CEUREG XXII Forum,
Session IV

Latest Changes to the Plant Protection Products Regulation in Russian Federation

V.N. Rakitskii, T.A. Sinitskaya, G.V. Masaltsev

"FSCH named after F.F. Erisman" of the Rospotrebnadzor

29-30 October 2018

Vienna, Austria

Summary of Legislative and Regulatory Acts

- Federal Law «On safe handling of pesticides and agrochemicals» (on 19.07.1997 № 109-FL with revisions).
- Federal Law «On sanitary-epidemiologic population wellbeing» (on 30.03.1999 № 52-FL, with revisions).
- Federal Law «On quality and safety of food» (on 02.01.2000 №29-FL).
- Federal Law «On technical regulation» (on 27.12.2002 № 184-FL).
- Federal Law «On consumer rights protection» (in edit. Federal Laws on 09.01.1996 № 2-FL, on 17.12.1999 № 212-FL).
- Uniform sanitary-epidemiologic and Hygienic requirements for goods, which are subject to sanitary-epidemiologic surveillance (control), approved by the Decision of the Customs Union Commission on 28.05.2010, № 299.
- Decision of the Customs Union Commission № 721 «On the application of international standards, recommendations and guidelines» on 22.06.2011.
- Russian Federation Government Act «On provision of harmonization of the Russian sanitary-epidemiologic requirement, veterinary-sanitary and phytosanitary measurements with international standards» on 28.09.2009 № 761.

Summary of Legislative and Regulatory Acts (Cont.)

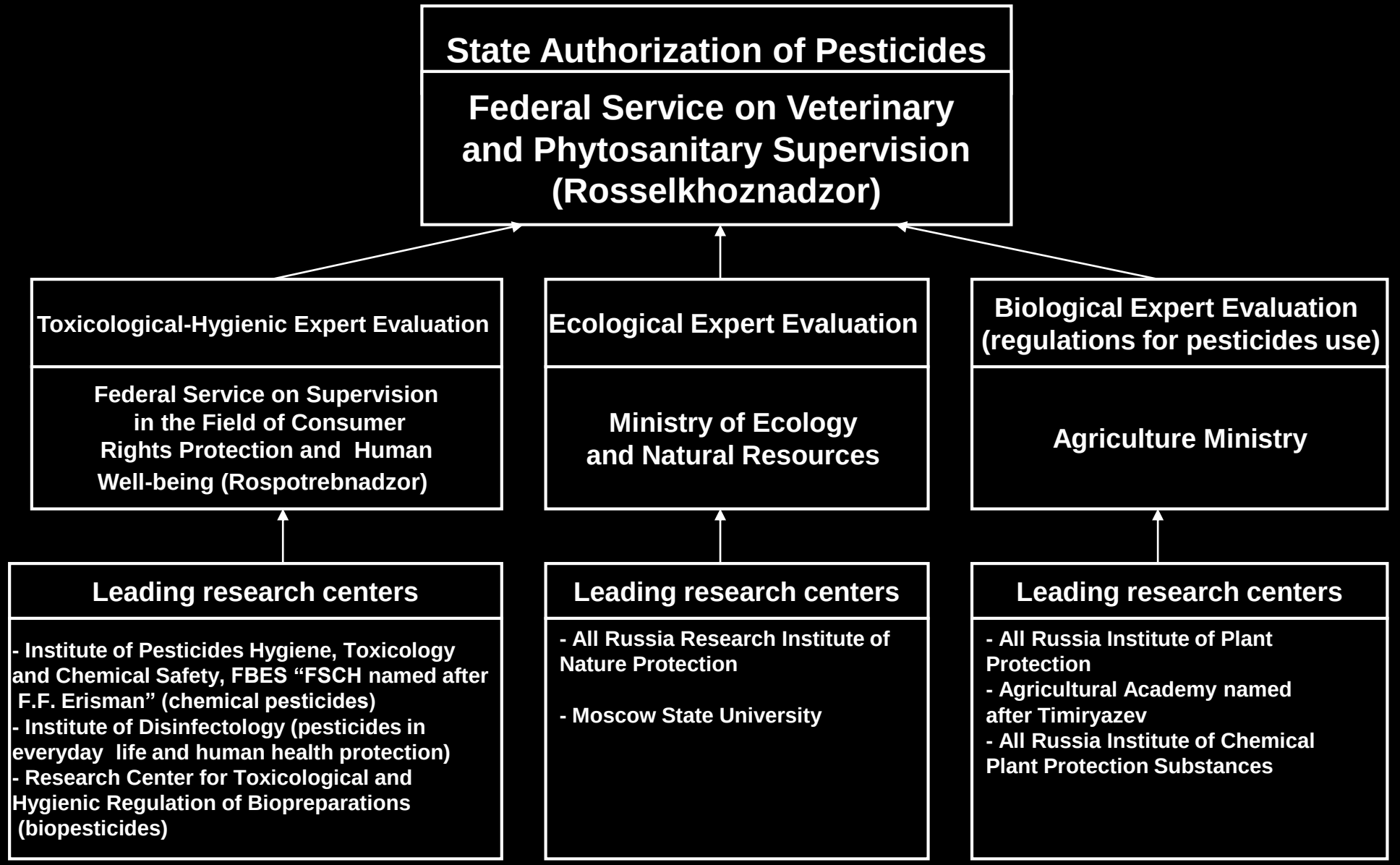
- Order of the Federal Agency on Consumer Rights Protection and Human on 01.08.2006 № 225 «On sanitary-epidemiologic expert evaluation of pesticides and agrochemicals».
- «Hygienic requirements for the safety of the processes of evaluation, storage, transportation, offtake, application, deactivation and disposal of pesticides and agrochemicals». Sanitary rules and norms. SanR&N 2.2.2584-10.
  - Enacted by the Head Government Sanitary Physician of the Russian Federation' Act from 25.05.2010.
- «Hygienic requirements for the safety and nutritional value of food.» Sanitary rules and norms. SanR&N 2.3.2.1078-01.
  - Enacted by the Head Government Sanitary Physician of the Russian Federation' Act on 14.11.2001 № 36 from 01.09.2002.
- Hygienic Norms for pesticides content levels in objects of the environment. HN 1.2.3539-18. Enacted by the Head Government Sanitary Physician of the Russian Federation' Act on 10.05.2018 № 33.

These documents are accepted by the experts of the Customs Union countries and are enacted as intergovernmental normative acts by the Decision of the Customs Union Commission.

Summary of Legislative and Regulatory Acts (Cont.)

- «The scientific justification for maximum residue levels of pesticides in food.» Methodology Guidelines MG 1.2.2960-11, 29.07.2011.
- «Risk assessment of the effects of pesticide residues in food on population». Methodology Guidelines MG 1.2.3216-14, 22.08.2014.
- Hygienic recommendations for study of quality of pesticide-treated food. № 01-19/139-17 on 29.12.1995.
- Hygienic classification of pesticides according to the degrees of hazard (Annex № 1 to SanR&N 1.2.2584-10, enacted on 02.03.2010).
- Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC.
- Codex Alimentarius Commission. Procedural Manual (Joint FAO/WHO Food Standards Programme).

System of State Authorization of Pesticides in the Russian Federation



HYGIENIC CLASSIFICATION OF PESTICIDES

(SanR&N 1.2.2584-10, 3d version 1996, 2001 and 2010)

a) General toxicity and stability in soil

(Publication is in Regulatory Toxicology and Pharmacology 28, 79-84, 1998)

	CLASS OF HAZARD			
INDEX	**1**	**2**	**3**	**4**
	Extremely hazardous	**Highly hazardous**	**Moderately hazardous**	**Slightly hazardous**
Mean lethal dose after intragastric administration, mg/kg	**< 50**	**51-200**	**201-1000**	**> 1000**
Mean lethal dose after skin application, mg/kg	**< 100**	**101-500**	**501-2000**	**> 2000**
Mean lethal concentration in the air, mg/m^3	**< 500**	**501-2000**	**2001-20000**	**> 20000**
Stability (soil)	**Time of degradation to non-toxic components > 1 year**	**Time of degradation to non-toxic components- 6-12 month**	**Time of degradation to non-toxic components – 2-6 month**	**Time of degradation to non-toxic components during 2 month**

Effect	1	2	3		4
			3A	3B	
Skin irritation	Skin lesions followed by scab formation, severe edema spreading beyond a targeted section by more than 1 mm, and abrupt hyperemia. These symptoms of irritation are maintained for more than 3 days.	Pronounced erythema and edema (1 mm rising). These symptoms are maintained during not less than 3 days.	Evident erythema and/or edema. These signs of irritation are maintained during not less than 2 days.	Weak (hardly discernible) erythema and/or edema. These symptoms of irritation disappear for 1 day.	No irritating action.
Irritating effect on eyes mucous membranes	Lesions (irreversible) of eye tissues or very pronounced hyperemia of conjunctive, pronounced edema – lids are nearly completely closed, cornea is opaque, iris is not visible, no response to light, very intense excretions moisten lids and skin around eyes. These signs of irritation are maintained for more than 3 days.	Pronounced hyperemia of conjunctive and cornea (deep diffusive reddening), evident edema: lids are half closed; cornea is opaque, iris is not visible, reaction towards light is maintained; intense excretions moisten lids and skin around eyes. These signs of irritation are maintained during not less than 3 days.	Evident hyperemia of conjunctive and cornea (some vessels are poorly discernible), edema with partial lids turning inside out, iris details are poorly discernible, eyes excretions moisten lids. These symptoms are maintained for not less than 2 days.	Weak hyperemia of conjunctive and/or cornea (vessels are injected), not pronounced edema, much eye moistening. These signs of irritation disappear during a day.	No irritating action.

Notes: Experimental animals are rabbits (3-6 animals in group).
Reaction is considered significant if it is evident for not less than 34% of animals.
Periods of observation of experimental animals: 14 –21 days after the exposure.

b) Allergic reactions

1	2		3		4
Sufficient evidence of allergic reactions in humans in epidemiological studies and/or in clinico-allergologic	**Limited evidence of allergic reactions in humans in epidemiological studies and/or in clinico-allergological studies (when the possibilities of specific allergo-tests are limited) together with sensitizing effects in experimental animals**		**Sufficient evidence of sensitizing effect in experimental animals**		**Lack of sensitizing effect in the standard set of tests**
studies confirmed by specific allergo-tests together with/or without evidence of sensitizing effects in experimental animals	**<u>Subclass 2A</u> Sufficient evidence of an extremely strong sensitizing effect in experimental animals: positive effect is produced by all methods of sensitization in 100% animals with high statistical significance (P < 0.001-0.01) of differences between the indices of specific allegro-tests *in vivo* and *in vitro***	**<u>Subclass 2B</u> Sufficient evidence of a strong sensitizing effect in experimental animals: positive effect is produced by all methods of sensitization in 50% animals with statistical significance (P < 0.01-0.05) of differences between the indices of specific allergo-tests *in vivo* and *in vitro***	**<u>Subclass 3A</u> Moderate allergen: sensitizing effect in more than 30% experimental animals with statistical significance (P < 0.05) of differences in the most sensitive specific allergo-tests *in vivo* and *in vitro***	**<u>Subclass 3B</u> Weak allergen: sensitizing effect in less than 30% animals without statistical significance in specific allergo-tests *in vivo* and *in vitro***	

c) Teratogenicity, embriotoxicity, reproduction toxicity

	1	2	3	4
Teratogenicity* * If multiple or rare anomalies are observed, the compound can be upgraded to a higher class of hazard	**Teratogenicity in humans is proven in epidemiological studies or, exceptionally, in isolated observations in humans together with evidence of dose response teratogenicity in experimental animals including doses non-toxic for the mothers**	**Dose-response teratogenicity in descendants including doses non-toxic for the mothers together with significant increase of anomalies in animals at dose-levels toxic for the mothers**	**Teratogenic effects in descendants at dose-levels toxic for the mothers**	**Lack of teratogenicity in the frame of standard set of tests**
Embryotoxicity* * If multiple or rare embryotoxic effects are observed, the compound can be upgraded to a higher class of hazard	**Embryotoxicity in humans is proven in epidemiological studies or, exceptionally, in isolated observations in humans together with dose-response embryotoxicity in experimental animals including doses non-toxic for the mothers**	**Dose-response embryotoxicity in experimental animals including doses non-toxic for the mothers, or embryotoxic effects exceeding spontaneous background in experimental animals at dose-levels toxic for the mothers**	**Some embryotoxic effects at dose-levels toxic for the mothers**	**Lack of embryotoxicity in standard set of tests**
Reproduction toxicity* * If multiple or rare reproductive disturbances are observed, the compound can be upgraded to a higher class of hazard	**The influence on the reproductive function in humans is proven in epidemiological studies or, exceptionally, in isolated observations in humans together with dose-response reproductive toxicity in experimental animals including dose-levels non-toxic for mothers and fathers**	**Dose-response alterations of the reproductive function indices in experimental animals including dose-levels non-toxic for mothers and fathers, or reproductive disturbances exceeding spontaneous background in experimental animals at dose-levels toxic for mothers and fathers**	**Influence on isolated indices of reproductive function in experimental animals at dose-levels toxic for mothers and fathers**	**Lack of the reproductive toxicity manifestations in standard set of tests**

d) Mutagenicity

1	2			3	4
Sufficient evidence of mutagenicity in humans in epidemiological studies (mutations	**The degree of evidence of mutagenicity in humans varies from, on the one hand, almost sufficient to, on the other hand, their complete absence together with sufficient evidence of mutagenicity in mammals**			**Sufficient evidence of mutagenicity in standard laboratory genetic objects (non-mammals;**	**Lack of mutagenicity in standard set of tests for gene and chromosome**
in germ and somatic cells) or, exceptionally, limited evidence of mutagenicity in humans (mutations in somatic cells) together with sufficient evidence of mutagenicity in mammals (dose-effect in somatic and germ cells *in vivo*)	**<u>Subclass 2A</u> Isolated epidemiological observations of mutagenicity in human somatic cells together with dose-effect mutagenicity is somatic and germ cells of mammals *in vivo***	**<u>Subclass 2B</u> Lack of evidence in humans together with dose-effect of mutagenicity in somatic and germ cells of mammals *in vivo***	**<u>Subclass 2C</u> Lack of mutagenicity in mammals, but presence of reproducible results in mammals at dose levels lower than MTD together with sufficient evidence of mutagenicity in standard genetic tests (non-mammals; mammals and human cells cultured *in vitro*). Lack of the dose - response in vivo in mammals, but presence of reproducible positive results in mammals at a single dose lower than MTD.**	**mammals and human cultured cells *in vitro*) and/or reproducible positive results in mammals at dose-levels equal or exceeding MTD**	**mutations**

e) Carcinogenicity*

1	2			3	4
	The degree of evidence of carcinogenicity in humans varies from, at one extreme, almost sufficient to, at the other extreme, no human data but with evidence of carcinogenicity in experimental animals			Sufficient evidence of carcinogenicity in experimental animals but with mechanism of carcinogenicity	Lack of carcinogenicity in two species of experimental evidence together
Carcinogenicity in humans together with sufficient evidence of carcinogenicity in experimental animals and evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity	<u>Subclass 2A</u> Limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals - or - sufficient evidence of carcinogenicity in experimental animals together either with evidence of similar mechanism of carcinogenicity that also operates in humans or with unusual manifestations of carcinogenicity	<u>Subclass 2B</u> Limited evidence of carcinogenicity in humans together with limited evidence of carcinogenicity in experimental animals - or - sufficient evidence of carcinogenicity in experimental animals with induction of tumours in organs with low incidence of spontaneous tumours or - exceptionally - only limited evidence of carcinogenicity in humans	<u>Subclass 2C</u> Sufficient evidence of carcinogenicity in ex-perimental animals with induction of tu-mours in organs with high incidence of spontaneous tumours - or - limited evide-nce of carcinoge--nicity in experimen-tal animals together with unusual manife-stations of carcino-genicity or with ge-notoxicity - or exce-ptionally - only human data which by their degree of evide-nce are classified between limited and inadequate evidence	which does not operate in humans - or - sufficient evidence of carcinogenicity in experimental animals but only at dose levels equal or exceeding maximum tolerated dose (MTD) - or - limited evidence of carcinogenicity in experimental animals together with the lack of genotoxicity	with the lack of genotoxicity

* (The terminology is taken from the IARC classification [IARC, 1995])

Russian Model Of Pesticides Risk Assessment For Operators

Evaluation Based On Exposure Levels

SF= Iav / MAC + Dav / MAL

- **Iav –** average content of a substance in the occupational air, mg/cm^3
- **Dav** – average content wash-out from operators skin, mg/cm^2
- **MAL** (TAL of skin contamination) – maximum acceptable (tentative acceptable) level of skin contamination with a substance (mg/cm^2)
- **MAC** (TSEL) occupational air– maximum acceptable concentration (tentative acceptable) level of a substance effect in the occupational air(mg/m^3)

Evaluation Based On A Taken Up Dose

SF= (Di + Dd) / ADEL

- **Di** – taken up inhalation dose, mg/kg
- **Dd** – absorbed dermal dose, mg/kg
- **ADEL** - acceptable daily level of exposure for operators, mg/kg

RISK FOR OPERATORS IS ACCEPTABLE AT SUMMARY SF ≤ 1.

Министерство здравоохранения Российской Федерации

Федеральный научный центр гигиены им.Ф.Ф.Эрисмана

УТВЕРЖДАЮ
Первый заместитель Министра
Здравоохранения Российской Федерации
Г.Г. Онищенко
« 30 » 01 2003 г.

ОПРЕДЕЛЕНИЕ КОМПЛЕКСНЫХ НАГРУЗОК ПЕСТИЦИДОВ И АГРОХИМИКАТОВ НА ОКРУЖАЮЩУЮ СРЕДУ

Методические рекомендации

№ 2001/173

Москва 2003 г.

The Assortment Index Of The Territorial Load Of Pesticides

- The first-ever proposed method of calculating the integral measure of the assortment index of the territorial load of pesticides, which is the product of the indicator of the average annual territorial load (kg / ha) and the average estimated score, reflecting the properties of the pesticides used, according to the current hygienic classification of pesticides by degree.
- It differs from the previously used method by employing 9 indicators that take into account the general toxic effects, specific, long-term effects and persistence in the soil.

System of analytical control of pesticides

During registration-related evaluation

Accredited organizations

- development, adaptation of methods on analytical control
- detection of residues of active ingredients of pesticides in food
- monitoring
- materials for sanitary-epidemiologic conclusion

During application

Accredited laboratories

- detection of residues of active ingredients of pesticides in plant products

↓

Setting of quantity levels

↓

Conclusion regarding whether quantity levels comply with the MRL normatives

↓

Decision making

Hygienic justification of minimizing risks to the health of the population of Russia (2011-2015)

- 2 methodological documents were created on the multi-component determination of the levels of residual quantities:
  - 19 active substances - herbicides of 11 chemical classes (sulfonylureas, aryloxycarboxylic, pyridinecarboxylic, benzoic acids, imidazolines, biphenylcarboxylic ethers, chloroacetamides, etc.) based on chromatographic methods (GLC, HPLC, MSD) in water and air. MG 4.1.3085-13.
  - 27 active ingredients of pesticides in crop production based on mass spectrometry in combination with GLC and HPLC - MG. "Multiple determination of pesticides of various chemical nature in plant products." MG 4.1.3351-16
- These methodical documents allow to exclude fragmented nature of the analysis, provide a transition to a qualitatively new level of chemical safety, and provides economical benefits by increasing productivity while maintaining high metrological parameters.

Государственное санитарно-эпидемиологическое нормирование
Российской Федерации

1.2. ОБЩИЕ ВОПРОСЫ.
ГИГИЕНА, ТОКСИКОЛОГИЯ, САНИТАРИЯ

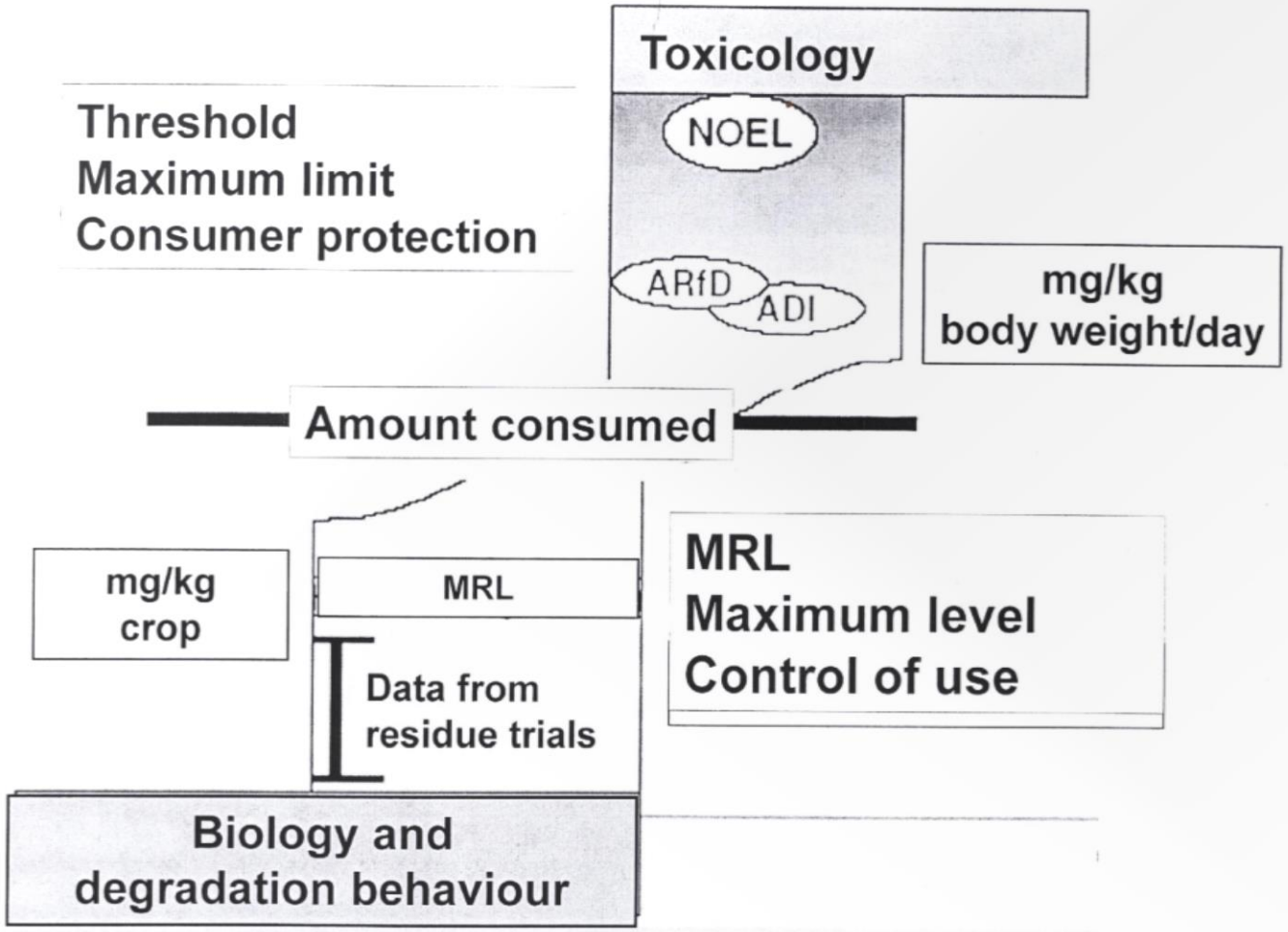
Оценка риска воздействия остаточных количеств пестицидов в пищевых продуктах на население

Методические указания
МУ 1.2.3216—14

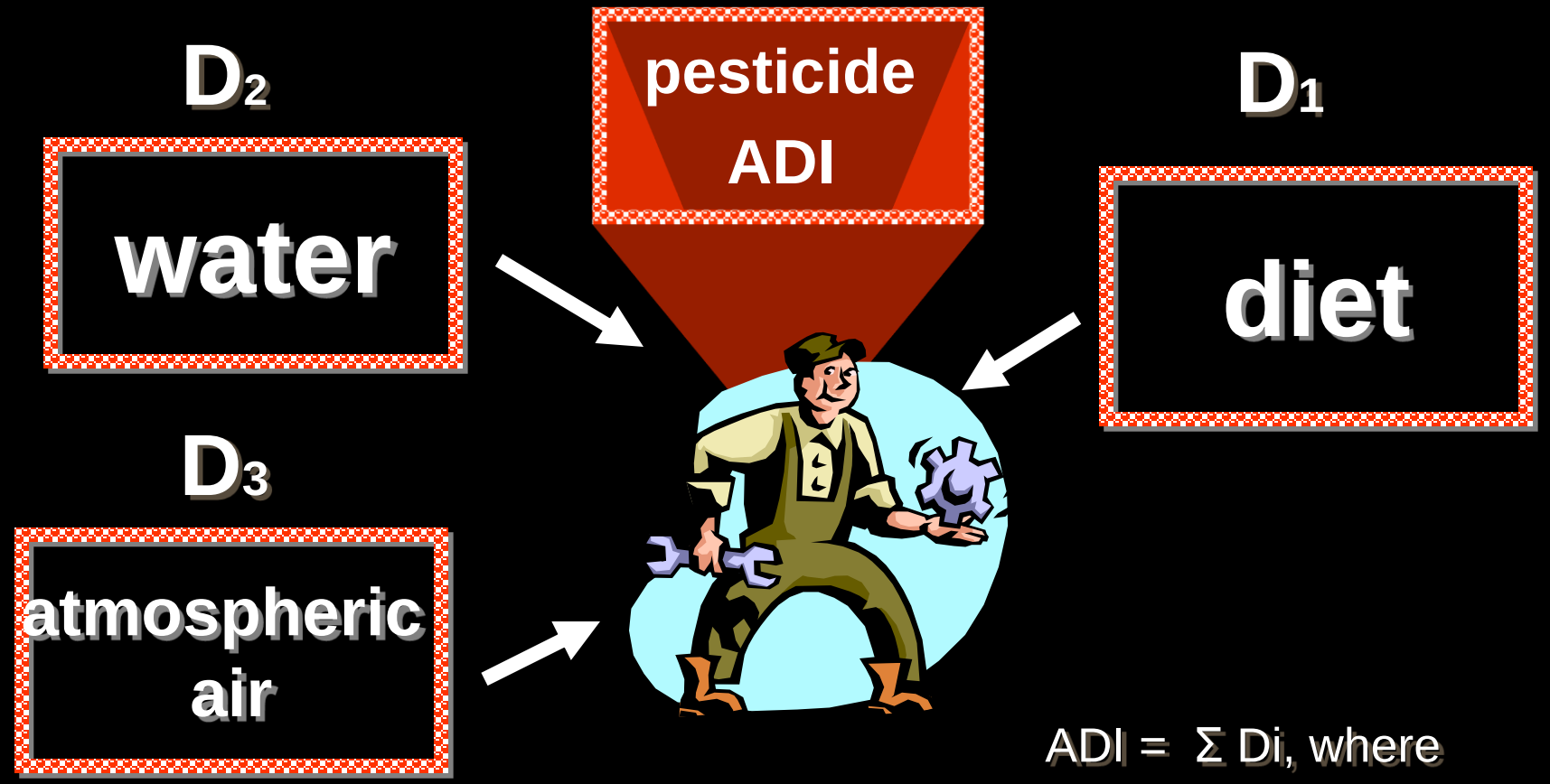
Издание официальное

Москва • 2014

Principle of dietary risk assessment



Principle of complex hygienic regulation



ADI = Σ Di, where

ADI – acceptable daily intake for an individual,

D_1 - acceptable dose which can get into a body with diet,

D_2 - acceptable dose which can get into a body with water,

D_3 - acceptable dose which can get into a body with atmospheric air.

Acceptable daily intake for man (ADI)

$$ADI = \frac{NOELch.or.}{\text{Reserve factor}} \quad \text{(mg/kg b.w.)}$$

where: **NOELch.or.** – A value of no observed effect level dose determined in chronic toxicological experiment with peroral administration

RF– reserve factor (min = 100)

When a substance is characterized by the specific and delayed effects, the reserve factor for hazardous pesticides increases up to 200 – 500 and in some cases - to 1 000 and more

Developed and harmonized according to the international standards:

3 322 MRLs

in plant commodities

EU – 1 119 MRLs

(Precedence was given to the priority lists)

CODEX ALIMENTARIUS - 2 203 MRLs

Thank You For Your Attention!