Brazilian Regulation on Pesticides

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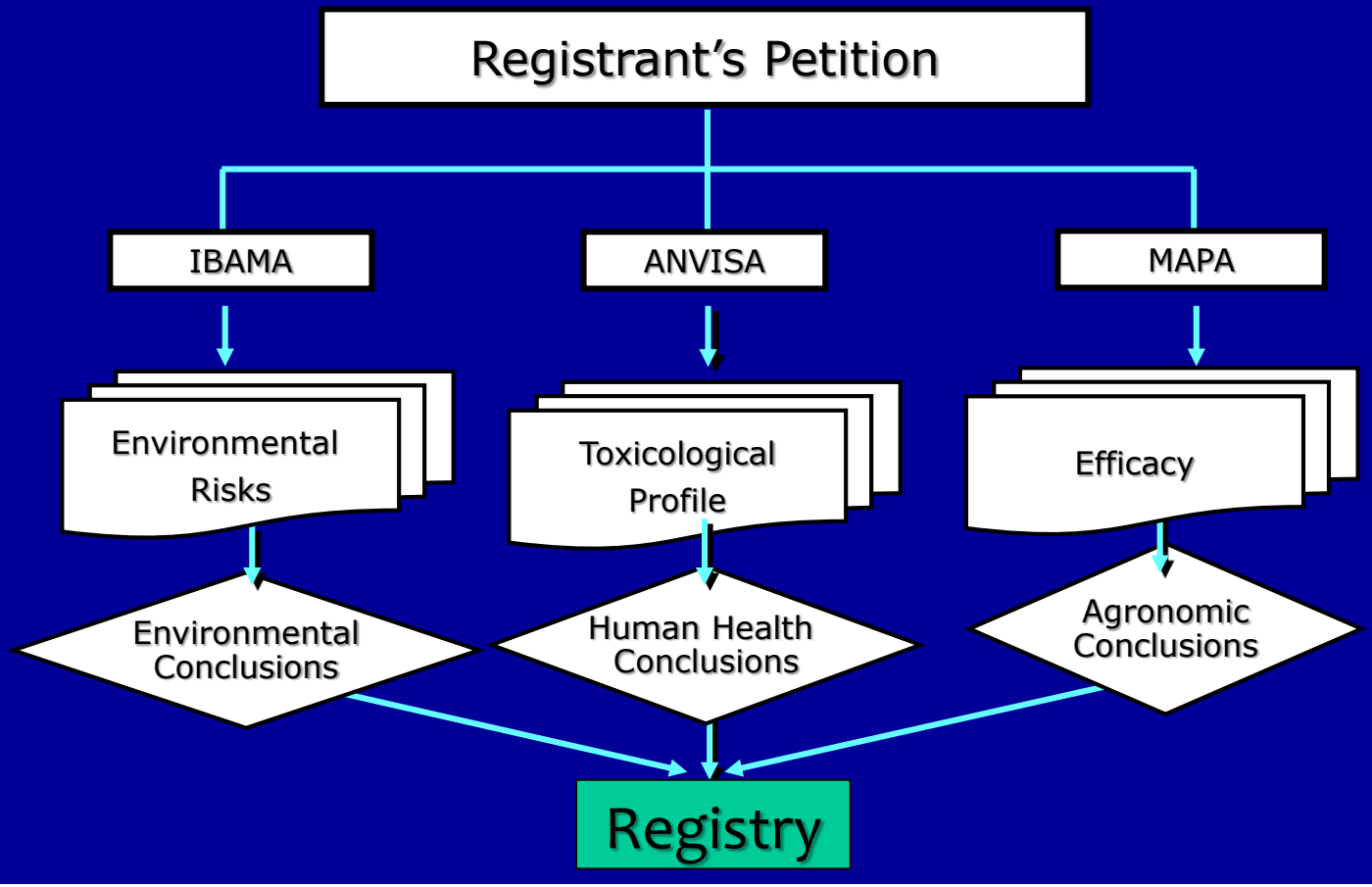
Overview of the Pesticides Registration Process

- Law 7802, July 11 of 1989
- Decree 4074, January 4th of 2002

- Art. 3º from the Law

The pesticides can only be produced, exported, imported, marketed and used if previously registered at the federal agency in accordance with the guidelines and requirements of federal agencies responsible for the health, the environment and agriculture.

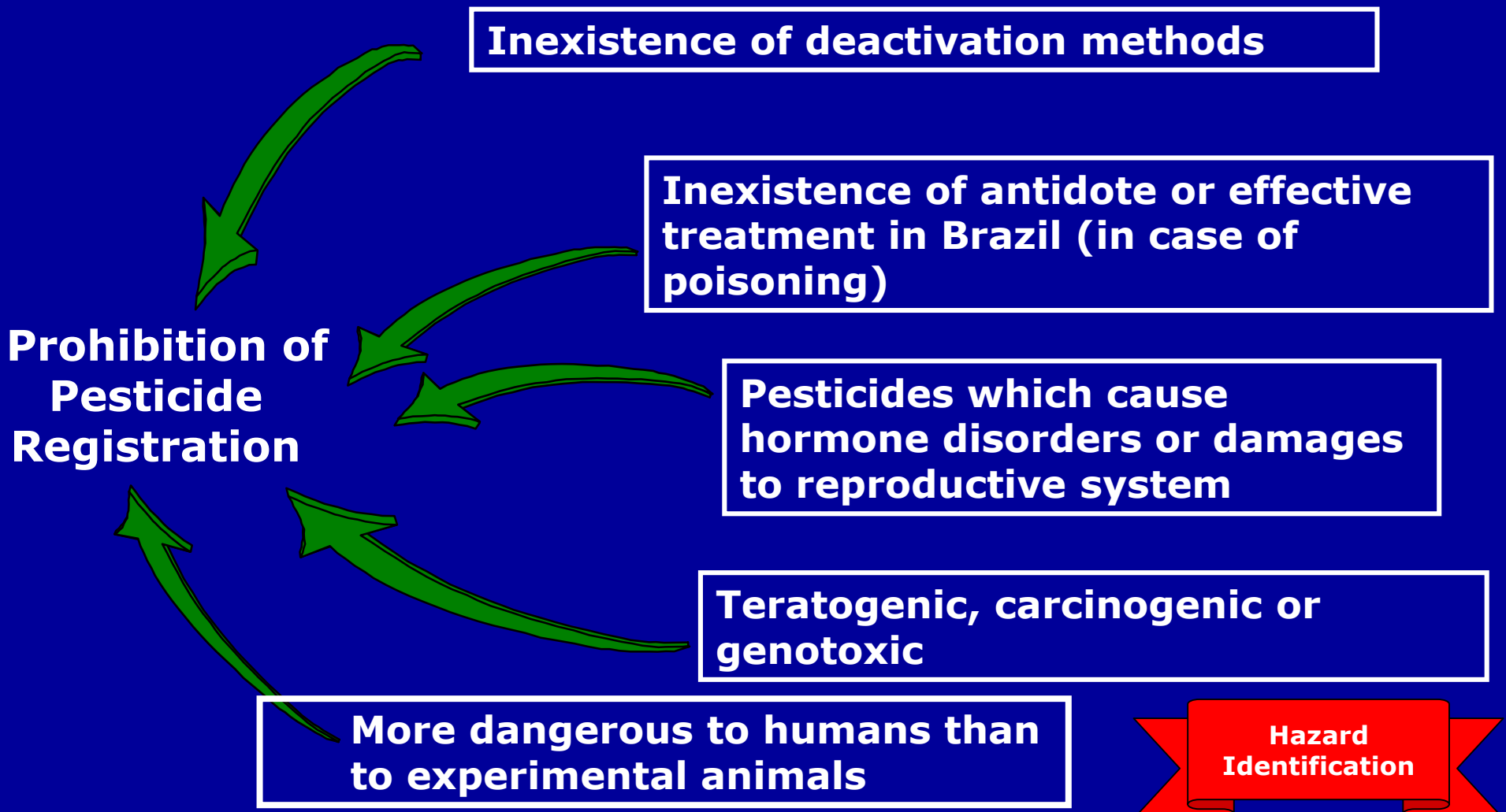
Overview of the Pesticides Registration Process



Anvisa's approach of Risk Assessment

The risk assessment in the context of health, is Anvisa responsibility and is only applied to pesticides that do not fall within the cut off criteria according to the Law nº 7.802/1989

Cut-off Criteria (according to the Law nº 7802/1989)



Hazard Identification of the Technical Products

Requirements for the toxicological assessment of the technical products

- ✓ Registrant Petition
- ✓ Identity of the product
- ✓ Physical and chemical characterization
- ✓ Toxicological studies

Toxicological and toxicokinetic Studies

Acute oral toxicity (oral LD50) ;
Acute dermal toxicity (LD50 skin) ;
Acute inhalation toxicity (LC50 inhalation) ;

Corrosion / acute skin irritation;
Corrosion / irritation acute;
Skin sensitization;

Studies on absorption, distribution, metabolism and excretion (ADME) in mammals and in vitro metabolism;

Mutagenicity studies to:

a. Gene Mutation Study in bacterial cells;
b. Gene Mutation Study in vitro mammalian cell;
c. Study chromosomal damage in vitro in mammalian cells; and
d. Study of chromosomal damage in vivo in somatic cells.

Oral repeated dose toxicity

a. oral repeated dose toxicity for ninety (90) days in rats;
b. oral repeated dose toxicity for ninety (90) days in mice;
c. oral repeated dose toxicity for ninety (90) days in non-rodents;
d. skin toxicity with repeated doses 21/28 (twenty-one / twenty-eight) days; and.
Study with repeated doses by other means;

Studies of chronic toxicity in rats

Carcinogenicity studies conducted in rats.
Carcinogenicity studies conducted in mices
Reproductive toxicity study for two generations or reproductive toxicity study of an extended generation, conducted with mice;
Toxicity study on prenatal development in mice;
Toxicity study on prenatal development in rabbits;
Neurotoxicity studies;
Study mode and / or mechanism of action;
Metabolism study in plants; and

Additional studies.

Labeling and Classification of the Formulated Products

Toxicological classification of the product is done according to the most restrictive acute study, following criteria of Ordinance No. 03/92.

CLASSIFICAÇÃO TOXICOLÓGICA

Classificação	DL_{50} Oral (mg/kg)		DL_{50} Dérmica (mg/kg)		CL_{50} Inalatória (mg/L/4h)	Irritação Dérmica	Irritação Ocular
	Sólido	Líquido	Sólido	Líquido			
Classe I Extremamente Tóxico	≤ 5	≤ 20	≤ 10	≤ 40	≤ 0,2	Ulceração ou corrosão na pele	**Opacidade** da córnea reversível ou não dentro de 7 d ou irritação persistente nas mucosas oculares
Classe II Altamente Tóxico	> 5 ≤ 50	> 20 ≤ 200	> 10 ≤ 100	> 40 ≤ 400	> 0,2 ≤ 2	Irritação severa, Draize-Cools ≥ **5**	**Sem** opacidade da córnea; irritação da mucosa ocular reversível em **7dias**.
Classe III Medianamente Tóxico	> 50 ≤ 500	> 200 ≤ 2000	> 100 ≤ 1000	> 400 ≤ 4000	> 2 ≤ 20	Irritação moderada, Draize-Cools ≥ **3** < **5**	**Sem** opacidade da córnea; irritação da mucosa ocular reversível em **72 h**.
Classe IV Pouco Tóxico	> 500	> 2000	> 1000	> 4000	>20	Irritação leve, Draize-Cools < **3**	**Sem** opacidade da córnea; irritação da mucosa ocular reversível em **24 h**.

Formulated products (PF) Requirements:

Quali-quantitative (range max / min / function)

- Declaration and laboratory Report
- Label template and leaflet
- Use display - and target culture
- Product mode of action
- Type of Employment - pre or post-emergence ...

Formulated products (PF) Requirements:

- Recommended Dose - Preparing the sauce
- Application Equipment
- Time, number and range of applications - According waste study

Final product, ready for use by the consumer

They have commercial name

Requirements for toxicological evaluation of formulated products

toxicological studies

- Acute oral toxicity (oral LD50);
- acute dermal toxicity (dermal LD50);
- acute inhalation toxicity (inhalation LC50);
- corrosion / acute eye irritation;
- corrosion / acute skin irritation;
- skin sensitization;
- mutagenicity studies:
  a. Gene Mutation Study in bacterial cells; and
  b. Study chromosomal damage in vitro in mammalian cells.
- Other studies.

- Residues Studies

Anvisa's approach of Risk Assessment

Public Consultation # 87

Currently the actions of Anvisa in the regulatory process of pesticides in Brazil are regulated by the Ordinance 3 of the National Health Surveillance Secretariat, 1992

Public Consultation # 87

Proposes an update of the requirements and criteria for evaluation and toxicological classification, risk assessment, the content of toxicological information on labels and leaflets and procedures for post-registration of pesticides change, their components and related products and wood preservatives within the Anvisa.

Innovations in risk assessment brought by Public Consultation # 87

Current Scenario

- Hazard Identification
- Dose-response analysis
- Exposure evaluation

  ✓ Dietary Chronic Risk Assesment in the registration process

- Risk Caracterization

Scenario arising

- Hazard Identification
- Dose-response analysis

  ✓ Update Anvisa classification criteria

  ✓ Current technical and scientific knowledge

Scenario arising

- Exposure evaluation
  - ✓ Dietary Chronic Risk Assesment in the registration process
  - ✓ Dietary Acute Risk Assesment in the registration process
  - ✓ Assessment of occupational exposure
- Risk Caracterization
- Risk communication improvement
- Improved decision-making

Scenario arising

- Application of the risk assessment in pesticide residue monitoring program

  - ✓ Acute and Chronicle Dietary risk assessment in post registration processes

  - ✓ Improvement of the Risk Communication

- Use the risk assessment on pesticide reassessment based on the food residue monitoring data.

Scenario arising

pesticides of classification based on acute toxicity

Via de exposição		Categoria 1 Extremamente toxico	Categoria 2 Altamente toxico	Categoria 3 Medianamente tóxico	Categoria 4 Pouco Tóxico
Oral (mg/kg p.c.)		≤ 5	>5 - ≤50	>50 - ≤300	>300
Cutânea (mg/kg p.c.)		≤ 50	>50 - ≤200	>200 - ≤1000	>1000
Inalatória	Gases (ppm/V)	≤ 100	>100 - ≤500	>500 - ≤2500	>2500
	Produtos sólidos e líquidos (mg/L)	≤ 0,05	>0,05 - ≤0,5	>0,5 - ≤1,0	>1,0

p.c. = peso corpóreo;
ppm/V = partes por milhão por volume

Some Challenges

- Consolidation of public consultation contributions
- Analysis team training
- Suit and rank products already registered
- Development of an occupational exposure model that reflects the conditions of tropical agriculture
- And so I goes…

THANK YOU!

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General Office of Toxicology - GGTOX

National Agency of Health Surveillance - ANVISA