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Toxicological Classification and Labelling of Plant Protection Products. Local and International Regulatory Criteria.

Juan Ignacio Pina

International Life Sciences Institute

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Pina, Juan Ignacio

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ILSI Argentina
Av. Santa Fe 1145, 4° Piso (1059)
Buenos Aires - República Argentina
Tel./Fax: (54-11) 4816-4384
E-mail: info@ilsi.org.ar
www.ilsi.org.ar

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Preface

On behalf of ILSI Argentina it is my pleasure to present to the scientific community a compilation work on **"TOXICOLOGICAL CLASSIFICATION AND LABELLING OF PLANT PROTECTION PRODUCTS. Local and International Regulatory Criteria".**

In April 2010 the **SSubcommittee of Plant Protection Products within the Technical Committee of Biosafety and Risk Analysis**, was created and since then has been in uninterrupted activity. One of the objectives of the Subcommittee is to develop OUTREACH and EDUCATION activities, and generate and disseminate technical and scientific material that contributes to the understanding of the general criteria of EVALUATION and CLASSIFICATION of Plant Protection Products, especially locally (Argentina) and regional.

This report is part of the **Series of Special Reports** of ILSI Argentina and constitutes an excellent presentation. It has been prepared by Eng. Juan Ignacio Pina, member of the Subcommittee of Plant Protection Products whose coordinator is Eng. Francisco Decono. This compilation covers a need for updated information on the interdisciplinary field of Agriculture, Toxicology, Chemistry, Biology and Public Health.

I invite you to share this document which is an example of ILSI´s commitment towards the understanding of the scientific and technological challenges.

Juan Carlos López Musi, Dr.

President - ILSI Argentina
(International Institute of Life Sciences)

Table of Contents

List of Tables

1. Acronyms

UNCED: United Nations Conference on Environment & Development.

EPA: Environmental Protection Agency.

FAO: Food & Agricultural Organization of the United Nations.

IFCS: Intergovernmental Forum on Chemical Safety.

OECD: Organization for the Economic Cooperation & Development.

ILO: International Labor Organization.

WHO: World Health Organization.

UNIDO: United Nations Industrial Development Organization.

UNEP United Nations Environment Program.

SAGPyA: Ministry of Agriculture, Livestock, Fisheries & Food.

SENASA: National Food Safety & Quality Service.

GHS: Global Harmonized System.

UNITAR: United Nations Institute for Training & Research.

WSSD: World Summit on Sustainable Development.

2. Introduction

Plant protection products play an important role within the totality of chemicals to which humans are exposed. These products are used to kill, repel, attract, regulate or stop the growth of pests in its broadest sense. A Plague is considered to be those harmful organisms that transmit diseases, compete for food and/or damage economic and cultural goods.

The use of plant protection products significantly increased after World War II. This relates to the changes in the models of production and crop that allowed doubling the production of agricultural food. In recent years they have become more important still, with the appearance on the market of genetically modified seeds in crops such as soybean, corn and cotton, among others.

The first pesticides used, organochlorinated, date from the 40s and the organophosphates and carbamates, from the 50s. Nowadays the chemical structures to which the different pesticides belong are varied.

These products have different degrees of selectivity on the organisms that they seek to control and may differentially affect other species, considered as ***non-target organisms***, including the human being. The ideal plant protection product would be that highly selective for the pest to be controlled and of very low toxicity to humans and other ***non-target organisms***.

Please note that as any chemical it can cause direct adverse effects on humans and other species, of which the man obtains food, pleasure or are essential for the maintenance of ecological balance. Since these substances have a wide variety of chemical structures, the modes of toxic action will also be different, as well as the risks of intoxication, depending on the chemical structure of the substance, forms of use, dose and frequency of application and exposure to them. Several situations as well as cases of acute and chronic exposures can be identified.

Both the dermal and inhalation are the most important pathways for the applicators of plant protection products, especially when applied as aerosols, fine droplets containing dissolved or suspended substance which are dispersed in the air. The inhalation pathway has good and rapid absorption of the toxic substance, which increases the risk of severe poisoning. The dermal pathway becomes important when the product applied has very low LD50 (very toxic) and if it is also fat soluble. This pathway is high risk in those applicators that do not use proper safety gear and practices, in order to avoid pesticide absorption by skin. The oral pathway is relevant in cases of accidental or intentional poisoning, or when the health and safety standards are not complied with, or from eating contaminated food.

The effects can be acute or chronic.

Acute effects generally include vomiting, diarrhea, abortion, headache, drowsiness, behavioral disorders, convulsions, coma, and death. They are associated to accidents by a single high dose whose symptoms start early.

Chronic effects may be different such as a higher incidence of developing certain cancers, leukemia, liver disorders, congenital malformations, and peripheral

neuropathy, or sometimes just malaise, persistent headaches, vague pains. They can be caused by repeated exposure to low doses and the symptoms or signs appear after a long time, even years after the exposure to the pesticide.

Although the use of these substances in agriculture is widespread, the list of substances used in this activity presents different levels of danger. This has led organizations such as FAO and the World Health Organization (WHO) to insist on the need to take precautions during their transportation, sale, handling, storage, preparation, application and disposal of related waste. Also, different countries and international organizations have established regulations to toxicologically classify plant protection products and subsequent label them.

This document presents a compilation of toxicological classification criteria and labelling of plant protection products locally and internationally: WHO, UN, United States and the European Union.

3. Toxicological Classification and Labelling of Plant Protection Products according to the World Health Organization

At international level, there is a classification of pesticide active ingredients according to the acute toxicity according to the WHO criteria. These guidelines correspond to a document published in 2009, based on an agreement of cooperation between several institutions (UNEP, ILO, FAO, WHO, UNIDO, UNITAR and OECD), under the International Program on Chemical Safety.

TABLE N° 1 - TOXICOLOGICAL CLASSIFICATION AND LABELLING OF PLANT PROTECTION PRODUCTS ACCORDING TO THE WHO (2009)

Toxicological Class	Warning phrase	LD50 of rats (mg/kg of live weight)	
		Oral	
		Oral	*Dermal*
Ia	Extremely dangerous	<5	<50
Ib	Highly dangerous	5 - 50	50 - 200
II	Highly dangerous	50 - 2000	200 - 2000
III	Slightly dangerous	>2000	>2000
U	Products that normally are not dangerous when used	5000 or more	

Source: *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification, 2009.*

4. Toxicological Classification and Labelling of Chemicals according to the Global Harmonized System of the United Nations

For a decade, the United States and other countries and interested parties worked on the development of a Global Harmonized System of Classification and Labelling of Chemicals (GHS). That was the main activity commissioned by the United Nations Conference on Environment and Development (UNCED) (1992). It was adopted by the World Summit on Sustainable Development (WSSD) (2002) and the Intergovernmental Forum on Chemical Safety (IFCS). The GHS is designed to provide a common and consistent approximation to define and classify the danger and to communicate that information in labels and safety data sheets.

The GHS classification criteria are based on the intrinsic danger, not on the risk. The classification is essentially equivalent to the danger identification step in the risk assessment paradigms. Consistent with the policy of the Office of the Pesticides Program of the United States Environmental Protection Agency (EPA), based on the best data available, the plant protection products are classified according to their toxicological danger. The GHS is not intended to harmonize the risk assessment or the risk management measures.

The GHS is neutral to evaluate the toxicity tests, and the methods used to estimate the danger to the health and the environment. The implementation of the system does not require the use of any particular protocol or the imposition of new information requirements. The classification is done with the available information, but the GHS acknowledges that agencies have authority to continue requesting information. The GHS does not specify test methods to estimate physical danger. It must also be considered that there is no distinction between liquid and solid products. The same criterion or range is established for both physical states of the substance.

TABLE N° 2 - CRITERIA OF CLASSIFICATION AND LABELLING OF CHEMICALS ACCORDING TO THE GLOBAL HARMONIZED SYSTEM OF THE UNITED NATIONS

Category of hazard	Criteria	Hazard communication elements	
1	DL_{50} (ingestion) ≤5 mg/kg of body weight	Symbol	
	DL_{50} (dermal route) ≤50 mg/kg of body weight		
	CL_{50} (gas) ≤100 ppm	Warning word	Danger
	CL_{50} (vapour) ≤0,5 mg/l	Danger indication	Fatal if swallowed Fatal in contact with skin Fatal if (gas, vapour, dust/mist) is inhaled
	CL_{50} (dust/mist) ≤0,05 mg/l		

Category of hazard	Criteria	Hazard communication elements	
2	DL_{50} (ingestion) >5 mg/kg of body weight but ≤ a 50 mg/kg of body weight	Symbol	
	DL_{50} (dermal route)>50 mg/kg of body weight but ≤ a 200 mg/kg of body weight		
	CL_{50} (gas) >100 ppm but ≤500 ppm	Warning word	Danger
	CL_{50} (vapour) >0,5 mg/l but ≤2,0 mg/l	Danger indication	Fatal if swallowed Fatal in contact with skin Fatal if (gas, vapour, dust/mist) is inhaled
	CL_{50} (dust/mist) >0,05 mg/l but ≤0,5 mg/l		

Category of hazard	Criteria	Hazard communication elements	
3	DL_{50} (ingestion) >50 mg/kg of body weight but ≤ a 300 mg/kg de body weight	Symbol	
	DL_{50} (dermal route) >200 mg/kg of body weight but ≤ a 1000 mg/kg of body weight		
	CL_{50} (gas) >500 ppm but ≤2500 ppm	Warning word	Danger
	CL_{50} (vapor) >2,0 mg/l but ≤10,0 mg/l	Danger indication	Toxic if swallowed Toxic in contact with skin Toxic if (gas, vapour, dust/mist) is inhaled
	CL_{50} (polvo/niebla) >0,5 mg/l but ≤1,0 mg/l		

Category of hazard	Criteria	Hazard communication elements	
4	DL_{50} (ingestion) >300 mg/kg de body weight but ≤ a 2000 mg/kg of body weight	Symbol	
	DL_{50} (dermal route) >1000 mg/kg of body weight but ≤ a 2000 mg/kg body weight		
	CL_{50} (gas) >2500 ppm but ≤ 20000 ppm	Warning Word	Warning
	CL_{50} (vapour) >10,0 mg/l but ≤ 20,0 mg/l	Danger indication	Harmful if swallowed Harmful in contact with skin Harmful if (gas, vapour, dust/mist) is inhaled
	CL_{50} (dust/mist) >1,0 mg/l but ≤5,0 mg/l		

Category of hazard	Criteria	Hazard communication elements	
5	DL_{50} (ingestion or dermal absorption) >2000 mg/kg of body weight but ≤ a 5000 mg/kg of body weight	Symbol	*No symbol*
	For gases, vapours, dust, mist, LC50 in the range equivalent to LD50 via oral (ingestion) and dermal (e.g., > 2000 but ≤ to 5000 mg/kg of body weight)		
	See also the additional criteria: a) Indication of significant effects in humans; b) Any mortality at Category 4; c) Significant Clinical signs at Category 4; d) Information from other studies	Warning Word	Warning
		Danger indication	May be harmful if swallowed May be harmful in contact with skin May be harmful if (gas, vapour, dust/mist) is inhaled

Source: *Globally Harmonized System of Classification and Labelling of Chemicals (GHS) – Fourth Revised Edition – United Nations, New York and Geneva, 2011.*

5. Toxicological Classification and Labelling of Plant Protection Products according to the National Food Safety & Quality Service

In Argentina, SENASA is the authority that regulates the classification and labelling of plant protection products, among other issues related to these products.

SENASA classifies formulated products and active ingredients of plant protection products according to the toxicological studies submitted by registrants.

The toxicological studies are:

1. Test of Acute Oral Toxicology (Lethal Dose 50)
2. Test of Acute Dermal Toxicology (Lethal Dose 50)
3. Test of Acute Inhalation Toxicology (Lethal Concentration 50)
4. Test of Ocular Irritation
5. Test of Dermal Irritation
6. Test of Sensitization

TABLE N° 3 - CRITERIA OF CLASSIFICATION AND LABELLING OF PLANT PROTECTION PRODUCTS ACCORDING TO SAGPyA RESOLUTION N° 350/1999 – Acute Dermal and oral toxicity

	DL_{50} of rats (mg/kg of live weight)			
	Oral		Dermal	
	Solid	Liquid	Solid	Liquid
Ia	5 or less	20 or less	10 or less	40 or less
Ib	5 - 50	20 - 200	10 - 100	40 - 400
II	50 - 500	200 - 2000	100 - 1000	400 - 4000
III	500 - 2000	2000 - 3000	More than 1000	More than 4000
IV	More than 2000	More than 3000		

Source: *SAGPyA Resolution N°350/99 and subsequent amending regulations.*

TABLE N° 4 - CRITERIA OF CLASSIFICATION AND LABELLING OF PLANT PROTECTION PRODUCTS ACCORDING TO SAGPyA RESOLUTION N° 350/1999 – Indications according to categories

WHO classification according to risks	Danger classification	Band color	Danger symbol	Words (*)
Ia Extremely dangerous	VERY TOXIC	Red PMS 199 C	Skull and crossbones	VERY TOXIC
Ib Highly dangerous	TOXIC	Red PMS 199 C	Skull and crossbones	TOXIC
II Moderately dangerous	HARMFUL	Yellow PMS C	St. Andrew´s cross	HARMFUL
III Slightly dangerous	WARNING	Blue PMS 293 C		WARNING
Products that normally are not dangerous when used		Green PMS 347 C		WARNING

(*) The word must be below the symbol and centered.
Source: *SAGPyA Resolution N°350/99 and subsequent amending regulations.*

TABLE N° 5 - CRITERIA OF CLASSIFICATION AND LABELLING OF PLANT PROTECTION PRODUCTS ACCORDING TO SAGPyA RESOLUTION N° 350/1999 – Inhalation toxicity

Class	Inhalation LC50 (mg/l)
I	≤0,2
II	>0,2 a 2
III	>2 a 20
IV	>20

Source: *SAGPyA Resolution N°350/99 and subsequent amending regulations.*

SAGPyA Resolution 350/1999 established the toxicological classification of products according to the type of formulation and the characteristics of the formulated products, considering different toxicological tests. From the tests of acute oral and dermal toxicity, the toxicological category or class for said routes of exposure is obtained. The category of greatest hazard is considered for the classification of the formulated product. The category defines the hazard classification, the color of the label, the danger symbol and the words that will appear in the label.

In 2011, SENASA submitted for public consultation a draft resolution amending the classification criteria that were established by SAGPyA Resolution 350/1999. On June 19, 2012 SENASA Resolution 302/2012 was published in the Official Gazette. It adjusts the criteria for the classification of plant protection products to the latest WHO publication (2009). Moreover, it incorporates the classification of products according to their eye and skin irritation and to their sensitization, considering the criteria used by the EPA.

The following provides the new criteria in force in Argentina for the classification and labelling of plant protection products:

TABLE N° 6 - SENASA RESOLUTION N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS – Acute Oral and Dermal Toxicity

Toxicological Class	Warning phrase	LD50 of rats (mg/kg of live weight)	
		Oral	Dermal
Ia	Extremely dangerous	<5	<50
Ib	Highly dangerous	5 a 50	50 - 200
II	Moderately dangerous	>50 a 2000	200 - 2000
III	Slightly dangerous	>2000 a 5000	>2000
IV	Products that normally are not dangerous when used	>5000	>5000

Source: *SENASA Resolution N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS.*

TABLE N° 7 - SENASA RESOLUTION N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS – Inhalation Toxicity

Class	Inhalation LC50 (mg/l)	Warning
I	≤0,2	VERY TOXIC
II	>0,2 a 2	HARMFUL
III	>2 a 20	WARNING
IV	>20	-

Source: *SENASA Resolution N°302/2012 - REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS.*

TABLE N° 8 - SENASA RESOLUTION N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS – Dermal Irritation

Class	Warning sign	Visible effects	Classification	Label
I	DANGER	Corrosive (destruction of tissue in the dermis and/or scarring)	CORROSIVE	Causes burns to skin
II	CAUTION	Severe irritation (severe erythema or edema) at 72 hours	SEVERE IRRITATION	Causes skin irritation
III	WARNING	Moderate irritation (mild erythema) at 72 hours	MODERATE IRRITATION	Avoid contact with skin and clothing
IV	WARNING	Mild or slight irritation (without irritation or slight erythema) at 72 hours	SLIGHT IRRITATION	Not required. OPTIONAL: Warning Category III

Source: *Resolution SENASA N°302/2012 - REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS.*

TABLE N° 9 - SENASA RESOLUTION N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS – Eye irritation

Class	Warning sign	Visible effects	Classification	Label
I	DANGER	Corrosive (destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	CORROSIVE	Causes irreversible eye damage
II	CAUTION	Corneal involvement or irritation reversal in 8-21 days	SEVERE IRRITATION	Causes temporary eye damage
III	WARNING	Corneal involvement or irritation reversal in 7 days or less	MODERATE IRRITATION	Causes moderate eye irritation
IV	WARNING	Minimal effects reversal in less than 24 hours	SLIGHT IRRITATION	Not required. OPTIONAL: Warning Category III

Source: *SENASA Resolution N°302/2012 - REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS.*

TABLE N° 10 - SENASA RESOLUTION SENASA N°302/2012 – REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS – Skin sensitization

Class	Classification	Label
I	Sensitising	Prolonged or repeated skin contact may cause allergic reactions in some people
II	Non-sensitising	-

Source: *SENASA Resolution N°302/2012 - REVIEW OF THE CRITERIA FOR THE TOXICOLOGICAL CLASSIFICATION OF PLANT PROTECTION PRODUCTS.*

6. Toxicological Classification and Labelling of Plant Protection Products according to the United States Environmental Protection Agency

The United States Environmental Protection Agency (EPA) considers six areas of acute toxicity-oral, dermal, inhalation, eye irritation, skin irritation and skin sensitization.

Statements regarding signal words, Danger for Humans and Domestic Animals, Personal Protective Equipment (Protection Standard for Non Workers) and First Aid are typically determined by the results of the six tests of acute toxicity performed with the formulated plant protection product. Tests of oral, dermal and inhalation acute toxicity evaluate the systemic toxicity via the exposure pathways mentioned. Tests of eye and skin primary irritation measure the irritation or corrosion, while the test of skin sensitization evaluates the potential of contact allergic dermatitis. ***With the exception of the test of skin sensitization***, each test of acute toxicity is assigned to a toxicity category based on the results obtained (see Table 11). The results of these six tests of acute toxicity must be informed in order to determine the appropriate labelling.

TABLE N° 11 - CLASSIFICATION OF PESTICIDES ACCORDING TO THE ACUTE TOXICOLOGY - EPA

Test	Category I	Category II	Category III	Category IV
Acute Oral	Less or equal to 50 mg/kg	>50 a 500 mg/kg	>500 a 5000 mg/kg	>5000 mg/kg
Acute Dermal	Less or equal to 200 mg/kg	>200 a 2000 mg/kg	>2000 a 5000 mg/kg	>5000 mg/kg
Acute Inhalation [1]	Less or equal to 0,05 mg/liter	>0,05 a 0,5 mg/litro	>0,5 a 2 mg/liter	>2 mg/liter
Primary Eye Irritation	Corrosive (irreversible destruction of ocular tissue) or corneal damage or irritati on persisting for more than 21 days	Daño a la	Damage to the cornea or other ocular damage disappears in 8-21 days	Minimal effects th at disappear within 24 hours
Primary Skin Irritation	Corrosive (destruction of tissue in the epidermis and/or scarring)	Irritación severa a	Severe irritation at 72 hours (severe erythema or edema)	Slight to mild irritation at 72 hours (no irritation or slight erythema)

[1] *4 hours of exposure*

Source: *Label Review Manual – Chapter 7 – Precautionary Statements – US EPA Office of Pesticide Programs – August 2007.*

TABLE N° 12 - WARNING PHRASES ACCORDING TO THE TOXICOLOGICAL CLASSIFICATION

Toxicological Category	Warning Phrase
Toxicological Category I	*DANGER* (DANGER)
Toxicological Category II	*WARNING* (ADVERTENCIA)
Toxicological Category III	*CAUTION* (CAUTION)
Toxicological Category IV	Not required

Source: *Label Review Manual – Chapter 7 – Precautionary Statements – US EPA Office of Pesticide Programs – August 2007.*

7. Toxicological Classification and Labelling of Plant Protection Products according to the European Union

The active ingredients and formulated products are regulated by different regulations. The current regulation for active ingredients is Guideline 67/548 and for formulated products Guideline 99/45.

However, the principles, symbols and warnings of the toxicological classification are set out in the Guideline on Dangerous Substances. This legislation has been amended numerous times and is extremely complex.

In the EU, the current legislation on classification is progressively replaced by new regulations, considering the Global Harmonized System developed by the United Nations. The schedule established by the new regulations of the European Community N° 1272/2008 fixes the change of the classification and labelling system for active substances in 2010 and for formulated products in 2015, without limitation to do it in advance.

8. Comparison of different selected regulatory systems on the classification and labelling of Plant Protection Products

8.1. Acute Oral Toxicity

TABLE N° 13 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE ACUTE ORAL TOXICITY

Test	Physical State	WHO/FAO/ILO (2009)			SGA (2011)			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			UE - Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning Phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Acute Oral Toxicity - LD50 of rats (mg/kg of live weight)	Solid	Ia	<5	Extremely dangerous	1	≤5	Danger	Ia	<5	Extremely dangerous	Ia	<5	Extremely dangerous	I	≤50	Danger	1	≤5	Danger
		Ib	5-50	Highly dangerous	2	>5 y ≤50	Danger	Ib	5-50	Extremely dangerous	Ib	5-50	Highly dangerous	II	50-500	Warning	2	>5 y ≤50	Danger
		II	50-2000	Moderately dangerous	3	>50 y ≤300	Danger	II	50-500	Moderately dangerous	II	50-2000	Moderately dangerous	III	500-5000	Caution	3	>50 y ≤300	Danger
		III	>2000	Slightly dangerous	4	>300 y ≤2000	Warning	III	500-2000	Slightly dangerous	III	>2000	Slightly dangerous	IV	>5000	-	4	>300 y ≤2000	Warning
		U (IV)	>5000	Products that normally are not dangerous when used	5	>2000 y ≤5000	Warning	IV	>2000	Products that normally are not dangerous when used	IV	>5000	Products that normally are not dangerous when used	-	-	-	-	-	-

Test	Physical State	OMS/FAO/ILO (2009)			SGA (2011)			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			UE - Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning Phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Acute Oral Toxicity - LD50 of rats (mg/kg of live weight)	Liquid	Ia	<5	Extremely dangerous	1	≤5	Danger	Ia	<20	Extremely dangerous	Ia	<5	Extremely dangerous	I	<5	Danger	1	≤5	Danger
		Ib	5-50	Highly dangerous	2	>5 y ≤50	Danger	Ib	20-200	Extremely dangerous	Ib	5-50	Highly dangerous	II	5-500	Warning	2	>5 y ≤50	Danger
		II	50-2000	Moderately dangerous	3	>50 y ≤300	Danger	II	200-2000	Moderately dangerous	II	50-2000	Moderately dangerous	III	500-5000	Caution	3	>50 y ≤300	Danger
		III	>2000	Slightly dangerous	4	>300 y ≤2000	Warning	III	2000-3000	Slightly dangerous	III	>2000	Slightly dangerous	IV	>5000	-	4	>300 y ≤2000	Warning
		U (IV)	>5000	Products that normally are not dangerous when used	5	>2000 y ≤5000	Warning	IV	>3000	Products that normally are not dangerous when used	IV	>5000	Products that normally are not dangerous when used	-	-	-	-	-	-

8.2. Acute Dermal Toxicity

TABLE N° 14 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE ACUTE DERMAL TOXICITY

Test	Physical State	WHO/FAO/ILO (2009)			SGA (2011)			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			UE - Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning Phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Acute Oral Toxicity - LD50 of rats (mg/kg of live weight)	Solid	Ia	<50	Extremely dangerous	1	≤50	Danger	Ia	<10	Extremely dangerous	Ia	<50	Extremely dangerous	I	≤200	Danger	1	≤50	Danger
		Ib	50-200	Highly dangerous	2	>50 y ≤200	Danger	Ib	10-100	Highly dangerous	Ib	50-200	Highly dangerous	II	200-2000	Warning	2	>50 y ≤200	Danger
		II	200-2000	Moderately dangerous	3	>200 y ≤1000	Danger	II	100-1000	Moderately dangerous	II	200-2000	Moderately dangerous	III	2000-5000	Caution	3	>200 y ≤1000	Danger
		III	>2000	Slightly dangerous	4	>1000 y ≤2000	Warning	III	>1000	Slightly dangerous	III	>2000	Slightly dangerous	IV	>5000	-	4	>1000 y ≤2000	Warning
		U (IV)	5000 o mayor	Products that normally are not dangerous when used	5	>2000 y ≤5000	Warning	-	-	-		5000 o mayor	Products that normally are not dangerous when used	-	-	-	-	-	-
Acute Oral Toxicity - LD50 of rats (mg/kg of live weight)	Liquid	Ia	<50	Extremely dangerous	1	≤50	Danger	Ia	<10	Extremely dangerous	Ia	<50	Extremely dangerous	I	≤200	Danger	1	≤50	Danger
		Ib	50-200	Highly dangerous	2	>50 y ≤200	Danger	Ib	10-100	Highly dangerous	Ib	50-200	Highly dangerous	II	200-2000	Warning	2	>50 y ≤200	Danger
		II	200-2000	Moderately dangerous	3	>200 y ≤1000	Danger	II	100-1000	Moderately dangerous	II	200-2000	Moderately dangerous	III	2000-5000	Caution	3	>200 y ≤1000	Danger
		III	>2000	Slightly dangerous	4	>1000 y ≤2000	Warning	III	>1000	Slightly dangerous	III	>2000	Slightly dangerous	IV	>5000	-	4	>1000 y ≤2000	Warning
		U (IV)	5000 o mayor	Products that normally are not dangerous when used	5	>2000 y ≤5000	Warning	-	-	-		5000 o mayor	Products that normally are not dangerous when used	-	-	-	-	-	-

8.3. Acute Inhalation Toxicity

TABLE N° 15 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE ACUTE INHALATION TOXICITY OF SOLID FORMULATED PRODUCTS

Test	Physical State	WHO/FAO/ILO (2009)			SGA (2011)			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase		Limits	Warning Phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Inhalation Acute Toxicity - LC50 of rats (mg/kg of live weight)	Solid	-	-	-	1	LC50 ≤100 ppm (gas) LC50 ≤0,5 mg/L (vapour) LC50 ≤0,05 mg/L (dust, mist)	Danger	I	≤0,2	-	I	≤0,2	Muy tóxico	I	≤0,05 mg/L	Very toxic	1	LC50 ≤100 ppm (gas) LC50 ≤0,5 mg/L (vapour) LC50 ≤0,05 mg/L (dust, mist)	Danger
		-	-	-	2	LC50 >5 y ≤500 ppm (gas) LC50 >0,5 y ≤2,0 mg/L (vapour) LC50 >0,05 y ≤0,5 mg/L (dust, mist)	Danger	II	>0,2 - 2	-	II	>0,2 - 2	Nocivo	II	>0,05 - 0,5 mg/L	Harmful	2	LC50 >5 y ≤500 ppm (gas) LC50 >0,5 y ≤2,0 mg/L (vapour) LC50 >0,05 y ≤0,5 mg/L (dust, mist)	Danger
		-	-	-	3	LC50 >500 y ≤2500 ppm (gas) LC50 >2,0 y ≤10,0 mg/L (vapour) LC50 >0,5 y ≤1,0 mg/L (dust, mist)	Danger	III	>2 - 20	-	III	>2 - 20	Cuidado	III	>0,5 - 2 mg/L	Warning	3	LC50 >500 y ≤2500 ppm (gas) LC50 >2,0 y ≤10,0 mg/L (vapour) LC50 >0,5 y ≤1,0 mg/L (dust, mist)	Danger
		-	-	-	4	CL50 >2500 y ≤20000 ppm (gas) CL50 >10,0 y ≤20,0 mg/L (vapour) CL50 >1,0 y ≤5,0 mg/L dust, mist)	Warning	IV	>20	-	IV	>20	-	IV	>2 mg/L	-	4	CL50 >2500 y ≤20000 ppm (gas) CL50 >10,0 y ≤20,0 mg/L (vapour) CL50 >1,0 y ≤5,0 mg/L (dust, mist)	Warning
		-	-	-	5	CL50 >2500 y ≤5000 mg/L (gas, vapour, dust & mist)	Warning	-	-	-	-	-	-	-	-	-	-	-	-

TABLE N° 16 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE ACUTE INHALATION TOXICITY OF LIQUID FORMULATED PRODUCTS

Test	Physical State	WHO/FAO/ILO (2009)			SGA (2011)			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase		Limits	Warning Phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Inhalation Acute Toxicity - LC50 of rats (mg/kg of live weight)	Liquid	-	-	-	1	LC50 ≤100 ppm (gas) LC50 ≤0,5 mg/L (vapour) LC50 ≤0,05 mg/L (dust, mist)	Danger	Ia	<40	Extremely dangerous	Ia	<40	Very toxic	I	≤0,05 mg/L	Danger	1	LC50 ≤100 ppm (gas) LC50 ≤0,5 mg/L (vapour) LC50 ≤0,05 mg/L (dust, mist)	Danger
		-	-	-	2	LC50 >5 y ≤500 ppm (gas) LC50 >0,5 y ≤2,0 mg/L (vapour) LC50 >0,05 y ≤0,5 mg/L (dust, mist)	Danger	Ib	40-400	Extremely dangerous	Ib	40-400	Harmful	II	>0,05 - 0,5 mg/L	Warning	2	LC50 >5 y ≤500 ppm (gas) LC50 >0,5 y ≤2,0 mg/L (vapour) LC50 >0,05 y ≤0,5 mg/L (dust, mist)	Danger
		-	-	-	3	LC50 >500 y ≤2500 ppm (gas) LC50 >2,0 y ≤10,0 mg/L (vapour) LC50 >0,5 y ≤1,0 mg/L (dust, mist)	Danger	II	400-4000	Moderately dangerous	II	400-4000	Warning	III	>0,5 - 2 mg/L	Caution	3	LC50 >500 y ≤2500 ppm (gas) LC50 >2,0 y ≤10,0 mg/L (vapour) LC50 >0,5 y ≤1,0 mg/L (dust, mist)	Danger
		-	-	-	4	CL50 >2500 y ≤20000 ppm (gas) CL50 >10,0 y ≤20,0 mg/L (vapour) CL50 >1,0 y ≤5,0 mg/L dust, mist)	Warning	III	>4000	Slightly dangerous	III	>4000	-	IV	>2 mg/L	-	4	CL50 >2500 y ≤20000 ppm (gas) CL50 >10,0 y ≤20,0 mg/L (vapour) CL50 >1,0 y ≤5,0 mg/L (dust, mist)	Warning
		-	-	-	5	CL50 >2500 y ≤5000 mg/L (gas, vapour, dust & mist)	Warning	-	-	-	-	-	-	-	-	-	-	-	-

8.4. Primary Eye Irritation

TABLE N° 17 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE PRIMARY EYE IRRITATION OF SOLID FORMULATED PRODUCTS

Test of Primary Eye Irritation	Physical State	WHO/FAO/ILO (2009)			SGA			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Primary Eye Irritation	Solid	-	-	-	1	1. At least in one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or not fully reverse normally within the observation period of 21 days; 2. At least in 2 of 3 animals tested, a positive response of: - Corneal opacity ≥3 and/or - Iritis> 1.5; Calculated as the average values of the values at 24, 48 and 72 hours of application of the testing substance.	Irreversible effects on eyes	-	-	-	I	Corrosive (irreversible destruction of eye tissue) or corneal damage or irritation persisting for more than 21 days.	Corrosive. Causes irreversible eye damage.	I	Corrosive (irreversible destruction of eye tissue) or corneal damage or irritation persisting for more than 21 days.	Danger	1 2	If, when applied to the eye of an animal, the substance causes: - At least in one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or not fully reverse within the normal observation period of 21 days; and/or - At least in 2 of 3 animals tested a positive response of: - Corneal opacity ≥ 3 and/or - Iritis> 1.5 Calculated as the average values of the tests at 24, 48 and 72 hours of the application on material to be evaluated.	Irreversible effects on eyes
		-	-	-	2A	1. At least 2 of 3 animals tested positive response of: - Corneal opacity ≥1; and/or - Iritis≥1; and/or - Redness of the conjunctiva ≥2; and/or - Edema of the conjunctiva (chemosis) ≥2 Calculated as the average values of the tests at 24, 48 and 72 hours of application of the testing substance, and which completely reverse in the normal observation period of 21 days.	Eye irritant	-	-	-	II	Corneal involvement or irritation reversal in 8-21 days.	Severe irritant. Cause temporary eye damage.	II	Damage to the cornea or other eye damage disappears in 8-21 days.	Warning		If, when applied to the eye of an animal, the substance causes: - At least in 2 of 3 animals tested positive response of: - Corneal opacity ≥ 1 and/or - Iritis ≥ 1, and/or - Redness of the conjunctiva ≥ 2 and/or - Edema of the conjunctiva (chemosis) ≥ 2 Calculated as the average values of the tests at 24, 48 and 72 hours of application of the testing substance, and which completely reverse within the normal observation period of 21 days.	Eye irritant
		-	-	-	2B	A substance whose effects abovementioned reverse within 7 days of observation is included within this category.	Slightly eye irritant	-	-	-	III	Cornea involved reversal of irritation in 7 days or less.	Moderately irritant. Causes moderate eye irritation.	III	Damage to the cornea or other eye damage disappears in 7 days or less.	Caution		-	-
		-	-	-	-	-	-	-	-	-	IV	Reversal of minimal effects in less than 24 hours.	Slightly irritant. Optional: Category III warning.	IV	Minimal effects disappear within 24 hours.	-		-	-
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-

TABLE N° 18 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE PRIMARY EYE IRRITATION OF LIQUID FORMULATED PRODUCTS

Test of Primary Eye Irritation	Physical State	WHO/FAO/ILO (2009)			SGA			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Primary Eye Irritation	Liquid	-	-	-	1	1. At least in one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or not fully reverse normally within the observation period of 21 days; 2. At least in 2 of 3 animals tested, a positive response of: - Corneal opacity ≥3 and/or - Iritis> 1.5; Calculated as the average values of the tests at 24, 48 and 72 hours of application of the testing substance.	Irreversible effects on eyes	-	-	-	I	Corrosive (irreversible destruction of eye tissue) or corneal damage or irritation persisting for more than 21 days.	Corrosive. Causes irreversible eye damage.	I	Corrosive (irreversible destruction of eye tissue) or corneal damage or irritation persisting for more than 21 days.	Danger	1	If, when applied to the eye of an animal, the substance causes: - At least in one animal effects on the cornea, iris or conjunctiva that are not expected to reverse or not fully reverse within the normal observation period of 21 days; and/or - At least in 2 of 3 animals tested a positive response of: - Corneal opacity ≥ 3 and/or - Iritis> 1.5 Calculated as the average values of the tests at 24, 48 and 72 hours of application on testing substance.	Irreversible effects on eyes
		-	-	-	2A	1. At least in 2 of 3 animals tested positive response of: - Corneal opacity ≥1; and/or - Iritis≥1; and/or - Redness of the conjunctiva ≥2; and/or - Edema of the conjunctiva (chemosis) ≥2 Calculated as the average values of the tests at 24, 48 and 72 hours of application of the testing substance, and which completely reverse in the normal observation period of 21 days.	Eye irritant	-	-	-	II	Corneal involvement or irritation reversal in 8-21 days.	Severe irritant. Cause temporary eye damage.	II	Damage to the cornea or other eye damage disappears in 8-21 days.	Warning	2	If, when applied to the eye of an animal, the substance causes: - At least in 2 of 3 animals tested positive response of: - Corneal opacity ≥ 1 and/or - Iritis ≥ 1, and/or - Redness of the conjunctiva ≥ 2 and/or - Edema of the conjunctiva (chemosis) ≥ 2 Calculated as the average values of the tests at 24, 48 and 72 hours of application of the testing substance, and which completely reverse within the normal observation period of 21 days.	Eye irritant
		-	-	-	2B	A substance whose abovementioned effects reverse within 7 days of observation is included within this category.	Slightly eye irritant	-	-	-	III	Cornea involved reversal of irritation in 7 days or less.	Moderately irritant. Causes moderate eye irritation.	III	Damage to the cornea or other eye damage disappears in 7 days or less.	Caution		-	-
		-	-	-	-	-	-	-	-	-	IV	Reversal of minimal effects in less than 24 hours.	Slightly irritant. Optional: Category III warning.	IV	Minimal effects disappear within 24 hours.	-		-	-
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-

8.5. Primary Dermal Irritation

TABLE N° 19 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE PRIMARY DERMAL IRRITATION OF SOLID FORMULATED PRODUCTS

Test	Physical State	WHO/FAO/ILO (2009)			SGA			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Primary Skin Irritation	Solid	-	-	-	1	A corrosive is a testing material that produces destruction of skin tissue, called visible necrosis, through the epidermis and into the dermis, in at least 1 of 3 animals evaluated after exposure up to 4 hours.	Corrosive	-	-	-	I	Corrosive (destruction of tissue in the dermis and/or scarring).	Corrosive. Causes skin burns.	I	Corrosive (destruction of tissue in the epidermis and/or scarring).	Danger	1	A corrosive is a testing material that produces destruction of skin tissue, called visible necrosis, through the epidermis and into the dermis, in at least 1 of 3 animals evaluated after exposure up to 4 hours.	Corrosive
		-	-	-	2	1. Average value ≥2,3 ≤4,0 for erythema/sores or for edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours after patch removal or, if the reaction is delayed, of degrees on 3 consecutive days after the onset of the skin reaction; 2. Inflammation that persists to the end of the observation period normally 14 days in at least 2 animals, particularly considering alopecia (in a limited area), hyperkeratosis, hyperplasia, and scaling; 3. In some cases where there is pronounced variability between the response of the animals, with very definite positive effects related to chemical exposure a single animal but less than the abovementioned criteria.	Irritant	-	-	-	II	Severe irritation (severe erythema or edema) at 72 hs.	Severe irritant. Causes skin irritation.	II	Severe irritation at 72 hours (severe erythema or edema).	Warning	2	1. Average value ≥2,3 ≤4,0 for erythema/sores or for edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours after patch removal or, if the reaction is delayed, the degrees on 3 consecutive days after the onset of skin reaction; 2. Inflammation that persists to the end of the observation period normally 14 days in at least 2 animals, particularly considering alopecia (in a limited area), hyperkeratosis, hyperplasia, and scaling; 3. In some cases where there is pronounced variability between the response of the animals, with very definite positive effects related to chemical exposure a single animal but less than the abovementioned criteria.	Irritant
		-	-	-	3	≥1,5 average value of <2.3 for erythema/sore or for gradation edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours or, if reactions are delayed, of degrees on 3 consecutive days after the appearance of skin reactions (when not included in the abovementioned irritant category)	Slightly irritant	-	-	-	III	Moderate irritation (moderate erythema) at 72 hs.	Moderate irritant. Avoid contact with skin and clothing.	III	Moderate irritation at 72 hours (moderate erythema).	Caution	3	-	-
		-	-	-	-	-	-	-	-	-	IV	Slight irritation (no irritation or slight erythema) at 72 hs.	Slight irritant. Optional: Warning Category III.	IV	Slight irritation at 72 hours (no irritation or slight erythema).	-		-	-
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-

CUADRO N° 20 - COMPARISON OF CATEGORIES, LIMITS AND WARNINGS REGARDING THE PRIMARY DERMAL IRRITATION OF LIQUID FORMULATED PRODUCTS

Test	Physical State	WHO/FAO/ILO (2009)			SGA			SAGPyA – Res. 350/99 (1999)			SENASA – Res. 302/12 (2012)			EPA			Reg CE 1272		
		Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase	Category	Limits	Warning phrase
Primary Skin Irritation	Solid	-	-	-	1	A corrosive is a testing material that produces destruction of skin tissue, called visible necrosis, through the epidermis and into the dermis, in at least 1 of 3 animals evaluated after exposure up to 4 hours.	Corrosive	-	-	-	I	Corrosive (destruction of tissue in the dermis and/or scarring).	Corrosive. Causes skin burns.	I	Corrosive (destruction of tissue in the epidermis and/or scarring).	Danger	1	A corrosive is a testing material that produces destruction of skin tissue, called visible necrosis, through the epidermis and into the dermis, in at least 1 of 3 animals evaluated after exposure up to 4 hours.	Corrosive
		-	-	-	2	1. Average value ≥2,3 ≤4,0 for erythema/sores or for edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours after patch removal or, if the reaction is delayed, of degrees on 3 consecutive days after the onset of the skin reaction; 2. Inflammation that persists to the end of the observation period normally 14 days in at least 2 animals, particularly considering alopecia (in a limited area), hyperkeratosis, hyperplasia, and scaling; 3. In some cases where there is pronounced variability between the response of the animals, with very definite positive effects related to chemical exposure a single animal but less than the abovementioned criteria.	Irritant	-	-	-	II	Severe irritation (severe erythema or edema) at 72 hs.	Severe irritant. Causes skin irritation.	II	Severe irritation at 72 hours (severe erythema or edema).	Warning	2	1. Average value ≥2,3 ≤4,0 for erythema/sores or for edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours after patch removal or, if the reaction is delayed, the degrees on 3 consecutive days after the onset of skin reaction; 2. Inflammation that persists to the end of the observation period normally 14 days in at least 2 animals, particularly considering alopecia (in a limited area), hyperkeratosis, hyperplasia, and scaling; 3. In some cases where there is pronounced variability between the response of the animals, with very definite positive effects related to chemical exposure a single animal but less than the abovementioned criteria.	Irritant
		-	-	-	3	≥1,5 average value of <2.3 for erythema/sore or for gradation edema in at least 2 of 3 animals evaluated at 24, 48 and 72 hours or, if reactions are delayed, of degrees on 3 consecutive days after the appearance of skin reactions (when not included in the abovementioned irritant category).	Slightly irritant	-	-	-	III	Moderate irritation (moderate erythema) at 72 hs.	Moderate irritant. Avoid contact with skin and clothing.	III	Moderate irritation at 72 hours (moderate erythema).	Caution	3	-	-
		-	-	-	-	-	-	-	-	-	IV	Slight irritation (no irritation or slight erythema) at 72 hs.	Slight irritant. Optional: Warning Category III.	IV	Slight irritation at 72 hours (no irritation or slight erythema).	-		-	-
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-	-

9. Glossary

Alopecia: Alopecia or hair loss is the partial or total loss of hair on skin areas normally with hair.

Hepatic impairment: Changes or failure of the liver function.

LC 50 (Lethal Concentration 50): Concentration of toxic agent that causes the death of 50% of the test population. See also: Indices of toxicity.

EC 50 (Effective Concentration 50): Concentration of toxic agent that produces significant adverse effects in 50% of the test population. See also: Indices of toxicity.

LD 50 (Lethal Dose 50): Dose, statistically calculated, of a toxic agent (substance, element or chemical compound and physical agent) that is expected to produce the death of 50% of the organisms in a population under a defined set of conditions.

Corrosive: A substance that produces destruction of the epidermal tissue (necrosis), visible through the epidermis and into the dermis.

Dosage: Amount of substance to which an organism is exposed and the time during said organism was exposed. The adverse effect or damage is a function of both the dose and the exposure conditions.

Erythema: It is a dermatological medical term for a skin redness conditioned by inflammation due to an excess of blood flow by vasodilatation. See also: Inflammation.

Sores: The sore itself is devitalized skin tissue whose main component is the skin and sometimes the underlying tissue, that become hard, dry and of pearly white, grayish or blackish color.

Hyperkeratosis: Condition characterized by the thickening of the outer layer of skin that is composed of keratin, which is a strong protective protein.

Hyperplasia: It is the increase in size of an organ or tissue, because its cells have increased in number. It may occur in tissues whose cells can multiply. This physiological process is also known as *"hypergenesis"*.

ADI (Acceptable Daily Intake): It refers to the dose of a product that can be ingested daily by an individual throughout his lifetime without appreciable health risk". It is expressed in mg/kg/day. Usually the ADI results from dividing the NOAEL (safety factor) by 10 and then by 10 again (safety factor by individual variations and by groups of hypersensitive individuals). Briefly, and in general, the ADI is one hundredth part of the NOAEL. See also: NOAEL.

Indices of Toxicity: Indices of toxicity are determined in the process of "toxicological evaluation" and the rest of toxicity parameters derive from them. These indices are a quantitative measure of the toxicity of a substance determined experimentally in laboratory animals. There are two types:

a) Indices of Acute toxicity: LD50, LC50

b) Indices of toxicity - repeated doses: NOAEL, LOAEL.

Inflammation: Inflammation is the form of expression of many diseases. It is a nonspecific response to aggressions from the outside, and is generated by inflammatory agents. The inflammatory response occurs only in vascularized connective tissues and emerges with the defensive aim to isolate and destroy the harmful agent and repair the damaged tissue or organ. Therefore it is considered a mechanism of immunity, stereotyped, in contrast to the adaptive immune reaction specific for each type of infectious agent. The inflammation is identified by the suffix –itis (colitis, conjunctivitis, etc.). The biggest problem arising from inflammation is when the defense directs both to harmful and harmless agents, so as to cause injury to healthy tissues or organs.

Skin irritation: Reaction of the skin resulting from a single or multiple exposures to a physical or chemical agent on the same area. It is characterized by inflammation and it can result in localized necrosis. It can occur along with several disorders or diseases. The skin irritation that causes a desire to scratch the affected area in search of relief is known as "itch". The itch can be generalized (when spread in several parts of the body) or localized (located in a specific area). They are classified according to the injuries they cause, as follows:

- Severe
- Moderate
- Slight

LOAEL (Lowest Observed Adverse Effect Level): Minimum concentration or amount of substance that causes adverse effects observable in test animals.

Congenital malformation: Abnormality in fetal development, especially when it is a structural defect.

Peripheral neuropathy: Peripheral nervous system disease.

Necrosis: Irreversible death of body tissue due to insufficient blood supply, whether from injury, radiation or chemicals. The condition is called gangrene when the tissue is dead in several areas.

Harmful: Harmful, pernicious or damaging element or substance; a substance that in certain doses and circumstances can be harmful to human health or cause alterations in the environment.

NOAEL (No Observable Adverse Effect Level): The NOAEL is defined as the greatest concentration or amount of substance that causes no observable damage in test animals under defined conditions.

Pesticide: Any substance or mixture of substances intended to destroy, prevent, repel, or mitigate any pest. The term pesticide can be used to designate compounds that are herbicides, fungicides, insecticides, or any other substances used to control pests. It may be a chemical substance, biological agent (such as a virus or bacteria), antimicrobial, disinfectant used against pests such as insects, fungi, viruses, bacteria or to eliminate plant pathogens or microorganisms.

Pesticides can be classified according to the chemical family to which they belong. The most important are:

- Organophosphate
- Organochlorinated
- Carbamates
- Triazines

Danger: A biological, chemical or physical agent that may cause a harmful effect to the health under defined conditions.

Dangerous: A dangerous material is any solid, liquid or gaseous substance whose physical, chemical or biological characteristics may cause damage to humans, the environment and the property. It could be classified according to its LD 50:

- Extremely dangerous
- Highly dangerous
- Moderately dangerous
- Slightly dangerous

Intrinsic danger: A danger that is proper, constitutive, internal or characteristic of an element or substance itself and not by external causes.

Risk: Depending on the specific scientific area, different definitions are often used, which generally do not conceptually differ between themselves. From a toxicological point of view, the risk is a function of the danger and of the exposure to that danger:

RISK = f (EXPOSURE, DANGER)

In order for a risk to exist, exposure to a dangerous substance and that exposure representing a health hazard are needed. Both the danger and the exposure are needed, if any of them is equal to zero then there is no risk.

Sensitizing substances: Substances and preparations that by inhalation or skin penetration can cause a reaction of hypersensitization in such a way that a further exposure to the substance or preparation causes characteristic negative effects.

Toxicity: The toxicity occurs every time that a substance comes into contact with a body surface such as the skin, eyes or mucosa of the digestive or respiratory system. The dose of the chemical or quantity with which it comes into contact is important to analyze how "toxic" a substance can be.

Acute toxicity: The acute toxicity determines the effects of a single and very high dose of a substance. Usually, the end of the test is the animal's death. The acute toxicity is expressed by the lethal dose 50 (LD 50), which represents more or less the dose of the substance that causes death in 50% of the animals.

Chronic toxicity: Long term toxic effects that can be kept at about the tenth part of the average life of the species. They are related to changes in the metabolism, growth or survival skills (death and reduction of the reproductive capacity).

Toxic: Any physical or chemical agent that alters any fundamental biochemical balance for life. The dose is the poison, not the substance.

Toxic substances are classified according to their LD 50 or LC 50:

- Very toxic
- Harmful
- Warning

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http://eur–lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31967L0548:ES:HTML

6. Guideline 1999/45/CE of the European Parliament and the Council of May 31, 1999 on the approximation of the legal provisions, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous substances.

http://eur–lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31999L0045:ES:HTML

7. Regulation (CE) N° 1272/2008 of the European Parliament and the Council of December 16, 2008 on classification, labelling and packaging of substances and mixtures, which amends and repeals Guidelines 67/548/CEE and 1999/45/CE and modifies Regulation (CE) Nº 1907/2006.

http://eur–lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:01:ES:HTML

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12. Appendix - About the Author

By Francisco C. Decono

Juan Ignacio Pina eis a young Agricultural Engineer graduated in 2006 from the Faculty of Agronomy of the University of Buenos Aires -FAUBA-. He is a Member of the Subcommittee of Plant Protection Products of ILSI Argentina.

He has a strong academic background; Second Level Master in Technologies for the Transformation of Food Products of the Faculty of Agriculture - University of Perugia, Italy (2006 - 2007), graduated "cum laude"; Bachelor on Agri-food Management (2000 - 2007 FAUBA). He also participated in an exchange program with the Autonomous University of Madrid, Spain in 2003.

Since 2008 he has worked in the area of Regulatory Affairs at recognized producers and marketers of plant protection products. He currently works as Regulatory Affairs Coordinator of Crop Protection and Lawn & Garden areas for Argentina at Syngenta Agro S.A.

He performs educational activities since he was a student – 2000. Currently he is First Teaching Assistant of Agri-food Systems - FAUBA- since 2006 to date in Workshop III of Agricultural Engineering and Management of Agri-food Chains of the Degree Course in Agri-food Management.

Other areas of expertise include Coordination of Working Teams and participation in research projects of the FAUBA and the University of Bologna.

He is a member of both the Subcommittee of Good Agricultural Practices of the Professional Council of Agricultural Engineering and the Technology Commission of the Chamber of Agricultural Health and Fertilizers (CASAFE).

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Argentina

Toxicological Classification and Labelling of Plant Protection Products.

Local and International Regulatory Criteria.

Juan Ignacio Pina

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