J. ENVIRON. TOXICOL.
Vol. 20, No. 4, 375～383 (2005)

Risk Assessment of Iron dichloride in OECD High Production Volume Chemicals Program

Heekyung Bae※, Mi Kyoung Kim, Kyungsook Ahn, Yeonki Choi, Hyunju Koo, Hyun-Mi Kim, Jin-Gyun Na, Kwang-Soo Choi and Myungjin Kim

Environmental Exposure Assessment Division National Institute of Environmental Research, Kyongseodong, Seogu, Incheon 404-708, Korea

염화제일철에 대한 인체 및 생태 위해성평가

배희경※, 김미경, 안경숙, 최연기, 구현주, 김현미, 나진균, 최광수, 김명진

국립환경과학원 환경노출평가과

요 약

염화제일철은 2004년 OECD SIDS 프로그램으로 한국에서 위해성평가가 수행된 대량생산 화학물질로 1998년 화학물질 유통량조사에 의하면 우리나라에서 연간 100,000톤이 생산되었다. 본 연구에서는 염화제일철의 인체 및 환경적 영향에 대한 독성잠재성을 평가하기 위하여 OECD 테스트가이드라인에 따라 독성시험을 수행하였다.

인체영향을 확인하기 위한 급성경구독성시험과 급성경피독성시험에서 랫드의 반수치사량은 각각 300～2,000 mg/kg b.w.과 ＞2,000 mg/kg b.w.이었다. 반복독성시험의 무유해용량 (NOAEL)은 수컷 랫드는 125 mg/kg b.w./day, 암컷 랫드는 250 mg/kg b.w./day였고, 생식 및 발생독성시험에서 무유해용량은 암수 랫드 모두 500 mg/kg b.w./day로 관찰되었다. 약한 피부자극성을 보였으며, 안부식성 물질임이 관찰되었다. *S. typhimurium* 과 *E. coli* 균주를 이용한 복귀돌연변이시험에서 최고 농도인 5,000 μg/plate에서 유전독성을 보이지 않았으며, 마우스를 이용한 생체내 (*in vivo*) 소핵시험에서도 최고 농도인 50 mg/kg bw/day에서 소핵유발빈도의 증가를 보이지 않아 본 시험물질은 돌연변이 유발 물질이 아닌 것으로 평가되었다. 어류 (*Oryzias latipes*), 물벼룩 (*Daphnia magna*), 조류 (*Pseudokirchneriella subcapitata*)를 이용한 수생생물에 대한 급성독성시험 결과, 96시간 *Oryzias latipes*의 반수치사농도는 46.6 mg/L이었고, 48시간 *Daphnia magna*의 반수영향농도는 19.0 mg/L이었다. 또한 *Pseudokirchneriella subcapitata*의 72시간 반수영향농도는 성장률을 이용한 계산법으로 6.9 mg/L이었으며, 면적계산법으로는 3.8 mg/L의 성장저해가 관찰되었다. 어류와 조류의 경우는 부분적으로 pH의 변화에 따른 영향으로 평가할 수 있는데 어류시험에서 pH 중성시험용액에서는 100 mg/L 이상의 독성값을 나타내었고, 조류에서는 농도 12 mg/L 이상에서 pH 7 아래로 떨어짐을 확인할 수 있었다.

염화제일철은 생산 및 사용공정에서 작업자에게 흡입 혹은 피부로 노출될 가능성이 있으나 밀폐공간에서 사용되므로 노출이 적은 것으로 평가되었다. 3종의 수생생물의 독성결과로부터 염화제일철은 수생환경에서 중간정도의 해가 있으며, 우리나라에서는 직접적인 염화제일철의 소비자 노출은 없으나 환경중 노출이 우려됨에 따라 제19차 OECD 대량생산화학물질 초기위해성평가회의에서 환경 분야에 대해서

※To whom correspondence should be addressed.
Tel: +82-2-833-2521, E-mail: hkybae@to21.co.kr

는 추가연구 후보물질로 권고되었고, 인체 분야에서는 인체에 대한 유해성과 사용 패턴을 고려하여 추가 연구 우선순위가 낮은 물질로 권고되었다.

Key words : Iron dichloride, risk assessment, ecotoxicity, toxicity, exposure

INTRODUCTION

The OECD Screening Information Data Set (SIDS) is a cooperative effort of OECD countries designed to collect the information of risk assessment on High Production Volume (HPV) chemicals. The goals of the work include the collection of data needed for the initial assessment of these chemicals and the generation of data that are lacking. The SIDS initial assessment reports and the other background SIDS documents are in many cases a unique source of information, which has not been available before. Iron dichloride was implemented according to this program in 2004 and the chemical was produced about 100,000 tonnes/year in 1998 in Korea. European capacity of iron dichloride is estimated to be 250,000 tonnes /year of which about 80,000 tonnes/year is produced by the steel industry in 2004 (European Commission, 2004). In Korea, the chemical is mainly used as a supplementary cohesion agent to treat dye wastewater in textile, dye and paper manufacturing industries. A minimum set of hazard information on iron dichloride and the evaluation of the existing data and/or newly tested study draw conclusion on the potential risk of iron dichloride.

GENERAL INFORMATION ON EXPOSURE

Iron dichloride is a solid inorganic substance, white rhombohedral crystals and sometimes has a green tint and very hygroscopic. Its commercial form is liquid (Budavari *et al*., 1998). It is freely soluble in water with solubility of 650 g/L H_2O at 25°C (Lide, 2002). Vapor pressure, partition coefficient in n-octanol/ water and stability test in water according to the OECD TG 111 are not applicable for the salt of an inorganic substance (Table 1). In Korea, iron dichloride is produced by reaction of scrap iron with waste liquid hydrochloric acid in the continuous closed reactor and this chemical is mainly used as a supplementary cohesion agent to treat dye wastewater in textile, dye and paper manufacturing industries and as a raw material for iron trichloride production. In Europe iron dichloride is used for wastewater treatment, H_2S reduction, pigment and soil immobilization (European Commission, 2004).

1. Environmental exposure and fate

Iron dichloride is produced in a closed system and wastewater containing this chemical is recycled in manufacturing process. In the wastewater plants of textile, dye and paper manufacturing industries, dye sewage is treated with iron dichloride. Ferrous ion is oxidized to ferric ion, which is precipitated to form slurry. The slurry contains ferric hydroxide ($Fe(OH)_3$) and the supernatant of treated dye sewage is discharged to downstream. Environmental exposure of iron dichloride is expected to be very low and mostly ferric ion would be released (NIER[a], 2004). Photodegradation and biodegradation are not relevant for an inorganic compound. Environmental fate modeling cannot be performed with the available data. Bioaccumulation is not expected.

2. Human exposure

As for human exposure, there is a potential for exposure to workers via inhalation and dermal routes during the packaging or processing the raw material, cleaning of reaction tank or filtration after the reaction. But occupational exposure is controlled with personal protective equipment like goggles and gas filter mask and with ventilation in Korea. The sub-

Table 1. Identity and physical−chemical properties of iron dichloride

Elements	Summary
OECD name	Iron dichloride
Synonym	Iron chloride ($FeCl_2$) Ferrous chloride Ferrous chloride ($FeCl_2$) Ferrous dichloride Iron protochloride Iron (2+) chloride Iron (II) chloride Iron (II) chloride ($FeCl_2$) Iron (II) chloride (1 : 2)
CAS number	7758−94−3
Molecular formula	$FeCl_2$
Structural formula	Cl —— Fe —— Cl
Degree of purity	35.3% (Liquid, The Commercial Product)
Impurity	0.0005% Lead (Pb) 0.00094% Cadmium (Cd) 0.1% Manganese (Mn) 0.1% Free acid 0.1% Iron trichloride ($FeCl_3$) 16.9% Iron (Fe) 0.00946% Copper (Cu) 0.00443% Nickel (Ni) >40% water
Physical−chemical properties	Solid
Physical state	Liquid (The Commercial Product)
Water solubility	650 g/L at 25°C
Melting point	No data available
Boiling point	No data available
Vapour pressure	No data available
Classification in Korea	No classified as toxic chemicals in the Toxic Chemicals Control Act, Republic of Korea

stance is not classified as a hazardous chemical, which is monitored annually for workplace exposure in Korea. Monitoring data of iron dichloride for occupational exposure is not available. ACGIH TLV of iron dichloride is TWA 1 mg (Fe)/m^3. In the manufacturing factories, workers may be exposed to the mist of hydrochloric acid but monitoring data by personal air sampling of hydrochloric acid were under TLV−ceiling of 5 ppm (NIER[a], 2004). There is no direct use and there are no consumer products containing iron dichloride in Korea.

HAZARDS TO THE HUMAN HEALTH

1. Toxicokinetics, metabolism and distribution

Intestinal mucosa is the principal site for absorption of iron (Bingham *et al*., 2001). Generally, 2 ~15% of iron is absorbed by the gastrointestinal tract. Absorption is occurred in two steps. Ferrous ion is absorbed from the intestinal lumen into the mucosal cells and then transferred to plasma by transferrin (Bingham *et al*,. 2001; Klaassen, 2001). An adult human contains 3~5 g of iron usually.

About 65% of total body iron is found in blood as haemoglobin. About 10% of body iron is found in myoglobin and iron-requiring enzymes. The rest of iron (25%) constitutes the body iron pool as protein-iron complex (ferritin and hemosiderin), which are found in liver, bone marrow and spleen (Bingham *et al*., 2001; Klaassen, 2001). Excess ingested iron is excreted in bile, sweat, feces and urine. Total iron excretion is of the order of 0.5 mg/day (Klaassen, 2001).

2. Acute toxicity

The acute effects of iron dichloride exposure have been examined via oral and dermal routes in rats according to the toxicity test performed by OECD TG 423 and 402 (NIER[b], 2004; NIER[c], 2004). The LD_{50} value in acute oral toxicity of rats was between 300 and 2,000 mg/kg b.w. The typical clinical signs of tested animals at 2,000 mg/kg b.w. were nasal discharge, hypoactivity, piloerection, prone position, reddish change and edema on ears, fore-legs and hind-legs. At 300 mg/kg b.w., all animals showed hypoactivity and piloerection on day 1 and some animals showed soft stool on day 2. These clinical signs were recovered to the normal status from day 3. The necropsy of the tested animals at 2,000 mg/kg b.w. was showed hemorrhage on lymphatic nodes, stomach intestine and thymus. And there were hypertrophy of pancrease and spleen. In one dead animal of 300 mg/kg b.w., hemorrhage on lymphatic nodes and intestine was observed. There was no abnormality by microscopic examination of the survived animals of 300 mg/kg b.w. group after sacrificed on day 15.

Acute iron poisoning by accidental ingestion of iron-containing medicine is one of the most common toxicologic emergencies in young children. Toxic doses of elemental iron range from 20 mg/kg b.w. to more than 60 mg/kg b.w. Iron exerts both local and systemic effects, which is a result of cell death and tissue damage caused by metabolic acidosis. Ingestion of more than 250 mg/kg b.w. of elemental iron is potentially lethal (McGuigan, 1996; Klaassen, 2001).

The acute lethal dose (LD_{50}) in acute dermal toxicity was greater than 2,000 mg/kg of b.w. Following the test guideline (TG 402), the limit test (2,000 mg/kg b.w.) was performed in 5 male and 5 female Sprague-Dawley rats. Because there was no animal death during the test period, the study was concluded.

3. Repeated dose toxicity

The repeated dose toxicity study was conducted according to the OECD TG 422, Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Screening Test (NIER[d], 2004). The NOAEL values were 125 mg/kg b.w./day for male rats and 250 mg/kg b.w./day for female rats. The Sprague-Dawley rats were orally administered with iron dichloride at 0, 125, 250 and 500 mg/kg b.w./day for 42 days to male rats and 42～54 days to female rats. The clinical signs such as blackish stool and salivation were observed during the test period, but these were recovered within the recovery period. In the mortality results, while all male rats survived, there were three female deaths in 500 mg/kg b.w./day. Two of them were dead on day 38 and on day 46 of the treatment period, and the third one was dead during the recovery period, on day 51. The cause of death was gastrointestinal damages by the test substance. Water consumption was increased in both sexes of 500 mg/kg b.w./day treated groups. The rate of body weight gain showed statistically significant decrease in 250 and 500 mg/kg b.w./day male treated groups. For female rats, the dose-related change was not observed. Cases of diffuse black colored liver and hemorrhage with diffuse black pigmentation in necropsy opinion were caused by the test substance in male 500 mg/kg b.w./day group, but these were recovered during the recovery period.

Absolute and relative weights of liver and adrenal glands were changed in 250 and 500 mg/kgb.w./day for male groups and 500 mg/kg b.w./day for female

group. Cases of hemosiderin deposits in hepatocyte and hyperplasia of zona fasciculate in adrenal cortex were observed. The sensory reactivity, the auricle reflex and corneal reflex tests, in male and female test groups were not different from control groups. There were no specific findings in urinalysis. In analysis of blood, statistically significant differences were found in mean cell volume (MCV), eosinophils (EOS), platelet (PLT), cholinesterase (CS), and triglycerides (TG). But these were within the biologically normal range and there were no dose-dependent changes.

4. Reproductive/Developmental toxicity

Reproduction and developmental toxicity study of iron dichloride was performed in accordance with OECD TG 422 (NIER[d], 2004). Sprague-Dawley rats were treated orally at 0, 125, 250 and 500 mg/kg b.w./day. Male and female animals were dosed for 42 days and 42~54 days, respectively. For the reproduction toxicity, there was no significant difference in mating data and in pre and post implantation loss rate between the control and the treatment groups. NOAEL value was 500 mg/kg b.w./day for both sexes. For the developmental study, the crown rump length (CRL) of female neonates on postpartum day 4 was significantly shorter in 125 mg/kg b.w./day group. The decrease did not correlate with body-weight changes, which is a main growth and developmental index. There was no dose-dependence of CRL decrease. Therefore, it was concluded that the test substance did not influence the growth of neonates. There was a case of acaudate in 500 mg/kg b.w./day group. Because of the low frequency of occurrence, a teratogenic effect was not showed. The NOAEL for the developmental toxicity was 500 mg/kg b.w./day.

5. Genetic toxicity (*in vitro* and *in vivo*)

Bacterial reverse mutation test, OECD test guideline 471, was performed by GLP (NIER[e], 2004). Iron dichloride did not increase reverse mutations of *Salmonella typhimurium* (strains TA 98, TA 100, TA 1535 and TA 1537) and *Escherichia coil* (strain WP2 *uvr*A) with and without metabolic activation system at 33.3, 100, 300, 1,000, 3,000 and 5,000 μg/plate. There was no statistically significant difference up to the maximum test concentration of 5,000 μg/plate ($p > 0.01$). Precipitation was noted at doses of 1,000 μg/plate and above greater than 300 μg/plate. It was concluded that iron dichloride did not exhibit mutagenic activity to any test strains under the test conditions. Mammalian erythrocyte micronucleus test was negative in accordance with OECD TG 474 (NIER[f], 2004). Six mice per experimental and control groups were employed. Iron dichloride was dissolved in corn oil, and administered to the mice by intraperitoneal injection. It is concluded that iron dichloride did not induce gene mutation up to the dose of 50 mg/kg b.w./day. In the wing spot test of *Drosophila melanogaster*, trans-heterozygous larvae for the wing-hair mutations *mwh* and *flr* were orally treated at the third instar stage with iron dichloride. Negative result was obtained when the wings were inspected at the adult stage for spots expressing phenotypes of the markers (Ogawa *et al*., 1994).

6. Skin/Eye irritation

External contact of the eye with acidic iron salts such as the sulfate or chloride has caused transient irritation and inflammation. On prolonged contact with the conjunctiva they have been known to cause a local brown discoloration. Skin and eye contact may produce severe irritation and burns (OHM/TADS, 1985). Acute skin irritation study of iron dichloride was performed in rabbits according to the OECD TG 404 (NIER[g], 2004). 500 mg of iron dichloride was applied on the skin of male rabbits and the clinical signs were observed for 14 days. No dead animal during the test period and normal pattern of body weight increase was observed. However, there were erythema, scars and edema on the application sites of iron dichloride.

The eye irritation result was more severe. This toxicity test was performed to OECD TG 405 (NIER[h],

2004). Test animals were female rabbits. 100 mg of iron dichloride applied into a conjunctival sac of one eye and clinical signs were observed. Although there was no dead animal and normal body weight increase was observed, quite severe clinical changes were observed. The level 3 of opacity area (greater than three−quarters) was seen in cornea within 1 hour after the treatment. The degree of opacity was increased to the level 4 in 3 days and the iris was not discernible through the opacity. These cornea lesions were not recovered within the test periods. Iris was also affected by iron dichloride. Hyperaemia and destructed light−reactivity were seen on day 2 after the treatment. Severe redness, edema and swelling were also observed in conjunctiva within 1 hour. This swelling caused partial eversion of lids and more than half of lids were closed. Although the pathological lesions were recovered partially, the eyelids were transformed abnormally.

The results of histopathological examination showed lymphocyte infiltration in the conjunctiva and severe granulomatous legions in cornea. A purulent inflammation and corneitis were also observed in stroma of cornea. These symptoms were not reversible within the test period. However, the clinical signs showed in the early state were recovered within 21 days because the histopathological changes were not observed in the iris. As the result, iron dichloride caused severe corrosive effect on eyes.

7. Initial assessment for human health

The LD_{50} by acute oral toxicity test of iron dichloride for rats was between 300 and 2,000 mg/kg b.w. that showed moderate toxicity. Iron dichloride was less toxic by dermal application with the LD_{50} greater than 2,000 mg/kg. The erythma and edema induced on the application sites were very weak and recovered easily. The skin irritancy was low. Iron dichloride showed corrosive effects on the eyes. The pathological effects appeared immediately after the exposure. Severe opacity of cornea was induced and was not recovered within the test period. Although Grade 4 edema in conjunctiva was recovered within the test period, morphological changes occurred. Iron dichloride is a corrosive irritant on eyes. The NOAEL valu-

Table 2. Summary of toxic effects of iron dichloride

Acute toxicity	LD_{50} (rat, oral) = 300 ~ 2,000 mg/kg b.w. LD_{50} (rat, dermal) = 2,000 mg/kg b.w.
Repeated dose toxicity	NOAEL (rat) = 125 (male) and 250 (female) mg/kg b.w./day Male rat : dose−dependent decreases in mean bodyweight, increased water consumption and the organ weights of liver and adrenal glands in a dose−dependent manner, black colored liver, and hemorrhage in stomach Female rat : death, increased liver weight, and intermittently increased water consumption
Reproductive/Developmental toxicity	NOAEL = 500 mg/kg b.w./day for each sex No significant differences on fertility index (mating, fertility and gestation data), mean litter size, birth rate, survival rate, sex ratio and body weights of litters were exhibited compared to the controls.
Genetic toxicity	Not a mutagen Bacterial reverse mutation test (*in vitro*) : Negative Mammalian erythrocyte micronucleus test (*in vivo*) : Negative
Skin irritation/Corrosion	Weak irritant
Eye irritation/Corrosion	Corrosive
Human exposure	Acute poisoning : vomiting, abdominal pain, diarrhea, liver failure, coma

Table 3. Effects of iron dichloride on aquatic organisms

Organisms	Species	Results	Test condition
Fish	*Oryzias latipes*	LC_{50} (96 hrs) = 46.6 mg/L	OECD TG 203 (static, measured conc.)
Invertebrate	*Daphnia magna*	EC_{50} (48 hrs) = 19.0 mg/L	OECD TG 202 (static, measured conc.)
Algae	*Pseudokirchneriella subcapitata*	EC_{r50} (72 hrs) = 6.9 mg/L EC_{b50} (72 hrs) = 3.8 mg/L $NOEC_r$ = 2.4 mg/L $NOEC_b$ = 1.1 mg/L	OECD TG 201 (static, measured conc.)

es for the repeated toxicity were 125 mg/kg b.w./day in male rats and 250 mg/kg b.w./day in female rats, the changes of body weights, clinical signs, water consumption, organ weights, necropsy opinions, and histopathology were the determining factors for NOAEL. In the reproduction and developmental toxicity, there was no significant difference up to the maximum test concentration between the control and the test groups. The NOAEL was 500 mg/kg b.w./day for both sexes. Iron dichloride was not a mutagen according to the bacterial reverse mutation test and mammalian erythrocyte micronucleus test (Table 2).

HAZARDS TO THE ENVIRONMENT

1. Aquatic effects

Iron dichloride has been tested for aquatic toxicity in three trophic levels including fish, daphnia, and algae. Results are summarized in Table 3. All of the aquatic acute tests were performed in accordance with the principles of GLP. In acute toxicity tests of fish and algae, the test solution became acidic. A preliminary test was conducted to show the effect of pH on fish. 100 mg/L of iron dichloride was dissolved and pH of the test solutions was adjusted to 3.5, 4.0, 4.5, 5.0, 5.5 and 6.0. The mortality was affected at pH 3.5 only. Increase of mortality at 96 hours presumed on account of lower pH gradient. In case of algae, the test solutions of 12, 22 and 44 mg/L concentration became acidic after 72 hours. The acidic condition of test solution affected growth of algae. Differently from fish and algae, the pH of test solutions for daphnia remained neutral due to the buffering action of M4 medium (NIER[i], 2004; NIER[j], 2004; NIER[k], 2004).

Reproduction test of *Salmo gairdneri* for iron dichloride tetrahydrate ($FeCl_2 \cdot 4H_2O$) was studied. Spermatozoa, ova and fertilization were tested by 1985 method of Billard and Roubaud. The gametes were exposed independently for 40 min to iron dichloride tetrahydrate added into diluents. The ovum diluent (insemination diluent, ID) was a NaCl solution (osmotic pressure: 250 mOsm kg^{-1}, pH 9.0, Tris 20 mM, glycine 50 mM). The spermatozoa were diluted at 10^{-1} and 10^{-2} of ID and the same diluent with K^+ added; they were immobile in this diluent (a conservation diluent). Insemination was carried out after the gametes had been washed. Ova and spermatozoa were mixed together in ID containing the test chemical (insemination test). Iron dichloride tetrahydrate in solution had toxic effects on spermatozoa from less than the concentration of 0.005 mg/L at an insemination dilution of 10^{-2} and from 0.73 mg/L at an insemination dilution of 10^{-1}. A similar sensitivity was found for ova (from 0.73 mg/L) and a higher sensitivity for fertilization (from 0.08 mg/L) (Billard and Roubaud, 1985).

2. Initial assessment for the environment

Iron dichloride is freely soluble in water and due to its inorganic properties no data are applicable for vapor pressure and partition coefficient in n−octanol/

water. Photodegradation and biodegradation are not relevant for an inorganic compound. Environmental fate modeling cannot be performed with the available data. Bioaccumulation is not expected.

The following acute toxicity tests with aquatic organisms are available:

Oryzias latipes: LC_{50} (96 hrs) = 46.6 mg/L

Daphnia magna: EC_{50} (48 hrs) = 19.0 mg/L

Pseudokirchneriella subcapitata EC_{r50} (72 hrs) = 6.9 mg/L, EC_{b50} (72 hrs) = 3.8 mg/L

For fish and algae, the observed effects are partially due to pH effects. For fish, no mortality was observed up to 100 mg/L in a neutralized solution. For algae, test solutions dropped below pH 7 at test concentrations of 12 mg/L and above. No data are available for terrestrial organisms. From the endpoint of aquatic organisms of the three trophic levels, iron dichloride is moderate toxic in aquatic environment.

CONCLUSIONS

Based on the results from several ecotoxicology and toxicology data, iron dichloride is considered to possess properties indicating a hazard for human health (corrosive) and environment and is also needed to perform an exposure assessment, and if then necessary a risk assessment due to the possibility of environment exposure. Iron dichloride is produced in a closed system and exposure to workers during the processing of the chemical is low. Consideration should be given to the ongoing assessment of other iron salts in the OECD HPV Chemicals Program. Therefore, iron dichloride was recommended as a candidate for further work in environment and currently of low priority for further work in human health in OECD SIAM 19 held in 2004.

ACKNOWLEDGMENT

We would like to thank LGLS, Korea Institute of Toxicology, Korea Testing and Research Institute for Chemical Industry, and Biotoxtech for supplying the results and the recommendations.

REFERENCE

Billard R and Roubaud P. The effect of metals and cyanide on fertilization in rainbow trout (Salmo gairdnen), Water Res 1985; 19(2): 209−214.

Bingham E. Barbara Cohrssen and Charles H. Powell (eds.). Patty's toxicology. 5th ed. New York: John Wiley & Sons, Inc. 2001; 176−177.

Budavari S, O'Neil M, Smith A, Heckelman and Kinneary J. The Merck Index, An Encyclopedia of Chemicals, Drugs and Biologicals, 12nd Edition on CD−ROM Version 12: 2, Chapman & Hall /CRC., 1998.

European Commission. Integrated Pollution Prevention and Control−Draft Reference Document on Best Available Techniques in the Large Volume Inorganic Chemicals−Solid and Others Industry Draft August 2004, http://eippcb.jrc.es.

Klaassen CD. Casarett and Doull's Toxicology. 6th ed. New York: Macmillan Publishing Co., 2001. chapter 23.

Lide DR. ed., CRC Handbook of Chemistry and Physics on CD−ROM, Version, Chapman & Hall /CRC 2002.

McGuigan MA. Acute iron poisoning, Pediatric Annals 1996; 25: 33−38.

National Institute of Environmental Research (NIER[a]), Korea, Survey on circulation volume and use pattern of iron dichloride in Korea, 2004.

National Institute of Environmental Research (NIER[b]), Korea, Iron dichloride (CAS No.: 7758−94−3): Acute oral toxicity study in rats (Study No. S784), Tested by LG Life Sciences/Toxicology Center, 2004.

National Institute of Environmental Research (NIER[c]), Korea, Iron dichloride (CAS No.: 7758−94−3): Acute dermal toxicity study in rats (Study No. S785), Tested by LG Life Sciences/Toxicology Center, 2004.

National Institute of Environmental Research (NIER[d]), Korea, Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in rats (Study No. B04024), Tested by Biotoxtech, 2004.

National Institute of Environmental Research (NIER[e]), Korea, Iron dichloride (CAS No.: 7758−94−3): Reverse mutation in four histidine−requiring strains of *Salmonella typhimurium* and one tryptophan−requiring strain of *Escherichia coli*. (Study No. S786), Tested by LG Life Sciences/Toxicology Center, 2004.

National Institute of Environmental Research (NIER[f]), Korea, Iron dichloride (CAS No.: 7758−94−3): Induction of micronuclei in the bone marrow of treated mice (Study No. S787), Tested by LG Life Sciences/Toxicology Center, 2004.

National Institute of Environmental Research (NIER[g]), Korea, Iron dichloride (CAS No.: 7758−94−3): Acute dermal irritation study of iron dichloride, 98% (CAS No: 7758−94−3) in rabbits, Tested by KOTRIC, 2004.

National Institute of Environmental Research (NIER[h]), Korea, Iron dichloride (CAS No.: 7758−94−3): Acute eye irritation study of iron dichloride, 98% (CAS No: 7758−94−3) in rabbits, Tested by KOTRIC, 2004.

National Institute of Environmental Research (NIER[i]), Korea, The acute toxicity of iron dichloride to fish (Report No. EG04007), Tested by KRICT, 2004.

National Institute of Environmental Research (NIER[j]), Korea, The acute toxicity of iron dichloride to *Daphnia magna* (Report No. EG04008), Tested by KRICT, 2004.

National Institute of Environmental Research (NIER[k]), Korea, Growth inhibition test of iron dichloride to algae (Report No. EG01003), Tested by KRICT, 2001.

Ogawa HI, Shibahara T, Iwata H, Okada T, Tsuruta S, Kakimoto K, Sakata K, Kato Y, Ryo H and Itoh T. Genotoxic activities *in vivo* of cobaltous chloride and other metal chlorides as assayed in the *Drosophila* wing spot test, Mutation Research 1994; 320: 133−140.

OHM/TADS, Developed by office of water and waste management of the United States environmental protection agency. 1985.