State regulation of pesticides in Ukraine. Toxicological aspects

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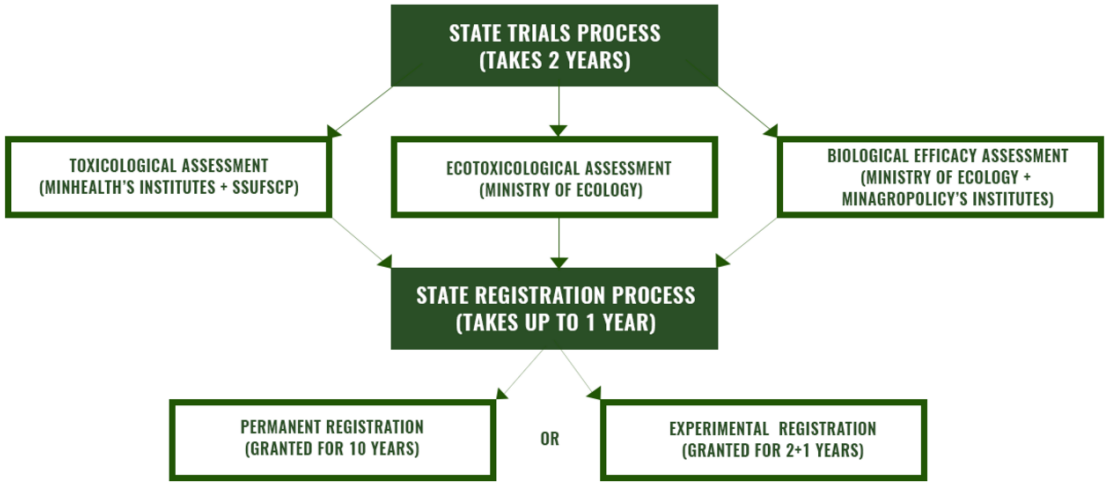
STATE TRIALS AND STATE REGISTRATION

Before the product comes to the market it shall be assessed and registered



Garmonization with EU legislations

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Association Agreement
between the European Union and the European Atomic Energy Community and their member states, of the one part, and Ukraine, of the other part

Accreditation and authorization

Registration trials	*Accreditation*	*Authorization*
Biological (efficacy)	**-** **GEP ?**	**National Academy of Agrarian Science *and* Ministry of Ecology**
Ecotoxicologycal	**-**	**Ministry of Ecology**
Toxicological	**GLP**	**Ministry of Health**
Field studies (residues and OE)	**ISO 17025** **GLP ?**	**Ministry of Health**

Accreditation and authorization

SNAS SLOVAK NATIONAL ACCREDITATION SERVICE

Karloveská 63, 840 00 Bratislava 4, Slovak Republic

STATEMENT
OF GLP COMPLIANCE

No. G-042

Slovak National Accreditation Service certifies

conformity with GLP according to the Law No. 67/2010 Coll, the OECD Principles of GLP and Directive 2004/10/EC, of the European Parliament and of the Council, in the test facility:

L.I. Medved's Research Center of Preventive Toxicology, Food and Chemical Safety, Ministry of Health, Ukraine
Center for preventive and regulatory toxicology
Heroiv oboroni 6, 03023 Kiev, Ukraine
ID number: 01897914

Area of expertise: Toxicology studies, toxicokinetics studies, mutagenicity studies, physical-chemical studies, field studies.

The above mentioned test facility is included in the Slovak National GLP Compliance Programme and is inspected by Slovak National Accreditation Service on a regular basis.

Prof. Mykola Prodanchuk MD - director, is the statutory body of the test facility, who manages and represents it and acts on its behalf.

This statement is granted on 09.03.2015 and is valid until 09.03.2020.

Bratislava, 09.03.2015

SLOVENSKÁ NÁRODNÁ AKREDITAČNÁ SLUŽBA
SNAS

Martin S e n č á k
Director

ЕКОГІНТОКС

GLP accredited studies

- OECD 402 OECD Guideline for Testing of Chemicals «Acute Dermal Toxicity”
- OECD 403 OECD Guideline for Testing of Chemicals «Acute Inhalation Toxicity”
- OECD 404 OECD Guideline for Testing of Chemicals «Acute Dermal Irritation/Corrosion”
- OECD 405 OECD Guideline for Testing of Chemicals «Acute Eye Irritation/Corrosion”
- OECD 492 «In vitro Eye Irritation»
- OECD 431 «In vitro Skin Corrosion»
- OECD 439 «In vitro Skin Irritation»
- OECD 406 OECD Guideline for Testing of Chemicals “Skin Sensitisation”
- OECD 420 Acute Oral Toxicity – Fixed Dose Procedure”
- OECD 421 “Reproduction/developmental toxicity screening test”
- OECD 422 Combined Repeated Dose Toxicity Study Reproduction/Developmental Toxicity Screening Test”
- OECD 423 Acute Oral Toxicity – Acute Toxic Class Method
- OECD 425 Acute Oral Toxicity: Up-and-Down Procedure
- OECD 426 OECD Guideline for Testing of Chemicals “Developmental Neurotoxicity Study”
- OECD 408 OECD Guideline for Testing of Chemicals „Repeated Dose 90-day Oral Toxicity Study in Rodents”
- OECD 410 OECD Guideline for Testing of Chemicals "Repeated Dose Dermal Toxicity: 21/28-day Study"
- OECD 451 OECD Guideline for Testing of Chemicals „Carcinogenicity Studies”
- OECD 452 OECD Guideline for Testing of Chemicals „Chronic Toxicity Studies”
- OECD 453 OECD Guideline for Testing of Chemicals „Combined Chronic Toxicity\Carcinogenicity Studies„
- OECD 414 OECD Guideline for Testing of Chemicals „Prenatal Developmental Toxicity Study” in Rodents
- OECD 443 reproductive block of “Extended One-Generation Reproductive Toxicity Study”
- OECD 424 OECD Guideline for Testing of Chemicals „Neurotoxicity Study in Rodents”
- OECD 471 OECD Guideline for Testing of Chemicals „Bacterial Reverse Mutation Test”
- OECD 474 OECD Guideline for Testing of Chemicals „Mammalian Erythrocyte Micronucleus Test”
- OECD 475 OECD Guideline for Testing of Chemicals „Mammalian Bone Marrow Chromosome Aberration Test”
- OECD 489 In Vivo Mammalian Alkaline Comet Assay
- OECD 487 In Vitro Mammalian Cell Micronucleus Test

Formulations data requirements

	Regulations/ Guidelines
Acute oral toxicity **(on 1-2 species of animals, rats, mice)**	**OECD 420 (FDP)** **OECD 423 (ATC)** **OECD 425 (UDP)**
Acute dermal toxicity **(for 1 animal, rat or rabbit)**	**OECD 402**
Acute inhalation toxicity **(for 1 species of animals, rats)**	**OECD 403**
Irritating to skin *and* **mucous membranes of the eyes**	**OECD 404,** ***OECD 431***, ***OECD 439*** **OECD 405,** ***OECD 492***
Sensitizing properties	**OECD 406, OECD 429**

Generic a.i. data requirements *(biological equivalence)*

Dossier	**Must have all sections from physicochemical parameters to toxicological and hygienic characteristics of the active substance and the formulation.** **The same requirements as to the original a.i.**
Toxicological section of the dossier	**Should include separate subsections of open data analysis on acute, subchronic and chronic toxicity, irritating and sensitizing properties, mutagenic, carcinogenic and teratogenic activity, reproductive toxicity of a.i.**
Own data for active ingredient - generic	**Original protocols of acute toxicity with various routes of entry into the body, irritating and sensitizing properties, subchronic toxicity and mutagenic activity**

Generic a.i. data requirements *(biological equivalence)*

If the lowest dose for ADI calculation obtained by the long-term effects (carcinogenicity, teratogenicity, reproductive toxicity)

+

experimental studies on the limiting effect

Generics (examples): acetamiprid

90-Day oral toxicity in rats
NOAEL: 12.4 mg/kg/day (bodyweight decrease and liver effects - increased weight and centrilobular hepatocyte hypertrophy)
90-Day oral toxicity in mice
NOAEL: 106.1 mg/kg/day(body and liver weight changes)
90-day dog study
NOAEL: 13 mg/kg/day (growth retardation in ♂)
Long term toxicity/Carcinogenicity in rats
the systemic NOAEL: 7.1 mg/kg/day (body weight reductions in ♀ and histopathological changes in the liver in ♂)
NOAEL for carcinogenic effects: 7.1 mg/kg/day (an increased incidence of adenocarcinoma in the mammary gland)
Reproductive toxicity (2-generation study), rats
Parental systemic NOAEL: 17.9 mg/kg /day offspring NOAEL: 17.9 mg/kg/day reproductive NOAEL: 51 mg/kg/day
Developmental rat study
maternal NOAEL: 16 mg/kg/day, developmental NOAEL: 16 mg/kg/day
acute neurotoxicity rat study
NOAEL: 10 mg/kg/day (♂/♀)
subchronic neurotoxicity rat study
systemic NOAEL: 14,8 mg/kg/day
rat developmental neurotoxicity study
NOAEL: 2,5 mg/kg/day (↓auditory startle responses)
ADI= 0.025 mg/kg/day) (Rat developmental neurotoxicity study NOAEL=2,5 mg/kg/d, UF=100.

Generics (examples): acetamiprid

ADI – 0,025 mg/kg/day

Lowest NOAEL **2,5 mg/kg/day** *(Rat developmental neurotoxicity study)*

Acute toxicity, irritating and sensitizing properties, subchronic toxicity, mutagenic activity

and

OECD 426 Developmental Neurotoxicity Study

Generics (examples): imidacloprid

ADI – 0,06 mg/kg/day

Lowest NOEL **5,7 mg/kg/day** *(Rat, systemic toxicity, chronic toxicity study)*

Acute toxicity, irritating and sensitizing properties, subchronic toxicity, mutagenic activity

Köszönöm a figyelmet!

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