

# Department of Physiology and Pharmacology Doctorate course in Toxicology CYCLE XXXII

Research doctorate thesis

# **Toxic Industrial Chemicals and Civil Protection.**

Methods of analysis for damage estimation as a result of accidental releases and not, export profiles and stockpiles of antidotes.

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# 1 Dedication

"Out of the night that covers me, Black as the pit from pole to pole, I thank whatever gods may be For my unconquerable soul.

In the fell clutch of circumstance I have not winced nor cried aloud. Under the bludgeonings of chance My head is bloody, but unbowed.

Beyond this place of wrath and tears Looms but the Horror of the shade, And yet the menace of the years Finds and shall find me unafraid.

It matters not how strait the gate, How charged with punishments the scroll, I am the master of my fate: I am the captain of my soul."

William Ernest Henle

## 2 Abstract

The risk of accidents caused by the dispersion of hazardous chemicals is a real and everpresent risk. Leaks can occur in the transport phases of the leaks rather than as a result of accidental or caused industrial accidents. The European Union, through the application of product regulations (REACH, CLP, Biocide product and Plant Protection Product) aims to guarantee safe use of chemicals within the Union and with PIC Rgulations promotes the shared responsibility during the export dangerous chemicals ban or severely restricted in UE. The study of inhalation toxicity the substances listed in the PIC Regulation is therefore a fundamental element for predicting the damage to the exposed population. In order to quantify the damages, predictive methods were used to indicate the quantitative estimates of the damages, allowing, on the basis of the results, to hypothesize and update adequate stocks of antidotes. Attention has also been paid to the fight against ionizing radiation with the proposal of a kit to reduce the damage to the health of personnel possibly exposed. As a result, emphasis was placed on the risk of transporting Liquid Petroleum Gas (LPG) at

As a result, emphasis was placed on the lisk of transporting Equild Feroleum Gas (EFG) at low temperatures, in terms of the high risk of explosion and flammability. The risk of missing an update of the equipment of the advanced second level medication posts, which lack medicinal oxygen in their supplies, was highlighted. Substances with a high inhalation toxicity higher than some war weapons such as Soman, Sarin, Tabun and Vx have been identified, highlighting a risk both for operators in the sector and for the population possibly exposed. Export flows of PICs from Europe to other continents over the last 16 years were analyzed.

### 3 Resume

Prevention is the word that best describes my doctoral thesis.

The ability to prevent accidents involving the release of chemical substances that may affect the health of people who may be exposed is the main objective behind my doctoral research. The prevention implemented through in silico methods for the estimation of the dispersion of chemical substances and through methods for the quantitative estimation of the damage with the aim of adapting what are the antidotal stocks present for the needs of civil protection.

In the mean time, Hazardous Materials (HazMat), as well as representing a risk of inhalation for people possibly exposed, may represent a risk of radiological nature, these substances may be present as a residue of the processing processes of the nuclear industry, rather than nuclear medicine. In the event of a risk of exposure to ionizing radiation, my research focused on idealizing a first aid kit to reduce damage from ionizing radiation.

Prevention is establish restriction and also applying the enforcement on the restricted substance within EC and in the meantime to stimulate the capacity building on the concern of these substance in the other countries especially those developing countries or with transition economy. Prevention in the end for professional users of these substances that may be involved in transport processes rather than in the use phases as in the case of plant protection products.

The approach to research has therefore been broad from the toxicological characteristics, to the dynamics of release up to the adaptation of antidotal stocks, going so far as to hypothesize a cyber attack as the origin of a release of chemicals.

The research was therefore developed assuming the damage following the release of "HazMat" chemicals of industrial origin, starting from the substances listed in the European Prior Informed Consent "PIC" Regulation No. 649/2012, which lists certain chemicals that given their toxicity are subject to restrictions or ban on their use in the European territory and for which attention Is put on in the export phase. The research also focused on the substances present in the Seveso III Directive, for a total of 489 substances.

Toxicological information was obtained by consulting databases such as: Toxnet, Cameo, Toxin and Toxin Target Database, PubChem, database of the Environmental Protection Agency (EPA) and European Chemistry Agency (ECHA). The information not available in the following databases have been found through the consultation of Safety Data Sheets or thanks to the help of programs such as the Qsar Toolbox that through Read Across or Trend Analysis has allowed me to fill the information gap. The distribution scenarios were simulated using the Environmental Protection Agency's ALOHA software, while the quantitative damage estimates were made using the TNO Organization's Green Book.

In addition to estimating the toxicological damage of an inhalation nature, I focused on adapting the antidotal stocks following the release of chemicals, comparing the equipment indicated in the Legislative Decree no. 105 of 26 June 2015 for the Advanced Second Level Medication Posts (AMP). Part of my research was focused on the protection from chemical substances of a radiological nature, assuming a special first aid kit to be used in case of a release of ionizing radiation, both for purely "operational" needs of a military nature and for civil protection needs.

A comparative analysis of the risk of toxicity among the substances of the PIC regulation related to pesticides was carried out with some organophosphorus commonly used as chemical warfare agents: Sarin (GB), Soman (GD), Tabun (GA) and VX highlighting the inhalation risks related to the use of these substances, both for operators and for the population within the European Community and in importing countries.

As result, different problems have been identified:

- Transport of LPG at low temperatures in terms of tank explosion risks, rather than high butane flammability at low temperatures;
- Failure to update the lists relating to the equipment of the advanced second level medication posts with particular reference to the essence of medicinal oxygen among the basic equipment for the treatment of patients;
- A self-medication kit for countering damage from ionizing radiation following radiological accidents which may involve HazMat has been suggested;
- 25 substances belonging to the PIC and Seveso III regulations with an inhalation toxicity comparable to or higher than the Soman, Sarin, Tabun and Vx weapons of war have been identified thanks to the consultation of the Databases or thanks to computational chemistry techniques;
- The export flows of the substances listed in the PIC Regulation (Pesticides use, Industrial use) were analyzed.

The chemicals were then ordered on the basis of their toxicity using a parameter that relates the duration of exposure and the concentration of the chemical.

The results show that there is a significant risk in the use of HazMat substances with regard to the inhalation risk, in Europe and in the countries to which these substances are exported highlighting that the issue of the management of hazardous chemicals should be addressed through a comprehensive approach. the thesis shows how at the same time these substances can lend themselves to a distorted use, different from that for which they were produced. The research also shows that antidotes are not always up to date with regard to both inhalation exposure and possible radiological emergency.

## 4 Introduction

The risk of accidents involving chemical substances of an industrial nature, which by their nature represent a risk to both, inhalation toxicity and exposure to possible ionizing radiation, is a real and current risk.

Some examples of accidents involving the transport of chemicals such as Liquid Petroleum Gas (LPG) are the accident in Viareggio in 2009 that led to the death of 33 people (11 of whom lost their lives in the immediate vicinity of the event, two more for heart attack, and dozens were injured)[1]. The increase in the risk of transporting these goods is also due to the increase in traffic and transported goods [2]. There are estimates in the world that speak of 1000 deaths and 10,000 injuries in the period from 1940 to 2005 with damage to property and infrastructure during the transport of dangerous goods such as LPG [3]. The Major Hazard Incident Data Service (MHIDAS) producedes by Aea technology, on the risk of transporting dangerous goods has also highlighted the fact that a considerable number of accidents have occurred in the transport of dangerous goods [4]. The risk of toxicity may also occur with the release of industrial chemicals. An example is the Minamata disease, so called as it was noticed the first time in Minamata (city in the Prefecture of Kumamoto/ JPN) area affected by the release of mercury into the wastewater of the chemical industry Chisso Corporation that lasted from, 1932 to 1968, is mercury that entered the food chain as a result of a biomagnification phenomenon caused considerable damage with consequences on the population potentially exposed for a total of 2,265 victims of which 1,784 died [5], with more than 10,000 people who received compensation from the company Chisso. The industrial accident occurred in the town of Bophal (India) on December 3, 1984, caused the leakage of 40 tons of methyl isocyanate, which led to 4,000 deaths and more than 50,000 contaminated [6]. In the case of Bophal, the combination of incorrect maintenance of the plant with unfavorable weather conditions (presence of thermal inversion) had a decisive and negative impact on the outcome of the tragedy. Therefore, when we talk about chemical risks, there is always a correlation not only between the chemical risk itself and the health of exposed people but also with environmental risk, like in the case of the accident occurred in Italy at Seveso. The spill of dioxin involved 37,000 people and as many as 80,000 animals (later slaughtered to prevent the introduction into the food chain) [7]. In the case of Seveso, the costs of land reclamation were also considerable, including the removal of contaminated land with the repositioning of unpolluted land. The total expense of the operation has been estimated at ITL 66 billion [8]. The Seveso accident prompted the Member States of the European Union to adopt a common policy on the prevention of major industrial risks from 1982 onwards. The European Directive called "Seveso Directive" (European Directive 82/501/EEC, implemented in Italy by the Presidential Decree of 17 May 1988, n. 175 in its first version) imposes the member states to identify their sites at potential risks. The current Seveso Directive in force is the third edition from 24 July 2012 and Directive 2012/18/EU of 4 July 2012 which was published in the Official Journal of the European Union no. 197. Effective on 13 August of the same year, to be transposed by the Member States by 1 June 2015. Italy transposed it into its legal system with legislative decree no. 105 of 26 June 2015.

Accidents may also include the release of radiological chemicals that have originated as waste from nuclear medicine rather than as waste from industrial processes involving the production of nuclear energy. A certainly important example is the Chernobyl disaster that caused the deaths of many people with estimates ranging from the 6,000,000 deaths of Greenpeace worldwide over the course of the 70 years [9] for tumors directly or indirectly related to radiation exposure. Official estimates provided by the UN (WHO; UNSCEAR, IAEA) speak of 65 deaths confirmed with more than 4000 cases of thyroid cancer [10]. Other notable radiological accidents were those at the Three Mile Island nuclear power station in the USA (1979) which led to the release of small quantities of radioactive gases and radioactive iodine into the environment [11], in Tokaimura / Japan (1999), where a small explosion in the nuclear plant generated the release into the atmosphere of a radioactive cloud that caused the death of two people and the contamination of 687 people [12]. Another accident occurred in Fukushima / Japan (2011) where, following a tsunami and the consequent breakdown of the cooling pumps of the plant, was a leak of radioactive material in units 1, 2 and 3 of the reactors. As a result of the accident, one person was killed and 16 were injured, with 184,000 people evacuated [13]. Other examples of radiological accidents caused by incorrect disposal of waste from nuclear medicine are those in Goiânia/ Brazil (1987), where an old device used in radiotherapy was stolen from an abandoned hospital and passed through various interlocutors. It is estimated that it has contaminated about 250 people by killing four of them and has been classified with level 5 of the IAEA INES scale [14].

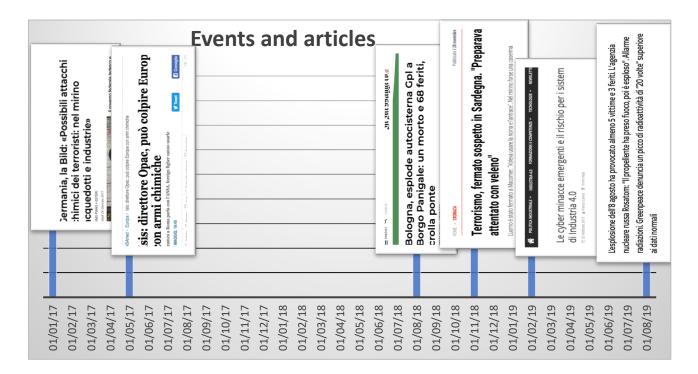
Even more relevant is the risk, in possible, war scenarios are examined, of the use of nuclear devices could lead to enormous and priceless consequences on the health of the exposed [15]. Just think that only between the United States and Russia is an estimated quantity of about 14,000 nuclear devices ready to explode [16].

The scenario is further complicated if disasters due to natural causes, disregarding man and war risks, are associated with the risk of terrorist attacks using the so-called "dirty bombs",

which are nothing more than low-power bombs capable of releasing chemical-radioactive material. This risk is also real in Italy as underlined by the Carabinieri Corps through its Commander of the Environmental Protection Unit Gen. Raffaele Vacca [17].

When we talk about HazMat, therefore, there is either a risk arising in everyday work situations but also in the light of recent news reporting a growing risk of misuse of these substances for terrorist purposes. A useful example to better understand the double possibility of using these substances, is the chlorine molecule, used in industrial processes as a chemical substance, and at the same time used as a toxic asphyxiating substance, very toxic from low concentrations.

In the following figure (*Fig.* 1) some examples of actual news events or newspaper articles that warn about the chemical risk involved in my PhD thesis:



*Fig. 1 from left to right in chronological order, in correspondence to the columns, are reported newspaper articles dealing with real events or real risks related to the distorted use of chemicals.* 

A real risk is, that certain chemical substances may, for various reasons, come into contact with the population or the environment, causing damage to people and property.

The European Community has decided to regulate the use and import of certain substances that by their nature represent a toxicological risk for the population and the environment by chemical products legislation: 1907/2006 called Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and 1272/2008 called Classification, Labelling and Packaging (CLP).

The objectives of the REACH Regulation are to improve knowledge of the risks and dangers arising from chemicals already on the market (before September 1981) and new substances placed on the market (after September 1981) while maintaining and strengthening the competitiveness and capabilities of the European chemical industry.

REACH consists of XV Titles divided into 141 articles and 17 technical annexes. The REACH also regulates the entry of substances into the EU, especially if they are imported in quantities exceeding one ton per year. The REACH Regulation lays down procedures for the collection and evaluation of data on the properties and hazards of substances. Substance manufacturers have to register substances and work together with other agencies to do so. The ECHA obtains the information and assesses it in accordance with the individual registrations and the Member States of the European Union which assess the selected substances to determine any risks to the population and the environment. The Scientific Committees of ECHA togheter the MSs then determine whether the risks of the substances can be managed or not. If the risks are too high, the authorities may ban them, reduce their use or make them subject to authorization.

The PIC Regulation, on the other hand, has the task of regulating the import and export of hazardous chemicals and requires companies wishing to export such substances to non-EU countries to do so. The purpose of the PIC Regulation Implements in EU the Rotterdam Convention is to promote shared responsibility and cooperation in international trade in hazardous chemicals, to protect human health and the environment by providing developing countries with useful information on how to safely store, transport, use and dispose of hazardous chemicals. The PIC Regulation shall apply to banned or severely restricted chemicals listed in Annex I containing industrial chemicals, pesticides and biocidal products. The export of these chemicals is subject to two types of requirements: export notification and explicit consent. The PIC Regulation also applies to chemicals that are banned for export in accordance with Annex V and to the packaging and labelling of all exported chemicals, as packaging and labelling must comply with relevant EU legislation. Chemicals including drugs, radioactive materials, waste, chemical weapons, food and food additives, feed, genetically modified organisms and pharmaceuticals (except disinfectants, insecticides and pesticides) are covered by other EU legislation and therefore do not fall under the scope of the PIC Regulation.

Furthermore, the PIC Regulation does not apply to chemicals exported for research or analysis in quantities not likely to have an effect on human health or the environment and in quantities not exceeding 10 kg from each exporter to each importing country per calendar year. The PIC Regulation shall apply from 1 March 2014. As of this date, ECHA is

responsible for the administrative and technical aspects of the new Regulation. The Agency's main task is to prepare and send export notifications to non-EU importing countries and to maintain a database of explicit notifications and consents from importing countries. ECHA also provides technical and scientific assistance and guidance to the industry, the designated national authorities of both the EU and third countries, as well as to the European Commission.

The substances listed in the PIC Regulation are therefore subject to restrictions on use, import and export with the aim of reducing the risk to the population and the environment.

This Regulation implements, within the European Union, the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade [18].

Another European Directive that deals with the normal production of industrial chemicals considered hazardous is the Seveso III Directive. The European Directive called "Seveso Directive" (European Directive 82/501/EEC, implemented in Italy by the Presidential Decree of 17 May 1988, n. 175 in its first version) requires member states to identify their sites at risk. The Directive provides for:

- the census of establishments at risk, with identification of dangerous substances
- the existence of a prevention plan and an emergency plan in each establishment at risk
- cooperation between operators to limit the domino effect
- monitoring of urbanization around sites at risk
- information for the inhabitants of neighbouring areas
- the existence of an authority responsible for inspecting sites at risk

The Directive does not cover military installations and the risks associated with the emission of ionizing radiation. In Italy, regional environmental protection agencies are responsible for monitoring sites at risk. The Directive therefore lists all the sites that produce chemical substances considered dangerous with a quantity exceeding specific threshold levels indicated in the tables in the annex to the Directive.

During my PhD I then analyzed several aspects directly related to HazMat highlighting the risks related to transport at low temperature, the lack of adaptation of antidotal stocks especially the lack of medicinal oxygen among the minimum equipment in the advanced posts of second level medication. I assumed a first aid kit for the reduction of damage from

ionizing radiation, related the toxicity of the chemicals listed in the PIC Regulation and Seveso III regulations with some Chemical Warfare Agents (CWA), highlighting that the risk of inhalation is a real risk especially if these substances are used for a different use from that assumed when they were placed on the market or for professional users (as in the incorrect use of pesticides). Finally, I highlighted the cybernetic risk in the age of companies 4.0 [19].

# 4.1 Toxicological Reference Indices

In this PhD thesis several toxicological reference indices have been used. The purpose of these indices is to quantify the risk of toxicity from inhalation or ingestion of chemicals.

The first reference index is the LC50 or lethal concentration 50 which indicates the concentration of chemical substance in the air that can cause the death of 50% of exposed people. This reference value generally refers to an exposure of 4 hours. If it refers to time periods other than four hours, the duration of the exposure should be specified. LC50 inhalation has been determined in the past through the use of guinea pigs to which the chemical was inhaled at different concentrations until the death of 50% of the guinea pigs (animals used in the experiments were mice, rats, hamsters and dogs for example).

The second toxicological index used is the LD50 Lethal Dose 50 is nothing more than the lethal concentration of the toxic substance such as creating death in 50% of the subjects once ingested. The lethal dose 50 is not the parameter used in the thesis for the determination of inhalation toxicity, but it can be an indicator in the broad sense of the systemic toxicity of the compound analyzed.

Over time, there has also been a growing awareness of the need to minimize the suffering of animals used in experiments. In part, the adoption of the REACH Regulation (EC) No 1907/2006 has already had the effect of raising awareness among industry on the need of using alternative methods for the estimation of inhalation toxicity by accepting and encouraging the use of computational chemistry estimation methods for the determination of inhalation damage. These "alternative" estimation methods can be used in the compilation of toxicological dossiers that companies must provide when registering the substance to the ECHA under REACH regulation procedures.

In addition\_the Directive 2010/63/EU on the protection of animals used for scientific purposes" limits the use of animals in science was tightened up, limiting it "only when, in order to obtain the result sought, it is not possible to use another scientifically valid method or testing strategy that is reasonably and practically applicable and does not involve the use

of live animals". In Italy, the Legislative Decree no. 26 of 4 March 2014 implemts the Directive and defines the criteria according to which animals like guinea pigs may be used and the strategies necessary for the maximum reduction of guinea-pig suffering in cases where the use of animal guinea-pigs is an essential factor.

It also encourages the principle of the "3 Rs" hypothesized in 1959 by two British academics, Rex Burch and William Russel, members of the Universities federation of animal welfare (EFAW) who hypothesized a model that researchers should use for harm reduction showing a greater sensitivity in alleviating suffering in experimental subjects [20]. The model is based on three principles: Replacement, Reduction and Refinement. With these three principles the researcher should try to replace his animal model with an alternative model, then he should try to reduce as much as possible the number of individuals to be used in his experimental protocol, to conclude with the last R, it tends to refine the experimental conditions to which the animals are subjected.

Another value collected during my thesis and in the database consultation, is the Immediately Dangerous to Life or Health (IDLH), defined by the American National Institute for Occupational Safety and Health (NIOSH) as the highest concentration of toxic substance to which a healthy person can be exposed for a period of 30 minutes, without suffering irreversible effects on health or without the effects of exposure preventing the escape.

Among the values consulted are also the Military Exposure Guidelines (MEG). These values allow to identify the maximum toxicity to which military personnel can be exposed. Such values consider the toxicity in air, water and soil. The values are given in Guide TG230 "Environmental Health Risk Assessment and Chemical Military Exposure Guidelines (MEGs) issued by the Army Public Health Center (APHC). In the thesis were collected, where available, MEG toxicity data at 1h.

Other values sought in the thesis indicators of inhalation toxicity were the Acute Exposure Guideline Levels (AEGLs). These values are developed by the Environmental Protection Agency (EPA). AEGLs are calculated for five different periods: 10 minutes, 30 minutes, 1 hour, 4 hours and 8 hours. They are classified in order of one to three, where the AEGL1 is dedicated to concentrations of toxic substance expressed in (ppm or mg/m3) of lower flow rate, capable of generating in exposed symptoms such as irritation and sensory effects, symptomatic and asymptomatic. AEGL3 is instead dedicated to concentrations of toxic substance that can generate a risk to the life of the exposition. Within the thesis I considered

the AEGL3 at 10 minutes, which is those concentration of toxic substance to which people can be exposed for a maximum period of 10 minutes putting at risk their survival.

The last parameters taken into consideration are the Protective Action Criteria for Chemicals (PACs). The PACs are used by the ALOHA software and allow to classify the danger zones in zones easily distinguishable on the map on toxicity level–the approach considers a hierarchical classification that first makes AEGLs values available, then if AEGLs values are not available, searches for values within the Emergency Response Planning Guidelines (ERPGs) and if these values are either not available, as an extreme ratio within the Temporary Emergency Exposure Limits (TEELs).

## 4.2 Inhalation toxicity

Irritant gases are those, that when inhaled, dissolved in the water of the mucous membrane of the respiratory tract and cause an inflammatory response, usually due to the release of acid or alkaline radicals. Exposure to irritant gases mainly affects the airways, causing tracheitis, bronchitis and bronchiolitis. Other inhalation medications may be directly toxic (e.g. cyanide, carbon monoxide) or cause damage by simply replacing O2 and causing asphyxiation (e.g. methane, carbon dioxide).

The effect of inhalation of irritant gases depends on the magnitude, duration of exposure and the specific agent.

Chlorine, phosgene, sulphur dioxide, hydrochloric acid, hydrogen sulphide, nitrogen dioxide, ozone and ammonia are among the most important irritant gases. Hydrogen sulfide is also a powerful cellular toxin, which blocks the cytochrome system and inhibits cellular respiration. Common exposure involves mixing ammonia at home with detergents containing bleach and chloramine, an irritating gas, is released.

Respiratory damage is related to the concentration and water solubility of the gas and the duration of exposure.

The most water-soluble gases (e.g. chlorine, ammonia, sulphur dioxide, hydrochloric acid) dissolve in the upper respiratory tract and immediately cause irritation of the mucous membranes, alerting people to the need of avoiding the exposure. Permanent damage to the upper respiratory tract, distal airway and lung parenchyma only occurs, if leakage from the gas source is prevented.

Less soluble gases (e.g. nitrogen dioxide, phosgene, ozone) cannot be dissolved until they enter the respiratory system, often reaching the lower airways. These agents are less able to cause early warning signals (phosgene at low concentrations has a pleasant smell) and are more likely to cause severe bronchiolitis. Often It has a delay of  $\ge$  12 h before symptoms of pulmonary edema develop.

The most serious and immediate complication is acute respiratory distress syndrome, which usually occurs immediately but can be also delayed up to 24 hours. Patients with significant involvement of the lower airway may develop a bacterial infection.

Some patients develop obliterative bronchiolitis which evolves into acute respiratory distress syndrome 10 to 14 days after acute exposure to certain agents (e.g. ammonia, nitric oxide, Sulphur dioxide, mercury). Obliterative bronchiolitis can occur and evolve into pneumonia when granulation tissue accumulates in the terminal airways and alveolar ducts during the body's repair processes. A minority of these patients develop late pulmonary fibrosis.

Soluble irritant gases cause severe burns and other irritating manifestations to the eyes, nose, throat, trachea and main bronchi. Strong coughs, hemoptysis, wheezing, vomiting and dyspnea are frequent. The upper airways may be obstructed by edema, secretions or laryngospasm. Gravity is generally dose-related. Insoluble gases cause less immediate symptoms but may cause dyspnea or coughing.

Patients who develop acute respiratory distress syndrome have increasing dyspnea and increased demand for O2.

Other risks related to inhalation toxicity are represented by chemicals belonging to the category of organophosphorus. This category includes both some of the pesticides I am researching and the chemical weapons used as a means of comparing toxicity.

The mechanism of action of the phosphoric organs is based on the link that these substances make with acetyl choline esterase, the enzyme that has the task of degrading excess acetylcholine. The lack of degradation of acetylcholine generates a hyper presence of the substance in intersynaptic spices generating an effect defined in toxicosyndromic as "killer B's" (Bronchorrhea and Bronchospasm), which manifests itself with muscarinic syndrome.

Muscarine symptoms predominate with miosis, increased oral secretions, bradycardia, diaphoresis, bronchospasm, bronchorrhea, vomiting, nausea, diarrhea, urinary incontinence, lacrimation, confusion, coma, lethargy, seizure, and possible death. Nicotine symtoms includes weakness and muscle fasciculations.

Below is a table showing some of the databases consulted during the PhD thesis for the estimation of the toxicity of inhaled chemicals (Tab. 1):

DATABASE Name	Number of Chemicals	Data	Donator(s)	Physical chemical properties	Environmental fate and transport	Ecotox Information	Human health hazard
Chemical Reactivity COLIPA	358	829	European Cosmetics Association (COLIPA)	$\checkmark$	-	-	-
Experimental pKa	14725	25422	Liverpool John Moores University, UK	$\checkmark$	-	-	-
GSH Experimental RC50	1460	2843	Unilever; International QSAR Foundation; University of Tennessee, Knoxville, USA	$\checkmark$	-	-	-
Phys-chem EPISUITE	25987	49509	Syracuse Research Corporation (SRC), USA	$\checkmark$	$\checkmark$	-	
pKa OASIS	1930	2309	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria	$\checkmark$	-	-	-
ECHA CHEM	11743	668041	European Chemicals Agency (ECHA)	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Bioconcentration NITE	767	1558	National Institute of Technology and Evaluation (NITE), Japan	-	$\checkmark$	-	-
<b>Bioaccumulation Canada</b>	499	2626	Environment Canada	-	$\checkmark$	-	-
Biota-Sediment Accumulation Factor US-EPA	311	24351	United States Environmental Protection Agency (EPA), USA	-	$\checkmark$	-	-
Biodegradation in soil OASIS	216	218	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria	-	$\checkmark$	-	-
REACH Bioaccumulation database (normalised)	220	1822	European Chemicals Agency (ECHA), Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria;	-	√	-	-
kM database Environment Canada	702	1535	Environment Canada	-	$\checkmark$	-	-
Hydrolysis rate constant OASIS	349	349	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria	-	$\checkmark$	-	-

Bioaccumulation fish CEFIC LRI	539	1124	CEFIC, LRI, Belgium	-	$\checkmark$	-	-
ЕСОТОХ	11320	887115	United States Environmental Protection Agency (EPA), USA	-	$\checkmark$	$\checkmark$	-
Biodegradation NITE	1373	1373	National Institute of Technology and Evaluation (NITE), Japan	-	$\checkmark$	-	-
Aquatic ECETOC	738	9487	European Center of Ecotoxicology and Toxicology (ECETOC), Belgium	-	-	$\checkmark$	-
Food TOX Hazard EFSA	1298	10541	European Food Safety Authority (EFSA)	-	-	$\checkmark$	$\checkmark$
Aquatic Japan MoE	659	4563	Ministry of Environment (MOE),Japan	-	-	$\checkmark$	-
Aquatic OASIS	2390	4826	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria; United States Environmental Protection Agency (EPA), USA; University of Knoxville, Tennessee, USA; Ministry of Economy, Trade and Industry (METI), Japan	-	-	~	-
Micronucleus ISSMIC	563	1022	Istituto Superiore di Sanità (ISS), Rome, Italy; Federal Office of Public Health (FOPH), Switzerland	-	-	-	$\checkmark$
ToxRefDB US-EPA	406	3591	United States Environmental Protection Agency (EPA), USA	-	-	-	$\checkmark$
Micronucleus OASIS	557	557	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria	-	-	-	$\checkmark$
Skin Irritation	354	351	National Institute for Public Health and the Environment (RIVM), Netherlands; European Center for the validation of Alternative methods (ECVAM), European Union; European Center of Ecotoxicology and Toxicology (ECETOC), Belgium; School of Pharmacy and Chemistry, Liverpool John	-	-	-	✓

			Mooroe I Initromiter				
			Moores University, UK				
December Medicted Effects	3333	5326	Laboratory of Mathematical				
Receptor Mediated Effects	3333	5526	Chemistry (LMC), Bourgas, Bulgaria	-	-	-	√
Rep Dose Tox Fraunhofer ITEM	949	5321	Fraunhofer Institute for Toxicology and	_	-	-	$\checkmark$
			Experimental Medicine, Germany European Cosmetics				
Dendritic cells COLIPA	257	933	Association (COLIPA)	-	-	-	$\checkmark$
Biocides and plant protection ISSBIOC	299	1196	Istituto Superiore di Sanità (ISS), Rome, Italy	-	-	-	✓
Skin sensitization ECETOC	39	42	European Center of Ecotoxicology and Toxicology (ECETOC), Belgium	-	-	-	$\checkmark$
Rodent Inhalation Toxicity Database	206	364	International QSAR Foundation	-	-	-	$\checkmark$
Acute Oral toxicity	10154	10154	Alex Tropsha, UNC Eshelman School of Pharmacy, North Carolina, USA; Martin Todd, USEPA, Cincinnaty, USA	-	-	-	$\checkmark$
ToxCastDB	1813	54669	United States Environmental Protection Agency (EPA), USA	-	-	-	$\checkmark$
Cell Transformation Assay ISSCTA	352	760	Istituto Superiore di Sanità (ISS), Rome, Italy	-	-	-	$\checkmark$
Repeated Dose Toxicity HESS	700	440396	National Institute of Technology and Evaluation (NITE), Japan	-	-	-	$\checkmark$
Keratinocyte gene expression LuSens	79	148	Givaudan International AG, Switzerland	-	-	-	$\checkmark$
Genotoxicity pesticides EFSA	706	17127	European Food Safety Authority (EFSA)	-	-	-	$\checkmark$
ZEBET database	362	908	Federal Institute for Consumer Health Protection and Veterinary Medicine (BgVV)	-	-	-	✓
Developmental & Reproductive Toxicity (DART)	716	1430	Procter & Gamble	-	-	-	$\checkmark$
Human Half-Life	1105	2045	Arnot Research & Consulting Inc., Canada	-	-	-	$\checkmark$
Skin Sensitization	1279	2667	Unilever; Procter & Gamble; ExxonMobil; Organization for Economic Co- operation and Development (OECD)	-	-	-	$\checkmark$

REACH Skin sensitisation database (normalised)	2072	2842	European Chemicals Agency (ECHA), Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria;	-	-	-	$\checkmark$
GARD Skin sensitization	130	131	SenzaGen AB	-	-	-	$\checkmark$
Yeast estrogen assay database	213	238	University of Knoxville, Tennessee, USA	-	-	-	$\checkmark$
Transgenic Rodent Database	208	3041	Centre for NanoHealth, Institute of Life Science, Swansea University, UK	-	-	-	~
Genotoxicity & Carcinogenicity ECVAM	744	9186	European Reference Laboratory for Alternatives to Animal Testing, EURL ECVAM	-	-	-	√
Carcinogenic Potency Database (CPDB)	1530	3501	University of California, Berkeley, USA	-	-	-	$\checkmark$
Carcinogenicity&mutagenicit y ISSCAN	1148	4518	Istituto Superiore di Sanità (ISS), Rome, Italy	-	-	-	$\checkmark$
Toxicity Japan MHLW	252	2914	Ministry of Health, Labour and Welfare, Japan	-	-	-	$\checkmark$
Genotoxicity OASIS	7985	30447	Laboratory of Mathematical Chemistry (LMC), Bourgas, Bulgaria	-	-	-	~
Keratinocyte gene expression Givaudan	323	1089	Givaudan International AG, Switzerland	-	-	-	$\checkmark$
Eye Irritation ECETOC	128	146	European Center of Ecotoxicology and Toxicology (ECETOC), Belgium	-	-	-	~
Toxicity to reproduction (ER)	53	303	National Institute of Environmental Health Sciences (NIEHS)	-	-	-	~
Developmental toxicity ILSI	193	4991	International Life Sciences Institute (ILSI), USA	-	-	-	$\checkmark$
MUNRO non-cancer EFSA	608	1461	European Food Safety Authority (EFSA)	-	-	-	$\checkmark$
Bacterial mutagenicity ISSSTY	7367	41634	Istituto Superiore di Sanità (ISS), Rome, Italy	-	-	-	$\checkmark$
Developmental toxicity database (CAESAR)	292	292	Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy, Emilio Benfenati	-	-	-	$\checkmark$
ADME database	6026	11969	Liverpool John Moores University, UK; Lhasa Limited, UK	-	-	-	$\checkmark$

Tab. 1 Databases consulted with reported number of molecules and aspects analyzed in the single database.

The correct use of databases avoids in vivo testing and represents an important source of data from which computational chemistry software can draw for the estimation of the toxicity of chemicals.

#### 4.3 The radiation damage

The radiation consists of electromagnetic waves of varying frequencies or particles. About 80% of the radiation comes from natural sources, such as cosmic radiation, ultraviolet light and natural radioisotopes, in particular radon gas. The remaining 20% comes from artificial sources, such as some instruments used in medicine and dentistry, products that emit radio waves or microwaves, and nuclear power plants. The effects of nuclear radiation have become apparent to the world as a result of nuclear explosions. The nuclear bombs dropped on Hiroshima and Nagasaki in 1945, in addition of causing immediate damage such as acute injuries and deaths, have caused an increase in the incidence of various forms of cancer. Therapeutic radiation also tends to release radiation with a well-known harmful effect. An example is the increased incidence of aplastic and neoplastic anemia in the skin, brain and hematopoietic system in radiologists at the beginning of the 20th century. Other cases from children treated with radiation between 1910 and 1959 for the treatment of benign lesions or for the treatment of cases of enlarged thymus, showed an increase in the incidence of alterations and thyroid tumors, lymphomas and leukemias. In addition, exposure of the fetus to radiation can cause solid tumors, leukemia, mental retardation and congenital malformations. The study of these accidental or deliberate exposures to radiation has made it possible to define the relationship between dose, irradiation time and acute and chronic harmful effects. However, it should be noted that these exposures were associated with higher doses of radiant energy than those that the population receives from natural or artificial sources, greater than the radiation that patients absorb through diagnostic procedures such as chest x-rays or mammography, or those that are absorbed by operators in the field of nuclear energy.

The effects of high radiation exposure are well known in the population, while the damage from low radiation exposure is not yet well known. In addition, some accidents that have affected nuclear power plants such as Windscale in England in 1957, Three Mile Island in Pennsylvania in 1979, and Chernobyl in the former Soviet Union in 1986, have increased the level of alert to cancer cases in close correlation with radioactivity in the medical, industrial and military fields. Microwaves, infrared rays, ultraviolet light, electrical energy and radio waves, and in general all electromagnetic radiation characterized by high wavelength and low frequency, are called non-ionizing radiation. Non-ionizing radiation only produces vibrations and rotations in the atoms of biological molecules.

The energy of radiation with a low wavelength and high frequency causes the expulsion of electrons and therefore the ionization of the target biological molecules. Examples of ionizing radiation are x-rays and  $\gamma$ -rays.

The origins of ionizing radiations can be different. In fact, they can be of electromagnetic nature, like the x-rays, produced by the roentgen tubes or the  $\gamma$ -rays emitted by natural sources or of cast nature corpus. Radiation is emitted during the natural decay of radioisotopes or during the artificial acceleration of subatomic particles. These corpusculated radiations are classified according to the type of emitted particle:  $\alpha$  particles,  $\beta$  particles (electrons), protons, neutrons, mesons or deuterons. The energy of these particles is measured in millions of electron volts (MeV). Radioisotopes decay either because they capture electrons or because of the emission of  $\alpha$  or  $\beta$  particles. The  $\alpha$  particles, which are formed by two neutrons and two protons, have a high ionization capacity, but at the same time a low penetrating power due to their size. The argument is different for type  $\beta$ radiations, which are nothing more than radiations emitted by the nucleus of an atom, which have little ionizing power but greater penetration capacity than the particles  $\alpha$ . The unit of measure of the decay of the radioisotopes is expressed in curie (Ci) equal to  $3,7 \times 10^{10}$ disintegrations per second, and in becquerel (Bq) equal to one disintegration per second. The time with which the radioisotope decays is expressed in half time  $(t^{1/2})$  and varies from a few seconds to centuries. The use of radioisotopes with high half-life is not recommended because of the continuous release of corpuscular radiation and  $\gamma$ -rays. For example, in the first half of the 20th century, radio-based paints were used to paint watch dials, just as they were used to treat cancer. The physical characteristic of this element (its high half-life of 1638 years) and its tendency to concentrate in bone tissue, caused the late appearance of bone tumors.

In the case of ionizing radiation, the dose is measured with reference to different units of measurement:

- Roentgen: charging unit produced by X-rays or γ-rays, which ionize a specific volume of air;
- Gray: expresses the radiation dose produced by the absorption of 1 joule of energy per kilogram of tissue;
- Rad: the amount of radiation that produces the absorption of 100 erg of energy per gram of tissue;
- Rem: the amount of radiation causing a biological effect equivalent to exposure to a dose of X-rays or γ-rays of 1 radiation;

• Sievert (Sv): the radiation dose causing a biological effect equivalent to exposure to an X-ray or γ-ray dose of 1 Gy: 1 Sv equals 100 rem.

In order to have a better quantification of the energy transferred per unit of tissue, so as to approach the biological effects of radiation, the following units of measurement have been identified:

- Linear energy transfer (**LET**) expresses the energy yielded per unit of distance travelled (eV/ $\mu$ m). The value changes depending on the type of ionizing radiation. The higher the LET, the lower the LET for type  $\alpha$  radiation, the lower the LET for type  $\beta$  radiation, and the lower the LET for  $\gamma$  and X-rays. Therefore, the particles that will interact more with the tissues, crossing little distance will be the  $\alpha$  and the  $\beta$ , while those that will interact less with the tissues penetrating however more deeply, will be the  $\gamma$ - and the X-rays. So, if equivalent amounts of energy affect an organism in the form of  $\alpha$  particles or  $\gamma$ -rays,  $\alpha$  particles will eventually cause significant damage in a small area, while  $\gamma$ -rays will eventually dissipate energy during the longest path and will eventually produce considerably less damage per unit of tissue.

- Relative biological effectiveness (**RBE**) is nothing more than a ratio between the LETs from various types of radiation and the LETs of  $\gamma$ -rays from cobalt and supervolt X-rays with an RBE value of 1 unit.

Ionizing radiations determine the radiolysis of water, producing free oxygen radicals, so cellular lesions from X-rays or  $\gamma$ -rays are greater in the presence of pressurized oxygen. In contrast, scavengers of free radicals and antioxidant agents can protect against radiation damage.

The dose of ionizing radiation influences what is the acute effect of ionizing radiation: for high doses (above 10 Gy) will be necrosis of the tissues concerned, at intermediate doses (1-2 Gy) will be a cytocidal effect of the proliferating cells, while at doses below 0.5 Gy no histopathological changes are observed. At a low level of radiation, however, there is subcellular damage that has as its main objective the DNA, but most cells are able to repair the cellular damage. If the cells have suffered significant DNA damage or are unable to repair this damage, they go into apoptosis. In surviving cells, late effects of radiation such as chromosome aberrations, mutations and genomic instability may occur. Some cells with DNA damage may undergo neoplastic transformation, especially rapidly growing cell populations that are highly sensitive to the effects of ionizing radiation.

Most alterations result from exposures above 0.5 Gy and acute cell death of vascular endothelium cells can cause late functional alterations of organs even months or years after exposure to radiation. In acute cases, ionizing radiation can cause a series of lesions to the DNA, with the formation of covalent bonds between DNA and proteins and between the two strands of DNA, degradation of the nitrogen bases, oxidation, cleavage of phosphodiester bridges and partial or total rupture of the DNA chain. These damages can be caused by corpuscular radiation or X-rays or  $\gamma$ -rays, or indirectly due to oxygen radicals by the action of products derived from lipid peroxidation. DNA damage can lead the cell to apoptosis thanks to the expression of some genes involved in DNA repair and responsible for stopping the cell cycle. Among the protagonists of cell repair mechanisms, is the protein p53, which is able to induce the arrest of the cell cycle to allow DNA repair and in some cases responsible for triggering apoptosis.

The study of oxidative stress is of recent interest, until 1985 there was little talk of oxidative stress. Nowadays the topics of fighting against oxidative stress are the order of the day, in the most disparate magazines. Meanwhile it is known that in our organism are pro oxidative and antioxidative phenomena that are in continuous equilibrium and that with time in a physiological or pathological way, this equilibrium can move in one direction or the other, giving rise to oxidative stress, defined as "alteration of the relationship between pro oxidants and antioxidants in favor of pro oxidants" which may then determine a potential cellular damage. The alteration of the pro-oxidant phenomena can be due to an increase in the production of radicals or to a decrease in the antiradical defenses (e.g. decrease in the thiol groups, cysteine, glutathione etc...). For this reason, if in every days life we were subjected to an overexposure of ionizing radiation caused by an NBC event, these would lead to the formation of radicals that in turn would lead to the depletion of the defenses of the entire body. In the case of an NBC event, exposure to free radicals would be in massive and concentrated doses and could lead to cellular damage to the person affected.

#### What are free radicals?

Surely oxygen radicals and nitrogen are free radicals. The free oxygen radicals are formed by the molecular oxygen by energy intervention (ionizing radiation). The formation of the super oxide radical is one of the most aggressive and oxidizing radicals found in nature. The latter will yield its radical by the intervention of a hydrogen and a molecule of water with the formation of hydrogen peroxide, which is a cellular poison. It's not a good thing having it in your body but it's useful to eliminate a radical. By the intervention of another hydrogen, the hydroxyl radical is formed, which is less oxidizing than the superoxide radical but has a greater aptitude for diffusion, tends to destroy less the molecule with which it comes into contact but has a greater range of action. At the end of the chain, water is formed. The electron is dispersed, but in the meantime substances with an extremely short life (nanoseconds, picoseconds) are formed, which will cede the electron to the next molecule and will form electronic fields and the molecules from which the electron has passed will not remain unharmed. For example, the passage of electrons is able to change the tertiary structure of the protein.

Another category of radicals are the nitrogen radicals. I.e. nitric oxide NO has been considered for years a poison, toxic substance or exchange product, today considered one of the most important mediators of the body especially as a vasodilator at the level of the brain..

It's not a neurotransmitter but a neuromodulator. Neurons produce nitric oxide as a modulator of intrasynaptic communication with role at the cellular level and at the vascular level with drugs with vasodilator function. However, the Nitrogen Oxide (NO) exists in radical form, a substance that tends to assume an electron in the external orbital and with the characteristic that you can combine with the radical superoxide.

### How do you combat oxidative problems?

There are the antiradical systems. The three most important antiradical system are the superoxide dismutase system, the catalase system and the reduced/oxidized glutathione system (GSH/GSSG). It is a very dynamic system, starting from four superoxides that are attacked by the superoxide dismutase which is an enzyme that recognizes the superoxide in the substrate and with the intervention of 4 (four) hydrogen released from a hydrogen donor, Nicotinamide Adenine Dinucleotide (NADH). To make the reaction there must be NADH. If there is no H, It Is Impossible to have the reaction. There must be a sufficient charge of NADH in the body to dismute the superoxide in two molecules of oxygen and two molecules of hydrogen peroxide. The molecular oxygen leaves and remain two molecules of hydrogen peroxide there is the enzymatic way of catalase. The enzymatic pathway uses catalases that catalyzes the transformation of two molecules of hydrogen peroxide there and one of oxygen.

An example of enzyme activity is the use of hydrogen peroxide. Normally, in our body no oxygen bubbles are formed because it catalyzes hydrogen peroxide because it mainly meets the reaction mediated by glutathione which is a tripeptide, composed of: glutamic acid,

glycine and cysteine. Three amino acids linked together by a peptide bond. Glutathione is a very small peptide with the characteristic of having a free SH group within the cysteine, an excellent donor of reducing equivalents, and therefore by intervention of the enzyme glutathione peroxidase the hydrogen peroxide is catalyzed. Two hydrogen are released from the SH group of glutathione (two molecules of glutathione are consumed in the reaction) and four molecules of water and two molecules of oxidized glutathione called GSSG are formed. The oxidized glutathione (GSSG) will be originated after the transfer of the two hydrogen from the GSH glutathione, after the transfer the two sulfide groups will bind with a disulphide bridge through a cysteine bridge giving rise to a GSSG. In the reaction balance we will need two molecules of GSH, to meet the glutathione peroxidation and originate at the end of the reaction four molecules of water and two molecules of oxidized glutathione (GSSG).

Oxidized glutathione is a non-toxic compound, therefore well tolerated by the body. The problem will arise when other molecules of hydrogen peroxide arrive. The GSSG no longer works because the hydrogen released by the non-oxidized glutathione will be exhausted. In the total balance, however, another enzyme must be mentioned, glutathione reductase. It will take the oxidized glutathione, a hydrogen from NADH, to give it to the GSSG. In the end we will again have four molecules of GSH and at the expense of the nicotinamide adenine dinucleotide (NADH) that having given up a hydrogen, it will become NAD+.

If the subject has outgoing equivalents, the reaction can work. If you do not have NADH because it has undergone many oxidative processes (drinks a lot of alcohol, alcoholic beverages, does not eat vegetables), It has no equivalent of oxidizers and reducing reactions will be worse and is more susceptible to oxidative stress.

Glutathione also does other things. In particular, what interests in NBC, is the neutralization of xenobiotics from the outside, as well as facilitating the transport of amino acids intracellularly. Where do free radicals come from? Are there any endogenous sources? In this thesis I will try to list some of the defense systems against NBC radicals, in the case of a possible attack, or a possible exposure of ionizing radiation.

# 5 Purpose

The purpose of my research was therefore to analyze the risks related to inhalation toxicity in the substances listed in the PIC Regulation, comparing these toxicities with the inhalation toxicities of some chemicals used in the war industry, with the aim of highlighting any risks for operators and in the distorted use of the same.

In this occasion, I analyzed the "countermeasures" available and proposed solutions with the aim of mitigating the damage to populations that may be affected..

Thus, my attention will be oriented towards PIC substances as these substances are placed under particular attention by the European Union because of their toxicity. In particular, the EU wants to increase the attention also in other countries that in the absence of regulation both in terms of prohibition or restriction, can import very dangerous substances whether they are aware of it or not.

My analysis of the substances will therefore initially focus on the issues related to the risk related to the transport of the same. Then I will estimate the impact on the population exposed in the event of an accident in a company Seveso III with the release of the chemical produced, with the opportunity I will estimate the antidotal equipment in terms of both quality and quantity.

My research will therefore be aimed at analyzing the following aspects:

- Risk analysis related to the transport of these chemicals especially with the occurrence of particular climatic conditions;
- Estimation of the antidotal equipment of drugs and medical devices following the release of a chemical substance from a Seveso III company;
- Research into antidotes to combat ionizing radiation;
- Toxicity analysis of the 489 substances ordered taking into account their inhalation toxicity;
- Analysis of export profiles of substances over the last 16 years.

### 6 Materials and Methods

In the course of my research, 489 chemical substances were analyzed within the European PIC Regulation (industrial and pesticide) and within the SEVESO III Regulation. The toxicological information was collected by consulting the following databases: EPA database, ECHA database, TOXNET, Technical Guide 230 (Environmental Health Risk Assessment and Chemical Exposure Guidelines for Deployed Military Personnel) of the U.S. Army Public Health Command (USAPHC), The Toxin and Toxin Target Database (T3DB), the book "HazMat Data for first response, transportation, storage, and security" Second Edition, by Rivhard P.Pohanish 2004 (ISBN: 0471-27328-7), Material Safety Data Sheet (MSDS), Libraries available through the Qsar ToolBox. The databases are free and have been consulted according to the order shown in tab. 2. I have analysed the PIC substances listed in the Pic Regulation taking into account several aspects. The database in which the data were collected was thus built, the first column contains the letters relating to the columns of the excel file. In the second column the description of the parameter analysed relative to the letter of the first column is given. For space reasons, the final table of the thesis will show only some of the parameters reported in the database, the excel file will be an annex of the doctoral thesis.

Column of						
the elaboration	Type of information					
xls folder						
А	Reference regulation					
В	Substance name					
С	Chemical Abstracts Service (CAS)					
D	Presence in the Chemical Facility Anti-Terrorism Standard (CFATS) regulation					
Е	ECHA Reference Regulation					
F	If present in ECHA databases					
G	If present in EPA databases					
Н	If present in TOXNET databases					
Ι	If present on CAMEO					
J	If present in the TG230 guide					
K	If present in t3db					
L	If it's in the book "HazMat Data"					
М	Toxicological levels of Immediately Dangerous to Life or Health ( <b>IDLH</b> ), Military Exposure Guidelines ( <b>MEG</b> ) or other indicators.					
N	Possible toxicity values Protective Action Criteria for Chemicals (PAC)3					

The following table (**Tab.2**):

depending on exposure and species.RLC50 toxicity levels on humans and guinea pigsSIf used, method of analysis through Qsar (Trend Analysis=TA, Read Across=RA)TToxicity values expressed in Parts Per Million (ppm)UExposure time and species concerned.VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	0	Toxicological levels, if any Access Acute Exposure Guidelines Levels (AEGLs) Values at 10'
depending on exposure and species.RLC50 toxicity levels on humans and guinea pigsSIf used, method of analysis through Qsar (Trend Analysis=TA, Read Across=RA)TToxicity values expressed in Parts Per Million (ppm)UExposure time and species concerned.VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of the substance within the Emergency Response Guidelines Regulation	Р	Possible levels of exposure <b>MEG</b> at 10'
SIf used, method of analysis through Qsar (Trend Analysis=TA, Read Across=RA)TToxicity values expressed in Parts Per Million (ppm)UExposure time and species concerned.VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAEAny restrictions and reference regulationsAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	Q	Toxicities detected by Data Base <b>(DB): Lethal</b> Concentration <b>50</b> (LC50), Lethal Dose 50 (LD50) depending on exposure and species.
TToxicity values expressed in Parts Per Million ( <b>ppm</b> )UExposure time and species concerned.VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code ( <b>UN</b> )ACClass UN codeADSubclass UN codeAEAny restrictions and reference regulationsAF <b>EPA encoding</b> AGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AIPresence of the substance within the Emergency Response Guidelines Regulation	R	LC50 toxicity levels on humans and guinea pigs
UExposure time and species concerned.VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAEAny restrictions and reference regulationsAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AIPresence of the substance within the Emergency Response Guidelines Regulation	S	If used, method of analysis through Qsar (Trend Analysis=TA, Read Across=RA)
VHuman LC50 expressed in ppm.WParameter "a" of the Probit function.XPhysical state of the chemical at room temperatureYBoiling pointZBoiling point in degrees CelsiusAAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAEAny restrictions and reference regulationsAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AIPresence of the substance within the Emergency Response Guidelines Regulation	Т	Toxicity values expressed in Parts Per Million ( <b>ppm</b> )
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AAPossible link to the reference databaseABUN Code (UN)ACClass UN codeADSubclass UN codeAEAny restrictions and reference regulationsAFEPA encodingAGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	Y	Boiling point
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ADSubclass UN codeAEAny restrictions and reference regulationsAF <b>EPA encoding</b> AGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	AB	UN Code (UN)
AE       Any restrictions and reference regulations         AF       EPA encoding         AG       Indications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)         AH       Presence of any restrictions, export notifications, import of the PIC Regulation.         AI       Presence of the substance within the Emergency Response Guidelines Regulation	AC	Class UN code
AF       EPA encoding         AG       Indications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)         AH       Presence of any restrictions, export notifications, import of the PIC Regulation.         AI       Presence of the substance within the Emergency Response Guidelines Regulation	AD	Subclass UN code
AGIndications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	AE	Any restrictions and reference regulations
AHPresence of any restrictions, export notifications, import of the PIC Regulation.AIPresence of the substance within the Emergency Response Guidelines Regulation	AF	EPA encoding
AI         Presence of the substance within the Emergency Response Guidelines Regulation	AG	Indications of ECHA toxicity (e.g. carcinogenic, mutagenic, skin sensitizing, etc.)
	AH	Presence of any restrictions, export notifications, import of the PIC Regulation.
AI Any notes on use	AI	Presence of the substance within the Emergency Response Guidelines Regulation
	AJ	Any notes on use

*Tab. 2 Information sought for each substance in the different columns.* 

Therefore, for each of the 489 substances, I have searched all the information reported in the previous table in the Databases, Software, books and Msds previously listed:

1) With 201 substances the toxicological information was obtained through the consultation of the Database, Software, Books and Msds as previously indicated.

2) For 288 substances the information was not available.

- a. In this case an analysis was carried out with the Qsar ToolBox software using read-across analyses for 27 substances , Read across analysis is a type of analysis based on structural chemical similarity between chemicals;
- b. Trend Analysis for 189 substances. Tren Analysis is an analysis between substances similar for toxicological characteristics with parameters such as: molecular mass, length of the carbon chain or other physical-chemical properties but which also takes into account the toxicological effects);

c. For the remaining 72 substances, no results could be obtained, as the availability of related chemicals by type was insufficient to reconstruct a regression line.

In the following table (**Tab.3**) the report of the substances analyzed by the software or not analyzable.

Regulations source of the substance	Read Across Analysis	Trend Analysis	Not analyzable
PIC (Industrial use)	22	49	18
PIC (Pesticides use)		128	49
Seveso III	5	12	5
Total	27	189	72

 Table 2 List of non-scheduled substances through consultation of DBs, books and MSDSs. Divided between not calculable and those analyzed with the Qsar Toolbox software divided by reference regulation and analysis technique.

Below are the parameters entered in the Qsar toolbox during the analysis.

### 6.1 Using the Qsar toolbox

The Qsar toolbox is a free software provided by ECHA, which allows companies that have to submit dossiers to obtain useful information without carrying out animal testing. The Qsar toolbox using CAS number of the chemical under evaluation, requests to define the target end point the final objective , in my analysis is Human Health Hazard in particular Acute Toxicity, LC50 and the inhalation exposure route. After this entries information, it is possible to go in the Profiling section where the methods of profiling substances can be defined , taking into account among those suggested by the Qsar Toolbox (they are considered plausible by the Qsar tool box in relation of the structure of the substance). After is possible consult different databases and Inventories in order to estimate the LC50inal.

#### Databases:

- Chemical Reactivity COLIPA, Echa CHEM database, Experimental pka database, GHS Experimetal RC50, Phys-chem EPISUITE, Bioaccumultaion database Canada, Bioaccumulation Fish CEFIC LRI), Bioconcentration NITE, Biodegradation in soil OASIS, Biodegradation NITE, Biota-Sediment Accumulation Factor US-EPA, ECOTX, Hydrolisis rate constant OASIS, Km database Environmental Canada, Phys-chem EPISUITE, Acquatic ECETOC, Acquatic Japan Moe, Acquatic OASIS, Acute Oral Toxicity, Bacterial mutagenicity ISSSTY, Biocides and plant protection ISSBIOC, Cancerogenic Potency Database (CPDB), Carcinogenicity & mutagenicity ISSCAN, Cell Transformation Assay ISSCTA, Dendritic cells COLIPA, Developmental & Reproductive Toxicity (DART), Developmental toxicity ILSI, ECVAM Genotoxicity & Carcinogenicity, Eye Irritation ECETOC, Genotoxicity OASI, Human Half Life, Keratocyte expression gene Givaudan, Keratocyte expression gene LuSens, Micronucleus ISSMIC, Micronucleus OASIS, MUNRO non-cancer EFSA, REACH Skin sensitization database (normalized), receptor Mediated Effects, Repose Tox Fraunhofer ITEM, Repeated Dose toxicity HESS, Rodental Inhalation Toxicity Database, Skin Irritation, Skin Sensitization, Skin Sensitization ECETOC, ToxCastDB, Toxicity Japan MHLW, Toxicity to reproduction (ER), ToxRefDB US-EPA, Transgenic Rodental Database, Yeast estrogen assay database, ZEBET database.

The Inventories consulted are:

- Canada DSL, COSING, DSSTOX, ECHA PR, EINECS, HPVC OECD, METI Japan, NICNAS, REACH ECB, TSCA and US HPV Challenge Program.

Only acute toxicity data by inhalator route are selected at a later stage.

Subsequently the categorization of the substances according to the analysis criteria is defined. In my case the analysis criterion was the criterion of "Respiratory sensitization". Then the substances were grouped, taking into account only the acute toxicity. Subsequently, the "Data Gap Filling" criterion was selected, which for some substances was the Trend Analysis rather than the Read Across, and finally the inhalation toxicity of reference are analyzed by using a regression curve that estimates the toxicological concentration of the inhalation sought. In case of read across or trend analysis simulations, the system also allows the selection of inconsistencies between grouped chemicals belonging to different chemical classes in order to homogenize the results and increase the  $r^2$  of the regression line. For non-analyzable substances, the system has not been able to group a sufficient number of chemicals to build a regression line suitable for the minimum statistical requirements.

The Qsar toolbox is therefore a fundamental tool for obtaining toxicological information that has not been available in the databases or in the msds consulted. Once I had obtained the LC50 estimates for the substances analyzed, I proceeded trying to identify a technique capable of initially allowing me to estimate the damage on the populations possibly exposed

and at the same time to sort the chemicals according to a particular parameter reported in the functions used for the models of vulnerability.

## 6.2 Using the Probit function and vulnerability models.

The Probit model is a non-linear regression model used when the dependent variable is dichotomous. In our case it is used to obtain an estimate of the persons possibly involved in the event of a release of a chemical substance.

The models of vulnerability reported in this section are models that allow us to estimate the inhalation toxicity of the substances analyzed by providing a value that in an absolute sense can indicate the toxicity of the substance analyzed and put into system in the model of Probit determines a possible estimate of the exposed.

In the case of my research, the results obtained have been obtained by different animals (guinea pigs, mice, rats), with different exposure times (minutes, seconds and hours) and different units of measurement (e.g.  $mg/m^3$ , mg/l, ppm etc..) were related to each other through a parameter used in the quantitative estimates of the damage reported in the Green book of the TNO Organization (1992).

In this text, using the functions of Probit, it is possible to estimate the damage caused by exposure to different chemical substances, using a calculation useful for determining the percentage of exposure, taking into account the concentration of the chemical and the exposure time.

The Probit function used within the Green Book is therefore composed as follows,

$$Pr=a+b1 \ln C + b2 \ln t$$

In the function, a and b are parameters of the function provided in the Green Book for the possible estimation of the exposed (in the book are reported the parameters of 20 substances from data obtained in animal testing). In other cases, such as those relating to the search for toxicity of unknown substances is conventionally attributed to the parameter b value of one.

C is the value of the concentration of the substance analyzed expressed in  $mg/m^3$  or ppm.

The value 't' is an estimate of the duration of exposure to the substance in minutes.

If b=b2 and n=b1/b2 are set, the most commonly used formula is obtained:

#### $Pr=a+b \ln (C^n t)$ .

Coefficients a and b were calculated for 20 substances, while for the remaining substances the estimation of the exposures was made possible thanks to the following computations:

For example the values taken from the Irving-Sax for the GA Taburn relative to the value CL50 <sub>(ihl - mus)</sub> 30' that is the value of the lethal concentration median (CL50) in air, statistically evaluated, which is expected to cause death, during exposure or within a certain time, consecutive to an inhalation exposure, of 50% in mice treated for a period of time equal to 30'. This value is equal to: GA Taburn ==> LC50 <sub>(ihl - mus) 30'</sub> = 15 mg/m<sup>3</sup>

However, this value must be multiplied by the correction factor (fd), which is a factor that allows to relate the toxicity values obtained from the guinea pig with the toxicity values hypothesized for humans, thanks to a safety factor that is the correction factor. In case of mouse is fd (mus) = 0.5

LC50 (human) = fd x 30 minutes LC50 (animal).

$$LC50_{(human)} = 0.5 \text{ x } 15 = 7.5 \text{ mg/m}^3$$

At this point, I have set b=1 and n=2 and obtain from the Probit function the constant "a"

$$a=5-\ln\{[LC50_{(human)}]^n\}x30 \rightarrow a = 5 - \ln\{[7,5]^2\}x30 = -2,431$$

The establishment of vulnerability models applicable to the human being requires two steps: the determination of the LC50 (human) and the calculation of the probit constants.

The calculation of LC50 (human) is based on the known LC50 (animal) values. The latter, if necessary, are converted into values corresponding to a minute exposure time of 30 minutes. Therefore, extrapolation is done with the help of an extrapolation factor. This factor has been taken into account for both, systemically acting and locally acting substances.

For substances that act locally, the differences between animals and humans in terms of respiration volume per minute and lung area are taken into account. The influence of factors such as: differences in the way of breathing (through the nose or not), the sensitivity of lung tissue, and the influence of the lungs on the rest of the body, is taken into account by providing a safety factor.

For systemically acting substances, the respiration volume per minute also plays a role. A safety factor has also been established for these substances, in which, in this case, the differences in kinetic and dynamic drugs are taken into account. In addition, for both types of substances, a difference is considered in relation to the state of activity: for the animal in the test (resting condition) and for a human being in the accidental circumstances (possible escape behavior).

Finally, based on the number of animal species for which you have activity: known data, the extrapolation factor is adapted (or not) in the sense of a less conservative assessment.

An extrapolation method has been developed in which measurable differences (such as breathing volume per minute, lung area) are quantified in the best possible way, while for lesser-known values a safety factor is provided. This leads to a cash extrapolation factor given to support as much as is possible to obtain it.

The methodology used to calculate the probit constants is based on LC50 as more and more accurate data from the animal study are available for these values. By fixing the value of b equal to 1.0, a conservative hypothesis is made for concentrations < LC50, which is appropriate for increasing the vulnerability of the population exposed to a disaster.

The calculation of the "a" probit constant is obtained, then, using the LC50 (human) and fixing b = 1.0.

The methodology used in this study to derive probit functions is valid especially for substances for which little toxicity data is available.

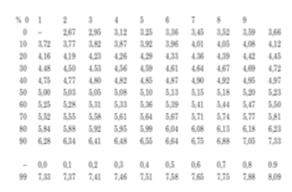
Whenever a user wishes to offer a better substantiated probit function based on sufficient toxicity data, this should be judged by a panel of experts.

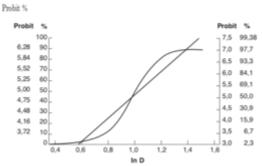
With regard to parameter "*a*", which reflects the difference in sensitivity between the animal and the human being, an attempt was made to arrive at the most well-founded assessment possible. Parameter "*a*" is valid for the fatal danger. To the best of our knowledge, adequate values of this parameter for other types of injuries cannot be provided with certainty. It might be suggested, for future research into acute toxicity, to try obtaining better definitions for these other types of hazards. In this respect, it is worth considering cases such as: 50% damage to the lungs and long-lasting disorders of the respiratory system and the digestive process. However, certain toxicity data for these other types of lesions can only be established when this field is more clearly defined.

Despite the proper foundation of the results, probit constants for humans are nothing more than an indication. A lot of research is still needed to establish really certain dose/effect ratios.

However, the vulnerability models presented in this thesis are mainly for the use of so-called "quantitative risk analysis". Uncertainties in these vulnerability models must therefore be considered in the context of other sometimes relatively large uncertainties, which also play a role in risk analysis. In this respect, we can mention: the effect models, the probability models, the population data, etc..

In this context, however, the vulnerability models presented here can effectively contribute to the calculation of the risks of a given activity, mainly in a relative sense (risk reduction, comparison between the various activities).





*Fig. 2 table used to calculate the percentage of exposed persons* 

Parameter "*a*" reflects the difference in sensitivity between the animal and the human being and is the parameter that is best suited for the assessment of the fatal inhalation hazard. It is therefore naturally suitable to match substances that have different LC50 data obtained on different guinea pigs and with different exposure times. The Probit function, once developed with both variables, does not provide an absolute estimate of the number of people exposed but a percentage estimate of the people possibly involved. By interpolating the absolute value obtained with the percentage obtainable from the table in the figure (Fig.2), the percentage of the persons involved is obtained.

My research is therefore aimed at obtaining the parameter "*a*" to order substances taking into account an order of dangerousness in terms of inhalation toxicity. Finally, to obtain a reference value of toxicity in absolute terms, the hazard, will also be related to the LC50 of traditional gases used in the past in conflicts such as war: Tabun, Sarin, Soman and Vx.

# 6.3 Representation of exposure scenarios

Once the inhalation toxicity of the substances had been estimated, in order to obtain an estimate of the suitability or otherwise of the antidotal stocks, it was necessary to carry out analytical techniques to simulate the dispersion of the chemical and the relative quantitative estimate of the exposed population.

The simulation of the release of substances has been made thanks to the software of the Environmental Protection Agency ALOHA<sup>®</sup> (Arial Location Hazardous Atmosphere), which allows to estimate the propagation of the toxic cloud taking into account parameters such as: the amount of substance stored, any pressures inside the tank, presence of release systems, operating temperatures, presence or absence of flame or explosions, container filling percentage, height of the release point and size of the same and many other parameters that allow to recreate in an appropriate manner the dynamics of substance release.

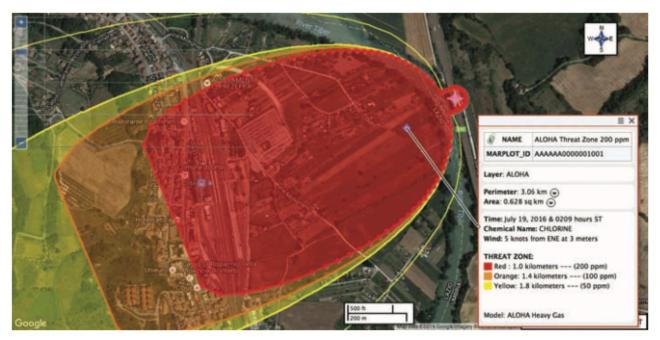


Fig. 3 Example of simulated gas release representation with ALOHA and MARPLOT.

ALOHA through its dispersion models has allowed to stratify the propagation zones of chemical clouds dividing them by concentration thresholds in AEGL 1, 2 and 3 relatively by the less toxic AEGL1 levels up to the AEGL3 levels considered more toxic (Fig.3). AEGLs are expressed in ppm or  $mg/m^3$ , and therefore allow the concentration of the toxic substance and its risk on the population to be clearly and unambiguously identified.

This has allowed to obtain a simple and immediate visualization on the map of the chemical risk of easy intuition for the operators of the sector and for the operators of the rescue if involved. The division into zones that takes into account the concentration of the chemical substance is very useful for determining the area of the exposed and through the functions of probity obtain an estimate of the percentage of people involved. This information could be integrated with any population present in the area involved, in order to obtain a real estimate of the exposures. This function is present in the ALOHA functions for the territory of the United States, but is not present in other states.

The limit of ALOHA is the 2D representation of the territory, which does not take into account the orographic conformation. This means that phenomena such as the canalization of the currents, rather than any thermal inversions due to the conformation of the same are not represented, thus influencing significantly on the representation of the dispersion of the cloud, both in a sense of over and underestimation of the same. Moreover, ALOHA allows the static reconstruction of the event, but in the simulations obtainable on the Italian territory it does not allow a "real time" adjustment of the movement of the cloud and therefore a "tailored" estimate of the exhibits. In order to overcome this problem, I have thought of adapting risk control by adopting concentric circles that take into account the maximum distance that can be obtained from the toxicological level considered.

The concentric risks circles also allow for the correct positioning of any coordination and control stations, also taking into account the possible risk of a change in wind direction. In summary, since I could not obtain a dynamic simulation of the release, I considered a precautionary approach of the risk scenario. This approach is, in my view, very useful in the event that any command or rescue outposts have to be placed on the ground in such a way that they are protected from any chemical risks.

The map (Fig. 4) representation of the release was made possible thanks to MARPLOT<sup>®</sup>, a system present in the EPA tool that allows the immediate visualization of the dispersion bell in 2D (limit of the same software that does not take into account the terrain orography). Within the same IT package provided by the EPA there is the CAMEO software<sup>®</sup>, which allows you to consult EPA database, and matches data with the criteria for the classification of substance established at United Nations level (Global Harmonised System on classification and labelling of chemical – GHS).

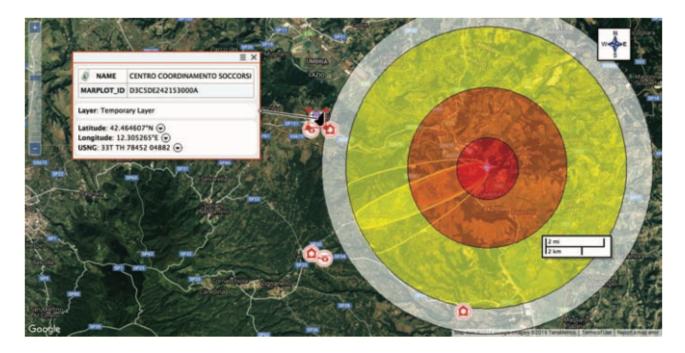


Fig. 4 Concentric representation of the toxicological risk scenario is a precautionary approach to risk that also takes into account any change in wind direction

These criteria are implemented in UE with the regulation CLP.So CAMEO software<sup>®</sup> gives quickly information on the dangerous classification of the substance. In addition , CAMEO software<sup>®</sup> offers information on the presence or absence of the substance under study in the Emergency Response Guidebook (ERG), any risk indications, recommendations in case you decide to intervene, toxicological values and chemical-physical properties, toxicological values of reference, and information of a regulatory nature taking into account American laws. The presence or otherwise of these substances in the Chemical Facility Anti-Terrorism Standards (CFATS) Regulation is of interest for comparison purposes, and chemicals are classified in this Regulation taking into account their usability for terrorist purposes.

ALOHA, MARPLOT and CAMEO are therefore essential for the simulation of the release of substances, for the graphic representation and for a possible integration of an informative nature to the databases already consulted. In particular, CAMEO has been useful to identify some peculiarities in terms of use in common life, rather than reactivity of the same compounds. The presence or not of the information obtainable from CAMEO has been one of the parameters taken into consideration in the compilation of the Database of reference of the thesis.

#### 6.4 Antidotes and valuation of antidotal stocks

The knowledge of the toxicity of chemicals, the use of techniques for the quantitative estimation of exposures and the use of simulation tools to estimate the release of chemicals allowed me to perform the assessment of stocks of antidotes (drugs, medical devices and personal protective equipment) in terms of adequacy, appropriateness and updating.

For the part concerning my research project on the evaluation of possible antidotal stocks, in a work presented with a poster at the 18th National Congress of Toxicology, entitled "Optimization of the stockpile of sanitary materials (drugs, medical devices, personal protective equipment and medicinal oxygen) for the management of chemical risk in Hospital Pharmacies adjacent to the production areas of ethylene oxide: an operative proposal". I have analyzed the adequacy of antidotal stocks of drugs, medical devices and medical oxygen taking into account the exposure scenario calculated with ALOHA and represented with MARPLOT; the estimation of exposures on the population through the use of methods for quantitative damage estimation attributable to the function of Probit of the Green Book, in relation to the equipment provided in Italian legislative decree n.196 of 25 August 2003 which describes the minimum equipment of drugs, medical devices and aids that must be present in a place of advanced medication of second level. The results of the simulation that made it possible to determine the number of exposures was the basis for the study of the adaptation of antidotal stocks taking into account the therapeutic protocols reported in TOXNET in the specific case for the fight against ethylene oxide poisoning.

The approach aimed at mitigating the risk of exposure to hazardous substances also from a dual-use perspective has been directed at reducing the damage from ionizing radiation possible in the event of exposure to chemicals capable of emitting radiation. This risk is possible both in the case of exposure to low-intensity nuclear devices, which may involve nuclear installations, and in the case of accidental exposure to medical radiological waste, such as in the case of Goiana in Brazil in 1987. In this case, my research has been directed to the strengthening of the biochemical mechanisms naturally present in the body intended to reduce the damage from ionizing radiation up to the hypothesis of a complementary set to be used in case I want to mitigate the negative effects of ionizing radiation.

# 6.5 Analysis of regulations

Some regulations aim to regulate the import rather than the placing on the market of chemicals in order to reduce the risk of exposure for both, the operators and the civil population potentially involved.

The PIC regulation supports the important flow information on concern and risk management of certain chemical substances severally restricted or ban within the European Union. These input could stimulate national measures to manage risks in the importing countries, concerning that possible risk of exposure for the populations that may be involved. From an international point of view, therefore, the possible collaboration between what the European Union, through the PIC Regulation, considers dangerous and toxic and what is prohibited in the African continent as potential toxic waste, such as to endanger any exposed, whether they are professional operators or not, is of importance.

In the global context that aims to a strategic approach and sound management of chemicals and waste the Basel Convention is an other pilaster. In this perspective, some African countries are doing relevant actions as indicated in the Bamako Convention. This Convention assumes a strategic importance especially from an international point of view. The Convention was originally signed by 12 nations of the African Union in Bamako (Mali, January 1991) and came into force in 1998. By now it has been signed by 29 members. Among the aims are the prohibition of HAZMAT and radioactive waste import in African countries, the minimization of handling toxic waste between different African states, the prohibition of discharge and incineration of hazardous waste at sea and in inland waters, the guarantee that waste is disposed correctly, the promotion of production of materials with low environmental impact, the establishment of precautionary principle [21].

The problem of the toxic chemical, capable of contaminating any exposure, is particularly important also from a *dual-use* point of view, in particular the use of these toxic substances could lend itself to a distorted use for terrorist purposes.

The United States of America, through the Department of Homeland Security (DHS), has developed the Chemical Facility Anti-Terrorism Standards (CFATS).

CFATS is the Nation's first regulatory program focused specifically on security at high-risk chemical facilities. The Cybersecurity and Infrastructure Security Agency (CISA) manages the CFATS program by working with facilities to ensure they have security measures in place to reduce the risks associated with certain hazardous chemicals and prevent them from being exploited in a terrorist attack. CFATS deals with chemicals that can be used for

terrorist purposes by analyzing them under three types of risk (release, theft or sabotage). Substances shall be published in lists according to their chemical name and CAS number. Therefore, it has been implemented a program by the United States that is perfectly suited to what is meant by the search for a possible distorted use of chemicals beyond their intended use at the time of production or marketing. This list is well suited to control chemicals in their supply chain and during any uses in the industrial production chain. It would also be more useful in a view of customs intelligence.

In Italy, this task falls within the competence of the Customs Agency and the State Monopolies, in particular within the competence of the Anti-Fraud and Control Department, which has the task of monitoring and analyzing through the creation and management of databases the trade flows and other information held by the Agency, in order to develop risk profiles to guide and make more effective the control activity.

To carry out intelligence activities on the commercial flows at risk, also through the management of the Analysis Room. To maintain and coordinate the chemical laboratories of the Agency. Carry out mutual assistance and administrative cooperation activities.

To take care of and coordinate, within the scope of its activities, the implementation of the strategies of analysis, prevention and repression of the illicit, also within the framework of the Convention with the National Anti-Mafia and Anti-Terrorism Directorate, proceeding directly, or with the collaboration of the territorial structures, to actions of contrast of the crimes of competence, with particular regard to the cases connected to hypotheses of association or relative to international money laundering and the financing of terrorism[22]. In this control perspective, the establishment of a list of highly toxic chemicals by inhalation that could be used for purposes other than those foreseen when they were placed on the market would be of strategic importance for normal customs intelligence operations and for the security of European citizens. An operation to prevent the threat based on the risk potentials due to the use of these substances.

The PIC Regulation and the consultation of its databases, in this key offers an excellent support, both for the identification of the highly toxic chemicals already identified by ECHA, and for the necessary import and export authorizations that must be carried out to import and export these substances. Notifications, requests and consents therefore represent a very important source of information for the reconstruction of possible flows of chemical substances. This framework would be more important if the vision would be taken to a European level as customs control policies are not homogeneous between the different ports within the European Union [23].

In conclusion, the European Union regulations has data from which to draw and obtain the necessary information and tools for the control of HazMats. All this while waiting for the

European Union to develop in turn CFATS similar to those in use in the USA. During the course of my research, I will check the presence of the chemicals of the PIC Regulation in the CFATS.

# 7 Results

The first results obtained during the thesis is the one related to the estimation of the risk inherent to the safety during the transport of HazMats.

The first substance analyzed in the article published in the Journal of Military Medicine [24] was chlorine. This article experimented with the first simulations using ALOHA® and provided a first estimate of the exposures following the release of chlorine caused by a road accident involving a tanker. The article highlighted the high capacity of chlorine to disperse over large surfaces and the high inhalation toxicity that characterizes this chemical element. The article sets out some of the basics of the regulation of the transport of hazardous chemicals and refers to the risk of safety in the transport of hazardous chemicals, especially in the light of recent European regulations concerning Transportable Pressure Equipment (T-PED) [25]. The article analyzed the dynamics of release of the chemical with an emphasis on the high incidence of mortality in the population. Attention has also been paid to the replacement of the fleet of vehicles, highlighting the progressive ageing of tanks weighing over 3.5 tons with relative risk to road safety and the related risk of lack of maintenance of the fleet, especially in implementation of the provisions of the T-PED Directive. Last but not least, it was highlighted how a more widespread knowledge of Safety Data Sheets can be a very important element in the hands of rescuers and how they can contribute in an important way to the massive spread of notions of first aid.

The second section of the results will be dedicated to the estimation of antidotal endowments following exposure to industrial toxic chemicals, the estimation will be made following a release simulation followed by an estimation of the population involved. On the estimation of the exposures, taking into account the therapeutic protocols and the reception capacity of a second-level MPA, the antidotal endowments will be estimated in quantitative and qualitative terms.

The third section of the results will examine the risk of ionizing radiation and how this risk can be reduced by using a special set of active substances that can enhance the mechanisms of radiation damage reduction and at the same time reduce the negative effects of exposure. The last section will compare all the chemicals analyzed, both industrial chemicals and pesticides. The substances will be sorted according to their inhalation toxicity LC50 derived from databases or obtained by computational chemistry methods. Finally, the data obtained in this way will be related to each other through the use of a parameter "a" derived from the models of vulnerability that can relate the concentration of toxic substances and the duration of exposure.

A final analysis will take into account the export flows of the chemicals analyzed.

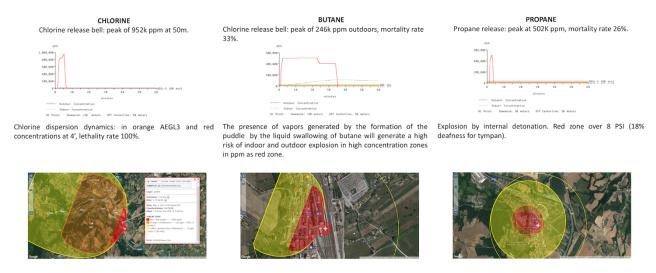
## 7.1 Vulnerability models and release estimation

The issue of the transport of HazMat was again addressed in a paper published in the context of the 1st Scientific International Conference on CBRNe (SICC2017) held in Rome between 22 and 24 May 2017 [26]. In this work, initially presented with a poster during the conference and subsequently elaborated as a paper in the proceedings of the congress, entitled "*Safety in the Transport of Hazardous substances in residential Areas: Cases of the Release of TIC (Chlorine, Propane and Butane) at Low Temperatures*", it emerged that the risk of transporting LPG and chlorine, especially at low temperatures, is relevant.

The substances were analyzed taking into account their release in four different types of scenarios:

- 1. release of substances without flames (with detection of concentrations at 50 meters from the point of release indoor and outdoor);
- scenario with the development of Boiling Liquid Expanding Vapour Explosions (BLEVEs) for propane and butane with the relative development of a fireball capable of providing 10 kWm<sup>2</sup> of heat transfer;
- 3. analysis of minimum flammability of chemicals;
- 4. controlled tank explosion charge of propane only or butane only with estimate of shockwave and damage generated.

In the case of the release without the development of flames, it is immediately evident a different behavior for the three substances analyzed, with a strong propensity to expansion for chlorine and propane and a low propensity for butane by virtue of its greater specific weight as shown in the figure (Fig.5)



*Fig. 5 releases in order from the left to the right: chlorine, butane and propane.* 

In the second case, related to the simulation of BLEVEs, the analysis was carried out on the only two flammable substances, propane and butane. Chlorine is not flammable and therefore has not been subjected to simulation. As a result, similar thermal waves in terms of size and intensity were obtained in the case of both propane and butane. The analysis also made it possible to identify different zones, dividing them into those capable of being lethal following 10" of exposure, those capable of generating second-degree burns following 60" exposure and those capable of generating third-degree burns following 60" exposure (Fig. 6).



*Fig.* 6 *BLEVE generated by butane and propane*.

The third scenario hypothesized related the concentration of more than 60% of toxic vapors with the possibility of development of explosions and fires caused by a trigger. In particular, the simulation models have reported the LEL (Lower Explosion Limit), i.e. the limits within the concentration ranges are defined within which the air-steam or flammable gas mixture is properly ignited by verifying the ignition of the mixture. A lower limit necessary for the ignition of the vapor or air-gas mixture, defined as LEL, is conventionally identified. In the specific case of simulation, the lower limit was set at 60% of the concentration. The opposite situation is the Upper Explosive Limit (UEL), which indicates excessive saturation of the environment that cannot trigger a fire or explosion reaction. The simulation showed the tendency of both, propane and butane, to generate explosions, if properly triggered. In particular the behavior of butane has been characterized in terms of flammability and aptitude to explosion in conjunction with the presence of low temperatures (between -0.5 and -0.7 ° C). The presence of low temperatures, taking into account the chemical-physical characteristics of butane, means that once it has escaped from the tank, it forms a puddle capable of slowly releasing toxic vapors into the atmosphere, generating both, a raised toxicity of the butane cloud and a high risk of fire due to the saturation of the environment (Fig.7).

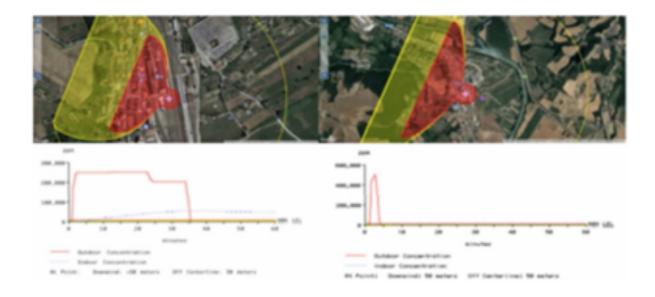


Fig. 7 Dynamic of release of butane (left) and propane (right): in red the area with LEL>60%, in yellow the area with >10% LEL.

The figure showing the dynamics of release of propane and butane shows that the concentration of butane is lower in absolute terms to propane but greater in persistence, such as to generate levels above the limits of explosion and ignitability for a period of time of 36 minutes, compared to 4 minutes of time of release of propane. This dynamic of high levels of toxicity manifests itself either indoors and outdoors, but it assumes worrying levels of danger if we consider the persistence of the environment's butane and its ability to form high concentrations in the air, such as to endanger any rescuers arrived at the scene of the accident.

In the fourth type of simulation, the hypothesis of a triggered detonation of the tank containing the two gases capable of exploding, propane or butane, was taken into consideration. Also, in this case, the loading conditions of the tank were the same in an attempt to generate a comparison that can be more than ever superimposed between the two different chemical substances.

Three levels of shock waves were analyzed: more than 8 psi capable of causing damage to infrastructure, more than 3.5 psi (and less than 8 psi) capable of causing damage to people, and a pressure band between 1 and 8 psi capable of breaking glasses (Fig. 8).



*Fig. 8 Shock wave generated by detonation (left butane, right propane), different colors with different intensity, from the highest (red) to the lowest (yellow).* 

The pressure measured at 50 m from the point of explosion for both, propane and butane, was also taken into account.

For propane, a pressure of 34.1 psi was observed at 50 m, while for butane, a pressure of 17.5 psi was observed. In general, with regard to the effects of pressure damage following the explosion, propane has shown a greater propensity to develop shock waves of greater importance than butane both in terms of pressure in the absolute sense and in terms of the surface involved.

The study then analyzed the toxicity of chemical substances in terms of mortality on the exposed showing a high mortality of chlorine of 100% at 50 meters from the point of release against the respective mortality of butane of 33% and propane of 26%.

These results have been obtained thanks to the application of the vulnerability models reported in the Green Book of the TNO Organization, where thanks to the use of the parameters "a" and "b", it has been made possible to determine the percentage of mortality of the exposed. These results are obtained thanks to the dispersion estimates simulated with the ALOHA software. In the specific case for the determination of the percentage of exposures, the parameters "a" and "b" were easily accessible, as already present in the tables in the green book, while for propane and butane it was necessary to obtain the parameter "a" with the use of methods previously described in the section materials and methods.

The models of vulnerability have also been useful in obtaining the estimate of the damage from burns following exposure to thermal waves by grouping the results into three classes of analysis: potentially lethal in 60" with thermal waves greater than 10kWm<sup>2</sup>, thermal waves capable of generating second degree burns in 60" and thermal waves capable of generating pain in 60".

In this case, the Probit function used was a variant of the one described above:

$$Pr = -36.38 + 2.56 \ln (t^*q^{4/3})$$

Where in function *t* it represents the exposure to the thermal wave in seconds, *q* the intensity of the thermal wave expressed in  $kWm^2$ , with the only difference that the parameter *q* assumes by default a value equal to 1.25 times the times that it is used in the calculation of the mortality of the exposed.

For an exposure of 60" to 10 kWm<sup>2</sup> there is a mortality of 70% of the exposures, 99% of firstdegree burns, 16% of second-degree burns, and 9% of third-degree burns. The vulnerability model as conceived tolerates a sum of the types of burns for a total of more than 100%, because the model itself takes into account the complications that may occur in the continuation of the disease.

The work also estimated the damage obtained as a result of the explosion generated by the shock wave. In this case, the Green Book assumes another Probit function:

$$Pr = -12.6 + 1,524 \ln Ps$$

Where, in the proposed function, *Ps* are the pressures expressed in Pascal (in the simulation the data were obtained with the release simulation expressed in Psi, hence the need to convert the values from Psi to Pa, in the specific case 8 Psi are equal to 55.185 Pa). Simulations have shown that following the explosion of the butane transport tank, there is a 60% incidence of trauma to the eardrums for people exposed to 50 m away from the point of explosion. In the case of propane, the incidence of damage to the eardrums for those exposed to 50 m distance rises to 90%.

The study therefore highlighted the risk of transporting HazMats in the event of TIC (Toxic Industrial Chemicals) accidents and highlighted the high risk generated by the transport of propane at temperatures close to zero degrees Celsius, both in terms of inhalation toxicity for exposed people, and in terms of the possibility of explosions due to the high concentration of saturation in the air. The risk of explosion is important both for those exposed at the scene of the accident, whether it is an outdoor or indoor explosion, but especially if we take into account the possible risks for rescuers who have intervened at the scene of the accident.

The poster presented in the framework of SICC2017 was such appreciated by the committee that it was awarded as Best Poster Award by the scientific committee of the project. The article was later published in Springer's ebook entitled "Enhancing CBRNE Safety & Security: Proceedings of the SICC 2017 Conference". Alongside the research carried out in the databases, in order to obtain information on the substances sought, research continued into techniques for estimating the simulation of the release of chemicals, aimed at greater accuracy in the reconstruction of risk scenarios. This time, in addition to the analysis of the exposed as such, an attempt has been made to provide a solution for adjustments to the stocks of antidotes present in the event of a health emergency. I have therefore sought an approach aimed at suggesting practical solutions with the aim of reducing any consequences for exposed populations.

# 7.2 Adaptation of antidotal stocks and exposure to HazMat.

The work presented at the 18th National Congress of the Italian Society of Toxicology (SITOX) entitled "Optimization of the "stockpile" of sanitary material (drugs, medical devices, personal protective equipment and medicinal oxygen) for the management of chemical risk in Hospital Pharmacies adjacent to ethylene oxide production areas: an operative proposal" was aimed at providing a proposal to deal with the release of ethylene oxide from a hypothetical chemical industry at significant accident risk (SEVESO III) following a cyber-attack.

The aim of the work was therefore to hypothesize antidotal stocks to be provided to the Hospital Pharmacies adjacent to the production sites of the substances covered by the SEVESO III directive. The chemical substance subject to the simulation was ethylene oxide, a substance present in the lists of substances attenuated by the Seveso III Regulation. The antidotal stocks analyzed used for the congruity in relation to the hypothesized scenarios, were those present in the Resolution of 22 May 2003, which establishes the minimum levels of equipment of drugs and medical devices that must be present in the Advanced Medication Post (AMP) of second level with treatment capacity for 50 people.

For the estimation of the complaints, it was taken of the document of the San Marino Committee on Bioethics "Bioethics of Disasters" and the regulations that define oxygen as a medicine (Italian Legislative Decree 219/2009) and antidote.



Fig. 9 Simulation of EO release

The dynamics of ethylene oxide (OE) dispersion were carried out through the use of the ALOHA software<sup>®</sup> (Fig. 9), the estimation of the exposures was made thanks to the application of the vulnerability models provided in the Green book. The validation of the therapeutic protocols has taken place through the use of TOXNET.

The LC50 ethylene oxide was estimated using the Qsar ToolBox with the application of trend analysis. From the simulation was obtained an LC50 of 691 ppm, the dynamics of gas dispersion was made with the help of the software ALOHA, the dynamics of OE dispersion was achieved through google maps. Parameter "a" was obtained from the LC50 simulated according to the above methods.

Mortality was calculated with 200 meter intervals, the average mortality was obtained by applying the harmonic mean of the detected mortalities. The choice of the harmonic mean was made because the mortality value was simulated taking into account the space. The simulation showed a harmonic mean mortality of 12.10 %.

Since there were no real numbers of exposed persons available, the estimate of complaints was made in percentage terms, taking into account the ability to receive complaints from the II level AMP. The calculation therefore revealed a potential mortality rate of 6 people. According to the Catastrophe Bioethics Committee, 15% of the total exposure could be disabled, and the disability itself would be a factor that could duplicate the mortality of the people involved. In view of the potential for exposure to death-creating concentrations, disabled people would be the victims of EO poisoning. The remaining 44 people should still be treated as a yellow code given the extent of the toxic cloud and the high levels of EO above AEGL3.

Also, in this case with OE a tank explosion simulation (BLEVEs) containing OE has been carried out and the results have been reported in the following table (Tab. 4)

Zone	Threat Zone	Area	Perimeter
RED- 10.0 kW/m <sup>2</sup> potentially lethal within 60"	366 m	0.422 km <sup>2</sup>	2.30 km
ORANGE – $5.0 \text{ kW/m}^2$ , $2^{nd}$ degree burns within $60''$	523 m	0.859 km <sup>2</sup>	3.29 km
YELLOW – 2.0 kW/m <sup>2</sup> pain in 60"	820 m	2.12 km <sup>2</sup>	5.16 km

#### Tab. 3 Results of OE Bleve release simulation

The dynamics of the tank explosion on the territory with the generation of thermal wave is represented below (Fig. 10):



Fig. 3 Geographic Information System (GIS) representation of OE's BLEVEs

Like in the previous case, the thermal wave calculated with the dedicated Probit function gave as a result to 10kWm<sup>2</sup> 9% mortality, 99% first degree burns, 16% second degree burns and 9% third degree burns.

The results obtained were compared with the therapeutic protocols provided in TOXNET, highlighting as more critical the lack of medicinal oxygen among the antidotal endowments provided for level II level MPAs. In particular, the treatment of pulmonary edema for the treatment of six people with what is included in the lists was analyzed.

The test showed that the supply of 500 ml physiological solutions, which can be used for infusional treatment in case of hypovolemia and for eye washing always following contamination with OE, was adequate. The 5% glucose solution used in the treatment of

pulmonary oedemas is adequate in the equipment of the AMP, as is the equipment of Ringer Lactate. Furosemide, nitroglycerin and morphine are also adequately equipped.

From the consultation of the list in the Resolution of May 22, 2003, these shortcomings emerge:

- 1. absence of walking aids for disabled persons such as wheelchairs;
- 2. lack of individual protection devices for first responders such as Tyvek suits, FFP3 masks, gloves with chemical protection;
- 3. Absence of emergency medical devices such as adult / pediatric intraosseous infusion systems, disposable laryngoscopes, adult / pediatric manual respiratory units, nasopharyngeal and oropharyngeal tubes, nasal atomizer systems for the emergency administration of drugs;
- 4. Absence of medicinal oxygen among the pharmaceutical equipment to be always available and of the relative electromedical for the administration (at least 6 portable pulmonary ventilators).

In particular, the absence of medicinal oxygen can be quantified considering the requirement of 15 L / minute of medicinal oxygen to be administered to emergency patients as foreseen by the protocols. The need for medicinal oxygen per patient can be summarized as per **Tab. 5**.

Oxygen Cylinders at 200	1 person	2 people	3 people	4 people	5 people	6 people
atm	<sup>2</sup> 24h	-24h	-24h	-24h	-24h	-24h
2 liters	54	108	162	216	270	324
5 liters	22	44	66	88	110	132
7 liters	16	32	48	64	80	96
40 liters	3	6	9	12	15	18

#### Tab. 4 Consumption of cylinders of different sizes depending on the patients.

In the case of burn damage following the explosion, the results of comparison between the defined drug list and the simulated needs are the following:

- 1. Introduction of drugs such as antibiotics like 2g ceftriaxone, thermostable adrenaline with injector, gauze of silver sulfadiazine and connectivine;
- 2. Introduction of medical devices such as adult / pediatric suction and suction tubes, anti-burn paints of various sizes, sterile tongue depressors and splashproof visors.

The simulations provided an estimation of the number of people exposed both to episodes of toxic inhalation and burn damage. Based on the processed numbers, the stocks of drugs and devices in the II level AMPs were then tested, revealing a total absence of the medical oxygen and related electromedical products useful for oxygen administration, even during the transport phases. A more general lack emerged in terms of non-modernization of medical devices usable in the emergency. Lacks have also emerged in terms of the aids that can be used by disabled people. Even at the level of the consistencies of drugs and medical devices, taking into account the treatment protocols and the number of exposed persons, the consistency of stockpiles appeared to be improvable and necessary to increase for some items.

From this study emerges the need to modernize and expand the response capacity of Hospital Pharmacies adjacent to the production sites of SEVESO III substances such as ethylene oxide, encouraging the management of pharmaceutical warehouses together with the needs of hospital departments however based on a criterion of efficiency and warehouse management originating from the First In - First Out method.

The greatest limit of the simulation consists in the inability of the software to estimate the three-dimensional conformation of the terrain (which takes into account the presence of buildings or hills). The study also hypothesizes the management of "caregivers" generally associated with the presence of the disabled person. European legislation and current laws increasingly aim to protect the environment and people, whether they are employees of companies at risk of a major accident than residents in the vicinity of the implants. On the other hand, the greater development of information technologies and relative risks of cyberattacks have increased the risk of a distorted use of the substances present on the national territory against the civilian population. The current composition of the National Reserve Antidotes must therefore be adapted to new threats against population security, whether these are of a malicious or negligent nature. The introduction of adequate stocks of drugs like medicinal oxygen as a basic element in the treatment of intoxication from chemicals of industrial origin, and of medical devices that ensure a more rapid and safe administration of drugs is an ever-increasing priority, as is the adoption of personal protective equipment for First Responders and dedicated aids for disabled people involved. It is also clear, that considering as strategic stocks some pharmaceutical specialties of current use in Hospital Pharmacy (HP) in "sensitive" places leads to a reduction in the response times of pharmaceutical logistics, quickly facing a chemical event. Because of the possibility of several incidental scenarios, the essential task of the "competent" HP, which is appropriately identified, is attributable to the implementation of all the procedures necessary to allow an adequate planning of the interventions and prevention, as much as possible, of the extension of damage to people, and constitutes a "resource" even in the national strategic sphere.

The work presented by means of a poster was such appreciated by the Scientific Evaluation Committee of the congress that it was awarded as one of the posters worthies of a SITOX scholarship (Fig. 12).

# 7.3 The HazMats and radiation protection.

Research into the adaptation of antidotal stocks has also been directed towards finding substances that can reduce the damage caused by exposure to ionizing radiation. This risk is present, as already discussed in the introductory phase of the thesis, not only in countries that may in some way be involved in industrial accidents related to the nuclear energy industry, but also in countries that may be exposed to radioactive waste from nuclear medicine rather than a deliberately distorted use of radioactive substances for terrorist purposes.

In this thesis, a complementary set of equipment was hypothesized to be used in the event that military rather than civilian personnel are exposed to this type of risk. Therefore, only the concept of antidotal defense adjustment has been developed, rather than the search for mortality of these substances.

The three substances have been analyzed in the light of their activity spectrum as a function of their activity. In particular, the following activity classes and subclasses were analyzed in order to reduce damage from ionizing radiation (**Tab. 6**):

Activity Class	Subclass
, , , , , , , , , , , , , , , , , , ,	Blocker of oxygen consumption
Protectants against all type of radiological	Free radical scavengers (exogenous and
effects	endogenous)
	DNA repair booster
Protectants against Type I early radiation	Inhibitors of death signaling pathways
r rolecturits against 1 ype 1 early radiation	Growth factors
Protectants against Type II early and Type	Blockers of radiation inflammation and
1 Toleciunis uguinsi 1 ype 11 euriy unu 1 ype III	chemiotaxis
111	Blocker of autocrine/paracrine pathways
Protectants against Type IV stochastic	Antimutagenic keepers of genomic
effects	Antinuugenie keepers of genomie
Protectants against Type V bystander	
effects	

Tab. 5 Summary of the molecule's activities respect to the protection from different types of damage.

Protection against all types of radiation.

As regards the activity of protection against all types of radiation effects, the three molecules showed activity against the identified subclasses. As for the ability to block oxygen consumption, amifostine is the only one to have shown activity [27-30], the decrease in the flow of oxygen to cells leads to a reduction in the formation of reactive species of oxygen (ROS). Regarding the ability to exogenous and endogenous scavengers, all three molecules showed activity. Amifostine has shown activity as a single molecule [31] or in combination

with vitamin E [32]. Resveratrol has shown an important action as a protector against endogenous and exogenous free radicals, in particular highlighting a high antioxidant capacity [33] with effects also on the respiratory chain of rats [34], and capability of acting as cellular scavenger and of prostaglandin antagonist [35-36].

Other positive effects of Resveratrol have been observed in the modulation of reactive oxygen species in in vivo fibroblasts [37].

The activity of antioxidant and antiradical l-carnitine against the effects induced by ionizing radiation is reported in several publications [38-46], as well as in association with vitamin E [47]. For DNA repair activity, both amifostine and resveratrol showed particular protective activity against DNA damage, especially amifostine showed protective ability against direct genome damage and damage induced by genome rupture by free radical [48-52]. Resveratrol showed activity in damage modulation and activities against double-strand breaks [53-54].

Type I radiation protection.

The three molecules showed activity for inhibitors of death signaling pathways: resveratrol showed anti-apoptotic activity against the cells of the bronchial epithelium following exposure of cigarette smoke [55], as well as demonstrated activity in modulation on apoptosis and oxidation in human blood mononuclear cells [56], as well as radioprotective and antioxidant activity in the hippocampus due to activation of Sirt1[57]. L-carnitine showed a mitigating action on UVA radiation damage induced on epithelial tissues by down regulation of oxidative stress, p38 c-Fos signaling and pro-inflammatory cytokines [58], it also showed an aging modulation and protective activity on cells and besides against testicular dysfunctions caused by gamma-ray irradiation in mice [59-60]. Counteracting damage related to increased growth factors has been demonstrated for resveratrol both in ovarian cancer cells [61] and in mechanisms to counter cell proliferation and oxidative DNA damage [62].

Protective mechanisms against early type II and type III damage.

Both resveratrol and amifostine have shown activity in protecting against type II and III damage. For the category of radiation inflammation and chemotaxis blockers, resveratrol has shown activity against inflammatory mechanisms by suppressing p65 and kinase activity Ikappa B [63], also showing neuroprotective activity in diabetic neuropathies by inhibiting the action of NF-kappaB [64], as evidenced by an anti-inflammatory activity in

the activation of SIRT1 and in the limitation of NLRP-3 [65], as well as a protective activity against long-term exposure to electromagnetic fields [66]. L-carnitine has demonstrated a mitigating action of inflammatory effects following UVA damage on the skin [67], and on the modulation of inflammation by acting on the microRNA, cytokine and p53 pathways [68]. In regards the action of the autocrine/paracrine pathways as a blocker, l-carnitine was the only molecule that showed some activity [69-72].

### Protective action against stochastic type IV effects.

The anti-mutagenic effects of the three molecules in this category are analyzed. All three molecules showed effects, in particular amifostine showed anti-mutagenic effects acting on the protein p53 and on the repression of the c-myc gene [73-76] also resveratrol showed an anti-mutagen action [77-78], as well as l-carnitine [79].

#### Protectants against Type V Bystander effects

In this category of compounds, the only molecule that showed activity was amifostine. In particular, we have shown that WR-1065, the active metabolite of amifostine, protects against radiation-induced cell death and delayed genomic instability [80]. Another study suggests that WR-1065, the active metabolite of amifostine, mitigates radiation-induced delayed genomic instability [81].

### Operational proposal for radiation protection.

With regard to the hypothesized dosages, the operational proposal must take into account the type of administration taking into account the peculiarity of the hypothesized kit. Pharmacological solutions involving continuous infusion were not considered, while oral and subcutaneous administration in a single dose was preferred. In the light of these factors, the following dosages have been assumed. Different dosages of amifostine have been proposed depending on the routes of administration. They can range from 74-222 mg / m<sup>2</sup> in continuous infusion [82], up to 740-900 mg/m<sup>2</sup> [83], again for continuous infusion methods. The choice of the dose of amifostine was also influenced by the route of administration according to the hypothesized use, in fact the proposed dose of 267 mg / m<sup>2</sup> [84] considered an average body area of 1.8 m2 for an adult person, then a dose of 480 mg of amifostine will be administered subcutaneously in a single dose.

This dosage can provide protection against radiation damage without showing in vivo the typical side effects of amifostine [85-89]. This dose helps to immediately delay the negative

effects arising from exposure to ionizing radiation and will therefore require hospitalization and treatment in hospital facilities. For resveratrol, too, the hypothesized dosage takes into account the route of administration; in this specific case, the proposed dose will be 100 mg/kg to ensure a plasma concentration between 10-50  $\mu$ m, capable of totally reducing chromosome aberrations in subjects exposed to 3Gy of total body irradiation [90-91]. Taking into account the average weight of 70 kg, the quantity assumed will be 7 grams. L-carnitine has shown activity against in vivo radiation in guinea pigs with intraperitoneal administration at dosages between 200 and 300 mg/kg [92]; since the hypothesized actual result of oral dosage in vivo guinea pigs is 300 mg/kg [93], taking into account the weight of 70 kg, there will be a solution of 21 grams of 1-carnitine to be administered when necessary.

In conclusion, since there is no pharmacological information in the scientific literature on the simultaneous administration of the three molecules of an antagonistic or synergistic character, the study shows that their administration can offer complete coverage against the types of damage from ionizing radiation hypothesized. The amifostine dosage tested on human volunteers showed no side effects such as hypotension and vomiting [94-95], and the resveratrol and l-carnitine formulations and formulations at the hypothesized concentrations are able to provide shielding protection against damage due to ionizing radiation. The administration of antidote should be performed in the run-up to the event (30 minutes before) or in the immediate post-event to immediately mitigate the deterministic and stochastic effects of ionizing radiation. Additional therapies will then have to be followed in the second level health facilities.

# 7.4 Toxicity of pesticides and industrial substances in relation to CWA

In order to understand the risk potential of exposure to these substances, they have been compared with the inhalation toxicities of chemical weapons, called Chemical Warfare Agents (CWA), historically used during wartime conflicts, such as Tabun, Sarin, Soman and VX.

The comparison was useful to highlight two aspects. The first inherent to the safety of the operators involved who for professional use can inhale these products that as in the case of pesticides are administered by means of an aerosol The second to investigate potential "*dual use*" for criminal purposes, where the use of highly toxic substances with high toxicological properties available on the market could be a tool to carry out violent actions or terror on the population.

Then a study aimed at identifying toxic substances with the aim of improving the quality of life of professionals and at the same time reducing the risks that certain substances may be used for terrorist purposes.

The database research and computational chemistry activity carried out on the 489 substances sought in the PIC and SEVESO III regulations led to the identification, by means of the reference parameter "a", of 26 substances with toxicity greater than or equal to Tabun, Sarin and comparable to that of Soman and VX.

Below I will start with a list of identified chemicals sorted by their toxicity. The substances reported are those with higher inhalation toxicity (parameter "a") than Tabun and Sarin.

#### PROPANIL

Regulation	PIC Pesticides		
	TIC T esticides		
Name and address	Propanyl	chemical formula	
Cas Number	709-98-8		CH6
Presence on	NO	Kind of Animal/Time	Dat the auropattion
CFATS	NO	exposition	Rat 4h exposition
References	CLP/ESR/PIC	Estimate Lc50 Human (ppm)	0,3125
Presence DB	Echa, Epa, Toxnet, Cameo, T3db	"a" parameter	1,845662696
Meg	NO	Physical state	Solid
Tox Pac 3	21 mg/m3	Boiling Point	351 °C
Tox Aegl 3 to 10'	NO	A Classification	3077 (9.9)
Meg to 1h	NO	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	LC50 Rat inhalation >1.25 mg/L air/4 hr	Advise	Miscellaneous hazardous material
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	1,25	Use in Europe	Banned
NOTES Colorless to brown crystals. Non corrosive. Used as an herbicide.			

The following table lists the properties of Propanil (Tab.7):

Tab. 6 Propanil analysis

# DIELDRIN

# The following table lists the properties of Diedrin (Tab.8):

Regulation	PIC Pesticides		
Name and address	Dieldrin		
Cas Number	60-57-1	chemical formula	~ I fil.
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition
References	CLP/ESR/PIC	Estimate Lc50 Human (ppm)	0,2075
Presence DB	Echa, Epa, Toxnet, Cameo, T3db, HazMat Book	"a" parameter	2,664608955
IDLH	50 mg/m3	Physical state	Solid
Tox Pac 3	450 mg/m3	Boiling Point	175 °C Melting point
Tox Aegl 3 to 10'	NO	A Classification	2761 (6.1, 6.1)
Meg to 1h	NO	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	LC50 Rat inhalation 13 mg/m3	Advise	Poison / Possible Carcinogenic
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,83	Use in Europe	Banned
NOTES	Organochlorine pesticides.		

Tab. 7 Dieldrin analysis

# OMETHOATE

The following table lists the properties of the Omethoate (Tab.9):

Regulation	PIC Pesticides		ньс
Name and address	Omethoate		Not
Cas Number	1113-02-6	chemical formula	H <sub>y</sub> C H <sub>y</sub> C
Presence on	NO	Kind of Animal/Time	Bat 1h avecition (had)
CFATS	NO	exposition	Rat 1h exposition (bad)
References	CLP/ESR/PIC	Estimate Lc50 Human	0,375
		(ppm)	
Presence DB	Echa, Toxnet, T3db.	"a" parameter	2,867313944
IDLH		Physical state	liquid
Tox Pac 3		Boiling Point	135°C
Tox Aegl 3 to 10'	NO	A Classification	2810 (6.1, 6.1)
Meg to 1h	NO	PIC Restriction	PIC/Ex. No.

LC50	LC50 Rat inhalation 1,5 mg/L/1h	Advise	Poison
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals	1.5 mg/L	Use in Europe	Banned
(ppm)	1.0 1167 1	ose in Europe	bullica
NOTES	//		

Tab. 8 Omethoate analysis

#### NICOTINE

# The following table lists the properties of Nicotine (Tab.10):

Regulation	PIC Pesticides		^	
Name and address	Nicotine		N	
Cas Number	54-11-5	chemical formula	CH <sub>0</sub>	
Presence on	NO	Kind of Animal/Time	Rat 20 minutes exposition	
CFATS	NO	exposition	(bad)	
References	CLP/ESR/PIC	Estimate Lc50 Human (ppm)	0,575	
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat.	"a" parameter	3,111038203	
IDLH	5 mg/m3	Physical state	liquid	
Tox Pac 3	35 mg/m3	Boiling Point	246°C	
Tox Aegl 3 to 10'	NO	A Classification	1654 (6.1, 6.1)	
Meg to 1h	NO	PIC Restriction	PIC/Ex. No./Ex. Co.	
LC50	LC50 Rat inhalation 2,3 mg/L/20'	Advise	Poison	
TA Or RA	~	Presence in ERG TAB.1	NO	
Lc50 in Animals (ppm)	2,3	Use in Europe	Banned	
NOTES	Toxic by inhalation, ingestion, and skin absorption. More dense than water.			

Tab. 9 nicotine analysis

# CADMIUM

# The following table lists the properties of the Cadmiun (Tab.11):

		1	
Regulation	PIC Industrial	chemical formula	Cd
Name and address	Cadmium		
Cas Number	7440-43-9		
Presence on	NO	Kind of Animal/Time	Rat 30 minutes exposition
CFATS	NO	exposition	(bad)
References	CLP/PIC/SVHC	Estimate Lc50 Human (ppm)	0,435
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat, TG230.	"a" parameter	3,263621114
IDLH	9 mg/m3	Physical state	solid
Tox Pac 3	4.7 mg/m3	Boiling Point	765°C
Tox Aegl 3 to 10'	8.5 mg/m3	A Classification	2570 (6.1, 6.1)
Meg to 1h	4.7 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.63 mg/m3	Advise	Poison, Carciogenic; Possibly Mutagenic, Possibly Toxic to Reproduction.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	1,74	Use in Europe	Listed in Annex V.
NOTES			

Tab. 10 Cadmium analysis

# LINDANE

The following table lists the properties of the Lindane (Tab.12):

Regulation	PIC Pesticides	chemical formula	CI
Name and address	Lindane		CIMIN
Cas Number	58-89-9		Ē

Presence on	NO	Kind of Animal/Time	Rat 30 minutes exposition
CFATS	NO	exposition	(bad)
References	CLP/PIC/ESR	Estimate Lc50 Human (ppm)	0,39
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat.	"a" parameter	3,482019698
IDLH	50 mg/m3	Physical state	solid
Tox Pac 3	1000 mg/m3	Boiling Point	323°C
Tox Aegl 3 to 10'	//	A Classification	2761 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	1.56 mg/L	Advise	Poison, Skin Sensiting.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	1,56	Use in Europe	Listed in Annex V.
NOTES	Organochlorine pesticides, solid, toxic. Colorless solid with a musty odor; pure material is odorless. Used as a pesticide and scabicide.		

#### CADMIUM OXIDE

Tab. 11 Lindane analysis

# The following table lists the properties of Cadmiun Oxide (Tab.13):

Regulation	PIC Industrial	chemical formula	OCd
address	Cadmium Oxide		
Cas Number	1306-19-0		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition (bad)
References	CLP/PIC/SVHC	Estimate Lc50 Human (ppm)	0,38
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat, TG230.	"a" parameter	3,533970671
IDLH	9 mg/m3	Physical state	solid
Tox Pac 3	5.4 mg/m3	Boiling Point	1559°C
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	10 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	7.98 mg/m3	Advise	Poison, Carcinogenic, Possibly Mutagenic, Possibly Toxic to Reproduction
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	1,52	Use in Europe	Substances subject to export controls or banned from export from the EU under the PIC regulation.
NOTES	Is a component of silver alloys, phosphors, semiconductors, glass and ceramic glazes. Formerly used by veterinarians to kill worms and parasites.		

Tab. 12 Cadmium Oxide analysis

## CADMIUM CHLORIDE

# The following table lists the properties of Cadmiun Chloride (Tab.14):

Regulation	PIC Industrial	chemical formula	
Name and address	Cadmium Chloride		CI- Cd <sup>2+</sup> CI-
Cas Number	10108-64-2		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition (bad)
References	CLP/PIC/SVHC	Estimate Lc50 Human (ppm)	0,2675
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat, TG230.	"a" parameter	4,236074044
IDLH	9 mg/m3	Physical state	solid
Tox Pac 3	7.6 mg/m3	Boiling Point	960°C
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	15 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.01 mg/m3	Advise	Poison, Carcinogenic, Mutagenic, Toxic to Reproduction
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	1,07	Use in Europe	Substances subject to export controls or banned from export from the EU under the PIC regulation.
NOTES	Cadmium chloride is used in photography, in fabric printing, in chemical analysis, and in many other uses.		

Tab. 13 Cadmium Chloride analysis

### CADMIUM SULFATE

#### The following table lists the properties of Cadmiun Sulfate (Tab.15):

Regulation	PIC Industrial	chemical formula	Cd2+
Name and address	Cadmium Sulphate		
Cas Number	10124-36-4		0

Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition (bad)
References	CLP/PIC/SVHC	Estimate Lc50 Human (ppm)	0,2525
Presence DB	Echa, EPA, Toxnet, Cameo, T3db, HazMat, TG230.	"a" parameter	4,351490679
IDLH	9 mg/m3	Physical state	solid
Tox Pac 3	8.7 mg/m3	Boiling Point	1000°C
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	17 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.59 mg/m3	Advise	Poison, Carcinogenic, Mutagenic, Toxic to Reproduction
TA Or RA		Presence in ERG TAB.1	NÔ
Lc50 in Animals (ppm)	1,01	Use in Europe	Substances subject to export controls or banned from export from the EU under the PIC regulation.
NOTES	Poisonous Gases May Be Pro	oduced In Fire.	

Tab. 14 Cadmium Sulfate anlysis

# TRIAZOPHOS

The following table lists the properties of Triazophos (Tab.16):

Regulation	PIC Pesticides	chemical formula	
Name and address	Triazophos		state
Cas Number	24017-47-8		о н,с
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 1 h exposition (evil)
References	CLP/PIC	Estimate Lc50 Human (ppm)	0,1525
Presence DB	Echa, EPA, Toxnet, Cameo.	"a" parameter	4,666836804
IDLH		Physical state	liquid
Tox Pac 3	12 mg/m3	Boiling Point	0°C Melting Point
Tox Aegl 3 to 10'	//	A Classification	3018 (6.1, 6.1)
Meg to 1h	17 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	LC50 Rat inh. 0.61 mg/L 1h	Advise	Poison.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,61	Use in Europe	Banned
NOTES	Organophosphorus pesticides, liquid, toxic. Yellowish oil. Used to control insects, mites, and nematodes.		

Tab. 15 Triazophos analysis

## CADMIUM DI(ACETATE)

#### The following table lists the properties of Cadmium Di(acetate) (Tab.17):

Regulation	PIC Industrial	chemical formula	са <sup>2+</sup> H5C-Қ <sup>0-</sup> H5C-Қ <sup>0</sup> -	
Name and address	Cadmium Deacetate			
Cas Number	543-90-8			
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition (bad)	
References	CLP/PIC	Estimate Lc50 Human (ppm)	0,2125	
Presence DB	Echa, EPA, Toxnet, Cameo.	"a" parameter	4,6964292	
IDLH	9 mg/m3	Physical state	Solid	
Tox Pac 3	9.6 mg/m3	Boiling Point	//	
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)	
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.	
LC50	8.01 mg/m3	Advise	Poison.	
TA Or RA	· · · · · · · · · · · · · · · · · · ·	Presence in ERG TAB.1	NO	
Lc50 in Animals (ppm)	0,85	Use in Europe	Severly Restricted	
NOTES				

Tab. 16 Cadmium Di(acetate) analysis

#### CADMIUM NITRATE

#### The following table lists the properties of Cadmium Nitrate (Tab.18):

Regulation	PIC Industrial	chemical formula	
Name and address	Cadmium Nitrate		
Cas Number	10325-94-7		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition (bad)
References	CLP/BPR/PIC	Estimate Lc50 Human (ppm)	0,2075
Presence DB	Echa, EPA, Toxnet, Cameo, HazMat, TG230.	"a" parameter	4,744050497
IDLH	9 mg/m3	Physical state	Solid
Tox Pac 3	9.9 mg/m3	Boiling Point	132°C
Tox Aegl 3 to 10'	//	A Classification	3087 (5.1, 6.1)
Meg to 1h	19 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.03 mg/m3	Advise	Oxidizier, Poison, Carcinogenic, Mutagenic, A majority of data submitters agree this substance is Toxic to Reproduction.
TA Or RA		Presence in ERG TAB.1	NO

Lc50 in Animals (ppm)	0,83	Use in Europe	Severly Restricted
NOTES	Toxic oxides of nitrogen and	cadmium oxide fume may	/ form in fires.

Tab. 17 Cadmium Nitrate analysis

## TOLYLFLUANID

# The following table lists the properties of Tolylfluanid (Tab.19):

Regulation	PIC Pesticides	chemical formula	$H_3C$ N F S $CH_3$ F $CH_3$ $H_3C$ $CH_3$ $H_3C$ $CH_3$ $H_3C$ $CH_3$ $CH_3$ $H_3C$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$ $CH_3$
Name and address	Tolyfluanid		cıČcı
Cas Number	731-27-1		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition (bad)
References	CLP/BPR/PIC	Estimate Lc50 Human (ppm)	0,065
Presence DB	Echa, Toxnet.	"a" parameter	4,986097095
IDLH	//	Physical state	Solid
Tox Pac 3	//	Boiling Point	93°C Melting Point
Tox Aegl 3 to 10'	//	A Classification	2811 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	LC50 Rat inh. 0.26 mg/L	Advise	Skin Sensitising
TA Or RA	0	Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,26	Use in Europe	Banned
NOTES	Toxic oxides of nitrogen and	cadmium oxide fume may	y form in fires.

Tab. 18 Tolylfluanid analysis

#### TAXOPHENE

The following table lists the properties of Taxophene (Tab. 20):

Regulation	PIC Pesticides	chemical formula	
Name and address	Taxophene		H <sub>3</sub> C N S CI
Cas Number	8001-35-2		сн,
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition (male) nose only.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,065

Presence DB	Echa,Epa,Toxnet,Cameo,t3db.	"a" parameter	4,986097095
IDLH	200mg/m3	Physical state	Solid
Tox Pac 3	200mg/m3	Boiling Point	65°C Melting Point
Tox Aegl 3 to 10'	//	A Classification	2761 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	LC50 Rat inh. 0.26 mg/L (4 hr nose only)	Advise	Poison, Possibly Carcinogenic.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,26	Use in Europe	Listed in Annex V pary 1 ed Annex I part 3 It is not possible to export this chemical.
NOTES	Yellow, waxy solid with a pleasant piney odor. Used as an insecticide, primarily for cotton and early growth stages of vegetables.		

Tab. 19 Taxophene analysis

### CADMIUM BROMIDE

# The following table lists the properties of Cadmium Bromide (Tab. 21):

Regulation	PIC Industrial	chemical formula	Br- Cd2+ Br-
address	Cadmium Bromide		
Cas Number	7789-42-6		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,18
Presence DB	Echa,Epa,Toxnet,Cameo,t3db, HazMat, TG230.	"a" parameter	5,028399475
IDLH	9 mg/m3	Physical state	Solid
Tox Pac 3	11 mg/m3	Boiling Point	//
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	22 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.02 mg/m3	Advise	Poison.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,72	Use in Europe	Severly Restricted
NOTES	//		

Tab. 20 Cadmium Bromide analysis

### CADMIUM FLUOROBORATE

The following table lists the properties of Cadmium Fluoroborate (Tab. 22):

Regulation	PIC Industrial	chemical formula	F F Cd ↔
Name and address	Cadmium Fluoroborate		F
Cas Number	14486-19-2		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 30 minutes exposition.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,17
Presence DB	Echa, HazMat.	"a" parameter	5,142716302
IDLH	9 mg/m3	Physical state	Liquid
Tox Pac 3	//	Boiling Point	//
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	7.95 mg/m3	Advise	Poison.
TA Or RA	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,68	Use in Europe	Severly Restricted
NOTES	Poisonous Gases May Be Produ	ıced In Fire.	

Tab. 21 Cadmium Fluoroborate analysis

### AZOCYCLOTIN

The following table lists the properties of Azocyclotin (Tab. 23):

Regulation	PIC Pesticides	chemical formula	
Name and address	Azocyclotin		
Cas Number	41083-11-8		N
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,05
Presence DB	Echa,Epa,Toxnet,t3db.	"a" parameter	5,510825624
IDLH	9 mg/m3	Physical state	Solid
Tox Pac 3	//	Boiling Point	210°C Melting Point
Tox Aegl 3 to 10'		A Classification	3146 (6.1, 6.1)
Meg to 1h		PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	0,2 mg/1 4h rat	Advise	Poison.

TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,2	Use in Europe	Banned
NOTES	Poisonous Gases May Be Produced In Fire.		

Tab. 22 Azocyclotin analysis

#### CADMIUM DISTEARATE

# The following table lists the properties of Cadmium Distearate (Tab. 24):

Regulation	PIC Industrial	chemical formula	
Name and address	Cadmium Distearate		
Cas Number	2223-93-0		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,0725
Presence DB	Echa, Epa, Toxnet, t3db, Cameo, HazMat, TG230.	"a" parameter	6,847140053
IDLH	9 mg/m3	Physical state	Solid
Tox Pac 3	28 mg/m3	Boiling Point	//
Tox Aegl 3 to 10'	//	A Classification	2570 (6.1, 6.1)
Meg to 1h	55 mg/m3	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	8.06 mg/m3	Advise	Poison.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,29	Use in Europe	Severly Restricted
NOTES	Solid. Used as a lubricant and stabilizer for polyvinyl chloride.		

Tab. 23 Cadmium distearate analysis

### CYFLUTHRIN

The following table lists the properties of Cyfluthrin (Tab. 25):

Regulation	PIC Pesticides	chemical formula	H,C - C - C - C - C - C - C - C - C - C -
Name and address	Cyfluthrin		₽.
Cas Number	68359-37-5		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.

References	CLP / PIC / BPR	Estimate Lc50 Human (ppm)	0,025
Presence DB	Echa, Epa, Toxnet, t3db, Cameo.	"a" parameter	6,897119985
IDLH	//	Physical state	liquid
Tox Pac 3	//	Boiling Point	60°C Melting Point
Tox Aegl 3 to 10'	//	A Classification	3352 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC/Ex. No./Ex. Co.
LC50	0,1 mg/L 4h rat (m)	Advise	Poison.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,1	Use in Europe	Banned
NOTES	A viscous amber partly crystalline oil. Used as an insecticide.		

Tab. 24 Cyfluthrin analysis

#### MONOCROTOPHIOS

# The following table lists the properties of Monocrotophos (Tab. 26):

Regulation Name and	PIC Pesticides	chemical formula	
address	Monocrotophos		-
Cas Number	6923-22-4		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,02
Presence DB	Echa, Epa, Toxnet, t3db, Cameo.	"a" parameter	7,343407088
IDLH	//	Physical state	Solid
Tox Pac 3	3.5 mg/m3	Boiling Point	125°C Melting Point
Tox Aegl 3 to 10'	//	A Classification	3018 (6.1, 6.1)
Meg to 1h	//	PIC Restriction	PIC
LC50	0,08 mg/L 4h rat (m)	Advise	Poison, Possibly Mutagenic.
TA Or RA		Presence in ERG TAB.1	NO
Lc50 in Animals (ppm)	0,08	Use in Europe	Banned
NOTES	Organophosphorus pesticides, liquid, toxic. Colorless crystals with a mild ester odor, commercial product is a reddish-brown solid. Very toxic.		

Tab. 25 Monocrotophos analysis

# METHOMYL

#### The following table lists the properties of Methomyl (Tab. 27):

Regulation	PIC Pesticides	Chemical formula			
Name and address	Methomyl		Hyc Hyc		
Cas Number	16752-77-5				
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.		
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,015		
Presence DB	Echa, Epa, Toxnet, t3db, Cameo.	"a" parameter	7,918771232		
IDLH	//	Physical state	Solid		
Tox Pac 3	23 mg/m3	Boiling Point	78°C Melting Point		
Tox Aegl 3 to 10'	//	A Classification	2811 (6.1, 6.1)		
Meg to 1h	//	PIC Restriction	PIC/Export No/Export Cons.		
LC50	0,06 mg/L 4h rat (m)	Advise	Poison, Possibly Mutagenic.		
TA Or RA	••••••••••••••••••••••••••••••••••••••	Presence in ERG TAB.1	YES		
Lc50 in Animals (ppm)	1006		Banned		
NOTES	Toxic solids, organic, n.o.s White crystalline solid with slight sulfurous smell. Used as a nematocide, and an insecticide on vegetables, tobacco, cotton, alfalfa, soy beans, and corn.				

Tab. 26 Methomyl analysis

#### CHLORFENVINPHOS

The following table lists the properties of Chlorfenvinphos (Tab. 28):

Regulation	PIC Pesticides	Chemical formula		
Name and address	Chlorfenvinphos			
Cas Number	470-90-6			
Presence on CFATS	NO	Kind of Animal/Time exposition Estimate Lc50 Human	Rat 4h exposition.	
References	References CLP / PIC		0,0125	
Presence DB	Echa, Epa, Toxnet, t3db, Cameo.	"a" parameter	8,283414346	
IDLH	500  mg/m3	Physical state	Liquid	
Tox Pac 3	Tox Pac 3 //		170°C Melting Point	
Tox Aegl 3 to 10' //		A Classification	3018 (6.1, 6.1)	
		PIC Restriction	PIC/Export No	
LC50	0,05 mg/L 4h rat (m)	Advise	Poison.	

TA Or RA		Presence in ERG TAB.1	YES
Lc50 in Animals (ppm)	0,05	Use in Europe	Banned
NOTES	Used as a foliage insecticide soil insects. Organophospho:	for potatoes, rice, maize, a rus pesticides, liquid, toxic	nd sugar cane. Used to control

Tab. 27 Chlorfenvinphos analysis

#### FENTANYL ACETATE

## The following table lists the properties of Fentanyl Acetate (Tab. 29):

Regulation	PIC Pesticides	Chemical formula		
Name and address	Hontanyl A cotato			
Cas Number	900-95-8			
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.	
References	CLP / PIC	Estimate Lc50 Human (ppm)	0,011	
Presence DB	Echa, Epa, Toxnet, Cameo t3db.	"a" parameter	8,539081089	
IDLH	//	Physical state	Solid	
Tox Pac 3	28 mg/m3	Boiling Point	123°C Melting Point	
Tox Aegl 3 to 10'	//	A Classification	3146 (6.1, 6.1)	
Meg to 1h	//	PIC Restriction	PIC/Export No	
LC50	0,044 mg/L 4h rat (m)	Advise	Poison, Possibly Carcinogenic, Possibly Toxic to Reproduction.	
TA Or RA		Presence in ERG TAB.1	YES	
Lc50 in Animals (ppm)	0,044	Use in Europe	Banned	
NOTES	Causes skin irritation and may cause respiratory irritation. Organotin compounds, solid.			

Tab. 28 Fentanyl Acetate analysis

#### PHOSGENE

The following table lists the properties of Phosgene (Tab. 30):

Regulation	SEVESO III	Chemical formula			
Name and address	Phosgene				
Cas Number	75-44-5				
Presence on CFATS	YES	Kind of Animal/Time exposition	Mouse 30 minutes exposition (bad).		

References	SEVESO III	Estimate Lc50 Human (ppm)	0,0235	
Presence DB	Echa, Epa, Toxnet, Cameo TG230, HazMat.	"a" parameter	9,100312334	
IDLH	2 mg/m3	Physical state	Gas	
Tox Pac 3	0.75 mg/m3	Boiling Point	7,5°C	
Tox Aegl 3 to 10'	3.6 mg/m3	A Classification	1076 (2.3/2.3,8)	
Meg to 1h	3 mg/m3	PIC Restriction	//	
LC50	0.047 mg/L 4h mouse (m)	Advise	Poisonous Gas / Flammable Gas	
TA Or RA		Presence in ERG TAB.1	YES	
Lc50 in Animals (ppm)	0,047	Use in Europe	Banned	
NOTES	Colorless gas or very low-boiling, volatile liquid (b.p. 8.3°C, 48°F) with an odor of new- mown hay or green corn. Extremely toxic. Warning properties of the gas inhaled are slight, death may occur within 36 hours			

Tab. 29 Phosgene analysis

#### CADUSAFOS

The following table lists the properties of Cadusafos (Tab. 31):

Regulation	Pic Pesticides	Chemical formula	H <sub>b</sub> C H <sub>b</sub> C		
Name and address	Cadusafos		Сн		
Cas Number	95465-99-9		CH		
Presence on CFATS	NO	Kind of Animal/Time exposition	Rat 4h exposition.		
References CLP		Estimate Lc50 Human (ppm)	0,0065		
Presence DB	Echa, Toxnet.	"a" parameter	9,591267281		
IDLH	//	Physical state	Liquid		
Tox Pac 3	//	Boiling Point	112°C		
Tox Aegl 3 to 10'	//	A Classification	3381 (6.1,6.1)		
Meg to 1h	//	PIC Restriction	PIC/ Export Co./Export No.		
LC50	0,026 mg/L 4h rat (m)	Advise	Poisonous		
TA Or RA		Presence in ERG TAB.1	NO		
Lc50 in Animals (ppm) 0,026		Use in Europe	Banned		
NOTES	//				

Tab. 30 Cadusafos analysis

## TABUN

The following table lists the properties of the Tabun (Tab. 32):

Regulation	CWA	TRAINING	
Name and address	Tabun		$H_3C^{-1}CH_3$ $H_3C^{-1}CH_3$
Cas Number	77-81-6		
Presence on CFATS	//	Kind of Animal/Time exposition	Mouse 4h exposition (bad).
References	Chemical Warfare Agents	Estimate Lc50 Human (ppm)	1,13
Presence DB	Toxnet.	"a" parameter	1,354367353
LC50	15mg/m3 30 min Mouse	Physical state	Liquid
TA Or RA		Boiling Point	246°C
Lc50 in Animals (ppm)	2,26	Presence in ERG TAB.1	//
NOTES	//	Use in Europe	Banned

Tab. 31 Tabun analysis

#### SARIN

The following table lists the properties of Sarin (Tab. 33):

Regulation	CWA	Chemical formula	
Name and address	Sarin		ĊH <sub>3</sub> ĊH <sub>3</sub>
Cas Number	107-44-8		
Presence on CFATS	//	Kind of Animal/Time exposition	Mouse 1h exposition (bad).
References	Chemical Warfare Agents	Estimate Lc50 Human (ppm)	1,13
Presence DB	Toxnet.	"a" parameter	1,38979856
LC50		Physical state	Liquid
TA Or RA		Boiling Point	158°C
Lc50 in Animals	1,57	Presence in ERG	//
(ppm)		TAB.1	
NOTES	//	Use in Europe	Banned

Tab. 32 Sarin analysis

## SOMAN

The following table lists the properties of Soman (Tab. 34):

Regulation	CWA	Chemical formula		
Name and address	Soman		F `	
Cas Number	96-64-0			
Presence on CFATS	//	Kind of Animal/Time exposition	Mouse 30 minutes exposition (bad).	
References	Chemical Warfare Agents	Estimate Lc50 Human (ppm)	0,065	
Presence DB	Toxnet.	"a" parameter	7,065538637	
LC50	LC50 1mg/m3 30 min Mouse	Physical state	Liquid	
TA Or RA		Boiling Point	198°C	
Lc50 in Animals (ppm)	0,13	Presence in ERG TAB.1	//	
NOTES	//	Use in Europe	Banned	

Tab. 33 Soman analysis

VX

The following table lists the properties of the Vx (Tab. 35):

Regulation	CWA	Chemical formula	
Name and address	VX		
Cas Number	50782-69-9		
Presence on CFATS	//	Kind of Animal/Time exposition	Rat 4h exposition.
References	Chemical Warfare Agents	Estimate Lc50 Human (ppm)	0,003656
Presence DB	Toxnet.	"a" parameter	10,74213233
LC50	0.16 mg/m3 rat male 4H	Physical state	Oil Liquid / vapour
TA Or RA		Boiling Point	298°C
Lc50 in Animals (ppm)	0,0146	Presence in ERG TAB.1	//
NOTES	//	Use in Europe	Banned

Tab. 34 Vx analysis

In the following table the substances are listed in order of inhalation toxicity estimated on the basis of parameter 'a' in **Tab. 36**:

REGULATIONS	NAME	CAS	LC50	PPM	TIME/SPECIES	LC50 HU. PPM	PARAMETER ""a"	STATE
Cwa	Tabun	77-81-6	Lc50 15 mg/m <sup>3</sup> 30 Min Mouse	2,26	30' Mouse	1,13	1,354367353	Liquid
Cwa	Sarin	107-44-8	Lc50 9mg/m <sup>3</sup> 60 Min Mouse	1,57	60' Mouse	0,785	1,38979856	Liquid
Pic Pesticides	Propanyl	709-98-8	Lc50 Rat Inhalation >1.25 Mg/L Air/4 Hr	1,25	4h Rat	0,3125	1,845662696	Solid
Pic Pesticides	Dieldrin	60-57-1	13 mg/m <sup>3</sup>	0,83	4h Rat	0,2075	2,664608955	Solid
Pic Industr.	Hexamethyldistannane	661-69-8	Ld50=7.6 mg/Kg	0,76	Rat	0,19	2,84082349	Solid
Pic Pesticides	Omethoate	1113-02-6	Lc50 Rat Male Inhalation >1.5 Mg/L/1 Hr	1,5	1h Rat	0,375	2,867313944	Liquid
Pic Pesticides	Nicotine	54-11-5	Lc50 (20 Min) 2.3 Mg/l Air	2,3	20' Accrued	0,575	3,111038203	Liquid
Pic Industr.	Cadmium	7440-43-9	8.63 g/m <sup>3</sup>	1,74	30' Rats	0,435	3,263621114	Solid
Pic Pesticides	Lindane	58-89-9	1.56 mg/l	1,56	30' Rat	0,39	3,482019698	Solid
Pic Industr.	Cadmium Oxide	1306-19-0	///	1,52	///	0,38	3,533970671	Solid
Pic Industr.	Cadmium Chloride	10108-64-2	///	1,07	///	0,2675	4,236074044	Solid
Pic Industr.	Cadmium Sulfate	10124-36-4	///	0,94	///	0,235	4,495142148	Solid
Pic Pesticides	Triazophos	24017-47-8	Lc50 Rat Inh. 0.61 Mg/1	0,61	1h Rat	0,1525	4,666836804	Liquid
Pic Industr.	Cadmium Acetate (5743-04-4 Echa)	543-90-8	///	0,85	///	0,2125	4,6964292	Solid
Pic Industr.	Cadmium Nitrate	10325-94-7	///	0,83	///	0,2075	4,744050497	Solid
Pic Pesticides	Tolylfluanid	731-27-1	Lc50 Rat Inh. 0.26 Mg/L	0,26	4h Rat	0,065	4,986097095	Solid
Pic Pesticides	Toxaphene	8001-35-2	Lc50 Rat Inh. 0.26 Mg/l (4 Hr Nose Only)	0,26	4h Rat	0,065	4,986097095	Solid
Pic Industr.	Cadmium Bromide	7789-42-6	///	0,72	///	0,18	5,028399475	Solid
Pic Industr.	Cadmium Fluoroborate (Cadmium Tetrafluoroborate)	14486-19-2	///	0,68	///	0,17	5,142716302	Liquid
Pic Pesticides	Azocyclotin	41083-11-8	0.2 mg /1	0,2	4h Rat	0,05	5,510825624	Solid
Pic Industr.	Cadmium Stearate	2223-93-0	///	0,29	///	0,0725	6,847140053	Solid
Pic Pesticides	Cyfluthrin	68359-37-5	0.1 mg/l	0,1	4h Rat	0,025	6,897119985	Liquid Viscous
Cwa	Soman	96-64-0	Lc50 1 mg/m <sup>3</sup> 30 Minutes Mouse	0,13	30' Mouse	0,065	7,065538637	Liquid
Pic Pesticides	Monocrotophos	6923-22-4	0.08 mg/1	0,08	4 Hr Rat	0,02	7,343407088	Solid
Pic Pesticides	Methomyl	16752-77-5	0.06 mg/l	0,06	4 Hr Rat	0,015	7,918771232	Solid
Pic Pesticides	Chlorfenvinphos	470-90-6	0.05 mg/l	0,05	4h Rat	0,0125	8,283414346	Liquid
Pic Pesticides	Fentin Acetate	900-95-8	0,044 mg/1	0,044	Air/4 Hr Rat	0,011	8,539081089	Solid
Seveso III	Carbonyl Dichloride (Phosgene)	75-44-5	0,047 mg/1	0,047	Mouse 30'	0,0235	9,100312334	Gas
Pic Pesticides	Cadusafos	95465-99-9	0,026 mg/1	0,026	4h Rat	0,0065	9,591267281	Liquid
Cwa	VX	50782-69-9	0.16 mg/m <sup>3</sup>	0,0146	4h Rat (m)	0,003656	10,74213233	oil liquid/vapo

Tab. 35 Substances of high inhalation toxicity ordered by parameter "a".

The ECHA therefore, by means of export applications and notifications, allows us to trace the reconstruction of the substances included in the PIC Regulation and their export worldwide as shown in the figure below, which represents all exports from 2003 to 2019 of all substances covered by the PIC Regulation (Fig. 11).

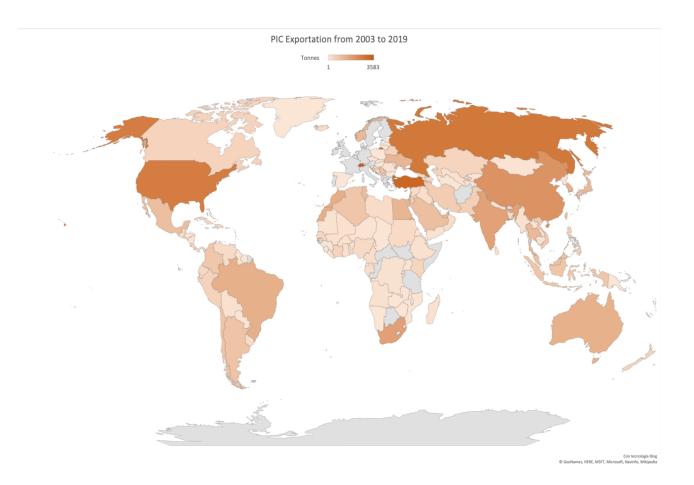


Fig. 4 export levels of PIC substances in tons from 2003 to 2019 worldwide.

The graph shows that many of the substances considered dangerous for the population have been exported to Africa and to the countries that have adhered to the Bamako Convention since 1998.

The same pesticides and industrial substances whose use is Banned in Europe are now exported and used in these countries and in emerging nations less sensitive to environmental issues where there is a more compliant regulatory regime regarding the use of these substances.

## 8 Discussion

During the research, several critical factors concerning HazMat were highlighted. The first one in temporal order was the risk inherent to the transport of LPG at low temperatures, in particular the behavior of butane, capable of generating a puddle capable of releasing vapors such as to saturate the air and therefore capable of triggering any fire or explosion reactions with the arrival of rescue.

Butane itself has shown high saturation capacity outdoors and indoors such as to put at risk of inhalation poisoning the populations possibly exposed.

Subsequently, attention was turned to the risks related to the release of chemicals, especially in companies at risk of major accidents, in this case, following a cybernetic attack, the adaptation of the stock of antidotes was analyzed to meet the need. The analysis revealed the lack of medicinal oxygen among the mandatory "drugs" as well as a non-upgrading of medical devices to what are the current guidelines for first aid.

A countermeasure was also hypothesized to face radiological emergencies, in this case a complementary set of equipment was hypothesized to defend against ionizing radiation. The kit with dosages and formulations suitable for use in the field takes on a double value, both for the protection of the Armed Forces possibly involved, and for any needs of civil protection.

In addition, the inhalation toxicity of the substances has been calculated and acquired in the PIC and Seveso III Regulations, highlighting, thanks to an indicative toxicity parameter normally used in the calculation of vulnerability models, a high toxicity risk for both certain industrial substances and pesticides.

The identified parameter allowed to compare different toxicity values acquired on in vivo guinea pigs (of different typologies) and for different exposure times, facilitating the comparison with the data obtained from the analysis through the computational chemistry acquired thanks to the Qsar Tool Box.

This type of analysis has also made it possible to test the goodness of European regulations that prohibit the use in the vast majority of cases (in relation to the toxic substances identified) within the European Union.

The analysis of the substances has therefore made it possible to identify substances normally used in industry or agriculture that can express an inhalation toxicity greater than or equal to some known chemical weapons generally attributable to the family of organophosphorus. This consideration therefore emphasizes both the risk to operators in the sector who have to operate with substances of very high toxicity and the risk of them being misused for terrorist purposes.

The analysis of export profiles has made it possible to identify countries that are parties to the Bamako Convention and that currently import many of the chemical substances whose use has been banned within the European Union.

The analysis of the substances has also made it possible to make considerations about the toxicities identified inhalation and the UN legislation on the transport of hazardous substances, which has been shown to be appropriate to the levels of toxicities identified.

With regard to the various levels of toxicity identified in the different databases, the absence of toxicity data on pesticides in the TG230 guide, highlighting a possible risk for the military population of an industrial nature only, completely omitting the risk inherent in any exposure from pesticides.

## 8.1 Limits of analysis

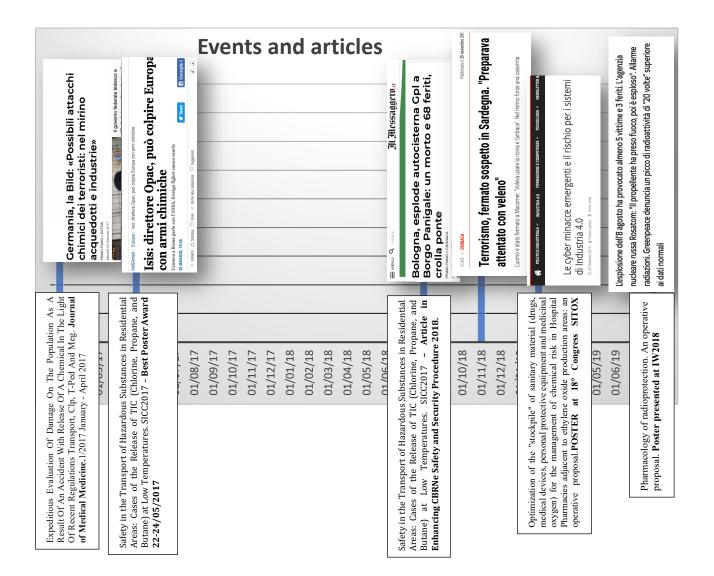
One of the major limits to the research conducted is certainly to be found in simulation software that, although reliable as in the case of ALOHA,<sup>®</sup> do not allow to obtain a representation of the dispersion on the ground three-dimensional. The simulations obtained with the QSAR toolbox, although useful and in some cases allowed by the ECHA as useful data for the presentation of the Dossier, have statistical limits due to the low number of comparable samples in obtaining the regression lines of the software. They are an indispensable tool to obtain an idea of inhalation toxicity with a datum able to approach with good approximation to the actual datum, but the absence of animal testing is a big limit to obtaining the exact datum.

With regard to radiation protection and the pharmacological approach assumed, although it is based on data obtained in vivo on guinea pigs, there is a lack of real in vivo testing that can determine the possible synergy of the three compounds identified.

# 9 Conclusion

Prevention, therefore, is the word that best represents my doctoral thesis. The set of all the procedures and measures that are put in place with the ultimate aim of reducing the damage to professional operators and persons possibly exposed.

The following graph shows the newspaper articles with their dates and the publications or posters presented at the various congresses (**Tab. 37**):



#### Tab. 36 list of events and publications produced

The first article published in the Journal of Military Medicine 1/2017 January - April 2017 entitled "Expeditious evaluation of damage on the population as a result of an accident with release of a chemical in the light of recent regulations transport, clp, t-ped and meg." It

highlighted the risk related to the transport of chlorine and highlighted how this chemical could have important effects on the population possibly involved in terms of terrorist risk.

On 24 January 2017 the newspaper "Messaggero" came out online with the article entitled Germany, the Bild: "Possible chemical attacks by terrorists: in the viewfinder aqueducts and industries" [96] the following words are reported in the article: "*It is also believed possible attacks on plants or transport of the chemical industry, it reads again.* "*The report describes in detail the risks to which the population is exposed in the case of a chemical attack, and how security agencies, hospitals and rescue organizations are prepared to deal with such cases. The document speaks of "a determined and technically competent terrorist group" which "may be able to use the potential of hazardous chemical material present in Germany for its own purposes in the context of an attack". Own production and use of chemicals for "large scale attacks" are largely excluded, the report adds."* 

As part of the 1st Scientific International Conference on CBRNe held from 22 to 24 May 2017 in Rome was presented a poster entitled "*Safety in the Transport of Hazardous Substances in Residential Areas: Cases of the Release of TIC (Chlorine, Propane, and Butane) at Low Temperatures.* ". The work presented highlighted the dangers of transporting LPG and chlorine both by road and rail, in particular the risk of release of propane at low temperatures and the associated risks of fire and explosion due to air saturation due to the formation of a butane puddle. The work also highlighted the risks of explosion, in terms of BLEVEs and shock waves, highlighting the risks related to the possible misuse of chemicals for terrorist purposes.

On 6 August 2018 a tank carrying LPG exploded in Bologna Borgo Panigale causing the death of one person and the injury of sixty-eight [98].

At the SICC2017 congress, OPCW Director General Ahmet Uzumcu spoke about the real risks of ISIS attacks with chemical weapons in Europe [97], in particular in relation to the risk associated with the return of foreign fighters to Europe and the associated risk of using chemical weapons.

The risk of attacks with the use of biocides or industrial substances is part of my PhD research was partly revealed on 28 November 2018, with the arrest of a suspected terrorist accused of preparing an attack with poison or chemical weapons [99].

On 25 February 2019 an online article warned about emerging cyber threats and the risk to industry 4.0 systems, the article entitled "Emerging cyber threats and the risk to industry 4.0 systems" [100], in line with the risks highlighted by the cyber-attacks on the Stuxnet model

to companies at risk of major accident as presented at the 18th National Congress of the Italian Society of Toxicology in Bologna with the poster entitled "*Optimization of the* "stockpile" of sanitary material (drugs, medical devices, personal protective equipment and medicinal oxygen) for the management of chemical risk in Hospital Pharmacies adjacent to ethylene oxide production areas: an operative proposal". In addition to focusing on IT infrastructures, the poster analyzed the equipment of the second level Advanced Medication Posts, highlighting some shortcomings in terms of drugs and devices and highlighting the role of hospital pharmacies adjacent to companies at risk of major accidents as an antidotal measure for the safety of the population.

With regard to the risk of exposure to ionizing radiation in the thesis have listed several possibilities of contamination with radiation in history, and it was assumed a complementary kit for reducing damage from ionizing radiation, the poster was presented at the IW2018 which was held on 8 November 2018 in Rome, the poster entitled "Pharmacology of radioprotection. An operative proposal", hypothesized a complementary set composed of three different molecules able to reduce the damage from ionizing radiation. The article is currently being published in the proceedings of the congress.

The nuclear accident in Russia on August 8th, which generated radiation 16 times higher than the permitted limit and caused the death of five Russian scientists [101], once again demonstrated the need for antidotes to reduce damage from ionizing radiation and reduce recurrences after the exposure phase.

In conclusion, the prevention of HazMat events is the basis of my PhD research that through the application of European Regulations and modern computer technologies and databases aims to reduce the harm to people, whether they are professional operators in the broad sense or citizens involved in civil protection emergencies.

My research therefore partly presumes that more attention will be given to identified chemicals which are already banned for use within the European Union, but which, because of their toxicity, could be used improperly in a different way from the one they were produced for. Could this be the prelude to the adoption of parameters on the CFATS model which are currently missing in Europe?

# 10 List Abbrevation

AEGLs	Access Agute Exposure Guidelines Levels
ALOHA	Access Acute Exposure Guidelines Levels Arial Location Hazardous Atmosphere
AMP	Advanced Medical Post
APHC	
BLEVEs	Army Public Health Center Boiling Liquid Expanding Vapor Explosions
BPR	Boiling Liquid Expanding Vapor Explosions Biogradul Broducts Regulation
CAMEO	Biocidal Products Regulation
CAMEO	Computer-Aided Management of Emergency Operations Chemical Abstracts Service
CFATS	_
CWA	Chemical Facility Anti-Terrorism Standard
DB	Chemical Warfare Agents Database
DB	Basic Date
DHS ECHA	Department of Homeland Security European Chemistry Agency
EFAW	Universities federation of animal welfare
EPA	Environmental Protection Agency
ERG	Emergency Response Guidebook
ERPGs	Emergency Response Planning Guidelines
Fd	Correction Factor
GA	Tabun
GB	Sarin
GD	Soman
GHS	Global Harmonized System
GIS	Geografic Information System
GSH	Glutathione
HAzMat	Hazardous Materilas
HP	Hospital Pharmacy
IDLH	Immediately Dangerous to Life or Health
ITL	Italian Lira
IT	Information Technology Lethal Concentration 50
LC50	Lethal Dose 50
LD50	
LEL	Lower Explosion Limit
LET	Linear Energy Transfer
LPG	Liquid Petroleum Gas
MEG	Military Exposure Guidelines
MHIDAS	Major Hazard Incident Data Service
MSDS	Material Safety Data Sheet
NADH NIOSH	Nicotinamide Adenine Dinucleotide National Institute for Occupational Safety and Health
NITE	National Institute for Occupational Safety and Health National Institute of Technology and Evaluation
NO	Nitric Oxide
PAC	Protrective Action Criteria for Chemicals
PIC	European Regulation Prior Informed Consent "PIC" n° 649/2012

Ppm	parts per million
RA	Read Across
RBE	Relative Biologic Effectiveness
REACH	Registration Evaluation, Authorization and restriction of Chemicals
ROS	radical species of the oxygen
Seveso III	the "Seveso III" Directive and the transposing legislative decree, no. 105
Directive	of 26 June 2015
SITOX	Italian Society of Toxicology
SOD	Super Oxide Dismutase
TA	Trend Anlysis
TEELs	Temporary Emergency Exposure Limits
UN	United Nations
USAPHC	United State Army Public Health Command

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# 12 Awards



Fig. 5 Best Poster Award at 1st Scientific International Conference on CBRNe



Fig. 6 Best Poster in 18° National Congress of Italian Society of Toxicology.



Fig. 7 Best Poster Award 2<sup>nd</sup> Conference on Innovations in Food Science & Human Nutrition – 13 September 2019 London

# 13 Paper

- 1. Ciccotti M. 2017. Expeditious damage assessment on population after a chemical substance release, in the light of the latest regulations on transport, clp (classification labeling packaging legislation), t-ped (transportable pressure equipment directive) and meg (military exposure guidelines). Journal of Military Medicine 1/2017 January-April 2017.
- 2. Ciccotti M, Spagnolo F, Palmery M. 2018. Safety in the Transport of Hazardous Substances in Residential Area: Cases of the Release of TIC (Chlorine, Propane, and Butane) at Low Temperatures. Enhancing CBRNe Safety & Security: Proceedings of the SICC 2017 Conference. Springer. doi.org/10.1007/978-3-319-91791-7
- Ciccotti M, Raguzzini A, Sciarra T, Catasta G, Aiello P, Buccolieri C, Reggi R, Palmery M, Lista F, Peluso I. 2018. Nutraceutical-based Integrative Medicine: Adopting a Mediterranean Diet Pyramid for Attaining Healthy Ageing in Veterans with Disabilities.Current Pharmacology Design. 2018;24(35):4186-4196. doi:10.2174/ 1381612824666181003113444.
- 4. Ciccotti M, Carbone D, Ciccotti M.E., Peluso I. Buccolieri C, Scimonelli L, Munzi D, Di Muzio M, Sciatta T, and Palmery M, and Lista F. Pharmacology of radioprotection. An operative proposal. In press on "IW CBRNe 2018. Countering radiological and nuclear threats", It will be published on the "CBRNe book series" by the end of November 2019.
- 5. Sciarra T, Ciccotti M, Aiello P, Minosi P, Munzi D, Buccolieri C, Peluso I, Palmery M and Lista F. Polypharmacy and Nutraceuticals in Veterans: Pros and Cons. Opinion article on Frontiers In Pharmacology. 10 september 2019 <u>https://doi.org/10.3389/fphar.2019.00994</u>

# 14 Poster

- Ciccotti M, Spagnolo F, Palmery M. Safety in the Transport of Hazardous Substances in Residential Area: Cases of the Release of TIC (Chlorine, Propane, and Butane) at Low Temperatures. Presented at SICC 2017, Rome 22-24 May 2017. BEST POSTER AWARD
- 2. Ciccotti M, Di Muzio M, Ciccotti M.E., Carbone D, Scimonelli L, Buccolieri C, Buccolieri V, Lista F, Palemry M and Sciarra T. Optimization of the "stockpile" of sanitary material (drugs, medical devices, personal protective equipment and medicinal oxygen) for the management of chemical risk in Hospital Pharmacies adjacent to ethylene oxide production areas: an operative proposal. Presented at 18° National Conference of Italian Society of Toxicology, Bologne 13 april 2018. BEST POSTER AWARD
- 3. Ciccotti M, Carbone D, Ciccotti M.E., Peluso I. Buccolieri C, Scimonelli L, Munzi D, Di Muzio M, Sciatta T, and Palmery M, and Lista F. Pharmacology of radioprotection. An operative proposal. Presented at "IW CBRNe 2018" 8 november 2018.
- Ciccotti M, Spagnolo F, Scimonelli L, Carbone D, Peluso I, Palmery M. Pesticides, inhalation toxicity and risk for operators. Presented at 2<sup>nd</sup> Conference on Innovations in Food Science & Human Nutrition – 13 September 2019 London. BEST POSTER AWARD

15 Table of Results

REGUL ATION	SUBSTANCE	CAS	DHS CFACTS	IDLH	TOX PAC 3	TOX AEGL 3 a 10'	MEG 1h	LC50	TA o RA	PPM	Time/s pecies	LC50 Hu. Ppm	parameter "a"	Physi cal State	Ebollition Poin	Ebollition Point in C	Link DB	UN			RESTRICTI ONS	CODIF EPA
PIC INDUST R.	1,1,1-Trichloroethane	71-55-6		700 ppm		4200 ppm	2.3000 mg/m3	20.616 ppm		20616	30' mice	10308	-23,68494	liquid a 20°C	74,1 °C	74,1	ECHA/CA MEO	2831	6.1	6.1		poison
PIC INDUST R.	1,1,1,2-Tetrachloroethane	630-20-6			13 ppm		1.500 mg/m3	8.600 mg/m3		1252,82	4 H Rats	313,205	-22,93562	Insol uble in water	266,9	130,5	CAMEO	1702	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	Triethyltin chloride	994-31-0						115.000 ppm	RA	115.000	human		-21,7065722		206°C	206	ECHA	2788	6.1	6.1	Pre registration	poison
SEVESO III	3-metilpiridina (cfr. nota 21)	108-99-6	NO		300 ppm			110.000 ppm	RA	110.000	human		-21,61766867	liquid			2313	3	3		Flammable Liquid	
SEVESO III	3-(2-etilesilossi)propilammina	5397-31-9	NO					92900 ppm	RA	92900	Human		-21,27975523				2810	6.1	6.1		Poison	
PIC INDUST R.	Butoxydibutylchlorostannane	14254-22-9						92600 ppm	RA	92600	Human		-21,27328622		138°C	138	SDS	2920	8	8+3	Pre Registration	poison
PIC INDUST R.	3,3'-dichlorobenzidine	91-94-1			140 ppm			74700 ppm	TA	74700	Human		-20,8436	solid	788	420	ECHA/CA MEO	2811	6.1	6.1	Annex VII REACH	poison
SEVESO III	Metanolo	67-56-1	NO	6000 ppm	7200 ppm	40000 ppm	93000 mg/m3	64000 ppm		64000	rat 4 h	16000	-19,84132693	liquid	64.°C		1230	3	3 /6 .1		Flammable liquid / Poison	РВТ
PIC INDUST R.	Dibutyltin compounds, ( DIBUTYLTIN-BIS(LAURYL MERCAPTIDE)	1185-81-5						13300 ppm	RA	13300	Human		-17,39223601	Solid Brow n	200	93,333333	ECHA/CA MEO	2788	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	N,N,N',N'-tetraphenyl[1,1'- biphenyl]-4,4'-diamine	15546-43-7			QSAR !?			13.100 ppm	TA	13.100	///		-17,3619324			х	ECHA				CLP	
SEVESO III	2-naftilammina	91-59-8	NO		140 mg/m 3		300 mg/m3	9740 ppm	RA	9740	human		-16,76919017	solid	306°C		1650	6.1	6.1		Poison	с
PIC INDUST R.	1,1,2,2-Tetrachloroethane	79-34-5		100 ppm	150 ppm		600 mg/m3	34.700 mg/m3		1252,82	30' Rats	313,205	-16,6973	liquid a 20°C	295 ° F	146	ECHA/CA MEO	1702	6.1	6.1	Annex VII REACH	poison

SEVESO III	2-metil-3-butenenitrile (cfr. nota 21)	16529-56-9	NO					3000 ppm		3000	rat 4h	750	-16,49337406	liquid			3273	3	3 6.1		Flammable Liquid, Poison	С / М
PIC INDUST R.	Ammonium 2-sec-butyl-4,6- dinitrophenolate	6365-83-9			?			8480 ppm	RA	8480	Human		-16,49212884								Annex III	
PIC INDUST R.	Chloroform	67-66-3		500 ppm	3200 ppm	4000 ppm	16000 mg/m3	9,770 ppm		9770	4 h Rats (F)	2442,5	-16,08219369	liquid	143	61,666667	ECHA/CA MEO	1888	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	Commercial octabromodiphenyl ether (including hexabromodiphenyl ether and heptabromodiphenyl ether)							///		9770	///	2442,5	-16,08219369				6.1					
PIC INDUST R.	Ethylene dichloride (1,2- dichloroethane)	107-06-2					1.2E+03 mg/m3	7.758 mg/L air		7758	4H Rats	1939,5	-15,6210099									
PIC INDUST R.	Carbon tetrachloride	56-23-5		200 ppm	340 ppm	700 ppm	33000 mg/m3	34500 mg/m3		5483,74	2 H mouse	2741,87	-15,62028264	liquid	170,1	76,722222	ECHA/CA MEO	1846	6.1	6.1	Community Corap	poison
PIC INDUST R.	2,2',4,4'-tetrachlorobiphenyl	2437-79-8						LD50: 1010 mg/kg	TA	1840	rats	460	-15,51568062	solid							Annex III	
SEVESO III	Benzene	71-43-2	NO	500 ppm	4000 ppm	9700 ppm	13000 mg/m3	9980 ppm		9980	mouse	4990	-15,43157976	liquid	80.9°C		1114	3	3		Flammable liquid.	С / М
SEVESO III	Acrilato di metile (cfr. nota 21)	96-33-3	NO	250 ppm	1000 ppm		750 mg/m3	1350 ppm		1350	rat 4h	337,5	-14,89635867	liquid	80.1°C		1919	3	3		Flammable Liquid	Ss
PIC INDUST R.	Trimethyltin hydroxide	56-24-6						3640 ppm	RA	3640	Human		-14,8006753				ECHA					
PIC INDUST R.	Triethyltin hydroxide	994-32-1 (56-24-6)						3640 ppm	RA	3640	Human		-14,8006753		114°C	114	ECHA /SDS	3146	6.1	6.1	Pre registration	poison
SEVESO III	Tetraidro-3,5-dimetil-1,3,5- tiadiazina-2-tione (cfr.nota 21)	533-74-4	NO					8400 mg/m3		1265,68	rat 4h	316,42	-14,76736854	solid	106°C	melting	3077	9	9		Miscellaneo us hazardous material	

PIC INDUST R.	1,1-Dichloroethene (VINYLIDENE CHLORIDE, STABILIZED EPA)	75-35-4	si		1000 ppm		4000 mg/m3	168.13 mg/L		168,13	60' Rats	42,0325	-14,75991	liquid a 20°C	31,45 °C	31,45	ECHA/CA MEO	1303	3	3	Annex VII REACH	infiamma bile
SEVESO III	1-bromo-3-cloropropano (cfr. nota 21)	109-70-6	NO					6.5 mg/L		1260	rat 4h		-14,75837292	liquid	143.3°C		2688	6.1	6.1		Poison	
SEVESO III	Ammoniaca Anidra	7664-41-7	SI	300 ppm	1100 ppm	2700 ppm	770 mg/m3	3360 mg/m3		4823,67	1 h mouse	2411,835	-14,67063086	Gasso so	-33°C		1005	2.2	2.3 /8		Non Flammable Gas, Poisonous Gas, Corrosive	
PIC INDUST R.	1,1,2-Trichloroethane	79-00-5		100 ppm	500 ppm		500 mg/m3	35,7 mg/m3		6,42	uomo	1200	-14,66079259	liquid a 20°C	235	112,77778	ECHA/CA MEO	NO			Annex VII REACH	poison
SEVESO III	Acido cloridrico	7647-01-0	SI	50 ppm	100 ppm	620 ppm	150 mg/m3	4 701 ppm		4710	rat	1177,5	-14,62293658	GAS/ liquid	51°C		1789	8	8		Corrosive	R
PIC INDUST R.	Binapacryl	485-31-4			QSAR !?			13.100 ppm		13.100	rats	3275	-14,58934368			66	ECHA/CA MEO				CLP e REACH	
PIC INDUST R.	Dioctyltin compounds (DI(N- OCTYL)TIN-S,S'- BIS(ISOOCTYLMERCAPTOACETA TE))	26401-97-8		25 mg/m 3						3160			-14,51785199	Clear yello w visco us liquid				2788	6.1	6.1	PIC	poison
PIC PESTICI DES	Bis(tris(2-methyl-2- phenylpropyl)(tin) oxide	13356-08-6	NO				LD50 Rat acute oral 2631 mg/kg			3060			-14,45353777	solid	235		2811	6.1	6.1		6.1 - Poison	
PIC INDUST R.	4-aminobiphenyl and its salts	92-67-1		273 ppm	99 mg/m c		200 mg/m3	390 ppm	RA	390	rats	1059,5	-14,3632	solid	576	302,22222	ECHA/CA MEO	3077	9	9	Annex VII REACH e SVHC	miscellan eous
PIC PESTICI DES	Fenbutatin oxide	13356-08-6	NO				LD50: 1450 mg/kg (Oral, Mouse)	2910 ppm	TA	2910			-14,3530141	solid	138	MP	2811	6.1	6.1		6.1 - Poison	

SEVESO III	Ossido di propilene	75-56-9	SI	400 ppm	870 ppm	1300 ppm	2100 mg/m3	4000 ppm		4000	rat 4 h	1000	-14,29614948	liquid	35°C		1280	3	3		Flammable liquid	C/M
SEVESO III	1,2-dibromoetano	74-95-3	NO		200 ppm		7500 mg/m3	40 g/m3		5626,02	2 h rat Inhal.	1406,505	-14,28521811	liquid	93.85°C		2664	6.1	6.1		Poison	
PIC PESTICI DES	Ethoxysulfuron	126801-58-9	NO					3600 ppm		3600	4h ratto	900	-14,08542845	solid	145		3077	9	9		9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Chlorotrioctylstannane	2587-76-0	NO				LD50 Rat oral 29200m g/kg		RA	2460			-14,01703064	solid								Ss
PIC PESTICI DES	Calciferol	50-14-6	NO					2440 ppm	ТА	2440			-14,00070402	solid	115	MP	2811	6.1	6.1		6.1 - Poison	
PIC INDUST R.	3,3'-dimethoxybiphenyl-4,4'- ylenediammonium dichloride	20325-40-0			QSAR !?			9700 ppm		9700	rats	2425	-13,98837099			267	ECHA				CLP e REACH	
PIC PESTICI DES	Cholecalciferol	67-97-0	NO				42.5mg/ kg LD50 rat	2410 ppm	TA	2410			-13,97596143	solid	496.4		2811	6.1	6.1		6.1 - Poison	
PIC INDUST R.	Decachloro-1,1'-biphenyl	2051-24-3						LD50: 1010 mg/kg	TA	2400	rats	2400	-13,96764541								Annex III	
PIC INDUST R.	Nonachloro-1,1'-biphenyl	53742-07-7						LD50: 1010 mg/kg	ТА	2310	rats	577,5	-13,89120299	solid							Annex III	
PIC INDUST R.	Carbamic acid, (4-methyl-1,3- phenylene)bis-, bis[2- [ethyl](perfluoro-C4-8- alkyl)sulfonyl]amino]ethyl] ester	68081-83-4						2150 mg/kg		2150	LD50		-13,74764362									
PIC INDUST R.	Pentachloroethane	76-01-7			1200 mg/m 3		5.0E+02 mg/m3	4238ppm		4238	2h rats	1059,5	-13,7185965	liquid	159.8 °C	159,8	ECHA/CA MEO/TN	1669	6.1	6.1	Annex III ed Annex VII	poison

PIC INDUST R.	Allyltriphenylstannane	76-63-1					LD50=100 mg/kg		2080	mouse (IV)	1040	-13,68144373				TN				Pre registration	
PIC INDUST R.	1,1'-Biphenyl, chloro derivs.	1336-36-3		5 mg/m 3	260 mg/m 3 (Pol ychlor inated biphe nyl )	5.0E+00 mg/m3	LD 50 4,5 g/kg		2020	rats	505	-13,62290296	solid /liqui d	Very High		ECHA/TO XNET	2315/34 25	9	9	Annex III	miscellan ous
PIC INDUST R.	2,2',4,4',6,6'-hexachlorobiphenyl	33979-03-2					LD50: 1010 mg/kg	TA	2020	rats	505	-13,62290296	solid							Annex III	
PIC INDUST R.	Triethyltin bromide	2767-54-6		25 mg/m 3			LC50= 16400 mg/m3		1403,01	mouse	701,505	-13,58709498	liquid	223°C	223		3265	8	8	Pre registration	corrosive
SEVESO III	gasoli	68334-30-5	NO		20000 mg/m 3	500 mg/m3	3.6 mg/1		1970	rat 4 h		-13,57277503	liquid	163°C		1202	3	3		Flammable liquid.	
PIC INDUST R.	Pentachloro[1,1'-biphenyl]	25429-29-2					LD50: 1010 mg/kg	TA	1930	rats	482,5	-13,53174795	solid							Annex III	
SEVESO III	Policloruro dibenzofurani e policloruro dibenziodiossine (con TCDD) cifra 20	1746-01-6	NO		0.0085 mg/m 3	0.0075 mg/m3	22.0 ug/kg		1920	rat male LD50	480	-13,52135831	solid	305°C	melting	2811	6.1	6.1		Poison	
PIC PESTICI DES	Aldrin	309-00-2	NO	100 mg/m 3		39 mg/kg Ratto LD50	1900 ppm	TA	1900			-13,50041571	solid	145		2761	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	DDT	50-29-3	NO	210 mg/m 3		150-300 mg/kg MOUSE LD50	1900 ppm	TA	1900			-13,50041571	solid	110		2761	6.1	6.1		6.1 - Poison	

PIC PESTICI DES	Cyhexatin	13121-70-5	NO				190 mg/kg rat oral	1880 ppm	TA	1880			-13,47925149	solid	228		2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Cyhexatin	13121-70-5	NO				LD50 Rat oral 190 mg/kg			1880			-13,47925149	solid	121	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Triphenyltin hydride	892-20-6	NO				DL50 Orale - Topo - 81 mg/kg			1870			-13,4685848	solid	156		3077	9	9	9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Tridemorph	24602-86-6	NO				DL50 Orale - ratto - 650 mg/kg			1840			-13,43623908	liquid	25	MP	3082	9	9	9 - Miscellaneo us hazardous material	R
SEVESO III	cheroseni	8008-20-6	NO				1100 mg/M3	5280 mg/cu		1820	rat 4h		-13,41438094	liquid	146°C		1223	3	3	Flammable liquid.	C/M
PIC PESTICI DES	Tritylium hexafluoroarsenate	437-15-0	NO						TA	1820			-13,41438094								
PIC PESTICI DES	Chlordane	57-74-9	NO	500 mg/m 3				1820 ppm	TA	1820			-13,41438094	liquid	175		2995	6.1	6.1 ,3	6.1 - Poison 3 - Flammable liquid	
PIC PESTICI DES	Triphenylsulphonium hexafluoroarsenate(1-)	57900-42-2	NO						TA	1780			-13,36993467								
PIC PESTICI DES	Nonylphenol	25154-52-3	NO	320 mg/m 3			LD50 Rat oral 1620 mg/kg	1780 ppm		1780			-13,36993467	liquid	293		3145	8	8	8 - Corrosive	
SEVESO III	Ossido di etilene	75-21-8	SI	800 ppm	200 ppm	360 ppm	360 mg/m3	5029 ppm		5029	rat 1 h	1257,25	-13,36770871	gas	10.7°C		1040	2.3	2.1	Poisonous Gas/ Flammable Gas	C/M/PB T

PIC PESTICI DES	Ethylene oxide	75-21-8	SI	200 ppm			5029 ppm		5029	1h rat inhalati on	1257,25	-13,36770871	gas	10.7		1040	2.3	2.3 /2 .1	2.3 - Poisonous gas / 2.1 - Flammable gas	C/M/PB T
PIC PESTICI DES	Vinclozolin	50471-44-8	NO				LC50 Rat inhalation >29,100 mg/cu m/4hr		2486,81	4h rat	621,7025	-13,34556229	solid	108	МР	3077	9	9	9 - Miscellaneo us hazardous material	R/Ss
PIC INDUST R.	2,4,4'-trichlorobiphenyl	7012-37-5					LD50: 1010 mg/kg	TA	1740	rats	435	-13,32447817	solid						Annex III	
PIC PESTICI DES	Fenpropathrin	39515-41-8	NO			LD50 Rat male oral 70.6 mg/kg (in corn oil)	1730 ppm	TA	1730			-13,31295076	solid	45	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Hexamethyldistannane	661-69-8	NO			LD50 rat 7690ug/ kg (7.69mg /kg)		TA	1730			-13,31295076	solid	182		3146	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Amitraz	33089-61-1	NO			39 mg/kg LD50 (rat)	1720 ppm	TA	1720			-13,30135652	solid	86	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Propargite	2312-35-8	NO			LD50 Rat (male) acute oral 2639 mg/kg	1720 ppm	TA	1720			-13,30135652	solid	x		2810	6.1	6.1	6.1 - Poison	
PIC INDUST R.	Tribenzyltin chloride	3151-41-5					LD50=175 mg/kg		1700	rat	425	-13,27796444								poison
SEVESO III	Miscele di ipoclorito di sodio con conc. Inferiore al 5% ex H400	7681-52-9	NO			500 mg/m3	1700 ppm	RA	1700	Human		-13,27796444	liquid	101 °C		1791	8	8	Corrosive	

PIC PESTICI DES	Trifluralin	1582-09-8	NO	78 mg/m 3		LD50 Rat oral >10,000 mg/kg			1680			-13,25429553	solid	96		3077	9	9		9 - Miscellaneo us hazardous material	
PIC INDUST R.	Dichlorobiphenyl	25512-42-9					LD 50 2230mg/kg	TA	1650	rats	1650	-13,21825852	solid			ECHA/CA MEO/TN	2315	9	9	Annex III	miscellan ous
PIC INDUST R.	4,4'-dichlorobiphenyl	2050-68-2					LD50: 1010 mg/kg	TA	1650	rats	412,5	-13,21825852	solid							Annex III	
SEVESO III	Propilammina (cifr 21)	107-10-8	NO		100 ppm	600 mg/m3	2310 ppm		2310	rat 4 h	577,5	-13,19805581	liquid	47.2 °C		1277	3	38		Flammable Liquid, Corrosive	
PIC INDUST R.	Creosote, wood	8021-39-4					11700 mg/m3		2304,39	rat	576,0975	-13,19319276	liquid							Annex VII REACH	
PIC PESTICI DES	Diphenyldiarsenic acid	4519-32-8	NO					TA	1590			-13,14417597									
PIC PESTICI DES	4-(diethylamino)-2- ethoxybenzenediazonium hexafluoroarsenate	63217-33-4	NO					TA	1570			-13,11885918									
PIC PESTICI DES	Binapacryl	485-31-4	NO			58 mg/kg rat oral	1560 ppm	TA	1560			-13,10607958	solid	66	MP	2811	6.1	6.1		6.1 - Poison	R
PIC PESTICI DES	Terbufos	13071-79-9	NO	2.2 mg/m 3		LD50 Rat male oral 2 mg/kg	1560 ppm	TA	1560			-13,10607958	liquid	69		3018	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	3-methyl-4-(pyrrolidin-1- yl)benzenediazonium hexafluoroarsenate	27569-09-1	NO					TA	1550			-13,0932178									
PIC PESTICI DES	Technazene	117-18-0	NO			LD50 Rat oral 250 mg/kg	1550 ppm	TA	1550			-13,0932178	solid	304		3077	9	9		9 - Miscellaneo us hazardous material	Ss

PIC INDUST R.	2-chlorobiphenyl	2051-60-7					LD50: 1010 mg/kg	ТА	1550	rats	387,5	-13,0932178	solid /liqui d								
PIC INDUST R.	3-chlorobiphenyl	2051-61-8					LD50: 1010 mg/kg	TA	1550	rats	387,5	-13,0932178		284.5°C	284,5						
PIC INDUST R.	4-chlorobiphenyl	2051-62-9					LD50: 1010 mg/kg	TA	1550	rats	387,5	-13,0932178	solid	556	291,11111		3432	9	9	Annex III	miscellan ous
PIC PESTICI DES	Phosalone	2310-17-0	NO			LD50 Rat oral 85 mg/kg bw	1540 ppm	TA	1540			-13,08027277	solid	47.5	MP	2811	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	Rotenone	83-79-4	NO			DL50 Orale - Ratto - 60 mg/kg	1540 ppm	TA	1540			-13,08027277	solid	210		2588	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	HCH (mixed isomers)	608-73-1	NO	1000 mg/m 3		LD50 Rat oral 100 mg/kg	1530 ppm	TA	1530			-13,06724341	solid	112		2761	6.1	6.1		6.1 - Poison	
PIC INDUST R.	Polybrominated biphenyls (PBB) except hexabromo-biphenyl	67774-32-7					LD50 21,500 mg/kg		2150	rats	537,5	-13,05449644	liquid			TOXNET					
PIC PESTICI DES	Oxadiargyl	39807-15-3	NO				1510 ppm	TA	1510			-13,04092724	?			3077	9	9		9 - Miscellaneo us hazardous material	
PIC INDUST R.	Hexachloroethane	67-72-1		300 ppm	300 ppm	3.0E+03 mg/m3	LD50 Mouse ip 4500 mg/kg		1500	(260 ppm!?)		-13,02763816	crysta lline solid	368,2	186,77778	ECHA/CA MEO	2811	6.1	6.1	Annex III ed Annex VII	poison
SEVESO III	Dicloruro di zolfo	10545-99-0					1500 ppm	RA	1500	human		-13,02763816		59°C							
PIC PESTICI DES	Benfuracarb	82560-54-1	NO			105mg/ kg LD50	1500 ppm	TA	1500			-13,02763816	solid	25	MP	2810	6.1	6.1		6.1 - Poison	

PIC PESTICI DES	Chlorobenzilate	510-15-6	NO	550 mg/m 3		1040 mg/kg rat male	1490 ppm	TA	1490			-13,01426018	solid	146		3077	9	9		9 - Miscellaneo us hazardous material	
SEVESO III	benzotricloruro	98-07-7	NO	Potent ial huma n carcin ogen	5.3 mg/m 3	10 mg/m3	6g/kg		1480	rat	370	-13,00079212	liquid	89°C		2226	8	8		Corrosive	C / Ss
PIC PESTICI DES	Diniconazole-M	83657-18-5	NO			LD50 male 639 mg/kg rat	1480 ppm	TA	1480			-13,00079212	solid	х		х	х	x			
PIC PESTICI DES	Fentin chloride	639-58-7	NO	38 mg/m 3		LD50 Rat oral 190 mg/kg			1480			-13,00079212	solid	240		3146	6.1	6.1		6.1 - Poison	
PIC INDUST R.	Trichlorobenzene	12002-48-1					LD50 = 756-766 mg/kg	TA	1480	rats	370	-13,00079212	liquid	213°C		ECHA/CA MEO/TN	2321	6.1	6.1	Annex III	poison
PIC PESTICI DES	Ethoxyquin	91-53-2	NO			DL50 Orale - Ratto - 800 mg/kg	1470 ppm	TA	1470			-12,98723274	liquid	123		х	x	x			
PIC PESTICI DES	Propisochlor	86763-47-5	NO			DL50 Orale - ratto - 3.433 mg/kg	1460 ppm	TA	1460			-12,97358081	solid			x	x	x		х	Ss
PIC PESTICI DES	Dinoterb	1420-07-1	NO	12 mg/m 3		LD50 Oral - Rat - 26 mg/kg	1440 ppm	TA	1440			-12,94599417	solid	220		2811	6.1	6.1		6.1 - Poison	R
PIC PESTICI DES	Fenarimol	60168-88-9	NO			LD50/R at:2,500 mg/kg	1440 ppm	TA	1440			-12,94599417	solid	117	MP	3017	6.1	6.1 /3		6.1 - Poison / 3 - Flammable liquid	

PIC INDUST R.	Dinoseb	88-85-7			5.4 mg/m 3		10 mg/m3	LD50 Rat, adult male oral 27 mg/kg	TA	1440	rat	1440	-12,94599417	Oran ge brow n liquid	38-42°C melting point	38	ECHA/CA MEO/TN	2779	6.1	6.1	Candidate List SVHC	poison
PIC PESTICI DES	Coumafuryl	117-52-2	NO				25mg/k g LD50 ratto	1430 ppm	TA	1430			-12,93205683	solid	124	MP	2811	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Pebulate	1114-71-2	NO				LD50 Rat oral 921 mg/kg	1420 ppm	TA	1420			-12,91802168	liquid	142		3082	9	9		9 - Miscellaneo us hazardous material	
SEVESO III	Piperidina	110-89-4	SI		110 ppm	370 ppm	380 mg/m3	2000 ppm		2000	4 h rat	500	-12,90985512	liquid	107°C		2401	8	83		Corrosive, Flammable Liquid	
PIC PESTICI DES	Alachlor	15972-60-8	NO				929 mg/kg (Rat LD50)	1400 ppm	TA	1400			-12,88965241	solid	100°C 0.02 mm Hg		2588	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	Diphenylamine	122-39-4	NO	220 mg/m 3			LD50 Rat oral 2 g/kg	1390 ppm	TA	1390			-12,87531543	solid	302		2811	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Iminoctadine	13516-27-3	NO					1390 ppm	TA	1390			-12,87531543	solid	558		3588	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Bensultap	17606-31-4	NO				1100 mg/kg (700 mg/m3)	1380 ppm	TA	1380			-12,86087494	solid			3077	9	9		9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Flurprimidol	56425-91-3	NO				DL50 Orale - ratto - maschio - 914 mg/kg	1360 ppm	TA	1360			-12,83167734	solid	264		x	х	x		х	
PIC INDUST R.	4,4'-bi-o-toluidine	119-93-7			36 mg/m 3		meg water	///		1350	///		-12,81691712	solid	392	200	ECHA/CA MEO	NO			Non nel PIC Annex III REACH	
PIC INDUST R.	Monomethyl-Tetrachlorodiphenyl methane; Trade name: Ugilec 141	76253-60-6						LD50 4600mg/kg (1330 ppm Human)	RA	1330	human		-12,78706582				ECHA/TO XNET				Annex III ed Annex VII	
PIC INDUST R.	Nonylphenols C6H4(OH)C9H19 (Isononylphenol)	11066-49-2			260 mg/m 3			1330 ppm	RA	1330	Human		-12,78706582	liquid	579	303,88889	ECHA/CA MEO	3145	8	8	Annex III	corrosive
PIC INDUST R.	Potassium 2,3,4,5-tetrachloro-6-[[[3- [[(heptadecafluoroocty1)sulphony1]o xy]pheny1]amino]carbony1]benzoate	57589-85-2						1330 ppm	RA	1330	Human		-12,78706582									
PIC INDUST R.	N- ethylheptadecafluorooctanesulphon amide	4151-50-2						1330 ppm	RA	1330	Human		-12,78706582									
PIC INDUST R.	Heptadecafluoro-N-(2- hydroxyethyl)-N- methyloctanesulphonamide	24448-09-7						1330 ppm	RA	1330	Human		-12,78706582									
PIC INDUST R.	N-ethylheptadecafluoro-N-(2- hydroxyethyl)octanesulphonamide	1691-99-2						1330 ppm	RA	1330	Human		-12,78706582									

PIC INDUST R.	Heptadecafluorooctanesulphonic acid, compound with 2,2'- iminodiethanol (1:1)	70225-14-8				1330 ppm	RA	1330	Human	-12,78706582									
PIC INDUST R.	Potassium heptadecafluorooctane-1- sulphonate	2795-39-3				1330 ppm	RA	1330	Human	-12,78706582									
PIC INDUST R.	Ammonium heptadecafluorooctanesulphonate	29081-56-9				1330 ppm	RA	1330	Human	-12,78706582									
PIC INDUST R.	Heptadecafluoro-N- methyloctanesulphonamide	31506-32-8				1330 ppm	RA	1330	Human	-12,78706582									
PIC INDUST R.	Chloro-1,1'-biphenyl	27323-18-8				1330 ppm	RA	1330	Human	-12,78706582								Annex III	
PIC INDUST R.	Heptachloro-1,1'-biphenyl	28655-71-2				1330 ppm	RA	1330	Human	-12,78706582								Annex III	
PIC INDUST R.	Tetrachloro(tetrachlorophenyl)benze ne	31472-83-0				1330 ppm	RA	1330	Human	-12,78706582								Annex III	
PIC INDUST R.	Tris (2,3-dibromopropyl) phosphate	126-72-7				1330 ppm	RA	1330	Human	-12,78706582		5.5°C Punto Fusione	5,5		3082	9	9	Annex III - Pre Registration process	canceroge nic
SEVESO III	cloruro di dimetilcarbamoile	63449-41-2	NO			1330 ppm	RA	1330	human	-12,78706582	solid	29-34°C	melting	3267	8	8/ 6.1		Corrosive	
PIC PESTICI DES	4-(ethylamino)-2- methylbenzenediazonium hexafluoroarsenate	63217-32-3	NO				TA	1330		-12,78706582									

PIC PESTICI DES	Chlordimeform	6164-98-3	NO				5.800 mg/m3	TA	1330	1h mammi fero ?!?	-12,78706582	solid	164		2810	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Propham	122-42-9	NO			LD50 Rat (male) oral 3724 mg/kg	1300 ppm	TA	1300		-12,74143647	solid	90	MP	3077	9	9	9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Procymidone	32809-16-8	NO			7800mg /kg mo use LD50	1290 ppm	TA	1290		-12,72599238	solid	166		х	Х	x	Х	R
PIC PESTICI DES	2-Naphthyloxyacetic acid	120-23-0	NO			LD50 = 599 mg/Kg Rat			1270		-12,69474174								Ss
PIC PESTICI DES	Paraquat-dichloride	1910-42-5	NO	9.6 mg/m 3			1mg/m3/6 H rat		1270		-12,69474174	solid	400	MP	2781	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Tricyclazole	41814-78-2	NO			DL50 Orale - Ratto - 250 mg/kg			1270		-12,69474174	solid	187	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Phenylarsine oxide	637-03-6	NO					TA	1260		-12,67893138		145	MP					C/Sr
PIC INDUST R.	Lithium heptadecafluorooctanesulphonate	29457-72-5					0,21 mg/1		1250	Uomo 0,16 mg/1 donna	-12,66299504				EPA/ECH A				
PIC PESTICI DES	Carbaryl	63-25-2	NO	600 mg/m 3		230 mg/kg LD50	1250 ppm	TA	1250		-12,66299504	solid	143	MP	2757	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	N-(p-arsenosophenyl)-1,3,5-triazine- 2,4,6-triamine	21840-08-4	NO	~				TA	1240		-12,6469307								
PIC PESTICI DES	Malathion	121-75-5	NO	390 mg/m 3		LD50 Mouse oral 1025 mg/kg	1240 ppm	TA	1240		-12,6469307	liquid	156		3018	6.1	6.1	6.1 - Poison	Ss
PIC PESTICI DES	Monolinuron	1746-81-2	NO			LD50 oral Rat 1800mg /kg (1600mg /kg)	1240 ppm	TA	1240		-12,6469307	solid	80	MP	3077	9	9	9 - Miscellaneo us hazardous material	

PIC PESTICI DES	Chlozolinate	84332-86-5	NO				1230 ppm	TA	1230		-12,63073628		81		1145	3	3		3 - infiammabil e	
PIC PESTICI DES	Flurenol	467-69-6	NO			DL50 Orale - ratto - > 10.000 mg/kg	1230 ppm	TA	1230		-12,63073628	solid	162	MP	3082	9	9		9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Metoxuron	19937-59-8	NO			LD50 oral Rat 1600mg /kg (1600mg /kg)	1220 ppm	TA	1220		-12,61440966	solid	126	MP	3077	9	9		9 - Miscellaneo us hazardous material	
PIC INDUST R.	3,3'-dimethoxybenzidine	119-90-4			380 mg/m 3	400 mg/m3	///		1210	//	-12,59794866	solid		137	ECHA/CA MEO	2811	6.1	6.1	Non nel PIC Annex III REACH	poison
PIC PESTICI DES	Monuron	150-68-5	NO			LD50 2 500 mg/kg bw (rat)	1200 ppm	TA	1200		-12,58135105	solid	185		3077	9	9		9 - Miscellaneo us hazardous material	
PIC INDUST R.	Benzidine	92-87-5			61 mg/m 3		2.5 mg/L		1190	96 H Notropi s Iu	-12,56461455	solid	753	400,55556	ECHA/CA MEO	1885	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	Benzidine dihydrochloride	531-85-1			QSAR !?		6,93 mg/1		1190	///	-12,56461455	solid	572	300	ECHA/CA MEO	NO			Non nel PIC Annex III REACH	
PIC PESTICI DES	Strychnine	57-24-9	NO			LD50 Rat oral 2350 ug/kg	1180 ppm	ТА	1180		-12,54773682	solid	284	MP	1692	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Naled	300-76-5	NO			LD50 Rat oral 160 mg/kg	1140 ppm	TA	1140		-12,47876446	solid	110		3018	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Thallium sulphate	7446-18-6	NO	21 mg/m 3		LD50 Brown rat oral 16 mg/kg	1140 ppm	TA	1140		-12,47876446	solid	632	MP	1707	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Indolylacetic Acid	87-51-4	NO			Lethal dose: >500 mg/kg ratto	1120 ppm	TA	1120		-12,44336531	solid	168.5	MP	х	х	x		х	
PIC PESTICI DES	Chloropicrin	76-06-2	NO	1.4 ppm	2 ppm		1100 ppm	TA	1100		-12,4073283	solid	112		1583	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Crimidine	535-89-7	NO	0.41 mg/m 3		1.2 mg/kg ratto LD50	1100 ppm	TA	1100		-12,4073283	solid	140		2588	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Triethyltin hydroxide	994-32-1	NO						1100		-12,4073283									
PIC INDUST R.	Sodium 2-(1-methylpropyl)-4,6- dinitrophenolate	35040-03-0			?		1020 ppm	RA	1020	Human	-12,25631319								Annex III	

PIC INDUST R.	Bromotrimethylstannane	1066-44-0		ACUT E TOX 2 ricavo da SDS				1020 ppm	RA	1020	Human		-12,25631319	liquid	165°C	165	SDS	2788	6.1	6.1	Pre registration	poison
PIC PESTICI DES	Iron bis(arsenate)	10102-50-8	NO							1010			-12,2366086				1608	6.1	6.1		6.1 - Poison	
PIC INDUST R.	[[1,1'-biphenyl]-4,4'- diyl]diammonium sulphate	531-86-2			QSAR !?			1000 ppm		1000	rats		-12,21670794	solid	х	х	ECHA/CA MEO	NO			Non nel PIC Annex III REACH	
SEVESO III	Acetilene	74-86-2	SI		400000 ppm	2500 ppm	6000 mg/m3	850000 ppm		979	dog	244,75	-12,17426067	gas	-84°C		1001	2.1	2.1		Flammable Gas	
PIC PESTICI DES	Trisodium arsenite	13464-37-4	NO						TA	963			-12,14130421									
PIC PESTICI DES	Trinickel bis(arsenate)	13477-70-8	NO						TA	963			-12,14130421									
PIC PESTICI DES	Tricalcium diarsenite	27152-57-4	NO						TA	963			-12,14130421									
PIC PESTICI DES	Calcium arsenate	7778-44-1	NO	270 mg/m 3			LD50: 20 mg/kg (Oral, Rat)		ТА	963			-12,14130421	solid	1455	MP	1573	6.1	6.1		6.1 - Poison	С
PIC PESTICI DES	Arsenic acid, magnesium salt	10103-50-1	NO				LD50 Mouse oral 315 mg/kg			963			-12,14130421	solid			1622	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Dimethylarsinic acid	75-60-5	NO	140 mg/m 3				6.9 mg/1/2 hr rat		959			-12,13297953	solid	196°C	MP	1572	6.1	6.1		6.1 - Poison	С
PIC PESTICI DES	Ethylene dichloride (1,2- dichloroethane)	107-06-2	NO	300 ppm				1000 ppm		1000	432 min rat	250	-12,11134742	liquid	83		1184	3	3/ 6.1		3 - Flammable Liquid / 6.1 - Poison	С
PIC PESTICI DES	Trimethyltin chloride	1066-45-1	NO	120 mg/m 3			LD50 Rat oral 12,600 ug/kg			947			-12,10779557	solid	37	MP	3146	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Zinc arsenate	13464-44-3	NO						TA	936			-12,08442833				1712	6.1	6.1		6.1 - Poison	С
PIC PESTICI DES	Trilithium arsenate	13478-14-3	NO						TA	936			-12,08442833									
PIC PESTICI DES	Tris(pentane-2,4-dionato- O,O')silicon hexafluoroarsenate	67251-38-1	NO						ТА	913			-12,03466914									
PIC PESTICI DES	Slimes and Sludges, copper refining	67712-00-9	NO						TA	913			-12,03466914									

PIC PESTICI DES	Triethyl arsenite	3141 12 6	NO					ТА	909			-12,02588757									
PIC PESTICI DES	2,6-dimethyl-4-(1- naphthyl)pyrylium hexafluoroarsenate	84282-36-0	NO					ТА	906			-12,01927599									
PIC PESTICI DES	2,6-dimethyl-4-phenylpyrylium hexafluoroarsenate	84304-15-4	NO					TA	906			-12,01927599									
PIC PESTICI DES	4-cyclohexyl-2,6-dimethylpyrylium hexafluoroarsenate	84304-16-5	NO					TA	906			-12,01927599									
PIC PESTICI DES	Dimethenamid	87674-68-8	NO				4990 ug/L		1280	4h rat	320	-12,01728091	solid	127		3082	9	9		9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Dicloran	99-30-9	NO	480 mg/m 3		2400 mg/kg LD50 ratto	21600 mg/m3		2551,18	1h ratto	637,795	-12,01037839	solid	130		2811	6.1	6.2		6.1 - Poison	
PIC PESTICI DES	Roxarsone	121-19-7	NO					TA	899			-12,00376345				1577	6.1	6.1		6.1 - Poison	С
SEVESO III	1,3 propansultone	1120-71-4	NO		110 mg/m 3	20 mg/m3	100 mg/kg		865	rat	216,25	-11,9266564	solid	180°C		2811	6.1	6.1		Poison	С
PIC INDUST R.	4-nitrobiphenyl	92-93-3		156 ppm	440 mg/m 3	500 mg/m3	LD 50 2230 mg/kg		223	rats	55,75	-11,91273523	solid	644	340	ECHA/CA MEO	2811	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	3,3'-dichlorobenzidine dihydrochloride	612-83-9			QSAR !?		859 ppm		859	rats		-11,91273523	solid		232	ECHA/CA MEO	3077	9	9	PIC ed altri regolamenti	miscellan eous
PIC INDUST R.	<ul> <li>[1,1'-biphenyl]-4,4'-diamine, reaction products with 1-methyl-2,4- dinitrobenzene and sodium sulfide (Na2(Sx)) (3,3'- DIMETHOXYBENZIDINE)</li> </ul>	1326-43-8			380 mg/m 3	400mg/ m3	///		859	///		-11,91273523	solid		137	CAMEO	2811	6.1	6.1	ESR e REACH	poison

PIC INDUST R.	[1,1'-biphenyl]-4,4'-diamine, reaction products with 4-methyl-1,3- benzenediamine and sulfur	1326-63-2		REAZ COM P			///	859	///	-11,91273523			х						
PIC INDUST R.	Acetamide, N-(2-methylphenyl)-, reaction products with [1,1'- biphenyl]-4,4'-diamine and sulfur, leuco derivatives	1326-73-4		REAZ COM P			///	859	///	-11,91273523			х						
PIC INDUST R.	[1,1'-biphenyl]-4,4'-diamine, reaction products with 4-(6-methyl-2- benzothiazolyl)benzenamine and sulfur	1326-75-6		REAZ COM P			///	859	///	-11,91273523			х						
PIC INDUST R.	Disodium 8,8'-[[1,1'-biphenyl]-4,4'- diylbis(azo)]bis(7- hydroxynaphthalene-1-sulphonate)	2302-97-8		REAZ COM P			///	859	///	-11,91273523			х						
PIC INDUST R.	Benzidine acetate (3,3'- DICHLOROBENZIDINE 91-94-1)	36341-27-2		140 ppm		2000 mg/m3	///	859	///	-11,91273523	solid	788	420	ECHA/CA MEO	2811	6.1	6.1	Annex III REACH e vari	poison
PIC INDUST R.	3,3',5,5'-tetramethylbenzidine	54827-17-7	1	29 mg/m 3		60 mg/m3	///	859	///	-11,91273523	solid		168,5	ECHA/CA MEO	NO			Annex III REACH e vari	
PIC INDUST R.	3,3',5,5'-tetramethyl[1,1'-biphenyl]- 4,4'-diamine dihydrochloride	64285-73-0		COM E PRIM A ?	NDB		///	859	///	-11,91273523			х					Annex III REACH e vari	
PIC INDUST R.	3,3'-dichlorobenzidine dihydrogen bis(sulphate)	64969-34-2		QSAR !?			///	859	///	-11,91273523	solid		х	CAMEO	NO			Annex III REACH e vari	
PIC INDUST R.	3,3'-dichlorobenzidine sulphate	74332-73-3	,	QSAR !?			///	859	///	-11,91273523	solid		х	CAMEO				Annex III REACH e vari	

PIC INDUST R.	[1,1'-Bipheny]]-4,4'-diamine, reaction products with 4-(6-methyl-2- benzothiazolyl)benzenamine, 4-(6- methyl[2,6'-bibenzothiazol]-2'- yl)benzenamine and sodium sulfide	90268-15-8		REAZ COM P		///		859	///		-11,91273523			х						
PIC INDUST R.	2,7-Naphthalenedisulfonic acid, 4- amino-5-hydroxy-, coupled with 4- amino-5-hydroxy-2- naphthalenesulfonic acid, diazotized 4-aminobenzenesulfonic acid and diazotized [1,1'-biphenyl]-4,4'- diamine	90431-98-4		REAZ COM P		///		859	///		-11,91273523			x						
PIC INDUST R.	4,4'-[[1,1'-biphenyl]-4,4'- diyldiazo]bis[4,5-dihydro-5-oxo-1- (4-sulphophenyl)-1H-pyrazole-3- carboxylic] acid, sodium salt	94199-52-7		REAZ COM P		///		859	///		-11,91273523			x						
PIC INDUST R.	2,2'-[[1,1'-biphenyl]-4,4'- diylbis(azo)]bis[N-(4-chlorophenyl)- 3-oxobutyramide]	94249-03-3		REAZ COM P		///		859	///		-11,91273523			х						
PIC INDUST R.	3,3-Diaminobenzidine tetrahydrochloride	868272-85-9		QSAR !?		///		859	///		-11,91273523			300	ECHA				CLP	
PIC PESTICI DES	Sodium arsenate dibasic heptahydrate	10048-95-0	NO				TA	834			-11,85366419	solid	180		1685	6.1	6.1		6.1 - Poison	С
PIC INDUST R.	Tris-aziridinyl-phosphinoxide	545-55-1				LD50=37m g/kg		824	rat	206	-11,82953844	solid	90°C	90		2501	6.1	6.1	Annex III - Pre Registration process	poison

PIC PESTICI DES	Ferbam	14484-64-1	NO			LC50 Rat inhalati on 0.4 mg/L/4 hr	818 ppm	TA	818		-11,81492205	solid	185	MP	3077	9	9	9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Acephate	30560-19-1	NO			700 mg/KG (Rat LD50)	774 ppm	TA	774		-11,70434113	solid	92		3018	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Methamidophos (Soluble liquid formulations of the substance that exceed 600 g active ingredient / 1)	10265-92-6					770 ppm		770		-11,69397841								
PIC PESTICI DES	Scilliroside	507-60-8	NO			LD50 Rat oral 430 ug/kg	762 ppm	TA	762		-11,67309049	solid	169	MP	х	х	x	х	
PIC PESTICI DES	Tristrontium diarsenate	13464-68-1	NO					TA	759		-11,66520094								
PIC PESTICI DES	Tribarium diarsenate	13477-04-8	NO					TA	759		-11,66520094								
PIC PESTICI DES	Tricobalt diarsenate	24719-19-5	NO					TA	759		-11,66520094								
PIC INDUST R.	N,N'-diphenylbenzidine	531-91-9			QSAR !?		755 ppm		755	rats	-11,65463288	solid		247		NO		Non nel PIC Annex III REACH	
PIC PESTICI DES	Pentahydroxyarsorane	7786-36-9	NO						721		-11,56247566								
PIC PESTICI DES	Potassium dihydrogenarsenate	7784-41-0	NO	240 mg/m 3		LD50 Rat oral 14.0 mg/kg			698		-11,49763559	solid	287	MP	1677	6.1	6.1	6.1 - Poison	с
PIC PESTICI DES	Ammonium copper arsenate	32680-29-8	NO					TA	661		-11,38870506								

PIC PESTICI DES	Trilead diarsenate	3687-31-8	NO	460 mg/m 3			LD50,be low 50mgkg (rabbit,r at)		TA	632			-11,29897617				1617	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	1,3-dichloropropene	542-75-6	NO	120 ppm	NTR	NO		4,650 mg/m3		605,19	2h mouse	302,595	-11,2122823	liquid	104		2047	3	3		3 - Flammable liquid	Ss
PIC PESTICI DES	Iron arsenate	10102-49-5	NO							591			-11,16482942									с
PIC PESTICI DES	Sodium dimethylarsinate	124-65-2	NO	510 mg/m 3			LD, = 2600 mgkg (rat)		ТА	586			-11,14783696				1688	6.1	6.1		6.1 - Poison	С
PIC PESTICI DES	Ammonium dihydrogenarsenate	13462-93-6	NO						ТА	585			-11,14442108									
PIC PESTICI DES	Cartap	15263-53-3	NO				225 mg/kg ratto	583 ppm	TA	583			-11,13757175	solid	131	MP				SDS assen te		
PIC PESTICI DES	Sodium metaarsenate	15120-17-9	NO						TA	494			-10,80626842									
PIC PESTICI DES	Sodium dioxoarsenate	7784-46-5	NO	170 mg/m 3						494			-10,80626842				1686	6.1	6.1		6.1 - Poison	С
PIC PESTICI DES	Arsenic acid	7778-39-4	NO	190 mg/m 3			LD,, less than 50 mg/kg.		TA	482			-10,75708561	liquid a			1553	6.1	6.1		6.1 - Poison	с
PIC PESTICI DES	Trisilver arsenate	13510-44-6	NO						ТА	478			-10,74041885									

PIC PESTICI DES	Trisilver arsenite	7784 08 9	NO						ТА	478			-10,74041885			1683	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	1,3-dichloropropene (CIS) (1Z)-1,3- dichloroprop-1-ene	10061-01-5	NO			NO		670 - 744 ppm		670	4H rat	167,5	-10,72260563	liquid	104	2047	3	3		3 - Flammable liquid	Ss
PIC PESTICI DES	1,2-dibromoethane (EDB)	106-93-4	NO	46 ppm	170 ppm	NO		14 300 mg/m3		1861,13	30 min rats	465,2825	-10,68648688	liquid	131	1605	6.1	6.1	PAC T/Pr e Regis tratio n	6.1 - Poison Inhalation Hazard	С
SEVESO III	Solfuro di idrogeno	7783-06-4	SI	100 ppm	50 ppm	76 ppm	70 mg/m3	634 ppm		634	1 h mouse	317	-10,61214811	Gasso so	-60°C	1053	2.3	2.3 /2 .1		Poisonous Gas, Flammable Gas	
PIC PESTICI DES	Lead hydrogen arsenate	7784-40-9	NO	460 mg/m 3			LD50: 175 mg/kg (Oral, Rat)			448			-10,61078385			1617	6.1	6.1		6.1 - Poison	C/R
PIC PESTICI DES	Disodium 4-[(o-arsonophenyl)azo]- 3-hydroxynaphthalene-2,7- disulphonate	3688-92-4	NO						ТА	445			-10,59734595								С
PIC PESTICI DES	Disodium 3,6-bis[(o- arsonophenyl)azo]4,5- dihydroxynaphthalene-2,7- disulphonate	62337-00-2	NO							441			-10,57928713								
PIC PESTICI DES	Trisodium arsenide	12044-25-6	NO					413 ppm	TA	413			-10,44809257								
PIC PESTICI DES	Tripotassium arsenide	12044-21-2	NO							413			-10,44809257								
PIC PESTICI DES	Trilithium arsenide	12044-22-3	NO							413			-10,44809257								

SEVESO III	Solfuro di nichel	12035-72-2	NO	10 mg/m 3 (TLV 0,1 mg/m 3)						400			-10,38412648	solid			3077	9	9		Miscellaneo us	C/Ss
PIC INDUST R.	Tetramethyl lead	75-74-1	SI	40 mg/m 3	40 mg/m 3		5.2E+01 mg/m3	LC50: 8500 mg/cu m/30 min		777,38	30' mouse	388,69	-10,3267616	liquid	230	110		1649/34 83	6.1	6.1/3	Annex III, PBT vPvB	poison
PIC PESTICI DES	Diarsenic triselenide	1303-36-2	NO				LD50 rat > 5gm/kg (5000mg /kg)		ТА	374			-10,24970898		260	MP						
PIC PESTICI DES	Tricopper arsenide	12005-75-3	NO							362			-10,18448581									
SEVESO III	idrazina	302-01-2	SI	50 ppm	35 ppm	64 ppm	46 mg/m3	252 ppm		252	Mouse 4 h	126	-10,15320274	liquid	113°C		2029	8	8,3 ,6. 1		Corrosive/F lammable/ Poison	C / Ss
SEVESO III	triammide esametil fosforica	680-31-9	NO		17 ppm		1000 mg/m3	2400mg/kg		240	LD 50 mouse	120	-10,05562241	liquid	232°C		2810	6.1	6.1		Poison	C / M
PIC PESTICI DES	Diammonium hydrogenarsenate	7784-44-3	NO							331			-10,00543413				1546	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Acifluorfen	50594-66-6	NO					6900 mg/m3		466,48		116,62	-9,998480495	solid	100°C 47% H20		3077	9	9		9 - Miscellaneo us hazardous material	
SEVESO III	Triossido di arsenico	1327-53-3	NO	5 mg/m 3	9.1 mg/m 3	11 mg/m3	9,1 mg/m3	45 mg/kg	TA	4,5	Mouse	326	-9,974992144	solid	460°C		1561	6.1	6.1		POISON	Cancer.
PIC PESTICI DES	Methyl bromide	74-83-9	NO	740 ppm				302 ppm		302	inhalati on /8 hr	75,5	-9,822051416	gas	3		1955	2.3	2.3		2.3 - Poisonous gas	

PIC PESTICI DES	Chlorthal-dimethyl	1861-32-1	NO					5700 mg/m3		419,83	4 h ratto	104,9575	-9,787749936	solid	155	MP	х	x	x		
PIC PESTICI DES	Propachlor	1918-16-7	NO				LD50 Rat oral 710 mg/kg	LC50: 3580 mg/m3 (Inhalation, Rat)		413,49	4h rat	103,3725	-9,757316862	solid	110		2811	6.1	6.1	6.1 - Poison	Ss
SEVESO III	Biossido di nichel	12035-36-8	NO	10 mg/m 3	1300 mg/m 3					290			-9,740959228	solid			3288	6.1	6.1	Posion	S/Ss
SEVESO III	1,2-dimetilidrazina,	540-73-8	NO	15 ppm	11 ppm	65 ppm	27 mg/m3	400 ppm		400	rat 4 h	100	-9,690979295	liquid	81°C		2382	6.1	6.1 /3	Poison / Flammable Liquid	С
PIC PESTICI DES	Ethalfluralin	55283-68-6	NO				LD50 Rat oral > 5000 mg/kg	4.980 mg/m3		365,36	4h rat	91,34	-9,509816539	solid	256	MP	3077	9	9	9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Arsenic sulfide	1303-33-9	NO						TA	252			-9,460055557	solid	707		1557	6.1	6.1	6.1 - Poison	
SEVESO III	Bis(2-dimetilamminoetil)metil ammina	3030-47-5	NO					290 ppm		290	6 h rat	72,5	-9,453277155	liquid	201°C						
PIC PESTICI DES	Lithium hexafluoroarsenate	29935-35-1	NO						TA	245			-9,403713803								
PIC PESTICI DES	Iron arsenide	12044-16-5	NO							243			-9,387320268								С
PIC PESTICI DES	Cinidon-ethyl	142891-20-1	NO					5300 mg/m3		328,69	4h ratto	82,1725	-9,298280316	solid			3077	9	9	9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Isoxathion	18854-01-8	NO					4.2 g/cu		327,76	LC50 Rat m/4 hr	81,94	-9,292613468	solid	160		2810	6.1	6.1	6.1 - Poison	

PIC PESTICI DES	Diarsenic pentaoxide	1303-28-2	NO	150 mg/m 3			LD50 Mouse oral 55 mg/kg		TA	227			-9,251097417		315	MP	1599	6.1	6.1	6.1 - Poison	С
PIC PESTICI DES	Diarsenic trioxide	1327-53-3	NO	9.1 mg/m 3	11 mg/m 3		LD,, = 45 mgikg.		TA	227			-9,251097417		465						с
PIC PESTICI DES	Zirconium arsenide	60909-47-9	NO						ТА	226			-9,24226738								
PIC PESTICI DES	Nickel arsenide	27016-75-7	NO						TA	226			-9,24226738								C/Ss
PIC PESTICI DES	Hexachlorobenzene	118-74-1	NO	91 mg/m 3			LD50 Rat oral 3500 mg/kg	3600 mg/m3		309,1	ratto 4h	77,275	-9,175379899	solid	226		2729	6.1	6.1	6.1 - Poison	С
PIC PESTICI DES	Trimagnesium diarsenide	12044-49-4	NO					216 ppm	TA	216			-9,151754197								
PIC PESTICI DES	Copper diarsenite	16509-22-1	NO						ТА	216			-9,151754197								
SEVESO III	Bromo	7726-95-6	SI	3 ppm	8.5 ppm	19 ppm	56 mg/m3	750 ppm		750	9 minuti Mouse	375	-9,051076629	solid	59°C		1744	8	6.1	Poison/corr osive	
SEVESO III	Fluoro	7782-41-4	SI	25 ppm	13 ppm	36 ppm	20 mg/m3			197		98,5	-8,967604839	gas	-188.13		1045	2.3	2.3 /5 .1 /8	Poisonus Gas/Oxidiz er/Corrosiv e	
PIC INDUST R.	DBB (Di-µ-oxo-di-n-butylstannio- hydroxyborane),	75113-37-0						256 ppm		256	rat	64	-8,79840509							Annex VII REACH	
PIC PESTICI DES	Flufenoxuron	101463-69-8	NO				LD50 Rat oral >3 g/kg	5.000 mg/m3		250,12	4H rat inhalati on	62,53	-8,751931807	solid	169	MP	х	х	x	Х	

SEVESO III	Cloro	7782-50-5	SI	10 ppm	20 ppm	50 ppm	58 mg/m3	700 ppm		700	rat 30'	175	-8,73076933	gas	- 34°C		1017	2.3/5.1	8	Poison/oxi dizer/corro sive	
SEVESO III	Ossigeno	7782-44-7	NO					0.5 a 5 g/KG		161	rat	40,25	-8,564006112				1073	2.2	2.2 / 5.1	Non Flammable Gas / Oxidizer	
PIC PESTICI DES	Hydrogen hexafluoroarsenate	17068-85-8	NO						TA	160			-8,551545012								
PIC PESTICI DES	Pentafluoroarsorane	7784-36-3	NO						TA	160			-8,551545012	gas	-52,8						
PIC PESTICI DES	Trifluoroarsine	7784-35-2	NO						TA	159			-8,539005786	oleos o	-8,5	MP					
PIC PESTICI DES	Praseodymium arsenide	12044-28-9	NO					158 ppm	TA	158			-8,526387448								
PIC PESTICI DES	Erbium arsenide	12254-88-5	NO						ТА	158			-8,526387448								
PIC PESTICI DES	Lanthanum arsenide	12255-04-8	NO						ТА	158			-8,526387448								
PIC PESTICI DES	Niobium arsenide	12255-08-2	NO						TA	158			-8,526387448								
PIC PESTICI DES	Neodymium arsenide	12255-09-3	NO						TA	158			-8,526387448								
PIC PESTICI DES	Samarium arsenide	12255-39-9	NO						TA	158			-8,526387448								

PIC PESTICI DES	Yttrium arsenide	12255-48-0	NO			TA	158		-8,526387448								
PIC PESTICI DES	Tribarium diarsenide	12255-50-4	NO			TA	158		-8,526387448								
PIC PESTICI DES	Tricalcium diarsenide	12255-53-7	NO			TA	158		-8,526387448								
PIC PESTICI DES	Trisilver arsenide	12417-99-1	NO			TA	158		-8,526387448								
PIC PESTICI DES	Gallium arsenide	1303-00-0	NO			TA	158		-8,526387448	solid	29,78	MP	1577	6.1	6.1	6.1 - Poison	C/R
PIC PESTICI DES	Indium arsenide	1303-11-3	NO			TA	158		-8,526387448		942	MP					
PIC PESTICI DES	Cobalt arsenide	27016-73-5	NO			TA	158		-8,526387448								
PIC PESTICI DES	Europium arsenide	32775-46-5	NO			TA	158		-8,526387448								
PIC PESTICI DES	Arsenic	7440-38-2	NO		LD50: 763 mg/kg (Oral, Rat)	ТА	158		-8,526387448	solid	612		1558	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Dysprosium arsenide	12005-81-1	NO				158		-8,526387448								
PIC PESTICI DES	Gadolinium arsenide	12005-89-9	NO				158		-8,526387448								
PIC PESTICI DES	Holmium arsenide	12005-92-4	NO				158		-8,526387448								

PIC PESTICI DES	Lutetium arsenide	12005-94-6	NO							158			-8,526387448									
PIC PESTICI DES	Manganese arsenide	12005-95-7	NO							158			-8,526387448									
PIC PESTICI DES	Terbium arsenide	12006-08-5	NO							158			-8,526387448									
PIC PESTICI DES	Thallium arsenide	12006-09-6	NO							158			-8,526387448									
PIC PESTICI DES	Thulium arsenide	12006-10-9	NO							158			-8,526387448									
PIC PESTICI DES	Ytterbium arsenide	12006-12-1	NO							158			-8,526387448									
PIC INDUST R.	Asbestos fibres: Chrysotile	601-650-3			3.3 mg/m 3		250 f/CC	///		223		55,75	-8,522393744	solid	1112	600	ECHA/CA MEO	2212	9	9	Annex VII REACH	miscellan eous
PIC INDUST R.	3,3',5,5'-Tetramethylbenzidine dihydrochloride hydrate	207738-08-7			QSAR !?			CL50 Inalazione - ratto - 1.900 mg/m3		157,57	///		-8,52093699			x	ECHA				CLP	
PIC INDUST R.	Lead compounds	7439-92-1		100 mg/m 3	700 mg/m 3		1.0E+02 mg/m3	5000 ppm for 5 days		154	Coturni x japonica		-8,475102586	solid	3164	1740	ECHA/CA MEO				Annex VII	tossico
PIC PESTICI DES	Aluminium arsenide	22831-42-1	NO						TA	150			-8,42246797									
SEVESO III	Triossido di zolfo	7446-11-9	SI		48.87 ppm	82.46 ppm	48.87 ppm	1375 mg/m3		419,94	1h rat	104,985	-8,401979528	solid	44,8°C		1829	8	8/ 6.1		Corrosive/ Poison Inhalation Hazard	
PIC PESTICI DES	Thiocyclam	31895-22-4	NO					LC50 Rat Inh.> 4500mg/m 3		405,45	1 rat	101,3625	-8,331750963	solid	х		2811	6.1	6.1		6.1 - Poison	

PIC PESTICI DES	Heptachlor	76-44-8	NO	700 mg/m 3				200 mg/l		200	4 hr ratto	50	-8,304684934	solid	95		2761	6.1	6.1	6.1 - Poison	
SEVESO III	Trifloruro di boro	7637-07-2	SI	25 ppm	88 mg/m 3	110 mg/m3	110 mg/m3	387 ppm		387	1h rat	96,75	-8,238605226	Gasso so	-100°C		1008	2.3	2.3 /8	Poisonous Gas, Corrosive	
PIC PESTICI DES	Diazinon	333-41-5	NO					2330 mg/cu		187,18	4H Rat	46,795	-8,172191643	liquid	120		3018	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Iron diarsenide	12006-21-2	NO							129			-8,12082219								
PIC PESTICI DES	Nickel diarsenide	12068-61-0	NO						TA	112			-7,838195124								C/Ss
PIC PESTICI DES	Vamidothion	2275-23-2	NO				LD50 Rat oral 64 mg/kg	lethal concentrati on (50) 1730 mg/m3		147,21	4h rat	36,8025	-7,691770479	solid	43	MP	1648	3	3	3 - Flammable liquids, corrosive, n.o.s.	
PIC PESTICI DES	Zinc diarsenide	12044-55-2	NO						TA	103			-7,670655358								
SEVESO III	Nitrato di potassio cf 17	7757-79-1	SI		600 mg/m 3		500 mg/m3	3750 mg/kg		375	rat	93,75	-7,482460711	solid	400°C		1486	5.1	5.1	Oxidizer	
PIC PESTICI DES	Diphenyliodonium hexafluoroarsenate	62613-15-4	NO					1750mg/m 3 rat inha	TA	91,03			-7,423575627								С
PIC PESTICI DES	Fluoroacetamide	640-19-7	NO	19 mg/m 3			LD50 Rat oral 4 to 15 mg/kg	550 mg/m3		174,51	30 ' inhalati on mouse	87,255	-7,338867114	solid	108	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Potassium hexafluoroarsenate	17029-22-0	NO					280mg/m3 /4H rat		30,02	rat 4H		-7,284366576								С

PIC PESTICI DES	Quintozene	82-68-8	NO				LD50 Rat oral greater than 12000 mg/kg	lethal concentrati on (50 percent kill): 1400 mg/m3		115,91		28,9775	-7,213678257	solid	327		3077	9	9	9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Antimony arsenate	28980-47-4	NO						TA	81,9			-7,212195363								
SEVESO III	4,4'-metilen-bis-(2-cloroanilina) e/o suoi Sali	101-14-4	NO		21 ppm		500 mg/m3	1140 mg/kg		114	rat	28,5	-7,180447098	solid	110°C	melting	3077	9	9	Miscellaneo us	С
SEVESO III	dimetilnitrosammina	62-75-9	NO		10 mg/m 3		100 mg/m3	57 ppm		57	4 h mouse	28,5	-7,180447098	liquid	151°C		2810	6.1	6.1	Poison	С
PIC PESTICI DES	Chlorfenapyr	122453-73-0	NO				441 mg/kg (Oral, Rat)	1900 mg/m3 ratto		113,97		28,4925	-7,179920713	solid	101	MP	2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Arsenic trichloride	7784-34-1	SI	240 mg/m 3			LD50: 145 mg/kg		TA	79,4			-7,150194118	oleos o	0	MP	1560	6.1	6.1	6.1 - Poison Inhalation Hazard	с
PIC PESTICI DES	Nitrofen	1836-75-5	NO					LC50 Rat inhalation 205 mg/L /1 hr		205	1h rat	51,25	-6,967775798	solid	180		3077	9	9	9 - Miscellaneo us hazardous material	C/R
SEVESO III	solfato di metile	77-78-1	NO	7 ppm	1.6 ppm	4 ppm	8.3 mg/m3	98 ppm		98	mouse 60'	49	-6,877985158	liquid	188°C		1595	6.1	6.1 /8	Poison Inhalation Hazard / Corrosive	C / Ss
PIC PESTICI DES	Cyanazine	21725-46-2	NO				149 mg/kg LD50	906 mg/ m3		92,03	4H Rat	23,0075	-6,752279423	solid	168	MP	2811	6.1	6.1	6.1 - Poison	
SEVESO III	Nitrato d'ammonio cf 13	6484-52-2	SI		440 mg/m 3		500 mg/m3	88.8 mg/L		88,8	rat 4 h	22,2	-6,680823501	solid	210°C		2067	5.1	5.1	Oxidizer	
SEVESO III	solfato di dietile	64-67-5	NO		11 ppm		150 mg/m3	0.88 g/kg		88	rat LD 50	22	-6,66272383	liquid	209°C		1594	6.1	6.1	Poison	C / M

PIC PESTICI DES	Arsenic tribromide	7784-33-0	NO						TA	56,5			-6,469678658	solid	31	MP						
PIC INDUST R.	Asbestos fibres	77536-66-4			3.3 mg/m 3		250 f/CC	///		223		55,75	-6,442952202	solid	1112	600	ECHA/CA MEO	2212	9	9	Annex VII REACH	miscellan eous
SEVESO III	1,2-dibromo-3cloropropano	96-12-8	NO		4.3 ppm		150 mg/m3	1480 mg/m3		153,12	rat 1 h	38,28	-6,384199695	liquid	6°C	melting	2872	6.1	6.1		Poison	C / M / R
PIC PESTICI DES	Oxydemeton-methyl	301-12-2	NO					LC50 Rat inhalation 1500 mg/cu m/ 1Hr		148,92	1 h rat	37,23	-6,328574338	liquid	106		2784	3	3,6 .1		3 - Flammable liquid / 6.1 - Poison	
PIC PESTICI DES	Zineb	12122-67-7	NO				LD50: 1850 mg/kg (Oral, Rat)	Lowest published lethal concentrati on: 800 mg/m3/4 H		70,94	4h rat	17,735	-6,2317191	solid	157	MP	2771	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	Fenthion	55-38-9	NO	35 mg/m 3			LD50 Rat male oral 190- 315 mg/kg	800 mg/m3		70,28	4H rat	17,57	-6,213024728	liquid	88		3018	6.1	6.1		6.1 - Poison	
PIC INDUST R.	Tetraethyl lead	78-00-2		40 mg/m 3	40 mg/m 3		6.2E+01 mg/m3	LC 50: 850 mg/m <sup>3</sup>		64,25	rats	16,0625	-6,033613649	liquid	392	200		1649	6.1	6.1	SVHC, PBT vPvB	poison
PIC PESTICI DES	Triammonium arsenate	24719-13-9	NO						TA	43,8			-5,960465016									
SEVESO III	Fosfina (triioduro di fosforo)	7803-51-2	SI	50 ppm	3.6 ppm	7.2 ppm	5 mg/m3	59.2 ppm		59,2	60 min mouse	29,6	-5,869893285	gas	-87°c		2199	2.3	2.3 /2 .1		Poisonous Gas / Flammable Gas	

PIC PESTICI DES	Ethion	563-12-2	NO	38 mg/m 3			LD50 Rat oral 47 mg/kg	864 mg/m3	54,95	4h ratto	13,7375	-5,720897563	liquid	165		3018	6.1	6.1	6.1 - Poison	
PIC INDUST R.	Octabromodiphenyl ether	32536-52-0						60gm/m3	1,83	1h rats	27,45	-5,719076898				ECHA/TO XNET			Annex III	
PIC PESTICI DES	Trichlorfon	52-68-6	NO	57 mg/m 3				LC50 Rat inh. 533 mg/cu m/4hr	50,62	4h rat	12,655	-5,556743711	solid	100		2783	6.1	6.1	6.1 - Poison	Ss
PIC PESTICI DES	Cyanamide	420-04-2	NO	400 mg/m 3			280 mg/kg ratto LD50	86mg/m3	50,02	4H Rat	12,505	-5,532896052	solid	260		2811	6.1	6.1	6.1 - Poison	Ss
PIC PESTICI DES	Carbosulfan	55285-14-8	NO					1530 mg/m3	98,3	1h ratto	24,575	-5,497803894	liquid	25	MP	2810	6.1	6.1	6.1 - Poison	Ss
SEVESO III	Etilenimina	151-56-4	SI	100 ppm	9.9 ppm	51 ppm	17 mg/m3	56 ppm	56	2 h rat Inhal.	14	-5,065606402	liquid	56°C		1185	6.1	6.1 / 3	Poisono Flammable liquid	С / М
PIC PESTICI DES	Thiodicarb	59669-26-0	NO				LD50 Rat oral 66 mg/kg	LC50 Rat inh. 520 mg/cu m/4 hr	35,87	4 h rat	8,9675	-4,867852784	solid	173	MP	2757	6.1	6.1	6.1 - Poison	Ss
PIC PESTICI DES	Dichlobenil	1194-65-6	NO					250 mg/cu	35,54	4h rat	8,885	-4,849367847	solid	270		3082	9	9	9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Fenitrothion	122-14-5	NO				LD50 Rat oral 500 mg/kg	378 mg/m3	33,34	4H ratto	8,335	-4,721565956	liquid	118		3017	6.1	6.1	6.1 - Poison / 3 - Flammable liquid	

SEVESO III	benzidina	92-87-5	NO	Potent ial huma n carcin ogen	61 mg/m 3		130 mg/m3	309 mg/kg	30,9	rat	7,725	-4,569562569	solid	402°C		1885	6.1	6.1	Poison	с
PIC PESTICI DES	Aldicarb	116-06-3	NO	1.8 mg/m 3				200 mg/m3	25,7	5 h di inalazio ne Ratto	6,425	-4,424175736	solid	99	Fonde e decompone	2757	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Anthraquinone	84-65-1	NO	790 mg/m 3				244 mg/m3	28,65	4h ratto	7,1625	-4,418357087	solid	377					Not dangerous	C /Ss
PIC PESTICI DES	Bitertanol	55179-31-2	NO					717 mg/m3	51,95	1h ratto	12,9875	-4,222319275	solid	136	MP	2811	6.1	6.1	6.1 - Poison	Ss
SEVESO III	2,6 Diisocianato di toluene	91-08-7	NO	2.5 ppm	0.51 ppm	0.65 ppm	3.6 mg/m3	91 mg/m3	12,78	4 h mouse	6,39	-4,19010746	liquid	129 °C		2078	6.1	6.1	Poison	SS/Sr
PIC PESTICI DES	Warfarin	81-81-2	NO	350 mg/m 3				lethal concentrati on (50 percent kill): 320 mg/m3 rat	25,38	4h rat	6,345	-4,175973126	solid	161	МР	3027	6.1	6.1	6.1 - Poison	R
PIC INDUST R.	Biphenyl-3,3',4,4'-tetrayltetraamine	91-95-2		87 ppm				619 mg/kg LD 50	61,9	rats	15,475	-3,879649019			176	ECHA			CLP REACH E PIC	
PIC PESTICI DES	Thiobencarb	28249-77-6	NO					LC50 Rat inh. > 42.8 mg/L (1h)	42,8	1 h rat	10,7	-3,834832045	liquid	126		3082	9	9	9 - Miscellaneo us hazardous material	
PIC INDUST R.	Dinoseb acetate	2813-95-8			?			60.1 mg/kg	60,1	rats	15,025	-3,820628343							Annex III	
SEVESO III	2,4 Diisocianato di toluene	584-84-9	NO	2.5 ppm	0.51 ppm	0.65 ppm	3.6 mg/m3	10 ppm	10	4 h mouse	5	-3,699514748	solid /liqui d	252°C		2078	6.1	6.1	Poison	SS/Sr

PIC PESTICI DES	Pentachlorophenol	87-86-5	NO	150 mg/m 3			LD50: 27 mg/kg (Oral, Rat)	CL50 Inalazione - Ratto - 355 mg/m3	32,59	1h rat	8,1475	-3,289766826	solid	309	3155	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Permethrin	52645-53-1	NO				LD50 Rat oral 600 mg/kg	CL50 Inalazione - Ratto - 485 mg/m3	30,31	1h rat	7,5775	-3,144711222	solid	220	3077	9	9		9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Furathiocarb	65907-30-4	NO					214 mg/m3	13,68	Ratto - 4 h	3,42	-2,939920025	solid	160	2811	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	2-aminobutane	13952-84-6	NO	31 ppm				11.2 mg/L	11,2	60 min Mouse	5,6	-2,539877758	liquid	64	2735	8	8	Anne x III/ Pre Regis tratio n	8 - Corrosive	
PIC PESTICI DES	Dichlorvos	62-73-7	NO	200 mg/m 3				198 mg/m3	21,91	1h ratto	5,4775	-2,495642147	liquid	140	2783	6.1	6.1		6.1 - Poison	Ss
SEVESO III	Monossido di nichel	1313-99-1	NO	10 mg/m 3	1300 mg/m 3		13 mg/m3	50 mg/kg	5	mouse	2,5	-2,313220387	solid	600°C	3288	6.1	6.1		Poison	C/R/Ss/ Sr
SEVESO III	Arsina (triioduro di arsenico)	7784-42-1	SI	3 ppm	0.5 ppm	0.91 ppm	1.6 mg/m3	20 ppm	20	1h rat	5	-2,313220387	gas	-62°c	2188	2.3	2.1		Poisonous Gas / Flammable Gas	
PIC PESTICI DES	Butralin	33629-47-9	NO					9.35 mg/l	9,35	4h ratto	2,3375	-2,178802888	solid	310	1993	3	3		3. Combustibl e / Flammable Liquid	
PIC PESTICI DES	Chlormephos	24934-91-6	NO	42 mg/m 3				88 mg/m3	9,17	4h ratto	2,2925	-2,139924774	liquid /soli d	81	3018	6.1	6.1		6.1 - Poison	

PIC PESTICI DES	Phosphamidon	13171-21-6	NO	21 mg/m 3				LC50 Rat inhalation 102 mg/cu m/4 hr	8,32	4h rat	2,08	-1,945374711	liquid	120	degrada	3018	6.1	6.1	6.1 - Poison	
SEVESO III	ossido di bis(clorometile)	542-88-1	SI	Potent ial huma n carcin ogen	0.18 ppm	0.23 ppm	0.85 mg/m3	5-7 ppm	6	6h rat	1,5	-1,697034248	liquid	104°C		2249	6.1	6.1 /3	Poison / Flammable Liquid	С
SEVESO III	ossido di clorometile	107-30-2	SI	Potent ial huma n carcin ogen	2 ppm	2.6 ppm	6.6 mg/m3	5-7 ppm	6	6h rat	1,5	-1,697034248	liquid	59°C		1239	6.1	6.1 /3	Poison / Flammable Liquid	С
PIC PESTICI DES	Parathion	56-38-2	NO	2 mg/m 3	3.6 mg/m 3			LC50 Rat 84.0 mg/cu m/4 hr (Inhalation )	7,05	4h rat	1,7625	-1,614105435	gas	375		1967	2.3	2.3	2.3 - Poisonous gas	
PIC PESTICI DES	Chlorate Sodium	7775-09-9	SI	240 mg/m 3				5.59 mg/1	5,59	4.5 h ratto	1,3975	-1,267791811	solid	248	MP	1495	5.1	5.1	5.1 - Oxidizer	
PIC PESTICI DES	Fenvalerate	51630-58-1	NO					101 g/cu	5,88	m/4 hr rat inhalati on	1,47	-1,251163725	solid	39.5	MP	2811	6.1	6.1	6.1 - Poison	Ss
PIC PESTICI DES	Cyclanilide	113136-77-9	NO					5.15 mg/l	5,15	4 h ratto	1,2875	-0,98604363	solid	190	MP	2811	6.1	6.1	6.1 - Poison	
SEVESO III	Isocianato di metile	624-83-9	SI	3 ppm	0.2 ppm	1.2 ppm	0.47 mg/m3	5 ppm	5	rat 4 h	1,25	-0,926926026	liquid	39°C		2480	6.1	6.1 /3	Posion Inhalation Hazard / Flammable liquid	Ss/Sr

PIC PESTICI DES	Dicofol	115-32-2	NO				5 mg/L	5	4 h ratto	1,25	-0,926926026	solid	139		3082	9	9		9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Carbofuran	1563-66-2	NO	3.7 mg/m 3			85mg/m3	9,93	1H ratto	2,4825	-0,912876796	solid	150	MP	2757	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Endosulfan	115-29-7	NO	180 mg/m 3		LD50 Rat oral 18 mg/kg	80 mg/m3	4,81	4h ratto	1,2025	-0,849444369	solid	70	MP	2761	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Chinomethionat	2439-01-2	NO				4.7 mg/L	4,7	4 h ratto	1,175	-0,803175219	solid	171	MP	3077	9	9		9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Cyhalothrine	68085-85-8	NO				83 mg/cu	4,51	4h ratto	1,1275	-0,720644508	solid	25	MP	2902	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	Acetochlor	34256-82-1	NO			764 mg/Kg (Rat LD50)	3.99 mg/L	3,99	4H Rat	0,9975	-0,475632663	liquid	172		3082	9	9		9 - Miscellaneo us hazardous material	Ss
PIC PESTICI DES	Fentin hydroxide	76-87-9	NO				60.3 mg/cu	3,99	4 hr Rat inhalati on	0,9975	-0,475632663	solid	121	MP	2786	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Hexazinone	51235-04-2	NO			LD50 Rat oral 860 mg/kg	7.480 mg/m3	7,48	ratto - 1 h	1,87	-0,346221424	solid	116	MP	3077	9	9		9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Methidathion	950-37-8	NO	160 mg/m 3			3.6 mg/L	3,6	LC50 Rat inhalati on (4 hr)	0,9	-0,269917892	solid	38	MP	2811	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Methyl-parathion	298-00-0	NO	3.5 mg/m 3	6.4 mg/m 3		34 mg/cu	3,16	Inhalati on m/4 hr	0,79	-0,009194256	solid	119		3017	6.1	6.1 (3)		6.1 - Poison \ 3 - Flammable liquid	
PIC INDUST R.	Nonylphenol ethoxylates (Ć2H4O)nC15H24O	9016-45-9			5400 mg/m 3	5.0E+02 mg/m3	28 mg/m3	2,22	8h rats	0,555	0,003788227	liquid or solid			ECHA/CA MEO/TN	3082	9	9	Annex XVII of REACH.	miscellan eous
PIC PESTICI DES	Dinobuton	973-21-7	NO				80 mg/m3	5,99	1h rat inhalati on	1,4975	0,098061336	solid	56	MP	2811	6.1	6.1		6.1 - Poison	

SEVESO III	Pentossido di arsenico	1303-28-2	NO	5 mg/m 3	150 mg/m 3	0.01 mg/m3 TLV	7.7 mg/m3	8 mg/kg	8	rat	2	0,212508257	solid	315°C		1559	6.1	6.1	POISON	Cancer.
PIC INDUST R.	Heptadecafluorooctane-1-sulphonic acid	1763-23-1						LC50 of 5.2 mg/L	5,2	1h rats	1,3	0,380926909	liquid			ECHA/TO XNET				
PIC PESTICI DES	Simazine	122-34-9	NO				LD50 7 500 mg/kg bw	LC50 (4 h) 2.21 mg/L air (rat)	2,21	4h rat	0,5525	0,705964768	solid			3077	9	9	9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Ametryn	834-12-8	NO					2.2 mg/L	2,2	4h ratto albino	0,55	0,715035078	solid	346		2763	6.1	6.1	6.1 - Poison	
CWA	TABUN	77-81-6						LC50 15mg/m3 30 min Mouse	2,26		1,13	1,354367353	liquid	246	162,13 MW					
CWA	SARIN	107-44-8						LC50 9 mg/m3 60 min. mouse	1,57		0,785	1,38979856	liquid	158						
PIC PESTICI DES	Propanil	709-98-8	NO					LC50 Rat inhalation >1.25 mg/L air/4 hr	1,25	4h rat	0,3125	1,845662696	solid	351		3077	9	9	9 - Miscellaneo us hazardous material	
PIC PESTICI DES	Dieldrin	60-57-1	NO	450 mg/m 3			LD50 Rat oral 38.3 mg/kg	13 mg/m3	0,83	4h rat	0,2075	2,664608955	solid	175.5	MP	2761	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Omethoate	1113-02-6						LC50 Rat male inhalation >1.5 mg/L/1 hr	1,5	1h rat	0,375	2,867313944	liquid	135		2810	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Nicotine	54-11-5	NO	35 mg/m 3			LD50 Rat oral 188 mg/kg	LC50 (20 min) 2.3 mg/L air (rat) !?	2,3	20 min rat	0,575	3,111038203	liquid	246		1654	6.1	6.1	6.1 - Poison	

PIC INDUST R.	CADMIUM	7440-43-9		9 mg/m 3	4,7 mg/m 3	8.5 mg/m3	4,7 mg/m3	8.63 mg/m³	1,74	30' Rats	0,435	3,263621114	solid	1409	765	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH e SVHC	poison
PIC PESTICI DES	Lindane	58-89-9	NO	1000 mg/m 3				1.56 mg/L	1,56	30' inhalati on	0,39	3,482019698	solid	323		2761	6.1	6.1		6.1 - Poison	
PIC INDUST R.	CADMIUM OXIDE	1306-19-0		9 mg/m 3	5,4 mg/m 3		10 mg/m3	///	1,52	///	0,38	3,533970671	solid	2838	1558,8889	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH e SVHC	poison
PIC INDUST R.	CADMIUM CHLORIDE	10108-64-2		9 mg/m 3	7.6 mg/m 3		15mg/ m3	///	1,07	///	0,2675	4,236074044	solid	1760	960	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH e SVHC	poison
PIC INDUST R.	CADMIUM SULFATE	10124-36-4		9 mg/m 3	8,7 mg/m 3		17 mg/m3	///	0,94	///	0,235	4,495142148	solid		1000	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH e SVHC	poison
PIC PESTICI DES	Triazophos	24017-47-8	NO	12 mg/m 3			LD50 Rat oral 66 mg/kg	LC50 Rat inh. 0.61 mg/L	0,61	1h rat	0,1525	4,666836804	liquid	0	MP	3018	6.1	6.1		6.1 - Poison	
PIC INDUST R.	CADMIUM ACETATE (5743-04-4 ECHA)	543-90-8		9 mg/m 3	9,6 mg/m 3			///	0,85	///	0,2125	4,6964292	solid		х	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	CADMIUM NITRATE	10325-94-7		9 mg/m 3	9,9 mg/m 3		19 mg/m3	///	0,83	///	0,2075	4,744050497	solid		132	ECHA/CA MEO	3087	5.1	6.1	Annex VII REACH	oxidizer/ poison
PIC PESTICI DES	Tolylfluanid	731-27-1	NO					LC50 Rat inh. 0.26 mg/L	0,26	4h rat	0,065	4,986097095	solid	93	MP	2811	6.1	6.1		6.1 - Poison	Ss
PIC PESTICI DES	Toxaphene	8001-35-2	NO	200 mg/m 3				LC50 Rat inh. 0.26 mg/L (4 hr nose only)	0,26	4h rat	0,065	4,986097095	solid	65	MP	2761	6.1	6.1		6.1 - Poison	

PIC INDUST R.	CADMIUM BROMIDE	7789-42-6		9 mg/m 3	11 mg/m 3		22 mg/m3	111	0,72	///	0,18	5,028399475	solid		х	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH e PIC e CLP	poison
PIC INDUST R.	CADMIUM FLUOROBORATE (cadmium tetrafluroborate)	14486-19-2		9 mg/m 3	QSAR !?			///	0,68	///	0,17	5,142716302	liquid		х	CAMEO	NO			Annex VII REACH	No
PIC PESTICI DES	Azocyclotin	41083-11-8	NO					0.2 mg /1	0,2	4h ratto	0,05	5,510825624	solid	210	MP	3146	6.1	6.1		6.1 - Poison	
PIC INDUST R.	CADMIUM STEARATE	2223-93-0		9 mg/m 3	28 mg/m 3		55 mg/m3	///	0,29	///	0,0725	6,847140053	solid		x	ECHA/CA MEO	2570	6.1	6.1	Annex VII REACH	poison
PIC PESTICI DES	Cyfluthrin	68359-37-5	NO					0.1 mg/L	0,1	4h ratto	0,025	6,897119985	liquid viscos o	60	MP	3352	6.1	6.1		6.1 - Poison	
CWA	SOMAN	96-64-0						LC50 1mg/m3 30 min Mouse	0,13		0,065	7,065538637	liquid	198	182,175 MW						
PIC PESTICI DES	Monocrotophos	6923-22-4	NO	3.5 mg/m 3				0.08 mg/L	0,08	4 hr rat	0,02	7,343407088	solid	125		3018	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Methomyl	16752-77-5	NO	23 mg/m 3				0,06 mg/1	0,06	inhalati on 4 hr rat	0,015	7,918771232	solid	78	MP	2811	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Chlorfenvinphos	470-90-6	NO	500 mg/m 3				0.05 mg/L	0,05	4H ratto	0,0125	8,283414346	liquid	170		3018	6.1	6.1		6.1 - Poison	
PIC PESTICI DES	Fentin acetate	900-95-8	NO	28 mg/m 3				0.044 mg/l	0,044	air/4 hr ratto	0,011	8,539081089	solid	123	MP	3146	6.1	6.1		6.1 - Poison	
SEVESO III	Dicloruro di carbonile (fosgene)	75-44-5	SI	2 ppm	0.75 ppm	3.6 ppm	3 mg/m3	0.047 mg/L	0,047	mouse 30 min espo	0,0235	9,100312334	gas	7.5°C		1076	2.3	2.3 /8		Poisonous Gas	
PIC PESTICI DES	Cadusafos	95465-99-9	NO					0.026 mg/1	0,026	4h ratto	0,0065	9,591267281	liquid	112		3381	6.1	6.1		6.1 - Poison	

PIC INDUST R.	Polychlorinated terphenyls (PCT) (Terphenyl, chlorinated)	61788-33-8						LD 50: 2100mg/kg		mouse	0	#NUM!	solid							Annex III	
PIC INDUST R.	Creosote oil, acenaphthene fraction	90640-84-9						2000 mg/kg LD 50		rat	0	#NUM!	liquid							Annex VII REACH	
PIC INDUST R.	Creosote oil	61789-28-4						LD50 Mouse oral 433 mg/kg		Mouse		#NUM!	liquid	х	х	TN				Annex VII REACH	poison
PIC INDUST R.	Tetraethylammonium heptadecafluorooctanesulphonate	56773-42-3						LD 50 190 mg/kg	0	rat	0	#NUM!	solid	182°C	182	ECHA/TO XNET					
SEVESO III	Formaldeide	50-00-0	SI	20 ppm	56 ppm	100 ppm	69 mg/m3	42 mg/kg	4,2	mouse		#NUM!	gas	- 101 °C		3077	9	9		Miscellaneo us Hazardous material	C/Ss
SEVESO III	GPL	68476-85-7	NO	2000 ppm	400000 ppm		35000 mg/m3				0	#NUM!	liquid	-0.5°C		1075	2.1	2.1		Flammable Gas	C/M/R
PIC INDUST R.	Benzidine sulphate	21136-70-9			QSAR !?								solid	х	х	ECHA	1885	6.1	6.1	Annex III REACH e vari	poison
PIC INDUST R.	Tar acids, coal, crude	65996-85-2			250 ppm		1000 mg/m3						liquid	350	176,66667	ECHA/CA MEO	2076	6.1	6.1	Annex VII REACH	poison
PIC INDUST R.	Creosote oil, high-boiling distillate	70321-79-8											liquid	х	х					Annex VII REACH	poison
PIC INDUST R.	Distillates (coal tar), naphthalene oils	84650-04-4											liquid	х	х					Annex VII REACH	
PIC INDUST R.	Extract residues (coal), low temp. coal tar alk.	122384-78-5											liquid							Annex VII REACH	
PIC INDUST R.	Creosote	8001-58-9											liquid							Annex VII REACH	
PIC INDUST R.	Anthracene oil	90640-80-5											liquid							Annex VII REACH	

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PIC INDUST R.	2-sec-butyl-4,6-dinitrophenol, compound with 1-aminopropan-2-ol (1:1)	71735-19-8			?															Annex III	
PIC INDUST R.	2-sec-butyl-4,6-dinitrophenol, compound with 2,2'-iminodiethanol (1:1)	53404-43-6			?																
PIC INDUST R.	2-sec-butyl-4,6-dinitrophenol, compound with 2,2',2''- nitrilotriethanol (1:1)	6420-47-9			?																
PIC INDUST R.	Monomethyl-Dichloro-Diphenyl methane; Trade name: Ugilec 121 or Ugilec 21	85705-05-1																			
PIC INDUST R.	Monomethyl-dibromo-diphenyl methane; Trade name: DBBT	99688-47-8														ECHA/TO XNET				Pre registrazion e	
PIC INDUST R.	1-Decanaminium, N-decyl-N,N- dimethyl-, salt with 1,1,2,2,3,3,4,4,5,5,6,6,7,8,8,8- heptadecafluoro-1-octanesulfonic acid (1:1	251099-16-8																			
PIC INDUST R.	Stannane, triphenyl-, mono(C9-11 neofatty acyloxy) derivs.	90552-69-5																			
SEVESO III	Triossido di nichel	1314-06-3																			C/Ss
SEVESO III	Idrogeno	1333-74-0	SI		400.00 0 ppm	TLV 25 ppm	30.000 mg/m3	0.5 a 5 g/KG			rat	0	gas	- 259 °C		1049	2.1	2.1		Flammable Gas	
SEVESO III	Naftalene	91-20-3	NO	250 ppm	500 ppm		1300 mg/m3	490 mg/kg		49	rat	х	solid	218°C		1334	4.1	4.1		Flammable solid.	
SEVESO III	oli combustibili	68476-30-2	NO		20000 mg/m 3		500 mg/m3	3.6 mg/l			rat 4 h		liquid	202°C		1202	3	3		Flammable liquid.	C/M

SEVESO III	Acrilato di terbutile (Cifr. 21)	1663-39-4	NO			6.75 mg/L		Mouse		liquid	119.2°C				Ss
PIC PESTICI DES	Diarsenic tritelluride	12044-54-1	NO												
PIC PESTICI DES	Dichromium arsenide	12254-85-2	NO												
PIC PESTICI DES	Triantimony arsenide	12255-36-6	NO												
PIC PESTICI DES	Germanium arsenide	12271-72-6	NO												
PIC PESTICI DES	Arsenic sulfide	12612-21-4	NO				TA								
PIC PESTICI DES	Trisodium arsenate	13464-38-5	NO				TA								С
PIC PESTICI DES	6,6'-dihydroxy-3,3'-diarsene-1,2- diyldianilinium dichloride	139-93-5	NO								190	MP			
PIC PESTICI DES	Oxophenarsine	306-12-7	NO												
PIC PESTICI DES	Neoarsphenamine	457-60-3	NO												
PIC PESTICI DES	Oxophenarsine hydrochloride	538-03-4	NO												
PIC PESTICI DES	Tris[(8α,9R)-6'-methoxycinchonan-9- ol] bis(arsenate)	549-59-7	NO												
PIC PESTICI DES	Sulfarsphenamine	618-82-6	NO												
PIC PESTICI DES	Trimanganese arsenide	61219-26-9	NO												

PIC PESTICI DES	Antimony arsenic oxide	64475-90-7	NO											
PIC PESTICI DES	Arsenic bromide	64973-06-4	NO							1555	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Cobalt arsenide	65453-05-6	NO											
PIC PESTICI DES	Silicic acid (H4SiO4), zinc salt (1:2), arsenic and manganese-doped	68611-46-1	NO											
PIC PESTICI DES	Bis(pentane-2,4-dionato- O,O')boron(1+) hexafluoroarsenate(1-)	68892-01-3	NO											
PIC PESTICI DES	Antimony oxide (Sb2O3), mixed with arsenic oxide (As2O3)	68951-38-2	NO											
PIC PESTICI DES	Lead alloy, base, dross	69011-59-2	NO											
PIC PESTICI DES	Lead, antimonial, dross	69029-51-2	NO											C/R
PIC PESTICI DES	Flue dust, lead-refining	69029-67-0	NO											C/R/M/ Ss
PIC PESTICI DES	Disilver arsenide	70333-07-2	NO											
PIC PESTICI DES	Thallium triarsenide	84057-85-2	NO											
PIC PESTICI DES	Tris[(8α)-6'-methoxycinchonan-9(R)- ol] arsenite	94138-87-1	NO											
PIC PESTICI DES	Gallium zinc triarsenide	98106-56-0	NO											

PIC PESTICI DES	Vanadium(4+) diarsenate (1:1)	99035-51-5	NO												
PIC PESTICI DES	Strychnidin-10-one, arsenite (1:1)	100258-44-4	NO												
PIC PESTICI DES	Slimes and Sludges, copper electrolytic refining, decopperized, arsenic-rich	100995-81-1	NO												
PIC PESTICI DES	Arsenic acid (H3AsO4), magnesium salt, manganese-doped	102110-21-4	NO												
PIC PESTICI DES	Slimes and Sludges, copper-lead ore roasting off gas scrubbing, arsenic- contg.	102110-62-3	NO												
PIC PESTICI DES	Sodium hexafluoroarsenate(V)	12005-86-6	NO												
PIC PESTICI DES	Sodium cacodylate trihydrate	6131-99-3	NO												С
PIC PESTICI DES	Arsenic acid, copper(2+) salt	29871-13-4	NO												
PIC PESTICI DES	Tristrontium diarsenide	39297-24-0	NO												
PIC PESTICI DES	Arsenic acid, sodium salt	7631-89-2	NO	270 mg/m 3		LD50: 41 mg/kg (Oral, Rat)	ТА			180	1685	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Disodium hydrogenarsenate	7778-43-0	NO				TA								С

PIC PESTICI DES	Mercury hydrogenarsenate	7784-37-4	NO				ТА						1623	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Manganese hydrogenarsenate	7784-38-5	NO				TA										
PIC PESTICI DES	Arsenic triiodide	7784-45-4	NO					0		solid	146	MP	1557	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Flue dust, arsenic-contg.	8028-73-7	NO										1562	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Lead arsenite	10031-13-7	NO	280 mg/m 3									1618	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Arsenic acid, copper salt	10103-61-4	NO								1100	MP					
PIC PESTICI DES	Arsenic acid, calcium salt	10103-62-5	NO			LD,, =20mgi kg.							1573				
PIC PESTICI DES	Strychnine arsenate	10476-82-1	NO														
PIC PESTICI DES	Diiron arsenide	12005-88-8	NO														
PIC PESTICI DES	Trizinc diarsenide	12006-40-5	NO							solid							С
PIC PESTICI DES	Digallium arsenide phosphide	12044-20-1	NO														

PIC PESTICI DES	Captafol	2425-06-1	NO		2.5 g/kg LD50				solid	162	MP	3077	9	9	9 - Miscellaneo us hazardous material	C / Ss
PIC PESTICI DES	Didecyldimethylammonium chloride	7173-51-5	NO		LD50 Rat oral 84 mg/kg				solid	180		2923	8 (6.1)	8 (6. 1)	8 - CORROSIV E SOLID, TOXIC, N.O.S.	
PIC PESTICI DES	Pyrazophos	13457-18-6	NO		DL50 Orale - ratto - 218 mg/kg				solid			2811	6.1	6.1	6.1 - Poison	
PIC PESTICI DES	Tributyltin Compounds, with the exception of those specified elsewhere in this annex (FLUORIDE)	1983-10-4	NO			1550 ppm	1550		liquid			2788	6.1	6.1	6.1 - Poison	R

16 Selection Of Chemichals

REGULATION	SUBSTANCE	CAS	IDLH mg/m <sup>3</sup>	TOX PAC 3	TOX AEGL 3 a 10'	MEG a 1h A	LC50	PPM	TIME/A NIMAL	LC50 Hu. Ppm	PARAMETER "a"	STATE
CWA	TABUN	77-81-6					LC50 15mg/m <sup>3</sup> 30 min Mouse	2,26		1,13	1,354367353	liquid
CWA	SARIN	107-44-8					LC50 9 mg/m3 60 min. mouse	1,57		0,785	1,38979856	liquid
PIC PESTICIDES	Propanil	709-98-8					LC50 Rat inhalation >1.25 mg/L air/4 hr	1,25	4h rat	0,3125	1,845662696	solid
PIC PESTICIDES	Dieldrin	60-57-1	450			LD50 Rat oral 38.3 mg/kg	13 mg/m <sup>3</sup>	0,83	4h rat	0,2075	2,664608955	solid
PIC PESTICIDES	Omethoate	1113-02-6					LC50 Rat male inhalation >1.5 mg/L/1 hr	1,5	1h rat	0,375	2,867313944	liquid
PIC PESTICIDES	Nicotine	54-11-5	35			LD50 Rat oral 188 mg/kg	LC50 (20 min) 2.3 mg/L air (rat)	2,3	20 min rat	0,575	3,111038203	liquid
PIC INDUSTR.	CADMIUM	7440-43-9	9	4,7 mg/m <sup>3</sup>	8.5 mg/m <sup>3</sup>	4,7 mg/m <sup>3</sup>	8.63 mg/m <sup>3</sup>	1,74	30' Rats	0,435	3,263621114	solid
PIC PESTICIDES	Lindane	58-89-9	1000				1.56 mg/L	1,56	30' inhalati on	0,39	3,482019698	solid
PIC INDUSTR.	CADMIUM OXIDE	1306-19-0	9	5,4 mg/m <sup>3</sup>		10 mg/m <sup>3</sup>	7,98 mg/m <sup>3</sup>	1,52	///	0,38	3,533970671	solid
PIC INDUSTR.	CADMIUM CHLORIDE	10108-64-2	9	7.6 mg/m <sup>3</sup>		15mg/m <sup>3</sup>	8,01 mg/m <sup>3</sup>	1,07	///	0,2675	4,236074044	solid
PIC INDUSTR.	CADMIUM SULFATE	10124-36-4	9	8,7 mg/m <sup>3</sup>		17 mg/m <sup>3</sup>	8,59 mg/m <sup>3</sup>	1,01	///	0,2525	4,351490679	solid
PIC PESTICIDES	Triazophos	24017-47-8	12			LD50 Rat oral 66 mg/kg	LC50 Rat inh. 0.61 mg/L	0,61	1h rat	0,1525	4,666836804	liquid
PIC INDUSTR.	CADMIUM DI(ACETATE) (5743 -04-4 ECHA)	543-90-8	9	9,6 mg/m <sup>3</sup>			8,01 mg/m <sup>3</sup>	0,85	///	0,2125	4,6964292	solid
PIC INDUSTR.	CADMIUM NITRATE	10325-94-7	9	9,9 mg/m <sup>3</sup>		19 mg/m <sup>3</sup>	///	0,83	///	0,2075	4,744050497	solid
PIC PESTICIDES	Tolylfluanid	731-27-1					LC50 Rat inh. 0.26 mg/L	0,26	4h rat	0,065	4,986097095	solid

PIC PESTICIDES	Toxaphene	8001-35-2	200				LC50 Rat inh. 0.26 mg/L (4 hr nose only)	0,26	4h rat	0,065	4,986097095	solid
PIC INDUSTR.	CADMIUM BROMIDE	7789-42-6	9	11 mg/m3		22 mg/m3	///	0,72	///	0,18	5,028399475	solid
PIC INDUSTR.	CADMIUM FLUOROBORATE ( cadmium tetrafluroborate)	14486-19-2	9				111	0,68	///	0,17	5,142716302	liquid
PIC PESTICIDES	Azocyclotin	41083-11-8					0.2 mg /1	0,2	4h rat	0,05	5,510825624	solid
PIC INDUSTR.	CADMIUM STEARATE	2223-93-0	9	28 mg/m <sup>3</sup>		55 mg/m <sup>3</sup>	///	0,29	///	0,0725	6,847140053	solid
PIC PESTICIDES	Cyfluthrin	68359-37-5					0.1 mg/L	0,1	4h rat	0,025	6,897119985	liquid
CWA	SOMAN	96-64-0					LC50 1mg/m <sup>3</sup> 30 min Mouse	0,13		0,065	7,065538637	liquid
PIC PESTICIDES	Monocrotophos	6923-22-4	3.5				0.08 mg/L	0,08	4 hr rat	0,02	7,343407088	solid
PIC PESTICIDES	Methomyl	16752-77-5	23				0,06 mg/l	0,06	inhalati on 4 hr rat	0,015	7,918771232	solid
PIC PESTICIDES	Chlorfenvinphos	470-90-6	500				0.05 mg/L	0,05	4H rat	0,0125	8,283414346	liquid
PIC PESTICIDES	Fentin acetate	900-95-8	28				0.044 mg/l	0,044	air/4 hr rat	0,011	8,539081089	solid
SEVESO III	Dicloruro di carbonile (fosgene)	75-44-5	2 ppm	0.75 ppm	3.6 ppm	3 mg/m <sup>3</sup>	0.047 mg/L	0,047	mouse 30 min espo	0,0235	9,100312334	gas
PIC PESTICIDES	Cadusafos	95465-99-9					0.026 mg/l	0,026	4h ratto	0,0065	9,591267281	liquid
CWA	VX	50782-69-9					0,16 mg/m3 rat male 4H	0,01462	4 h rat	0,003656	10,74213233	oil liquid/va por