ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 799

[OPTS-42054B; FRL-3431-9]

Testing Consent Orders on Aniline and Seven Substituted Anilines

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This document announces that EPA has signed enforceable testing consent orders both with manufacturers (including importers) who have agreed to perform certain health and environmental effects tests on aniline and with manufacturers who have agreed to perform certain health and/or environmental effects tests on seven substituted anilines that they manufacture. These chemical substances were designated by the Interagency Testing Committee (ITC) for priority testing. Elsewhere in this issue of the **Federal Register**, the Agency announces its decision to terminate rulemaking for certain other category members for health and environmental effects and chemical fate.

EFFECTIVE DATE: Effective on August 19, 1988.

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SUPPLEMENTARY INFORMATION: This rule adds aniline (CAS No. 62-53-3), 2-chloroaniline (CAS No. 95-51-2), 4-chloroaniline (CAS No. 106-47-8), 3,4-dichloroaniline (CAS No. 95-76-1), 2-nitroaniline (CAS No. 88-74-4), 4-nitroaniline (CAS No. 100-01-06), 2,4-dinitroaniline (CAS No. 97-02-9), and 2,6-dichloro-4-nitroaniline (CAS No. 99-30-9) to the list of chemical substances and mixtures ("chemicals") subject to testing consent orders in 40 CFR 799.5000.

I. ITC Recommendation

In its Fourth Report to EPA, published in the **Federal Register** of June 1, 1979 (44 FR 31866), the ITC recommended that all chemicals in the category defined as "aniline and anilines substituted in one or more positions with a chloro, bromo, or nitro group, or any combination of one or more of these substituent groups" be considered for health effects, chemical fate and environmental effects testing. The ITC recommended testing for chronic health effects with emphasis on blood and nervous system disorders, teratogenicity, carcincogenicity, mutagenic effects, and epidemiology studies. The ITC also recommended chemical fate and environmental effects testing.

In response to the ITC, EPA published an Advance Notice of Proposed Rulemaking (ANPR) for the anilines category (49 FR 108, January 3, 1984). In the ANPR, EPA identified 20 individual chemicals in production in 1982, reviewed the available health and environmental effects information on the chemicals, indicated tentative data gaps in available health and environmental effects information, and requested public comments on a scheme to test representative category members rather than all category members. The ANPR named six subcategories (aniline, monochloroanilines, polychloroanilines, mononitroanilines, polynitroanilines, and halo-nitroanilines) and seven representative subcategory members (aniline; 4-chloroaniline; 3,4-dichloroaniline; 4-nitroaniline; 2,4-dinitroaniline; 2-chloro-4-nitroaniline; and 2-bromo-4,6-dinitroaniline) for possible health and environmental effects testing consideration under section 4(a)(1)(A) of TSCA. In response to the ANPR, EPA received comments and new information from the Aniline Association and the Substituted Anilines Task Force (SATF), an industry group organized as a special project of the Synthetic Organic Chemical Manufacturers Association, whose members manufacture or import one or more of the substituted anilines (Refs. 1 and 2). Comments were also received from Sodyeco Inc., Eastman Kodak, and Upjohn Company (Refs. 3 through 5). The Aniline Association and SATF provided results of surveys of processors to determine the potential for human exposure and environmental release. The exposure and release data supplied by the SATF and some of the data supplied by the Aniline Association were submitted as Confidential Business Information (CBI) (Refs. 6 and 7).

II. Testing Consent Order Negotiations

In the **Federal Register** of August 11, 1986 (51 FR 28758) and in accordance with the procedures established in 40 CFR 790.28, EPA requested that persons interested in participating in or monitoring testing negotiations on aniline and seven substituted anilines contact the Agency. EPA held public meetings on August 12, 1986; October 14, 1986; January 15, 1987; and February 19, 1987 to discuss testing appropriate for these eight chemicals. On or before July 7, 1988, five manufacturers of aniline and four manufacturers of substituted anilines signed eight separate Testing Consent Orders with EPA. Under one Order, the five manufacturers of aniline agreed to conduct or provide for the conduct of the following tests: *In vivo* mouse micronucleus assay, grammarid acute effects test, and daphnid chronic effects test. Under seven separate Orders, the manufacturers of the seven substituted anilines agreed to conduct or provide for the conduct of the following tests for each of the substituted anilines they manufacture: *In vivo* cytogenetics (*in vivo* mouse micronucleus assay) for 2-chloroaniline, 4-chloroaniline, 3,4-dichloroaniline, 2-nitroaniline, 4-nitroaniline, 2,4-dinitroaniline; gammarid acute effects, daphnid chronic effects, and rainbow trout acute effects (with trigger to rainbow trout early-life stage) for 2-chloroaniline; and algae acute effects, daphnid acute effects (with trigger to grammarid acute and daphnid chronic effects), and rainbow trout early life-stage test for 2,6-dichloro-4-nitroaniline. The test standards to be followed and the testing schedule for each test are specified in each Order. Procedures for submitting study plans, modifying the Order, monitoring the testing, and other provisions were also included in each Order.

The following table presents the disposition by EPA of the 20 anilines

category members reported to be in production in 1982.

ANILINES CATEGORY MEMBERS DISPOSITION

CAS No.	Chemical name	Disposition
62-53-3	Aniline	(1)
95-51-2	2-Chloroaniline	(1)
108-42-9	3-Chloroaniline	(2)
106-47-8	4-Chloroaniline	(3)
608-27-5	2,3-Dichloroaniline	(3)
554-00-7	2,4-Dichloroaniline	(3)
95-82-9	2,5-Dichloroaniline	(3)
95-76-1	3,4-Dichloroaniline	(3)
634-93-5	2,4,6-Trichloroaniline	(3)
1817-73-8	2-Bromo-4,6-dinitroaniline	(3)
88-74-4	2-Nitroaniline	(3)
99-09-2	3-Nitroaniline	(3)
100-01-6	4-Nitroaniline	(3)
97-02-9	2,4-Dinitroaniline	(3)
121-87-9	2-Chloro-4-nitroaniline	(3)
6282-25-6	2-Chloro-5-nitroaniline	(3)
89-63-4	4-Chloro-2-nitroaniline	(3)
635-22-3	4-Chloro-3-nitroaniline	(3)
99-30-9	2,6-Dichloro-4-nitroaniline	(4)
827-94-1	2,6-Dibromo-4-nitroaniline	(3)

[1] Consent Order: health and aquatic effects testing.
[2] Decision to terminate rulemaking found elsewhere in this issue of **Federal Register**.
[3] Consent Order: health effects testing.
[4] Consent Order: aquatic effects testing.

III. Technical Summary

A. Manufacture, Use And Release

Aniline is produced by five manufacturers (DuPont, First Mississippi Corp., Rubicon, Mobay Chemical Corp., and U.S.S. Chemical Corp.) at five locations in the United States. Production was about 790 million pounds in 1984 (Ref. 1). The production volumes for substituted anilines range from less than 1000 pounds to 10 million pounds. The manufacturers of the substituted anilines have provided EPA with exact production volumes for 1982 as CBI (Ref. 8). The TSCA section 8(b) confidential chemical inventory update reports that there has not been a significant increase in production of these chemicals from levels reported in 1982.

The manufacturers and processors of aniline and substituted anilines report that the chemicals are used consumptively as chemical intermediates (Refs. 7 and 9). Aniline is used to produce isocyanates, rubber processing chemicals, dyes, and hydroquinone, for drug manufacture, and for other uses including production of herbicides, synthetic fibers, and photographic chemicals. The primary use for most of the substituted anilines is as intermediates in dye and pigment production. 3,4-Dichloroaniline and 2-chloroaniline are used primarily as pesticide intermediates. 4-Nitro-aniline and 2-nitroaniline are used solely as intermediates for phenylenediamines.

Manufacturers of aniline report that approximately 2.5 million pounds were disposed of by deep well injection, 2.5 million pounds were incinerated, 130,000 pounds went to regulated landfills, 49,500 pounds were released to air, and 14,700 pounds were released to water. The manufacturers of aniline have provided to EPA site-specific aquatic release volumes for 1984 as CBI (Ref. 10). Total estimated aquatic release of aniline by processors was 85,155 pounds at 22 locations with the range of location-specific release between 22,000 pounds (3 locations) and 1,000 pounds or less (14 locations) (Ref. 11). Both manufacturers and processors of substituted anilines have provided EPA with release volumes for 1982 as CBI.

B. Human Exposure

1. *Occupational exposure.*—a. *Aniline.* The Aniline Association has provided EPA with information on potential occupational exposure from aniline manufacturing and processing operations (Refs. 1 and 7). The Association reports that there is little or no occupational exposure to aniline because: Few workers are potentially exposed for short periods; production occurs in an enclosed, continuous process mostly in open-design plants (plant not enclosed in a building); and rigorous workplace controls and industrial hygiene practices are used to protect workers from the known acute toxic effects of aniline. Also, most manufacturers and processors require that employees wear rubber suits and gloves for protection in potential exposure situations such as reactor entry, special work procedures, and sampling and maintenance operations, because the greatest potential for exposure is through dermal contact (aniline is absorbed very rapidly through the skin). Air monitoring and medical surveillance results show control practices are effectively preventing exposures to aniline (Ref. 1). Aniline has excellent acute indicator properties; the olfactory detection level is 0.5 to 1 ppm, and acute exposure causes cyanosis, a condition evidenced by bluish skin discoloration due to deficient blood oxygenation.

The Aniline Association survey data reported that 487 workers involved in manufacturing are potentially exposed to airborne aniline concentration levels between 0.001 to 1.4 ppm, with 97 percent of workers below 1 ppm. An additional 1,524 workers involved in internal and outside processing of aniline are potentially exposed to levels ranging from 0.001 to 5 ppm with 99.9 percent of total worker hours at exposures below 2 ppm. The Occupational Safety and Health Administration's (OSHA) inspection summary data time-weighted averages (TWA) were all below 0.25 ppm and serve to support the Association's conclusions (Ref. 12). The OSHA permissible exposure limit (PEL) for aniline is 5 ppm (Ref. 13). The American Conference of Governmental Industrial Hygienists (ACGIH) TWA recommended exposure limit is 2 ppm for aniline (Ref. 14).

b. *Substituted anilines.* The SATF has provided EPA with confidential information on potential occupational exposure from manufacturing and processing operations of substituted anilines (Refs. 6 and 8). The SATF also reports that there is little or no occupational exposure to the substituted anilines currently in production because very few employees are potentially exposed. The SATF reports that production occurs over short time periods in a closed continuous process during which the chemical is consumed; that workplace controls and industrial hygiene practices are used to protect workers from the known or suspected acute toxic effects of the substituted anilines, and that air monitoring and medical surveillance results show control practices are effectively preventing exposures to the substituted anilines. Some substituted anilines also have excellent acute effects indicator properties like those of aniline.

A study by one manufacturer/processor to evaluate the effects of potential airborne exposure of manufacturing workers to 4-chloroaniline on various biological (blood) parameters reported that: (1) All the methemoglobin levels measured fall within what has been traditionally regarded as a normal range, (2) a small statistically significant elevation in methemoglobin following the work shift was observed among employees involved in 4-chloroaniline manufacture and the matched comparison group suggesting the observed increase in methemoglobin among workers may not be work-related, and (3) there was no correlation between post-exposure methemoglobin and 4-chloroaniline air sampling data within the narrow range of low level exposures typical in this work setting (Ref. 15). A major manufacturer/processor of chloro- and nitroanilines reports an average of 3 cases per year or methemoglobinemia, defined as oxygen saturation below 90 percent, observed at the their main plant over the last 10 years (Ref. 16). Over the

last 5 years, no methemoglobinemia was observed.

2. *Consumer exposure.* There is no known or suspected consumer exposure to any of the aniline category members as a result of TSCA-covered activities because they are wholly consumed chemical intermediates.

C. Environmental Exposure

There are few monitoring data available for aniline and the substituted anilines in wastewater of sediment. Ewing et al. in 1977 sampled surface waters from 204 sites near heavily industrialized areas across the U.S. Aniline and substituted anilines were not detected at concentrations above 1 ppb (Ref. 17). In another study wastewater, receiving waters and sediments near a plant manufacturing a broad range of chemicals were analyzed for organic pollutants (Ref. 18). One sample of wastewater contained 0.02 ppm of aniline. Aniline was not detected in river water or sediments. Chloroaniline (isomers unspecified) was not detected in wastewater or river water but was found in sediment at 1 to 2 ppm. Plant and sampling locations were not reported.

Games and Hites in 1977 measured organic compounds in untreated and treated effluent originating from a dye manufacturing plant (Ref. 19). Results showed the presence of six aniline compounds. The compounds included aniline, chloroaniline, dichloroaniline, nitroaniline, tribromoaniline and bromodinitroaniline. The concentrations ranged from 36 to 480 ppb for raw wastewater to 7 to 96 ppb for treated effluent.

USEPA data in the STORET system include a total of 46 data points or observations on environmental levels of aniline in streams, and 42 data points or observations on levels of 2-nitroaniline in streams (Ref. 20) The mean residual level of aniline was 9.47 ppb, with maximum and minimum values of 13 and 1 ppb, respectively; the STORET data were collected between August 1978 and August 1980. The mean residual level for 2-nitroaniline was 0.39 ppb with maximum and minimum values of 1.7 and 0.1 ppb, respectively; the STORET data were collected between January 1983 and May 1985.

D. Physicochemical Properties

1. *Water solubility, vapor pressure, and octanol/water partition coefficient* EPA has estimated water solubilities, vapor pressures, and the log octanol/water partition coefficients (log P) of aniline and six representative substituted anilines, and these data are presented in the following table:

PHYSICAL AND CHEMICAL PROPERTIES OF ANILINE AND SIX SUBSTITUTED ANILINES

Chemical	CAS Number	Empirical formula	Molecular weight	Water solubility (mg/L)	Log octanol/water partition coefficient (Log KOW)	Soil sorption coefficient (KOC)	Vapor pressure	Henry's law constant
Aniline	62-53-3	C_6H_7N	93.13	[1] 35,000	[1] 0.90	47	0.473 25° C	0.17×10^{-5}
2-Chloroaniline	95-51-2	C_6H_6C1N	127.57	3,900	1.91	261	0.22 25° C	0.95×10^{-5}
4-Chloroaniline	106-47-8	C_6H_6C1N	127.57	[1] 3,900	1.83	236	9.8×10^{-3} 25° C	0.54×10^{-5}
3,4-Dichloroaniline	95-76-1	$C_6H_5C1_2N$	162.02	[1] 51	2.69	691	5.8×10^{-3} 25° C	0.24×10^{-5}
2-Nitroaniline	88-74-4	$C_6H_6N_2O_2$	138.13	1,200	1.69	198	3.8×10^{-3} 25° C	0.55×10^{-5}
4-Nitroaniline	100-01-6	$C_6H_6N_2O_2$	138.13	800	1.39	136	2.9×10^{-4} 25° C	0.66×10^{-5}
2,6-Dichloro-4-Nitroaniline	99-30-9	$C_6H_4C1_2N_2O_2$	207.02	49	2.45 to 3.29	1,000	1.45×10^{-5} 25° C	0.81×10^{-5}

[1] = Measured value.

Experimental values of some parameters are available for aniline, 4-chloroaniline, and 3,4-chloroaniline (Refs. 21 through 24). The calculated and experimental values indicate that, under equilibrium conditions, aniline, the chloroanilines, and the nitroanilines will remain in the water compartment, although other data suggest that anilines will bind chemically to sediment (see Unit III.D.3).

2. *Soil mobility.* The adsorption properties of aniline and some substituted anilines have been reported and EPA has estimated soil organic-carbon sorption coefficients (Koc) from calculated log P values using equations developed by Kenaga, and Kenaga and Goring (Refs. 25 and 26). (See table for these values.) The measured and estimated Koc values indicate that aniline and substituted anilines adsorb weakly to moderately to organic matter in soil and sediment and therefore can be considered moderately to highly mobile. However, there are experimental data to indicate that 4-chloroaniline and 3,4-chloroaniline and other aromatic amines chemically bind to organics in soil and sediment; therefore these and possibly other category members may be much less mobile in soil and sediment than predicted by the Koc (Refs. 27 through 31).

3. *Presistence.* Chemical fate data on aniline indicate that it is readily biodergradable and oxidizable in surface water and sewage sludge (Refs. 32 through 35). The overall experimental degradation half-life in surface water is less than 1 day (Refs. 36 and 43).

Data on 2-chloroaniline, 4-chloroaniline, and 3,4-dichloroaniline (DCA) indicate the major reaction in soil is chemical binding with the humic acid fraction (Refs. 27 through 31). After binding, the chloroaniline are not extractable as such. As the concentration of the chemicals in the soil increases, polymerization of these chemicals also occurs. The humic adsorption properties of the chloroanilines are believed to correlate with the organic content and pH of the soil (Ref. 37). Microbial metabolism occurs slowly in soil because the chloroanilines bind to soil organics (Refs. 38 through 42). The chloroanilines have relatively low log P values and are therefore not likely to bioconcentrate in fatty tissue of aquatic organisms, although their lower water solubilities and higher log P values indicate they are more likely to do so than aniline.

Photodegradation is likely to be a primary route of aquatic degradation of the chloroanilines (Refs. 43 through 45). The experimental half-life of DCA in distilled water, natural sea water, and Instant Ocean is less than 1 day (Ref. 43). The rates of biodegradation of monochloroanilines are estimated to be slower than aniline in the aquatic environment (Ref. 46). In aerobic environments 4-chloroaniline biodegrades faster than DCA. In anaerobic environments the reverse is true (Ref. 47). Some monochloroanilines

are reported to be degraded in activated sludge (Refs. 33 and 47).

Available data on the chemical fate of the nitroanilines and halogenated nitroanilines are limited. In semicontinuous activated sludge testing, 4-nitroaniline has been described as readily degradable and 2-nitroaniline as resistant to degradation (Ref. 48). 4-nitroaniline and 2,6-dichloro-4-nitroaniline (DCNA) undergo microbial degradation in pure culture (Refs. 49 and 50). The relatively low log P values indicate the nitroanilines and halogenated nitroanilines are not likely to bioconcentrate in aquatic organisms. The nitroanilines and halogenated nitroanilines may, like other aromatic amines, chemically bind to organics in soils and sediments, although there are no data to confirm this effect for these chemicals.

IV. Testing Program

A. Environmental Effects

In its Fourth Report to the EPA, published in the **Federal Register** of June 1, 1979 (44 FR 31866), the ITC recommended chemical fate testing because of suspected environmental effects and also because there were conflicting reports on the ability of animals, plants, and microbes to metabolize and tolerate these chemicals. The ITC recommended environmental effects testing because reports of occurrences of residues and their persistence in water and soil suggested a highly dispersive discharge into the environment and available data raised a concern that category members may produce adverse effects.

Using CBI supplied by manufacturers and processors and information from the open literature, EPA has calculated worst-case aquatic predicted environmental concentrations (PECs) for aniline, 2-chloroaniline, and 2,6-dichloro-4-nitroaniline, which were the category members judged to be released in significant amounts (Ref. 51). Because the Agency has few data on the fate of the substituted anilines in the environment, calculation of their PECs was based on the worst-case assumption that none of the substituted anilines are affected by physical or biological processes other than dilution in the discharge environment. For aniline, PECs were calculated using a measured overall degradation half-life of 17.5 hours (¾ day) which includes biodegradation, oxidation, photolysis, and hydrolysis in natural waters (Ref. 52). In addition, the concentration in the discharge environment was conservatively based on the lowest river flow rate that would not be exceeded 5 percent of the time. The PECs for aniline and the substituted anilines judged to be released in significant amounts are not described here because they are derived from CBI data.

The Agency has reviewed the available data on environmental effects and the potential for environmental exposure to other anilines category members currently in production (see Notice of Termination of Rulemaking for Certain Anilines Category Members appearing elsewhere in this issue of the **Federal Register**). The Agency has determined that, given the low anticipated and observed exposure to these chemicals and in the light of the environmental effects data available for this category, these chemicals do not reach levels in the environment that raise a concern for adverse effects.

EPA has estimated the potential for releases of anilines category members to adversely affect aquatic organisms by examining available aquatic toxicity data and by comparing acute vertebrate and invertebrate LC50's to the site-specific PECs calculated as described in Unit IV.A.2.

EPA has determined that concentrations of aniline, 2-chloroaniline, and DCNA in the aquatic environment resulting from manufacturing and processing could reach levels which may be harmful to aquatic organisms (i.e., LC50's of sensitive aquatic species of aniline, 2-chloroaniline, and DCNA are likely to be less than or equal to 1000 × the predicted environmental concentrations or less than or equal to 1 mg/L). Therefore, additional acute toxicity testing is needed to determine the effects of: Aniline on daphnids, 2-chloroaniline on gammarids and rainbow trout, and DCNA on algae and daphnids with trigger to gammarids. Testing to determine the chronic effects of aniline on dephanids, 2-chloroaniline from acute trigger to daphnid or gammarid and rainbow trout early life stage, and DCNA early life stage in rainbow trout is also needed to assess the potential long-term hazard of these chemicals to aquatic organisms.

The following is a summary of available aquatic effects information the Agency has considered in its decision to issue a Consent Order for aquatic effects testing of aniline, 2-chloroaniline, and 2,6-dichloro-4-nitroaniline. The 96-hour EC50 for aniline in freshwater algae (*Selenastrum capricornutum*) is 19 mg/L and the 48-hour EC50 for 2-chloroaniline in freshwater algae (*Scenedesmus pannonicus*) is 32 mg/L (Refs. 53 and 54). The 48-hour LC50 for aniline in *Daphnia magna* is 0.65 mg/L and the 48-hour EC50 for 2-chloroaniline in Daphnia magna is 0.46 mg/L (Refs. 55 and 54). The 96-hour LC50's for aniline and 2-chloroaniline in fathead minnows are 134 mg/L and 5.8 mg/L, respectively (Ref. 56). The 96-hour LC50 for aniline in rainbow trout is 8 mg/L (Ref. 57). The 96-hour LC50's for 2,6-dichloro-4-nitroaniline in bluegill sunfish and rainbow trout are 1.08 mg/L and 0.56 mg/L, respectively (Refs. 58 and 59).

B. Health Effects

In its Fourth Report 44 FR 31866, the ITC recommended that all chemicals in the anilines category be tested for chronic health effects with emphasis on blood and nervous system disorders, teratogenicity, caricinogenicity, mutagenic effects, and epidemiology studies. The ITC based its recommendations for chronic health effects (with emphasis on blood and nervous system disorders), for teratogenic effects testing, and for epidemiology studies on the potential for some category members to cause methemoglobinemia in humans. The ITC recommended mutagenic and carcinogenic effects testing because some category members were reported to cause mutagenic and/or carcinogenic effects, and the results raise a suspicion of these effects in untested members. The Agency in its ANPR for the aniline category, 49 FR 108, proposed testing for reproductive effects based on the potential for some category members to cause methemoglobinemia in humans.

The Agency has reviewed the available data on health effects and the potential for human exposure to the seven anilines category members named in the Consent Orders and the other anilines category members currently in production (see Notice of Termination of Rulemaking for Certain Anilines Category Members appearing elsewhere in this issue of the **Federal Register**). The Agency has determined that, given the low anticipated and observed exposure to these chemicals and in light of the health effects data available for the category, these chemicals do not reach levels in the workplace environment that raise a concern for chronic, developmental, and reproductive effects.

However, potential human exposure to aniline, 2-chloroaniline, 4-chloroaniline, 3,4-dichloroaniline, 2-nitroaniline, 4-nitroaniline, and 2,4-dinitroaniline resulting from manufacturing and processing is sufficient to raise a concern for effects on human health through adverse heritable mutagenic effects. Therefore, additional testing to characterize the

mutagenicity for seven category members is necessary.

This additional testing is necessary as part of a tiered testing approach which involves a program review to follow the development of the in vivo cytogenetics data and considers all available mutagenic and health effects data to determine the need for further mutagenic effects or other health effects testing. EPA is deferring any decision as to the need for carcinogenicity testing of the substituted anilines until it has received the results from all the mutagenicity testing to be performed under the Consent Orders. Data on the carcinogenic potential of aniline has been evaluated and judged to be adequate. The Agency will announce its decision on further mutagenicity or carcinogenicity testing needs in a separate rulemaking.

The following is a summary of available health effects information the Agency has considered in its decision to issue Consent Orders only for mutagenic effects testing of seven anilines category members.

1. *Acute effects.* The primary acute effect in mammals associated with exposure to aniline and some substituted anilines is an increase in methemoglobin levels in blood (Ref. 60). However, a recent study sponsored by American Hoechst shows that not all substituted anilines readily cause increased levels of methemoglobin in rats (Ref. 61). The study was designed to rate the methemoglobin-inducing potency of category members relative to aniline, using high doses to maximize the amount of methemoglobin produced. Doses were equimolar to 100 and 400 mg/kg of aniline. When test compounds induced the formation of methemoglobin above vehicle controls in a dose-dependent manner they were considered positive. For compounds classified as positive, the results of the 100 mg/kg equimolar does at 1 hour were then statistically compared with the 100 mg/kg aniline results to determine if the test compound was more potent, equipotent, or less potent than aniline. Test compounds that failed to induce methemoglobinemia at either time point (1 hour and 6 hours) or dose were considered negative.

Only 3-chloroaniline and 4-chloroaniline were significantly more potent methemoglobin producers than aniline. Four chemicals were equipotent to aniline: 3-nitroaniline, 4-nitroaniline, 2,4-dinitroaniline, and 3,4-dichloroaniline; and four were less potent than aniline: 2-chloroaniline, 4-chloro-3-nitroaniline, 2,3-dichloroaniline, and 3,5-dichloroaniline. The other eleven chemicals were negative.

Numerous reports and studies describe secondary effects from acute human and animal exposure to aniline, 4-chloroaniline, and 4-nitroaniline related to methemoglobinemia and resulting anoxia (Ref. 62). The secondary effects include cyanosis, and central nervous system symptoms which result from the decreased oxygen-carrying capacity of methemoglobic blood. Changes in blood chemistry and development of Heinz bodies also occur. Removal from exposure usually allows a normalization of hematologic conditions, followed by amelioration of secondary abnormalities.

2. *Metabolism.* Studies on the disposition and metabolism of aniline, 4-chloroaniline, 4-nitroaniline, 2,4-dinitroaniline, 2-bromo-4,6-dinitroaniline, 2,6-dichloro-4-nitroaniline, and 4-chloro-2-nitroaniline in rats indicate these chemicals are rapidly metabolized and excreted (Refs. 63 through 68). For example, the whole body half-life of these chemicals ranges from 1 to 7 hours; and within 2 to 3 days, clearance of chemical-derived radioactivity from the body was almost complete.

Aniline and some of the substituted members of the category (2-chloroaniline, 3-chloroaniline, 4-chloroaniline, 2,3-dichlororaniline, 2,4-dichloroaniline, 3,4-dichloroaniline, 3-nitroaniline, 4-nitroaniline, and 4-chloro-3-nitroaniline) are biotransformed in rats and other mammals into intermediates which initiate the formation of methemoglobin from hemoglobin (Ref. 60). There are two metabolic pathways involved in the metabolism of aniline and the other methemoglobin-forming members: (1) The hydroxylation of the aromatic ring carbons to produce phenols which are the precursors for conjugated products excreted in urine or bile or (2) the hydroxylation of the nitrogen atom to form phenylhydroxylamine and nitrosobenzene which convert hemoglobin to an oxidized form, methemoglobin, an irreversible oxygen carrier. However, the sensitivity to methemoglobin-forming anilines varies among mammals. Cats are the most sensitive and produce the highest and most sustained levels of methemoglobin. Humans, dogs, rats, and rabbits are less sensitive (order of decreasing sensitivities). The variation in sensitivity could be due to the extent to which the chemical is metabolized to phenylhydroxylamine or to the differences in the activities of enzymes that promote the reduction of methemoglobin in the red cell back to hemoglobin.

3. *Subchronic and chronic effects.* Results from prechronic or subchronic and chronic (oncogenicity) oral studies in rats or rats and mice for three methemoglobin-inducing chemicals (aniline, 4-chloroaniline, and 4-nitroaniline) have been reported (Refs. 69 through 75). Some common effects that result from long term exposure to aniline and 4-chloroaniline at doses (10 to 100 mg/kg/day) that induce significant methemoglobin include: Anemia, red blood cell Heinz bodies, dose-related increase in spleen weight and size, dose-related congestion of splenic pulp, increased red blood cell turnover rate, and dose-related increased pigment (hemosiderin engorgement) in spleen and in kidney and liver at high doses (> 10 mg/kg/day). At higher doses (30 to 100 mg/kg/day), a dose-dependent increased incidence of primary splenic sarcomas, principally in male rats, was reported for aniline and 4-chloroaniline (Refs. 69 and 75).

Results of a chronic oral study in rats using 4-nitroaniline indicate the administration of 4-nitroaniline at levels up to 9 mg/kg/day for 2 years did not cause any treatment-related oncogenic effects (Ref. 74). The study was designed to determine whether chronic or oncogenic effects occur from long-term exposure to 4-nitroaniline at doses that induce increased levels of methemoglobin in rats. Methemoglobin levels were increased over controls at mid (1.5 mg/kg/day) and high (9.0 mg/kg/day) dosage levels. Slight anemia was observed mainly at the high dosage level. At the low (0.25 mg/kg/day) dosage level, the only treatment-related change was slight brown pigment in splenic reticuloendothelial cells. The only treatment-related change at the mid and high dosage levels was accumulation of brown pigment in sinusoidal macrophages in the liver and in reticuloendothelial cells in the spleen. Results of an oral 90-day subchronic study in mice using 4-nitroaniline have been reported. Effects in both sexes given 30 and 100 mg/kg/day include: Methemoglobinemia, Heinz bodies, increased red blood cell turn over rate, increased spleen and liver weight, and pigment deposition within phagocytic cells of spleen, bone marrow and liver (Ref. 74). The National Toxicology Program (NTP) is sponsoring an oral chronic effects-oncogenicity study of 4-nitroaniline in mice at dose levels of 0, 3, 30, and 100 mg/kg/day (Ref. 76).

Subchronic inhalation studies using rats and mice with the methemoglobin inducers 3-chloroaniline, 3,4-dichloroaniline, and 4-nitroaniline report

the same type of effects that occur at lower doses and over shorter exposure periods in oral studies in rats and mice (Refs. 77 through 81). Subchronic oral exposure of rats to 4-chloro-3-nitroaniline resulted in reduced testes-weight-to-brain-weight ratio at 18 mg/kg/day and testicular atrophy along with other toxic effects at 90 mg/kg/day (Ref. 82). No treatment-related effects were observed at or below 100 ppm in the diet in two chronic/oncogenicity studies in rats and dogs for 2,6-dichloro-4-nitroaniline (DCNA), which does not induce significant methemoglobinemia in mammals (Ref. 83). An oncogenicity study of DCNA in mice is in progress (Ref. 84).

Because there is evidence from studies on the metabolism of methemoglobin-producing anilines for a non-genotoxic mechanism for the induction of hemangio- and fibrosarcomas in the spleen of rats from dietary exposure at high concentrations, and because EPA wants to review all relevant data on all the anilines before making a determination as to the need for oncogenicity testing, the Agency is deferring its decision on the need for additional data on oncogenic effects of substituted anilines until the results of the in vivo mutagenicity tests are available (Ref. 85). The available data on the oncogenic effects of aniline are adequate for TSCA risk assessment purposes.

Also, after reviewing the available reports and studies on the acute and chronic health effects of the anilines category the Agency has found no evidence of adverse hematologic or central nervous system effects that are not likely to be related to the decreased oxygen-carrying capacity of methemoglobic blood. The data provide no basis to believe that these chemicals may present an unreasonable risk of adverse hematologic or central nervous system effects at anticipated exposure levels as manufacturers and processors control potential human exposure below the threshold for methemoglobinemia. Therefore, the Agency has concluded that additional information on hematologic or central nervous system effects of aniline and substituted anilines is not necessary at this time.

4. *Developmental toxicity.* Aniline, a potent methemoglobin producer, was observed not to be developmentally toxic in rats at levels (100 mg/kg) that produced maternal and fetal toxicity commonly caused by methemoglobinemia (Ref. 86). Timed pregnant mice treated with aniline (500 mg/kg/day) during days 7 through 14 of gestation revealed no apparent effect on numbers of litters produced; however, offspring viability through the first three postpartum days was significantly lower than for the control group. Also, reductions in birth weight and weight gain were seen in aniline-treated litters (Ref. 87). No treatment-related maternal or embryotoxicity was observed below 125 mg/kg/day (oral administration) of 4-nitroaniline in New Zealand rabbits (Ref. 88). 4-Nitroaniline administered by gastric intubation to pregnant rats at a dose of 25 mg/kg/day from day 6 to 19 of gestation was not maternally or developmentally toxic (Ref. 89). At 85 mg/kg/day some maternal toxicity (increased spleen weight) and fetotoxicity (reduced fetal weight) were evident; however, no developmentally toxic effects were observed. At 250 mg/kg/day, 4-nitroaniline produced maternal toxicity, embryotoxicity and terata. No treatment-related maternal or developmental toxicity was observed at or below 300 mg/kg/day of 2-nitroaniline to pregnant rats after gavage administration on days 6 to 15 of gestation. Significant evidence of maternal toxicity was observed at 2-nitroaniline dosages of 600 mg/kg with a single malformation in one fetus each from two litters at that dosage (Ref. 90). Pregnant rats exposed to 1.1 and 1.7 mg/m^3 of 2,4-dinitroaniline developed maternal and embryotoxicity, but no other developmental toxic effects were observed (Ref. 91). Pregnant rabbits exposed to DCNA showed no maternal toxicity or developmental toxicity at 1,000 ppm in diet (Ref. 92). A second teratology study of DCNA in rats is in progress (Ref. 84).

The data provide no basis to believe that these chemicals may present an unreasonable risk of adverse developmental effects at anticipated exposure levels, as available data show no developmental effects that occur at exposure levels at which some category members cause methemoglobinemia and manufacturers and processors control potential human exposure below the threshold for methemoglobinemia. Therefore, the Agency has concluded that additional information on the developmental effects of aniline and the substituted anilines is not necessary for risk assessment purposes at this time.

5. *Reproductive effects.* Aniline administered subcutaneously in female rats (average weight 150 grams) for seven days at 50 mg/day caused alterations in steroidal hormone levels of the *corpora luteum* (Ref. 93). 4-Nitroaniline administered by gastric intubation at dose levels of 0.25, 1.5 and 9.0 mg/kg/day to the F0 and F1 generation of male and female rats during pre-mating growth and through ensuing mating, gestation, and lactation intervals showed no significant adverse effect on mortality rates or body weights in the F0 and F1 generations (Ref. 94). In the F0 generation, the male fertility index and pregnancy rate for the high dose group were lower than control data; however, only for the pregnancy rate was this difference from the control group statistically significant. In the F1 generation, mating, pregnancy, and fertility indices were comparable between control and treated groups. No adverse effects of treatment were indicated during either generation in parturition or litter size data, pup weight date, pup survival, or sex distribution data or dead pup observations. Likewise, gross and histopathological evaluation of selected tissues from F1 and F2 pups or adults to include testes/epididymides of F0 males (high dose group) did not reveal an adverse effect. The recent chronic study using aniline has no mention of long-term effects on reproductive organs (Ref. 69). Chronic studies on 4-chloroaniline and 4-nitroaniline have no mention of effects on reproductive organs (Ref. 70 and 74). 4-Chloro-3-nitroaniline caused testicular effects in rats after subchronic oral exposure at 90 mg/kg/day, but the animals showed other toxicities as well (Ref. 82). The NOEL was reported as close to but below 3.6 mg/kg/day. The 3.6 mg/kg/day dose produced a minimal toxic response. A sperm morphology vaginal cytology (SMVCE) study of 4-nitroaniline reported no effects of the chemical on mouse estrous cycles but reduced sperm motility in mice at 100 mg/kg/day (Ref. 95). An SMVCE study of 4-chloro-2-nitroaniline reported no effects on reproductive parameters in male rats; however, the chemical appeared to interfere with the relative frequency of estrous stages (600 and 1,200 mg/kg/day) (Ref. 96). This effect is likely to be caused by alteration in hormonal activity. A three generation reproductive study of DCNA reported no effects on reproductive parameters in male or female rats at 100 ppm and 10 ppm in diet (Ref. 97).

The data provide no basis to believe that these chemicals may present an unreasonable risk of adverse reproductive effects at anticipated exposure levels, as available reproductive effects data show no reproductive effects that occur at exposure levels at which some category members cause methemoglobinemia and manufacturers and processors control potential human exposure below the threshold for methemoglobinemia. Therefore, the Agency has concluded

that additional information on the reproductive effects of aniline and the substituted anilines is not necessary for risk assessment purposes at this time.

6. *Mutagenic effects.* The following data were considered by EPA for evaluating the risk of mutagenic injury to human health from exposure to seven category members.

a. Aniline is reported to have negative results in the following gene mutation assays: *Salmonella, E. coli,* WP2 uvr A, and *Aspergillus* (Refs. 98 through 101). Aniline is positive for the L5178Y TK, ± mouse lymphoma gene mutation assay and negative for the *Drosophila* sex linked recessive lethal assay (SLRL) (Refs. 102 through 104). Aniline is negative for sister chromatid exchange in human lymphocytes, and negative for chromosomal aberrations in cultured Chinese hamster ovary cells (Refs. 105 and 106). Aniline caused an increased frequency of sister chromatid exchange (SCE) *in vivo* in mouse bone marrow cells and *in vitro* with Chinese hamster ovary cells (Refs. 107 and 108). Aniline also caused a slight increase in frequency of SCE's in cultured human fibroblasts (Ref. 109). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

b. 2-Chloroaniline is negative in the *Salmonella* gene mutation assay, and there are no data on cytogenetic effects of 2-chloroaniline (Ref. 110). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

c. 4-Chloroaniline is reported to have positive results in the following gene mutation assays; *Salmonella, E. coli* pol A, *Aspergillis* and L5178Y TKI± mouse lymphoma (Refs. 101 and 111 through 113). 4-Chloroaniline is positive for sister chromatid exchange and chromosomal aberration effects *in vitro* (Ref. 114). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

d. 3,4-Dichloroaniline is reported to have negative results in the *Salmonella* gene mutation assay and positive results in the *Aspergillus* gene mutation assay (Refs. 99 and 115). There are no data on the cytogenetic effects of 3,4-dichloroaniline. EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

e. 2-Nitroaniline is reported to have positive results in the *Salmonella* gene mutation assay; there are no data available on the cytogenetic effects of 2-nitroaniline (Ref. 116 and 118). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

f. 4-Nitroaniline is reported to have positive results in the *Salmonella* and L5178Y TK± mouse lymphoma assays and negative results in the *Drosophila* SLRL assay (Refs. 117, 119 and 122). 4-Nitroaniline is weakly positive for sister chromatid exchange and chromosomal aberration effects *in vitro* (Ref. 120). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

g. 2,4-Dinitroaniline is reported to have positive effects in the *Salmonella* gene mutation assay and is negative in the *Drosophila* SLRL assay (Refs. 116, 121, and 123). 2,4-Dinitroaniline is also being tested for *in vitro* cytogenetics effects (Ref. 120). EPA believes that an *in vivo* cytogenetics test is necessary for risk assessment purposes, and manufacturers have agreed to perform the testing (mouse micronucleus).

V. Export Notification

The issuance of these Consent Orders subject any person who exports or intends to export aniline, 2-chloroaniline, 4-chloroaniline, 3,4-dichloroaniline, 2-nitroaniline, 4-nitroaniline, 2,4-dinitroaniline, and 2,6-dichloro-4-nitro-aniline to the export notification requirements of section 12(b) of TSCA. The specific requirements are listed in 40 CFR Part 707. EPA added and reserved subpart C of 40 CFR 799.5000 for a list of testing consent orders issued by EPA. This listing serves as notification to persons, who export or who intend to export chemical substances or mixtures which are the subject of testing consent orders, that 40 CFR Part 707 applies.

VI. Rulemaking Record

EPA has established a record for these Consent Orders (docket number OPTS-42054B). This record contains the basic information considered by the Agency in developing these Testing Consent Orders.

A. Supporting Documentation

(1) Testing Consent Orders between the five manufacturers/importers of aniline and the Agency.

(2) Testing Consent Orders between the four manufacturers/importers of seven substituted anilines and the Agency.

(3) Federal Register notices pertaining to this notice consisting of:

(a) Notice containing the designation of the Anilines Category to the Priority List (44 FR 107; June 1, 1979).

(b) Advance Notice of Proposed Rulemaking for the Anilines Category (49 FR 108; January 3, 1984).

(c) Notice soliciting interested parties for developing a Consent Order for Aniline and Seven Substituted Anilines (51 FR 28758; August 11, 1986).

(d) Notice of interim final rule on procedures for developing enforceable consent agreements (51 FR 23706; June 30 1986).

(4) Communications consisting of:

(a) Written letters.

(b) Contact reports telephone conversations.

(c) Meeting summaries.

(5) Reports—published and unpublished factual materials.

B. References

(1) LaRoe, Winn and Moerman, Counsel for Aniline Association. Comments of the Aniline Association on the Advance Notice of Proposed Rulemaking on the Need for Additional Testing of Aniline Under section 4 of TSCA. (1984).

(2) Cleary, Gottlieb, Steen and Hamilton, Counsel for Substituted Anilines Task Force. Comments on Advance Notice of Proposed Rulemaking for Chloro-, Bromo-, and/or Nitroanilines, for the Substituted Anilines Task Force of Synthetic Organic Chemical Manufacturers Association. (1984).

(3) Sodyeco Inc. Comments of Sodyeco Inc. on the Advance Notice of Proposed Rulemaking on the Need for Additional Testing of Anilines Under section 4 of TSCA. Letter of March 2, 1984 from B.W. Drum to TSCA Public Information Office.

(4) Eastman Kodak Company. Comments of Eastman Kodak on the Advance Notice of Proposed Rulemaking on the Need for Additional Testing of Aniline Under section 4 of TSCA. Letter of March 2, 1984 from R.F. Brothers to TSCA Public Information Office.

(5) Upjohn Company. Aniline and Chloro-, Bromo- and/or Nitroanilines: Response to the Interagency Testing Committee by Upjohn Company. Letter of February 28, 1984 from J.S. Mehring to TSCA Public Information Office.

(6) Cleary, Gottlieb, Steen and Hamilton. Comments on Advance Notice of Proposed Rulemaking for Chloro-, Bromo-, and/or Nitroanilines (Appendix A. Confidential Business Information) for the Substituted Anilines Task Force of the Synthetic Organic Chemical Manufacturers Association. (1984).

(7) LaRoe, Winn and Moerman. Comments of the Aniline Association on the need for additional testing of aniline under section 4 of TSCA. From: Aniline Association, August 26, 1983.

(8) Cleary, Gottlieb, Steen and Hamilton. Information relevant to EPA's determination of whether to require additional health or environmental effects testing of the substituted anilines under section 4 of TSCA. From: Substituted Anilines Task Force of the Synthetic Organic Chemical Manufacturers Association, July 18, 1983. (Appendix A. Confidential Business Information).

(9) Cleary, Gottlieb, Steen and Hamilton. Information relevant to EPA's determination of whether to require additional health or environmental effects testing of the substituted anilines under section 4 of TSCA. From: Substituted Anilines Task Force of the Synthetic Organic Chemical Manufacturers Association, July 18, 1983

(10) SOCMA. Synthetic Organic Chemical Manufacturers Association. Letter from A. Rautio of Synthetic Organic Chemical Manufacturers Association to M. McCommas, Office of Toxic Substances, USEPA. (Confidential Business Information). (1985).

(11) SOCMA. Letter from A. Rautio of Synthetic Organic Chemical Manufacturers Association to M. McCommas, Office of Toxic Substances, USEPA. (1985).

(12) OSHA. Occupational Safety and Health Administration. OHDS-4 Health Sampling Report for Aniline (Substance Code 0220) for Period June 1979 through May 1983. U.S. Department of Labor, Washington, DC. (1983).

(13) OSHA. U.S. Department of Labor. "Occupational Health Guidelines for Aniline." (1978).

(14) ACGIH. American Conference of Governmental Industrial Hygienists. "TLVs: Threshold limit values for chemical substances and physical agents in the work environment with intended changes." *Hygienic Guide Series: Aniline.* (1980).

(15) Monsanto. Monsanto Company. "Evaluation of blood methemoglobin levels for workers involved in production of *para*-chloroaniline." Unpublished company data. (1986).

(16) DuPont. Letter from T. Lewis of DuPont and Company to M. McCommas, Office of Toxic Substances, USEPA. (1984).

(17) Ewing, B.B. and Chian, E.S.K. "Monitoring to detect previously unrecognized pollutants in surface water." EPA Report No. 560/6-77-015 performed by University of Illinois for Office of Toxic Substances, USEPA. (1977).

(18) Jungclaus, G.A., Lopez-Avila, V., and Hites, R.A. "Organic compounds in an industrial wastewater: A case study of their environmental impact." *Environmental Science Technology.* 12:88-96. (1978).

(19) Games, L.A., and Hites, R.A., "Composition, treatment efficiency, and environmental significance of dye manufacturing plant effluents." *Analytical Chemistry.* 49:1433-1440. (1977).

(20) USEPA. U.S. Environmental Protection Agency. "Retrieval of data on anilines category from EPA's STORET System." Office of Toxic Substances, USEPA. (1985).

(21) Kirk-Othmer. Northcott, J. "Aniline and its derivatives." In: *Kirk-Othmer Encylopedia of Chemical Technology.* 3rd ed. Vol. 2. New York: Wiley-Interscience, pp. 309-321. (1978).

(22) Monsanto. "Aqueous solubility of 4-chloroaniline." Conducted by Monsanto Industrial Chemicals Company, St. Louis, MO. (1982).

(23) Beard, R.R., and Noe, J.T. In: *Patty's Industrial Hygiene and Toxicology.* New York, NY: John Wiley and Sons. Vol. 11a. (1981).

(24) Konemann, H., Zelle, R., and Busser, F. "Determination of log P values of chloro-substituted benzenes, toluenes, and anilines by HPLC on ODS—silica." *Journal of Chromatography* 178:559-565. (1979).

(25) Kenaga, E.E. and Goring, C.A.I. "Relationship between water solubility, soil sorption, octanol-water partitioning, and concentration of chemicals in biota." *ASTM Special Technical Publication STP.* 707:78-115. (1980).

(26) Kenaga, E.E. "Predicted bioconcentration and soil sorption coefficients of pesticides and other chemicals." *Ecotoxicology and Environmental Safety.* 4:26-38. (1980).

(27) Bollag, J.M., Minard, R.D., and Liu, S.Y. "Cross-linkage between anilines and phenolic humus constituents." *Environmental Science and Technology* 17:72-80. (1983).

(28) Saxena, A., and Bartha, R. "Binding of 3,4-dichloroaniline by humic acid and soil: mechanism and exchangeability." *Soil Science* 136(2):111-116. (1983).

(29) Saxena, A. and Bartha, R. "Modeling of the covalent attachment of chloroaniline residues to quinoidal sites of soil humus." *Bulletin of Environmental Contamination Toxicology* 30:485-491. (1983).

(30) Parris, G.E. "Covalent binding of aromatic amines to humate. 1-Reactions with carbonyls and quinones." *Environmental Science and Technology* 14:1099-1106. (1980).

(31) You, I-S, Jones, R.A., and Bartha, R. "Evaluation of a chemically defined model for the attachment of 3,4-dichloroaniline to humus." *Bulletin of Environmental Contamination Toxicology* 29:476-482. (1982).

(32) Malaney, G.W. "Oxidative abilities of aniline-acclimated activated sludge." *Journal of the Water Pollution Control Federation* 32:1300-1311. (1960).

(33) Pitter, P. "Determination of biological degradability of organic substances." *Water Research* 10:231-235. (1976).

(34) OECD Chemicals Testing Programme—Degradation/Accumulation Group. "Ring test programme 1981-1982. Assessment of biodegradability of chemicals by manometric respirometry." Commission of the European Communities report No. EUR 8631 EN. (1983).

(35) Lyons, C.D., Katz, S., and Bartha, R. "Mechanisms and pathways of aniline elimination from aquatic environments." *Applied and Environmental Microbiology* 48:491-496. (1984).

(36) Falco, J.W., Mulkey, L.A., and Swank, R.R. "A screening procedure for assessing the transport and degradation of solid waste constituents in sub-surface and surface waters. No. 23: Aniline." Proceedings of the 1st Annual Meeting for the Society of Environmental Toxicology and Chemistry, Washington, DC. (1980).

(37) Rippen, G., Ilgenstein, M., Klopffer, W., and Porenski, H.J. "Screening of the adsorption behavior of new chemicals: Natural soils and model adsorbents." *Ecotoxicology and Environmental Safety* 6:236-245. (1982).

(38) Bordeleau, L.M., and Bartha, R. "Biochemical transformations of herbicide-derived anilines in culture medium and in soil." *Canadian Journal of Microbiology* 18:1857-1864. (1972).

(39) Bollag, J.M., Blattman, P., and Laanio, T. "Adsorption and transformation of four substituted anilines in soil." *Journal of Agricultural and Food Chemistry.* 26:1302-1306. (1978).

(40) Kearney, P.C. and Plimmer, J.R. "Metabolism of 3,4-dichloroaniline in soils." *Journal of Agricultural and Food Chemistry.* 20:584-585. (1972).

(41) Hsu, T.S. and Bartha, R. "Hydrolyzable and nonhydrolyzable 3,4-dichloroaniline humus complexes and their respective rates of biodegradation." *Journal of Agricultural and Food Chemistry.* 24:118-122. (1976).

(42) Freitag, D., Scheunert, I., Klein, W., and Korte, F. "Long-term fate of 4-chloroaniline-14C in soil and plants under outdoor conditions. A contribution to terrestrial ecotoxicology of chemicals." *Journal of Agricultural and Food Chemistry.* 32:203-207. (1984).

(43) Miille, M.J., and Crosby, D.G. "Pentachlorophenol and 3,4-dichloroaniline as models for photochemical reactions in seawater." *Marine Chemistry.* 14:111-120. (1983).

(44) Miller, G.C., and Crosby, D.G. "Photooxidation of 4-chloroaniline and N-(4-chlorophenyl)-benzene sulfonamide to nitroso and nitro products." *Chemosphere* 12(9):1217-1227. (1983).

(45) Wolff, C.J.M., and Crossland, N.O. "Fate and effects of 3,4-dichloroaniline in the laboratory and in outdoor ponds: I. Fate." *Environmental Toxicology and Chemistry.* 4:481-487. (1985).

(46) Falco, J.W., Mulkey, L.A., and Swank, R.R. "A screening procedure for assessing the transport and degradation of solid waste constituents in sub-surface and surface waters: No. 49: Chloroaniline." Proceedings of the 1st Annual Meeting for the Society of Environmental Toxicology and Chemistry. Washington, DC (1980).

(47) Lyons, C., Bartha, R., and Katz, S. "Chlorine substitutions and biodegradability of anilines in aerobic and anaerobic test systems." In: Abstracts of the annual meetings, New Brunswick, NJ: Rutgers University, pp. 271-285. (1983).

(48) Monsanto. "Biodegradation testing of 2-nitroaniline and 4-nitro-aniline." Unpublished company data. (1975).

(49) Zeyer, J. and Kearney, P. C. "Microbial metabolism of 14C nitro-anilines to 14C carbon dioxide." *Journal of Agricultural and Food Chemistry* 31:304-308. (1983).

(50) Van Alfen, N.K. and Kosuge, T. "Microbial metabolism of the fungicide 2,6-dichloro-4-nitroaniline." *Journal of Agricultural and Food Chemistry* 22:221-224. (1974).

(51) USEPA. "Predicted environmental concentrations for selected substituted anilines." Confidential Business Information, prepared by M. McCommas, Test Rules Development Branch, Office of Toxic Substances. (1985).

(52) USEPA. Memo: Surface Water Concentrations of Aniline from P. Harrigan, Design and Development Branch, Office of Toxic Substances to M. McCommas, Test Rules Development Branch, Office of Toxic Substances, USEPA. Confidential Business Information. (1985).

(53) Calamari, D., Da Gasso, R., Galassi, S., Provini, A. and Vighi, M. "Biodegradation and toxicity of selected amines on aquatic organisms." *Chemosphere* 9:753-762. (1980).

(54) Canton, J.W., Sloof, W., Kook, H.J., Struys, J., Pouw, J.M., Wegman, R.C., and Piet, G.J. "Toxicity Biodegradability and Accumulation of a Number of C1/N-Containing Compounds for Classification and Establishing Water Quality Criteria." *Regulatory Toxicology and Pharmacology* 5:123–131. (1985).

(55) Adema, D.M.M. "*Daphnia magna* as a test animal in acute and chronic toxicity tests." *Hydrobiology*. 59:125–134. (1978).

(56) USEPA. Testing results report of USEPA Environmental Research Laboratory, Duluth, MN. (1985).

(57) Abram, F.S. and Sims, L.R. "The toxicity of aniline to rainbow trout, *Salmo gairdneri*." *Water Research* 16(8):1309–1312. (1982).

(58) Pitcher, F.A., and McCann, J.A. "Botran Technical: Bluegill ("*L. macrochirus*"): Test No. 742." U.S. Agricultural Research Service, Chemical and Biological Investigations Branch, Technical Services Division, Animal Biology Laboratory; unpublished study. CD:127912-A. (1974).

(59) Pitcher, F.A., and McCann, J.A. "Botran Technical: Rainbow Trout." U.S. Environmental Protection Agency, Chemical and Biological Investigations Branch, Technical Services Division, Animal Biology Laboratory, unpublished study. CDL: 165061-A. (1974).

(60) Kiese, M. *Methemoglobinemia: A Comprehensive Teatise*, CRC Press, Cleveland, OH. (1974).

(61) Reynolds, W. P., Roell, M. G. and Fleming, J. J. "Methemoglobin inducing potential of various substituted anilines in rats." Toxicology Section of Hoechst-Roussel Pharmaceuticals, Incorporated. Unpublished company data. (1984).

(62) USEPA. "Support Document: Health Effects of Anilines." submitted to Office of Toxic Substances by JRB Associates. (1981).

(63) McCarthy, D.J., Waud, W.R., Struck, R.F., and Hill, D.L. "Disposition and metabolism of aniline in Fischer 344 Rats and C57BL/6XC3HF, Mice." *Cancer Research* 45: 174–180. (1985).

(64) Sipes, I.G. and Carter, D.G., "Pharmacokinetics of xenobiotics: *p*-chloroaniline." University of Arizona, Tucson, Arizona for National Institute of Environmental Health Sciences, Research Triangle Park, NC. (1984).

(65) Matthews, H.B., Chopade, H.M., Smith, R.W., and Burka, L.T. "disposition of 2,4-dinitroaniline in the male F-344 rat." *Xenobiotica* 16:1–10. (1986).

(66) Chopade, H.M. and Matthews, H.B. "Disposition and metabolism of 2-bromo-4,6-dinitroaniline in the male F-344 rat." *Journal of Toxicology and Environmental Health* 17:37–50 (1986).

(67) Eberts, F.S. "Fate of 2,6-dichloro-4-nitroaniline in the rat." Abstracts of American Chemical Society meeting. Washington, DC. (1967).

(68) Chopade, H.M., and Matthews, H.B. "Disposition and metabolism of 4-chloro-2-nitroaniline in the male F-344 rat." *Journal of Toxicology and Environmental Health* 12:267–282. (1983).

(69) CIIT. Chemical Industry Institute of Toxicology: By Research Triangle Institute. Final Report on 104-week chronic toxicity study of aniline hydrochloride." Research Triangle, NC. (1982).

(70) NCI. National Cancer Institute. "Bioassay of *p*-chloroaniline for possible carcinogenicity." National Institutes of Health, U.S. Department of Health and Human Services. Carcinogenic Technical Report Series No. 189. (1979).

(71) NTP. National Toxicology Program. "Prechronic studies of *p*-chloroaniline: Repeated dose and subchronic in rats." Conducted by Battelle Laboratories, Columbus, OH. (1981).

(72) NTP. "Prechronic studies of *p*-chloroaniline: Repeated dose and subchronic in mice." Conducted by Battelle Laboratories, Columbus, OH. (1981).

(73) USEPA. Memo: NTP bioassay—*p*-chloroaniline. From Larry Rosenstein, Chemical Information and Analysis Group, Office of Toxic Substances to Don R. Clay, Director, Office of Toxic Substances. (1985).

(74) Monsanto. "Two-year chronic gavage study in rats: *Para*-nitroaniline." Conducted by Biodynamics Inc. for Department of Medicine and Environmental Health, St. Louis, MO. Unpublished company data. (1985).

(75) NTP. "Subchronic study of 4-nitroaniline in mice" conducted by Hazleton Raltech Inc., Madison, WI. (1983).

(76) USEPA. Memo from Dorothy Canter, Assistant to the Director, National Toxicology Program to Dr. Lawrence Rosenstein, Chemical Information and Analysis Group, Office of Toxic Substances. (1984).

(77) Dupont. "Subacute inhalation toxicity study of aniline in rats." Conducted by Haskell Laboratories, Newark, DE. Unpublished company data. (1982).

(78) Dupont. "Subacute inhalation toxicity study of *m*-chloroaniline in rats." Conducted by Haskell Laboratories, Newark, DE. Unpublished company data. (1982).

(79) Monsanto. "Four-week inhalation toxicity study of 4-nitro-aniline in male rats—BD80–508." Department of Medicine and Environmental Health, St. Louis, MO. Unpublished company data. (1984).

(80) Monsanto. "Four-week inhalation toxicity study of 2-nitro-aniline in male rats—BD82–270." Department of Medicine and Health, St. Louis, MO. Unpublished company data. (1983).

(81) DuPont. "3,4-Dichloroaniline inhalation subchronic in rats." Conducted by Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE. Unpublished company data. (1986).

(82) Kodak. Eastman Kodak Company. "A 90-day study of 4-chloro-3-nitro-aniline in rats by gavage administration." Toxicological Sciences Health and Environment Laboratories, Rochester, NY. Unpublished company data. (1984).

(83) Woodard, G. et al. "DCNA rat and dog chronic study." For Upjohn Company, Kalamazoo, MI. Unpublished company data. Confidential Business Information. (1965).

(84) USEPA. Office of Pesticide Programs. "Registration Standard for 2,6-dichloro-4-nitroaniline." (1983).

(85) Bus, J.S., and Popp, J.A. "Perspectives on the mechanism of action of the splenic toxicity of aniline and structurally related compounds." *Food and Chemical Toxicology* 25: 619–626. (1987).

(86) Price, C.J., Tyl, R.W., Marks, T.A., Paschke, L.L. Ledoux, T.A., and Reel, J.R. "Teratologic and postnatal evaluation of aniline hydrochloride in the Fischer 344 rat." *Toxicology and Applied Pharmacology* 77:465–478. (1985).

(87) NIOSH. National Institute for Occupational Safety and Health. "Screening of priority chemicals for reproductive hazards." By Borriston Laboratories Inc., Temple Hills, Maryland. (1983).

(88) Monsanto. "A teratogenicity study in rabbits with 4-nitroaniline." Conducted by Biodynamics, Inc. Unpublished company data. (1982).

(89) Monsanto. "A teratogenicity study with 4-nitroaniline in rats." Conducted by Biodynamics, Inc. Unpublished company data. (1980).

(90) Monsanto. "A teratology study in rats with o-nitroaniline." Conducted by Monsanto Company Environmental Health Laboratory, St. Louis, MO. Unpublished company data. (1985).

(91) Khipko, S.E. "Experimental study of the effect of 2,4-dichloro-aniline on embryogenesis." *Gigiena Trudy Professionalnykh Zabolevaniy* 82(6):47–49 (English translation) (1982).

(92) Wazeter, F.X., Buller, R.H., and Geil, R.G. "Somers test in Albino rabbit: 100–037." by International Research and Development Corp. for Upjohn Co., Kalamazoo, MI. Unpublished company data. Confidential Business Information. (1986).

(93) Hatakeyama, S., Kovacs, K., Yegheayan, E., and Blascheck, J.A. "Aniline-induced changes in the corpora lutea in rats." *American Journal of Obstetrics and Gynecology* 109:469–476. (1971).

(94) Monsanto. "4-Nitroaniline—two generation reproductive study." Conducted by Biodynamics Inc. Unpublished company data. (1983).

(95) NIEHS. National Institute of Environmental Health Sciences. "Sperm morphology/vaginal cytology report on 4-nitroaniline." By Environmental Health, Research and Testing Inc., Cincinnati, OH. (1983).

(96) NIEHS. "Sperm morphology/vaginal cytology report on 4-chloro-2-nitroaniline." By Environmental Health Research and Testing Inc., Cincinnati, OH. (1984).

(97) Lobdell, B.J., Johnstan, C.D., and Cronin, M.T.I. "U-2069: Effect on reproductive capacity through three generations in the rat." Prepared by Woodard Research Corp. for Upjohn Co., Kalamazoo, MI. Unpublished company data. Confidential Business Information. (1965).

(98) DeFlora, S. "Study of 106 organic and inorganic compounds in *Salmonella*/Microsome test." *Carcinogenesis* 2(4):283–298. (1981).

(99) Tanaka, K., Marai, S., and Mii, T. "Mutagenicity of extracts of urine from rats treated with aromatic amines." *Mutation Research* 79:173–176. (1980).

(100) Pai, V., Bloomfield, S.F., Jones, J., and Gorrod, J.W. "Mutagenicity testing of nitrogenous compounds and their *N*-oxidized products using trp + reversion in *E. coli*." In: Gorrod J.W., ed. Biological oxidation of

nitrogen. Amsterdam: Elsevier/North Holland Bio Med Press, 375–382. (1978).

(101) Prasad, I. "Mutagenic effects of the herbicide 3,4-dichloropropionanilide and its degradation products." *Canadian Journal of Microbiology* 16:369–372. (1970).

(102) Amacher, D.E., Paillet, S.C., Turner, G.N., Ray, V.A., and Salzburg, D.S. "Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation." *Mutation Research* 72:447–474. (1980).

(103) NTP. NTP Technical Bulletin No. 8, July 1982. Mouse lymphoma test results, page 6. (1982).

(104) Yoon, J.S., Mason, J.M., Valencia, R., Woodruff, R.C., and Zimmering, S. "Chemical mutagenesis testing in Drosophila. IV. Results of 45 coded compounds for National Toxicology Program." *Environmental Mutagenesis* 7:349–367 (1985).

(105) Takehisa, S., and Kanaya, N. "SCE induction in human lymphocytes by combined treatment with aniline and norharman." *Mutation Research* 101:165–172. (1982).

(106) Ishidate, M., and Odashima, S. "Chromosome test with 134 compounds on Chinese hamster ovary cells *in vitro*—a screening for chemical carcinogens." *Mutation Research* 48:337–354. (1977).

(107) Parodie, S., Pala, M., Russo, P. et al. "DNA damage in liver, kidney, bone marrow, and spleen of rats and mice treated with commercial and purified aniline as determined by alkaline elution and SCE induction." *Cancer Research* 42:2277–2283. (1982).

(108) Abe, S. and Sasaki, M. "Chromosome aberrations and sister chromatid exchanges in Chinese hamster cells exposed to various chemicals." *Journal of the National Cancer Institute* 58:1635–1641. (1977).

(109) Wilmer, J.L., Kligerman, A.D., and Erecson, G.L. "Sister chromatid exchange induction and cell inhibition by aniline and its metabolites in human fibroblasts." *Environmental Mutagenesis* 3:627–638. (1981).

(110) DuPont. "Mutagenic activity of 2-chloroaniline in Salmonella/Microsome assay." By Haskell Laboratories. Unpublished company data. (1978).

(111) Seuferer, S.L., Braymer, H.D., and Dunn, J.J. "Metabolism of diflubenzuron by soil microorganisms, and mutagenicity of the metabolites. *Pesticide Biochemical Physiology* 10(2): 178–186. (1979).

(112) Rosenkranz, H.S. and Poirer, L.A. "Evaluation of the mutagenicity and DNA modifying activity of carcinogens and non-carcinogens in microbial systems." *Journal of National Cancer Institute*. 62:873–892. (1979).

(113) NTP. NTP Technical Bulletin No. 8, July 1982. "Mouse lymphoma assay results for 4-chloroaniline." P. 6. (1982).

(114) NTP. NTP Technical Bulletin No. 9, April 1983. "SCEs and chromosome aberrations for 4-chloroaniline." P. 7. (1983).

(115) Monsanto. "Salmonella mutagenicity study with 3,4-dichloroaniline." Unpublished company data. (1981).

(116) Garner, R.C. and Nutman, C.A. "Testing of some azo dyes and their reduction products for mutagenicity using *Salmonella typhimurium* TA 1538." *Mutation Research* 44:9–19. (1977).

(117) Thompson, C.Z., Hill, L.E., Epp, J.K., and Probst, G.S. "The induction of bacterial mutation and hepatocyte unscheduled DNA synthesis by mono substituted anilines." *Environmental Mutagenesis* 5:803–811. (1983).

(118) Chiu, W.C., Lee, L.H., Wang, C.Y., and Bryan, G.T. "Mutagenicity of some commercially available nitro compounds for *S. typhimurium*." *Mutation Research* 58:11–22. (1978).

(119) Monsanto. "*Salmonella* mutagenicity assay of 4-nitroaniline." Conducted by Haskell Laboratory. Unpublished company data. (1980).

(120) NTP. National Toxicology Program. NTP Results Report. Page 82. August 1986.

(121) Muzzall, J.M. and Cook, W.L. "Mutagenicity test of dyes used in cosmetics with the *Salmonella*/Microsome test." *Mutation Research* 67(1):1–8. (1979).

(122) Valencia, R., Mason, J.M., Woodruff, R.C., and Zimmering, S. "Chemical mutagenesis testing in Drosophila. III. Results of 48 coded compounds tested the National Toxicology Program." *Environmental Mutagenesis* 7:325–348 (1985).

(123)Woodruff, R.C., Mason, J.M., Valencia, R., and Zimmering, S. "Chemical mutangenesis testing in Drosophila. V. Results of 53 coded compounds testing for the National Toxicology Program." *Environmental Mutagenesis* 7:677–702 (1985).

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List of Subjects in 40 CFR Part 799

Testing, Hazardous substances, Chemicals, Recordkeeping and reporting requirements.

Dated: August 8, 1988.

J.A. Moore,

Assistant Administrator for Pesticides and Toxic Substances.

Therefore, 40 CFR Part 799 is amended as follows:

PART 40—[AMENDED]

1. The authority citation continues to read as follows:

Authority: 15 U.S.C. 2603, 2611, 2625.

2. Section 799.5000 is amended by adding the following chemical substances in Chemical Abstract Service (CAS) Registry Number order to the table, to read as follows:

§ 799.5000 Testing consent orders.

* * * * *

CAS No. and substance or mixture name	Testing	Federal Register citation
62-53-3 Aniline	Health effects	(Insert FR date)
	Environmental effects.	Do.
88-74-4 2-Nitroaniline.	Health effects	Do.
95-51-2 2-Chloroaniline.	Health effects	Do.
	Environmental effects.	Do.
95-76-1 3,4-Dichloroaniline.	Health effects	Do.
97-02-9 2,4-Dinitroaniline.	Health effects	Do.
99-30-9 2,6-Dichloro-4-nitroaniline.	Environmental effects.	Do.
100-01-6 4-Nitroaniline.	Health effects	Do.
106-47-8 4-Chloroaniline.	Health effects	Do.

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