CHIMIA 48 (1994) Nr. 11 (November)

Ecological and Toxicological Aspects in Production and Application of Colorants

Chimia 48 (1994) 519–520

ISSN 0009–4293

Cooperation between Authorities and Industry, Illustrated by a Case Study on C.I. Disperse Blue 79:1

Eric A. Clarke* and **C. Tucker Helmes**[a])

ETAD is an international association formed in 1974 to represent the interests of the dye manufacturing industry on issues relating to the possible impact of dyes on health and the environment. The current membership of 37 companies worldwide includes leading manufacturers of organic colorants in Europe, U.S.A., Japan, Brazil, and India. At the founding assembly held on June 21, 1974, the Presidential Address emphasized the need for 'an effort to gain the trust of government authorities, and ... to offer them our help in their efforts to protect the health of man and his environment'. This cooperative stance has shaped the nature of ETAD's activities over the past twenty years and reflects the commitment of the industry to fulfil its responsibilities to society, and to assist its member companies by advocating the need for regulations to be cost-effective. Environmental protection is a global issue and it would be counterproductive if the imposition of overly stringent requirements in one region led to the closure of plants manufacturing to already high standards, to the benefit of producers in other regions which operate to lower standards.

The motivation for cooperation is

- to avoid unnecessary regulatory costs in the short-term
- to avoid future regulatory costs by demonstrating industry's commitment to a high level of protection for health and the environment. Pressure for overly stringent regulations arises from the often adverse public perception of the chemical industry.

The credentials of an industry group seeking cooperation with the authorities are

- representation of the industry
- recognition
- knowledge and expertise
- responsibility, reliability, and credibility

Following an overview of ETAD's efforts worldwide to cooperate with regulatory authorities, a case study will be presented in more detail.

Case Study: Voluntary Test Program to Address Health and Environmental Concerns about a Major Disperse Dye

Chronology

In its 19th report to EPA in November 1986, the Interagency Testing Committee (ITC) listed Disperse Blue 79 (the bromo/ethoxy analogue) in the 'recommended testing' category for chemical fate, environmental and health effects testing. The bromo/methoxy, chloro/methoxy and chloro/ethoxy analogues were recommended for similar testing by the ITC in its 20th report in May 1987. The ITC based its recommendations on the potential for significant exposure to C.I. Disperse Blue 79 as a high production volume azo dye and the need for test data.

During the period February to June 1987, ETAD submitted comments on the ITC recommendations to clarify the exposure issues and interpretation of available information on health and environmental effects. ETAD also identified the predominant analogue in U.S. commerce to be the bromo/methoxy analogue, C.I. Disperse Blue 79:1 (*Fig.*).

In August 1988, EPA announced its intention to pursue health effects testing under a TSCA Section 4 test rule or consent agreement. The agency held a public meeting in October 1988 to begin negotiations on the consent agreement, which was signed by the eight participating companies in September 1989.

Benefits

A consent agreement offers industry several advantages over waiting for the EPA to promulgate a test rule:

- Projects a cooperative industry image.
- Achieves reduction in the scope of some testing; *e.g.* pharmacokinetics/metabolism.
- Gains favourable testing schedule: *e.g.* developmental toxicity.

*Correspondence: Dr. E.A. Clarke
ETAD Executive Director
Clarastr. 4
Postfach
CH–4005 Basel
[a]) Executive Director of ETAD U.S. Operating Committee
Suite 300
1330 Connecticut Avenue, N.W.
Washington DC 20036-1702, USA

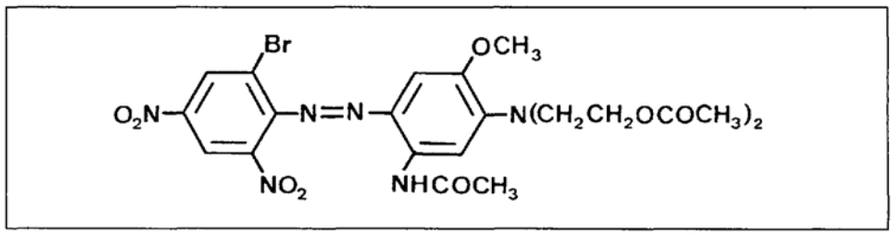


Figure. *C.I. Disperse Blue 79:1*

- Avoids the risk that additional unexpected tests would be required in a final test rule.

The agency benefits as less resources are needed than for a formal rule-making and the data required for evaluation of possible risks are available sooner.

Scope and Results of Test Program

Drosophila *SLRL Mutagenicity*

No induction of mutations in the post-meiotic germ cells.

90 Day Subchronic Toxicity

No treatment-related effects. NOEL > 2500 mg/kg/d.

Developmental Toxicity

Rat: Dose levels 0, 500, 1000, and 2000 mg/kg/d. An unexpectedly low but approximately equivalent pregnancy rate (44–56%) was observed across all dose groups. No demonstrable maternal or developmental toxicity in rats.

Rabbit: Dose levels 0, 100, 300, and 600 mg/kg/d. NOEL for maternal toxicity = 100 mg/kg/d. NOEL for developmental toxicity = 300 mg/kg/d. No evidence of teratogenicity at any dose level in rabbits.

Metabolism/Pharmacokinetics

Administration by gavage led to more than 95% overall recovery of the administered dose in feces and urine. Within 24 h, 85% of the dose was recovered in the feces and *ca.* 5% in the urine, indicating rapid elimination.

Early Life Stage Toxicity, Rainbow Trout

No significant concentration-related effects. NOEL greater than 4.8 µg/l, corresponding to water solubility limit.

Conclusions

The testing program provided evidence for the safety of Disperse Blue 79:1 under the conditions of the health and environmental studies conducted. The total costs of the program, *ca.* $ 600 000 for testing, administration and legal fees, were shared among the eight participating companies in the consent agreement. Following an evaluation of the data provided the EPA concluded that no further risk management of C.I. Disperse Blue 79:1 was required.

Chimia 48 (1994) 520–522

ISSN 0009–4293

On the Toxicology and Metabolism of Azo Dyes

Klaus Hunger*

An increasing number of regulations has somewhat led to the false impression that azo dyes in general must be considered hazardous in particular with respect to their cancerogenic and mutagenic properties. Based on the metabolic pathways and the structural features of azo dyes an assessment of the cancerogenic potential is being made.

1. Division of Azo Dyes

Two groups of azo dyes are to be considered:

- water-soluble dyes, mostly carrying sulfonate groups
- solvent-soluble dyes with non-polar substituents.

This division is justified by the different metabolic pathways of both groups.

2. Toxicological Properties

Azo dyes in general have a low toxic profile [1], certainly of most concern is the cancerogenic potential. In fact, only a very small number of the *ca.* 3000 different azo dyes on the market are cancerogenes, and these are not produced anymore by responsible manufacturers.

An assessment of the possible cancerogenic potential of azo dyes would help to decide early in the development of new products whether to proceed or to stop and save high expenses for toxicological investigations.

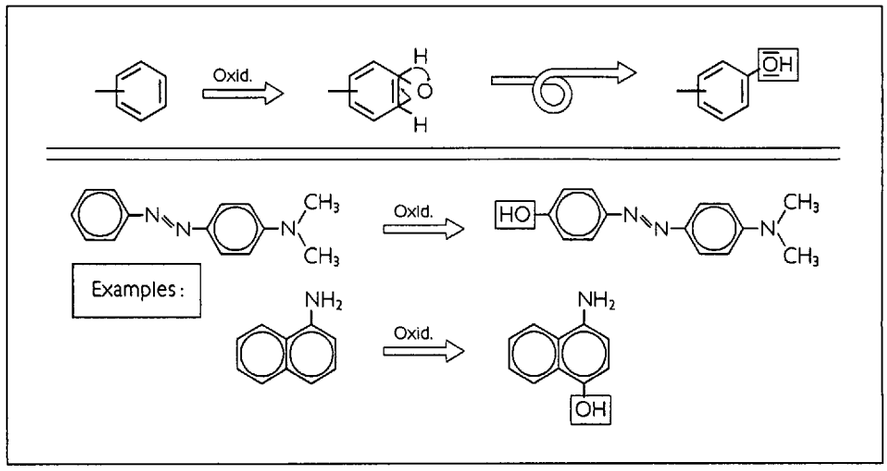
3. Metabolism

Enzymes catalyzing all metabolic reactions are unable to differentiate whether degradation products are hazardous for the organism. Oxidation and reduction reactions are the most important degradation mechanisms for azo dyes.

3.1. *Oxidative Metabolism*

Dyes with greater lipid solubility undergo preferably oxidation reactions. Oxidative processes are mainly catalyzed by

Scheme 1. C-*Hydroxylation* (ring hydroxylation)



*Correspondence: Dr. K. Hunger
Hoechst Aktiengesellschaft
D–65926 Frankfurt am Main