COMMITTEE OF EXPERTS ON THE TRANSPORT OF DANGEROUS GOODS AND ON THE GLOBALLY HARMONIZED SYSTEM OF CLASSIFICATION AND LABELLING OF CHEMICALS

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MISCELLANEOUS PROPOSALS OF AMENDMENTS TO THE MODEL REGULATIONS ON THE TRANSPORT OF DANGEROUS GOODS

Toxic by inhalation substances for consideration by the experts on the transport of dangerous goods

Addendum to ST/SG/AC.10/C.3/2008/49

Transmitted by the expert from the Netherlands

The project report announced is ST/SG/AC.10/C.3/2008/49, para 4 is reproduced overleaf.

National Institute
for Public Health
and the Environment

Letter report 601018001/2008
Sjöfn Gunnarsdóttir | Joke Herremans

Toxic by inhalation or not?

Information search and classification of 41 substances

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RIVM Report 601018001/2008

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Rapport in het kort

Toxic by inhalation or not? Information search and classification of 41 substances

De VN Model regulation Transport Gevaarlijke Goederen (VN-TDG) specificeert de criteria voor de classificatie van gevaarlijke stoffen. Deze classificatiecriteria maken gebruik van de fysisch chemische en toxicologische eigenschappen van stoffen. De correcte classificatie van stoffen is van essentieel belang voor veilig transport van gevaarlijke goederen.

In opdracht van het ministerie van Verkeer en Waterstaat, Programma Veiligheid heeft het RIVM voor 41 stoffen de noodzaak tot classificatie in de VN-TDG vervoerscategorie 6.1 beoordeeld. Deze categorie is van toepassing als stoffen toxisch zijn.
De resultaten hiervan zullen door het ministerie van Verkeer en Waterstaat worden ingebracht in het Subcomité Transport Gevaarlijke Goederen van de United Nations Economic and Social Council.

Over 41 stoffen is informatie verzameld om te kunnen bepalen of indeling in vervoerscategorie 6.1 noodzakelijk is en zo ja, welke verpakkingseisen gelden. De informatie over inhalatie toxiciteit en dampdruk van deze stoffen is afkomstig van openbare data bases.

De gevonden informatie was voldoende om het merendeel van de stoffen te classificeren. De meeste classificeerbare stoffen voldoen aan de criteria voor classificatie in vervoerscategorie 6.1 op grond van hun toxiciteit bij inhalatie.

Negen stoffen zijn zogenoemde isocyanaten. Voor twee isocyanaten is volledig informatie voor classificatie in de openbare databases gevonden terwijl voor de overige deze informatie ontbrak. Op basis van “read-across” kan echter worden geconcludeerd dat de zeven isocyanaten een vergelijkbare classificatie kunnen krijgen als de twee geclassificeerde isocyanaten.

Trefwoorden: Inhalatie toxiciteit, stofclassificatie, UN Model Regulation Transport Gevaarlijke Goederen.

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1 Goal of the project

The UN model regulation on Transport of Dangerous Goods specifies criteria for the classification of hazardous chemicals based on their physical-chemical and toxicological properties. Proper classification is critical to ensure safety and efficiency of the transport of dangerous goods.

Document UN/SCETDG/30/INF.74 lists 60 substances that are currently listed as substances that are (potentially) toxic via the inhalation route and whose classification is now undergoing a review. Agreement on classification has been reached for several substances (written in non-struck-through typeface in UN/SCETDG/30/INF.74) whereas more information was needed to complete the review for a number of substances (written in a struck-through typeface in UN/SCETDG/30/INF.74).

The goal of this project was to gather more information on the substances for which insufficient information has been available in order to answer the question whether they fulfil the criteria for classification in division 6.1 and/or its sub-categories.

2 Materials and methods

2.1 Information gathered

According to the UN model regulation on Transport of Dangerous Goods, classification in category 6.1 is dependent on the saturated vapour concentration (SVC) and LC50 value for the substance, and human exposure experience.

The search for information was primarily focused on collecting acute inhalation toxicity values (LC50) and vapour pressure values. Less emphasis was put on collecting relevant information on human exposure experience.

2.2 Information sources

The information sources used were publicly available and easily accessible. No attempt was made to evaluate the quality or the correctness of the information collected.

The following databases were used as the primary data sources:

- AEGL (http://www.epa.gov/oppt/aegl/)
  Developed by the National Advisory Committee. Intended for national and local authorities, and private companies to deal with emergencies involving spills or catastrophic exposures.

- Annex I of EU directive 67/548/EEC (http://ecb.jrc.it/classification-labelling/search-classlab/)
  Information for substances listed on Annex I have undergone an extensive peer-review and quality control check.

  Annex I of EU directive 67/548/EEC specifies three classification categories for substances that are toxic by inhalation:
  i) Very toxic by inhalation (T+, R26). Substances in this category have LC50 inhalation values of ≤ 0.25 mg/l/4h for aerosols and particulates, and of ≤ 0.5 mg/l/4h for gases and vapours. No lower limit is specified for this category.
  ii) Toxic by inhalation (T, R23). Substances in this category have LC50 inhalation values of 0.25 < LC50 ≤ 1 mg/l/4h for aerosols and particulates, and of 0.5 < LC50 ≤ 2 mg/l/4h for gases and vapours.
  iii) Harmful by inhalation (Xn, R20). Substances in this category have LC50 inhalation values of 1 < LC50 ≤ 5 mg/l/4h for aerosols and particulates, and of 2 < LC50 ≤ 20 mg/l/4h for gases and vapours.

- ATSDR (http://www.atsdr.cdc.gov/toxpro2.html#bookmark05)
  Toxiciological profiles for hazardous substances found at U.S. National Priorities List sites is created by the Agency for Toxic Substances and Disease Registry (ATSDR) by Congressional mandate. Peer-reviewed.

- Cameo Chemicals (http://cameochemicals.noaa.gov/)

CAMEO Chemicals is an online library of over 6000 data sheets for hazardous materials that are commonly transported, used, and/or stored in the United States. Developed jointly by National Oceanic and Atmospheric Administration (NOAA), the U.S. Environmental Protection Agency (EPA), and the U.S. Coast Guard.

- CICAD (http://www.who.int/ipcs/publications/cicad/en/)
  CICADs provide internationally accepted reviews (peer-reviewed) on the effects on human health and the environment of chemicals or combinations of chemicals.

- Emergency Response Planning Guidelines (ERPG; AIHA press, Fairfax VA, 2000)
  The ERPGs are developed by the ERPG committee of the American Industrial Hygiene Association. A list of references is provided.

- HSDB (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB)
  All data are referenced and derived from a core set of books, government documents, technical reports and selected primary journal literature. Each data entry has a quality review tag: "Peer reviewed" – reviewed by the Scientific Review Panel or a similar group, "QC reviewed" – quality control reviewed but not yet reviewed by the Scientific Review Panel, or "Unreviewed" – used for a limited number of data statements.

- IUCLID - The European Chemical Substances Information System (http://ecb.jrc.it/esis/)
  IUCLID is the basic tool for data collection and evaluation within the EU-Risk Assessment Programme. The data structure has been designed to describe the effects of substances on human health and the environment, in close collaboration between Member States, Industry and the European Chemicals Bureau (ECB). References for each entry are provided. Not peer-reviewed.

- OECD SIDS (http://www.chem.unep.ch/irptc/sids/OECDSIDS/indexcasnumb.htm)
  The data obtained from this link have undergone a quality check.

- TSCATS (http://www.syrres.com/Esc/tscats.htm)
  An online index to unpublished, nonconfidential studies covering chemical testing results that are submitted by U.S. industry to EPA under several sections of the Toxic Substance Control Act. About 9% of TSCATS documents are summarized in the RTECS database, 10% are available online in electronic form in the database itself and 16% include abstracts which summarize the data from a cited study. Only information that was publicly available in the form of a summary and free of charge was used from the TSCATS database for this search.

In summary, the primary data sources contain data that have been peer-reviewed and/or contain a reference for each citation. The quality of these data sources is at least comparable to and in some instances better than the data in the RTECS database (http://www.cdc.gov/niosh/rtecs/) that was used as the primary data source for accepted substances in document UN/SCETDG/30/INF.74. A description of the RTECS database states that it is a compendium of data extracted from the open scientific literature. For each citation, the bibliographic source is listed thereby enabling the user to access the actual studies cited. However, no attempt has been made to evaluate the studies cited in RTECS and the user has the responsibility of making such assessments.

When additional information was needed e.g. when possible errors were encountered or where large discrepancies were found in the data, additional data sources were used. These data sources included:
- PubMed (http://www.ncbi.nlm.nih.gov/sites/entrez/)
- CRC handbook of physics and chemistry

- the California Office of Pesticide Regulation (http://www.cdpr.ca.gov/docs/legbills/opramenu.htm)
- the International Program on Chemical Safety (http://www.who.int/ipcs/en/)
- DSSTox (http://epa.gov/ncct/dsstox/)

Material safety data sheets and safety data sheets were also included in the search. However, the information from these sources was not used in the final data analyses because of the often inconsistent information between (M)SDS for the same substance from two different suppliers and because the information found on these data sheets often contradicted more reliable data sources (e.g. Annex I of EU directive 67/548/EEC)

During the information collection, each substance was allocated a page in an Excel file where the raw data and the source of the data was were entered. Data sheets for individual substances and the Excel file are available upon request. An example of a data sheet for a substance can be found in Appendix I.

2.3 Vapour pressure

Only vapour pressure values for which the temperature was also noted were included in the data analyses. Furthermore, only experimentally obtained vapour pressure values (no modelled data) were used in the data analyses.

The UN model regulation on Transport of Dangerous Goods specifies that the SVC is expressed in ml/m^3 at 20 ˚C and standard atmospheric pressure. If vapour pressure values were on the Fahrenheit scale, the following equation (1) was used to convert them into the Celsius scale:

(1) $T_c = (5/9)*(T_f-32)$

where T_c is the temperature in degrees Celsius
T_f is the temperature in degrees Fahrenheit

Vapour pressure values at temperatures other than 20 ˚C were extrapolated to 20 ˚C using equation (2)[1]:

(2) $VP_{T1} = VP_{Ttest} * e^{(0.041* (T_1-T_{test}))}$

where VP_{T1} is the vapour pressure at 20 ˚C
VP_{Ttest} is the vapour pressure at the test temperature
T_{test} is the test temperature (K)
T_1 is the standard temperature (293.15 K (=20 ˚C))

This generalized equation has the advantage of being not dependent on the use of substance-specific values for the heat of vaporization that were often not available for the substances of interest. To assess whether this generalized equation was acceptable as a first approximation, substance-specific heat of vaporization values and equation (3) were used, and the results compared with the results obtained from the generalized results.

[1] MFW Waitz, JI Freijer, P Kreule and FA Swartjes (1996). The VOLASOIL risk assessment model base don CSOIL for soils contaminated with volatile compounds. RIVM report 715810014.

(3) $VP_{T1} = VP_{Ttest} * e^{(H_{vap}/R * [(1/T_{test})-(1/T_1)])}$

where VP_{T1} is the vapour pressure at 20˚C
VP_{Ttest} is the vapour pressure at the test temperature
H_{vap} is the heat of vaporization
R is the molar gas constant (here 8.314 J/mole K)
T_{test} is the test temperature (K)
T_1 is the standard temperature (293.15 K (=20˚C))

Reasonably comparable results were obtained for substances for which equation where both equation (2) and (3) could be used. This suggests that equation (2) is acceptable as a first approximation for the extrapolation of vapour pressure to 20 ˚C for the substances of interest.

The volatility values for the mixtures 1613 Hydrocyanic acid (≤ 20% aqueous solution) and 3294 Hydrogen cyanide (≤ 45% in alcohol) were calculated using the equations in section 2.6.2.2.4.7 of the UN model regulation on Transport of Dangerous Goods, using the vapour pressure of the pure liquid for calculations of partial pressures. In a worst case scenario, the maximum allowed percentage of HCN was used in the calculations (i.e. 20% and 45%). For 3294 Hydrogen cyanide (≤ 45% in alcohol), it was assumed that the alcohol was ethanol.

2.4 SVC

SVC was calculated from the vapour pressure values using equation (4)

(4) $SVC\ (ml/m^3) = VP/R*T * v_m * 1000$

where VP is the vapour pressure at 20˚C (Pa)
R is the gas constant (8.314 m^3 Pa/K mole)
T is the temperature (at 293 K (equals 20˚C)
v_m is the molar volume of ideal gas (24.1 L/mol at 20˚C)
1000 is the conversion factor between ml and L (1000 ml/L).

Where more than one SVC value was calculated for a substance, the average value was used in the final data analyses.

2.5 LC50 values

Only LC50 values obtained from experiments using common laboratory animals, such as mice, rats, rabbits and guinea pigs were used.

The UN model regulation on Transport of Dangerous Goods specifies that LC50 values should be based on 1-h exposure times. However, where only results from studies using 4-h exposure times are available, those results may be extrapolated to 1-h exposure results by multiplying the LC50 4-h value with 2 for vapours and with 4 for mists (2.6.2.2.4.2 and 2.6.2.2.4.5). In this study, every attempt was made to use only 1-h or extrapolated 4-h exposure values but such data were not available for all substances.

LC50 values were reported in the units mg/l, ml/m^3 (ppm) or mg/m^3. The UN model regulation on Transport of Dangerous Goods specifies that vapours should be reported in the unit ml/m^3 (ppm) whereas mists should be reported in the units mg/l. Equations 5 through 10 were used to convert the units into ml/m^3 or mg/l:

(5)	mg/l to ppm	[C (mg/l) * V_m (ml/mmol) * 1000 (l/m^3)] / [mw (mg/mmol)]
(6)	ppm to mg/l	[ppm (ml/m^3) * mw (mg/mmol)] / [V_m (ml/mmol) *1000 (L/m^3)]
(7)	mg/m^3 to ppm	[C (mg/m^3) * V_m (ml/mmol)] / [mw (mg/mmol)]
(8)	ppm to mg/m^3	[ppm (ml/m^3) * mw (mg/mmol)] / [V_m (ml/mmol)]
(9)	mg/m^3 to mg/l	[C (mg/m^3)] / [1000 (l/m^3)]
(10)	mg/l to mg/m^3	C (mg/l) * 1000 (l/m^3)

where C is the concentration in mg/l, ml/m^3 (ppm) or mg/m^3
V_m is the molar volume of gas

The databases AEGL and ERPG as well as study summaries were used to determine whether a substance was tested as vapour or mist. Nearly all of the substances were assessed to be vapours with the exception of 1892 Ethyldichloroarsine which is probably tested as a mist and 2474 Thiophosgene for which no information could be found and thus results for both vapour and mist are reported.

The LC50 values for the mixtures 1613 Hydrocyanic acid (≤ 20% aqueous solution) and 3294 Hydrogen cyanide (≤ 45% in alcohol) were calculated using the equations in section 2.6.2.2.4.7 of the UN model regulation on Transport of Dangerous Goods. For worst case scenario calculations, the maximum allowed percentage of HCN was used as input. For 1613 Hydrocyanic acid (≤ 20% aqueous solution) it was assumed that water was a non-toxic substance. Furthermore, for 3294 Hydrogen cyanide (≤ 45% in alcohol) it was assumed that the alcohol was ethanol.

3 Results

Table 1 Results of this study.
No entry indicates that no information was found for that parameter.

						Acute inhalation LC50 values (ml/m^3, 1-h exposure time)				
UN nr	**CAS nr**	**Name**	**Remarks**	**SVC or volatility (for mixtures)**	**Vapour/mist**	**Annex I[(a)] low**	**Annex I high**	**LC50 low**	**LC50 high**	**Remarks**
1135	107-07-3	Ethylene chlorohydrin		6890	Vapour		≤ 300	64	64	
1182	541-41-3	Ethyl chloroformate		39178	Vapour		≤ 222	145	200	(b)
1251	78-94-4	Methyl vinyl ketone		98773	Vapour			4.9	5.6	
1510	509-14-8	Tetranitromethane		11490	Vapour			35	300	
1541	75-86-5	Acetone cyanohydrin		1037	Vapour		≤ 283	20	20	(c)
1560	7784-34-1	Arsenic trichloride		11408						
1580	76-06-2	Chloropicrin		26064	Vapour		≤ 147	13.2	28.8	
1605	106-93-4	Ethylene dibromide		13560	Vapour	128 <	≤ 512	1833	1833	(d)
1613	74-90-8	Hydrocyanic acid	Pure	790179	Vapour		≤ 890	142	142	(e)
			20% in H_2O	80948 (HCN) 20731 (H_2O)				1396	1768	(g)
1670	594-42-3	Perchloromethyl mercaptan		5186	Vapour			10.1	35.4	
1672	622-44-6	Phenylcarbylamine chloride								
1722	2937-50-0	Allyl chloroformate		21459	Vapour					
1746	7787-71-5	Bromine trifluoride		9195	Vapour					
1810	10025-87-3	Phosphorus oxychloride		37302	Vapour		≤ 157	62.8	105	
1834	7791-25-5	Sulphuryl chloride		141056	Vapour			14	318	
1838	7550-45-0	Titanium tetrachloride		12707	Vapour			116.8	165	
1892	598-14-1	Ethyldichloroarsine		2813	Mist			1.6	1.6	(f)
2232	107-20-0	2-chloroethanal		131687	Vapour		≤ 307	200	239	
2382	540-73-8	Dimethylhydrazine (symm)		74990	Vapour	400 <	≤ 1602	1160	1160	
2407	108-23-6	Isopropyl chloroformate		43529	Vapour			247	300	

2438	3282-30-2	Trimethyl acetyl chloride		37499						
2442	76-02-8	Trichloro acetyl chloride		22875						
2474	463-71-8	Thiophosgene		136245	Vapour	210 <	≤ 838			
	463-71-9	Thiophosgene			Mist	1 <	≤ 4			
2477	556-61-6	Methyl isothiocyanate		19957	Vapour	330 <	≤ 1380	626	626	
2481	109-90-0	Ethyl isocyanate		145189						
2482	110-78-1	n-Propyl isocyanate								
2483	1795-48-8	Isopropyl isocyanate								
2484	1609-86-5	tert-Butyl isocyanate								
2485	111-36-4	n-Butyl isocyanate		22348	Vapour			3.7	146	
2486	1873-29-6	Isobutyl isocyanate								
2487	103-71-9	Phenyl isocyanate		3752	Vapour			3.9	12.6	
2488	3173-53-3	Cyclohexyl isocyanate		2148	Vapour					
2521	674-82-8	Diketene		10339	Vapour	1148 <	≤ 11462	178	620	
2605	6427-21-0	Methoxymethyl isocyanate								
2606	681-84-5	Methyl orthosilicate		12874	Vapour			190	300	
2644	74-88-4	Methyl iodide		434490	Vapour	170 <	≤ 680	442	849	
2668	107-14-2	Chloroacetonitrile		13110	Vapour	214 <	≤ 854			
2826	2941-64-2	Ethyl chlorothioformate		118004	Vapour					
3079	126-98-7	Methacrylonitrile		79393	Vapour	360 <	≤ 1436	72	1400	
3246	124-63-0	Methanesulphonyl chloride		3315	Vapour			50	250	
3294	74-90-8	Hydrocyanic acid	Pure	790179	Vapour		≤ 890	142	142	(e)
			45% in EtOH	430405 (HCN) 26654 (EtOH)				260	1622	(g) (h)

(a) Substances fall into one of the three categories ‘very toxic by inhalation’, ‘toxic by inhalation’ or ‘harmful by inhalation’. Each category has clearly fixed concentration limits in mg/l that are here converted into ppm, see section on ‘LC50 values’ in ‘2 Material and methods ‘.The highest and the lowest value in the category to which a substance belongs is listed. No lower limit is defined for the category ‘very toxic by inhalation’. Data obtained from Annex I of EU directive 67/548/EEC data are always extrapolated from 4 h.

(b) High variability was found in the reported vapour pressure data.

(c)	Based on 2-h exposure time without extrapolation.
(d)	Based on 0.5-h exposure time without extrapolation.
(e)	Numerous inhalation studies are available but most have exposure times less than 1 hour.
(f)	Probably tested as mist. LC50 values are based on a 0.167-h (10-min) exposure time without extrapolation. The LC50 value is 220 ppm/10 min if tested as vapour.
(g)	Values were calculated using equations in section 2.6.2.2.4.7 of the UN Model regulation on Transport of Dangerous Goods.
(h)	The type of alcohol is not specified in the UN transport list. It is here assumed to be ethanol.

Table 2 Classification according to the criteria for toxic by inhalation in section 2.6.2.2 of the UN model regulation on Transport of Dangerous Goods on the basis of the results in Table 1.
The classification is only based on inhalation LC50 values and saturated vapour concentrations and is given as division number and packing group. No entry indicates that sufficient information for classification was not found.

UN nr	CAS nr	Name	Present classification	Classification on the basis of the data for inhalation toxicity	Remarks
1135	107-07-3	Ethylene chlorohydrin	6.1 - 3 -I	6.1 - I	
1182	541-41-3	Ethyl chloroformate	6.1 - 3,8 - I	6.1 - I	(b)
1251	78-94-4	Methyl vinyl ketone	6.1 - 3,8 - I	6.1 - I	
1510	509-14-8	Tetranitromethane	5.1 - 6.1 - I	6.1 - I	
1541	75-86-5	Acetone cyanohydrin	6.1 - I	6.1 - I	(c) (i)
1560	7784-34-1	Arsenic trichloride	6.1 - I		
1580	76-06-2	Chloropicrin	6.1 - I	6.1 - I	
1605	106-93-4	Ethylene dibromide	6.1 - I	6.1 - I	(d) (i)
1613	74-90-8	Hydrocyanic acid, (≤ 20% HCN in H_2O.)	6.1 - I	6.1 -II	
1670	594-42-3	Perchloromethyl mercaptan	6.1 - I	6.1 - I	
1672	622-44-6	Phenylcarbylamine chloride	6.1 - I		
1722	2937-50-0	Allyl chloroformate	6.1 - 3,8 - I		
1746	7787-71-5	Bromine trifluoride	5.1 - 6.1,8 - I		
1810	10025-87-3	Phosphorus oxychloride	8 - II	6.1 - I	
1834	7791-25-5	Sulphuryl chloride	8 - I	6.1 - I	
1838	7550-45-0	Titanium tetrachloride	8 - II	6.1 - I	
1892	598-14-1	Ethyldichloroarsine (mist)	6.1 - I	6.1 - II	(f) (g)
2232	107-20-0	2-chloroethanal	6.1 - I	6.1 - I	
2382	540-73-8	Dimethylhydrazine, symmetrical	6.1 - 3 - I	6.1 - I	(i)
2407	108-23-6	Isopropyl chloroformate	6.1 - 3,8 - I	6.1 - I	
2438	3282-30-2	Trimethyl acetyl chloride	6.1 - 3,8 - I		
2442	76-02-8	Trichloro acetyl chloride	8 - II		
2474	463-71-8	Thiophosgene (vapour)	6.1 - II	6.1 - I	
		Thiophosgene (mist)	6.1 - II	6.1 - II	(h)
2477	556-61-6	Methyl isothiocyanate	6.1 - 3 - I	6.1 - I	(i)
2481	109-90-0	Ethyl isocyanate	3 - 6.1 - I		
2482	110-78-1	n-Propyl isocyanate	6.1 - 3 - I		
2483	1795-48-8	Isopropyl isocyanate	3 - 6.1 - I		
2484	1609-86-5	tert-Butyl isocyanate	6.1 - 3 - I		
2485	111-36-4	n-Butyl isocyanate	6.1 - 3 - I	6.1 - I	
2486	1873-29-6	Isobutyl isocyanate	3 - 6.1 - II		
2487	103-71-9	Phenyl isocyanate	6.1 - 3 - I	6.1 - I	
2488	3173-53-3	Cyclohexyl isocyanate	6.1 - 3 - I		
2521	674-82-8	Diketene	6.1 - 3 - I	6.1 - I	(k)
2605	6427-21-0	Methoxymethyl isocyanate	3 - 6.1 - I		
2606	681-84-5	Methyl orthosilicate	6.1 - 3 - I	6.1 - I	

2644	74-88-4	Methyl iodide	6.1 - I	6.1 - I	
2668	107-14-2	Chloroacetonitrile	6.1 - 3 - II	6.1 - I	
2826	2941-64-2	Ethyl chlorothioformate	8 - 3 - II		
3079	126-98-7	Methacrylonitrile	3 - 6.1 - I	6.1 - I	(i)
3246	124-63-0	Methanesulphonyl chloride	6.1 - 8 - I	6.1 - I	
3294	74-90-8	Hydrogen cyanide (≤45% HCN in EtOH)	6.1 - 3 - I	6.1 - I	(i) (m)

(b)	High variability was found in the reported vapour pressure data.
(c)	Based on 2-h exposure time without extrapolation.
(d)	Based on 0.5-h exposure time without extrapolation..
(e)	Numerous inhalation studies are available but most have exposure times less than 1-h.
(f)	Probably tested as mist. LC50 values based on 0.167-h (10-min)exposure time without extrapolation.
(g)	Based on a 10-min exposure time without extrapolation.
	The same classification applies if the substance was tested as vapour instead of mist as is now assumed.
(h)	Using highest LC50 value, the packing group is 6.1-III. However, thiophosgene may be an eye irritant.
	Tear gases are in packing group II although the toxicity data may place them in packing group III.
(i)	The packing group is 6.1-II if the highest LC50 is used.
(k)	The packing group is 6.1-III if the highest LC50 is used.
(m)	The type of alcohol is not specified in the UN transport list. It is here assumed to be ethanol.

Table 3 Classification according to the subcategories on toxic by inhalation on the basis of the results in Table 1.
The classification is only based inhalation LC50 values and saturated vapour concentrations. No entry indicates that sufficient information for classification was not found.

UN nr	CAS nr	Name	Remarks	LC50 < 200 ppm & SVC > 500LC50	Remarks	LC50 < 1000 ppm & SVC > 10LC50	Remarks
1135	107-07-3	Ethylene chlorohydrin		no		yes	
1182	541-41-3	Ethyl chloroformate	(b)	no		yes	
1251	78-94-4	Methyl vinyl ketone		yes		yes	
1510	509-14-8	Tetranitromethane		no		yes	
1541	75-86-5	Acetone cyanohydrin	(c)	no		yes	(g)
1560	7784-34-1	Arsenic trichloride					
1580	76-06-2	Chloropicrin		yes	(g)	yes	
1605	106-93-4	Ethylene dibromide	(d)	no		yes	(g)
1613	74-90-8	Hydrocyanic acid (pure)	(e)	yes	(g)	yes	
		Hydrocyanic acid (≤ 20% HCN in H_2O)		N/A		N/A	
1670	594-42-3	Perchloromethyl mercaptan		no		yes	
1672	622-44-6	Phenylcarbylamine chloride					
1722	2937-50-0	Allyl chloroformate					
1746	7787-71-5	Bromine trifluoride					
1810	10025-87-3	Phosphorus oxychloride		yes	(g)	yes	
1834	7791-25-5	Sulphuryl chloride		yes	(g)	yes	
1838	7550-45-0	Titanium tetrachloride		no		yes	
1892	598-14-1	Ethyldichloroarsine (mist)	(f)	N/A	(h)	N/A	(i)
2232	107-20-0	2-chloroethanal		yes	(g)	yes	
2382	540-73-8	Dimethylhydrazine symmetrical		no		yes	(g)
2407	108-23-6	Isopropyl chloroformate		no		yes	
2438	3282-30-2	Trimethyl acetyl chloride					
2442	76-02-8	Trichloro acetyl chloride					
2474	463-71-8	Thiophosgene (vapour)		no		yes	

		Thiophosgene (mist)						
2477	556-61-6	Methyl isothiocyanate		no			yes	(g)
2481	109-90-0	Ethyl isocyanate						
2482	110-78-1	n-Propyl isocyanate						
2483	1795-48-8	Isopropyl isocyanate						
2484	1609-86-5	tert-Butyl isocyanate						
2485	111-36-4	n-Butyl isocyanate		yes	(g)		yes	
2486	1873-29-6	Isobutyl isocyanate						
2487	103-71-9	Phenyl isocyanate		yes	(g)		yes	
2488	3173-53-3	Cyclohexyl isocyanate						
2521	674-82-8	Diketene		no			yes	(g)
2605	6427-21-0	Methoxymethyl isocyanate						
2606	681-84-5	Methyl orthosilicate		no			yes	
2644	74-88-4	Methyl iodide		yes	(g)		yes	
2668	107-14-2	Chloroacetonitrile		no			yes	
2826	2941-64-2	Ethyl chlorothioformate						
3079	126-98-7	Methacrylonitrile		yes	(g)		yes	(g)
3246	124-63-0	Methanesulphonyl chloride		no			yes	
3294	74-90-8	Hydrocyanic acid (pure)	(e)	yes	(g)		yes	
		Hydrocyanic acid (≤ 20% HCN in H_2O.)		N/A			N/A	

(b)	High variability was found in the reported vapour pressure data.
(c)	Based on 2-h exposure time without extrapolation.
(d)	Based on 0.5-h exposure time without extrapolation.
(e)	Numerous inhalation studies are available but most have exposure times less than 1-h.
(f)	Probably tested as mist. LC50 values based on 0.167-h (10-min)exposure time without extrapolation. LC50 value is 220 ppm/10 min if tested as vapour.
(g)	If highest LC50 value is used, the answer is 'no'.
(h)	If UN1892 Ethyldichloroarsine is tested as vapour, the answer is 'no'.
(i)	If UN1892 Ethyldichloroarsine is tested as vapour, the answer is 'yes' .
N/A	Not applicable since no formula was provided for calculating saturated vapour concentrations for mixtures.

Table 4 Brief summary of human experience after inhalation exposure to the substances listed in Table 1.

UN nr	CAS nr	Name	Human exposure experience
1135	107-07-3	Ethylene chlorohydrin	Fatal poisoning after 2 h exposure to 300 ppm. Route of exposure not specified in abstract. Non-fatal poisonings have occurred. Symptoms include lung, eye & nose irritation, nausea, vomiting, visual disturbances, brain & lung edema, coma.
1182	541-41-3	Ethyl chloroformate	Symptoms include lacrimation, respiratory, skin and eye irritation, pulmonary oedema of late onset. Exposure to the analogue methyl chloroformate at 190 ppm can result in death after 10 min.
1251	78-94-4	Methyl vinyl ketone	Respiratory, skin and eye irritant, inhalation of the substance may cause lung oedema.
1510	509-14-8	Tetranitromethane	Eye and upper respiratory tract irritation occur at airborne concentrations less than 1 ppm. Nasal irritation, burning eyes, dyspnoea, cough, chest oppression, dizziness, headache, methemoglobinemia and a few deaths attributed to exposure (route not clearly specified in abstract.
1541	75-86-5	Acetone cyanohydrin	Two human fatalities were reported after acetone cyanohydrin exposure (route not specified in abstract). Symptoms of exposure include palpitation, headache and vomiting.
1560	7784-34-1	Arsenic trichloride	Toxic and caustic owing to poisonous nature of arsenic and release of HCl in presence of water. Irritating to skin, eyes and mucous membranes.
1580	76-06-2	Chloropicrin	298 ppm and 119 ppm for 10 min and 30 min, respectively, is lethal to man. 15 ppm and 7.5 ppm for 1 min and 10 min, respectively, is intolerable to man. 1.3 ppm is the lowest irritant concentration. Irritating to eyes and mucous membranes.
1605	106-93-4	Ethylene dibromide	Two human fatalities after inhalation and/or dermal exposure to ethylene bromide residues in a tank. Inhalation causes drowsiness and pulmonary lesions.
1613 & 3294	74-90-8	Hydrogen cyanide (pure)	Well known human poison. 107-134 ppm may lead to death after 0.5 to 1 h. 134 ppm is likely fatal within 30 min, 178 ppm is likely fatal after 10 min, 267 ppm is immediately fatal.
1670	594-42-3	Perchloromethyl mercaptan	Eye irritant at 1.3 ppm. Nausea and eye, throat and respiratory tract irritant at 8.8 ppm. Brief exposures to low concentration may produce CNS depression, lung, liver and heart congestion. A human fatality was described after inhalation and dermal exposure, survivors developed lung oedema.
1672	622-44-6	Phenylcarbylamine	Lacrimator, irritant to skin and mucous membranes.

		chloride	
1722	2937-50-0	Allyl chloroformate	Irritating to eyes and respiratory tract.
1746	7787-71-5	Bromine trifluoride	Corrosive, exposure can severely irritate the nose, throat and lungs. Short-term high concentrations: serious lung injury. Lower concentrations: watering of eyes, difficulty in breathing after few minutes.
1810	10025-87-3	Phosphorus oxychloride	Vapour irritates eyes, causes dizziness, headache, weakness, anorexia, nausea, vomiting, chest pain, cough, dyspnoea, bronchitis, bronchopneumonia, pulmonary oedema and nephritis. Both chronic and acute cases of occupational intoxication have been recorded.
1834	7791-25-5	Sulphuryl chloride	Causes burns, irritating to respiratory system and eyes. 10 ppm for 1 min may cause severe toxicity, 4 ppm for more than a short time may lead to symptoms of illness. Pulmonary oedema of delayed onset was reported after inhalation of vapour.
1838	7550-45-0	Titanium tetrachloride	Death and corneal damage after inhalation to vapours. Death of a worker due to pulmonary oedema after inhalation of vapours after a splashing accident. Corrosive irritant to skin, eyes and mucous membranes, cough and chest pains can develop.
1892	598-14-1	Ethyldichloroarsine	Lacrimator, irritant to eyes, nose, respiratory tract and skin. Medial lethal dosage (MLD50) by inhalation - 3000 to 5000 mg/min/m3, depending on the period of exposure. Median temporarily incapacitating dosage (ICt50) by inhalation - 5 to 10 mg/min/m3.
2232	107-20-0	2-chloroethanal	Irritating to eyes, nose and throat.
2382	540-73-8	Dimethylhydrazine	Irritating to skin, eyes and mucous membranes.
2407	108-23-6	Isopropyl chloroformate	Irritating to eyes and respiratory tract, can produces delayed pulmonary oedema.
2438	3282-30-2	Trimethyl acetyl chloride	No relevant information was found.
2442	76-02-8	Trichloro acetyl chloride	Strong irritant to skin and tissue.
2474	463-71-8	Thiophosgene	Vapour is irritating to eyes, nose and throat.
2477	556-61-6	Methyl isothiocyanate	Lacrimator, irritant and vesicant.
2481	109-90-0	Ethyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2482	110-78-1	n-Propyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2483	1795-48-8	Isopropyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2484	1609-86-5	tert-Butyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2485	111-36-4	n-Butyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2486	1873-29-6	Isobutyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2487	103-71-9	Phenyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).

2488	3173-53-3	Cyclohexyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2521	674-82-8	Diketene	Lacrimator and eye, skin and respiratory tract irritant.
2605	6427-21-0	Methoxymethyl isocyanate	Isocyanates are considered to be respiratory sensitizers unless proven otherwise (67/548/EEC).
2606	681-84-5	Methyl orthosilicate	Inhalation of vapours can lead to fatal lung or kidney damage. Exposure to vapours causes delayed pain to eyes, tearing and redness. Estimated that 200-300 ppm are required for 15 min to produce minimal lesions, 1000 ppm to produce injury requiring hospitalization.
2644	74-88-4	Methyl iodide	Characteristics of poisoning include delay between exposure and onset of symptoms, early systemic toxicity with congestive changes in lungs and oliguric renal failure, prominent cerebellar and Parkinsonian neurological symptoms as well as seizure and coma in severe cases psychiatric disturbances that last from months to years. Fatal poisoning has been described, details are lacking in abstract.
2668	107-14-2	Chloroacetonitrile	Lacrimator and irritant. Lacrimation may provide adequate warning of exposure.
2826	2941-64-2	Ethyl chlorothioformate	No relevant information was found.
3079	126-98-7	Methacrylonitrile	Lacrimator, eye irritant. Mild irritant effects were noted in human volunteers exposed to concentrations of 2 and 14 ppm.
3246	124-63-0	Methanesulphonyl chloride	Corrosive to eyes, skin and mucous membranes.

3.1 Additional remarks

3.1.1 Vapour pressure

Vapour pressure values could be found for 34 substances. Because vapour pressure values for the mixtures 1613 Hydrocyanic acid (<20% aqueous solution) and 3294 Hydrogen cyanide (<45% in alcohol) were not found, only vapour pressure for pure HCN was collected.

3.1.2 LC50 values

LC50 values could be found for 26 substances. Because LC50 values for the mixtures 1613 Hydrocyanic acid (<20% HCN in water) and 3294 Hydrogen cyanide (<45% in alcohol) were not found, only LC50 values for pure HCN were collected.

Sixteen substances were classified for inhalation toxicity on Annex I of EU directive 67/548/EE. Although Annex I of EU directive 67/548/EEC classification does not provide exact LC50 values (see section on 'LC50 values' in '2 Materials and methods'), it gives a range of LC50 values within which the "true" LC50 value lies. Therefore, the boundaries (the lowest and the highest) were used as LC50 values in the final calculations.

Values in Annex I of EU directive 67/548/EEC or LC50 values based on 1-h or 4-h exposures times could not be located for three substances: 1541 Acetone cyanohydrin, 1605 Ethylene dibromide and 1892 Ethyldichloroarsine. In the results, the LC50 values used for these compounds are based on 2-h, 0.5-h and 10-min experimental exposure times, respectively. LC50 values based on shorter exposure times are often higher than LC50 based on longer exposure times. It is therefore possible that, if extrapolated to 1-h exposure times, the LC50 value for 1605 Ethylene dibromide and 1892 Ethyldichloroarsine will be lower than those reported here.

3.1.3 Classification of isocyanates based on read-across arguments

Of the substances included in this study, nine are isocyanates. Sufficient data for classification was located for two of these isocyanates and vapour pressure information was found for additional two. In read-across and category approaches, the unknown property of a substance is presumed equal to that of similar compounds with known properties. Such read-across and category approaches may be used to estimate the classification of the seven isocyanates for which insufficient or no information has been found.

The isocyanates included in this study are 2481 Ethyl isocyanate, 2482 n-Propyl isocyanate, 2483 Isopropyl isocyanate, 2482 t-Butyl isocyanate, 2485 n-Butyl isocyanate, 2486 Isobutyl isocyanate, 2487 Phenyl isocyanate, 2488 Cyclohexyl isocyanate and 2605 Methoxymethyl isocyanate. All are comparable in chemical composition (consisting of C, H, N and in one case O), structure (aryl, alkyl or alkoxy isocyanates with one isocyanate functional group) and size (ethyl to cyclohexyl and phenyl side groups). Further support for the use of a read-across approach for classification is the finding that a clear structure –activity relationship is observed for vapour pressure values for the four isocyanates for which vapour pressure information is available. The smallest isocyanate (2481 Ethyl isocyanate) has the highest vapour pressure, the intermediate in size isocyanate (2485 n-Butyl isocyanate) has lower vapour pressure whereas the largest isocyanates (2487 Phenyl isocyanate and 2488 Cyclohexyl isocyanate) have the lowest vapour pressures. Although not a substance of interest for this study,

available data for methyl isocyanate can support the read-across argument. A brief search using the HSDB and AEGL databases revealed that methyl isocyanate has 1-h (measured and extrapolated) LC50 value between 10 and 45 ppm, an average vapour pressure of 49215 Pa and SVC of 486083. These data show that the structure activity relationship for vapour pressure holds for methyl isocyanate as well since the vapour pressure of the smaller methyl isocyanate is higher than that for ethyl isocyanate. Furthermore, the LC50 values for methyl isocyanate (10-45 ppm) are comparable to those observed for 2485 n-Butyl isocyanate (3.7-146 ppm) and 2487 Phenyl isocyanate (3.9-12.6 ppm).

The two isocyanates that could be classified are 2485 n-Butyl isocyanate and 2487 Phenyl isocyanate. Both fulfil the criteria specified in section 2.6.2.2 for substances that are toxic by inhalation for inclusion in Division 6.1. Furthermore, both fulfil the criteria for inclusion in packing group I (Table 2). In addition, methyl isocyanate also fulfils the criteria for inclusion in Division 6.1, packing group I. It can therefore be argued that it is likely that the other isocyanates for which insufficient information was found, also fulfil the criteria for inclusion in Division 6.1, packing group I.

Furthermore, both 2485 n-Butyl isocyanate and 2487 Phenyl isocyanate fulfil the criterion of LC50 < 200 ppm & SVC > 500 LC50 except when the highest LC50 value is used when the fulfil the criterion of LC50 < 1000 ppm & SVC > 10 LC50 (Table 3). In addition, methyl isocyanate fulfils the criterion of LC50 < 200 ppm & SVC > 500 LC50 for all available LC50 values. It can therefore be argued that it is likely that the other isocyanates for which insufficient information was found, also fulfil these criteria in a similar manner.

4 Conclusions

Multiple acute inhalation LC50 values were found for some substances. In most cases, the range of the available LC50 values was reasonable and within what can be expected for experimental results. For only three substances is the range in LC50 values high (>19-fold). The reason for this large range was not sought out in detail. Table 1 lists the highest and the lowest experimental acute inhalation LC50 values and the limit values listed on Annex I of EU directive 67/548/EEC based on acute inhalation toxicity. This provides a general overview over the information that is available and allows independent classification of the data. In the classifications provided in Table 2 and 3, the data shown in Table 1 are classified using two classification criteria for acute inhalation toxicity. In these tables, the most conservative LC50 values (including limits of Annex I of EU directive 67/548/EEC) were used to classify the substances. Using the lowest LC50 is considered pragmatic since the most conservative LC50 value has in most cases been experimentally obtained or is otherwise specified by the limits of Annex I of EU directive 67/548/EEC. Classification using the highest LC50 values was also performed and compared with that obtained using the lowest LC50 value. The results of this comparison are discussed below.

Of the 41 substances of interest, no useful vapour pressure and/or acute inhalation LC50 values could be found for 13 substances (Table 1). For 28 substances, vapour pressure and LC50 values were found that were considered sufficient for classification according to the criteria specified for substances that are toxic by inhalation in section 2.6.2.2 of the UN Model Regulation on Transport of Dangerous Goods. Note that thiophosgene has a double listing, one as vapour and a second as mist because it was not clear from the available information whether the acute inhalation LC50 values were obtained using the mist- or vapour form of the substance. Furthermore note that for the substances 1541 Acetone cyanohydrin, 1605 Ethylene dibromide and 1892 Ethylenedichloroarsine, the LC50 values listed are based on exposure times other than the recommended 1-h or 4-h exposure times. These acute inhalation LC50 values were used in Tables 1, 2 and 3 without extrapolation or modifications since they give a better indication of the acute inhalation toxicity of the substance than no information. It may be possible to extrapolate these values to 1-h exposure times using Haber's Law ($C^n * t = k$). However, this extrapolation method was not recommended in the UN Model Regulation on Transport of Dangerous Goods and was therefore not used in this report.

All of the substances for which sufficient information was gathered fulfilled the criteria specified in section 2.6.2.2 for substances that are toxic by inhalation for inclusion in Division 6.1 (Table 2). Using the lowest (most conservative) acute inhalation LC50 value and assuming that thiophosgene was tested as vapour, 26 of the substances fulfilled the criteria for packing group I, 2 fulfilled the criteria for packing group II whereas none fulfilled the criteria for packing group III. If the highest (least conservative) LC50 value was used, 19, 8 and 1 substances were found to belong to packing group I, II and III, respectively.

The substances were also classified according to criteria for sub-categories for substances that are toxic by inhalation and that can be found in the Dangerous Goods List (chapter 3.2) of the UN Model Regulation on Transport of Dangerous Goods (Table 3). In this system, the substances are classified based on whether they fulfil the following criteria i) LC50 < 200 ppm and SVC > 500 LC50 or ii) LC50 < 1000 ppm and SVC > 10LC50. Substances tested as mists and mixtures without test data can not (easily) be classified using these criteria. Nine and 1 substances fulfilled the criteria for group 1 when the lowest and highest LC50 values, respectively, were used. Twenty-three and 17 substances fulfilled the criteria for group 2 when the lowest and the highest LC50 values, respectively, were used.

Human exposure experience information on the substances was collected (Table 4). This information has not been used to classify the substances in this report because the criteria for classification using human exposure experience information are ambiguous. This information may be used as supplementary information to confirm the classification of a substance.

Sufficient information for classification was found for two of the nine isocyanates of interest for this study. By using read-across approaches, it may be possible to argue that the seven isocyanates for which insufficient information was found can be classified in a comparable manner as the two isocyanates for which sufficient information was found.

5 Appendix I

An example of a data sheet for a substance included in this study.

UN number	CAS number	Name
1838	7550-45-0	Titanium tetrachloride

Molecular formula
NOAA (Cameo) TiCl4

Molecular weight
NOAA (Cameo) 189.73

Molecular form
NOAA (Cameo) liquid, fuming

Vapor pressure	Original data	Pascal and ˚C	General extrapolation Pascal @ 20˚C	General extrapolation **SVC**
NOAA	10.0 mm Hg @ 70.34 ° F	1333 Pa @ 21.3 ˚C	1264	12482
HSDB	1.31X10^{-2} atm @ 20 ˚C	1327 Pa @ 20 C˚	1327	13107
ATSDR	10 mm Hg @ 20 ˚C	1333 Pa @ 20 C	1333	13166
	9.6 mm Hg @ 22 ˚C	1327 Pa @ 22 C	1223	12075
				12707
MSDS	12.8 hPa @ 20 ˚C	Not used - judged to be a less reliable source		
	16.5 hPa @ 25 ˚C	Not used - judged to be a less reliable source		
	67 hPa @ 55 ˚C	Not used - judged to be a less reliable source		

	Original data			Correct units		**vapor, ppm, 1h**	
LC50 (vapor)	LC50	exposure time	species	ppm	h	**LC50**	Remarks
HSDB	100 mg/m3	2 h	mouse	12.7	2		
	460 mg/m3	4 h	rat (head)	58.4	4	116.8	4-h extrap.
	108000 mg/m3	2 min	rat (head)				
IUCLID	0.46 mg/l	4 h	rat	58.4	4	116.8	4-h extrap.
	1.1 mg/l	2 h	rat	139.6	2		
	1.3 mg/l	1 h	rat	165	1	165	1-h
	3 mg/l	30 min	rat	381	0.5		
	5.5 mg/l	15 min	rat	698	0.25		
	36 mg/l	5 min	rat	4569	0.083		
	108 mg/l	2 min	rat	13707	0.033		
	0.1 mg/l	2 h	rat	12.7	2		
ATSDR	460 mg/m3	4 h	rat	58.4	4	116.8	4-h extrap.
	108000 mg/m3	2 min	rat				
ERPG	460 mg/m3	4 h	rat	58.4	4	116.8	4-h extrap.

	1100 mg/m3	2 h	rat	139.6	2		
	1300 mg/m3	1 h	rat	165	1	165	1-h
						116.8	**min**
						165	**max**

Annex 1 (EU 67/548/EEC)	R34: Causes burns - corrosive		
MSDS	1300 mg/m3	1h rat	Not used - judged to be a less reliable source
	400 mg/m3		Not used - judged to be a less reliable source
	100 mg/m3	2h	Not used - judged to be a less reliable source

Human exposure experience

IUCLID Corneal damage was reported in five people who had been severely exposed to the fumes of TiCl4. In one fatal case, the victim exhibited sever conjunctivitis with extensive destruction of corneal tissue. The cause of death was reported to be pulmonary effects of exposure.

HSDB Observed damage to corneas in five human being who had been severely exposed to these fumes, with particularly several effects on cornea in patients who died from exposure

ATSDR One death was reported in the case of a worker who was accidentally splashed his whole body with titanium tetrachloride. The patient died from the complications of severe pulmonary injury caused by inhalation of titanium tetrachloride fumes

Case studies of humans acutely exposed to titanium tetrachloride fumes show the irritant nature of the inhaled chemical.

Although the degree of pulmonary injury can vary, exposure can result in an intense chemical bronchitis or pneumonia (Lawson 1961). Following an accidental acute exposure, three research workers experienced only mild irritant symptoms consisting of cough and tightness in the chest, which both lasted only a couple of hours and left no abnormalities on the chest X-ray (Ross 1985). More severe pulmonary effects were reported in two other incidents of accidental exposure to titanium tetrachloride.
One worker who was splashed with hot titanium tetrachloride suffered marked congestion of the pharynx, vocal cords, and trachea (Ross 1985). This exposure had long-term effects that included stenosis of the larynx, trachea, and upper bronchi. The second worker accidentally exposed to titanium tetrachloride hydrolysis fumes developed cough and dyspnea 20 minutes after exposure (Park et al. 1984). His symptoms progressed to severe upper airway distress that required intubation and ventilation. Further symptoms included hypoxia and diffuse pulmonary infiltrates suggestive of adult respiratory distress syndrome.
He gradually improved, but fiberoptic bronchoscopy 5 weeks after admission revealed erythema of the entire bronchial tree and the presence of 35-40 fleshy polypoid lesions. The presence of the polyps, according to the authors, was a sign of an exaggerated but normal reparative process of the tracheobronchial injury. This delayed complication has been seen in thermal respiratory injuries, indicating that the severe adverse respiratory effects seen in this case may, in part, be due to the exothermic nature of the titanium tetrachloride hydrolysis reaction. One year after the injury, his lungs appeared normal, but some degree of mild stenosis remained