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Umweltbundesamt

o-ANISIDINE: RISK REDUCTION

Elaboration of a Risk Reduction Strategy under Existing Substances Regulation (EEC) No 793/93

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BE-211

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Information on the rapporteur:

Rapporteur according Article 9 – 11 Reg. (EEC) 793/93 responsible for o-anisidine is the Federal Ministry of Agriculture, Forestry, Environment and Water Management in consultation with the Federal Environment Agency.

This draft risk reduction strategy has been prepared by the Federal Environment Agency on behalf of the Federal Ministry of Agriculture, Forestry, Environment and Water Management.

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SUMMARY

o-Anisidine (CAS-No. 90-04-0; EINECS-No. 201-963-1) is a substance on the second priority list of Commission Regulation (EC) 2268/95. It is used as an intermediate for a number of azo and naphthol pigments and dyes.

At present the produced quantity is < 1000 t/y. More than 90 % of the produced o-anisidine are processed to pigments which are utilised mainly for the printing of packings (cardboards, polymer and aluminium foil). To a minor extent and with decreasing tendency it is also processed to dyes which are used for paper and textile dyeing (ca. 3 % and 7 % respectively).

o-Anisidine is classified as a Category 2 carcinogen, a Category 3 mutagen and as toxic by inhalation, in contact with skin and if swallowed. Exposure to o-anisidine at the workplace is possible during production and processing and during formulation and use of o-anisidine based pigments. The main possible exposure routes are inhalational and dermal. The general population may come into contact with the substance during the use of consumer products coloured with pigments or dyes based on o-anisidine.

The risk assessment of o-anisidine[1] has identified a need for limiting the risks for the following situations:

At the workplace there is a risk due to dermal contact with o-anisidine during the installation of gas compensation pipes in the processing of o-anisidine because of repeated dose toxicity and genotoxic and carcinogenic properties of the substance.

For consumers there is a risk due to dermal contact of the general population with textiles and due to oral exposure of young children suckling clothes coloured with o-anisidine based dyes because of repeated dose toxicity and genotoxic and carcinogenic properties of the substance.

To reduce the risk at the workplace it is proposed to reach an Industry Commitment under which the concerned companies would commit themselves to determine what could be as low as technically possible (ALATP) in terms of reduction of workplace exposure, and would in a second step implement possible further measures identified. The principles of prevention and reduction of exposure as outlined in the Carcinogens Directive, reaching as far as to the option of replacement, should form the basis of the evaluation.

As far as consumers are concerned the proposal for the 19th amendment of Directive 76/769/EEC relating to restrictions on the marketing and use of azocolourants is considered to effectively minimise the risk arising from the release of o-anisidine from dyed textiles and clothes. Implementation of this amendment should be speeded up as far as possible. The effectiveness of the measure would have to be ensured by adequate monitoring programmes.

1 BACKGROUND

1.1 Introduction

o-Anisidine (CAS-No. 90-04-0; EINECS-No. 201-963-1) is a substance on the second priority list of Commission Regulation (EC) 2268/95. A risk assessment with Austria as Rapporteur

[1] European Union Risk Assessment Report o-anisidine; European Communities, 2002. The report may be downloaded from the homepage of the European Chemicals Bureau: http://ecb.jrc.it/existing-chemicals/

was carried out in the framework of Council Regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances. The reasons to select o-anisidine as a priority substance were its carcinogenicity and other health endpoints of potential concern as judged by structural analogy to other aromatic amines. In addition, its use as an intermediate for azo dyes and pigments raised questions as to potential exposure of consumers from dyed products.

1.2 Production and use

o-Anisidine is produced from 2-methoxy-nitrobenzene by catalytic reduction with hydrogen under pressure in an inert liquid medium. At present the produced quantity is < 1000 t/y. About 99 % of this amount are handled captively by the German reporting producing and processing company. In lower amounts it is also imported by several companies into Germany and France. For 1995 the world o-anisidine production was estimated to be about 15000 t/y, out of which China alone produced about 7000 t/y.

In the EU o-anisidine is used as an intermediate for a number of azo and naphthol pigments and dyes. More than 90 % of the produced o-anisidine are processed to pigments which are utilised mainly for the printing of packings (cardboards, polymer and aluminium foil). To a minor extent and with decreasing tendency it is also processed to dyes which are used for paper and textile dyeing (ca. 3 % and 7 % respectively).

o-Anisidine is found as a residue in the corresponding pigments in measurements of the German manufacturer in concentrations between 10 and 50 mg/kg. Data on o-anisidine residues in dyes are not available. In addition, the substance can theoretically emerge from the corresponding pigments and dyes by reductive cleavage of the azo bond, by hydrolysis and/or metabolic degradation. These reactions are especially important for the dyes due to their significantly higher water solubility as compared to the pigments.

2 THE RISK ASSESSMENT

2.1 Overview

o-Anisidine may be released into the environment mainly during its production and processing. The hydrosphere is expected to be the main target compartment. The PEC/PNEC ratios for the sewage treatment plant (STP), surface water and the sediment based on the local releases of o-anisidine at the production and processing facilities of the largest European producer are all well below 1. According to the risk assessment for the environment there is at present no need for risk reduction measures beyond those which are being applied already.

In terms of human health hazards o-anisidine is classified as toxic by inhalation, in contact with skin and if swallowed due to its capacity to induce methemoglobin formation, as found in cats to a degree relevant for humans. In rats and mice, the repeated oral administration resulted in haemolytic anaemia and changes in enzyme parameters or organ weights (liver, kidney, and spleen). o-Anisidine was shown to be carcinogenic in rats and mice after oral exposure. Tumours of the urinary system occurred at high incidences, especially of the bladder, which is also the main target organ in humans for this substance class of aromatic amines. The mutagenic effects of o-anisidine have to be considered in combination with its carcinogenicity. There is sufficient evidence that o-anisidine is mutagenic *in vitro*, while the *in vivo* assays gave contradictory results. Based on all the evidence o-anisidine is considered a genotoxic carcinogen.

o-Anisidine has not been tested adequately for sensitising properties and no test is available on developmental toxicity. It was decided to evaluate a possible need for tests in the light of the outcome of the risk reduction strategy.

Exposure of humans to o-anisidine is possible at the workplace during production and processing, and during formulation and use of o-anisidine based pigments. The main possible exposure routes are inhalational and dermal. Measurements are available on workplace exposure by inhalation during the production of o-anisidine and its processing to pigments. The dermal exposure concentrations were estimated.

The general population may come into contact with the substance during the use of consumer products coloured with pigments or dyes based on o-anisidine. From the use pattern of the substance the contact with printed packings and foils and with dyed textiles can be identified as most important. The main exposure routes appear to be dermal (skin contact with printed packings and foils and dyed textiles) and oral (young children sucking at dyed textiles).

In the exposure assessment of o-anisidine based products, i.e. pigments and dyes, the following distinctions have to be made:

- exposure to o-anisidine residues in pigments and dyes (in measurements of the German manufacturer o-anisidine is found as a residue in the corresponding pigments in concentrations between 10 and 50 mg/kg)
- exposure to o-anisidine from the cleavage of the azo bonds of dyes; this reaction will not occur significantly in pigments as these are much less water soluble and thus less bioavailable.

With respect to the environment the main target compartment of o-anisidine is the hydrosphere. However, indirect exposure via the environment by the intake of drinking water is not expected in consideration of the use pattern and as concentrations of o-anisidine in drinking water are not reported.

The risk assessment of o-anisidine has identified a need for limiting the risks for the following situations:

(1) At the workplace:
Dermal contact with o-anisidine during the installation of gas compensation pipes in the processing of o-anisidine due to repeated dose toxicity and genotoxic and carcinogenic properties of the substance (see Table 1).

(2) General population:
Dermal contact with textiles coloured with o-anisidine based dyes due to repeated dose toxicity and genotoxic and carcinogenic properties of the substance.

Oral exposure of young children suckling clothes which are coloured with o-anisidine based dyes due to repeated dose toxicity and genotoxic and carcinogenic properties of the substance (see Table 2).

In addition to these specific situations, the risk assessment shows that residual risks cannot be excluded concerning all the populations and uses of the substance with relevant exposure, since o-anisidine is identified as a genotoxic carcinogen for which a threshold cannot be reliably identified. In particular this applies to the following situations:

- Workplace exposure by inhalation in the production and processing of o-anisidine

- Workplace exposure by inhalation and by dermal contact during the formulation of o-anisidine based printing inks.

- General population in dermal contact with packing materials printed with o-anisidine based pigments.

- Man exposed indirectly via the environment.

Following the provisions of the Technical Guidance Document for risk assessment conclusions iii apply to these scenarios due to the carcinogenic properties of the substance. However, risk reduction measures already in place are considered sufficient with respect to this hazard, which is expressed as **conclusion iiia** in the risk assessment report.

Thus, only scenarios and endpoints referred to under (1) and (2) above are considered in this risk reduction strategy.

Table 1: Overview of the conclusions on the relevant workplace exposure scenarios for all toxicological endpoints

Endpoint	Acute Toxicity[a]		Irritation/ Corrosion		Sensitization		Repeated Dose Toxicity[a]		Muta-genicity[b]	Carcino-genicity		Fertility	Develop-mental Toxicity
Exposure scenario/route	Inh.	Der.	Inh.	Der.	Inh.	Der.	Inh.	Der.	Inh. Der.	Inh.	Der.	Inh. Der.	Inh. Der.
Production													
- Reaction vessel, distillation and filtration unit	ii	ii	ii	ii	[-]	[-]	ii	ii	iiia	iiia	iiia	ii	[-]
Processing													
- Operating - Cleaning, inspection, sampling	ii	ii	ii	ii	[-]	[-]	ii	ii	iiia	iiia	iiia	ii	[-]
- Installation of gas compensation pipes	ii	ii	ii	ii	[-]	[-]	ii	**iii**	Inh.: iiia Der.: **iiib**	iiia	**iiib**	ii	[-]
Formulation of printing inks	ii	ii	ii	ii	[-]	[-]	ii	ii	iiia	iiia	iiia	ii	[-]
Printing	ii	ii	ii	ii	[-]	[-]	ii	ii	Inh.: ii Der.: iiia	ii	iiia	ii	[-]

[a] the oral uptake of o-anisidine is assumed to be prevented by personal hygiene measures;
[b] o-anisidine is considered a genotoxic carcinogen. Mutagenicity and carcinogenicity have to be evaluated together. For the development of risk reduction strategies the classification concerning carcinogenicity is relevant.
[-] not (adequately) tested.

Table 2: Overview of the conclusions for the relevant consumer exposure scenarios for all toxicological endpoints

Endpoint / Exposure scenario	Route of exposure	Acute Toxicity	Irritation / Corrosion	Sensitization	Repeated Dose Toxicity	Mutagenicity[a]	Carcinogenicity	Fertility	Develop-mental Toxicity
Skin contact with packings printed with pigments	Dermal	ii	ii	[-]	ii	iiia	iiia	ii	[-]
Young children sucking textiles coloured with dyes	Oral	ii	ii	not applicable	**iii**	**iiib**	**iiib**	ii	[-]
Skin contact with dyed textiles	Dermal	ii	ii	[-]	**iii**	**iiib**	**iiib**	ii	[-]

[a] o-Anisidine is considered a genotoxic carcinogen. Mutagenicity and carcinogenicity have to be evaluated together. For the development of risk reduction strategies the classification concerning the carcinogenicity is relevant.
[-] not (adequately) tested

2.2 Effects relevant for risk reduction

2.2.1 Repeated dose toxicity

Data on effects in humans after repeated exposure are not available. In rats and mice, the repeated oral administration resulted in haemolytic anaemia and changes in enzyme parameters or organ weights (liver, kidney, spleen). From a valid oral subacute study with rats a NO(A)EL of 16 mg/(kg bw x d) was derived. This value was used for calculating the Margin of Safety. From a subchronic and a chronic oral study, where higher doses of o-anisidine were given, a NOEL cannot be derived. However, these studies show that the toxicity of o-anisidine does not increase significantly with duration of exposure. An acute i.v. study with cats (methaemoglobin formation at a single dose of 7.7 mg o-anisidine/kg bw) was not used as much higher plasma peak levels can be expected than after physiological routes of exposure.

No inhalation and dermal studies with repeated application are available for o-anisidine. In the risk assessment for non-carcinogenic effects for these routes of exposure a route to route extrapolation from the oral subacute study was performed.

2.2.2 Carcinogenicity

Data on carcinogenic effects in humans are not available. o-Anisidine (tested as hydrochloride) was carcinogenic in rats and mice, rats being more susceptible. It can be assumed that the carcinogenic effect of o-anisidine hydrochloride after oral administration is due to o-anisidine itself. In rats as well as in mice, tumours of the urinary system, especially of the bladder, occurred at high incidences. In addition, an increased incidence of tumours in the thyroid was observed in male rats. The bladder is also the main target organ in humans for this substance class of aromatic amines.

For continuous life time exposure, the T25 value for o-anisidine hydrochloride for rats was calculated to be 51.6 mg/(kg bw x d) (Dybing et al., 1997[2]). Multiplying this value with a correction factor for the molecular weight of o-anisidine (0.77), a T25 value of 39.7 mg/(kg bw x d) was obtained.

The International Agency for Research on Cancer (IARC, 1999[3]) and the German MAK Committee (DFG, 1996[4]) have rated o-anisidine as carcinogenic. In the European Union (Annex I of Directive 67/548/EEC[5]), it is classified as a Category 2 carcinogen.

[2] Dybing E, Sanner T, Roelfzelma H, Kroese D, Tennnant RW. T25: A simplified carcinogenic potency index: Description of the system and study of correlations between carcinogenic potency and species/site specificity and mutagenicity. Pharmacol Toxicol 1997; **80**: 272-279.

[3] IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans 1999; **73**: 49-58

[4] DFG. MAK- und BAT-Werte-Liste 1996. Verlag Chemie 1996, Weinheim.

[5] as amended by Commission Directive 2000/32/EC of 19 May 2000 adapting to technical progress for the 26th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.

2.3 Workplace

2.3.1 Dermal exposure during processing (subscenario "installation of gas compensation pipes")

According to industry (reporting company) the process of installation of gas compensation pipes for filling and emptying of tank wagons takes place at three different sites about 40 times per year at each site. The procedure itself takes between 5 (filling) and 15 (emptying) minutes. Workers are wearing protective gloves and breathing masks and receive special training twice per year, special operating instructions are available.

The following workplace concentrations (TWA values) were measured from air sampling during processing of o-anisidine:

0.05 – 0.15 mg/m^3 (long term)
0.05 – 0.09 mg/m^3 (short term)

For risk assessment on dermal exposure calculations with the EASE model were carried out. They showed that a dermal exposure to the substance during processing in general appears to be so low that it is not quantified. Only for the installation of gas compensation pipes a maximum dermal exposure concentration of 0.1 mg/cm^2 x d (0,6 mg/kg bw x d) was estimated (worst case assumptions: direct handling of the substance, incidental contact, non-dispersive operation). However, as stated in the risk assessment, the use of PPE is expected to substantially reduce contamination of the skin.

For dermal exposure a NAEL of 4 mg/kg bw for **repeated dose toxicity** was derived assuming 100 % dermal absorption and applying a factor of 4 for metabolic rate scaling from rats to humans. The calculated Margin of Safety was ≥ 7. Considering further that observations in the rat do not adequately reflect the higher human sensitivity to methemoglobin forming agents, a tentative factor for species to species extrapolation of 10 yields a MOS of < 1 for the installation of gas compensation pipes which is insufficient for worker health protection, so that for this specific workplace situation risk reduction measures are necessary.

Data concerning **carcinogenic effects** after repeated dermal exposure are not available. Therefore, a calculated T25 value of 39.7 mg/kg bw from the oral study was the starting-point for the risk assessment with regard to carcinogenic effects. This value was used for route-to-route extrapolation. For dermal exposure a T25 of 28.2 mg/kg bw was obtained, assuming 100 % absorption, applying a factor of 4 for metabolic rate scaling from rats to humans and adjusting lifetime exposure to occupational exposure. The calculated MOE is about 47 for the installation of gas compensation pipes leading to conclusion iiib.

2.4 Consumers

2.4.1 Exposure to dyed textiles

In the EU, the amount of o-anisidine used in the manufacturing of textile dyes shows a low and even further decreasing tendency (see section 2). Nevertheless, a significant amount of textiles dyed with colorants on the basis of o-anisidine may be imported from non-EU countries such as India and China.

Textiles coloured with o-anisidine based dyes may contain free o-anisidine. In addition, reductive cleavage of the azo bond may occur after resorption to form free o-anisidine. Further, the substance may emerge during the use of dyed products due to hydrolytic degradation of the dyes which have a much higher water solubility and, therefore, bioavailability than

pigments. Measured data on residues of o-anisidine in dyed textiles or its emergence by reductive cleavage of the azo bond due to metabolisation or hydrolysation are not available.

An estimation of the exposure situation was carried out with data on the dermal and oral exposure to azodyes and aromatic amines which were assumed to be formed from the dyes by reductive cleavage of the azo bond due to the metabolic activity of the skin and the gastrointestinal tract, respectively (on behalf of the European Commission Directorate General III by LGC, 1997[6]).

2.4.1.1 Young children sucking dyed textiles

For young children, who may come in contact with o-anisidine while sucking at dyed clothes, a MOS in the range of 31 - 13333 was calculated for **repeated dose toxicity**. The lower MOS is insufficient for the protection of the health of children, if one considers possible higher sensitivity of young children, frequent exposure and species differences (respective safety factors lead to MOS of 0,5 – 223). The risk characterisation for **carcinogenicity** based on a calculated T25 value of 9,9 mg/kg bw/d led to Margins of Exposure in the range of 76 – $3{,}3 \times 10^4$, which is insufficient for the protection of the health of children.

2.4.1.2 Dermal contact with dyed textiles

In the case of dermal contact of the general public with dyed textiles a MOS of 200 – 6.7×10^5 **for repeated dose toxicity** from a worst case approach is obtained, which may be insufficient for human health if one considers long term exposure and possible higher sensitivity of humans compared to rats (respective safety factors lead to MOS of 3,5 – $1{,}2 \times 10^4$). Margins of Exposure for **carcinogenicity** are in the range of 495 – $1{,}7 \times 10^6$, showing the necessity for risk reduction measures as well.

3 CURRENT RISK REDUCTION MEASURES

3.1 General

Classification and Labelling

The classification and labelling of o-anisidine was revised based on new information gathered during risk assessment and published in Commission Directive 2000/32/EC of 19 May 2000 adapting to technical progress for the 26th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances:

Carcinogen Category 2; R45	May cause cancer
Mutagen Category 3; R40	Possible risks of irreversible effects
T; R23/24/25	Also toxic by inhalation, in contact with skin and if swallowed

[6] LGC. Best estimate risk assessment calculations for dermal and oral exposure. LGC Ltd. 1997; Teddington/UK.

S-phrases:
S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
S53: Avoid exposure - obtain special instructions before use.

3.2 Workplace

3.2.1 EU legislation

For o-anisidine substance-specific regulations for the protection of the safety and health of workers do not yet exist at European level. However, as general regulations for occupational safety and health, in particular the following directives are of relevance:

- Framework Directive 89/391/EC on the introduction of measures to encourage improvements in the safety and health of workers at work
- Directive 89/656/EEC on the minimum health and safety requirements for the use by workers of personal protective equipment at the workplace (third individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC)
- Directive 90/394/EEC (last amended by Directive 1999/38/EC with the extension to mutagens) on the protection of workers from the risks related to exposure to carcinogens at work (sixth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC)
- Directive 92/85/EEC on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding (tenth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC)
- Directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work (Chemical Agents Directive; fourteenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC); will have to be implemented by 05 May 2001 by Member States and will replace Directive 80/1107/EEC on the protection of workers from the risks related to exposure to chemical, physical and biological agents at work.

Furthermore, Directive 91/155/EEC (last amended by Directive 93/112/EEC) defining and laying down the detailed arrangements for the system of specific information relating to dangerous preparations in implementation of Article 10 of Directive 88/379/EEC, requires that anyone placing on the market o-anisidine or preparations containing o-anisidine for which a labelling duty exists must provide a safety data sheet for the industrial user.

In regulating the Category 2 carcinogen o-anisidine at the workplace the Carcinogens Directive (90/394/EEC) plays a central and important role. It aims at the protection of workers from risks to their health and safety, including the prevention of such risks, arising or likely to arise from exposure to carcinogens at work.

Based on a determination and assessment of risks by the employer it provides a step-by-step approach for risk control: Replacement of the substance should be considered in the first place. Where it is neither technically possible to replace the carcinogen by a less dangerous substance nor to manufacture and use it in a closed system, the employer has to ensure that the level of exposure of workers is reduced to as low as is technically possible by the application of a series of measures.

These measures include the limitation of the quantities of a carcinogen at the place of work and keeping as low as possible the number of workers exposed or likely to be exposed, as

well as the design of appropriate work processes, engineering control measures, and methods for the evacuation of carcinogens at source.

Further requirements are the use of existing appropriate procedures for the measurement of carcinogens, the application of suitable working procedures and methods, the use of collective and/or – where exposure cannot be avoided by other means – individual protection measures, and the provision of information for workers.

Provisions are made for employers to ensure that workers receive sufficient information and appropriate training as well as for Member States who shall establish arrangements for carrying out relevant health surveillance of workers. Furthermore the possibility to set exposure limit values is laid down in the Directive.

3.2.2 National Occupational Exposure Limits (OEL)

An occupational exposure limit value for o-anisidine has not been specified at the European level. National limit values exist in 6 EU Member States (Table 3).

Table 3: Occupational exposure limits for o-anisidine in EU Member States

Country	Exposure limit	Limit value (ppm)[d]	Limit value (mg/m^3)[d]
Austria	TRK[a]	0.1	0.5
Denmark	MAC[b]	0.1	0.5
France	OEL[c]	0.1	0.5
Germany	TRK	0.1	0.5
Ireland	OEL	0.1	0.5
Netherlands	MAC	0.1	0.5

[a] TRK = Technical Guiding Concentration (8h – TWA, peak limitation cat. 4, i.e. over 15 minutes the average concentration may not exceed the fourfold TRK value, additional remark referring to the dermal resorption capacity of the substance); [b] MAC = Maximum Accepted Concentration (workplace); [c] OEL = Occupational Exposure Limit; [d] conversion factor: 1 ppm = 5.12 mg/m^3 for the gaseous phase at standard temperature and pressure

3.2.3 Practical implementation of current measures

As stated above o-anisidine is subject to far-reaching regulations in place for chemical agents in general and for carcinogens at the workplace in particular. However, it was shown in the risk assessment for o-anisidine that during the installation of gas compensation pipes in the processing of the substance, sufficient protection of workers cannot be assured.

3.3 Consumers

A need for limiting the risks for consumers was identified for the dermal contact with textiles coloured with o-anisidine based dyes and for oral exposure of young children sucking clothes which are coloured with o-anisidine based dyes.

3.3.1 EU legislation

o-Anisidine is classified as a Category 2 carcinogen according to the Dangerous Substances Directive 67/548/EEC (see section 3.1). Consequently it is taken up in

- Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations.

According to the provisions laid down in Annex I, Group 29, of that Directive o-anisidine may not be used in substances and preparations placed on the market for sale to the general public (in individual concentration equal to or greater than either the concentration specified in Annex I to Directive 67/548/EEC or in Annex I to Directive 88/379/EEC). The packaging of such substances and preparations must be marked with the sentence: “Restricted to professional users.” However, consumer products coloured with azodyes based on o-anisidine do not fall under this regulation.

Non-use of dyes which can release or be cleaved to carcinogenic aromatic amines, or are themselves classified as carcinogenic in accordance with Directive 67/548/EEC and Directive 88/379/EEC is a prerequisite in

- Commission Decision 96/304/EC establishing the ecological criteria for the award of the Community eco-label to bed linen and T-shirts.

Nevertheless this decision is not regarded as satisfactory in terms of risk reduction. Due to its voluntary nature the number of products which are labelled may contribute to a low extent to the total amount of products on the market. Furthermore, only a limited number of textile categories is included in this eco-label.

3.3.2 National legislation

In Austria, France, Germany, the Netherlands and Sweden the use of selected azodyes in textiles used for clothing, which can be degraded to aromatic amines classified as known animal carcinogens and supposed human carcinogens, is prohibited by law. This also holds for the import of coloured textiles. So far o-anisidine is not included in these lists of aromatic amines.

4 POSSIBLE FURTHER RISK REDUCTION MEASURES

4.1 Workplace

The Technical Guidance Document on development of Risk Reduction Strategies lists a series of possible measures related to Manufacture, Industrial and Professional Use, which include:

- controls on manufacture;
- restrictions on marketing and/or use;
- redesigning the process itself, or changing the substances or materials used in it;
- safe systems of work, e.g. specified standards of physical containment or extraction ventilation;
- application of good manufacturing practice, e.g. under ISO standards;
- classification and labelling;

- separation of personnel;
- monitoring and maintenance of equipment;
- dust suppression methods;
- occupational exposure limits and/or air monitoring;
- accurate hazard information, e.g. SDS, warning signs;
- biological exposure indices and/or biological monitoring;
- medical surveys;
- training
- use of personal protective equipment (PPE);
- licensing of operators or of certain operations;
- “end-of-pipe” controls;
- limit values for emission and effluent monitoring;
- environmental quality standards and/or environmental monitoring.

o-Anisidine is classified as a genotoxic carcinogen which implicates that it is not possible to identify a threshold below which risks to human health cease to exist. This has to be kept in mind during elaboration of possible further measures which have to ensure that exposure of workers is prevented or that the level of exposure is reduced to as low as is technically possible (ALATP). To fulfil these requirements the Carcinogens and Chemical Agents Directives follow a stepwise approach, which includes many of the possible measures listed above, thereby relating to the technical feasibility of measures and to the obligation of employers to keep themselves informed of the latest advances in technology and scientific findings concerning workplace design. Thus it seems appropriate to consider further risk reduction options for o-anisidine within the framework of existing controls such as the Carcinogens and Chemical Agents Directives.

The following options beyond those already applied may be considered for further reducing exposure to o-anisidine:

- **European Occupational Exposure Limit (OEL) Value**

An OEL to ensure an EU harmonised level of control for a carcinogen in the workplace can be established within the framework of the Carcinogens or the Chemical Agents Directives.

- **Industry commitment**

A commitment made by the industry concerned would aim to determine and implement what could be considered ALATP for the specific workstep under concern.

4.2 Consumers

The Technical Guidance Document on development of Risk Reduction Strategies lists a series of possible measures related to Domestic and Consumer Use which include:

- restrictions on the sale;
- product design changes;
- hazard warnings and/or use instructions on packaging;
- and several measures which are specific to substances and preparations.

In the matter in hand the risk for consumers arises from products which may under certain circumstances unintentionally release o-anisidine, thus risk reduction has to be targeted on this scenario.

Marketing and use restrictions are considered a very relevant option to reduce the risk emerging from the oral contact of young children and the dermal contact of the general population with textiles coloured with o-anisidine based dyes. In this context it has to be

taken into account that a considerable amount of coloured textiles is imported from the Far East where the use of azodyes on the basis of aromatic amines is more significant than in the EU.

Within the EU a “Proposal for a Directive of the European Parliament and of the Council amending for the 19th time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations” aims to restrict the use of azodyes, which can release certain aromatic amines, for dyeing of textiles and leather. o-Anisidine is included in the list of aromatic amines under concern. Furthermore, the textile and leather articles which may release o-anisidine in concentrations above 30 ppm may not be placed on the market. With this provision also imported articles liberating o-anisidine will be covered.

5 ASSESSMENT OF POSSIBLE FURTHER RISK REDUCTION MEASURES

The Technical Guidance Document on development of Risk Reduction Strategies requires that further risk reduction options be evaluated against the following criteria:

- effectiveness: the measure must be targeted at those significant hazardous effects and routes of exposure that had been identified by the risk assessment and it must be capable of reducing the risks that need to be limited within and over a reasonable period of time;
- practicality: the measure should be implementable, enforceable and as simple as possible to manage. Priority should be given to commonly used measures that could be carried out within the existing infrastructure (though not to the exclusion of novel measures);
- economic impact: a rough qualitative estimate of the impact of the measure on producers, processors, users and other parties on the basis of experience and judgement is regarded sufficient. However, regarding restrictions on marketing and use a more detailed analysis of the advantages and drawbacks of the measures should be provided.
- monitorability: monitoring possibilities should be available to allow the success of the risk reduction to be assessed.

5.1 Workplace

The outcome of the risk assessment for o-anisidine shows an elevated risk for workers in production and processing of the substance during one specific workstep, which is the installation of gas compensation pipes during processing.

5.1.1 European Occupational Exposure Limit (OEL) Value

So far an occupational exposure limit value for o-anisidine has not been specified at the European level. National limit values exist in 6 EU countries (Table 3), the limit being 0,5 mg/m^3 (0,1 ppm) in all of these countries. Production of o-anisidine in the EU is currently known to take place only in one company in one Member State, where it is also further processed. In lower amounts o-anisidine is also imported by several companies in the same and in one additional Member State. Both have established national exposure limit values for o-

anisidine. There are no data available if and by which techniques the importing companies further process o-anisidine.

In Germany the current TRK-value for o-anisidine is 0,5 mg/m^3; according to industry the detection limit is 0,05 mg/m^3 which is one tenth of the TRK. Data from the reporting company show that in measurements regularly performed at workplace (including the installation of gas compensation pipes) concentrations of o-anisidine were well below the TRK-value.

Effectiveness:
An established harmonised OEL would hold for all countries in the EU and for all workplace scenarios. Considering the current situation where risk occurred only during one specific workstep in the processing of o-anisidine in one company the introduction of a European OEL would not be of benefit for not affected Member States.

Practicality:
The legal basis would be through the Carcinogens Directive. Experience of countries with national OELs can be helpful for the establishment of a harmonised limit. Methods for monitoring are available.

Economic Impact:
All member states will be affected as far as the implementation into national law is concerned. Monitoring costs will not arise in addition to those already in existence to comply with the provisions of the Carcinogens Directive.

Monitorability:
Reporting industry already undertakes routine monitoring.

5.1.2 Industry commitment

The outcome of the risk assessment for o-anisidine shows that there is a not acceptable risk during installation of gas compensation pipes in the processing of the substance.

The existing legislative system for the safety at work with chemicals and/or carcinogens provides a set of general principles and measures to be adopted by industry in a stepwise approach. In regulating the Category 2 carcinogen o-anisidine at the workplace the Carcinogens Directive (90/394/EEC) plays a central and important role. Based on a determination and assessment of risks by the employer it provides a step-by-step approach for risk control: Replacement of the substance should be considered in the first place. Where it is neither technically possible to replace the carcinogen by a less dangerous substance nor to manufacture and use it in a closed system, the employer has to ensure that the level of exposure of workers is reduced to as low as is technically possible by the application of a series of measures.

Following this approach industry should determine under a commitment what could be considered ALATP for prevention or reduction of exposure, in consideration of the current state of the scientific and technical knowledge and practical feasibility. In a second step it would implement the further measures identified in order to minimise the risk arising from this specific workstep.

As already stated, within the existing legislative system for workplace safety the option of replacement of carcinogens should be considered in the first place. According to industry replacement of pigments based on o-anisidine by comparable organic pigments is not possible for technical reasons: As the colouring properties of azo pigments are influenced by the type of substitution on the aromatic ring, replacement of o-anisidine by other aromatic amines would lead to azo pigments that are different in shade and in other application properties.

However, there is a possibility for replacement of pigments based on o-anisidine by highly fast organic pigments, although they would fall into a price category many times higher.

Therefore it might be justified to evaluate, if comparable risk minimisation is achievable by other measures as well, taking into account the fact that the risk, although not acceptable, occurs at comparatively limited conditions of exposure (see section 2.3.1).

Effectiveness:
The determination of ALATP should be based on the principles of prevention and reduction of exposure outlined in the Carcinogens Directive, reaching as far as to the option of replacement. The foreseeable efficiency of these measures would be the criteria to abstain from replacement. Therefore possible further measures to minimise the risks would have to be efficient enough to justify the circumvention of the substitution principle.

Practicality:
Undertakings already carried out for compliance with the Carcinogens Directive could be considered as well as actions specially designed for this task. In that way such an Industry Commitment would also increase the effectiveness of the Carcinogens Directive. As the number of companies processing o-anisidine is very small coverage should not be a limiting factor. In general, voluntary agreements can be implemented more quickly than legislative options.

Economic Impact:
Data which are collected for assessment of risks according to Article 6 of the Carcinogens Directive should be readily available. Additional costs would arise in the assessment of what can be considered ALATP and in introducing new working methods. Beside the technical feasibility the analysis carried out by industry could comprise the economic feasibility of further measures as well.

Monitorability:
Monitoring by industry and Health and Safety inspectors would be necessary. In part it is already carried out within the scope of the Carcinogens Directive.

5.2 Consumers

For assessment of possible options for risk reduction it has to be kept in mind that exposure from domestic or consumer use will in general be unsupervised, that contrary to the workplace also susceptible individuals, like very young or very old people, will be exposed, and that not everybody will read or understand use instructions supplied. Restrictions on marketing and use of articles under concern would provide an effective tool to take into account these prerequisites.

With the proposed 19th amendment of Directive 76/769/EEC it is intended that azodyes which, by reductive cleavage of one or more azo groups, may release o-anisidine in concentrations above 30 ppm in finished articles or in dyed parts thereof may not be used in textile and leather articles which may come into direct and prolonged contact with the human skin or oral cavity. Consequently, these textile and leather articles may not be placed on the market.

The risks identified for o-anisidine arise during dermal contact with textiles coloured with o-anisidine based dyes and during oral exposure of young children suckling clothes which are coloured with o-anisidine based dyes. These scenarios will be covered by the restrictions proposed with the 19th amendment of Directive 76/769/EEC and thus lead to a minimisation of the risks. However, adequate monitoring programs will be imperative to ensure the effectiveness of the measure.

A detailed assessment of risk reduction by means of an EU wide ban on azodyes and products treated with azodyes was performed by RPA for DG Enterprise.[7] There it is recommended that restrictions on the use of azodyes should be harmonised at an EU level, what is also supported by industry, for which the introduction of national legislation has led to additional costs, that could be reduced by harmonised provisions. It is further recommended that one of the aims of harmonisation should be to address and solve some of the problems experienced by industry in fulfilling the requirements of national bans.

6 FURTHER RISK REDUCTION MEASURES RECOMMENDED

6.1 Workplace

An elevated risk for workers in production and processing of o-anisidine was determined for one specific workstep, which is the installation of gas compensation pipes during processing.

Measures to reduce this risk should be sought within the existing legislative system for the safety and health at work which provides a set of general principles and measures to be adopted by industry in a stepwise approach.

It is proposed to reach an Industry Commitment under which the concerned companies would commit themselves to determine what could be as low as technically possible (ALATP) in terms of reduction of workplace exposure, and would implement possible further measures identified in order to minimise the risk arising from this specific workstep. The principles of prevention and reduction of exposure as outlined in the Carcinogens Directive, reaching as far as to the option of replacement, should form the basis of the evaluation.

6.2 Consumers

The proposal for the 19th amendment of Directive 76/769/EEC relating to restrictions on the marketing and use of azocolourants is considered to effectively minimise the risk arising from the release of o-anisidine from dyed textiles and clothes. Implementation of this amendment should be speeded up as far as possible.

7 MARKETING AND USE RESTRICTIONS

Marketing and use restrictions are proposed to reduce the risk for consumers in dermal or oral contact with textiles coloured with o-anisidine based dyes. This measure is already proposed with the 19th amendment of Directive 76/769/EEC. An analysis of the advantages and drawbacks and of the availability of alternatives is not considered necessary within this risk reduction strategy as it was already performed in the preliminary stages of the negotiations for the 19th amendment[7].

[7] Analysis of the Advantages and Drawbacks of Banning Azo-dyes and Products Treated with Azodyes, by Risk & Policy Analysts Limited, Final Report-July 1997

8 POSSIBLE MONITORING ARRANGEMENTS

8.1 Workplace

Adequate monitoring of the implementation of the industry commitment for example via regular reports should be arranged within the participating parties.

8.2 Consumers

After implementation of the proposed 19th amendment of Directive 76/769/EEC relating to restrictions on azocolourants adequate monitoring programs will be imperative to ensure the effectiveness of the measure.

9 ORGANISATIONS CONSULTED

Clariant as reporting company

FCIO-Federation of Chemical Industry in Austria, member of CEFIC

Central Labour Inspectorate, Federal Ministry of Economic Affairs and Labour