Evaluations for Establishing Voluntary Operating Standards for chlorine dioxide

- Gas product -

2014 March

Japan chlorine dioxide Manufacturers Association

<Background of deliberation>

February 13, 2013 19th Japan Chlorine Dioxide Industry Association Standards Committee

February 21, 2013 5th Japan Chlorine Dioxide Industry Parent Committee, 20th Japan Chlorine Dioxide Industrial Standards Committee

March 22, 2013 21st Japan Chlorine Dioxide Industry Standards Committee

April 26, 2013 The 22nd Japan Chlorine Dioxide Industry Standards Committee

May 30, 2013 The 23rd Japan Chlorine Dioxide Industry Standards Committee

June 24, 2013 The 6th Japan Chlorine Dioxide Industry Parent Committee, 24th Japan Chlorine Dioxide Industrial Standards Committee

July 16, 2013 The 25th Japan Chlorine Dioxide Industry Standards Committee

August 22, 2013 The 26th Japan Chlorine Dioxide Industry Standards Committee

September 18, 2013 27th Japan Chlorine Dioxide Industry Association Standards Committee

September 20, 2013 7th Japan Chlorine Dioxide Industry Parent Committee 28th Japan Chlorine Dioxide Industrial Standards Committee

October 23, 2013 The 29th Japan Chlorine Dioxide Industry Standards Committee

November 19, 2013 30th Japan Chlorine Dioxide Industry Association Standards Committee

December 20, 2013 31st Japan Chlorine Dioxide Industry Association Standards Committee

January 22, 2014 The 32nd Japan Chlorine Dioxide Industry Standards Committee

January 23, 2014 8th Japan Chlorine Dioxide Industry Parent Committee, 33rd Japan Chlorine Dioxide Industrial Standards Committee

<Parent Committee Roster>

Akika Nishikawa (Chairman)

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<List of committee members of the Japan Chlorine Dioxide Industry Standards Committee>

Noriaki Moriguchi (Chairperson)

Hiroaki Koyama (Vice Chairman)

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I. Summary

Chlorine dioxide (ClO2) is a powerful oxide, including influenza-containing viruses, germs, and mushrooms.

End-use products that use these gases are SPATIAL SANITIZER products.

Used for the safe use of sugar, bacterium, and odor prevention measures.

Some criteria are required.

There is little insight into the security of chlorine dioxide gas.

Dalhamn is approx. 10ppm per rat

Exposure of chlorine dioxide gas (Note 1) for 9 days in 4 hours/day and 14 days, and all deaths during the administration period

It is reported.

On the other hand, exposures of about 0.1 ppm, 5 hours a day, and about 10 weeks are not among the deaths

The company said there were no clinical signs of poisoning or toxicity.

Paulet & Desbrousses is in rats or

5 or 10 ppm of chlorine dioxide gas was exposed to rabbits for 2 hours/day and 30 days/day, resulting in increased leukopenia.

And for 2.5 ppm, four to seven hours per day, 30 or 45 days of exposure to pulmonary disease (bronchial and alveolitis)

For 1 ppm, five hours a day, five days a week, and ten weeks of exposures in rats, despite the evidence of bleeding alveolitis

Epidermal or substantive injury in addition to evidence of pulmonary venous congestion and slight edema around the tinulous bulbs

The company said it was not allowed.

In a recent study, Akamatsu and his colleagues reported 0.05 and 0.0 1 ppm for rats

No abnormal findings after 24 hours a day, 7 days a week, and 6 months of chlorine dioxide gas exposure

The company says it wants.

Ogata et al. conducted a follow-up study on Paulet & Desbrousses in rats (1)

We performed mil × 5h per day × 5d per week × 10 weeks) and reported no signs of toxicity.

One of the reasons for this is the Paulet & Desbrousses trial, although the authors say the cause is unknown.

Still, we speculate that there was large variability in chlorine dioxide gas concentrations, and thus the 1 ppm is smallest.

Toxicity (LOAEL) is assumed to approximate Non-Toxicity (NOAEL).

U.S. OSHA is responsible for inhaling chlorine dioxide from an occupational safety and health perspective
Set a standard of 0.1 ppm for exposure with an 8-hour weighted-average (PEL-TWA) of acceptable exposure levels.
You do.
World Health Organization (WHO) also estimates of available occupational exposure data (UK) and
By using the Estimation and Assessment of Substance Exposure (EASE) models
0.1 ppm is obtained for the maximum possible exposure concentration (8-hour-weighted mean) from the exposure concentration
Compared to the NOAEL, this is derived from a very limited number of observations.
Numbers that do not require concerns about airways or eye stimulation of workers exposed to chlorine dioxide in the workplace
The company says. U.S. Environmental Protection Agency (U.S. EPA) Paulet & Co. for 24-hour exposures
In a series of Desbrousses results, particularly in the lungs without substantial changes in pathology at 1 ppm exposures
1 ppm of LOAEL with an emphasis on venous congestion and slight edema around tinuous branches
The uncertainty coefficient (UF) multiplied by 3,000 times (10 times the individual variance multiplied by 3 times the species variance multiplied by the subacuteness test result)
Apply an extrapolation of 10 times from the results × 10 times using LOAEL, etc. and apply a reference concentration (RfC) of 0.00007.
As a ppm, the U.S. Administration for Disease Registration of Hazardous Substances (U.S. ATSDR) increased UFs by 300 times (10 times the individual variance)
Note 1) As used herein, "ppm" is the volume ratio of all gases, i.e., volume/volume (v/v). i.e.
The ratio of the volume of chlorine dioxide gas to the volume of air-mixed gas.
Three-fold difference in species × 10-fold extrapolation using LOAEL, etc., and the minimum-risk level (MRL) is 0.001 ppm.
It is set as.
However, the underlying Paulet & Desbrousses results are followed
They are rejected in their follow-up tests.
The Industry Association is fully aware of the safety of chlorine dioxide gas, and the following Indoor Concentrations Guidelines are noted in Note 2.

Chlorine dioxide was established as a voluntary standard by the Industrial Association. The guideline will be implemented by October 2015 and new knowledge will be obtained. Changes should be made based on the results of such changes.

1. Guideline values for indoor concentrations (voluntary standards of the Chlorine dioxide Industries Association) shall be 0.01 ppm Note 3.
2. Rationale
The Industrial Association has adopted the results of the first participants, which have been reaffirmed, as a NOAEL, and has also adopted a dichloromethane system.
Health effects on inhalation of chlorine chloride gas are limited to local injuries, the extent of which is concentration dependent.
This is probably the case, so the 1 ppm of labs multiplied by 5 h/day × 5 d/week × 10
1 ppm (2.8 mg/m3), which is the exposure amount after weekly administration, was used to calculate the indoor concentration guideline value.
I used.
The Indoor Concentration Guidelines (voluntary standards of the Chlorine dioxide Industries Association) set this NOAEL at 90
By dividing by UF (10-fold differences in individuals × 3-fold differences in species × 3-fold extrapolations from the results of sub-acute testing)
And that.
These figures are derived based on the Occupational Safety and Health Standards and are based on formal standards.
It is also supported by the values derived with reference to the evaluation of health effects of rudehyde.

II. Summary of substances subject to evaluation
Chlorine dioxide (ClO2) is a powerful oxide, including influenza-containing viruses, germs, and viruses?
It is thought to be useful for mushrooms, etc.
Ogata et al. 1) was effective in rats exposed to influenza virus and low concentrations of chlorine dioxide gas.
The company is considering the possibility of reducing influenza outbreaks due to chlorine dioxide gas exposures.
Mimura et al. 2) is a forward-looking cohort study in the presence of low concentrations of chlorine dioxide gas.
This suggests the possibility of reducing influenza infections.

Also, Morino et al. 3) is CO2.
It is reported that chlorofluorogas exposure reduces fungal mycelium growth.
To its mechanism of action
2) Significance of indoor concentration guideline value
Based on the scientific findings on toxicity currently available, humans consume air at that concentration for a lifetime
Calculated values that are deemed to be unaffected by adverse effects on health.
3. Meaning of chlorine dioxide gas's Independent Concentration Guidelines (voluntary standards of the Japan chlorine dioxide Manufacturers Association)
This is an indicator of the concentration of gas when chlorine dioxide gas is at a steady state. The concentration of gas is 2, immediately after the gas is generated (opened).
It does not regulate the concentration of chlorofluorocarbons.
Regarding the chlorine dioxide gas concentration level immediately after the occurrence of the gel-type and the solid-type
The rules shall be stipulated.
Introduction 4) is a test using model protein, and its effect is mainly on the denaturing action of protein.
This is because the triptophan and tyrosine groups of the constituent amino acids are covalent bonds.
The company expects to exert its effects by modifying.
Ogata 5) also type A influenza
In a viral surface protein, hemagglutinin, in a test with H1N1
Virus-making by Oxidizing the 153rd Amino Acid Tryptophan Residue
Changes in body structure, impairs receptor bonds with host cells, and deters viral infection
The company says.
For end-use products used in Japan, Gel is a product aimed at SPATIAL SANITIZER.
Types and solid (powders, granules, tablets, etc.) are available.
Gel-type products include offices, classrooms, residential rooms (bedrooms, living rooms, etc.), bathrooms, toilets, and washstands.
Removal type or hanging type around kitchens or around pets, etc., and viruses are excluded.
Use for elimination, SPATIAL SANITIZER, anti-molds, and deodorization purposes.
Solid type: chlorine dioxide generated solid type is water content and/or CO2 in the air.
Responding to carbon to naturally generate chlorine dioxide, such as residential rooms (bedrooms, living rooms, etc.), kitchens,

Virus removal, SPATIAL SANITIZER, and deodorization in entrances, washrooms, closets, lockers, etc.
Used for.
Also, mechanically generate chlorine dioxide and use air-conditioning facilities for airports, hotels, and hospitals
Removal, SPATIAL SANITIZER, anti-fungi, and fire of viruses floating in spaces at large-scale facilities, etc.
Low-concentration chlorine dioxide gas generators are also used for odor.

1. Chemical name, molecular formula, molecular weight, etc.

Japanese name	二酸化塩素
English name	chlorine dioxide
CAS No.	10049-04-4
Molecular formula	ClO2
Molecular weight	67.5

2. Physicochemical properties

Physical properties	Red to yellow gas at room temperature with pungent odor
Melting point	-59 ° C
Boiling point	11 ℃
Specific gravity	1.6 (water = 1, liquid: 5 ℃)
Water solubility	0.8 g / 100 mL (20 ° C)
Vapor pressure	101 kPa (20 ℃)
Relative vapor density (air = 1)	2.3
Explosion limit	10 vol% (air)

3. Assay (chlorine dioxide)
See Attachment for test methods.
4. Safety Studies
1) Pharmacokinetics and Metabolism
There are no data available on inhalational and dermal exposures to chlorine dioxide gas.
Chlorine dioxide itself is extensively absorbed and distributed throughout the body via these pathways
It is unlikely.
"Chlorine dioxide toxicokinetic data are limited, but unchanged dioxide data are

available," WHO6 concluded.
"It is unlikely that chlorine is significantly absorbed and distributed throughout the body by the dermal or inhalation routes."
It is stated.
This view is strongly supported by the results of the article 4).
This theory
According to the sentence, "chlorine dioxide reacts very quickly with protein and may enter the body."
Nevertheless, it reacts with proteins on the body surface at an early stage and reaches the blood and even the whole body.
"It's hard to think."
The U.S. ATSDR7 also "has a higher chlorine dioxide."
In doses adequate for direct systemic toxic effects of chlorine dioxide due to reactivity
It is unlikely to be absorbed.
Gastrointestinal, musculoskeletal, endocrine, skin, and metabolic effects
"No report was found," and U.S. EPA8. "Respiration of chlorine dioxide gas"
"No results on absorption into the organ pathway can be found," the researchers note....
2) Toxicity
(1) Acute toxicity
i) Inhalation exposure studies
Following exposure of 1 guinea pig to 150 ppm of chlorine dioxide gas for 44 minutes
The patient died.
No deaths occurred following exposure to the same concentration for 5 or 15 minutes.9)
Ii) Dermal exposure studies
Is it possible to confirm the dermal toxic results of chlorine dioxide gas exposures?
I got stuck.
As a reference, the results of dermal administration of the chlorine dioxide dissolved solution 10 and 11) are shown below.
Rats were dermally applied to the back for 24 hours with 2,000 mg/kg body weight of chlorine dioxide solution
No deaths or clinical signs were observed, and the lethal dose was 2,000 mg/kg body weight (subtotal).
The body weight was estimated to be 20 mg/kg or more as chlorate ion.
(2) Eye irritation
The results of the eye irritation test with chlorine dioxide gas cannot be confirmed.
I got it.

As a reference, the results of the intraconjunctival injection study of chlorine dioxide solution 12) are shown below.
To rabbits add 0.1mL of chlorine dioxide solution (1.858ppm as chlorite ion)
After intramembranous administration, mild redness and edema of the conjunctiva were observed from 24 hours after administration.
Redness disappeared from 72 hours to 5 days after administration, and edema disappeared after 72 hours.
No changes were observed in the cornea or iris.
(3) Short-term toxicity
Dalhamn (1957) 13) reported four studies in rats.
①3 In rats at very high concentrations of chlorine dioxide gas at 3-min intervals for 1 week
3 Exposure (approx. 3,400 ppm (Day 1)→1,100 ppm) by a stepwise reduction in spray dose
(8 Day) →800 ppm (Day 16).
The result is marked respiratory depression,
Body weight gain was observed in control rats, whereas body weight was decreased in exposed rats
I did.
Histological examination revealed new bronchopneumonia lesions and congestion at the renal corticomedullary junction in 3 animals
2 It was observed in animals.
②4 The rats were exposed to approximately 260 ppm of chlorine dioxide gas for 2 hours.
As a result,
Lacrimation and epistaxis were particularly prominent, and 1 animal died approximately 1 hour after exposure.
For survival
Three animals were necropsied immediately after 2 hours of exposure, and all four animals showed appearance of kidney, liver, spleen and lung.
Microscopic examination showed pulmonary edema and circulatory congestion.
③5 In rats at a chlorine dioxide gas of about 10 ppm 4 h/day for 9 days
The animals were exposed for a day.
Consequently, writhing due to rhinorrhea and dyspnea in exposed rats
The condition was observed, and the body weight was decreased.
1 animal 10 days after exposure, 2 animals 12 days after exposure, 13 days
The remaining two animals died later.

④5 Approximately 0.1 ppm of chlorine dioxide gas to a rat for 5 hours a day for about 10 weeks
I was exposed.
No notable changes were seen during the exposure period, no weight loss, and no kidneys, liver
Histological examination of the lung and lung was also normal.
Paulet & Desbrousses (1970)14) is four in rats and rabbits
Studies are reported.
① 10 ppm of chlorine dioxide gas for 5 male and female rats for 2 hours a day, 30 days
I was exposed.
Resulting in localized bronchopneumonia with nasal discharge, ocular hyperemia, and desquamation of the alveolar epithelium
There was.
Increases in red blood cell and white blood cell counts were observed, and weight gain was mildly suppressed.
It was controlled.
② Chlorine dioxide gas of 5 ppm was administered to 5 rats/sex and 4 rabbits at 2 hours/day
The animals were exposed for 30 days.
Similar effects on the respiratory tract were observed.
The severity was mild.
No significant changes in red blood cell or white blood cell counts were observed, and the body
No inhibition of weight gain was observed.

③ 2. 5 ppm of chlorine dioxide gas for 10 males and males, 7 hours a day, 30 days a day
I was exposed.
As a result of lymphocytic infiltration into the alveoli, alveolar congestion, alveolar hemorrhage, and epithelium
Erosion and inflammatory infiltration in the trachea were observed.
With few changes in RBC and WBC counts
Body weight gain was mildly suppressed.
Rats in this group will be necropsied 15 days after the end of exposure
However, recovery from lung injury was significant.
④ Eight rabbits were exposed to 2.5 ppm of chlorine dioxide gas for 4 hours a day for 45 days.

Alveolar congestion and alveolar hemorrhage were observed.
Red blood cell and white blood cell counts almost changed.
There was no increase in body weight and no adverse effect on body weight gain.
Rabbits in this group also completed exposure 15
Although necropsy was performed at a later date, recovery from lung injury was prominent.
The liver was 2.5, 5.0, and 10 ppm of chlorine dioxide moth in rats and rabbits.
It was not affected by soot exposure.
Paulet & Desbrousses (1972) 15) conducted an additional study on 8 rats
The 1 ppm was exposed to chlorine dioxide gas for 5 hours a day, 5 days a week, and 10 weeks.
That
Venous congestion and slight peribronchiolar oedema were observed in the lungs of exposed rats
However, no changes were observed in the epithelium or parenchyma.
Red blood cells and white blood cells
No changes in blood cell count or body weight gain were observed.
On the basis of these results, EPA use the lowest-observed-adverse-effect level (LOAEL) as the 1 ppm.
However
The key to this paper is how the chlorine dioxide gas is generated and how its concentrations are controlled.
The method and the method of measurement should not be described at all.
Paulet & Desbrousses (1974)16) 5, 10 and 15 ppm/10-15 rats
The animals were exposed to chlorine dioxide gas for 15 minutes twice or four times daily for 1 month.
Its consequences
1/10 and 1/15 rats exposed to fruit, 15 ppm at a time, 2 or 4 times a day, respectively
The patient died.
Weight loss was observed in both groups, and histological findings included nasal and ocular inflammation and increased secretions.
Alveolar catarrhality with more pronounced bronchiolar infiltration in the bronchitis 4 times daily exposure group
Injury was observed.
Pulmonary alveolar damage was observed 15 days after the end of exposure, similar to the findings in the control.

It was reversible because it was shown.
No changes were observed in the liver.
Alveolar irritation and reduced body weight gain were observed in ppm exposure, but not in 5 ppm exposure
Bed signs, weight gain, pulmonary histopathology or haematology parameters
No adverse effects were observed.
Ogata et al. (2013) 17 rat females aged 5 weeks acclimated for 1 week prior to testing
Expose 8 males to 1 ppm of chlorine dioxide gas for 5 hours a day, 5 days a week, and 10 weeks
A repeat test of Paulet & Desbrousses (1972) 15) was carried out.
1 hour after the start of exposure
Chlorine dioxide gas concentrations measured in the center of the chamber were 1.02 ± 0.07 throughout the entire study.
It was ppm.
Macroscopically, there were no differences in body weight over time and clinical signs.
The patient was in good health.
The macroscopic findings at necropsy were also normal, and the resected lung, liver,
The right and left kidney weights did not differ from those of the control group.
On blood and blood chemistry values
No effects on metabolism or bone marrow function were observed.
Appearance of bronchoalveolar lavage smears
No effects of chlorine dioxide gas on the respiratory tract were observed microscopically.
In the Paulet & Desbrousses study as one of the factors that differ in outcome
Speculate that the variability in chlorine dioxide gas concentrations may have been large (at low concentrations)
Precise control of chlorine dioxide gas concentrations requires considerable skill
Of the technique (test conditions) and the methods of determination are entirely lacking, and 1 ppm
As the lowest-observed-adverse-effect level (LOAEL) should be rewritten to the no-observed-adverse-effect level (NOAEL)
I'm doing.
(4) Medium-and long-term toxicity
Akamatsu et al. (2012)18) are 0, 0.05, and 0.1 ppm for sixteen males and females of approximately five-week age.
Chlorine dioxide gas was exposed for 24 hours a day, 7 days a week, for 6 months.
During the study period

The indoor chlorine dioxide gas concentrations were 0.054 ± 0.007 (0.047-0.060) ppm in the low-concentration group,
It was 0.103 ± 0.011 (0.075 to 0.120) ppm in the high-concentration group.
As a result, all study periods
No signs of toxic effects attributable to chlorine dioxide gas were observed throughout the study, and body weight gain, food, and body weight gain were observed.
Water intake, organ weights, blood and blood chemistry parameters, necropsy findings, and histopathology
In toxicities attributable to chlorine dioxide gas, including the target organ of respiration
Not possible
(5) Reproductive and developmental toxicity
No evidence of reproductive or developmental effects of chlorine dioxide gas
I got it.
As a reference, the chlorine dioxide dissolved solution is summarized in the following reports 10 and 11.
Teratogenic changes in fetuses of rats and rabbits during embryonic organogenesis
No transformation was observed.
There were no effects on pregnant dams.
(6) Carcinogenicity
It was not possible to confirm the carcinogenicity results of chlorine dioxide gas.
For reference, sodium chlorite is summarized in the following report 11).
Following long-term administration of sodium chlorite to mice or rats in drinking-water,
No significant increase in tumours was observed.
(7) Genotoxicity
It was not possible to confirm the genotoxicity results of chlorine dioxide gas.
As a reference, the chlorine dioxide dissolved solution is summarized in the following reports 10 and 11.
Negative for bacterial gene mutagenesis in reverse mutation assay
I got bad.
Positive clastogenicity to CHL/IU cells in chromosomal aberration test
It was judged to be sex.
Negative micronucleus test, clastogenicity or inhibition of spindle formation
It was concluded that there was no effect.
(8) EFFECTS ON HUMANS
For U.S. ATSDR7) informations on the mortality of humans exposed to chlorine dioxide gas,

Bleaching-tank workers died (Elkins 1959) after exposure for an indeterminate period of time
It is stated that the concentration in the tank was 19 ppm.
U.S. ATSDR7) is also the primary source of chlorine dioxide gas from limited human data
To respiratory tract irritation and to eye irritation by workers in a sulfite pulp production facility
In response to a relatively high level of chlorine dioxide gas due to device failure
With Gloemme and Lundgren 1957 of eye discomfort with chlorine
She noted that she was also exposed to sulfite.

5. Evaluation by international organizations
1) U.S. OSHA 19), Industrial Health and Safety Experts Conference ACGIH 20
The ACGIH is based on the tolerable concentrations of chemicals to which workers are exposed in the workplace.
8-h weighted mean (TLV-TWA) of 0.1 ppm, 15-min limit (TLV-STEL)
The criterion of 3 ppm is set at 0.
U.S. OSHA is also a dioic acid from the viewpoint of occupational safety and health
Acceptable exposure concentrations for inhaled exposure to chlorine are 0.1 on an 8-h weighted mean (PEL-TWA)
It is ppm.
In the Concise International Chemical Assessment Document 6, the World Health Organization (WHO)
Measurements of available occupational exposures (U.K.) and Estimation and Assessment of
Be considered from the exposures estimated using the Substance Exposure (EASE) models
A maximum-exposure level (8 h-weighted mean) of 0.1 ppm is obtained, with this value being extremely high
Chlorine dioxide in the workplace compared with NOAEL, although derived from limited data
As values that do not require concern about irritation of the respiratory tract or eyes of exposed workers
I have.
2) National Advisory Board on AEGL Development (AEGL Committee) 21
AEGL Committee dioxide, one of the business organizations of the National Academy of

Sciences
Guideline values for acute chlorine exposure are AEGL-1 at 8-hour exposure (so-called discomfort levels)
0.15 ppm, AEGL-2 (the so-called injury levels) 0.45 ppm, AEGL-3 (the so-called injury levels)
The lethal level is set at 0.98 ppm.
3) U.S. Environmental Protection Agency (U.S. EPA) 8)
U.S. EPA conducted a series of Paulet & Desbrousses results in terms of 24-hour exposures, 14
~16)、 Minimal peribronchiolar area without parenchymal changes, particularly in the pathology of 1 ppm exposures
The 1 ppm of LOAEL is to emphasize the presence of oedema and venous congestion in the lungs.
Uncertainty factor (UF) 3000-fold (10-fold individual difference × 3-fold species difference × extrapolation from subacute test)
10 Add 10-fold extrapolation using × LOAEL, etc. to 0.00007 ppm of reference concentration (RfC)
He says.
However, the formation of the Paulet & Desbrousses on which this criterion was based Performance 15) was denied in a subsequent follow-up 17) of Ogata et al.

4) U.S. Hazardous Substances and Diseases Registry (U.S. ATSDR) 7
On a series of Paulet & Desbrousses results 14-16 as in the RfC of U.S. EPA
UF300 fold (10-fold individual difference × 3-fold species difference × LOAEL, etc.) using LOAEL as the 1 ppm.
With an extrapolation of 10-fold and a minimal-risk level of 0.001 ppm
You have.
However, the results of the Paulet & Desbrousses on which the criteria for U.S. EPA were established 15)
This was denied in a follow-up 17) conducted by Ogata et al.
6. Setting chlorine dioxide gas Indoor Concentration Guidelines
1) Establishment of chlorine dioxide Industry Association Voluntary Standards
The indoor level guideline (voluntary standard of the Chlorine Dioxide Industry Association) is set at 0.01 ppm.
2) Summary of Studies, etc. as the Rationale for the Establishment
Guidelines for chlorine dioxide gas Indoor Concentrations by the chlorine dioxide

Industrial Association (voluntary standards of the Chlorine Dioxide Industry Association)
Is established from the following viewpoints, and the numerical values are derived based on occupational health and safety standards
This is supported by the numerical values and the numerical values derived from the health effect assessment of formaldehyde.
I got it.
(1) Establishment of a guidance value based on the results of toxicity studies in animals
Chlorine dioxide gas Inhaled injury is characterized by eye irritation and nasal/pharyngeal irritation
Congestion and oedema of blood vessels in the head, trachea, bronchi, lungs, etc. at high concentrations
Death results from dyspnea.
The damaging effect is local damage due to oxidative modification, and during exposure.
It is considered reversible because recovery is observed after stopping.
WHO6) the wound
Regarding adverse effects, "they are highly reactive, and health effects are limited to local injury.
"The toxicity is dose-dependent," said U.S. AEGL Commission 21, "chlorine dioxide."
Very reactive, and clinical signs result from direct chemical action on tissues
"I think it's possible....
U.S. ATSDR7 also "chlorine dioxide is highly reactive"
Thus, sufficient amounts of chlorine dioxide are absorbed to induce direct systemic toxicities
It is difficult to think.
Effects on the digestive system, musculoskeletal system, endocrine system, skin, and metabolism are described.
"No reports were found," the authors note...
Paulet & Desbrousses15) in rats, chlorine dioxide gas was 1 ppm × 5 h/day × 5
Minimal without epithelial or parenchymal damage in a study of inhalation exposure to d/week for 10 weeks
Report peribronchiolar oedema and pulmonary venous congestion and U.S. EPA8)
The lowest-observed-adverse-effect level (LOAEL) is the 1 ppm, with emphasis on this report, and this is uncertain
Coefficient (UF) 3,000-fold (10-fold individual difference × 3-fold species difference × extrapolation from subacute test results 10

0.00007 ppm as reference concentration (RfC) with 10-fold extrapolation using X LOAEL, etc.
He says.
On the other hand, U.S. ATSDR7 increased UF by 300-fold (10-fold individual difference × 3-fold species difference)
With an extrapolation of 10-fold using LOAEL and the lowest-risk level (MRL) of 0.001ppm
This is set.
However, the results of the Paulet & Desbrousses on which the evidence was based are as follows
The test was denied in the additional test 17) of Ogata et al.
After reviewing the Paulet & Desbrousses study with inhaled 1 ppm
Reported no abnormalities in rats and obtained in Paulet & Desbrousses studies
As the LOAEL of the 1 ppm should be modified to a no-observed-adverse-effect level (NOAEL)
Furthermore, similar results (respiratory injury observed in rats exposed to 1 ppm) were not obtained.
As one of the factors, fluctuation of the peak concentration in the test environment is mentioned.
Eyelashes
To chlorine dioxide gas concentrations in Paulet & Desbrousses trials
With a transiently high concentration of gas due to lack of precise control
It is suspected that the patient had suffered from the disease.
The Japan Industrial Association adopted the reconfirmed results as NOAEL.
As noted, the health-related effects of inhaled chlorine dioxide gas are limited to, and approached by, local injury.
Since the degree appears to be concentration-dependent, the 1 ppm of rats by Ogata et al. x 5 h/
Concentration of 1 ppm (2.8 mg/m3) in rooms, which is the exposures to 5 d/week for 10 weeks
It was adopted for the degree guideline value calculation.
The guideline values for indoor concentrations (voluntary standards of the Chlorine Dioxide Industry Association) are 90-fold higher than this NOAEL
Derived by dividing by UF.
As for individual differences, the breakdown is easy for infants and the elderly, etc.
Considering the susceptibility strata, extrapolate by a factor of 10, and for species

differences, U.S. AEGL Commission 21) said, "2.
Chlorine oxide is highly reactive, and clinical signs are due to direct chemical effects on tissues
May occur.
To species and individual differences in the effects at these sites of invasion
"It is expected that it will not be very large...
WHO's European territory
Regional Expert Committee 22) for the evaluation of formaldehyde: "In rats and humans, respiratory route
Despite anatomical and physiological differences in the pathways, the defense mechanisms of the respiratory pathway are similar
"They note...
Such chlorine dioxide characteristics or rats and baboons
A 3-fold similarity was considered.
In addition, the results of the subacute toxicity study were not included in the long-term study.
In episodes, the health-effect effects of chlorine dioxide are limited to local injury and their effects are reversible
Having.
Red pine et al. 18) chlorine dioxide gas up to 0.1 ppm for 6 months in rats
Exposure resulted in a 3-fold increase, considering that no abnormalities were observed.
Such considerations
Indoor concentration guideline value (voluntary standard of the Chlorine Dioxide Industry Association) calculated under 0.011 ppm
And.
Values derived as reference are shown below.
(2) Values derived with reference to Occupational Safety and Health Standards
ACGIH20) is the tolerable concentrations of chemicals to which workers are exposed in the workplace.
11
For 0.1 ppm with 8-hour weighted mean (TLV-TWA) and 15-minute limits
The standard of 0. 3 ppm is set in (TLV-STEL).
U.S. OSHA19) is also occupational safety
Eight-hour weighted normalization of allowable exposure concentrations for inhalational exposure to chlorine dioxide from a hygienic standpoint
The average value (PEL-TWA) is 0.0 1 ppm.

WHO is the Concise International Chemical Assessment Document
Measurements of available occupational exposures (U.K.) and Estimation and in subsection 6)
Exposures estimated using Assessment of Substance Exposure (EASE) models
0.1 ppm is obtained as the maximum-exposure-concentration (8 h-weighted mean) that can be derived from the concentration
As NOAEL, although derived from very limited evidence.
Comparatively, workers exposed to chlorine dioxide in the workplace are concerned about irritation of the respiratory tract and eyes
It is a numerical value that does not need it.
Red pine et al.18) studies in rats
And 0. 1 ppm of chlorine dioxide gas was exposed for 24 hours a day, 7 days a week, for 6 months and was abnormal.
It is reported that no case was observed.
The Japan Industrial Association uses chlorine dioxide gas's end-use products in everyday life
Considering this, the results of occupational safety and health or 6-month exposure studies have been obtained.
An additional 10-fold safety margin should be provided for 0.1 ppm.
In this case
The indoor concentration guideline (voluntary standard of the Chlorine Dioxide Industry Association) is 0.01 ppm.
(3) Numerical value derived with reference to the assessment of the health effects of formaldehyde
WHO's European Regional Expert Commission 22) concludes that formaldehyde in the air has a beneficial effect on the health of formaldehyde in the air.
Based on the assessment and the estimated threshold of cytotoxicity in the nasal mucosa and the results of epidemiological studies in humans, 1
Low-order values [0.08ppm (0.1 mg/m3)] are used as reference values.
In Japan,
This value is used as the indoor concentration guideline value 23) for formaldehyde.
I have.
The main symptoms of formaldehyde exposure are irritation of the eyes, nose and throat
Concentration-related discomfort, lacrimation, sneezing, nausea, dyspnea, if severe
It is fatal.
Formaldehyde is rapidly metabolized and after inhalation in rats and humans

No increase in blood concentration was observed.24)
The damaging effect was greater than the mean concentration.
— It is believed to be related to ku concentration.22)
Chlorine dioxide Inhalation-related injuries included eye irritation and nasal cavity, pharynx, trachea, and trachea
Causes congestion and edema of blood vessels in the bronchi, lungs, etc., resulting in dyspnea and death at high concentrations
You have.
In addition, WHO6 for chlorine dioxide, "Highly reactive and healthy
Acoustics are limited to local injury.
The toxicity is dose-related."
U.S. AEGL Board
Member 21) said: "chlorine dioxide is highly reactive and clinical signs are direct to the tissues.
"It is thought to be caused by chemical action....
U.S. ATSDR7 also "diacids"
Chlorine is highly reactive, and chlorine dioxide is a direct systemic toxic agent.
Sufficient absorption is unlikely.
Digestive organs, musculoskeletal system, endocrine system, skin,
12
"There are no reports describing metabolic effects."
Further Paulet &
Similar results were not obtained in Ogata et al. 17, which reviewed Desbrousses's study 15).
Peaked concentrations as one of the factors (respiratory injury seen with inhaled exposures to 1 ppm)
Lists the variation and suggests that the NOAEL of chlorine dioxide gas in rats is 1 ppm You have.
Based on these similarities, epidemiological studies in humans were conducted in chlorine dioxide.
10-fold is extrapolated to account for the lack of safety margins, and a safety margin of one order of magnitude lower is set.
And the indoor level guideline (self-administered standard of the Chlorine Dioxide Manufacturers Association) is 0.01 ppm.
(1) With similar values for both (2) and (3) for the damaging effect of chlorine dioxide gas It is a value that can be prevented.

7. Processing technology

・ Remove gas with fine water spray.

・ Decreased by autolysis but also eliminated by activated charcoal 25),26

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Test procedure

Exam name	Chlorine dioxide gas measurement method	Number of pages
		2

standard	Working hours
	100 minutes

reagent

Carbonate buffer composition and adjustment method

Sodium carbonate (Na2CO3) 0.159g Total volume 1000mL
Sodium bicarbonate (NaHCO3) 0.126g
About 1000mL distilled water (H2O)
Quantify sodium carbonate and sodium bicarbonate, respectively, and dissolve in distilled water to a total volume of 1000 mL.

Absorbing solution adjustment method (errands adjustment)

Potassium iodide (KI) 0.1g Buffer 500ml
Quantify potassium iodide and dissolve in 500 ml of buffer.

Chlorous acid standard solution (erase adjustment)

Weigh 1000ppm of chlorite ion standard solution and dilute it 178 times with distilled water to make 5.6 ㎎ / L. 1ml of this solution is a salt
Corresponds to 5.5 ㎍ of boric acid ion (2 ㎕ of chlorine dioxide).

Standard series adjustment

Take chlorite standard solution as shown in the table below in 4 test tubes with stoppers, and add absorbent to make each solution 10.0 ml.
To do. The chlorite ion concentration is measured by ion chromatography.

ClO2 concentration ppm * 1	0	0.01	0.03	0.05	0.1
Equivalent ClO2 amount ㎕	0	0.4	1.2	2.0	4.0
Chlorous acid standard solution ml	0	0.2	0.6	1.0	2.0

Note) * 1: Gas sampling volume 40 l (= 1 kg / min x 40 min)

machine	Instrument
Ion chromatography	・ Hole pipette of required amount ・ Erlenmeyer flask with required amount of stopper ・ Required volumetric flask ・ Required absorption bottle x 3 ・ Necessary amount of test tubes with stoppers x 4

Chlorine dioxide gas measurement method	
Sampling and analysis	Remarks
Take 10 ml of the absorbent on each of 3 sampling impingers. Aspirate and collect air containing chlorine dioxide gas at a rate of 1 L / min for 40 minutes. Using the absorption solution as a control solution, the chlorite ion concentration is measured by ion chromatography. [Chlorine dioxide concentration (ppm)] = ([chlorite ion concentration] x 10 / 67.5 x (22.4 x 293/273) / 40)	The measurement of chlorite ion concentration is a standard. Tests created by quasi-series measurements Use a quantity line.
IC conditions	
Perform analysis under the following analysis conditions. Body: DIONEX Column: Dionex Ionpac AS18 4mm Guard column: Dionex Ionpac AG18 4 ㎜ Suppressor: Dionex ASRS300 4 ㎜ Eluent concentration: NaOH or KOH 15 mM-80 mM (0-18 min (15 mM) → 18.1 min-25 min (80 mM) → After completion, return to 15 mM and stabilize for about 15 minutes (Total: 40 min) (In order to improve the separation of ClO2- ions, the concentration was changed from 25 mM to 15 mM. Since the analysis time becomes longer, the unnecessary peak in the latter half is 80 mM. Drive out.) Flow rate: 1.0ml / min Analysis time: 40 minutes Sample volume: 50 μl Cell temperature: 35 ° C Column: Room temperature	

References	OSHA Method No.ID-202 「Determination of Chlorine Dioxide in Workplace Atmospheres」	Career
Created date		Implementation start date
Author		