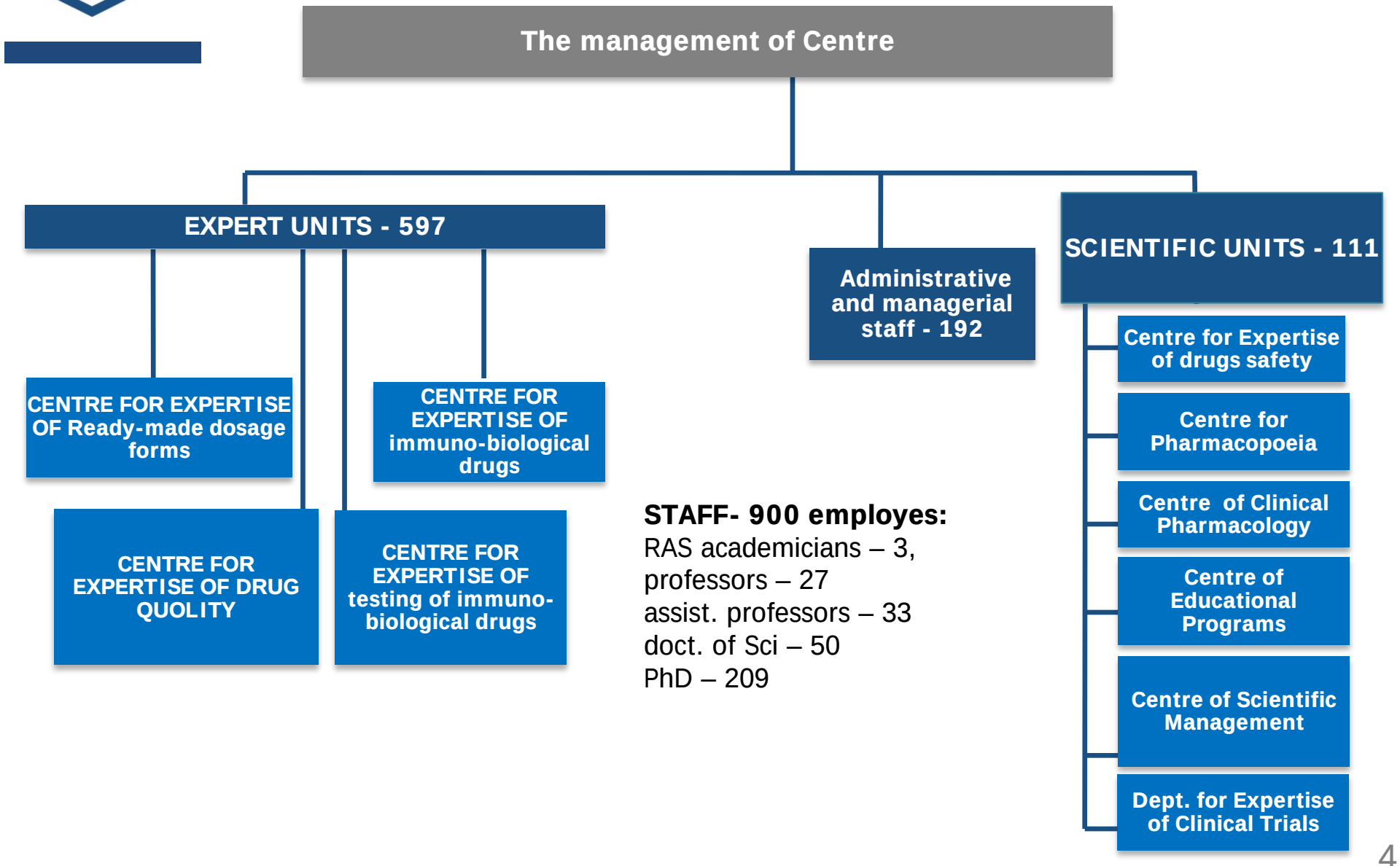
Federal State Budgetary Institution «Scientific Centre for Expert Evaluation of Medicinal Products» of the Ministry of Health of the Russian Federation

Personalized medicine: contribution to the evaluation of the efficacy and safety of drug therapy

R. Alyautdin,
Director of Centre for Expertise of Drug Safety

Structure of Scientific Centre for Expert Evaluation of Medicinal Products



STAFF- 900 employes:
RAS academicians – 3,
professors – 27
assist. professors – 33
doct. of Sci – 50
PhD – 209

Scientific expertise:

- Permission for clinical study of drugs
- State registration of medicines in the Russian Federation and the EAEU,
- Making changes to the marketing authorisation of drugs,
- An estimation of interchangeability of medicines,
- Formation of a group orphan drugs

Scientific research:

Centre of Clinical Pharmacology

pharmacokinetic laboratory

- Determination of the concentration of the drugs used in the blood plasma
- Study of the activity of cytochrome P-450 isoenzymes responsible for drug metabolism

pharmacogenetic laboratory

- Pharmacogenetic testing: detection of polymorphisms of genes encoding biotransformation enzymes and drug transporters

Centre for Expertise of Drug Safety

- Analysis of drugs efficacy and safety

Model of introducing personalized medicine technologies into practical health care

Academician RAS
V. Kukes

Centre of personalized medicine

Stage 1

The development of a "roadmap" of research on the personalization of specific diseases and interventions

Stage 2

Formation and maintenance of biobank and electronic register of patients with specific diseases

Stage 3

Associative research (including candidate gene)

Stage 4

Development of models / algorithms based on personalization based on bioinformational technologies

Stage 5

Clinical validation of algorithms / models of personalization: design of the research

Stage 6

Estimation of economic efficiency of the developed methods of personalization of adherence to clinical practice

Stage 7

Development of an organizational model for the implementation of personalized methods in medical practice

Who primarily needs the use of omics technology to personalize pharmacotherapy in clinical practice?

What should be the drug?

- Non-alternative drugs
- Drugs with a wide spectrum and severity of unwanted drug reactions
- With long-term (life-long) use of drugs (cardiovascular, psychotropic drugs, hormones, etc.)
- Drugs with narrow therapeutic spetrum

What should be the patient?

- Patient at risk of developing adverse reactions
- With a hereditary history of adverse reactions

Scientific targets of Pharmacogenomic lab

MEDICINES

- Statins
- Proton pump inhibitors
- Oral anticoagulants
- Beta2-adrenomimetics
- Antidepressants
- Bets-adrenoblockers

ENZIMES

- CYP 3A4, 2D6, 2C9
- VKORC1
- ABCB1

Pharmacogenomics and Personalized Medicine

Dovepress
open access to scientific and medical research

Open Access Full Text Article

SHORT REPORT

The frequency of *SLCO1B1*5* polymorphism genotypes among Russian and Sakha (Yakutia) patients with hypercholesterolemia

This article was published in the following Dove Press journal:
Pharmacogenomics and Personalized Medicine
25 May 2016
Number of times this article has been viewed

Dmitrij Alekseevitch Sychev[1]
Grigorij Nikolaevich Shuev[2]
Jana Valer'evna Chertovskih[3]
Nadezhda Romanovna Maksimova[3]
Andrej Vladimirovich Grachev[1]
Ol'ga Aleksandrovna Syrkova[2]

[1]Department of Internal Medicine and Clinical Pharmacology, Russian Medical Academy of Postgraduate Education, Moscow, [2]Faculty of Postgraduate Education, Far Eastern State Medical University, Khabarovsk, [3]Genetic Laboratory, Ammosov North-Eastern Federal University, Yakutsk, Russian Federation

Among the Yakuts, the C allele of SLCO1B1 * 5 was 2 times more common than in Russians - a lesser predisposition to statin myopathy

Table 1 Results of comparison of frequency of *C*-allele of *SLCO1B1*, Russian and Sakha (Yakutia) versus published data

Population	n	*TT* genotype	*TC* genotype	*CC* genotype	*T* allele[a]	*C* allele[a]	Comparison with Russian			Comparison with Sakha (Yakutia)		
							Chi-squared	*P*	OR (95% CI)	Chi-squared	*P*	OR (95% CI)
Russian Federation, Russians	1,071	665 (62%)	346 (32%)	60 (6%)	1,676 (78%)	466 (22%)	–	–	–	8.9	0.0028	2.2 (1.32–3.70)
Russian Federation, Sakha (Yakutia)	76	62 (82%)	11 (14%)	3 (4%)	135 (89%)	17 (11%)	8.9	0.0028	0.45 (0.27–0.76)	–		
Brazil[11]	216	152 (71%)	59 (27%)	5 (2%)	363 (84%)	69 (16%)	7.1	0.0078	0.68 (0.52–0.90)	1.69	0.19	1.5 (0.86–2.66)
China[12]	272	205 (75%)	62 (23%)	5 (2%)	472 (87%)	72 (13%)	19.3	<0.0001	0.55 (0.42–0.72)	0.28	0.59	1.2 (0.69–2.13)
China[13]	363	256 (71%)	95 (26%)	12 (3%)	607 (83%)	119 (17%)	9.4	0.002	0.70 (0.56–0.88)	2.2	0.136	1.56 (0.91–2.68)
China[14]	140	111 (79%)	27 (19%)	2 (2%)	249 (89%)	31 (11%)	16.8	<0.0001	0.45 (0.30–0.66)	0.0013	0.97	0.99 (0.53–1.85)
China[15]	373	281 (75%)	82 (22%)	10 (3%)	644 (86%)	102 (14%)	22.6	<0.0001	(0.45–0.72)	0.48	0.49	1.26 (0.73–2.17)
France[16]	724	519 (72%)	193 (26.5%)	12 (1.5%)	1,231 (85%)	217 (15%)	25.6	<0.0001	0.63 (0.53–0.75)	1.3	0.25	1.4 (0.83–2.37)
Japan[17]	64	44 (73%)	20 (27%)	0 (0%)	108 (84%)	20 (16%)	2.4	0.12	0.66 (0.41–1.08)	0.83	0.36	1.47 (0.73–2.95)

Note: [a]Number (allele frequency).

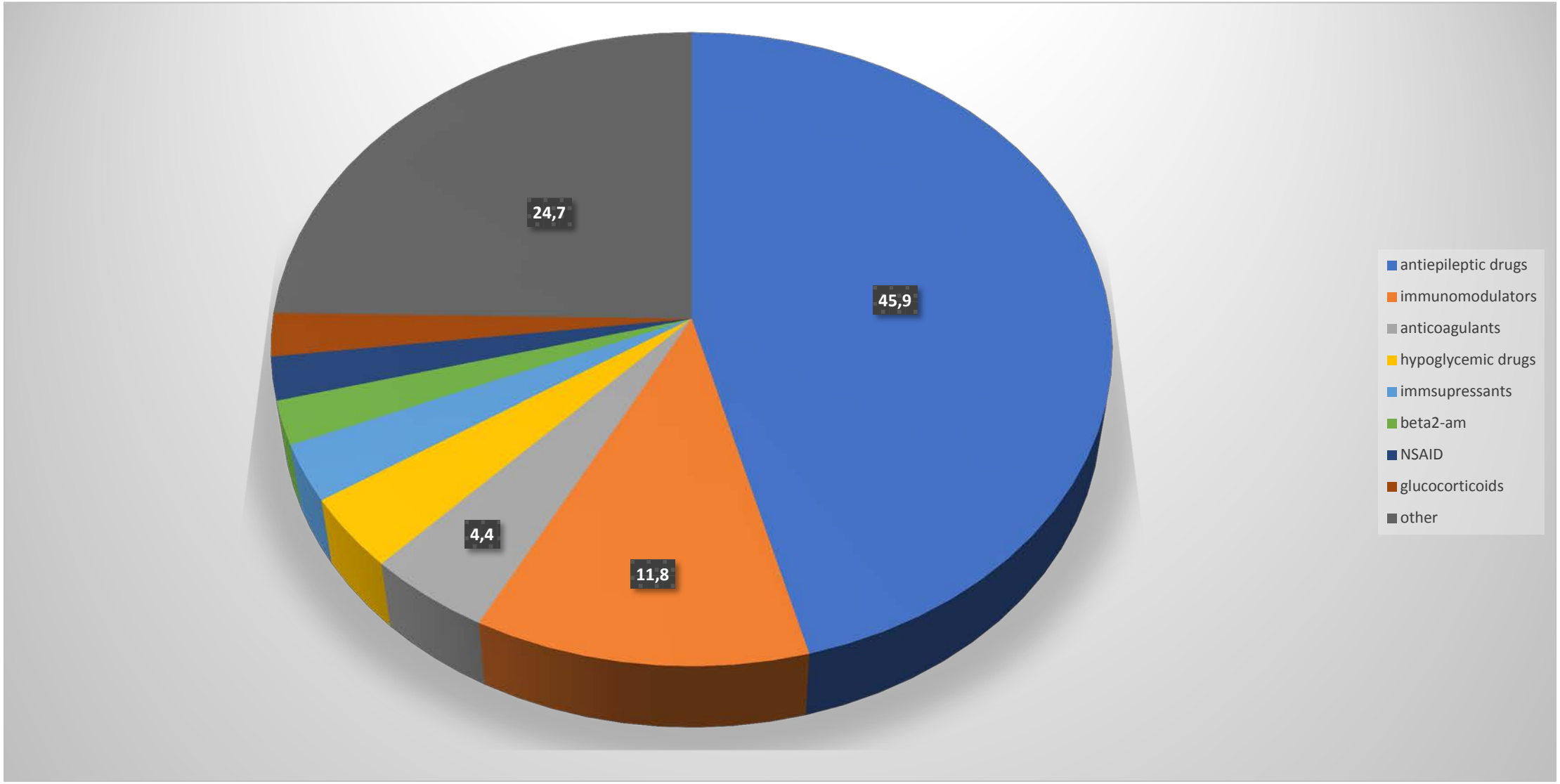
(82%), *TC* – 11 (14%), *CC* – 3 (4%) (Hardy–Weinberg's chi-square test was 5.13 *P*=0.077). In comparison with data from Brazil, France, the People's Republic of China, and Japan, *C*-allele frequency in the Sakha (Yakutian) population was not significantly different.

Conclusion: Thus, we have studied the incidence of pathologic *SLCO1B1 c.521C*-allele in Russian and Sakha hyperlipidemic patients. The presence of *SLCO1B1 C*-allele in patients with hyperlipidemia forces us to be more careful in hypolipidemic drug prescription, especially statins, according to a higher risk of statin-induced myopathy development. The fact that *SLCO1B1 C*-allele is rarer among Sakha patients, could be interesting from the point of studying adverse

Analysis of data from the Russian electronic database of spontaneous reports

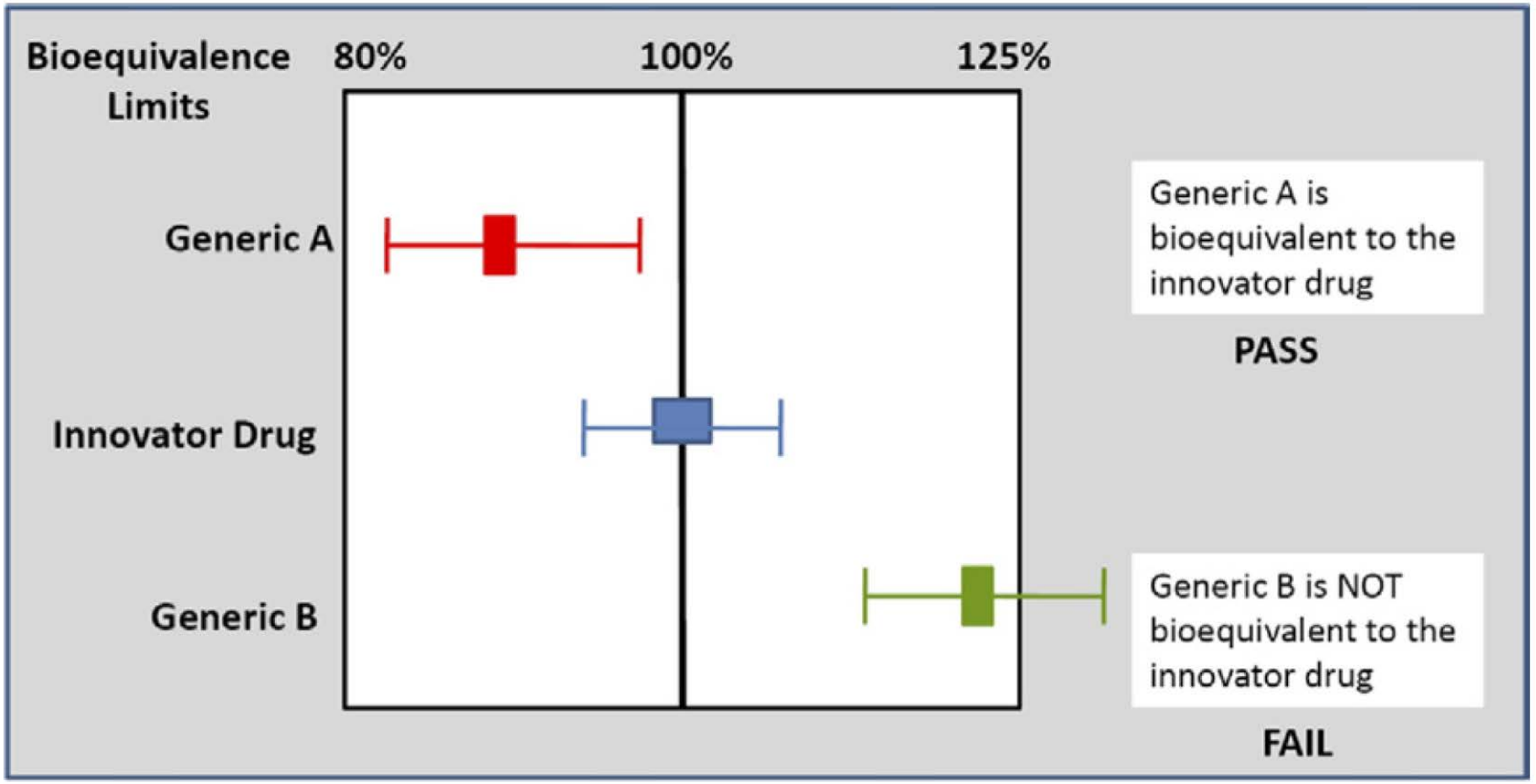
- An analysis of all spontaneous reports on adverse reactions over a period of 10 years has shown that reports on the drug inefficiency when replacing the reference drug with generic and vice versa were met at 1.9%.
- As result serious adverse reactions developed in 88,9% of all cases

Groups of medicines, most often showing inefficacy on replacing the reference drug with generic



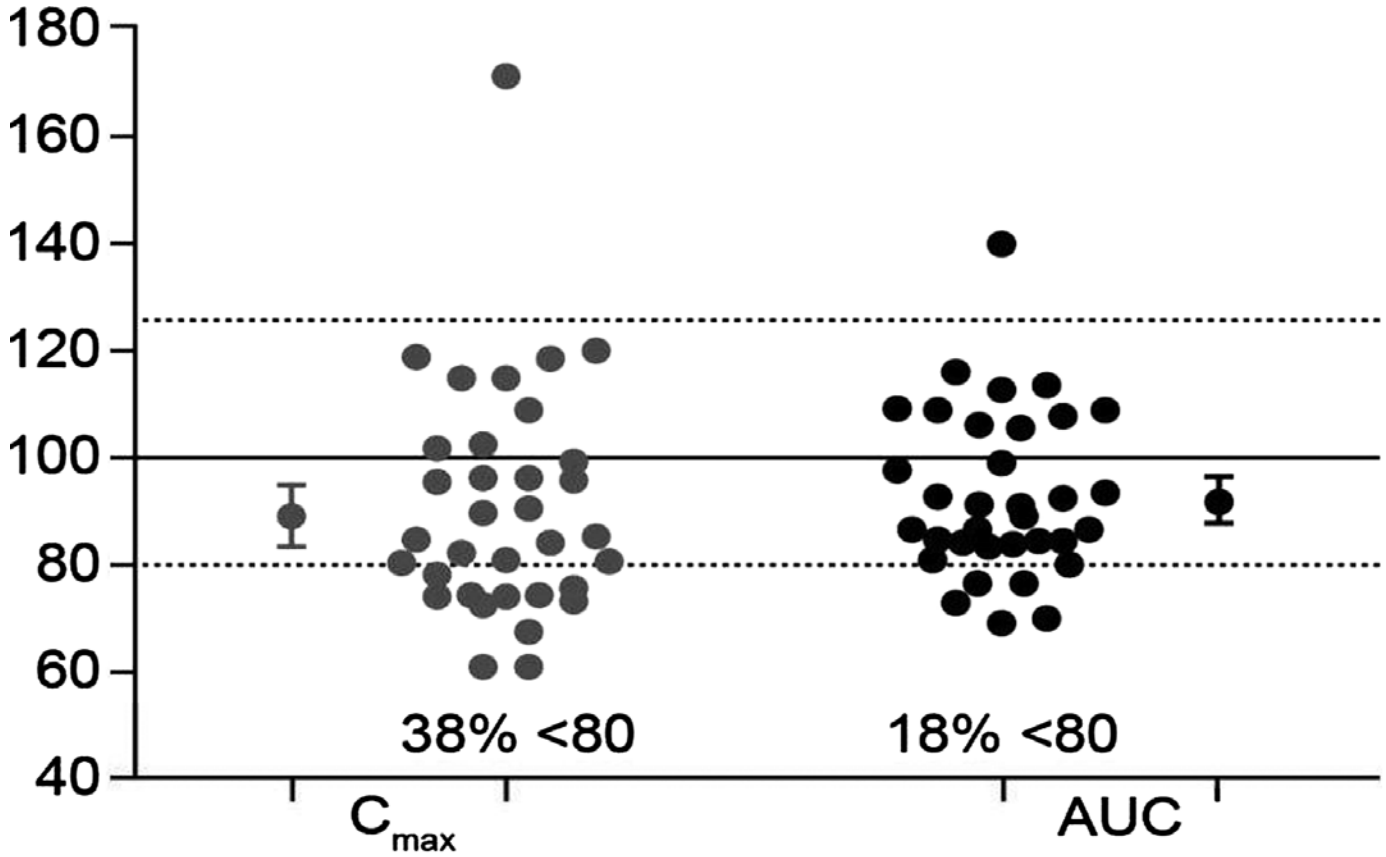
Bioequivalency

The established bioequivalence limits are 80% to 125%



Bioequivalency

The inefficiency of the drug is caused by individual characteristics of the organism

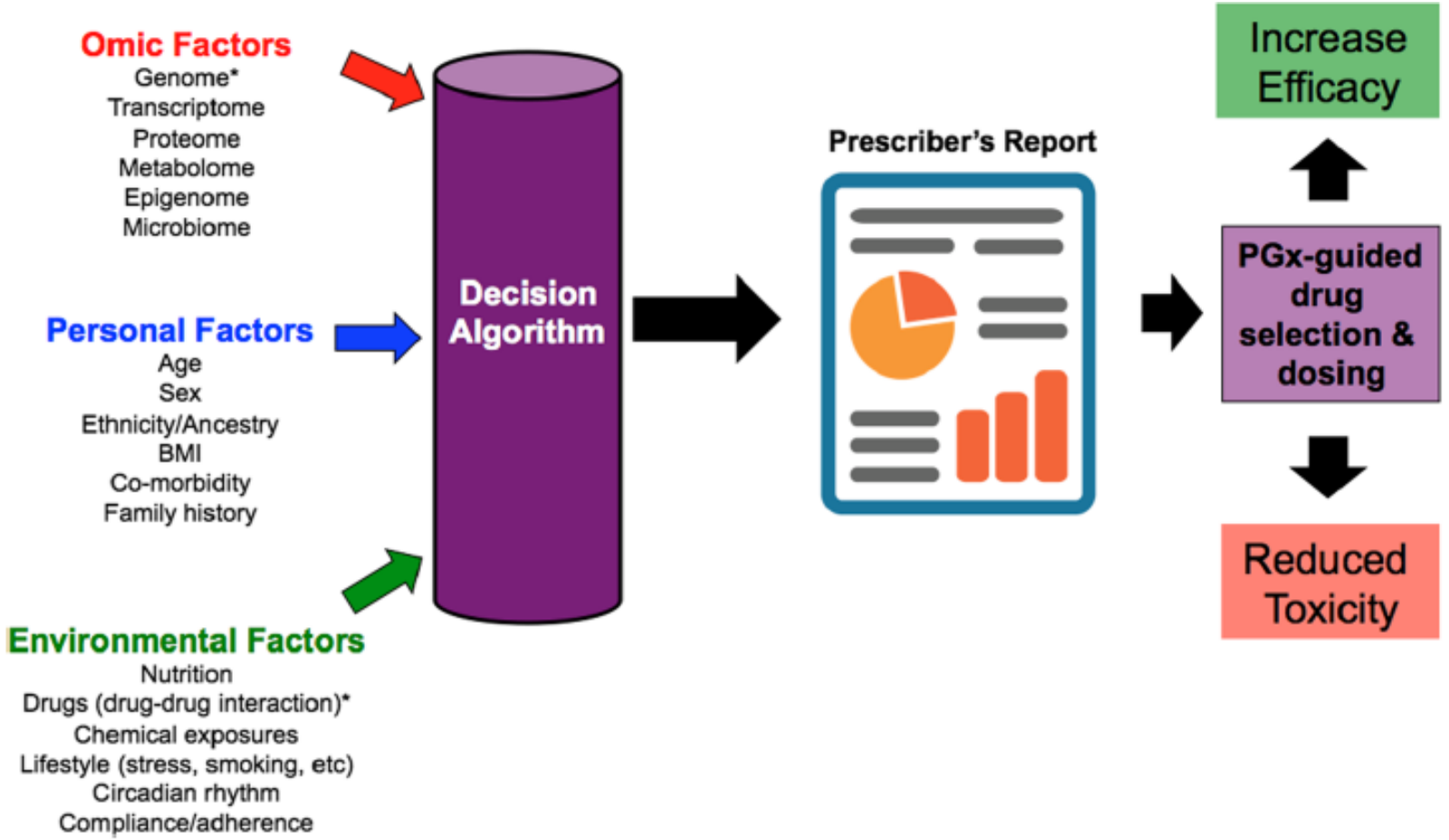


Composition of excipients included into the composition of the cyclosporine dosage form

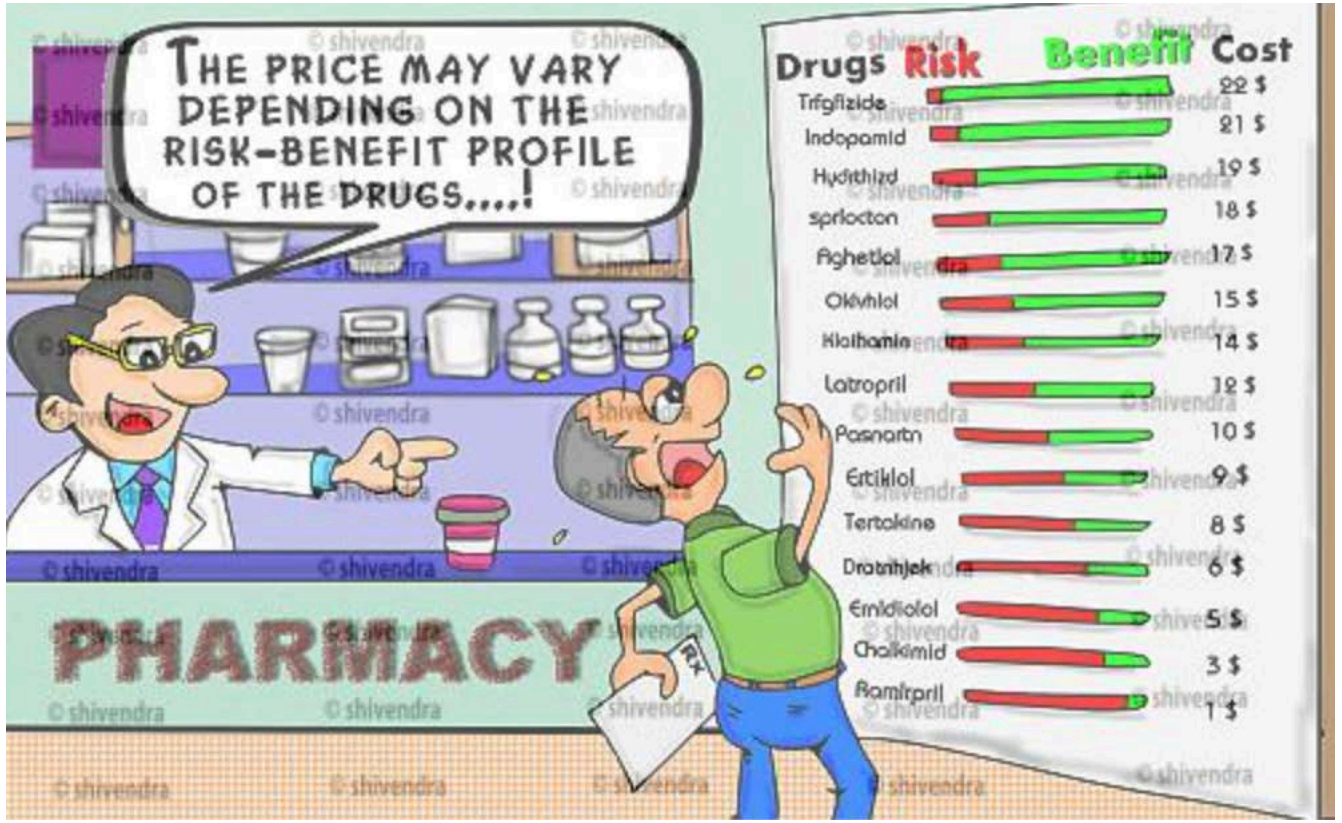
ORIGINAL DRUG	GENERIC DRUG
• Tocopherol • Ethanol • Propylene glycol • Mono, di, triglycerides • Corn oil • Hydrogenated Castor Oil	• PEG • Polysorbate 80 • Propylene glycol • Sorbitol • Titanium Oxide

Cause of inefficiency of the drug may be not only features of ADME active substance, but also excipients

Omics technology to clinical practice!



Selection of treatment on the basis of patient individual characteristics, taking into account the "set" of polymorphisms of certain genes makes it possible to make drug treatment effective and safe.



Thank you!