Federal Service for Veterinary and Phytosanitary Surveillance (FSVPS)

Russian State Centre for Quality and Standardization of Veterinary Drugs and Feed ("VGNKI")

The Center of the World Organization for Animal Health (OIE) for diagnosis, control of animal diseases and food safety in Eastern Europe, Central Asia and Transcaucasia

Overview of VGNKI activities in the field of national residue monitoring program of Russia and AMR

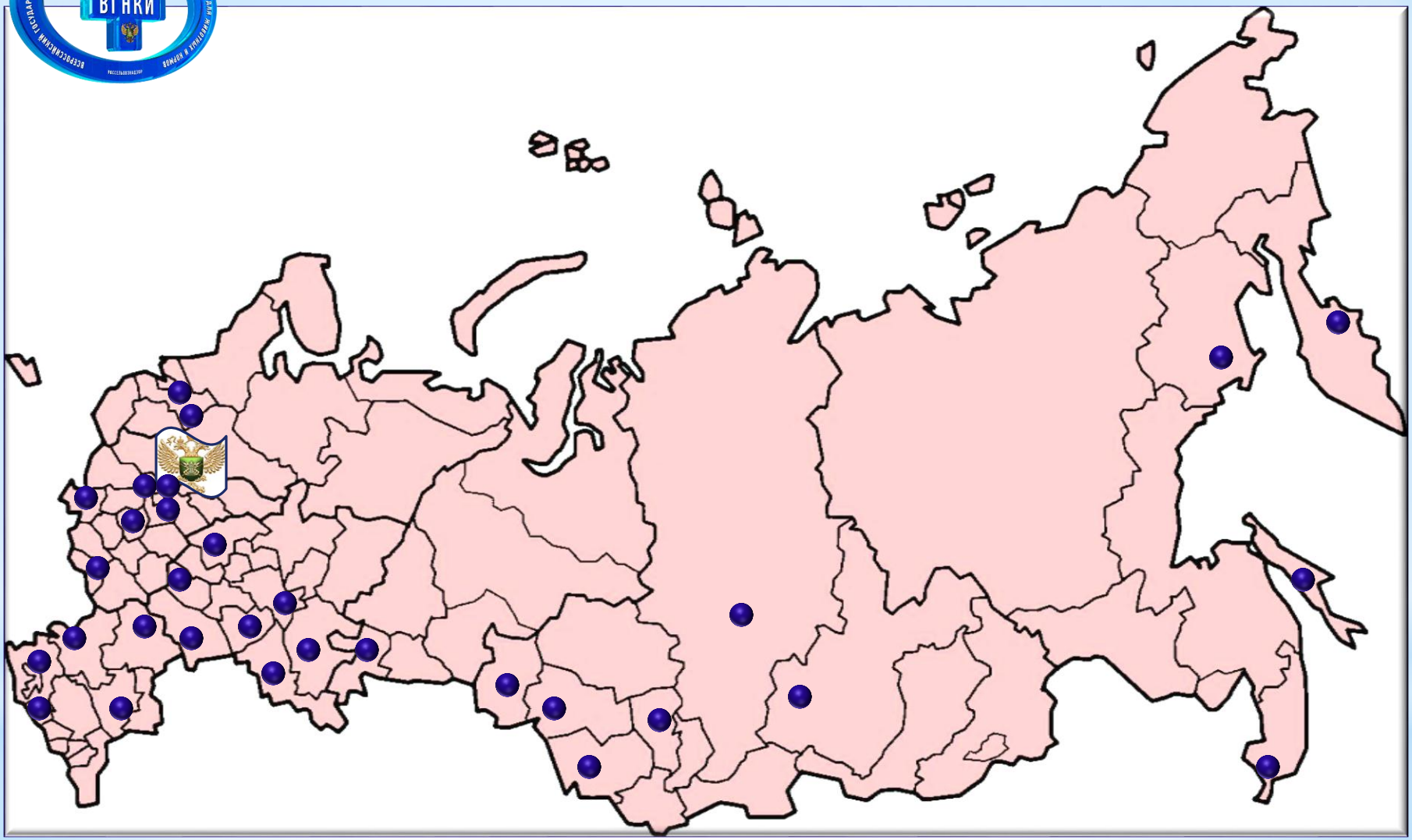
Overview of structure

Ministry of Agriculture

FSVPS
(Federal Service for Veterinary and Phytosanitary Surveillance)
Central Office

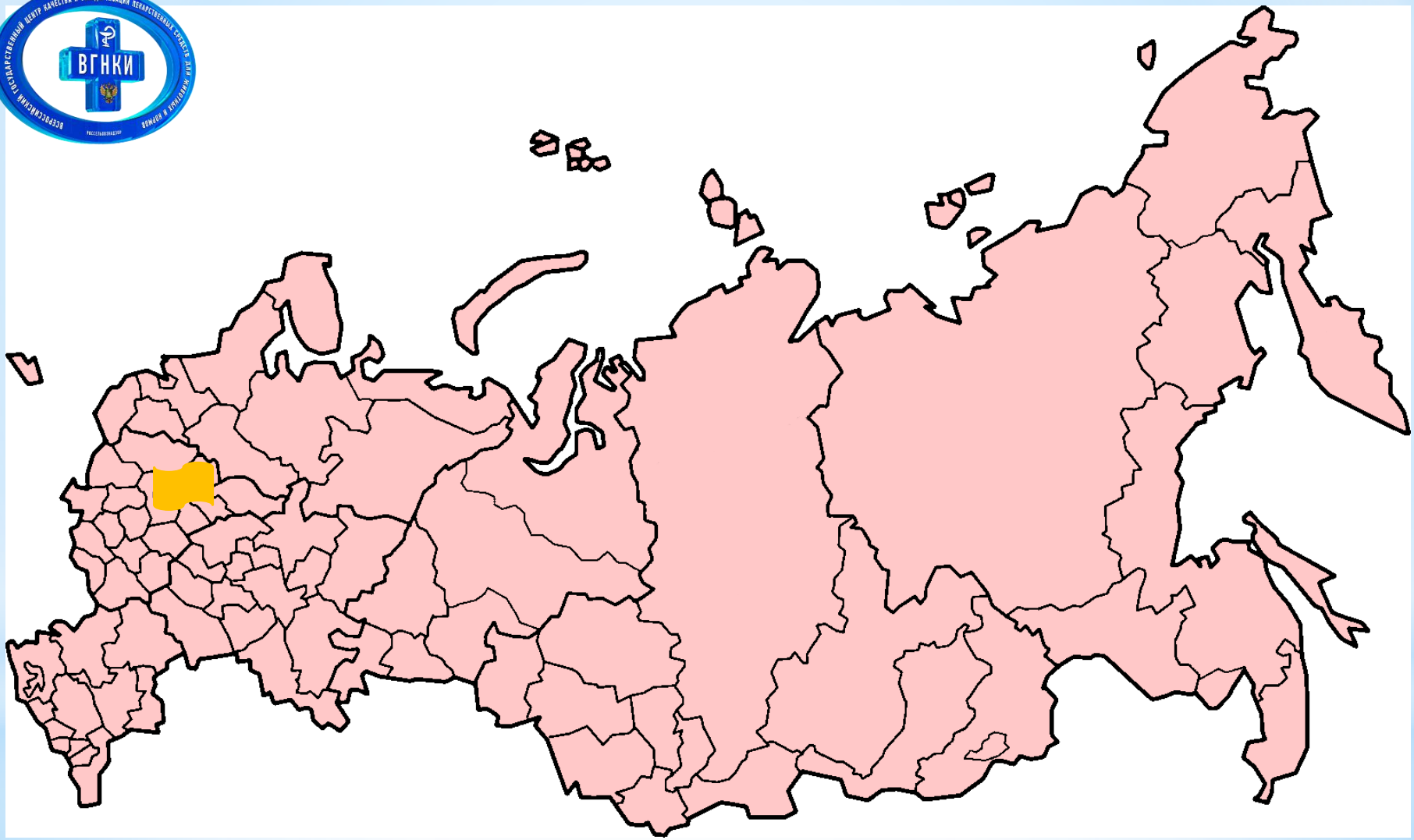
- FSVPS Regional Offices (59)
- Regional Laboratories (34)
- Research Institutes (3)
- Border Inspection posts


FSVPS Regional Offices



Regional laboratories

State Center for Quality of Veterinary Drugs and Feedstuff (VGNKI)



The Russian State Center for Quality and Standardization of Veterinary Drugs and Feed (VGNKI)

- In 1996 VGNKI received the status of the collaborating Center of the World Organization for Animal Health (OIE) for diagnostics and control of animal diseases in Eastern Europe, Central Asia and Transcaucasia

- In 2005 – the status of the collaborating Center on Food Safety

VGNKI serves as confirmatory laboratory in frame of monitoring program for control of residues of veterinary drugs and environmental contaminants

- In 2006-2015 screening and confirmatory methods (over 50) were developed to detect toxic elements, mycotoxins, PCBs, pesticides, hormones, tetracyclines, sulfonamides, metabolites of nitrofurans, coccidiostats, nitroimidazoles, amphenicols, anthelmintics, penicillins, quinolones, beta-agonists, triphenylmethane dyes, aminoglycosides, mycotoxins, NSAIDs, stilbenes, etc. in food and feed

The Russian State Center for Quality and Standardization of Veterinary Drugs and Feed (VGNKI)

VGNKI – Federal State institution that executes the government policy in quality assurance of drugs and feeding staff for animals and animal-based food products security by organizing the standardization framework in the territory of Russian Federation.

The institution takes a top position in the Ministry of Agriculture subordinate State divisions system and fulfills functions of the referent center of science and methods of the Federal Service for Veterinary and Phytosanitary Surveillance (Rosselkhoznadzor), all its departments and affiliates.

VGNKI - one of the largest centers of certification of veterinary drugs, feeding staff and feed additives in Europe. All its scientific, methodological and expert activity focused on goals achievement defined by the doctrine of food security.

VGNKI is the official center of OIE World Organization of Animal Health that executes food products security and animal diseases diagnostics and control in Eastern Europe, Central Asia and in South Caucasus region.

The institution is certified by RF Standardization, Metrology and Certification Committee (Gostandart) as the Veterinary Drugs and Feed certification and testing center.

The Russian State Center for Quality and Standartization of Veterinary Drugs and Feed (VGNKI)

Federal State Institution “The Russian State Center for Quality and Standardization of Animal Drugs and Feed” (VGNKI) organizes the system of the government policy in the field of quality and safety control of animal drugs, feeds and animal and plant food product for animal and human health security from common diseases.

VGNKI executes the security effectiveness control for the following products types circulated in the territory of Russian Federation:

- Preventive, diagnostic and treatment drugs and reproduction drugs for animals
- Vitamins, ferments, premixes, probiotics and feeds
- Feed supplements including GMO contained products

The Russian State Center for Quality and Standardization of Veterinary Drugs and Feed (VGNKI)

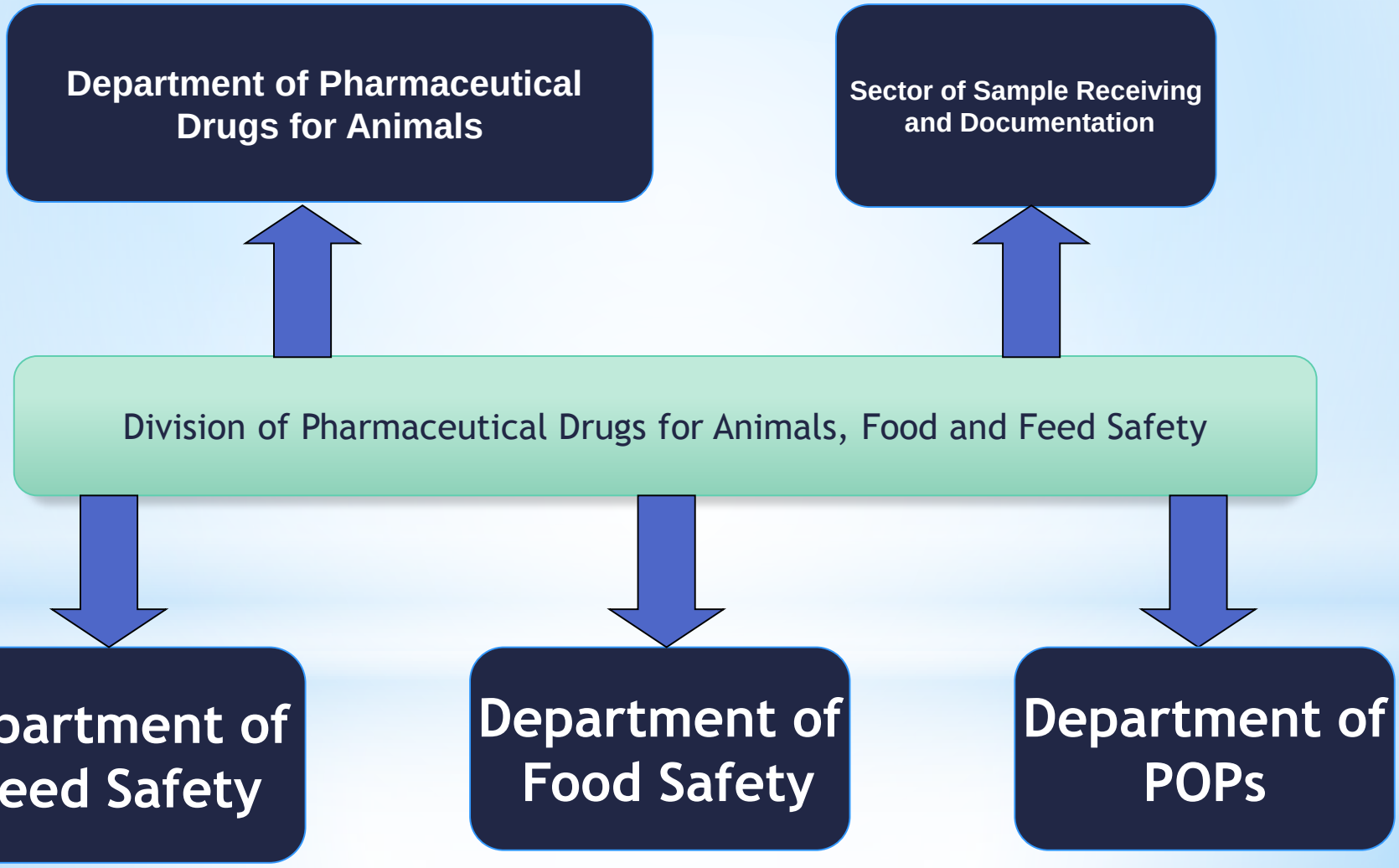
Diseases Diagnostics and Prevention

- The Institution Research laboratories regularly provide molecular diagnostics of animal diseases, viruses and contaminants.
- The institution disposes and maintains the National fund of micro-organism strains (bacteriums, viruses, fungis, chlamys, rickettsias and others) collection that can be applicable for creating and control of veterinary drugs and their providing for industrial enterprises, scientific research or veterinary studies institutions.
- “VGNKI” realizes permanent optimization of strains maintenance system, creates innovative conservation conditions and selection methods for microorganisms strains.

The Russian State Center for Quality and Standardization of Veterinary Drugs and Feed (VGNKI)

Innovations and Development

- Annually, under surveillance of Rosselkhoznadzor, “VGNKI” develops minimum 10 new methods, that allow it to provide products safety.
- Federal State Institution “VGNKI” is certified as a interlaboratory comparing tests coordinator (provider certificate № К 01.039 from 09.12.2013), what allows subordinated laboratories to confirm technical competence in the field of veterinary researches.
- Created the system of voluntary certification of veterinary staff “Vet-Expert” (registration number № ROCC RU.B1130.04 GLM0 from 14.11.2013), what allows creating a data base of competent veterinary specialists and experts.
- In "VGNKI" is created the organization of test laboratories accreditation (Federal Agency agreement for accreditation and expert organization of FSI "VGNKI" from 23.10.2013), that allows to evaluate and admit veterinary and testing laboratories of relative scientific trends.
- VGNKI has the certification for providing of measurement technics accreditation and paper works metrological evaluation, what allows the department to organize the works for measurements correspondence to metrological requirements by its own resources.
- The institution cooperates with Rosselkhoznadzor labs concerning national and international accreditation, activity coordination in the framework of cooperation with Codex Alimentarius, metrological provision of Rosselkhoznadzor labs.
- During next several years it is planned to reach microorganism strains optimal condition maintenance and transfer them into national standard samples.


Department of Pharmaceutical Drugs for Animals
Sector of Sample Receiving and Documentation
Division of Pharmaceutical Drugs for Animals, Food and Feed Safety
Department of Feed Safety
Department of Food Safety
Department of POPs

Main tasks of division

1. Development and validation of confirmatory and screening methods for control of drug residues and toxic substances in animal produce.
2. Testing of products of animal origin in the frame of National Monitoring Program.
3. Testing of feed additives and animal drugs for registration and certification in Russia.
4. Expert assessment of normative documents for feed additives and animal drugs
5. International collaboration. Participation in International Proficiency Tests.
6. Organization of Proficiency Tests for Regional Laboratories of Federal Service for Veterinary and Phytosanitary Surveillance

CONFIRMATION OF TECHNICAL COMPETENCE ACCORDING TO ISO/IEC17025:2005 STANDARD (january - september 2015)

PARTICIPATION OF DIVISION ANALYTICAL LABORATORIES IN 13 ROUNDS OF INTERNATIONAL PROFICIENCY TESTING ORGANIZED BY 4 REFERENCE CENTERS

UK **FERA**	➢ *Proficiency testing round on toxic elements determination in baby food: Cadmium (Z=-0,4), Chromium (Z=-0,7), Lead (Z=-0,2), Mercury (Z=-0,5), Selenium (Z=0,4).* ➢ *PT on Vitamins in dry cereal breakfast.*
NETHERLANDS **RIKILT- EU RL**	➢ *Aflatoxin M1 in milk: sample 1 (Z=-0,38), sample 2 (Z=-1,35).* *In Work:* ➢ *Antibiotics and coccidiostats in feed.* ➢ *Aflatoxin M1 in milk.* ➢ *Antibiotics in poultry meat.* ➢ *Resorcylic acid lactones in bovine urine.*
NORWAY Norwegian Institute of Public Health	➢ *Dioxins and Polychlorinated Biphenyls (PCDDs/PCDFs/dl-PCBs/non dl-PCBs in beef.* ➢ *Dioxins and Polychlorinated Biphenyls (PCDDs/PCDFs/dl-PT on PCBs/non dl-PCBs in salmon.*
FRANCE **BEPIA**	➢ *Dioxins and Polychlorinated Biphenyls (PCDDs/PCDFs/dl-PCBs/non dl-PCBs in soya feed.* ➢ *Dioxins and Polychlorinated Biphenyls (PCDDs/PCDFs/dl-PCBs/non dl-PCBs in bovine liver.*

CONFIRMATION OF TECHNICAL COMPETENCE ACCORDING TO ISO/IEC17025:2005 STANDARD

Participation in PROGETTO TRIESTE Program

TESTVERITAS

TEST VERITAS, Research Agency for Evaluation of Competence in Food and Feed Analysis Italy

Progetto Trieste is Proficiency testing for the evaluation and control of the laboratory performance in the analysis of food and feed contaminants

In 2015 году Laboratories of the Division of Pharmacological Drugs for Animals, Food and Feed Safety of took part in 17 rounds of 23 different xenobiotic groups determination.

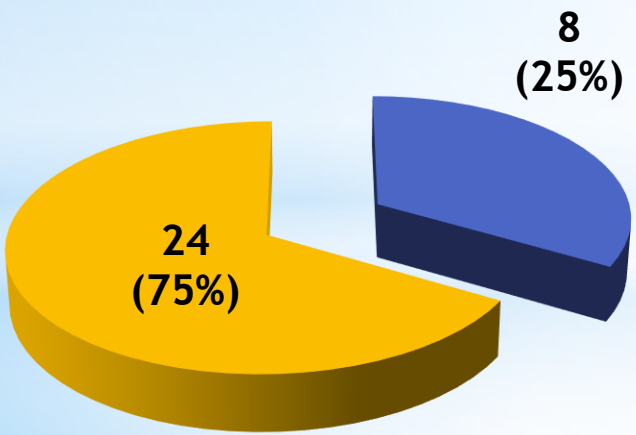
- ***Chloramphenicol and malachite green in lyophilized fish tissue***
- ***Quinolones in turkey heart tissue***
- ***Tetracyclines in beef***
- ***Sulfonamides in pork***
- ***Tetracyclines and sulfonamides in feed***
- ***Beta-agonists in swine liver***
- ***Corticosteroids in beef liver***
- ***Sulfonamides in honey***
- ***Tylosin in honey***
- ***Tetracyclin in honey***
- ***Avermectins in lyophilized cow milk***
- ***Metabolites of nitrofurans in lyophilized eggs***
- ***Tetracyclines and chloramphenicol in lyophilized eggs***
- ***Sulfonamides in lyophilized eggs***
- ***Tetracyclines and quinolones in lyophilized cow milk***
- ***Metabolites of nitrofurans in swine muscle tissue***

CONFIRMATION OF TECHNICAL COMPETENCE ACCORDING TO ISO/IEC17025:2005 STANDARD

VGNKI organizes proficiency testing schemes for regional FSVPS laboratories

Round 1
«Determination of nitrofuran metabolites in poultry»

In 2016
32 laboratories participated in this round

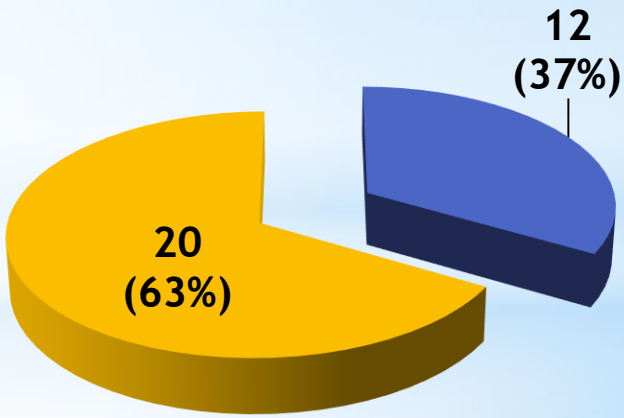


■ Confirmatory methods HPLC-MS/MS

■ Screening method ELISA

Round 2
«Determination of chloramphenicol in milk»

In 2016
32 laboratories participated in this round



Principles of National Monitoring Plan Development

According to Codex Alimentarius Commission principles, VGNKI uses Risk-based Approach while developing National Plan of Chemical Substances Monitoring in Food and Feed Materials (Codex Standard CAC/GL 62-2007 suggesting the risk profile evaluation, Codex standards 71-2009 and 80-2013)

Risk profile is a description of a food safety problem and its context developed for the purpose of identifying those elements of a hazard or risk that are relevant to risk management decisions (Codex definition).

Risk profile evaluation by VGNKI is relied on the principles and experience of the world most effective food safety systems (e.g. European Union, USA and Japan).

At the same time VGNKI takes into account the crucial differences between the risk profiles of Russia and the above-mentioned countries determined by the following:

-Differences in xenobiotic and veterinary drug use.

-Differences in consumption of various Food Products

- Differences in National Legislation (for ex.in Russia the MRL for tetracyclines are much stricter).

Principles of National Monitoring Plan Development

One of the main practical goals of VGNKI is permanent increase of the National Monitoring efficiency, which is possible only by implementation of the risk-based approach, including the risk profiles evaluation.

The key part of risk profile evaluation is the

Prioritization of xenobiotics analysis in specific food commodities, which is based on toxicological data and detection frequency.

Risk profile evaluation also includes careful analysis of the **following data**:

-Manufacturing conditions of food and feed materials

-Quantity of animal husbandry enterprises, livestock data

-Volume of imports,

-Consumption data for various food commodities in Russia

-Data about local sources of pollution by contaminants

-Legislation of exporting countries

-Data from Russian and International Veterinary Risk Alert Systems, scientific publications about xenobiotic findings in food and feed.

- Data about the efficiency and reliability of food safety systems in exporting countries.

Use of confirmatory multimethods to increase the testing efficiency

Confirmatory methods of drug residues detection are developed on the basis of a combination of methods **GC-MS/MS (Gas Chromatography-Mass Spectrometry), HPLC-MS/MS (High Performance Liquid Chromatography-Mass Spectrometry)** (methods of level I on Codex Alimentarius).

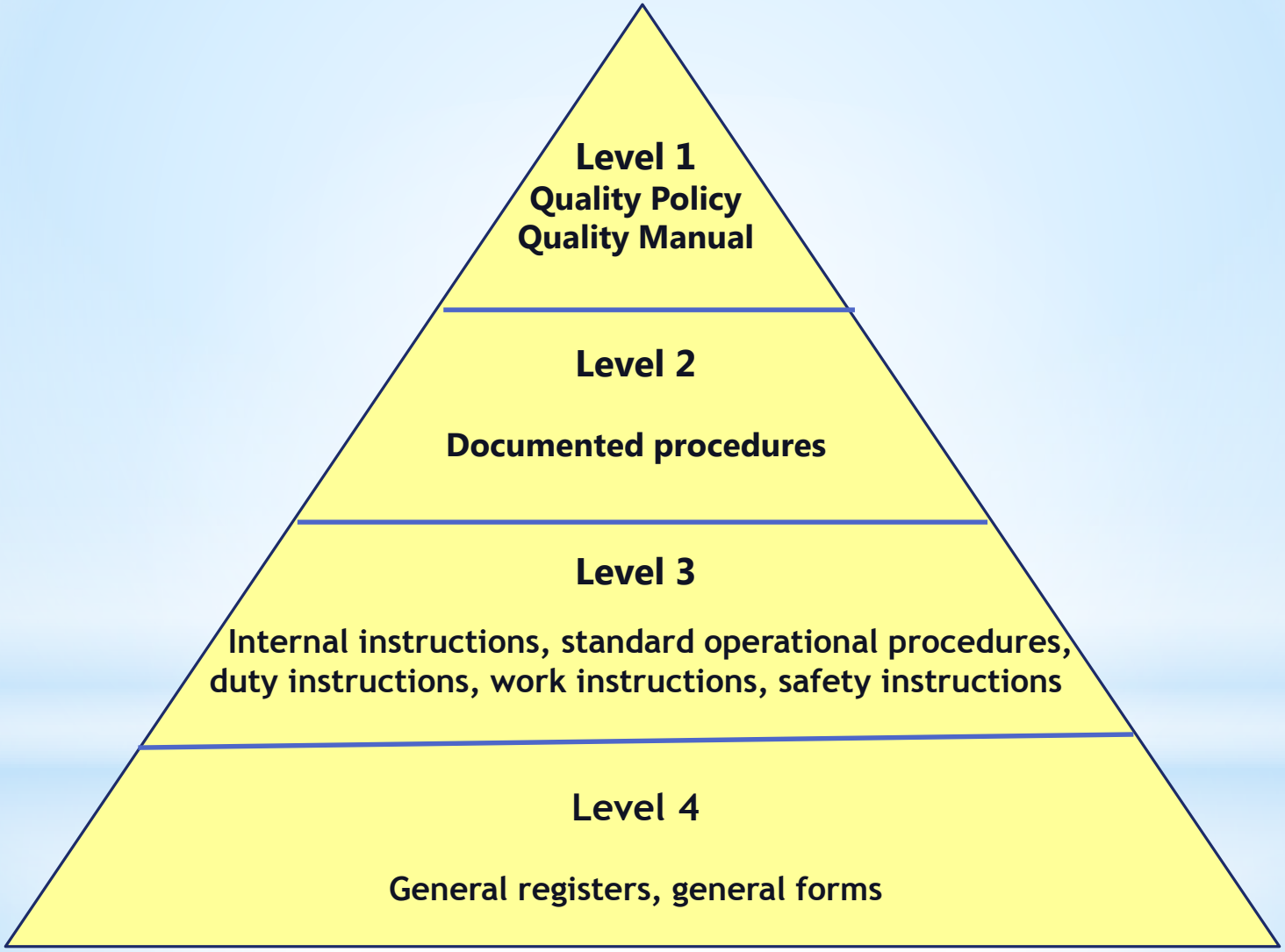
New perspective direction is development of multi-methods that allow to carry out simultaneous detection of many xenobiotics in a sample and essentially simplifies a problem of carrying out a large-scale monitoring and increases efficiency of techniques.

Application of HPLC-MS with tandem mass spectrometer detection allows to carry out reliable detection of several groups of the various chemical nature in one sample with the minimum preparation of the sample.

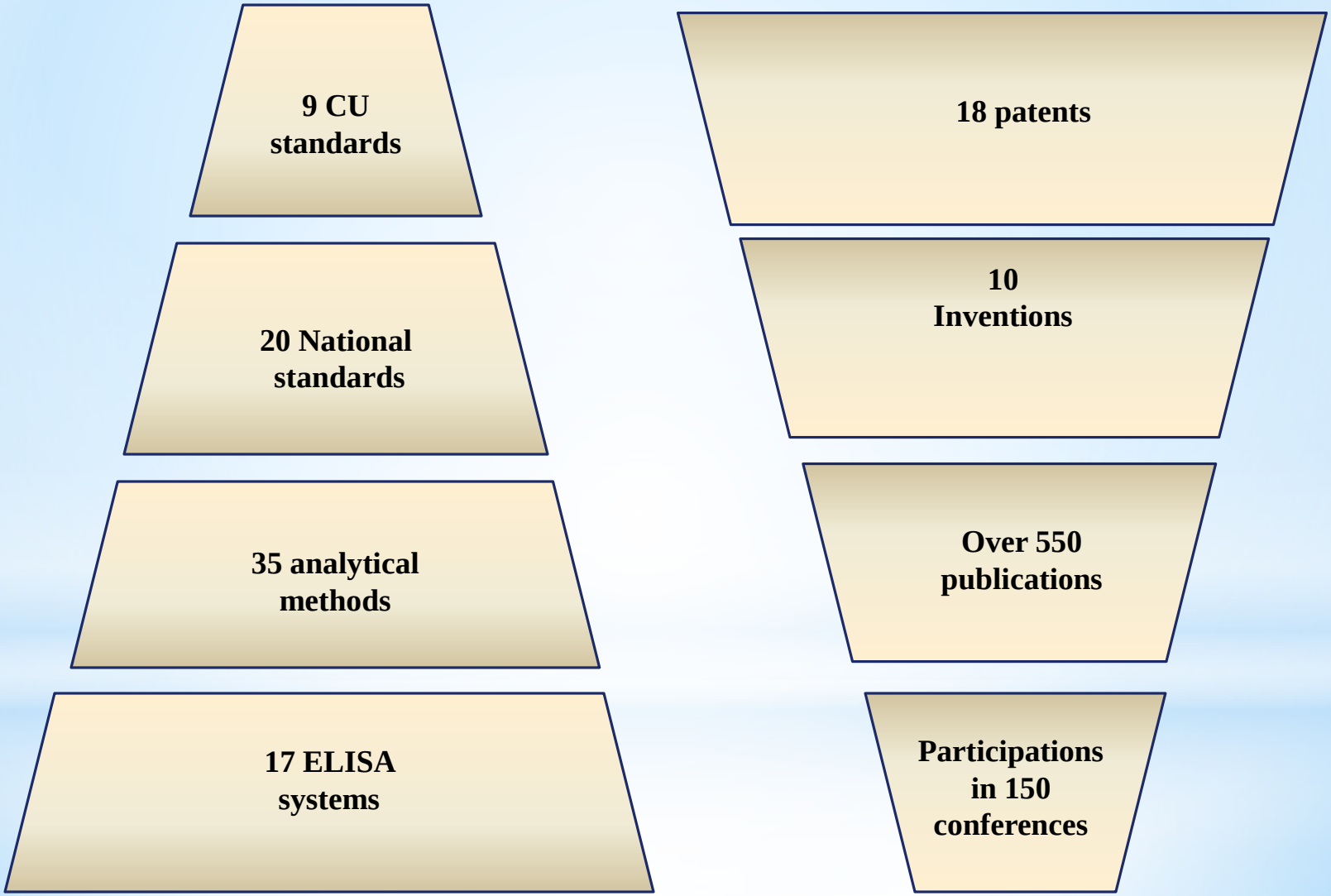
We have optimized conditions for quantitative determination **of more than 200 drugs, growth promoters and their metabolites** in food of animal origin

Quality assurance according to ISO/IEC 17025:2005

Structure of internal quality management documentation



Scientific Activity of the Division



Development of detection methods for veterinary drug residues and contaminants in livestock products

(as part of FCVPS Experimental Research Program in 2015-2017)

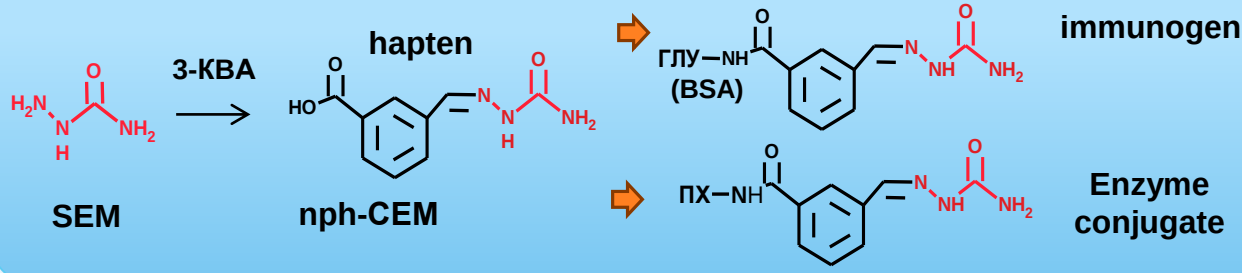
Part1 1. Development of screening method for semicarbazide detection based on solid-phase concurrent ELISA

Actuality

- Furacillin is quickly metabolized in the body, and it's metabolites may be detected in organs and tissues of livestock animals during 6 weeks after treatment. Semicarbazide has cancerogenic, mutagenic and genotoxic properties.
- The use of nitrofurans in animal production is banned in USA, Canada, EU, Argentina, Brazil and other countries! In Russia these drugs are also banned with maximum concentration as the level of method sensivity – 1 μg/kg.

Results and half-way conclusions

1.Hapten, immunogen and enzyme conjugate were synthesized.



2.183 polyclonal rabbit antsera were obtained using 6 immunization schemes with different adjuvants: Freund's complete adjuvant, Freund's incomplete adjuvant, Floravit®, Floravit purified fraction and various immunogen concentrations (nph-SEM-SLH).

3. Optimum conditions for direct solid-phase ELISA were found ensuring maximum sensivity and specificity.

№ serum	Immunogen	Enzyme conjugate	Incubation	IC_{50}, ng/ml
74/(10-12)	nph-SEM-SLH	Σ(nph-AOZ-HRP and nph-SEM-HRP)	1h at 4°C	8,0-20,0
44/(14-26)				2,0-8,0

Abbreviations:

SEM- semicarbazide
3-КВА – 3- carboxybenzaldehyde
nph-SEM – SEM nitrophenyl derivative
SLH – snail lymph hemocyanin
HRP- horseraddish peroxidase,
AOZ- Furazolidone metabolite
FLoravit® - culture liquid of fungus *Fusarium Sambucinum Fuckel*

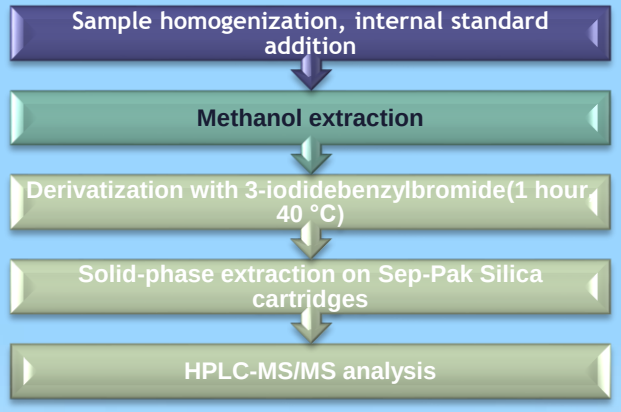
Part 2. *Development of confirmatory HPLC-MS method for thyreostat residues determination.*

Actuality

- Thyreostats (antithyroid drugs, goitrogens) – is a group of compounds blocking thyroid gland hormone biosynthesis and interfering with water release from tissues, that results in weight gain. Examples of thyreostats are thiouracil and it's derivatives (methyl-, propyl-, phenil-), metimazol (tapazol), 2-mercaptobenzimidazole.
- Despite of meat production increase, thyreostat treatment leads to impaired meat quality. Health risks associated with to thyreostat residues in food are the main problem.
- Consumption of food with thyreostat residues may result in hormonal disruptions due to thyroid gland disfunction (hypothyreosis). IARC stated that thiouracil and it's derivatives have carcinogenic properties.
- Thyreostat veterinary use is banned in EU (since 1981), USA, Australia, Customs Union and other countries.

Method characterization

Sample preparation scheme:



Metrological characteristics of the method:

Compound	Concentration range, µg/kg	Relative extended uncertainty with coverage factor k = 2, %	Repeatability limit, r, % (P = 0,95, n = 2)
6-Propyl-2-thiouracil	2-15	63	61
	15-30	30	28
6-Methyl-2-thiouracil	2 - 30	32	33
2-Mercapto-benzimidazole	0,4 - 8	59	58
	8 - 30	37	36
2-Thiouracil	2 - 8	69	83
	8 - 30	33	39
6-Phenyl-2-thiouracil	2 - 8	63	58
	8 -30	43	42

Conclusions

- Quick Sample preparation procedure for 5 thyreostats determination in animal feed, physiological liquids, organs and tissues was developed.
- Optimization of chromatographic separation procedure and mass spectrometry identification of analytes was performed.
- Metrological characteristics of the method were defined including concentration range, extended uncertainty, repeatability limit and reproducibility limit. Metrological certification report was made and forwarded to VGNKI Metrological Service for evaluation.

Development of HPLC-MS method for cephalosporins quantification in livestock products

Actuality

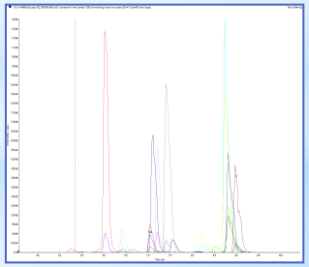
- Cephalosporins are a group of beta-lactam antibiotics with high antibacterial activity, but without full insensitivity to beta-lactamases (enzymes, produced by microorganisms). In order to increase drug stability, extend the range of antimicrobial activity and enhance the pharmacokinetic properties various semi-synthetic cephalosporin derivatives were synthesized. About 10% of patients with hypersensivity to penicillins and carbapenems are sensitive to cephalosporins.
- International legislation (Codex Alimentarius) and EU legislation prescribes systematic control of cephalosporin residues in livestock products.
- Current Customs Union legislation regulates 7 cephalosporins levels in food products of animal origin (ceftiofur, cefacetril, cefalexine, cefalonim, cefaperazone, cefquinome, cefapirine). Maximum Residue Levels for different cephalosporins are in range of 10-6000 mg/kg.
- In Customs Union countries there are no confirmatory methods of cephalosporin determination.

Method characterization

Compound	Precursor ion, m/z	Daughter ion, m/z	Collision energy, eV	Collision cell exit potential
Ceftiofur	523,8	241,0/126,1	24/55	20/20
Desfuroylceftiofur	430,1	285,1/126,1	21/35	13/15
Desfuroylceftiofur cysteine	549,2	183,1/241,3	35/28	15/20
Cefacetril	363,8	208,1/114,1	13/27	20/15
Cefalexine	347,8	158,4/106,3	16/35	10/14
Cefalonim	458,8	152,2/337,1	26/13	16/15
Cefaperazone	646,2	143,1/290,4	41/31	12/12
Cefquinome	529,3	134,1/396,3	20/18	13/15
Desacetyl cefapirine	381,8	112,0/292,1	30/20	14/15
Cefadroxil	363,8	226,1/347,1	23/8	16/15
Cefsulodine	533,2	123,3/331,2	18/20	20/14
Cefotaxim	455,8	125,2/277,1	70/20	7/14
Ceftriaxone	555,2	167,1/324,1	85/23	15/14
Ceftibuten	410,8	268,0/139,3	20/40	20/11
Cefpodoxime	558,3	410,2/156,2	20/40	30/13
Cefodizime	585,2	140,0/107,1	50/40	20/15
Cefpirome	514,9	120,2/401,3	21/27	15/20
Cefotiam	526,2	168,2/353,2	39/16	19/16
Cefuroxime	425,9	158,3/348,1	19/11	11/17
Cefaclor	367,8	118,0/106,1	46/37	6/20
Cefazoline	455,8	125,0/396,2	70/13	17/20
Cefetamet	511,9	241,2/126,2	23/26	20/18
Cefepime	482,2	241,0/126,2	23/43	23/20
Cefixime	453,8	285,1/126,0	20/39	20/18
Cefamandole	462,8	158,0/347,0	24/12	20/15

Results

- **The method was developed according to the calendar plan.**
- **Parameters of mass spectrometry identification were optimized for 25 compounds from cephalosporin group.**
- **Optimum conditions of reverse-phased chromatographic separation were selected.**

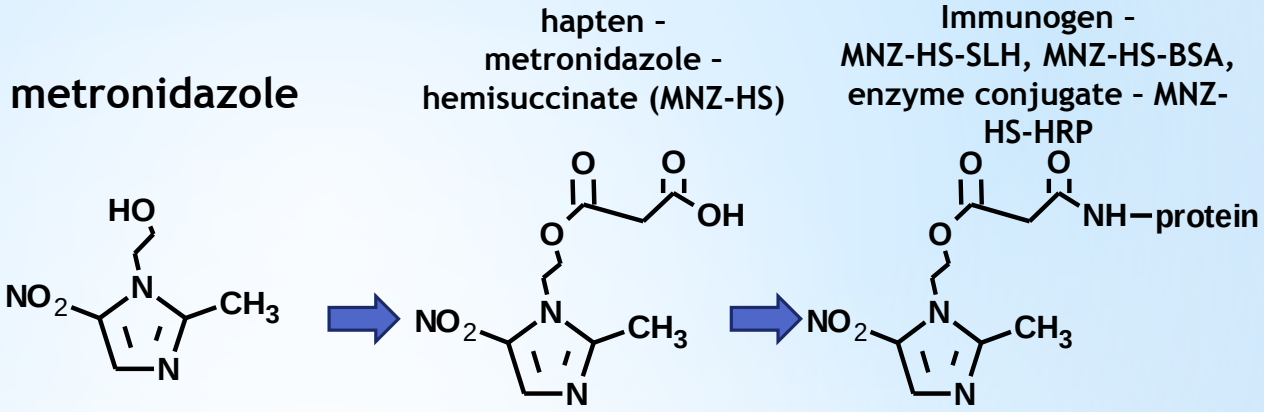


Chromatogram of standard solution of 25 antibiotics (10 ng/ml)

Development of solid-phase concurrent ELISA screening method for nitroimidazole residues determination in food products of animal origin.

Actuality

- **Nitroimidazoles are synthetic antimicrobial drugs, derivatives of 5-nitroimidazole. They are used for poultry coccidiosis and histomonosis and swine haemorrhagic enteritis treatment and prophylaxis.**
- **At the present day it is well know that almost all nitroimidazoles and their metabolites with nitroimidazole ring have genotoxic, mutagenic and cancerogenic properties.**
- **In EU, USA, Canada, Japan and other countries the use of nitroimidazoles in animal production is prohibited. In Russia these drugs are also banned with Maximum residue concentration as the level of method sensivity – 1 μg/kg (GOST R 54904-2012).**



Results and half-way conclusions

1. Metronidazole derivative Metronidazole succinate was synthesized using the succinic anhydride.
2. The derivative was used to produce conjugates with Snail lymph hemocyanin (SLH), Bovine serum albumin (BSA) and Ovalbumine (OVA) and Horseradish peroxidase (HRP).
3. 42 polyclolonal antisera were produced using Freund's complete adjuvant and Freund's incomplete adjuvant. Optimum conditions for direct solid-phase ELISA were found ensuring maximum sensitivity and specificity of the method.

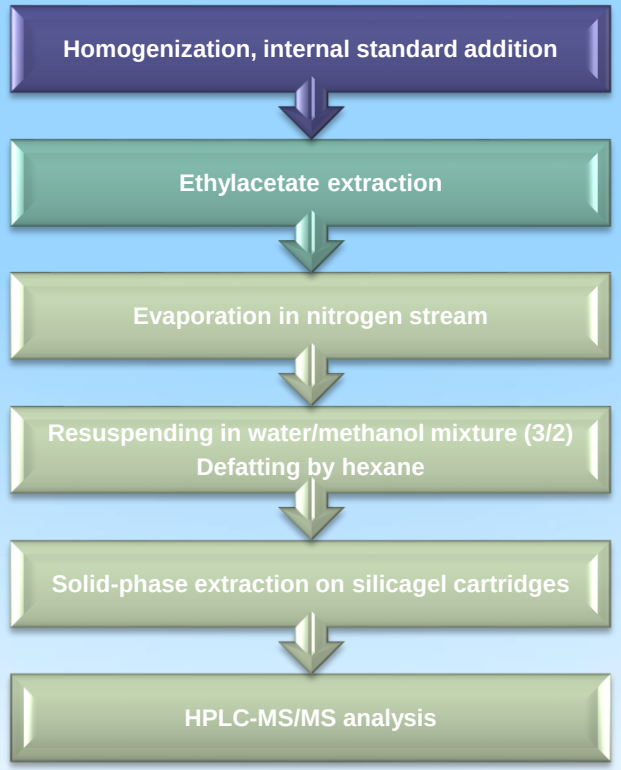
Development of HPLC-MS method for sedative drugs and adrenoblockers detection in animal tissues

Actuality

- Sedative drugs are used in animal production for weight loss and untimely death of animals due to stress conditions during transportation.
- Sedative drugs are also used for weight gain due decrease in animal activity and increase of feed consumption.
- Adrenoblockers are compounds that block receptors for adrenaline mediators.
- Т.к. седативные препараты и адреноблокаторы применяются за несколько часов до убоя, то велик риск их остаточного содержания в продукции животноводства, что может нанести вред здоровью человека.
- Animals are treated sedative drugs and adrenoblockers several hours before slaughter, that is the reason for high risk of residues accumulation in tissues and may thus result in health problems for consumer
- Any presence of sedative drugs in food products of animal origin is prohibited by Russian Legislation.

Method characterization

Sample preparation schmene:



Cocnlusions

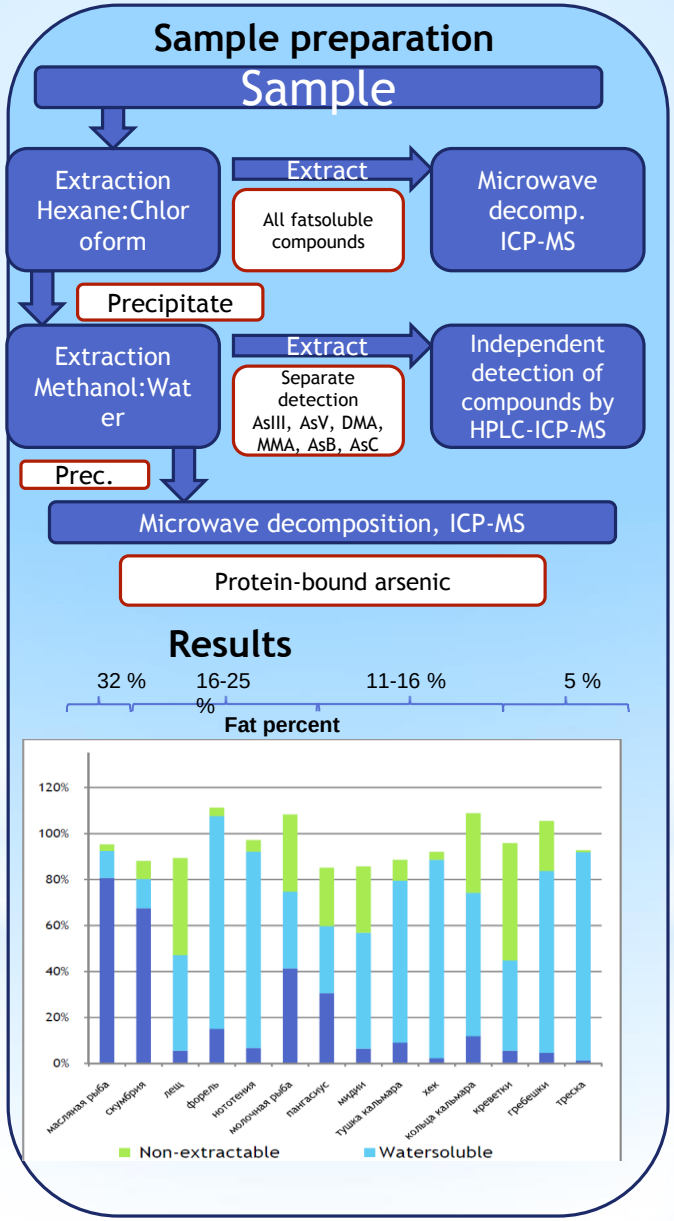
- Conditions of 19 sedative drugs chromatographic separation and MS detection were optimized.
- Sample preparation scheme for muscle tissue and liver was developed. Solvent volumes and solid phase extraction conditions were optimized.
- Pre-validation experiments were performed. Next we going to provide metrological characterization of the method: Concentration range, extended uncertainty, repeatability limit and reproducibility limit.

Development of HPLC-ICP-MS method of arsenic organic and inorganic compounds detection in fish and seafood.

Actuality

- Customs Union legislation regulates maximum levels of arsenic in fish, seafood and products thereof – 5 mg/kg.
- However, it is well known, that in these products arsenic may accumulate in various compounds with different biological and chemical properties. Inorganic arsenite and arsenate are the most toxic compounds, organic compounds monomethylarsenic acid and dimethylarsenic acid along with fatsoluble arsenic compounds are also toxic.
- Chemical composition of arsenic compounds depends on products type, fat percent and environmental conditions. For example, in low fat fish, squid and shrimps, 80-90% of arsenic may persist in non-toxic organic compounds form (arsenobetaine, arsenocholine, trimethylarsenic oxide, tetramethylarsenate ion), but in seafood with high percent of fat, up to 80% of arsenic may be in fatsoluble high toxic compound form. Thus, total arsenic content does not allow to estimate health risk of this products consumption.
- In this regard, in EU, USA and other countries, total arsenic levels are not regulated by legislation, but maximum levels for toxic inorganic compounds were established (As (III) – arsenites, As(V) – arsenates).
- In Russia there are no official methods of independent organic and inorganic arsenic compounds determination and thus health risk evaluation of fish and seafood consumption is complicated.

Sample preparation



Results

Results

- Extraction procedure conditions for fatsoluble, watersoluble and protein-bound arsenic compounds from fish and seafood tissues were optimized. ICP-MS detection conditions for fatsoluble arsenic compounds were also optimized.
- Method of HPLC watersoluble organic and inorganic arsenic compounds separation and ICP-MS arsenic quantification was proposed.
- Distribution of fatsoluble, watersoluble and non-extractable arsenic compounds in fish and seafood with different fat percent was evaluated.
- Chemical composition of watersoluble arsenic compounds was studied. We have shown, that non-toxic arsenobetaine is the main arsenic compound in crustaceans, fish and cephalopod tissues, but toxic arsenic compounds (arsenates, arsenates, dimethylarsenic acid) accumulate in clam tissues in significant amounts.
- HPLC-ICP-MS method of organic and inorganic arsenic compounds quantification in fish and seafood was developed.

Development of HPLC-ICP-MS method of organic and inorganic mercury compounds detection in food and feed.

Actuality

- It Is scientifically proved that in food and feed mercury may persist in various compound forms with different toxicity.
- Inorganic mercury half-life is the body is 80 days, organic mercury half-life – more than 600 days.
- In Russia methylmercury in seafood is not monitored, only total mercury is analyzed.
- WHO Maximum Levels of methylmercury are 0.5 mg/kg for non-predatory fish and 1 mg/kg for predatory fish.
- EU Maximum Level of methylmercury is 0.5 mg/kg.
- Swedish food hygiene specialists insist on lowering the Maximum Level of mercury in fish, because the limit of 1 mg/kg, although protecting consumers from acute toxicity, does not ensure the absence of long-term harmful health effects.
- In Russia there are no official methods of independent organic and inorganic mercury compounds determination and thus health risk evaluation for mercury is complicated.

Method characterization

Sample preparation

Homogenization

↓

Extraction of mercury compounds by 1% water solution of L-cysteine

↓

Heating at water bath for 120 min.

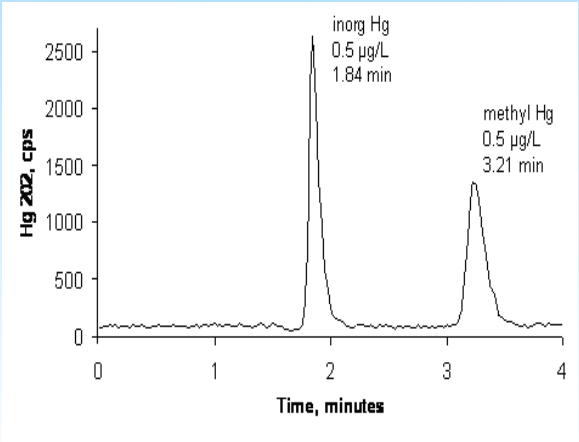
↓

Filtering through membrane filter

↓

HPLC-ICP-MS analysis

Chromatogram example
Retention times of inorganic mercury compounds and methylmercury



Results

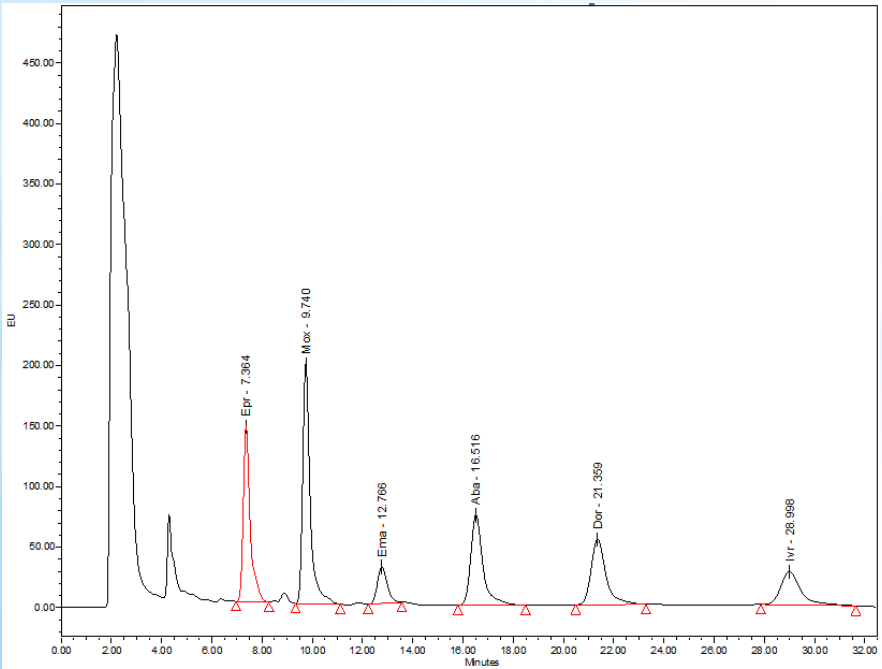
- Lyophilizates of sea organisms (fish, squid, shrimp, crab and mussel) as matrix standards were prepared.
- Using standard solutions of organic and inorganic mercury compounds chromatographic separation conditions were optimized (sorbent, mobile phase composition, gradient etc.)
- Sample preparation procedure was developed, extraction optimization is in work.
- Metrological characteristics were estimated, including sensitivity, reproducibility, and chromatographic separation measurement rate.
- Optimization of detection conditions in HPLC-ICP-MS system was started (generator power, argon and hydrogen streams, ion optics settings) for maximum sensitivity and minimal matrix interferences.

Development of HPLC-FLU method for macrocyclic lactone residues determination in livestock products

Actuality

- Antiparasitic drugs from the family of macrocyclic lactones, that are widely used in animal production, may be the cause of human and animal poisonings if consumed in excess amounts.
- Due to wide use of different macrocyclic lactones (abamectin, ivermectin, doramectin, emamectin, eprinomectin, moxidectin) development of the method for **simultaneous determination** of all mentioned compounds in livestock products is essential for the purposes of food safety.

Chromatogram of muscle tissue sample extract. Concentrations of analytes are 50 µg/kg.



Accuracy factors

Compound	Relative extended uncertainty for different concentration ranges, %			
	0,5 - 2,0 µg/kg	2,0 - 10,0 µg/kg	10,0 - 50,0 µg/kg	50,0 - 250,0 µg/kg
Abamectin	53	32	33	43
Ivermectin	66	27	35	37
Doramectin	41	32	28	33
Emamectin	60	22	27	44
Eprinomectin	61	42	27	37
Moxidectin	52	28	23	33

Conclusions

- Method of simultaneous determination of macrocyclic lactones residues in food products of animal origin (muscle, liver, fat, milk) was developed.
- Metrological characterization of the method was performed.
- Relative extended uncertainty, repeatability limit and reproducibility limit were measured.
- Technical report of metrological characterization was composed and forwarded to VGNKI Metrological Service.

Department of Pharmaceutical Drug Circulation Safety Control

The Department includes:

- **Laboratory of Drug Expert Review**
- **Laboratory of Drug Quality Control**
- **Sector of Sample Reception and Laboratory Reports Recording**

Department of Pharmaceutical Drug Circulation Safety Control

Major activities of the Department:

- Registration dossier expert review for a dossier authorization or confirmation of the dossier authorization.

- Sample testing of pharmaceutical veterinary drugs for:

a drug registration in the territory of the Russian Federation; confirmation of an official drug registration; amendments into registration documents covering registered drugs; registration of pharmaceutical substances in the State register of veterinary drugs.

- Quality control of samples of the pharmaceutical drugs, which are in circulation in the territory of the Russian Federation – under the public contract.

- Sample testing for compliance with regulatory documents requirements according to the current accreditation scope – under requirement of the Certification body;

- Development of state reference samples of antibiotics

- Participation in international proficiency testing programs.

Department of Pharmaceutical Drug Circulation Safety Control

Analytical equipment includes 6 HPLC with DAD, UV и FLU detectors.

In the framework of veterinary drug circulation control in the territory of the Russian Federation in 2016 the laboratory received 1459 veterinary drug samples for analysis as well as more than 408 samples for registration and mare than 100 samples for certification.
The tested samples represented various groups of antibiotics, vitamins, antiparasitic drugs, pesticides and desinfectants.

* Managing and developing of All-Russian microbial strains collection.

Maintaining and developing of microbial strain collection of All-Russian collection of strains, used in veterinary and animal breeding. The collection contains more than 25000 strains.

The Russian State Center for Quality and Standartization of Veterinary Drugs and Feed (VGNKI)

Division of biotechnology

- Department of animal infectious diseases gene diagnostics
- Department of GMO control
- Department of molecular biology
- Department of sanitary and clinical microbiology
- Department of research of biological objects
- Department of sampling and research results analysis
- Department of standardization and quality control of genetic material and drugs used in animal reproduction

Research themes

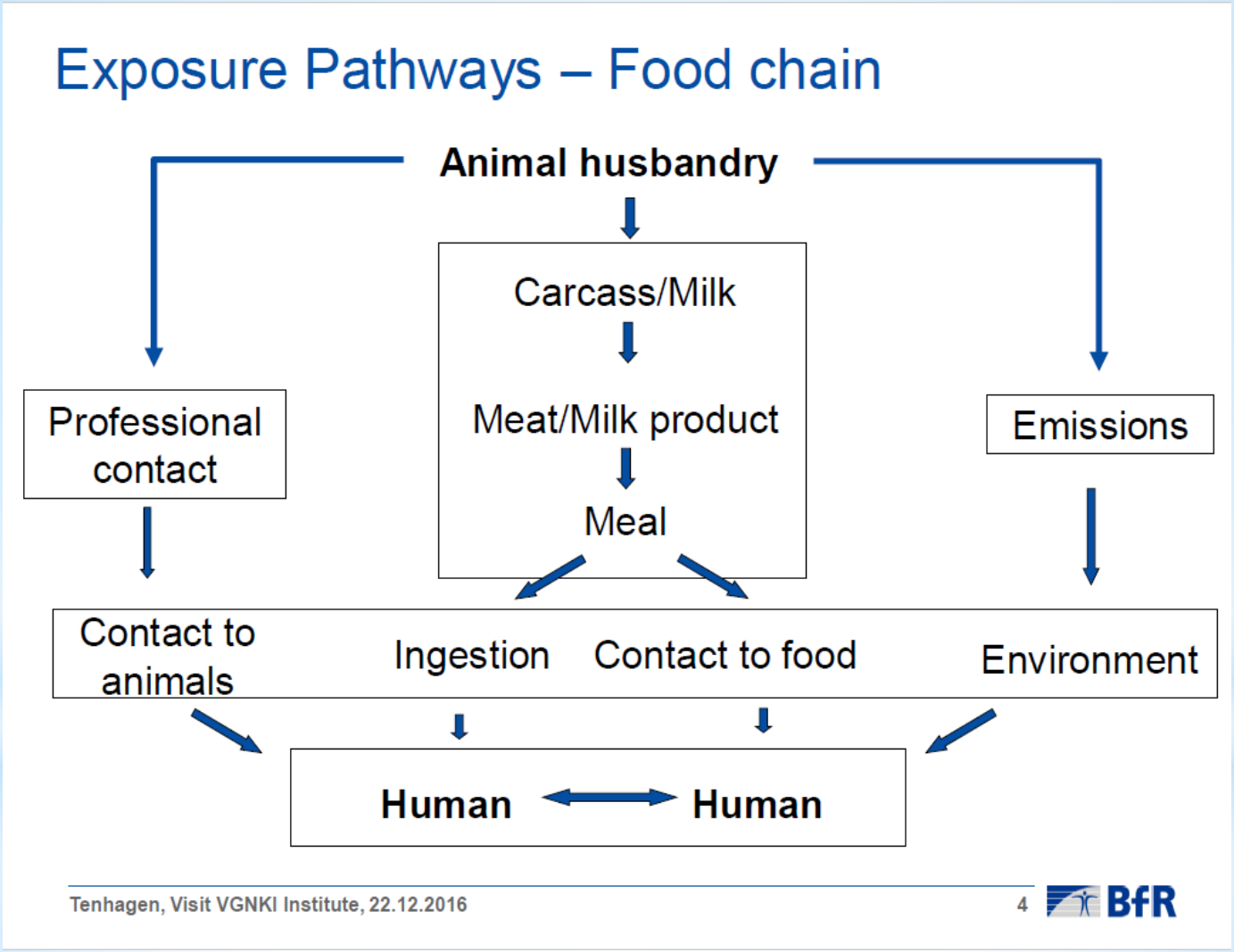
- Elaboration and validation of screening procedures for detecting GMO – lines of plant origin for improvement of the effectiveness of state control and monitoringof feed and feed supplement.

- Elaboration and implementation of molecular genetic complex of methods for GMO identification in feed and feed supplement (probiotic) within the framework of control over production with GMO.

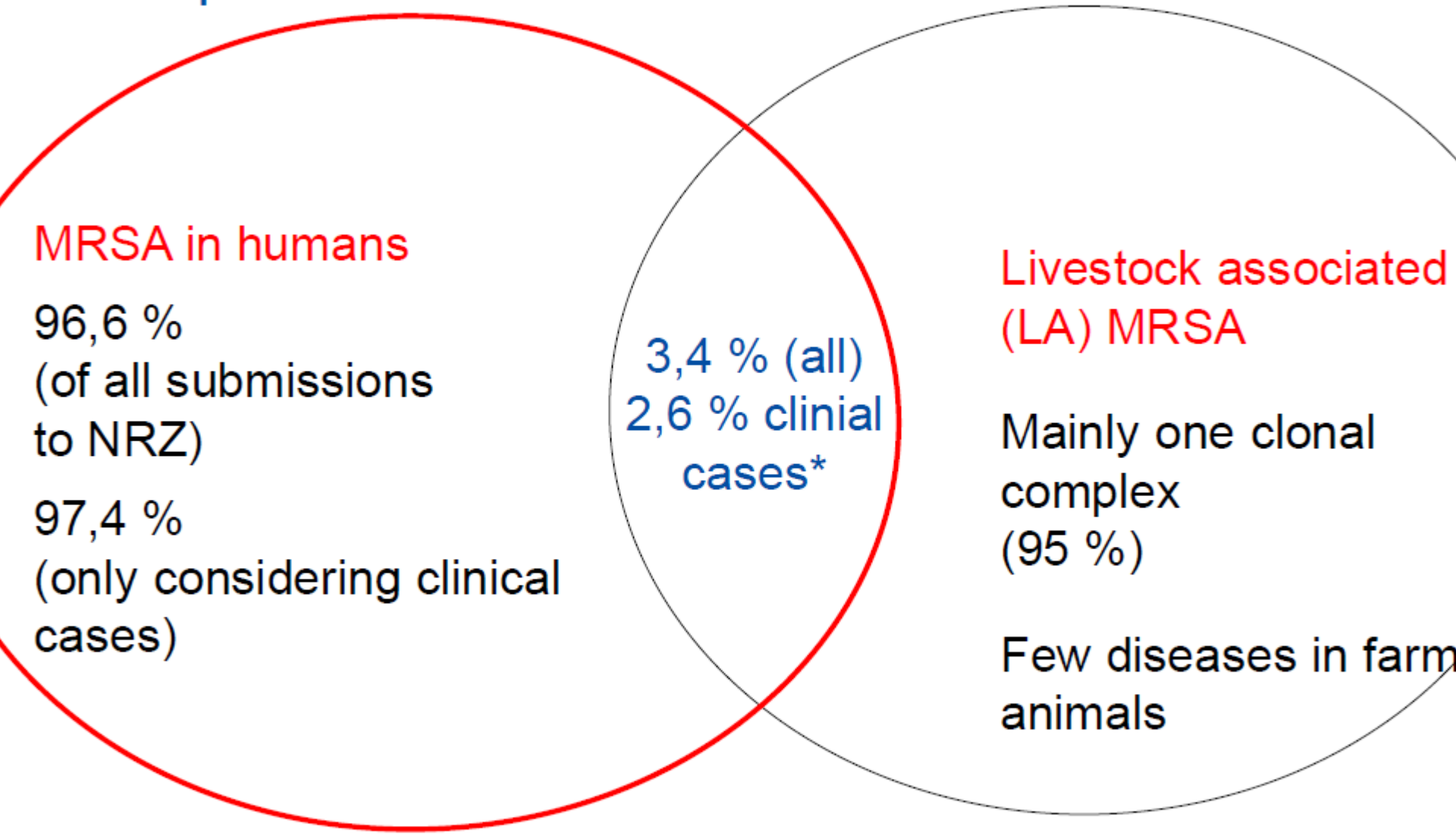
- Elaboration of test-systems for detecting agents causing infectious diseases of swine. Conducting research of strain of diamond-skin disease agent with use of PCR on a real-time basis.

- Elaboration of test-systems for detecting agents causing infectious diseases of cattle. Elaboration of method of detecting agent causing respiratory syncytial infection of cattle with use of PCR on a real-time basis.

Problem of zoonotic bacteria AMR

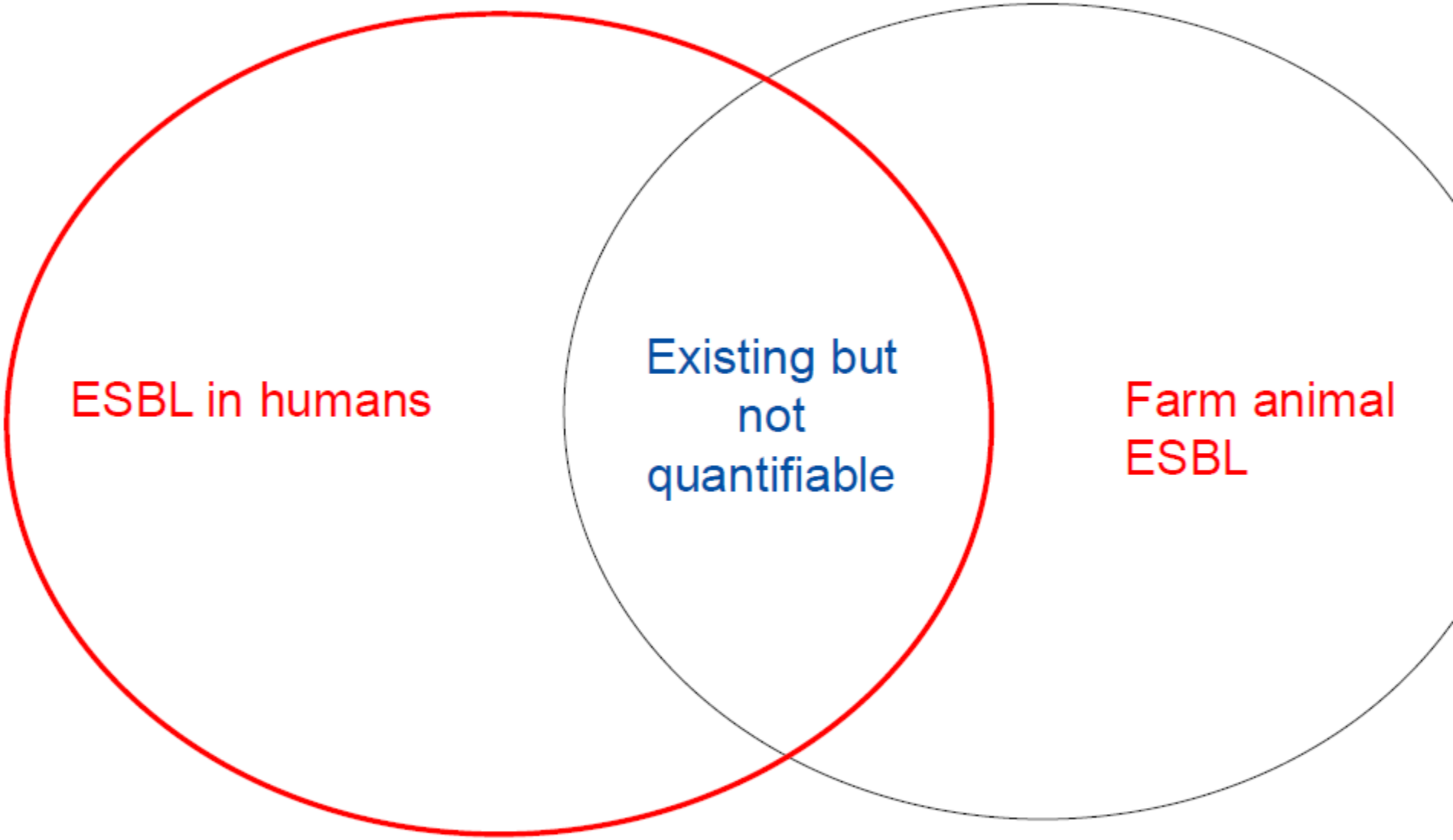


Example MRSA in farm animals and humans



Epid. Bull. 31/2015

ESBL in farm animals and humans



VGNKI activities in the field of antimicrobial resistance

* Monitoring of zoonotic bacteria resistance and veterinary use of antimicrobials play a crucial role in strategies aimed at minimization of resistant microorganisms distribution.
* In 2010-2015 VGNKI made a comparison of 200 Salmonella isolates from the VGNKI museum collection obtained in 1948-2009 and 108 isolates obtained in 2010-2012 from food products, feed and animal biomaterial.
* Recently isolated strains showed a 2-fold increase in ampicillin and doxicyclin and 1.8 –fold increase in streptomycin resistance. Also intermidiate resistance to critically important antimicrobials ciprofloxacin and norfloxacin raised significantly – by 3.9 and 5.6-fold, respectively.
* Being an OIE collaborating centre VGNKI is elaborating a National Program for AMR monitoring in livestock and food products of animal origin According to FAO/WHO and OIE recommendations.

VGNKI activities in the field of antimicrobial resistance

The main items are the following:

* VGNKI is the reference laboratory performing susceptibility testing and analysis of genetic determinants of AMR by internationally harmonized methods. VGNKI performs training of regional laboratories.
* Regional veterinary laboratories perform susceptibility tests of bacteria isolated from livestock and food products using harmonized methods of analysis.
* Data is collected by VGNKI, analyzed and passed to international organizations, including OIE etc.
* CLSI standard microdilution method was chosen to test sensivity of 4 groups of bacteria (*E. coli, Salmonella sp., Campylobacter spp., u Enterococcus spp)* isolated from food products (meat, milk, dairy, fish etc) and biomaterial of farm animals (carcasses, lavages, feces, swabs etc.). All 4 groups are recommended by OIE for the inclusion in the AMR monitoring.
* 30 antimicrobials from 12 groups were included in the program for susceptibility testing basing on the data of medical and veterinary importance, registration and sales volumes in Russia , effectivity, medical and veterinary importance etc.

Thank you for your attention.