 150 days) following the subsequent pre-emergent applications, without incorporation. The more rapid loss of trifluralin from these subsequent applications was considered to be due to increased losses by volatilisation from the soil surface when trifluralin is not incorporated. Dissipation of trifluralin was increased after incorporation of straw in both field and laboratory tests. The laboratory tests showed that volatilisation is reduced following incorporation of straw, although overall dissipation is increased. The reduced volatilisation is considered to be due to adsorption to the organic material. (Quoted from OSPAR, 2005).

Taking all available results from laboratory and field studies into account, it can be concluded that trifluralin is persistent in soil.

### Anaerobic biodegradation

Degradation of trifluralin under anaerobic conditions (non-GLP test according to EPA Subdiv. N 162-2, 1982) is more extensive than under aerobic conditions (32-58% AR after 60 days). One major metabolite, TR-4, up to 13.2% AR was formed in two out of the three tested soils but this metabolite was shown to degrade in one of the soils by the end of the study. The metabolites that could be attributed to anaerobic conditions were TR-4, TR-7, TR-14 and TR-16 (see Annex 1). These were formed by sequential reduction of the nitro groups on the parent molecule (TR-4 and TR-7) or by oxidative dealkylation of the N-propyl group on an aerobic metabolite (TR-13) followed by reduction of the nitro group (TR-14). Under anaerobic conditions the levels of evolved volatile components were less significant than under aerobic conditions. However, the levels of non-extractable radioactivity were higher (35-60% AR). Depending on the soil used in the experiment, anaerobic $DT_{50}$ was determined to be 23 to 54 days ($DT_{90}$ 77- 181 days; 22 °C) (quoted from OSPAR, 2005).

### Volatility

Volatility may be a major route of dissipation for trifluralin above the soil surface. Trifluralin evaporates when applied to the surface of soil with an amount of 41-68% of the applied radioactivity volatilized after 24 h. However, volatilisation is minimal (< 2% AR) when trifluralin is incorporated into the soil after application. In addition, the calculated photochemical oxidative degradation half-life of trifluralin in air is rapid (0.22 days). It is critical that the substance is incorporated into the soil shortly after application since otherwise significant volatilisation to air occurs (quoted from OSPAR, 2005).

### Conclusion for persistence

Half-life in water for trifluralin was determined in the water/sediment system to be 1-2 days. Half-life in sediment was calculated to be 7-15 days and 6-15 days in the total system. When applied to the water phase, most of the substance can volatilise from the system (53-77% AR). The short half-life in water does not represent a rapid degradation of trifluralin but rather a transfer to other environmental compartments, mainly sediment. Considerable levels of metabolites (up to 30% at certain points of time, some of them stable) indicate degradation of trifluralin in sediment, especially under anaerobic conditions, besides the formation of bound residues. Regardless of the short half-life in water and the moderately short half-life in sediment, trifluralin should be considered persistent in the water/sediment systems due to the low degree of mineralisation and the formation of high amounts of bound residues.

Trifluralin is shown to be persistent in soil with determined half-lifes greater than six month. Fulfilment of the criterion for persistence (P-) is further supported by the identification as “not readily biodegradable”. It should be emphasized that the strong tendency of trifluralin to adsorb to soil, sediment and suspended matter significantly reduces toxicity risks in the water phase because trifluralin will hardly be present there. On the other hand, trifluralin stays present in the sediment and probably adsorbed to suspended matter. Desorption from sediment to water appears to be low. With a resuspension of sediment and with the further dispersion of suspended matter, it could possibly be carried into the marine environment although likelihood for this pathway is low.

### 2.2.2 Bioaccumulation

Studies reported in the published literature give calculated and measured bioconcentration factors in the range of 2,280 to 11,500 for different fish species (see table 2.1). From the studies available, the GLP study from 1996 is considered to provide the most reliable endpoint data for bioaccumulation in fish. In this study a 28-day flow-through study on bluegill sunfish *(Lepomis macrochirus)* was performed and an uptake first-order rate constant ($K_1$) of 828 mL/g/day led to a whole body bioconcentration factor (BCF) of 5674. Residues were primarily trifluralin plus small amounts of N-dealkylated metabolites, alcohol metabolites and conjugates of alcohol metabolites. On removal to clean water, depuration was rapid with an elimination first-order rate constant ($K_2$) of 0.15 day-1. Metabolites and their conjugates accounted for around 6-7% of total residues (EUTTF, 1996 as quoted from OSPAR, 2005).

Based on the available results trifluralin posess a high potential for bioaccumulation and thus implies a risk for bioconcentration in various organisms at lower levels of aquatic and terrestrial food chains, and for biomagnification at higher trophic levels.

**Table 2.1 BCF values for trifluralin.**

| Species | Test duration | Exposure concentration µg/L | BCF (whole fish) | Reference[1] |
|---|---|---|---|---|
| *Lepomins macrochirus* | 28 d uptake | 2 | 5674 | EUTTF (2002) |
| *Lepomins macrochirus* | 35 d uptake | 8 | 1580 | EUTTF (2002) |
| *Pimephales promelas* | 35 d uptake | 0,3 | 8870 | EUTTF (2002) |

**Conclusion for bioaccumulation**

With measured weight-based BCF values greater than 5,000 fulfils the criterion for bioaccumulation.

### 2.2.3 Potential for Long-Range Environmental Transport

A new generation of POPs including trifluralin has been measured in Arctic air, seawater, and freshwater sediments (Canadian Arctic Contaminants Program, 2006). Despite a relatively short atmospheric half-life of 21-74 minutes, trifluralin was observed in air at three Arctic monitoring stations, Tagish, Alert and Dunai at concentrations up to 2.92; 0.64 and 0.13 pg/$m^3$, respectively. The half-life calculations are based solely on photochemical degradation and indicate that trifluralin should not reach the Arctic at measurable quantities even though relatively large amounts (>5 x $10^6$ kg) are applied annually to crops in western Canada and the USA. Current results indicate that other pathways such as transport on dry particulate or aerosol might be the primary mode of transport for trifluralin.

Trifluralin has a high potential for volatilization but is rapidly photolysed in air. Under aqueous photolysis the formation of the metabolites TR-6 (α,α,α-triflouro-5-nitrotoluene-3,4-diamine 3-nitro-5-(triflouromethyl)-1,2-benzenediamine) and TR-15 (2-ethyl-7-nitro-5-(triflouromethyl) benzimidazole have been demonstrated (EU DAR, 2005). The metabolites formed by photolysis in air should be identified in order to address the risk of long range transport of potential stable metabolites. Potential metabolites are shown in Annex 1.

Furthermore, the assessment of the potential for long-range transport of trifluralin can be based on physical properties. For this - apart from persistence - the vapour pressure and the Henry's Law Constant are considered to be the most relevant properties. As a rule of thumb, substances

with vapour pressures > 1.33 x $10^{-2}$ Pa will be entirely in the vapour phase and substances with vapour pressures < 1.0 x $10^{-4}$ Pa will be particulate (US ATSDR, 2004).

As a measure of values of these properties that would qualify for long-range atmospheric transport, the currently listed POPs are used. For already listed POPs, information was sought on the UNEP-POPs homepage[7].

Based on a comparison of trifluralin with already listed POPs (aldrin, heptachlor, dieldrin, endrin, chlordane, DDT, toxaphene and hexachlorobenzene), it is indicated that trifluralin with respect to solubility in water, vapour pressure and Heny's Law Constant are in the middle range of the listed POPs (see Table 2.2). The comparison indicates that atmospheric degradation of trifluralin is among the fastest.

**Table 2.2 Atmospheric oxidation half-life, water solubility, vapour pressure and log $K_{ow}$ for currently listed POPs and trifluralin**

| Substance | Atmospheric oxidation half-life (hours) (EPIWIN) | Water solubility (µg/L) | Vapour pressure (Pa) | Henry's Law Constant | Log $K_{OW}$ |
|---|---|---|---|---|---|
| **Aldrin** | 2.0 | 17-180 | 3.1 10-3 | 6,59E-02 | 5.2-7.4 |
| **Chlordane** | 25.5 | 56 | 1.3 10-4 | 6,38E-03 | 6.0 |
| **DDT** | 37.4 | 1.2-5.5 | 2.5 10-5 | 1,71E-03 | 4.9-6.9 |
| **Dieldrin** | 13.9 | 140 | 2.4 10-5 | 7,71E-03 | 3.6-6.2 |
| **Endrin** | 13.9 | 220-260 | 2.4 10-5 | 6,64E-05 | 3.2-5.3 |
| **Heptachlor** | 2.1 | 180 | 4.0 10-2 | 3,06E-01 | 4.4-5.5 |
| **Hexachlorobenzene** | 15,192 | 40 | 1.5 10-3 | 9,44E-01 | 3.0-6.4 |
| **Toxaphene** | 56.9 | 550 | 4.0 101 | 8,37E+00 | 3.2-5.5 |
| **Trifluralin** | 5.3-10.3 | 195-221 | 6.1 10-3 – 9.5 10-3 | 4,15E-03 | 5,27 |

A large number of numerical models, covering a wide range of complexity, have been developed for predicting how chemicals are transported, distributed and degraded in the various compartments of the environment. For evaluation of the potential long-range transport of trifluralin, a fugacity model, the EQC model[8] has been used. The EQC model facilitates a chemical-to-chemical comparison in a standard environment.

Model estimates for half-lifes and distribution of currently listed POPs and trifluralin in air, water, soil, sediment and persistence for the whole environment are presented in Tables 2.3 and 2.4, respectively.

**Table 2.3. Model estimates for half-lifes of currently listed POPs and trifluralin in air, water, soil, sediment and persistence for the whole environment**

| | Aldrin | Chlordane | DDT | Dieldrin | Endrin | Hexachlo- | Heptachlor | Toxaphene | Trifluralin |
|---|---|---|---|---|---|---|---|---|---|

[7] www. KIM??
[8] http://www.trentu.ca/academic/aminss/envmodel/models/EQC2.html

| | | | | | | robenzene | | | |
|---|---|---|---|---|---|---|---|---|---|
| Air | 1.0 | 50.6 | 74.7 | 27.8 | 27.8 | 951.0 | 1.0 | 114.0 | 10.7 |
| Water | 4320 | 4320 | 4320 | 4320 | 4320 | 4320 | 4320 | 4320 | 4320 |
| Soil | 8640 | 8640 | 8640 | 8640 | 8640 | 8640 | 8640 | 8640 | 8640 |
| Sediment | 38900 | 38900 | 38900 | 38900 | 38900 | 38900 | 38900 | 38900 | 38900 |
| Persistence | 9690 | 9150 | 10600 | 6150 | 6150 | 7210 | 7950 | 8300 | 5850 |

**Table 2.4. Model estimates for distribution (%) of currently listed POPs and trifluralin in air, water, soil, sediment and persistence for the whole environment**

| | Aldrin | Chlordane | DDT | Dieldrin | Endrin | Hexa-chloroben-zene | Heptachlor | Toxaphene | Trifluralin |
|---|---|---|---|---|---|---|---|---|---|
| Air | 0.00517 | 0.16 | 0.154 | 0.158 | 0.158 | 0.524 | 0.00758 | 0.237 | 0.0985 |
| Water | 1.03 | 1.26 | 0.868 | 3.61 | 3.61 | 1.34 | 1.28 | 2.01 | 2.63 |
| Soil | 42.9 | 45.7 | 40.4 | 69.2 | 69.2 | 70 | 52.1 | 51.9 | 70.9 |
| Sediment | 56 | 52.9 | 58.6 | 27 | 27 | 28.1 | 46.6 | 45.8 | 26.4 |

The above estimates indicate a significant persistence of trifluralin in water, soil and sediment, a persistence which is in the same range as those of the currently listed POPs. The half-life of trifluralin in air is 10.7 hours. An atmospheric half-life greater than 48 hours is a common criterion, either for long-range transport as such or for persistence. This numerical value is included in the following treaties and regulations: UNECE-LRTAP POPs Protocol, UNEP POPs Convention, NACEC-SMOC and Canada-TSMP (Franklin, 2006). As seen from the table, POP substances as aldrin, and heptachlor also possess an estimated half-life in air of less than 48 hours.

All in all the model estimation shows that trifluralin distributes and persists in the environment in same degree as already listed POPs.

### Conclusion for long-range transport

In summary, the above discussion shows that the available data on trifluralin are conflicting when it comes to long-range atmospheric transport in gaseous form. Whilst estimates based on the half-life of trifluralin might suggest a limited capacity for long-range transport, monitoring data show that transport does in fact take place as trifluralin was observed in air at three Arctic monitoring stations. Current results thus indicate that pathways such as transport on dry particulate or aerosol might be the primary mode of transport for trifluralin. Furthermore, transport of sediment particles in ocean currents as well as biotic transport could also contribute to long-range environmental transport of trifluralin.

Due to lack of monitoring data in biota, the assessment of the potential for long-range transport of trifluralin is also based on comparisons of the physical chemical properties of trifluralin with other recognised POPs. When the reliable values for water solubility and vapour pressure are used, the values given for trifluralin are comparable to other documented POP substances. Model estimation shows that trifluralin distributes and persists in the environment in the same degree as already listed POPs.

## 2.3 Exposure

### 2.3.1 Environmental concentrations

The available information regarding environmental concentrations of trifluralin is very limited.

In 1987, trifluralin was detected in several municipal water supplies in Saskatchewan at trace (nanogram per litre) levels. It was not detected in drinking-water supplies of 77 municipalities in Manitoba or Alberta (detection limits 0.05 to 0.5 mg/L). Trifluralin was detected in one of 91 wells at 41 mg/L in a 1984-survey in southern Ontario. Trifluralin has occasionally been detected at trace levels (below 1 mg/L) in surface waters in Manitoba. Trifluralin was not detected (detection limit 0.1 mg/L) in an eight-week sampling of irrigation water in southern Saskatchewan. Based on a concentration of 0.05 mg/L (or half the usual detection limit of 0.1 mg/L), the estimated median Canadian exposure is 0.08 mg/d, or $1 \times 10^{-6}$ mg/kg bw per day from drinking water. In Canada, trifluralin was not detected in a national survey of 120 foods (detection limit 4 ppb). In USA, trifluralin was not detected in over 27,000 food samples covering 27 crops (detection limit 10 ppb). The theoretical maximum dietary intake of trifluralin is estimated to be 0.0271 mg/d, or 0.00039 mg/kg bw per day for an adult, based on the assumption that the maximum permitted residues of 0.1 mg/kg are present in all wheat, peas, beans, tomatoes and turnips consumed. Actual residues and intakes are expected to be much lower than this estimate (quoted from Trifluralin. 1989[9]).

In the USA, trifluralin was found in 172 of 2047 surface water samples and in one of 507 groundwater samples analysed. The 85$^{th}$ percentile of the levels in all non-zero surface water samples was 0.54 μg/L. It was not found in 229 drinking-water supplies (mainly groundwater) analysed in Italy (quoted from WHO, 2003).

### 2.3.2 Human exposure

Exposure of workers, bystanders and consumers to trifluralin can be anticipated during production, application and as a result of residues in food crops (EFSA, 2005, EU DAR, 2005) although the Section 2.3.1 indicates that residues in food are extremely low. Information from residue trials in Northern European cereals indicates that chronic dietary exposure of consumers to trifluralin is very low, representing less than 2% of the Acceptable Daily Intake (ADI) of 0.015 mg/kg bw for adults and less than 4% for children and infants (EFSA, 2005, EU DAR, 2005). There is no evidence of bioaccumulation of trifluralin and it does not appear to have been detected in human adipose tissue, breast milk or in blood samples from the general population. There are very limited reports of poisoning cases or excessive occupational exposure. A recent study reported trifluralin residues on the hands of both occupationally exposed and non-occupationally exposed individuals (Bouvier *et al*., 2006).

[9]http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/water-eau/doc-sup-appui/trifluralin/trifluralin_e.pdf

## 2.4 Hazard assessment for endpoints of concern

### 2.4.1 Toxicity

#### Toxicokinetics in experimental animals and in man

Trifluralin is reported to be well absorbed in the rat, the only species for which robust data are available, following oral administration (EFSA, 2005, EU DAR, 2005). Over 80% of a dose of 1 mg/kg was absorbed within 48 hours of dosing and 72% of a dose of 40 mg/kg, as demonstrated in bile-cannulated rats (Pottenger *et al.,* 1995 as reported in EU DAR, 2005). The limited data available for other species indicate similar bioavailability. Trifluralin has been reported to be more extensively absorbed following oral than dermal administration (EU DAR, 2005). Following absorption, it is widely distributed in the body, with highest concentrations being found in fat, kidneys, liver, adrenals, skin and blood, followed by rapid excretion. Trifluralin is extensively metabolised in the rat via nitroreduction, N-dealkylation, hydroxylation, cyclisation reactions and direct conjugation. The latter appears to be the major metabolic route with conjugates (predominantly N-acetyl and glucuronide conjugates) representing approx. 75% of all urinary metabolites. Approx. 10% of the total administered dose in rats is represented by unchanged trifluralin in the faeces. Available data indicate that the metabolic pathway in rats and dogs is virtually identical (EU DAR, 2005). Biliary excretion is predominant, with over 80% of an administered oral dose in rats being detected in the faeces and 20% in the urine. Bioaccumulation has not been reported, and the elimination half-life in the rat has been estimated to be 16-18 hours (EU DAR, 2005). Residual radioactivity in the carcass accounted for 1.54–1.89% of the administered dose 168 hours after single low or high doses of trifluralin (Pottenger *et al.,* 1995 as reported in EU DAR, 2005). An elimination half-life of 65 hours has been reported in monkeys given a single dose of 2 mg/kg intravenously (Pottenger *et al.,* 1995 as reported in EU DAR, 2005). No robust data on the toxicokinetics of trifluralin in humans have been reported (EU DAR, 2005).

#### Toxicity of trifluralin in animal studies

The acute toxicity of trifluralin is low (EFSA, 2005, EU DAR, 2005, OSPAR, 2005) following oral, dermal and inhalation administration in experimental animal studies. The oral $LD_{50}$ is >5,000 mg/kg bw for rats and >2000 mg/kg bw for mice, rabbits and dogs, and the dermal $LD_{50}$ is >2,000 mg/kg bw in rats and rabbits. The four-hour $LC_{50}$ acute inhalation value has been determined to be >4.65 mg/L air. It is mildly irritant in skin and eye irritation studies and is a skin sensitiser. Trifluralin is also of relatively moderate toxicity in short to medium duration repeat dose toxicity studies in animals. In a 90-day study in rats decreased body weight gain (females), decreased packed cell volume, increased plasma alpha-1 globulin and albumin concentration and increased relative liver weight (males) were reported at a dose level of 50 mg/kg/day and above while, in another 90-day study, relative liver weight was increased, with a NOEL of 50 mg/kg/day. Repeat dose oral toxicity was greater in a study in dogs,, with decreases in a number of haematological parameters (leading to anaemia), increases in mean corpuscular volumes and blood cholesterol, increases in absolute and relative liver weight and abnormal stools. The NOAEL in this study was determined to be 2.4 mg/kg bw/day.

#### Genotoxicity

Trifluralin has provided largely negative results in a range of genotoxicity tests *in vitro*, including bacterial and mammalian mutagenicity assays, chromosome aberrations in Chinese Hamster

ovary cells or unscheduled DNA synthesis (EU DAR, 2005, OSPAR, 2005). However there was evidence of aneuploidy induction in an *in vitro* chromosome aberration study, positive effects in a Comet assay, and a weakly positive result was obtained in an initial *in vivo* micronucleus study (EU DAR, 2005). A more robust repeat micronucleus study showed no such effect, and overall trifluralin is not considered to have genotoxic properties.

### Long-term toxicity and carcinogenicity

In a 2-year chronic toxicity study in rats, decreased body weight gain and changes in some haematological and blood chemistry parameters were evident at a dose level of 128 mg/kg/day while an increased incidence of glomerulonephrosis accompanied by renal calculi was seen at 30 mg/kg/day and above. In a study in B6C3F1 mice administered trifluralin in the diet at a dose level of approx. 180 mg/kg bw/day and above, there was decreased body weight gain, decreases in some haematological parameters, increased liver weight and progressive glomerulonephrosis in the kidney. The NOEL in the mouse was 563 ppm in the diet, equivalent to approx. 40 mg/kg bw/day (EU DAR 2005, EFSA, 2005).

In a carcinogenicity study in B6C3F1 mice at dose levels of 563 ppm (40 mg/kg bw/day), 2,250 ppm (180 mg/kg bw/day) and 4,500 ppm (420 mg/kg bw/day) in the diet, trifluralin induced malignant liver tumours and benign lung tumours in females, and there was also a slight increase in malignant stomach tumours (EU DAR, 2005, EFSA, 2005, OSPAR, 2005). No evidence of carcinogenicity was seen in the males. This study had methodological deficiencies, and the material tested contained potentially carcinogenic impurities including N-nitroso-di-n-propylamine. No carcinogenic effect was seen in mice following administration of a purified trifluralin sample, representative of the current commercial material.

Trifluralin was also tested for carcinogenic potential in Fisher 344 rats at dose levels of 813, 3,250 and 6,500 ppm in the diet, equivalent to 30, 128 or 272 mg/kg/day in males and 37, 154 or 336 mg/kg/day in females. Hepatic adenomas were observed in males from the lowest dose level and and hepatocellular carcinomas from the middle dose level. Other carcinogenic effects included Leydig cell tumours, thyroid tumours and renal carcinoma in males and transitional cell carcinoma of the bladder in high dose females (EU DAR, 2005, EFSA, 2005, OSPAR, 2005). No NOAEL could be established in the study since liver adenomas were seen at the lowest dose tested (EU DAR, 2005, EFSA, 2005). In contrast, no evidence of carcinogenic potential was seen in a National Toxicology Programme (NTP) study where Osborne-Mendel rats were fed trifluralin in the diet up to a time-weighted average of 8000 ppm for two years (Thomas et al, 1978 as quoted in EU DAR, 2005) although the rapporteur for the EU draft risk assessment (EU DAR 2005) was not able to examine the complete test report for this and two other rat carcinogenicity studies, those of Worth et al, 1966 (as quoted in EU DAR, 2005) and thus could not reach a conclusion on their validity (EU DAR, 2005).

It has been concluded (EU DAR, 2005, EFSA, 2005) that trifluralin has carcinogenic potential in rats. The lack of genotoxic potential would suggest that the tumours seen have an underlying non- genotoxic mechanism, and it is likely that the urinary tract tumours can be attributed to the underlying renal toxicity seen in both the rat and the mouse. The mechanism of tumour formation in the other organs (liver, thyroid and testis) has not been identified, but may, in the case of thyroid and testis, have an underlying hormonal mechanism. However, based on weight of evidence, trifluralin is unlikely to pose a carcinogenic risk to humans. The International Agency for Research on Cancer has classified trifluralin as not classifiable as to its carcinogenicity in humans (IARC group 3) (IARC, 1999).

### Reproductive toxicity

An extensive database exists on the possible reproductive toxicity of trifluralin, including 1-, 2- and 3-generation studies in rats, a limited 1-generation study in dogs and a number of developmental toxicity studies in rats and rabbits. No direct effects on reproductive performance or fertility were observed, any effects seen were accompanied by maternal toxicity and were non-specific in nature. In a 2-generation rat reproduction study, a dose level of 40-54 mg/kg bw/day showed clear maternal toxicity, comprising reduced weight gain during pregnancy and blood changes indicative of anaemia, and effects on the offspring (reduced growth and survival during lactation). NOEL of 4.5–5.8 mg/kg bw/day was identified in this study, based on the effects seen in the foetus (EU DAR, 2005, EFSA, 2005, OSPAR 2005).

### Toxicity of trifluralin in humans

As indicated in Section 2.3.2, there are very limited reports of poisoning cases attributed to trifluralin or reports of excessive occupational exposure. Occupational health records for workers exposed to trifluralin and trifluralin-containing products indicate that irritant effects such as redness, rash, hives, vesicular change, bullae and pruritis are the most commonly reported health effects attributable to trifluralin. Epidemiological studies in exposed workers and in the general population have not indicated any relationship between increased cancer incidence rate, reproductive effects or asthma in populations with a known exposure to trifluralin (EU DAR, 2005, EFSA, 2005).

### Effects on endocrine systems

Trifluralin is one of 564 chemicals on the EU Working List of potential endocrine-disrupting substances under the EU Strategy for Endocrine Disrupters[10] although it has not been categorised as a high priority chemical. It has also been included on other lists of endocrine disrupting chemicals (PAN, 2001). However, the available toxicological studies in mammals, birds and fish indicate that effects in such studies are not specific to endocrine disruption and no adverse reproductive effects are seen below exposure levels that produce systemic toxicity in mammalian studies.

In a study involving administration of trifluralin to ewes at a dose level of 17.5 mg/kg given twice a week over a 43-day period during mid breeding season, statistical increases in cortisol, estradiol and insulin, and a decrease in LH were reported (Rawlings *et al*., 1998, as reported in OSPAR, 2005). The authors concluded, however, that a possible role of systemic toxicity in the induction of these effects could not be ruled out. Other studies reported negative results for estrogenic activity in an *in vitro* E-SCREEN assay with trifluralin. A recent study examining the effect of a range of endocrine disruptors on the lipopolysaccharide or bacterial lipopeptide activation of nuclear factor kappa Bs showed no effect of trifluralin in this system, while other known endocrine disruptors showed a positive response (Igarashi *et al*, 2006). The incidence of vertebral abnormalities in fish taken from trifluralin-treated environments was not significantly higher than those taken from non-treated environments and overall, it is concluded that there is no evidence to suggest that trifluralin exerts endocrine-modulating effects in the environment (OSPAR, 2005).

[10] http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm

### Conclusion on effects assessment and toxicity of trifluralin

Trifluralin is well absorbed via the oral route but is less readily absorbed via the dermal route and data on absorption via the inhalation route are lacking. Acute toxicity in animals is low and there are few reports of acute toxicity in humans. It is moderately toxic in short, medium and long duration, repeat dose toxicity studies in animals, producing changes in some haematological and blood chemistry parameters and renal damage at doses between 30-50 mg/kg bw/day. Largely negative results were obtained with trifluralin in a range of genotoxicity tests *in vitro* and *in vivo* and, overall trifluralin is not considered to have genotoxic properties. It has produced a range of tumours including renal and urinary tract tumours, liver, thyroid and testicular tumours in a carcinogenicity study in rats at doses of 30 mg/kg bw/day and above, although a similar carcinogenic potential was not seen in mice. Trifluralin does not have specific effects on reproductive performance or fertility and all in all it is concluded that there is no evidence to suggest that trifluralin exerts endocrine modulating effects in the environment

Table 2.5 summarises the outcomes of key toxicological studies on trifluralin, including the NOAEL/LOAEL derived in each study. The studies included in Table 2.5 have been selected on the basis of the importance of the endpoint investigated (e.g. reproductive toxicity, carcinogenicity, other key target organ toxicity), robustness of the reported studies (GLP status, conformity with current Test Guidelines, etc) and the dose level (NOAEL/LOAEL), at which effects were reported.

**Table 2.5 Summary of key toxicological studies on trifluralin.**

| Species | Study type | Effect | LOAEL/NOAEL (mg/kg bw/day) | Reference |
|---|---|---|---|---|
| Rat, CD | Oral 90-day feeding study | Decreased body weight gain (females), decreased packed cell volume, increased plasma alpha-1 globulin and albumin, increased relative liver weight (males) | LOAEL 50 mg/kg/day<br>NOAEL 5 mg/kg/day | Ashby & Finn, 1978 (as quoted in EU DAR, 2005) |
| Rat, Wistar | Oral 90-day feeding study | Increased relative liver weight | LOAEL 100 mg/kg/day<br>NOAEL 50mg/kg/day | Worth et al. 1977 (as quoted in EU DAR, 2005) |
| Dog, beagle | Oral 1-year, test substance administered by capsule | Small decreases in haematological parameters, increases in mean corpuscular volumes and blood cholesterol, increases in absolute and relative liver weight and abnormal stools. | LOAEL 40 mg/kg/day<br>NOAEL 2.4mg/kg/day | Adams et al. 1992 (as quoted in EU DAR, 2005) |
| Rat, Fischer 344 | 2-year oral feeding study | Decreased body weight gain and changes in haematological and blood chemistry parameters, increased incidence of glomerulonephrosis accompanied by renal calculi | LOAEL 30 mg/kg/day<br>NOAEL < 30 mg/kg/day | Emmerson, 1980a (as quoted in EU DAR, 2005) |

**Table 2.5. Summary of key toxicological studies on trifluralin (continued)**

| Species | Study type | Effect | LOAEL/NOAEL (mg/kg bw/day) | Reference |
|---|---|---|---|---|
| Mouse, B6C3F1 | 2-year oral feeding study | Decreased body weight gain, anaemia, increased liver weight and progressive glomerulonephrosis in the kidney. | LOAEL 180 mg/kg/day NOAEL 40 mg/kg/day | Emmerson, 1980b (as quoted in EU DAR, 2005) |
| Rat, Fischer 344 | 2-year oral feeding study | Renal carcinoma in males and transitional cell carcinoma of the bladder in high dose females. Hepatic adenomas in males from the lowest dose level and hepatocellular carcinomas from the middle dose level. Other carcinogenic effects included Leydig cell tumours, in the testis and thyroid tumours. | LOAEL 30 mg/kg/day NOAEL < 30 mg/kg/day | Emmerson, 1980a (as quoted in EU DAR, 2005) |
| Rat, CD | 2-generation reproduction study | Reduced body weight gain in parents, no effect on reproduction | NOAEL (parental) 15 mg/kg/day NOAEL (reproduction) 148 mg/kg/day | Hoyt, 1986 (as quoted in EU DAR, 2005) |
| Rat, CD | 2-generation reproduction study | Reduced maternal body weight gain, haematological changes, uterine atrophy and reduced ovarian weight. Decreased litter size, decreased live foetuses, preimplantation loss. | NOAEL (parental) 4.5–5.8 mg/kg/day NOAEL (reproduction) 40.7–52.8 mg/kg/day | Rubin et al, 1987 (as quoted in EU DAR, 2005) |
| Rat, CD | Developmental toxicity study | Reduced maternal body weight gain and food consumption, no effect on development | NOAEL (maternal) 225 mg/kg/day NOAEL (developmental) 475 mg/kg/day | Byrd, 1984 (as quoted in EU DAR, 2005) |
| Rat, CD | Developmental toxicity study | Maternal – adrenal enlargement and changes in the forestomach Foetal-decreased foetal weight and skeletal anomalies in the presence of maternal toxicity | NOAEL (maternal) 100 mg/kg/day NOAEL (developmental) 300 mg/kg/day | Borders & Salamon, 1985 (as quoted in EU DAR, 2005) |
| Rat, Harlan | Developmental toxicity study | No developmental toxicity | NOAEL (maternal) 2000 ppm NOAEL (developmental) 2000 ppm | Worth et al, 1977 (as quoted in EU DAR, 2005) |
| Sheep (female) | 43-week feeding study, trifluralin given twice weekly at 17.5 mg/kg | Statistical increases in cortisol, estradiol and insulin, and a decrease in LH were reported | LOAEL 17.5 mg/kg | Rawlings et al., 1998 |

### 2.4.2 Ecotoxicity

Most of the available test results for trifluralin are in the range of the water solubility of trifluralin (about 200 µg/L).

Trifluralin is shown to be very toxic to aquatic organisms (see Table 2.6). Although a herbicide, fish seem to be particularly sensitive to trifluralin. The lowest chronic endpoint is the 35-d NOEC of 0.3 µg/L and LOEC of 0.7 µg/L (measured concentration) for spinal cord deformation in the fathead minnow (*Pimephales promelas*) was derived from a study (1992), in which fish were constantly exposed to trifluralin under flow-through conditions (0.6-50 µg/L nominal) (EU DAR, 2005, EFSA, 2005, OSPAR, 2005).

The second lowest endpoint is the 2-generation NOEC of 1.3 µg/L on sheepshead minnow (*Cyprinodon variegatus*; 1978), based on a significant reduction in parental fecundity after 166 days exposure to measured trifluralin of 1.3-34.1 µg/L. This is not a significant difference to the endpoint of 1.14 µg/L (measured) after 48-day exposure to the early life-stages of rainbow trout (*Oncorhynchus mykiss*; 1990). Further information can be obtained from a non-standard laboratory study (1985) conducted with brown trout (*Salmo trutta*) on juvenile fish exposed for 24 hours to nominal trifluralin concentrations of 25-250 µg/L and subsequently held in clean water for up to one year. During this period the fish were periodically sampled, radiologically examined for vertebral lesions and analysed for trifluralin residues. Although no mortality occurred in any of the treatment groups during the exposure period, several fish were prostrate at the 100 and 250 µg/L exposure level and intramuscular haemorrhaging along the spinal column was evident. No adverse effects were observed in the control fish or those exposed to 25 µg/L. Based on these results, a NOEC for vertebral injury following acute exposure was considered to be 25 µg/L (quoted from OSPAR 2005).

Two sediment-dwelling organisms prowed to be less sensitive than fish. Comparably few tests with marine species have been reported, some of which are presented in Table 2.6. In these tests, the sensitivity of marine species is apparently comparable with the sensitivity of freshwater species of the same taxonomic group (quoted from OSPAR, 2005).

Considering the toxicity trigger of 0.01 mg/L (10 µg/L) for NOECs, the criterion for toxicity (T-) is fulfilled for trifluralin.

Several metabolites of trifluralin (see Annex 1) have attracted attention in soil, water and sediment dissipation tests. TR-4 was a major metabolite in one of the water/sediment systems (up to 27% AR) and also occurred with <10% in soil under anaerobic conditions. Low levels of TR-4 were observed at the respective end of the experiments, suggesting a further degradation of TR-4. The effects of TR-4 were tested on larvae of the midge *Chironomus riparius* sediment-water exposure system (NOEC 0.332 mg a.s./L nominal), earthworms (NOEC (14 d) 100 mg a.s./kg dry soil nominal) and soil microflora activity (< 25% deviation from control values after 29 days up to 2 mg a.s./kg dry soil). In relation to the corresponding PEC values for sediment and soil, toxicity values (PNEC) exceeded the trigger values by far, indicating that there is no unacceptable risk by this metabolite (quoted from OSPAR 2005).

TR-6 and TR-15 are major products of photolysis of trifluralin in aqueous sterile buffer. Acute ecotoxicity tests for TR-6 and TR-15 were performed with algae, daphnids and fish resulting in $EC_{50}$/$LC_{50}$ values of 1-5 mg/L. These two metabolites are thus much less toxic than the parent compound trifluralin. No information about the chronic toxicity of the metabolites towards aquatic organisms was found. Neither are ecotoxicity data available for TR-7 and TR-14. The risk from these metabolites is, however, considered to be low, based on their similarity to the previously tested metabolites. For example, TR-7 is structurally similar to TR-4 and TR-14 is structurally similar to TR-15. Since all three metabolites tested to date are less toxic than the par-

ent compound, trifluralin, and formed in smaller amounts, the risk from TR-7 and TR-14 is also likely to be low. Available toxicity values for metabolites are shown in Table 2.6.

**Table 2.6 Summary of key ecotoxicological studies on trifluralin (quoted from OSPAR 2005).**

| Taxonomic group and species | End point | Duration | Result mg/L | Reference |
|---|---|---|---|---|
| *Selenastrum capricornutum* | $EC_{50}$ Growth inhibition | 7 d (static) | 12.2 µg/L[a]<br>>5,560 µg/L (TR-6)<br>1,670 µg/L (TR-15) | EUTTF (2002) |
| *Lemna gibba* | $EC_{50}$ Growth inhibition | 14 (static) | 43.5 µg/L[a] | EUTTF (2002) |
| *Chironomus riparius* | NOEC Larval development | 28 d (static) | 250 µg/L (nominal) | EUTTF (2002) |
| *Daphnia magna* | $EC_{50}$ Mortality | 2 d (renewal) | 245 µg/L<br>3,520 µg/L (TR-6)<br>9,360 µg/L (TR-15) | EUTTF (2002) |
| *Daphnia magna* | NOEC Life cycle | 21 d (renewal) | > 50.7 µg/L | EUTTF (2002) |
| *Cancer magister* | NOEC Reproduction | 69 d | 15 µg/L | Frimmel et al. (2001) |
| *Lepomis macrochirus* | $LC_{50}$ Mortality | 4 d (flow through) | 89.2 µg/L | EUTTF (2002) |
| *Oncorhynchus mykiss* | $LC_{50}$ Mortality | 4 d (flow through) | 88.0 µg/L<br>1,000 µg/L (TR-6)<br>5,460 µg/L (TR-15) | EUTTF (2002) |
| *Salmo trutta* | NOEC Sublethal effects | 24h/365 d (static) | 25 µg/L (nominal conc) | EUTTF (2002) |
| *Cyprinodon variegatus* | NOEC Life cycle | 166 d (flow through) | 1.3 µg/L | EUTTF (2002) |
| *Oncorhynchus mykiss* | NOEC ELS | 48 d (flow through) | 1.14 µg/L | EUTTF (2002) |
| *Pimephales promelas* | NOEC Juvenile growth | 35 d (flow through) | 0.3 µg/L | EUTTF (2002) |

a) Test results in static test systems are based on measured initial concentrations because trifluralin was not detectable at the end of the tests.

### Conclusion

In relation to the aquatic toxicity of trifluralin, it has been shown that trifluralin is very toxic, especially towards fish. The lowest chronic endpoint is the 35-d NOEC of 0.3 µg/L and LOEC of 0.7 µg/L (measured concentrations). The effect measured was spinal cord deformation in the fathead minnow (*Pimephales promelas*). Other studies performed with fish have confirmed the high toxicity towards fish and considering the toxicity trigger of 0.01 mg/L (10 µg/L) for NOECs, the T-criterion is fulfilled for trifluralin.

TR-4 was shown to be the major metabolite in one of the water/sediment systems and is shown not to be toxic towards terrestrial and sediment-living organisms. TR-6 and TR-15 are the major products of photolysis of trifluralin, as previously described. In the acute ecotoxicity tests carried

out with TR-6 and TR-15, exposed algae, daphnids and fish showed $EC_{50}/LC_{50}$ values in the range of 1-5 mg/L. Information about the chronic toxicity of major metabolites for aquatic organisms is not available. All in all it must be concluded that most likely major degradation products from trifluralin most likely do not possess a critical acute toxicity towards terrestrial, sediment-living or aquatic organisms. Information about the chronic toxicity has not been found.

# 3 SYNTHESIS OF THE INFORMATION

Trifluralin is a synthetic fluorinated dinitroaniline herbicide which was first registered in 1963 and which is still produced and used widely.

According to available data, trifluralin is considered to be persistent in the environment. Trifluralin has a short half-life in water. Regardless of the short half-life in water and the moderately short half-life in sediment, trifluralin is considered persistent in the water/sediment systems due to the low degree of mineralisation and the formation of high amounts of bound residues. Trifluralin is persistent in soil and is shown to be "not readily biodegradable". Trifluralin rapidly photodegrades in air.

Volatility may be a major route of dissipation for trifluralin above the soil surface. Trifluralin is shown to evaporate when applied to the surface of soil (41-68% volatilisation).

With measured weight-based BCF values in the range 1,580-8,870, trifluralin is considered to have a high potential for bioaccumulation and biomagnification.

The acute toxicity of trifluralin in animals is low and there are few reports of acute toxicity in humans. It is moderately toxic in short, medium and long duration repeat dose toxicity studies in animals, producing changes in some haematological and blood chemistry parameters and renal damage. Trifluralin is not considered to have genotoxic properties. It has, however, produced a range of tumours including renal and urinary tract tumours, liver, thyroid and testicular tumours in rats although a similar carcinogenic potential was not seen in mice. Trifluralin does not have specific effects on reproductive performance or fertility and there is no convincing evidence to suggest that trifluralin exerts endocrine-modulating effects in the environment.

Trifluralin is very toxic to aquatic organisms, the most sensitive group being fish, for which chronic NOEC values as low as 0.3 µg/L are shown. Some of the major metabolites formed in water/sediment systems are shown not to be toxic to terrestrial and sediment-living organisms. The major products of photolysis of trifluralin are shown not to be of high acute toxicity towards aquatic organisms. The chronic toxicity of metabolites is not known.

Trifluralin is shown to be rapidly photodegraded in air and significant amounts of the parent compound trifluralin is thus not expected to be transported to distant locations of the marine environment via the air. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could contribute to long-range environmental transport of trifluralin. Trifluralin has been monitored in air at three arctic locations. Monitoring data in arctic biota are not available.

Due to lack of biotic monitoring data on trifluralin, the assessment of the potential for long-range transport of trifluralin is based on physical chemical properties as well as modelling. When the reliable values for water solubility and the vapour pressure are used, trifluralin is within the range of the currently listed POPs. Furthermore, model estimation shows that trifluralin distributes and persists in the environment to the same extent as currently listed POPs

Based on the available data, trifluralin should be considered as a POP, warranting global action. All in all, safe levels of exposure cannot be set for substances such as trifluralin, which are not only highly persistent and highly bioaccumulative but also chronically toxic towards aquatic organisms, because of the difficulties in assessing long-term effects of life-long exposure to even low concentrations.

Production and use of trifluralin continues and it is still extensively produced and used as a herbicide. When it is still used as pesticide, it will be directly released to the environment. Moreover, the high persistency of the substance has caused high contamination of soil and waters in the areas where it has been used and these contaminated sites can serve as a source of pollution for a long time.

# 4 CONCLUDING STATEMENT

It has been demonstrated that trifluralin is persistent in the environment. It has a high potential for bioaccumulation and biomagnification. There is monitoring data in arctic air that indicates long-range transport of the substance, but there are no monitoring data in biota from areas remote from sources. The physical and chemical properties as well as modelling of potential long range transport suggest that trifluralin can be transported over long distances bound to particles in air and water.

Trifluralin is associated with a range of harmful effects on primary aquatic organisms. The conclusion of the review of trifluralin under Directive 91/414/EEC is that registration of this substance cannot be continued. Due to its harmful properties and the potential risks posed by its production and use, global action is warranted.

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## *ANNEX 1: Metabolic pathways of trifluralin*

(Quoted from OSPAR, 2005).

**Metabolic Pathways of Trifluralin**

**Fig. 1: Proposed metabolic pathway of trifluralin in soil under aerobic conditions.**

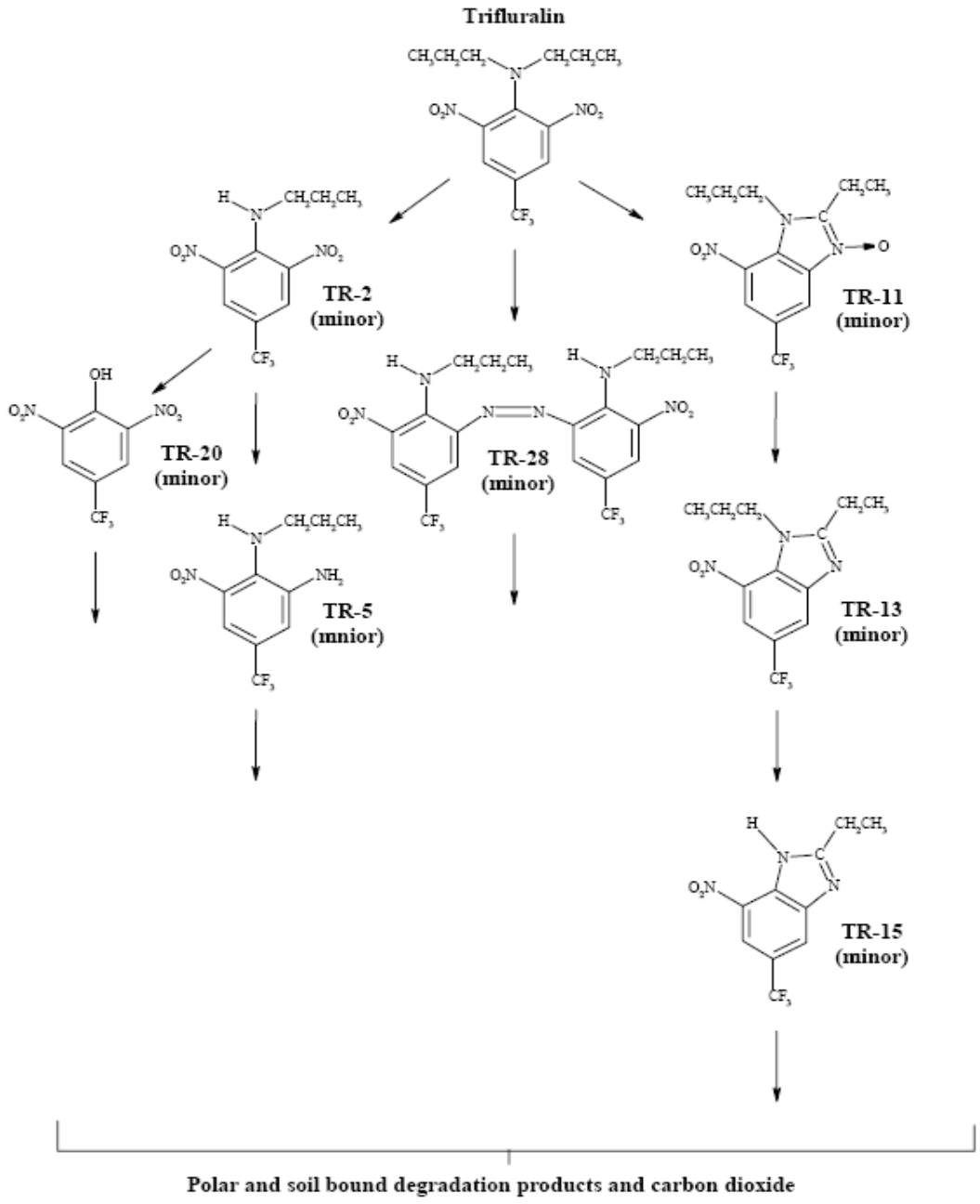


**Fig. 2:** **Proposed metabolic pathway of trifluralin in soil under anaerobic conditions.**

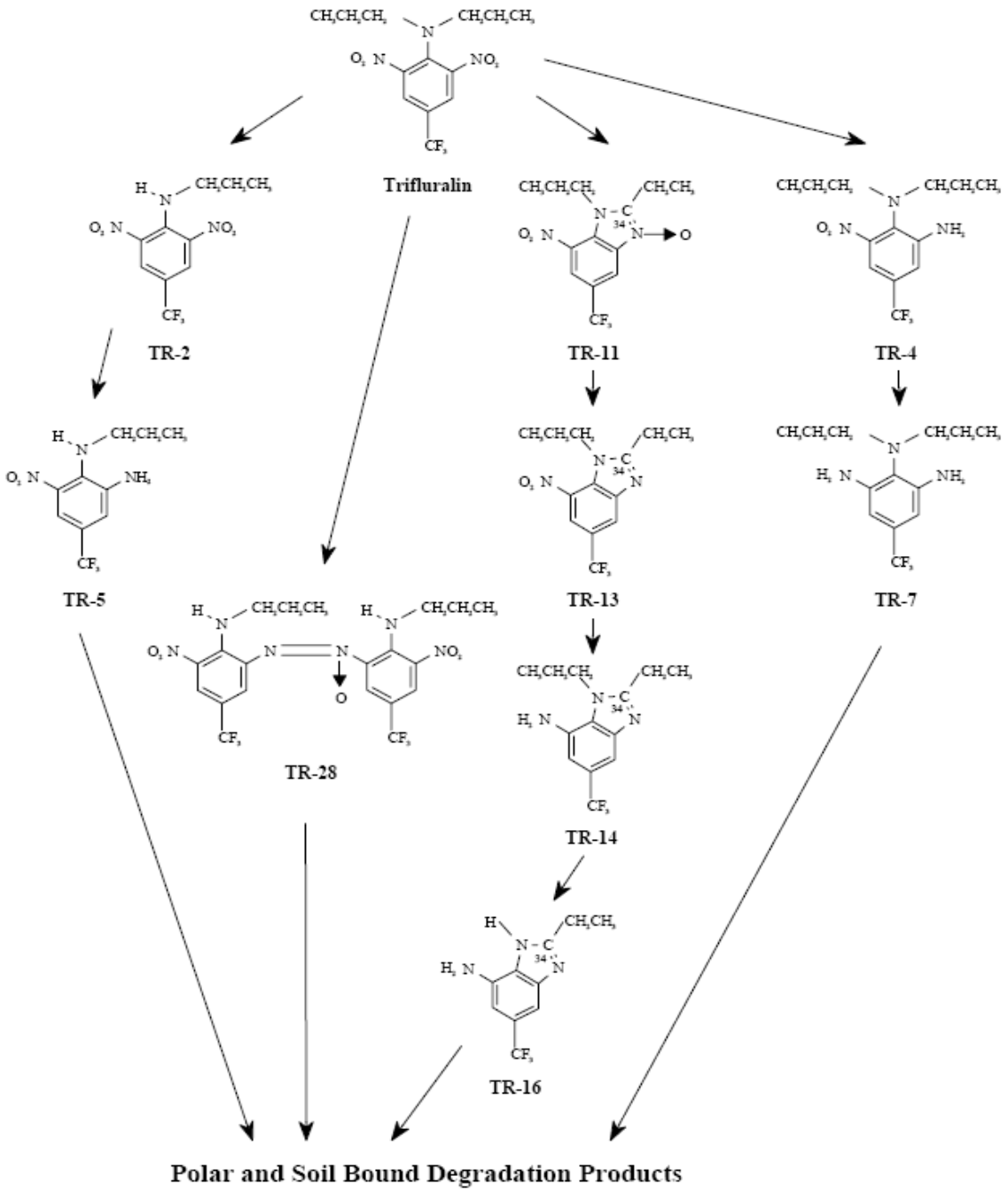


**Fig. 3:** **Proposed degradation pathway for the photolysis of trifluralin in aqueous sterile buffer solution.**

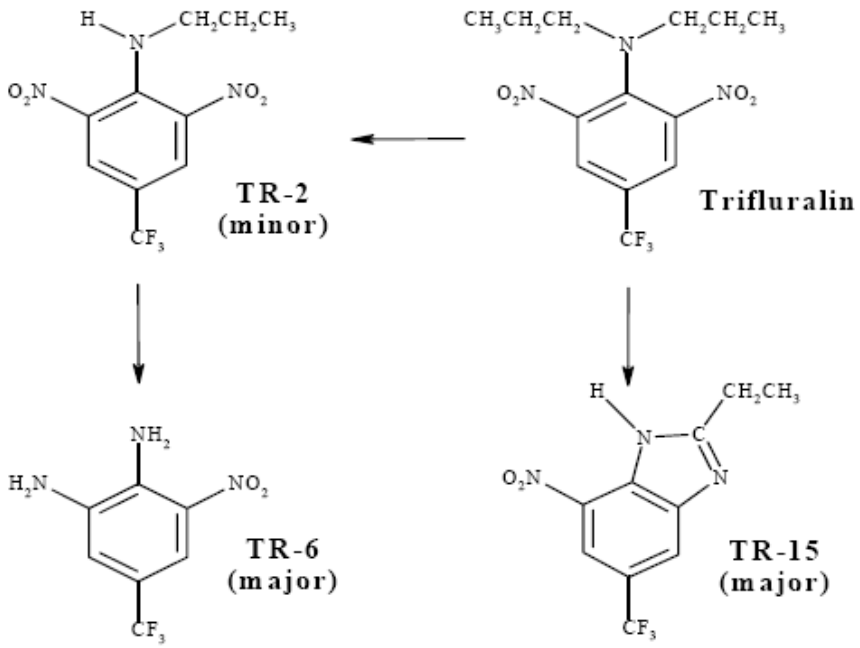
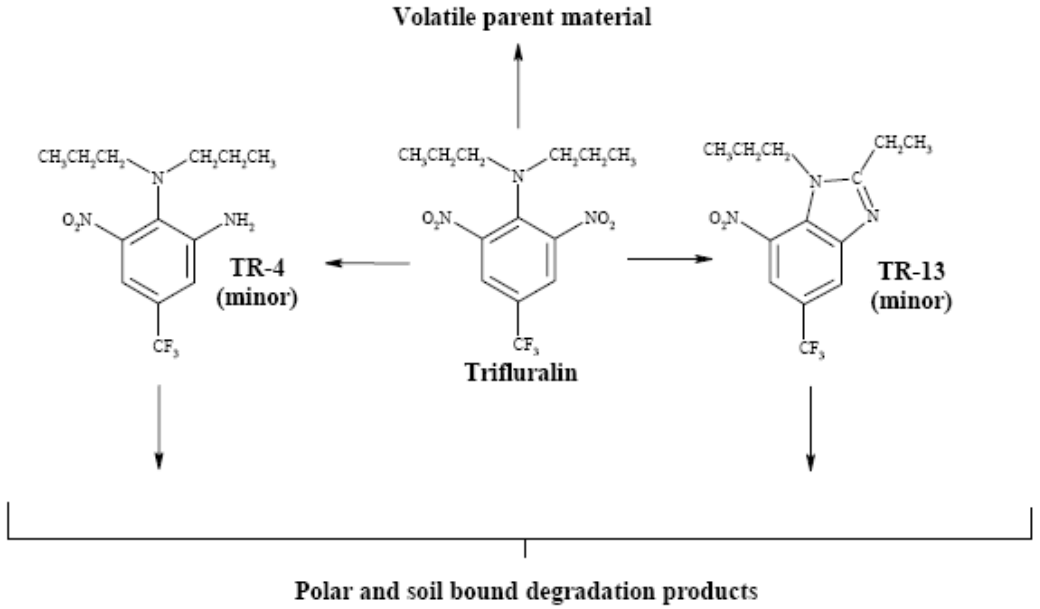



**Fig. 4:** **Proposed degradation pathway for trifluralin in a water/sediment system. A recent water/sediment-study (2004) indicated the occurrence of TR-7 (via TR-4) and TR-14 (via TR-13) as major metabolites in sediment.**




Note: The metabolite TR-4 is considered minor in the water phase and major in the sediment of the water/sediment system.