BUWAL Bundesamt für Umwelt, Wald und Landschaft
OFEFP Office fédéral de l'environnement, des forêts et du paysage
UFAFP Ufficio federale dell'ambiente, delle foreste e del paesaggio
SAEFL Swiss Agency for the Environment, Forests and Landscape

CH-3003 Berne, 16 novembre 2005

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Secretariat for the Rotterdam Convention
UNEP Chemicals
11-13, Chemin des Anémones
CH – 1219 Châtelaine, Genève

Votre référence

Votre communication du

Notre référence AMM / E463-1286

Objet **Notifications of Final Regulatory Action**

Dear Ms. Logan,

Please find enclosed 15 new notifications of final regulatory action from Switzerland for the following chemicals :

- 1,2 – dibromoethane P
- 1,2 – dichloroethane P
- 2 – naphthylamine and its salts I
- 4 – aminobiphenyl I
- 4 – nitrobiphenyl I
- Benzidine and its salts I
- Binapacryl P
- Dicofol P
- Ethylene oxide P
- Mirex P+I
- Pentachlorophenol P+I
- Tris (1-aziridinyl) phosphine oxide I
- Tris (2,3-dibromopropyl) phosphate I
- Monomethyl – dibromo – diphenyl – methane I
- Monomethyl-tetrachloro-diphenyl-methane and monomethyl-dichloro-diphenyl-methane I

Best regards

Maria a Marca

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

UNEP

FORM FOR NOTIFICATION OF FINAL REGULATORY ACTION TO BAN OR SEVERELY RESTRICT A CHEMICAL

IMPORTANT: See instructions before filling in the form

COUNTRY: SWITZERLAND

PART I: PROPERTIES, IDENTIFICATION AND USES

1.	IDENTITY OF CHEMICAL	
1.1	**Common name**	Benzidine and its salts
1.2	**Chemical name according to an internationally recognized nomenclature (e.g. IUPAC), where such nomenclature exists**	(1,1'-Biphenyl)-4,4'-diamine) (CAS # 92-87-5) (1,1'-Biphenyl)-4,4'-diamine, sulfate (1:1) (CAS# 21136-70-9) (1,1'-Biphenyl)-4,4'-diamine, dihydrochloride (CAS # 531-85-1) (1,1'-biphenyl)-4,4'-diamine, acetate (CAS# 36341-27-2) and other salts
1.3	**Trade names and names of preparations**	
1.4	**Code numbers**	
1.4.1	**CAS number**	92-87-5 (Benzidine) 21136-70-9 (Benzidine sulphate) 531-85-1 (Benzidine dihydrochloride) 36341-27-2 (Benzidine acetate)
1.4.2	**Harmonized System customs code**	2921 59 90 (CAS # 92-87-5 & 531-85-1)
1.4.3	**Other numbers (specify the numbering system)**	DC9625000 (RTECS), 1885 (UN), 202-199-1 (EC)

1.5	**Indication regarding previous notification on this chemical, if any**
1.5.1	✓ This is a first time notification of final regulatory action on this chemical.
1.5.2	☐ This is a modification of a previous notification of final regulatory action on this chemical. The sections modified are: _____ ☐ This notification replaces all previously submitted notifications on this chemical.

PLEASE RETURN THE COMPLETED FORM TO:

Interim Secretariat for the Rotterdam Convention
Plant Protection Service
Plant Production and Protection Division, FAO
Viale delle Terme di Caracalla
00100 Rome, Italy

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Fax: (+39 06) 5705 6347
E-mail: pic@fao.org

OR

Interim Secretariat for the Rotterdam Convention
UNEP Chemicals

11-13, Chemin des Anémones
CH – 1219 Châtelaine, Geneva, Switzerland

Tel: (+41 22) 917 8183
Fax: (+41 22) 797 3460
E-mail: pic@unep.ch

Date of issue of the previous notification: _____

1.6 Information on hazard classification where the chemical is subject to classification requirements

International classification systems	Hazard class
IARC	Group 1 (carcinogenic to humans)
UN Hazard Class (Pack Group)	6.1 (II)
Other classification systems	**Hazard class**
EU	Carc. Cat. 1 : R 45 may cause cancer Xn : R22 harmful if swallowed N : R 50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Switzerland	Carc. Cat. 1 : R 45 may cause cancer Xn : R22 harmful if swallowed N : R 50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

1.7 Use or uses of the chemical

1.7.1 ☐ **Pesticide**

Describe the uses of the chemical as a pesticide in your country:

1.7.2 ✓ **Industrial**

Describe the industrial uses of the chemical in your country:

Benzidine is a manufactured chemical that was used to produce azo-dyes for cloth, paper, and leather. In the past, benzidine also has been used in clinical laboratories for detection of blood, as a rubber compounding agent, in the manufacture of plastic films, for detection of hydrogen peroxide in milk, and for quantitative determination of nicotine. Most of these uses have been discontinued because of concerns about benzidine's potential carcinogenicity. Some dyes that may contain benzidine as an impurity still are used as stains for microscopy and similar laboratory applications.

1.8 Properties

1.8.1 **Description of physico-chemical properties of the chemical**

Empirical formula: $C_{12}H_{12}N_2/NH_2C_6H_4\text{-}C_6H_4NH_2$; molecular mass: 184.2; Physical state and appearance: white or reddish crystalline powder, turns dark on exposure to air and light; Boiling point: 401°C; Melting point: 128°C; Relative density (water = 1): 1.25; Solubility in water: none; Relative vapour density (air = 1): 6.36; Octanol/water partition coefficient as log Pow: 1.34

IPCS, CEC (1999): International Chemical Safety Card Benzidine (0224)
(http://www.inchem.org/documents/icsc/icsc/eics0224.htm)

1.8.2	**Description of toxicological properties of the chemical**

Exposure: Because benzidine may be produced only for captive consumption, its direct release into the environment is expected to be low. However, accidental releases from closed systems potentially could result in environmental exposure through inhalation, ingestion, or dermal contact. In the past, benzidine may have been released into wastewaters and sludges. Because benzidine is moderately persistent in the environment, exposure of populations living near former benzidine or benzidine-dye manufacturing or waste-disposal sites may still be of concern.

Mutagenicity: Benzidine is metabolized by cytochrome P-450 enzymes (via *N*-oxydation) to form electrophilic compounds that can covalently bind to DNA. Covalent binding products of benzidine with DNA have been described in the liver of mice and rats treated *in vivo*. Benzidine induced micronuclei, sister chromatid exchanges, DNA strand breaks and unscheduled DNA synthesis in cells of rodents treated *in vivo*. It induced unscheduled DNA synthesis in humans cells *in vitro*. It caused transformation of Syrian hamster embryo and BALB/c3T3 cells and induced chromosomal aberrations, sister chromatid exchanges, unscheduled DNA synthesis and DNA strand breaks in rodent cells *in vitro*; conflicting results were obtained for mutation. Benzidine induced aneuploidy, gene conversion and DNA damage in yeast, but not mutation. It was mutagenic to plants and bacteria.

Few data were available on the genetic and related effects of benzidine in humans. Workers exposed to benzidine-based dyes had higher levels of chromosomal aberrations in their white bloods cells than did unexposed workers.

Evidence for carcinogenicity to animals (*sufficient*): Benzidine and its salts were tested for carcinogenicity by oral administration in mice, rats, hamsters and dogs and by subcutaneous and intraperitoneal injection and inhalation in rats. Following oral administration of benzidine and its hydrochloride, significant increases in the incidences of benign and malignant liver neoplasms were observed in mice and hamsters and of mammary cancer in rats; benzidine induced bladder carcinomas in dogs. Following subcutaneous administration of benzidine and its sulphate to rats, a high incidence of Zymbal-gland tumours was observed. After intraperitoneal administration of benzidine to rats, a marked increase in the incidence of mammary gland and Zymbal-gland neoplasms was observed. The results of one study in rats by inhalation could not be evaluated. Two metabolites of benzidine, *N*,*N*'-diacetylbenzidine and *N*-hydroxy-*N*,*N*'-diacetylbenzidine, produced mammary gland and Zymbal gland tumours in rats following their intraperitoneal injection.

Evidence for carcinogenicity to humans (*sufficient*): Case reports and follow-up studies of workers in many countries have demonstrated that occupational exposure to benzidine is causally associated with an increased risk of bladder cancer. In one extreme instance, all five of a group of workers continuously employed in the manufacture of benzidine for 15 years or more developed bladder cancer. Earlier data suggesting that the incidence of this cancer in workers decreased after a reduction in industrial exposure have been supported by a study of a cohort of workers at a US benzidine-manufacturing facility, in which major preventive measures were instituted in 1950 to minimize worker exposure. The study period covered 1945-1979, and, overall, there was a clearly significant excess of bladder cancer incidence, which, however, declined in those first employed after 1950. Although a longer follow-up is required to evaluate fully the effect of preventive measures on cancer risks, the causal association is strengthened by these two independent observations. Few other epidemiological studies have examined the cancer risk associated with exposure to benzidine alone. In a study at a dyestuffs factory in Italy, it was possible to distinguish a very high bladder cancer risk (5 deaths observed, 0.06 expected) associated with benzidine production. The study was extended and updated, but the role of exposure to benzidine alone in the dramatically increased bladder cancer risk could not be examined further. Of 25 benzidine 'operators' at a plant in the USA, 13 developed bladder cancer; all cases had been exposed for six years or more. A surveillance programme of 179 active and 65 retired workers in a dyestuffs manufacture plant in Japan revealed nine cases of bladder cancer that occurred between 1968 and 1981; all of the cases had been engaged in benzidine production.

Other investigations have shown high incidences of cancer of the bladder and urinary tract after concomitant exposure to benzidine and 2-naphthylamine. Exposure to these two compounds was also associated with an increase in the occurrence of second primary cancers at sites other than the bladder, including the liver.

Among 1601 workers in the chemical-dye industry in China who were exposed to benzidine, methylnaphthylamine and dianisidine, 21 cases of bladder carcinoma were found. All had a history of exposure to benzidine, while no carcinoma was found among workers exposed to methylnaphthylamine or dianisidine. Suggestions of a dose-response relationship were provided by analysis according to length of exposure.
Bladder cancer was also found to be increased in ecological studies of areas where benzidine (as well as 2-naphthylamine and other compounds) was used, manufactured or stored.
Some studies have reported an association between benzidine exposure and cancer at other tissue sites (i.e. liver, kidney, central nervous system, oral cavity, larynx, esophagus, bile duct, gallbladder, stomach, and pancreas). The evidence for an association with benzidine is more limited for these cancers than for bladder cancer.

International Agency for Research on Cancer (IARC) – Summaries & Evaluations (1987), Suppl. 7, Benzidine (Group 1) (http://www.inchem.org/documents/iarc/suppl17/benzidine.html)

Department of Health and Human services, National Toxicology Programm (US), 11th Report on Carcinogens (2005) (http://ntp.niehs.nih.gov/ntp/roc/eleventh/profiles/s020benz.pdf)

1.8.3 Description of ecotoxicological properties of the chemical

The substance is toxic to aquatic organisms.
Based on available data, benzidine is not expected to persist in the environment.
Available data on the toxic effects of benzidine on aquatic organisms indicate that surface water concentrations in the range of 0.1 mg/L would be required before adverse effects on fish would be expected. Since its half-life in environmental media is less than a few weeks, concentrations of benzidine in surface water in the range of the estimated effect threshold are considered very unlikely. There is no information on the toxicity of benzidine to wildlife. However, due to the low accumulation of benzidine in aquatic organisms, adverse effects on aquatic-based wildlife due to decreased availability of prey are considered unlikely.
Due to its low volatility, and because it is expected to photooxidize rapidly in air, benzidine is not expected to contribute to ozone depletion, global warming or the formation of ground-level ozone.

National Office of Pollution Prevention (Canada), Existing Substances Evaluation, (http://www.ec.gc.ca/substances/ese/eng/psap/PSL1_benzidine.cfm#Synopsis)

PART II: FINAL REGULATORY ACTION

2. FINAL REGULATORY ACTION

2.1 The chemical is: ✓ **banned** **OR** ☐ **severely restricted**

2.2 Information specific to the final regulatory action

2.2.1 Summary of the final regulatory action

In Switzerland, benzidine and its salts are classified as category 1 carcinogens and cannot be obtained in a private capacity. As in the EU, the placing on the market and use of these substances are banned, as well as the preparations containing these substances at a concentration of 0.1% or more (Ordinance on the Reduction of Risks linked to Chemical products, ORRChem). As the ban already exists in the EU since 1989, no transition time has been fixed in Switzerland.
There is an exception on the use for analytical and research purposes. This exception takes into consideration that often no substitutes of these substances exist for analytical purposes.
The azo-dyes used in textiles or leather articles, that can release arylamines like benzidine and its salts, are also subject to the requirements of the Ordinance on Utility Articles (OUA) recently updated.

2.2.2	**Reference to the regulatory document**
	• Ordinance on the Reduction of Risks linked to the use of particularly dangerous substances, preparations and objects (Ordinance on the Reduction of Risks linked to Chemical products, ORRChem) of 18 May 2005; Annex 1.13 (RS 814.81) http://www.bk.admin.ch/ch/f/rs/8/814.81.fr.pdf (French) http://www.bk.admin.ch/ch/d/sr/8/814.81.de.pdf (German) http://www.bk.admin.ch/ch/i/rs/8/814.81.it.pdf (Italian) • Ordinance on Utility Articles (OUA) of 1 March 1995, Annex 3, Article 26a (RS 817.04) http://www.bk.admin.ch/ch/f/rs/8/817.04.fr.pdf (French) http://www.bk.admin.ch/ch/d/sr/8/817.04.de.pdf (German) http://www.bk.admin.ch/ch/i/rs/8/817.04.it.pdf (Italian)
2.2.3	**Date of entry into force of the final regulatory action**
	• ORRChem : 1st August 2005 • OUA : 1st July 1995, last update 5th May 2005

2.3	**Was the final regulatory action based on a risk or hazard evaluation?**	✓Yes θ No
	If yes, give information on such evaluation	
	Switzerland based its hazard evaluation of 2-naphthylamine on the evaluation performed by the EU : Azo-dyes (a collective term used to describe a group of synthetic dyes made from benzidine, toluidine and similar organic chemicals) account for approximately 70% of all organic dyes currently produced in the world. Since the middle of the 1990s, several OECD countries have banned the manufacture, import, export and sale of textiles and other products, that could come into contact with human skin for prolonged periods, and that are made with azo dyes which have the capacity to release, by reductive cleavage, hazardous arylamines. Germany was the first to impose the ban, followed by The Netherlands, Austria and Norway. In 1999, the European Union circulated a draft Directive that would apply the ban across its Member States. In the European Parliament Directive 2002/61/EC of July 2002, the EU has decided that by 11th September 2003 the harmonized legislation regarding azo dyes in consumer goods had to be enacted. 2-naphthylamine has been banned in Switzerland because its carcinogenicity. Switzerland considers that the conditions conerning exposure to the azo dyes are comparble to conditions in the EU. Therefore the EU prescriptions on the aromatic amines and nitrate aromatics have been transposed in the Swiss legislation in the new ordinance ORRChem.	
	Reference to the relevant documentation	
	• OECD, Joint Working Party on Trade and Environment, The development dimension of trade and environment: case studies on environmental requirements and market access, 2002 : http://www.oecd.org/dataoecd/23/15/25497999.pdf • Comments on the ordinance on the reduction of risks linked to the use of particularly dangerous substances, preparations and objects : http://www.bag.admin.ch/parchem/vernehm/f/Erlaeuterungen_ChemRRV_final_draft_f__VL.pdf (French) http://www.bag.admin.ch/parchem/vernehm/d/Erlaeuterungen_ChemRRV_final_draft_d__VL.pdf (German) http://www.bag.admin.ch/parchem/vernehm/i/Erlaeuterungen_ChemRRV_final_draft_i__VL.pdf (Italian)	

2.4	**Reasons for the final regulatory action**	
2.4.1	**Is the reason for the final regulatory action relevant to the human health?**	✓Yes θ No
	If yes, give summary of the known hazards and risks presented by the chemical to human health, including the health of consumers and workers	
	Animal carcinogenicity data : Benzidine is carcinogenic in the mouse, rat and hamster, and possibly the dog. Given orally, it has produced bladder carcinoma in the dog after a long latent period and liver tumours in the rat and hamster. Human carcinogenicity data : The epidemiological studies showed that occupational exposure to commercial benzidine alone was strongly associated with bladder cancer. In the same studies, exposure to 2-naphthylamine alone was similarly associated with bladder cancer. A number of case reports from several countries support the relationship between this neoplasm and occupational exposure to benzidine.	

Reference to the relevant documentation

- International Agency for Research on Cancer (IARC) – Summaries & Evaluations (1987), Suppl. 7, Benzidine (Group 1) (http://www.inchem.org/documents/iarc/suppl17/benzidine.html)

Expected effect of the final regulatory action

Minimizing cancer risks for population in Switzerland.

2.4.2	**Is the reason for the final regulatory action relevant to the environment?**	θ Yes	✓No

If yes, give summary of the known hazards and risks to the environment

Reference to the relevant documentation

Expected effect of the final regulatory action

2.5 Category or categories where the final regulatory action has been taken

2.5.1	**Final regulatory action has been taken for the chemical category**	✓ **Industrial**

Use or uses prohibited by the final regulatory action

ORRChem :

- According to Annex 1.13, the placing on the market and use of benzidine and its salts or preparations containing 0.1% weight or more of these substances are banned.
- According to Annex 1.10 on the substances classified as carcinogens, mutagens or toxic to reproduction, the packaging of substances and preparations subject to the prohibition must be marked: "Reserved for commercial use".

OUA : Articles cannot contain any of the azo-dyes that can release aromatic amines like 4-aminobiphenyl, by reduction of one or more azoic groups, to a concentration higher than 30 mg/kg of the article (art. 26a).
The utility articles that shall not contain any azo-dye are textiles and leather goods that come into contact with the human body like (Annex 3):
a. clothes, bed clothes, sleeping bag, toilets towels, wigs, hats, nappies and other hygienic articles
b. shoes, gloves, straps, belts, handbags, purses/wallets, briefcases
c. tissue or leather toys and toys that contain tissue or leather accessories
d. tissues intended as consumer goods

Use or uses that remain allowed

Exeptions of ORRChem :
- The ban does not concern the placing on the market and use for research purposes.

2.5.2	**Final regulatory action has been taken for the chemical category**	☐ **Pesticide**

Formulation(s) and use or uses prohibited by the final regulatory action

Formulation(s) and use or uses that remain allowed

2.5.3 Estimated quantity of the chemical produced, imported, exported and used, where available.		
	Quantity per year (MT)	Year
Produced		
Imported		
Exported		
Used		

2.6 Indication, to the extent possible, of the likely relevance of the final regulatory action to other states and regions

The impact of these laws has been felt most acutely in developing countries that produce leather and textiles with azo dyes, particularly Bangladesh, Colombia, Egypt, India, Pakistan and Sri Lanka. India, also a major manufacturer of synthetic dyes, saw two of its industries affected.

The adoption of import tolerances on arylamines, first by Germany and then by other European countries, could have had a highly disruptive effect on developing-country exporters. Because Germany announced its ban on azo dyes two years before applying it to imported textiles, however, developing countries did receive some forewarning of the impending regulatory change. The difficulties and controversies surrounding testing procedures (which have so far largely followed those of Germany) were, perhaps, a greater problem. In India, for example, it took the Government and local industry four years (1997-2001) to establish the testing facilities necessary to comply with the European standards.

The cost of compliance was considered high by textile exporters, and some of them alleged that the European prohibitions on azo dyes only came into effect once European manufacturers had developed patented substitutes. Nonetheless, the level of compliance appears now to be high. Samples tested at the eco-laboratories of the Textile Committee are reported to show a compliance rate of over 96% for textiles produced for export to Europe.

Considerable technical assistance has been provided by several European countries since the regulations were put in place — mainly in the form of workshops and factory visits by technical experts. But documentation is scarce on the effectiveness of these actions.

OECD, Joint Working Party on Trade and Environment, The development dimension of trade and environment: case studies on environmental requirements and market access, 2002 : http://www.oecd.org/dataoecd/23/15/25497999.pdf

2.7 Other relevant information that may cover:

2.7.1 Assessment of socio-economic effects of the final regulatory action

2.7.2 Information on alternatives and their relative risks

2.7.3 Relevant additional information

PART III : GOVERNMENT AUTHORITIES

Ministry/Department and authority responsible for issuing/enforcing the final regulatory action	
Institution	Federal Department of Environment, Transport, Energy and Communications
Address	Parliament Building North 3000 Berne, Switzerland
Telephone	+41 31 3225512 (General Secretary)
Telefax	+41 31 3242692 (General Secretary)
E-mail address	
Designated National Authority	
Institution	Swiss Agency for the Environment, Forests and Landscape Substances, Soil and Biotechnology Division
Address	3003 Berne Switzerland
Name of person in charge	Prof. Dr. Georg Karlaganis
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Date, signature of DNA and official seal: 15.11.05 Georg Karlaganis

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