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Initial Risk Assessment of Acetanilide in OECD High Production Volume Chemical Program

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ABSTRACT *: In Korea, 2,320 tonnes of acetanilide were mostly used as intermediates for synthesis in pharmaceuticals or additives in synthesizing hydrogen peroxide, varnishes, polymers and rubber. Only small amount of 120 kg were used as a stabilizer for hydrogen peroxide solution for hair colouring agents in 1998. Readily available environmental or human exposure data do not exist in Korea at the present time. However, potential human exposures from drinking water, food, ambient water and in work places are expected to be negligible because this chemical is produced in the closed system in only one company in Korea and the processing factory is equipped with local ventilation and air filtering system. Acetanilide could be distributed mainly to water based on EQC model. This substance is readily biodegradable and its bioaccumulation is low. Acute toxicity of acetanilide is low since the LD_{50} of oral exposure in rats is 1,959 mg/kg bw. This chemical is not irritating to skin, but slightly irritating to the eyes of rabbits. From repeated dose toxicity, the adverse effects in rats were red pulp hyperplasia of spleen, bone marrow hyperplasia of femur and decreased hemoglobin, hematocrit and mean corpuscular hemoglobin concentration. The LOAEL for repeated dose toxicity in rats was 22 mg/kg/day for both sexes. Acetanilide is not considered to be genotoxic. In a reproductive/developmental toxicity study, no treatment-related changes in precoital time and rate of copulation, impregnation, pregnancy were shown in all treated groups. The NOAELs for reproduction and developmental toxicity (offspring toxicity) are considered to be 200 mg/kg bw/day and 67 mg/kg bw/day, respectively. Ecotoxicity data has been generated in a limited number of aquatic species of algae (72 hr-E_bC_{50}; 13.5 mg/l), daphnid (48hr-EC_{50}; > 100 mg/l) and fish (Oryzias latipes, 96hr-LC_{50}; 100 mg/l). From the acute toxicity values, the predicted no effect concentration (PNEC) of 0.135 mg/l was derived using an assessment factor of 100. On the basis of these data, acetanilide was suggested as currently of low priority for further post-SIDS work in OECD.*

Key Words *: Acetanilide, Hazard assessment, SIDS (Screening Information Data Set), SIAM (SIDS Initial Assessment Meeting)*

I. INTRODUCTION

Currently it has been known that 100,000 chemicals are used in commerce world-wide. To investigate the potential risk of those substances, enormous tasks should be undertaken. Through a 1990 OECD Council Decision, member countries decided to undertake the investigation of the over 5000 high production volume (HPV) chemicals in order to determine whether there is a need to undertake further work to clarify and/or manage their potential risks in a co-operative way. These HPV chemicals include all chemicals reported to be produced or imported at levels greater than 1,000 tons per year in at least one member country.

Each country, often with the chemical industry, collects hazard information, carries out toxicity testing, and assesses the results for a portion of these HPV chemicals. When making the first evaluation of the chemical, a minimum set of data is necessary to determine its potential hazards.

To ensure that such data are available, OECD developed the Screening Information Data Set (SIDS). The SIDS outlines the minimum data elements essential for determining whether or not a chemical requires further investigation. When data gaps for a specific chemical are identified, testing is carried out by the sponsoring country or the chemical industry. Chemical industries may volunteer to play a significant role

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in providing data and initial assessments to the programme via member country. They can also assist in promoting the collection of information, and in ensuring that necessary tests are conducted in a timely manner. After co-operative initial hazard assessments are agreed by experts, member countries agree to the hazards of these chemicals to human health/environment with information about exposure and recommendations on any actions to be undertaken.

The most recent OECD HPV Chemicals List is that compiled in 1997, which contains 4,103 substances. There are currently close to 400 substances in the program which have been selected from the HPV List for investigation by member countries. As Korea has taken part in this SIDS program since 1999, several chemicals including disodium disulphite, acetanilide had been selected from the OECD list of HPV chemicals to prepare SIDS Initial Assessment Report (SIAR). Overall Korea is supposed to share 4.01% of total burden, which is 7 chemicals each year for the program according to the agreement among OECD member countries.

The purpose of this study is to provide a minimum set of hazard information on acetanilide, and through the evaluation of the existing data and/or newly tested study to draw conclusion on the potential risk of acetanilide.

II. PROCEDURE OF OECD SIDS PROGRAM

1. SIDS as a screening tool

The SIDS program represents a minimum data set

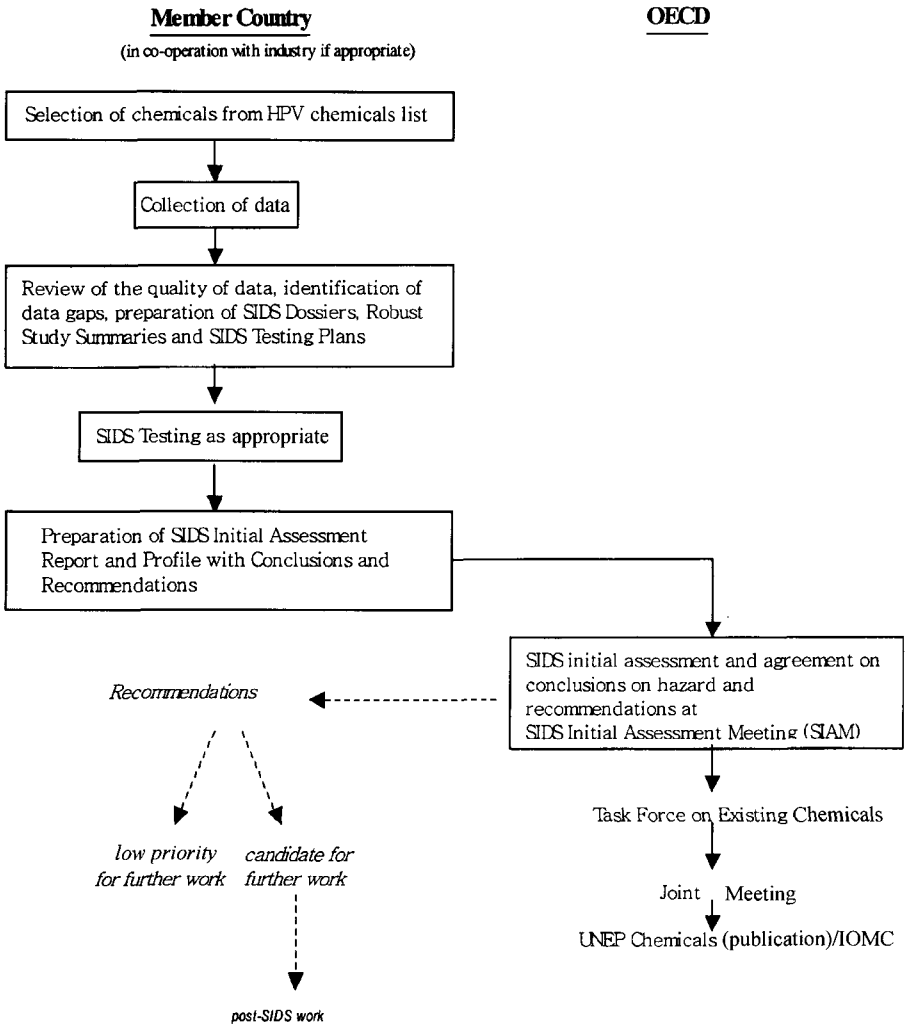


Fig. 1. SIDS process including post-SIDS work.

and thus used for initial or screening level of hazard assessments to make judgments on potential hazard and to set priorities for further work. The synopsis of the stages (Fig. 1) involved in the SIDS work is (1) collection of toxicity and exposure data (2) review of the quality of data, preparation of SIDS Dossiers and if existing data are not adequate, SIDS Testing Plans (3) SIDS Testing and/or collection of information, as appropriate (4) preparation of a SIDS Initial Assessment Report with conclusions on potential risk and recommendations on further work to be undertaken (5) co-operative initial assessment and agreement on conclusions and recommendations at the SIAM and confirmation at the Steering Group on Existing Chemicals and the Joint Meeting.

The conclusions present: (1) a summary of the hazards of the chemical, written with sufficient detail and clarity as to be informative and to assist countries with classification work and other hazard based national decision making, and (2) exposure information to put the hazard information into context such as domestic use pattern of acetanilide. The recommendation, based on these conclusions, can be either that the chemical is currently of low priority for further work or that it is a candidate for further work to clarify its potential risk.

2. Data collection and preparation of SIDS Dossier and Robust study summary

Acetanilide as a target substance was selected for investigation and the first activity involved collection of existing information on the substance and collating it in a SIDS Dossier. Additionally, industry also could be requested to provide data and full reports of studies. In order to assess hazard of acetanilide, data from Japan Chemical Industry Ecology-Toxicology & Information Center was used for the biodegradation, and data for water solubility, vapor pressure, photodegradation, biodegradation, skin and eye irritation were obtained from Clarient (Hoechst), Germany.

When no information is available for a given data element, calculation or estimates derived from Quantitative Structure Activity Relationships (QSARs) can be provided. For the assessment of acetanilide, models such as EPIWIN for photodegradation, EQC model for transport and distribution, and BCFWIN for bioaccumulation were used. Also testing were carried out if existing data were not adequate. In the case of acetanilide, testings for melting point, boiling point, partition coefficient, stability in water, toxicity to algae, acute toxicity to Daphnia, combined repeated dose toxicity study with the reproduction/developmental toxicity screening test, and mutagenic toxicity *in vivo* were conducted additionally to fill the data gaps.

In order to implement the refocused HPV Chemicals Programme in the most efficient way possible, it was agreed in 1999 that robust study summaries should be prepared as part of the SIDS Dossier. These summaries provide detailed information about the key studies upon which the SIDS initial assessment is to be based. Robust study summaries are to be prepared for the most valid and relevant study for any given SIDS endpoint.

Through this process, the most appropriate data for each elements as a key data were selected and used to finalize the assigned chemical on SIAM meeting.

3. Data quality and review

Several methods are available for assessing "data adequacy", and Klimisch scheme in particular has been recently proposed for use in Europe in developing the International Uniform Chemical Information Database (IUCLID). Klimisch *et al.* (1997) describe the method and propose that data evaluation be done systematically and that it include consideration of reliability, relevance, and adequacy. Klimisch *et al.* define adequacy as "the usefulness of data for risk assessment purposes". Klimisch *et al.* use their criteria in the following scoring system for evaluating data reliability as following:

1 = reliable without restrictions: studies or data generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline or in which all parameters described are closely related/comparable to a guideline method.

2 = reliable with restrictions: studies or data (mostly not performed according to GLP), in which the test parameters documented do not totally comply with

the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.

3 = not reliable: studies or data in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (*e.g.*, unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgment.

4 = not assignable: studies or data which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.).

SIDS Initial Assessment Meeting(SIAM) provides the final check of the quality and adequacy of the SIAR and the data behind it. Sponsor country (*e.g.* Korea) requested comments or advice from other SIDS Contact Points during about one month prior to SIAM in the process leading up to finalizations of a SIAR (through the electronic discussion groups). The SIDS Dossier - the adequacy and quality of data therein and any rationale for not undertaking SIDS testing - was reviewed by all stakeholders in the framework of the evaluation of the SIAR at and lead-

Table 1. Summary of the key studies in initial assessment of acetanilide

Elements	Species	Protocol
Melting Point		OECD TG 102
Boiling Point		OECD TG 103
Density		NA
Vapour Pressure		NA
Partition Coefficient (Log Pow)		OECD TG 107
Water Solubility		NA
pH		NA
pKa		NA
Oxidation: Reduction Potential		
Photodegradation		Estimation (AOPWIN)
Stability in Water		OECD TG 111
Monitoring Data		
Transport and Distribution		Estimation (EQC model: Fugacity Level I)
Biodegradation		Other (MITI, Japan)
Acute/Prolonged Toxicity to Fish	*Orizias latipes*	Other (Korean TG)
Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	Other (Korean TG)
Toxicity to Aquatic Plants e.g. Algae	*Selenastrum capricornutum*	OECD TG 201
Chronic Toxicity to Aquatic Invertebrates		
Toxicity to Soil Dwelling Organisms		
Toxicity to Terrestrial Plants		
Toxicity to Other Non-Mammalian Terrestrial Species (including Birds)		
Acute Oral Toxicity	Rat	OECD TG 401
Acute Inhalation Toxicity		
Acute Dermal Toxicity		
Skin Irritation	Rabbit	OECD TG 404
Eye Irritation	Rabbit	OECD TG 405
Skin Sensitization		
Repeated Dose Toxicity	Rat	OECD TG 422
Genetic Toxicity *in vitro*		
Bacterial Test (Gene mutation)	*S. typhimurium*	Other (Ames test)
Non-Bacterial *in vitro* Test (Chromosomal aberrations)	Chinese hamster cell	Other (cytogenetic)
Genetic Toxicity *in vivo*	Mouse	OECD TG 474
Carcinogenicity	Rat/mouse/hamster	Other
Toxicity to Reproduction	Rat	OECD TG 422
Developmental Toxicity/Teratogenicity	Rat	OECD TG 422
Experience with Human Exposure	Human	exposure in workplace, overdosing as a drug

ing up to the SIAM.

Careful consideration was made of the quality of the study, the method, the reporting of the results, the conclusions drawn and the results in order to complete a robust study summary. All key data used in hazard assessment of acetanilide were summarized as following (Table 1).

4. Preparation of SIAR for hazard assessment

The SIDS Initial Assessment Report (SIAR) is a relatively short document which forms part of a package of information for HPV chemicals along with the SIDS Initial Assessment Profile and SIDS Dossier. The SIAR clearly describes the hazards of the chemical and general exposure information to put those hazards in context. To ensure consistency and quality, the SIAR is divided into each of the sections described below.

· Chemical Identity (acetanilide);
· General Information on Exposure;
· Human Health Hazards;
· Hazards to the Environment;
· Conclusions and Recommendations; and
· References.

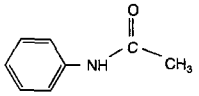
This study shows the SIAR which has systematically identified the human health and environmental hazards of acetanilide with clear reference to the SIDS Dossier for supporting information.

III. INITIAL RISK ASSESSMENT OF ACETANILIDE

1. Chemical identity and physicochemical properties

Physicochemical properties are as follows: melting point 113.7°C, boiling point 304°C at 760 mmHg, water solubility 4 g/l at 20°C, logPow 1.16 at 23°C (Table 2).

Table 2. Identity and Physicochemical Properties of acetanilide

Elements		Summary
OECD Name Synonym		Acetanilide Acetic acid anilide Acetaminobenzene Acetanil Acetanilid Acetoanilide Acetylaminobenzene Acetylaminobenzol Acetylaniline Antifebrin N-Acetyl aniline N-Acetyl-benzenamine N-Phenyl acetamide N-Phenyl acetic acid amide Phenalgene Phenalgin USAF EK-3
CAS Number		103-84-4
Molecular Formula		C_8H_9NO
Structural Formula		$CH_3CONHC_6H_5$ 
Degree of Purity		> 97% (industrial grade)
Physicochemical properties	Melting Point	113.7°C
	Water Solubility	4 g/l at 20°C
	Log Pow	1.16 at 23°C
	Vapour Pressure	0.002 hPa at 20°C
	Boiling Point	304°C at 760 mmHg
Classification in Korea		Not classified as toxic chemicals in the Toxic Chemicals Control Act, Republic of Korea

2. Exposure

Acetanilide is produced in a non-dispersive manner and mainly used as intermediates of synthesis in medicine and dyes, as additives for hydrogen peroxide and cellulose ester varnishes, and as a plasticizer in polymer industry as well as accelerator in the rubber industry.

Total production of acetanilide in Korea is about 2,300 tonnes/year and the import into Korea was less than 1% of the total production as of 1998 survey (MOE[a], 1998). Acetanilide is produced by only one company in Korea. Mostly it is used as an intermediate for synthesis of pharmaceuticals and dyes. Less than 0.2 ton/year were used as a stabilizer in hydrogen peroxide solution. Acetanilide is produced as a solid form with the purity of > 97% as industrial grade in Korea. US EPA reported that 196 tons of acetanilide were produced in 1998. Although acetanilide is used mainly as intermediates in the closed system, it may be released into the environment from its production and processing sites. No monitoring data are available in Korea at the present time.

1) Environmental fate

Acetanilide is not expected to undergo direct photolysis in water due to the lack of functional groups to absorb UV light (HSDB, 2000). However, it is expected to degrade rapidly in air by reaction with photochemically-produced hydroxyl radicals. The estimated half-life is about 31 hours (NIER[a], 2001). Hydrolysis of acetanilide is less than 10% in water solution of pH 4-pH 9 and the half life is longer than 1 year, measured using OECD TG 111 (NIER[b], 2001). Therefore, the chemical hydrolysis is not expected to be an environmentally important removal process in aquatic systems (Mabey *et al.*, 1978).

If released into water, biodegradation of acetanilide is expected to be an important removal process. The biodegradation of acetanilide is 68.7% at 14 days by MITI test, which is readily biodegradable (MITI, 1992). An estimated BCF of 1.56 by BCFWIN Model (NIER[a], 2001), based on logPow = 1.16 (NIER[c], 2001), implies that bioaccumulation of acetanilide in aquatic organisms is low (Franke *et al.*, 1994). If it is released into the soil, acetanilide is expected to exhibit very high mobility(Swann *et al.*, 1983) based on a measured K_{OC} of 27 (Briggs *et al.*, 1981). Acetanilide is not expected to volatilize from wet soil based on an estimated Henry's Law constant of 6.2×10^{-9} atm m^3/mole (NIER[a], 2001). No monitoring data of acetanilide in Korea were given.

The distribution of emitted acetanilide at equilibrium in the environmental compartments was obtained by Equilibrium Criterion model (EQC) of fugacity level I, and it showed the highest distribution of the chemical is in the water system (Water, 98.57%; Air, 0.13%; Soil, 1.26%; Sediment, 0.02%; biota and suspended sediment, 0.02%) (NIER[a], 2001).

2) Human exposure

Although limited monitoring data indicate that non-occupational exposure can occur from the ingestion of contaminated drinking water, the most probable human exposure would be occupational exposure through dermal contact or inhalation at workplaces where acetanilide is produced or used. NIOSH (National Occupational Exposure Survey 1981-1983) has statistically estimated that 9,000 workers (6,100 of these are female) are potentially exposed to acetanilide in USA.

No human exposure data are available in Korea at the present time. However, it seems that consumer exposure does not occur. Potential exposure to this chemical from drinking water, food and ambient water is expected to be negligible because it is produced in the closed system in only one company in Korea.

3. Human health hazards

1) Effects on human health

Toxicokinetics and metabolism. Acetanilide is converted to phenolic metabolite in the human body which gives it an analgesic effect, but some are converted to aniline (aminobenzene) which is toxic. It was found that single dose of 10 mg/kg of acetanilide resulted in 191.5±27.8 min. of blood plasma half-life in 25 subjects(human) and 14.1±2.8 liter/h of metabolic clearance rate (Kellerman *et al.*, 1978).

Acute toxicity. The acute effects of acetanilide exposure have been examined in mice, rats, guinea pigs, rabbits, cats and dogs. Data show wide range of LD_{50} depending on the species (Table 3). Oral LD_{50}

Table 3. Acute toxicity of acetanilide in experimental animals

Route	Animal	Value	Type	References
Oral	Rat	Male/Female:1959(1428-2429)mg/Kg Male:2033(1368-2858)mg/kg Female:1893(1218-2459)mg/kg	LD_{50}	Van den Heuvel *et al.*, 1990
	Mouse	1210 mg/kg bw	LD_{50}	Starmer 1971
Inhalation		No data		
Dermal		No data		
I.P	Rat	540 mg/kg bw	LD_{50}	Argus 1959
	Mouse	715 mg/kg	LD_{50}	Argus 1959

value ranged from 1,428~2,429 mg/kg bw for male and female rats with a combined average of 1,959 mg/kg bw. Based on this information, the acute oral toxicity of this chemical is likely to be low according to harmonized integrated hazard classification system. The adverse effects by oral observed in laboratory animals are ptosis, lethargy, abnormal gait, lacrimation, sedation, narcosis, paralysis and death after administration (Higgins *et al.*, 1993; Van den Heuvel *et al.*, 1990).

Repeated dose toxicity. MOE study (MOE[b], 2001) was conducted under the GLP using OECD test guideline 422 and selected as the key study for the repeated dose toxicity test. Details of the study are as follows;

Acetanilide was administrated to rats (male:12/dose, female:12/dose) by gavage at doses of 22, 67, 200 and 600 mg/kg/day. Males were dosed for 30 days and females were dosed for 39-50 days from 14 days before mating to day 3 of lactation. Cyanosis was observed at 600 mg/kg in males and females, and decreased locomotor activity was noted at 200 mg/kg in males as well as at 600 mg/kg in males and females. Salivation at 67, 200, 600 mg/kg and reddish tear at 600 mg/kg in males were shown as well. Four females at 600 mg/kg died at the day 21, 22, and 23 of pregnancy and the day 4 of lactation, respectively.

There were significant decreases in hemoglobin (HGB), hematocrit (HCT), mean corpuscular hemoglobin concentration (MCHC) at 22, 67, 200, 600 mg/kg and red blood cell (RBC) at 67, 200, 600 mg/kg and increase in mean corpuscular volume (MCV) at 67, 200, 600 mg/kg, mean corpuscular hemoglobin (MCH) at 200, 600 mg/kg and reticulocyte (RET) at 600 mg/kg for males respectively. Blood biochemistry revealed increases in aspartate aminotransferase (AST), arginine aminotrasferase (ALT), albumin (ALB), albumin/globulin ratio (A/G ratio) and total bilirubin in males at 200 and/or 600 mg/kg. Increased weights of spleen, liver, brain, heart, kidneys, and ovarys and decreased thymus weights were noted in rats. In histopathological examination, red pulp hyperplasia of spleen and bone marrow hyperplasia of femur were observed at 22, 67, 200, 600 mg/kg and extramedullary hematopoiesis of liver at 200 and 600 mg/kg in both sexes. Also significant increases of thymus atrophy were observed in females at 200 and 600 mg/kg. The Low observed adverse effect level (LOAEL) for repeated dose toxicity of acetanilide was 22 mg/kg/day for male and female.

Genetic toxicity or mutagenicity. Several *in vitro* studies show that acetanilide is non-mutagenic to Salmonella typhimurium with or without metabolic activation (Goldman *et al.*, 1977, 1980; Wheeler *et al.*, 1975; Ogawa *et al.*, 1987; Sugimura *et al.*, 1976; Zeiger *et al.*, 1988). Most of the studies with mammalian chromosomal aberration test, Bacillus subtilis recombination assay and SCE assay show negative results (Sasaki *et al.*, 1983; Yoshida, 1980; Ishidate *et al.*, 1978; Tanooka *et al.*, 1977).

Regarding *in vivo* study, mammalian erythrocytes micronucleus test was performed by MOE using OECD TG 474 and the results showed acetanilide is not genotoxic (NIER[d], 2001).

Carcinogenicity. Information on carcinogenicity is available from the studies performed in both male and female of rats, mice and hamsters. However, carcinogenicity studies showed no evidence of tumor in liver, mammary gland, etc. (Blunck *et al.*, 1975; Yamamoto *et al.*, 1970; Wright, 1967). Even the 4th generation studies using mouse strains of ABC-A

revealed that there was no appearance of tumor in the mammary gland (Wright, 1967). Human data are not available at present.

Reproduction/Developmental toxicity. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) was conducted using Sprague-Dawley rats (MOE[b)], 2001). In this study, the rats were exposed to acetanilide at doses of 22, 67, 200, and 600 mg/kg/day for 30 days for male and for 39-50 days for female. No treatment-related changes in precoital time and rate of copulation, impregnation, and pregnancy were observed in any exposure level group.

At 200 mg/kg/day dose, there was a decrease in body weight gain at day 4 after birth in both male and female pups. Perinatal deaths were increased, and cyanosis and icterus in offsprings were observed in 600 mg/kg/day dose group. Viability index on day 4 was decreased in 600 mg/kg /day dose group and the No observed adverse effect level (NOAEL) for reproduction is 200 mg/kg/day. The body weight of pups was decreased from the dose level of 200 mg/kg/day, and NOAEL for developmental toxicity (offspring toxicity) is considered to be 67 mg/kg /day.

Other: Irritation; Sensitization; Corrosivity. According to the study performed by using OECD TG 404 (acute dermal irritation/corrosion) and TG 405 (acute eye irritation/corrosion), acetanilide was not irritating to skin but slightly irritating to the eyes of rabbit (Hoechst AG, 1991). It is described that labelling is not required. There are no available data for skin sensitization.

2) Initial assessment for human health

Acetanilide is converted to phenolic metabolite in the body that gives it an analgesic effect, however some are converted to aniline (aminobenzene) that is toxic. LD_{50} of oral toxicity was 1,959 mg/kg bw for male and female rats. This chemical is not irritating to skin but slightly irritating to the eyes of rabbit. There is no information available on skin sensitization. In accordance with an OECD TG 422 (combined repeated dose with the reproduction/developmental toxicity screening test), acetanilide was given by gavage at doses of 22, 67, 200 and 600 mg/kg/day to male rats for 30 days and female rats for 39-50 days. The adverse effects were red pulp hyperplasia of spleen, bone marrow hyperplasia of femur and decreased HGB, HCT and MCHC. The LOAEL for repeated dose toxicity in rats was 22 mg/kg/day for both sexes.

In reproduction/developmental toxicity study, no treatment-related changes in precoital time and rate of copulation, impregnation, pregnancy were found in any treated group. However, the viability of offsprings at 600 mg/kg/day and the body weight of pups at 200 mg/kg/day were significantly reduced. The NOAELs for reproduction and developmental toxicity are considered to be 200 mg/kg/day and 67 mg/kg/day, respectively. Most of in vitro mutagenic toxicity studies including Ames assay, mammalian chromosomal aberration test, Bacillus subtilis recombination assay and Sister chromatid exchange (SCE) assay showed negative results. Regarding in vivo study, mammalian erythrocytes micronucleus test performed by OECD TG 474 also showed negative result. Therefore acetanilide is not considered to be genotoxic. There are some evidences that this chemical is not carcinogenic in rats, mice and hamsters.

4. Hazards to the environment

1) Aquatic Effects

Ecotoxicity data have been generated in a limited number of aquatic species of algae, daphnid and fish.

Table 4. Summary of effects of acetanilide on aquatic organisms

Species	Exposure duration	Results (mg/l)	References
Algae :			
-Selenastrum capricornutum	72 hr	E_bC_{50} = 13.5	MOE c), 2001
Daphnid :			
- Daphnia magna	48 hr	EC_{50} > 100	MOE d), 2001
Fish :			
- Oryzias latipes	96 hr	LC_{50} > 100	MOE e), 1997
- Lepomis macrochirus	96 hr	LC_{50} = 100	Dawson et al., 1975/1977
- Menidia beryllina	96 hr	LC_{50} = 115	Dawson et al., 1975/1977

No data on prolonged fish toxicity and toxicity to terrestrial organisms are available. Results are summarized in Table 4 (Table 4).

2) Initial assessment for the environment

The estimation by EQC model of fugacity level I reveals that the majority of acetanilide will be distributed to water (98.57%). The chemical is readily biodegradable (68.7%) and it has a low potential for bioaccumulation (1.56). From the lowest acute toxicity value of algae, daphnid and fish, the predicted no effect concentration (PNEC) of 0.135 was derived using an assessment factor of 100, which is based on the 72 hr-E_bC_{50} of algae, 13.5 mg/*l*.

IV. CONCLUSIONS

Carried out by Korean government initiative, the SIDS of acetanilide is lack of solid information on exposure profiles that domestic chemical industries could desirably have undertaken of providing, while readily available data at the moment was rough information for use pattern or quantity of chemical produced. To produce a sound scientific basis for national risk assessment, the voluntary participation of domestic chemical industries should be encouraged.

Acetanilide was recommended as low priority for further work due to its weak toxicity and relatively low production volume despite of lack of its detailed exposure data. Member countries at the 13th SIAM agreed on this recommendation and no need for further investigation of acetanilide. In the system of OECD SIDS program if, given the hazard and use situation described in SIAR, a chemical is considered to warrant further testing and/or assessment beyond the initial assessment, SIAM also can recommend that the chemical is a candidate for further work regarded as post-SIDS. Also it is expected that this conclusion and recommendation will be applied by OECD member countries for national and regional priority setting, and all information resulting from the OECD SIDS program will be available world-wide.

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