ACTO

ASSOCIATION OF CLINICAL TRIALS ORGANIZATIONS

ACTO NEWSLETTER № 30

Summary of 2024 results

MOSCOW 2025

CONTENTS

SUMMARY

In 2024, the Ministry of Health of Russia issued 17.3% fewer approvals for clinical trials compared to 2023: 629 versus 761. The number of approvals for international multicentre clinical trials (IMCTs) remained unchanged at 18, with ten of the 18 new projects in 2024 initiated by Russian sponsors. Activity in the IMCT sector had already declined to the lowest levels in the past 20 years during the second half of 2022 and has remained at this level.

The most significant decrease—27.5% (343 approvals vs 473 in 2023) — was recorded in the sector of bioequivalence studies for Russian generics. After the decline in IMCTs, this market segment became the largest in Russia (54.5% of all types of studies by the end of 2024), and its reduction had the greatest impact on the overall decrease in research volumes for the year. The reduction in the number of new bioequivalence studies by Russian sponsors is particularly notable, as this indicator had been growing steadily from 2020 to 2023, with 2024 being an exception.

The number of approvals for bioequivalence studies of foreign generics also decreased significantly — by 14.8% (104 vs 122 the year before). The number of approvals for local studies by Russian sponsors remained almost unchanged (-2.3%, 128 approvals vs 131 in 2023). The only type of research that saw an increase in the number of approvals issued was local research conducted by foreign sponsors – 36 vs 17 (111.8%).

In 2024, ACTO continued to monitor the practice of backdating entries on approved clinical trials in the Ministry of Health registry. In 2024, 23 cases were recorded where entries were added to the registry with delays (on average, by 23 days, with a maximum delay of 141 days). Additionally, four entries had not appeared in the registry by the time the newsletter was published.

Another concerning trend continued to develop in 2024 – sponsors of research on generics/biosimilars are not specifying the reference drug in the protocol's title. In 2023, 81 such cases were recorded, and in 2024, their number reached 124 (for comparison: in 2021, there were only two such cases). The share of comparative studies of generics and biosimilars in which the comparison drug is not indicated in the protocols increased from 0.5% in 2021 to 24% in 2024. This practice makes information about the studies less accessible to the public.

In addition to the above, the newsletter summarizing 2024 contains information on:

– types of drugs studied in local research;

– distribution of various types of research by therapeutic areas;

– most popular molecules in the research of generics and biosimilars;

– distribution of foreign sponsors who received approvals in 2024 to study their reproduced medications in Russia by countries;

– medical organizations that most frequently participate in conducting bioequivalence studies;

– sponsors and contract research organisations leading in the number of approvals for various types of research;

– situation in the clinical research markets of the neighbouring countries of the Russian Federation;

– development of the situation regarding a legislative amendment proposing radical changes in the process of obtaining informed consent.

VOLUME AND DYNAMICS OF THE RUSSIAN CLINICAL TRIALS MARKET

The year 2024 marked a significant reduction in the clinical trials market in Russia. During the year, the Ministry of Health issued 17.3% fewer approvals compared to 2023: 629[1] vs 761 (Table 1). For the first time in the past two years since the start of the war, this reduction was not caused by a decrease in the number of international multicentre clinical trials (IMCTs). In fact, the IMCT sector had no further to 'fall'; it already hit rock bottom back in 2023. Then, as in 2024, only 18 approvals were issued[2] for this type of trial. Looking ahead, it is worth noting that 10 out of the 18 protocols approved in 2024 belonged to Russian sponsors.

As seen in the table, the most significant annual decline was recorded in the sector of bioequivalence studies for Russian generics – at 27.5%: 343 approvals in 2024 compared to 473 in 2023. After the departure of IMCTs, this segment became the largest on the market. Its reduction by more than a quarter was the main reason for the overall market contraction at the end of the year. For foreign companies, the number of bioequivalence study approvals also decreased, though less significantly than for Russian sponsors – by 14.8% (104 approvals vs 122 the year before). Only the sector of local studies on therapeutic efficacy and safety was practically unaffected. Russian sponsors received three fewer approvals (128 vs 131 in 2023; -2.3%). Meanwhile, foreign sponsors obtained 19 more approvals (36 vs 17, which, against a low base, resulted in an increase of 111.8%).

Table 1

Approvals for Conduct Clinical Trials: 2024 vs 2023						
Year	**Total**	**International Multicenter CTs**	**Local CTs (Foreign Sponsors)**	**Bioequivalence Studies (Foreign Sponsors)**	**Local CTs (Local Sponsors)**	**Bioequivalence Studies (Local Sponsors)**
2024	629	18	36	104	128	343
2023	761	18	17	122	131	473
2024 г. vs 2023, %	-17.3%	0.0%	111.8%	-14.8%	-2.3%	-27.5%

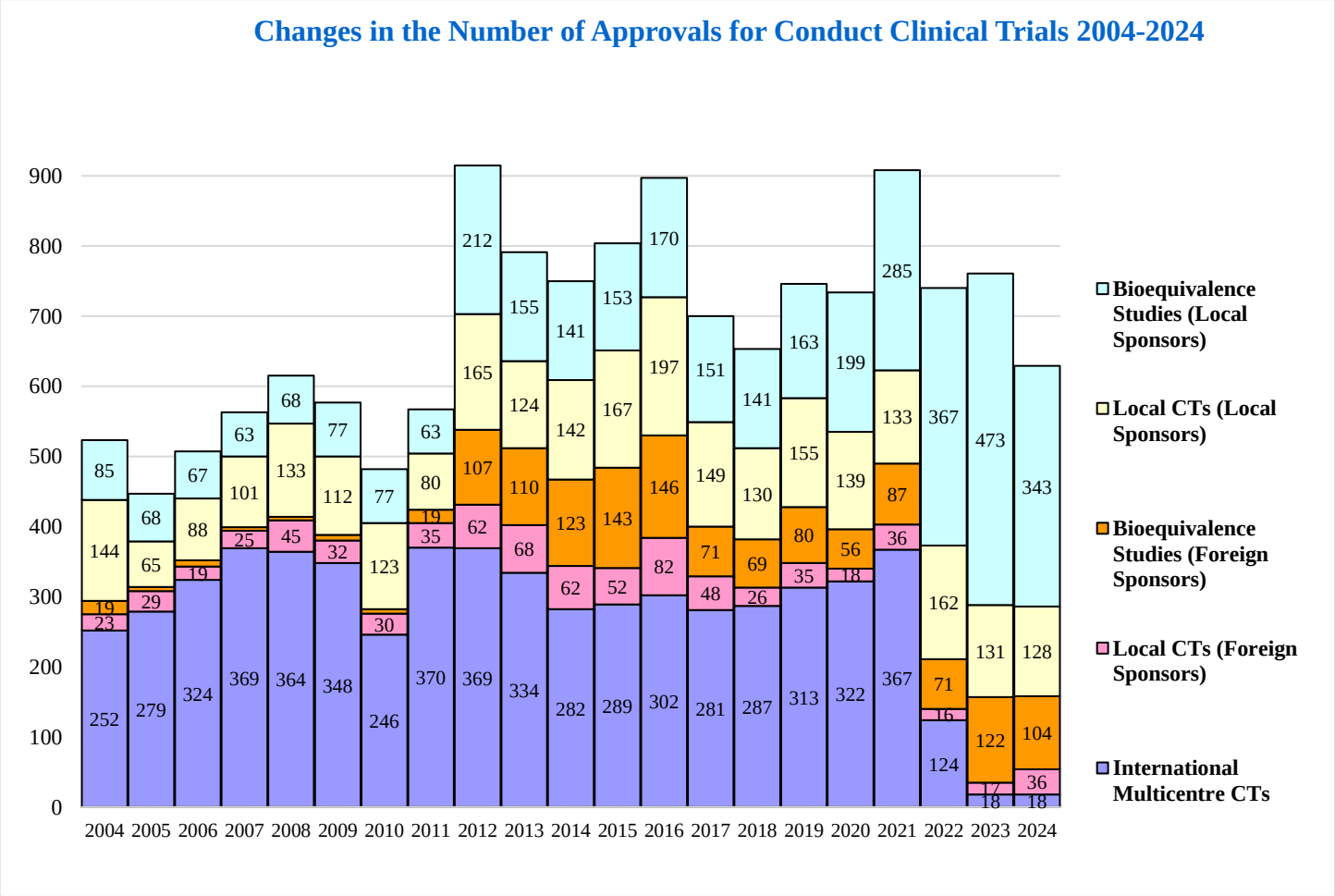
Data from www.grls.rosminzdrav.ru

Diagram 1 reflects the dynamics of the number of issued approvals from 2004 to 2024. Diagrams 2–6 show the same dynamics from 2012 (after the current legislation on the circulation of medicines came into force) separately for each type of study, broken down by half-year periods.

[1]Actually, there should be 633 registry entries for 2024. However, as of early March 2025, there are 629, with four numbers 'missing'. For more details, see page 9.

[2]We do not rely solely on entries in the Ministry of Health registry and classify trials as IMCTs only when information about their international status is confirmed by other sources, primarily international databases. According to the Ministry of Health's registry, 23 IMCT approvals were issued in 2024. However, we classified two studies conducted by Russian sponsors, one by an Indian sponsor, and one by a Belarusian sponsor as local trials since we did not find them in the aforementioned sources.

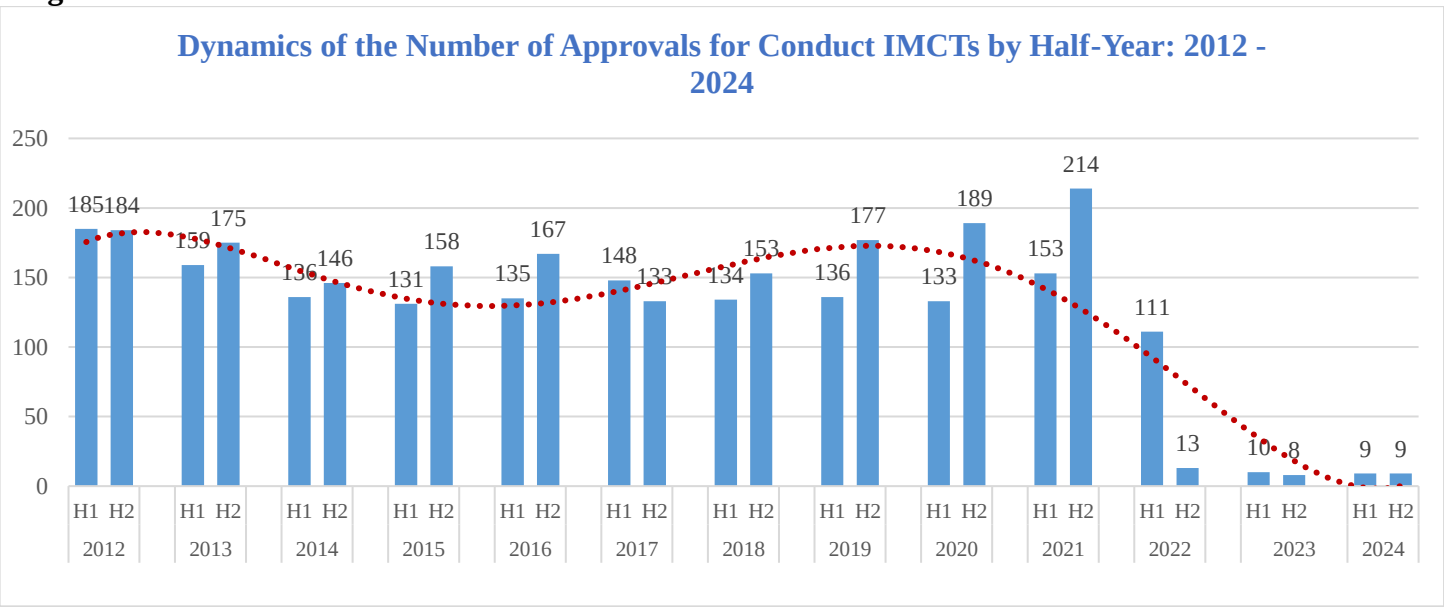
Diagram 1



Data from www.grls.rosminzdrav.ru

It is evident that the number of new IMCTs dropped to the lowest levels ever observed in the second half of 2022 and has since remained at this level (Diagram 2).

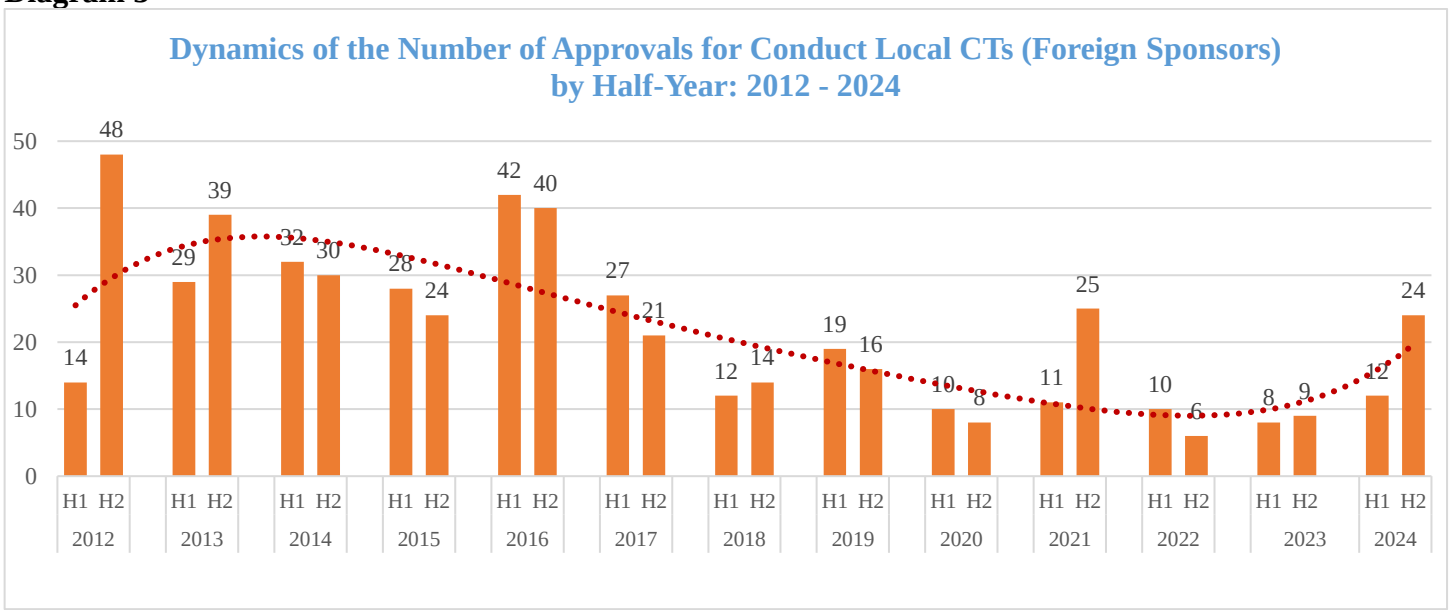
Diagram 2



Data from www.grls.rosminzdrav.ru

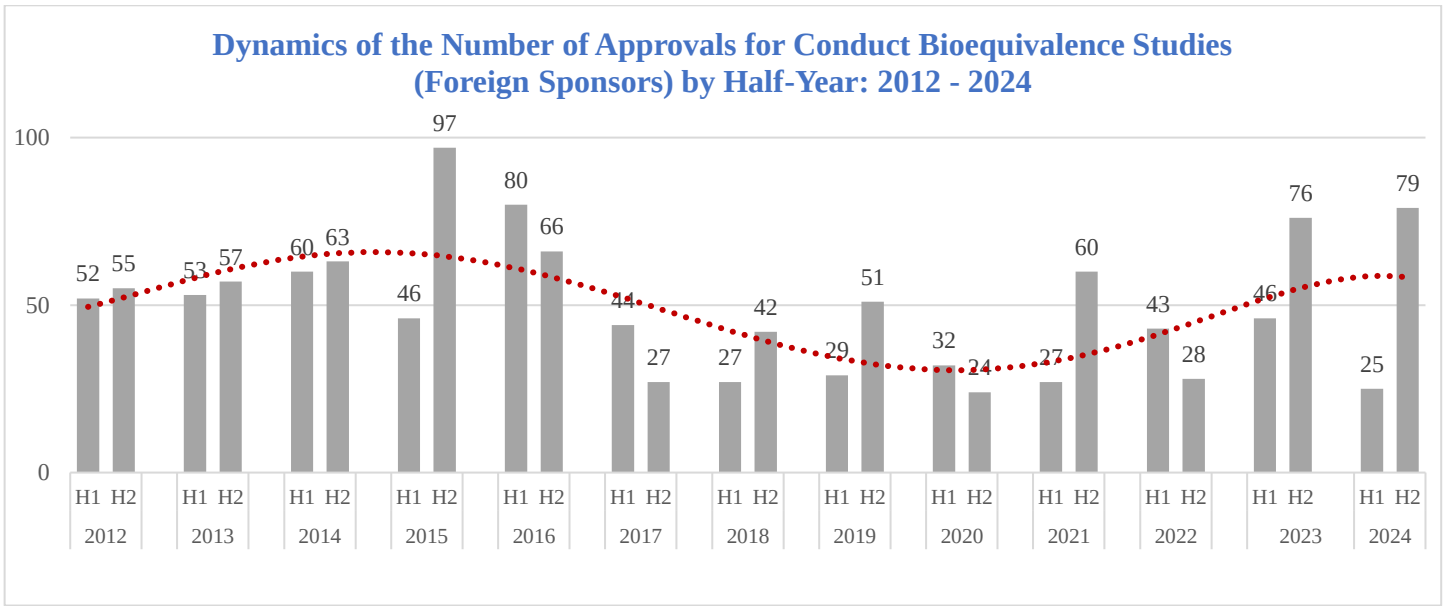
The number of approvals for foreign sponsors, both for local trials and for bioequivalence studies, fluctuates year by year but remains within the more or less usual fluctuation range of recent years (Diagrams 1, 3, and 4).

Diagram 3



Data from www.grls.rosminzdrav.ru

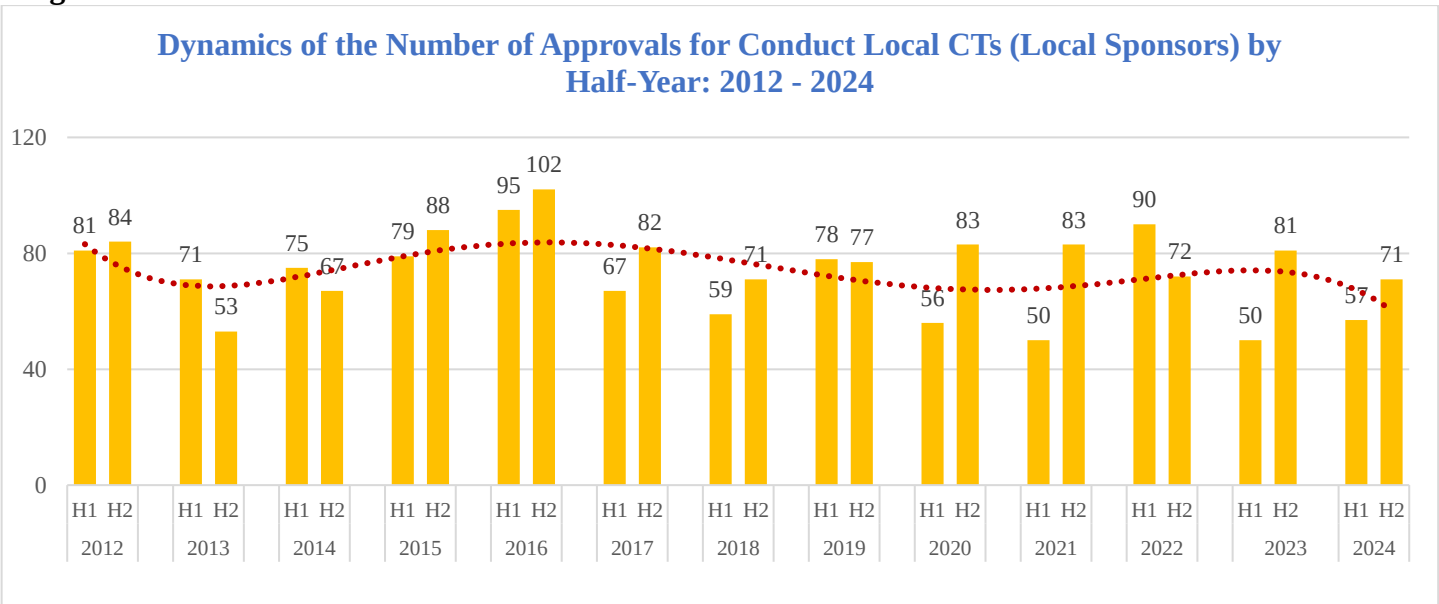
Diagram 4



Data from www.grls.rosminzdrav.ru

The number of approvals for local trials on the therapeutic efficacy and safety of domestically produced drugs in 2024 (128) is below the average for the period from 2012 to 2023 (149.5 approvals) but slightly above the decline observed in 2013 (124 approvals) (Diagrams 1 and 5).

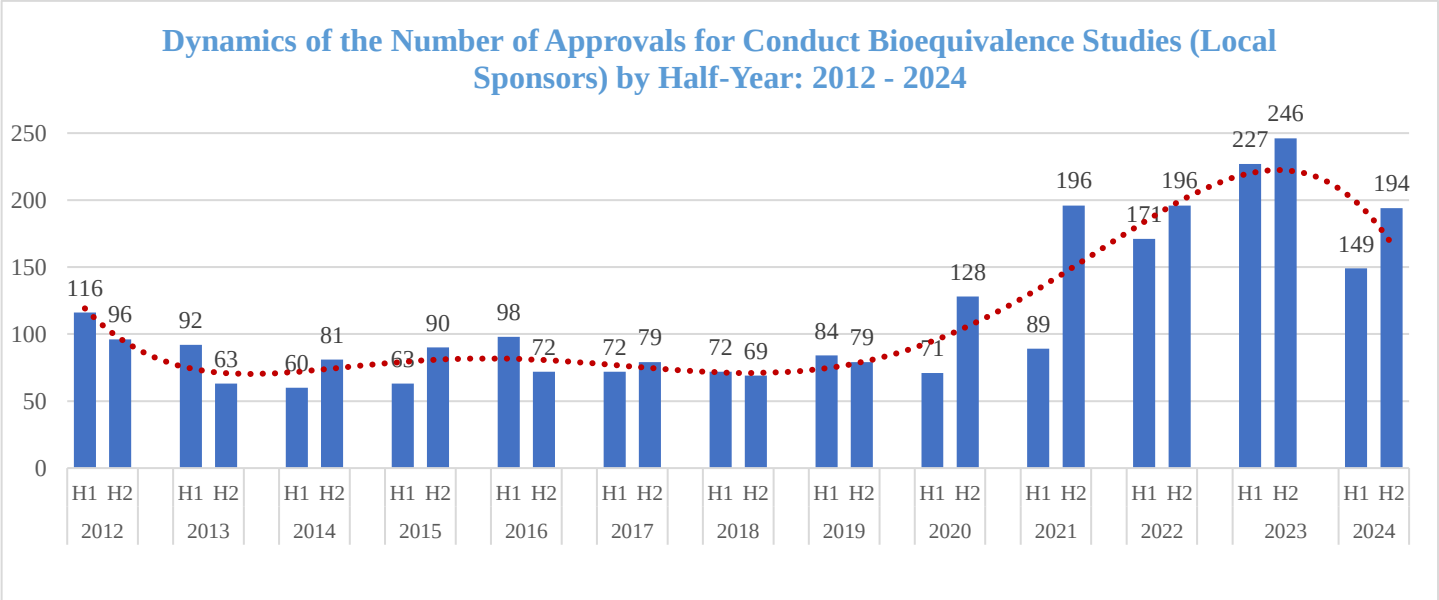
Diagram 5



Data from www.grls.rosminzdrav.ru

The bioequivalence research sector of Russian sponsors appears less stable (diagrams 1 and 6): from 2020–2023, the results of each year surpassed that of the previous year (a consequence of the pandemic? the expiry of patents for a large number of blockbusters? the general trend towards import substitution? a combination of all these factors?). However, the past year marked a turning point for this upward trend. The indicator for 2024 is still higher than the result for 2021 and any earlier year, but it is noticeably lower than for 2022 and 2023. The reasons for this remain speculative. This could be the result of the boom coming to an end, driven by the approaching expiry of patents on a range of pharmaceutical blockbusters. Alternatively, it may reflect broader processes in the Russian economy, which is undergoing challenging times. It will be interesting to see whether the reduction in the number of this type of research continues in 2025.

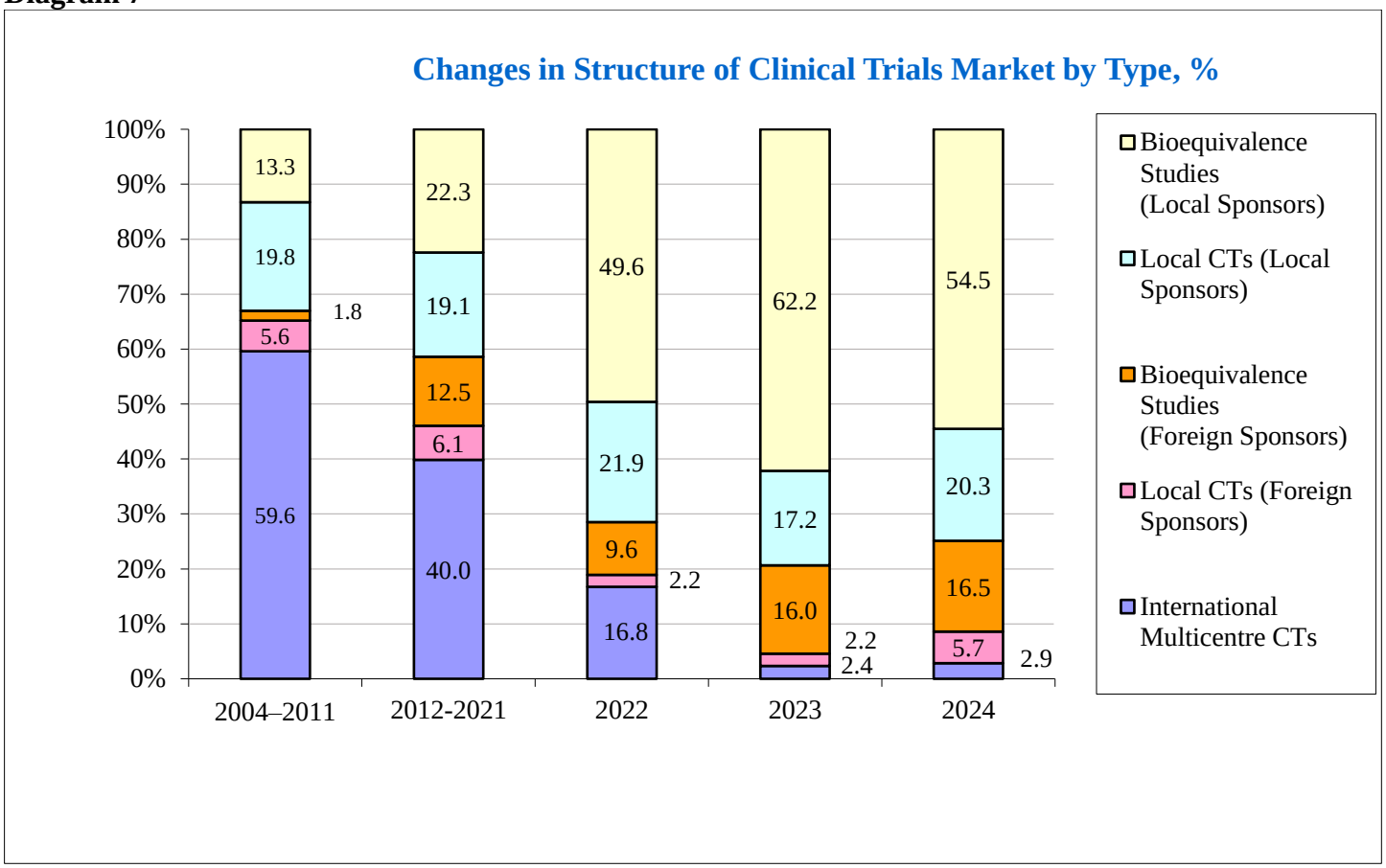
Diagram 6



Data from www.grls.rosminzdrav.ru

Diagram 7 shows how the shares of each type of trials have changed during different periods: before the adoption of the current legislation on the circulation of medicines (average indicator for 2004–2011), after its implementation and before the start of the war (average indicator for 2012–2021), and finally, over the past three years.

Diagram 7



Data from www.grls.rosminzdrav.ru

Until 2022, IMCTs dominated the market: during the "pre-reform" period, they accounted for an average of 59.6% of the total number of approvals, and after the adoption of the law "On Circulation of Medicines," their average share decreased to 40%. As we can see from diagram 1, this occurred not due to a decrease in the number of international projects, but due to an increase in the number of other types of trials, primarily bioequivalence studies.

After 2022, the market structure changed drastically. The share of IMCTs in 2022 decreased to 16.8%[3]. In 2023 and 2024, the share of IMCTs dropped to its historic low – less than 3%. Meanwhile, approximately 80% of all approvals now is accounted for by Russian sponsors. At the same time, local trials on the therapeutic efficacy and safety of domestic drugs still account for about 1/5 of the approvals issued annually. However, projects studying the bioequivalence of Russian generics have become the dominant market segment: 49.6% in 2022, 62.2% in 2023, and 54.5% in 2024. And despite a significant (-27.5%) reduction in the number of approvals issued for this type of trials in 2024, their share in the overall market structure decreased by only 7.7 percentage points year-on-year and still accounts for more than half of the total volume.

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In the newsletter summarising the results of 2023, we reported for the first time on the increasing instances of backdating entries about approved trials in the Ministry of Health registry. According to the procedure approved by the order of the Ministry of Health of Russia dated 26 August 2010 No. 754n *On the Procedure for Maintaining, Publishing, and Posting on the Official Internet Website of the Ministry of Health a Registry of Approved Clinical Trials of Medicinal Products for Medical Use*, the entries regarding the issuance of an approval

[3] This figure did not accurately reflect the actual state of affairs in the sector, as it only showed the number of approvals issued, without considering cases where foreign sponsors did not initiate subject recruitment for already approved trials.

for conducting a trial must be entered into the registry no later than one working day after the decision to issue the approval is made. This requirement was generally adhered to until 2023, when we first recorded systematic failures. Gaps began appearing in the register: an approval is issued under number 10, then 12, while number 11 may appear in the register several days, weeks, or even months later.

In total, there were 23 trials entered retrospectively into the Ministry of Health's register in 2024 (compared to 35 in 2023). The average delay in entering a record in 2024 was 23 days (one day longer than in 2023), the minimum was three days (the same as the previous year), and the maximum was 141 days (compared to 109 in 2023). At the same time, records of four approvals in the 2024 register had not appeared by the time the newsletter was released, despite sequential numbering suggesting that they should be present (approvals numbered 569, 574, 576, and 618).

In 2023, Ministry of Health employees resolved all remaining gaps in the register literally on the last working day of the year. In 2024, they did not consider it necessary to do so, despite our reminder. Two records from the previous year were added in January 2025, one in February, and four, as mentioned earlier, remained unaddressed. Therefore, the actual average delay in entering records in 2024 is greater than the figure we reported, but it is currently impossible to calculate due to the lack of data.

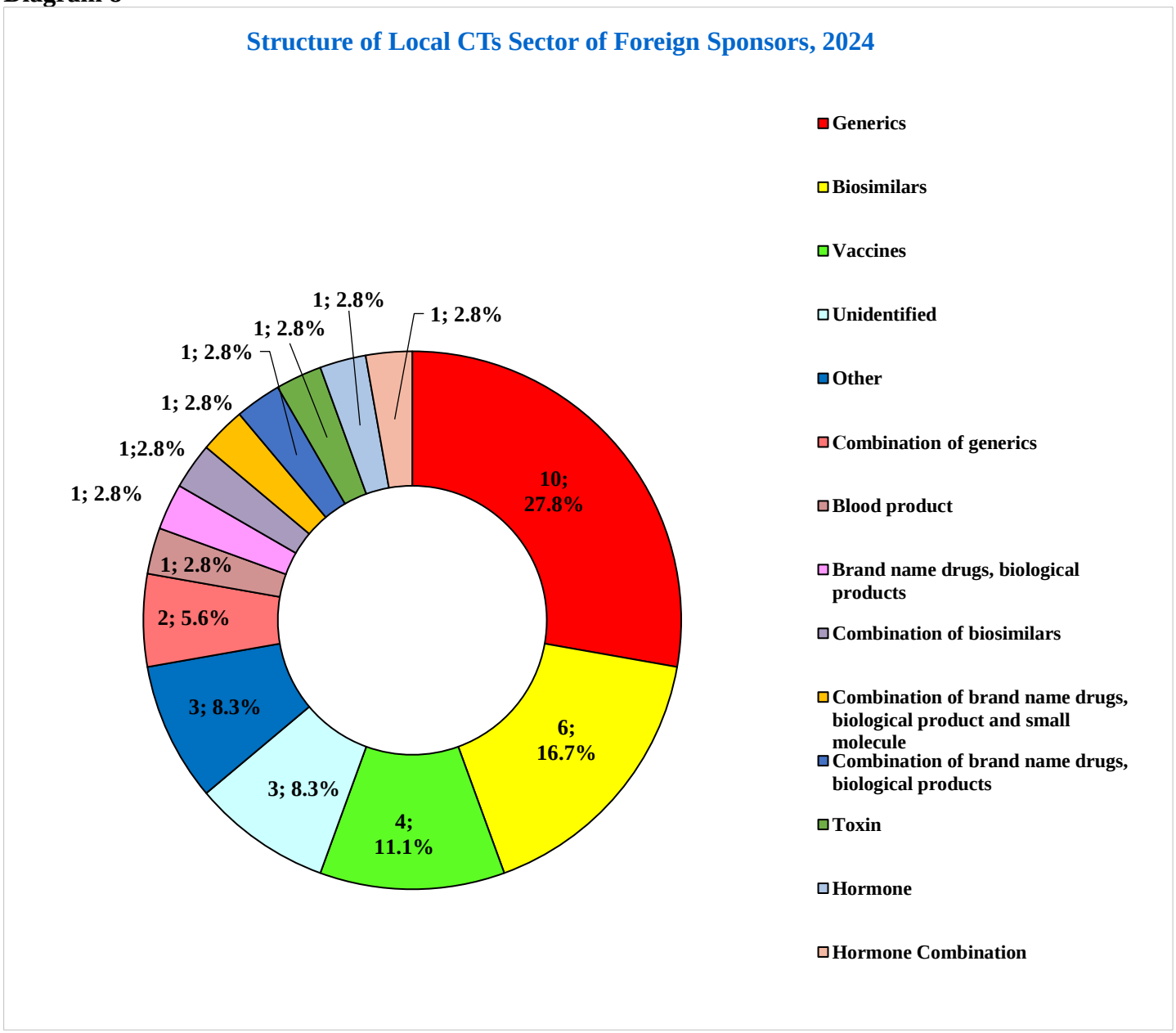
Notably, in 2024, the Ministry of Health Order No. 754n was replaced by a new order, Ministry of Health Order No. 708n dated 23 December 2024,*"On Approving the Procedure for Maintaining the Register of Approved Clinical Trials of Medicinal Products for Medical Use"*. According to the new order, entries in the register must be made simultaneously with the Ministry of Health of Russia's decision to issue an approval for conducting a clinical trial. That is, on the same day. The order came into force on 15 February 2025. However, there is still no understanding as to how closely the Ministry of Health intends to follow its own requirements.

STRUCTURE OF THE MARKET FOR LOCAL TRIALS

Diagrams 8 and 9 show the types of medicinal products studied in local protocols for therapeutic efficacy and safety by foreign and Russian companies, respectively. It should be noted that bioequivalence studies are not included here, and the overall share of generics is significantly higher than reflected in the statistics of this section.

In the structure of local studies by foreign sponsors (Diagram 8), the largest share (27.8%) was taken by generics – 10 approvals. Another two approvals (5.6%) were granted for their combinations. Six approvals were issued for the study of biosimilars (16.7%). These include two denosumab studies — Indian and Chinese — as well as Iranian pembrolizumab, ocrelizumab, and aflibercept, and Indian abatacept. Additionally, another trial by an Indian sponsor is investigating a combination of two monoclonal antibodies: doralimab and mirimabimab, used jointly with a vaccine for rabies prevention.

Diagram 8



Data from www.grls.rosminzdrav.ru

Four approvals were for vaccines (11.1%): Chinese and South Korean vaccines against chickenpox, the Cuban one against meningococcal infection, and a combined vaccine candidate based on virus-like particles of

the respiratory syncytial virus (RSV)/human metapneumovirus, recently acquired by AstraZeneca from the company Icosavax.

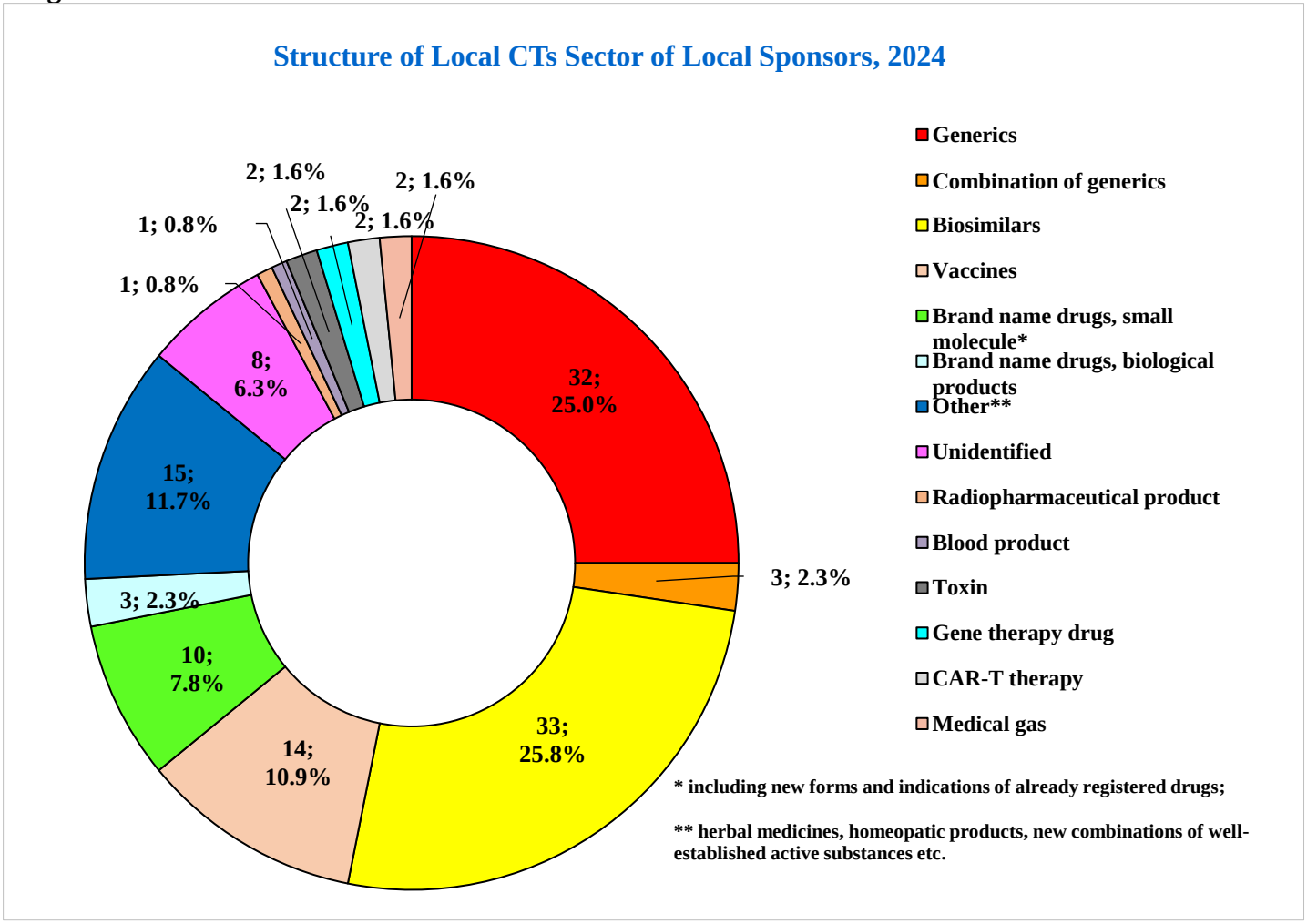
In addition, AstraZeneca is researching its valrustomig for cervical cancer, a combination of durvalumab and oleclumab for non-small cell lung cancer, as well as AZD0901, a conjugate of a biological molecule and a small molecule, for gastric or gastroesophageal junction adenocarcinoma.

The hormone estradiol and the combination of estradiol and progesterone have been put forward for study by the Bulgarian company Zentiva and the Belgian company Bezen Healthcare SA, respectively. Companies from Belarus have received approval to study immunoglobulin and botulinum toxin.

Three approvals (8.3%) were for the categories "other" and "unidentified" products (an acne treatment cream of unknown composition and two drugs about which even less is known).

In the structure of local studies by Russian sponsors (diagram 9), biosimilars hold the largest share at 25.8% (33 approvals). Generics follow closely at 25.0% (32 approvals), with another three approved trials (2.3%) relating to combinations of generics. By the end of 2024, the share of biosimilars does not significantly exceed the share of generics as it did in 2023. (27.5% vs 17.6%), but it significantly outperforms figures from earlier years, when the share was around 10% or less. More than half of the 33 approvals for biosimilars were accounted for by three companies: Generium and Geropharm (seven approvals each) and Grotex (four approvals). R-Pharm, Mabscale and Orphan-Bio received three approvals each, while Biocad obtained two.

Diagram 9



Data from www.grls.rosminzdrav.ru

Vaccines accounted for 10.9% (14 approvals) in the structure of local trials by Russian sponsors by the end of 2024. Three approvals (2.3%) were granted for original biological products by R-Pharm, SupraGen and the N.F. Gamaleya National Research Centre for Epidemiology and Microbiology.

Separately, we would like to highlight two additional groups of drugs identified among the approvals for research in 2024.

Firstly, the Federal State Budgetary Institution “National Medical Research Center for Hematology” of the Russian Ministry of Health received two approvals for the study of Utjephra (second-generation CAR T-cells specific for the CD19 antigen of B-cells): *an interventional, open-label, single-group phase I/II study to assess the tolerability, safety and efficacy of the anti-CD19 CAR-T medicinal product in adult patients with relapses and refractory forms of B-cell lymphoproliferative disorders*, as well as subsequent non-interventional follow-up of the same patients.

The solution, in our view, is groundbreaking, as Russia has lost many years attempting to 'promote the development' of cell technologies, which has produced the opposite effect – a sharp slowdown. It all began back in the 2010s, when the Ministry of Health declared that, in order to develop one of the most promising areas of biomedicine, separate legislation needed to be formed. The preparation of a draft federal law 'On Biomedical Cell Technologies' was announced. At the same time, a number of foreign sponsors were already prepared to offer Russia participation in research on their developments in this field. However, the initiative was halted at the dossier submission stage by an unequivocal decision from the Ministry of Health: 'We are preparing a new law, come back later.' Attempts by companies to explain that there was nothing preventing these products from being considered under the current legislation on the circulation of medicines led nowhere. The verdict remained unchanged: 'wait.' The law 'On Biomedical Cell Products' (BMCP) was only adopted in 2016. But this did not signify the start of the process. Firstly, for practical implementation, it was necessary to develop and adopt a large number of subordinate acts. Secondly, in itself, it was a poor copy of the first edition of the law 'On Circulation of Medicines', and some of its specific requirements (for example, conducting sample examinations of cell products to obtain approvals for clinical trials) appeared to be completely unfeasible for foreign companies. After attempting to discuss difficulties with representatives of the regulator, they gave up and began waiting for more favourable legislation to be adopted at the EAEU level (where they decided to take a logical approach, acknowledging that biomedical cell products, while specific, are nevertheless medicinal products and should generally be regulated under medicinal legislation). At the same time, some Russian research institutes were already prepared to test their developments. However, after trying to navigate the impenetrable jungle of Russian law, they were forced to retreat and 'go underground'. It seems there is neither clinical trial nor a registered product, but 'we have our patients, they need treatment, and we treat them in the way we believe is best for them'. 'To the madness of the brave, we sing a song…'. Only one representative of Russian developers has so far managed to break through the crucible of legislative thought. In December 2023, the company Generium became the first (and only) in Russia to receive a registration certificate for its product Ezitens® (spheroids from autologous human chondrocytes bound by a matrix) under the law "On BMCP." And as of the beginning of March 2025, the register still contains only this entry. Likewise, the BMCP clinical trial register contains only one entry regarding a study of the same product, which was approved for conduction in 2021.

And now, at last, a breakthrough! The Ministry of Health, it seems, has been forced to yield to common sense and references to the approach adopted in the EAEU, and has agreed to grant permission for the study of a product manufactured using CAR-T technology under the legislation "On Circulation of Medicines." Hallelujah! But it is very unfortunate that it took more than a decade for this elementary decision...

The second pleasantly surprising find in the 2024 register is the approvals of trials for two gene therapy products. One approval was granted to Gene Surgery LLC for a Phase IIa study to assess the efficacy and safety of the drug AntioncoRAN-M (stimotimagen copolymer plasmid) in patients with soft tissue sarcoma (Phase I was conducted in 2021). The second was granted to Lomonosov Moscow State University for a Phase I-II study of the drug MediReg® (a secretion of human mesenchymal stromal cells) in patients with severe spermatogenesis disorders.

But let us return to Diagram 9. Original drugs, represented by small molecules, received ten approvals (7.8%). Two approvals each (1.6%) were granted for botulinum toxin and medical gases, one (0.8%) for a radiopharmaceutical and clotting factor VIII.

The category "others" accounted for 11.7% (15 approvals) – bovine brain polypeptides, homeopathic remedies, and so on... Additionally, we were unable to identify eight approvals (6.3%). There are assumptions that at least four of them are represented by biological products, and two by small molecules (likely original). For more details on the growing challenges in identifying certain studies, see pp. 19–21.

STRUCTURE OF THE CLINICAL TRIALS MARKET BY THERAPEUTICS AREAS

Table 2 presents the distribution of IMCTs approvals issued in 2024 by therapeutic areas.

Table 2

Distribution of International Multicenter CTs by Therapeutic Areas, 2024			
Therapeutic Area	**Number of IMCTs**	**Share (%)**	**The number of planned participants**
Oncology	8	44.4%	2 106
Ophthalmology	2	11.1%	239
Oncohaematology	2	11.1%	225
Infectious Diseases (vaccine)	1	5.6%	400
Cardiology	1	5.6%	267
Dermatology/Rheumatology	1	5.6%	240
Rheumatology	1	5.6%	100
Haematology	1	5.6%	60
Other (type VI mucopolysaccharidosis)	1	5.6%	15
TOTAL	18	100.0%	3 652

Data from www.grls.rosminzdrav.ru

Eight out of 18 international protocols are in the field of oncology. Half of them were initiated by Russian companies. Biocad is investigating its development BCD-236 against breast cancer in Phase II and a biosimilar of nivolumab in Phase III for advanced skin melanoma. R-Pharm is testing two monoclonal biosimilars in IMCTs: cetuximab for squamous cell carcinoma of the head and neck, and pertuzumab against breast cancer. The Iranian CinnaGen Co. is also researching its pertuzumab analogue for breast cancer, while the Indian company Dr. Reddy's is investigating nivolumab for non-small cell lung cancer. Dr. Reddy's Laboratories Ltd. launches an additional study for 25 patients who completed participation in the previous oncology trial with durvalumab by AstraZeneca. The last but not least IMCT in oncology is the study by the American company Oncotelic Inc. for the first-in-class targeted therapy drug trabedersen: «*A randomised Phase IIb/III study evaluating the antisense oligonucleotide OT-101 targeting TGF-β2 in combination with the mFOLFIRINOX regimen versus mFOLFIRINOX alone in patients with advanced unresectable or metastatic pancreatic cancer*». A total of 455 patients are planned to be enrolled worldwide, 24 of them in Russia.

Another American company, Ascentage Pharma Group Inc., has included Russia in its Phase III IMCT evaluating olverembatinib in patients with the chronic phase of chronic myeloid leukaemia. In Russia, 25 patients are planned to be enrolled. Another study in oncohaematology is being conducted by Biocad, which is in Phase II/III evaluating its development BCD-248 in subjects with relapsed/refractory multiple myeloma.

Two IMCTs were approved in 2024 in the field of ophthalmology. Both concern biosimilars of Bayer's aflibercept – one by the South Korean company Altos Biologics Inc., the other by the domestic company Generium.

Two more IMCTs by Generium are dedicated to studying a biosimilar of canakinumab in patients with Still's disease and galsulfase in patients with mucopolysaccharidosis type VI. Both trials are a continuation and include patients from earlier studies.

Biocad has initiated research on its proprietary developments BCD-085 (netakimab) in children with moderate to severe plaque psoriasis and ANB-002 in patients with haemophilia B.

AstraZeneca has included Russia in its Baxdrostat study conducted within the Asian population with uncontrolled arterial hypertension (BaxAsia). GlaxoSmithKline has managed to obtain an approval for the continued study of its vaccine for the prevention of respiratory syncytial virus infection in older adults.

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Table 3 presents the approvals issued to foreign sponsors for the study of reproduced drugs (generics and biosimilars), broken down by therapeutic areas. Over the year, their total number decreased by 6%: 125 in 2024 vs 133 in 2023.

Table 3

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars) of Foreign Sponsors, 2024			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Cardiology and CVD/Surgery/Intensive care	31	24.8%	1 780
Obstetrics and gynecology	14	11.2%	1 091
Endocrinology	12	9.6%	880
Infectious Diseases (except HIV/HCV/tuberculosis)	8	6.4%	1 623
Neurology	8	6.4%	632
Urology	8	6.4%	510
Gastroenterology	7	5.6%	470
Psychiatry	6	4.8%	322
Oncology	5	4.0%	452
Analgesic and NSAIDs	5	4.0%	356
Pulmonology	4	3.2%	422
Allergology	3	2.4%	804
Rheumatology	3	2.4%	183
Dermatology	2	1.6%	703
Ophthalmology	2	1.6%	260
Haematology	2	1.6%	151
HIV	2	1.6%	101
Otorhinolaryngology	2	1.6%	64
Oncohaematology	1	0.8%	60
TOTAL	125	100.0%	10 864

Data from www.grls.rosminzdrav.ru

Cardiology and cardiovascular diseases take the leading position[4] with 31 trials (24.8% of the total number of approvals), which is fewer than in 2023 (49 approvals and also the first place). In 2024, obstetrics and gynaecology are in second place with 14 protocols (11.2%), which is significantly higher than in 2023 (two trials). Endocrinology ranks third with 12 studies (9.6%), slightly lower than the previous year (17 approvals and second place in 2023).

Infectious diseases share fourth place[5] with neurology and urology, each having eight approvals (6.4% each). In 2023, neurology and urology shared third place with nine trials (6.8%), while infectious diseases were in fifth place with seven protocols (5.3%).

In 2024, gastroenterology ranked fifth: seven protocols (5.6%) vs only three (2.3%) the previous year.

Thus, in 2024, there was a decrease in interest in the study of reproduced drugs in cardiology and endocrinology compared to 2023, while obstetrics and gynaecology significantly improved their positions. Infectious diseases, neurology and urology remained at the top of the table, with the number of new studies in these areas changing insignificantly.

[4] In recent years, we have been complementing the name of this area with surgery and intensive care due to the active demand for anticoagulants among manufacturers of reproduced drugs since the pandemic.
[5] Excluding HIV, hepatitis C and tuberculosis, which we traditionally consider separately.

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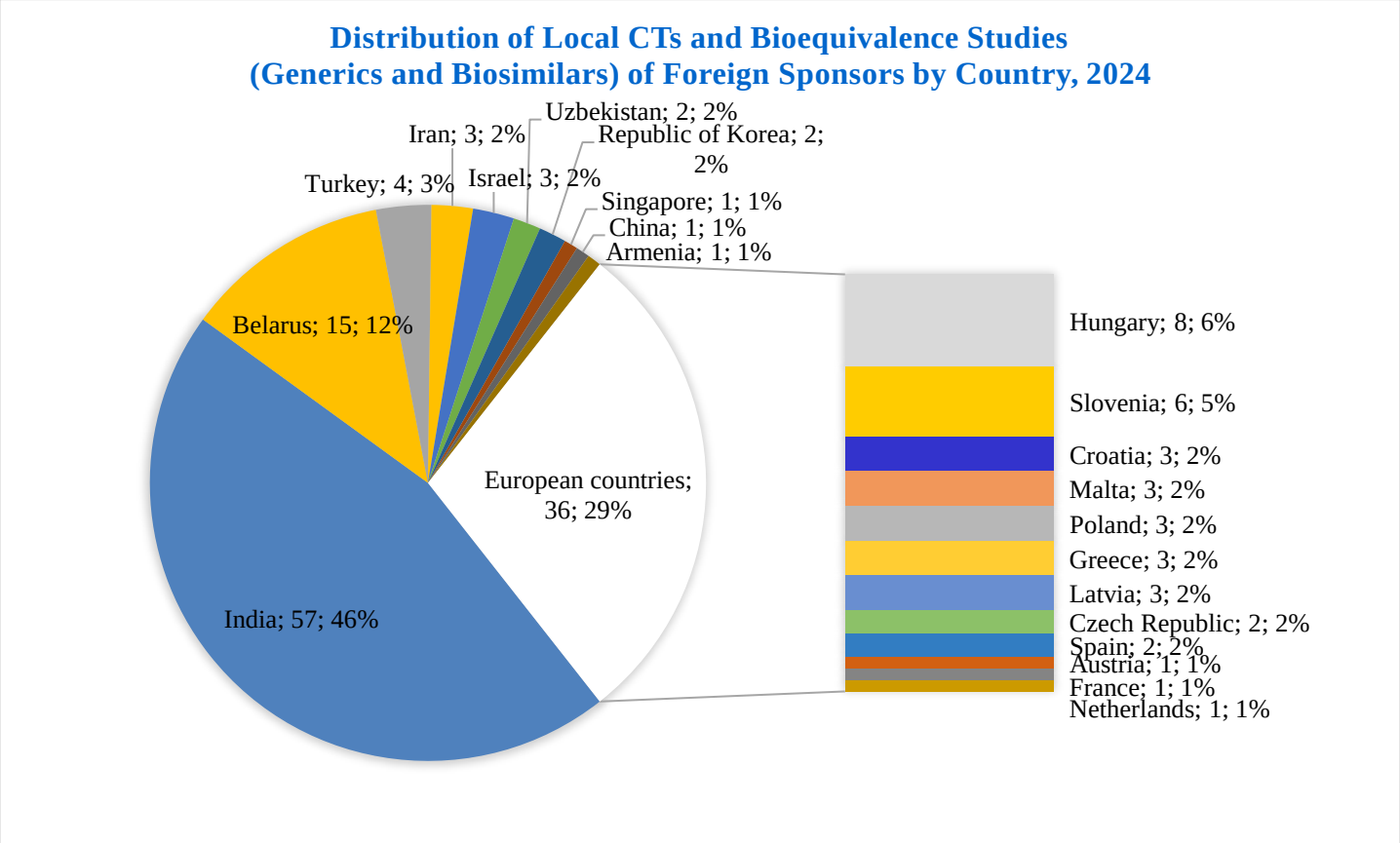
Since 2022, we have been analysing the specific countries from which foreign sponsors obtained approvals to study their reproduced drugs in Russia (diagrams 10 and 11).

Diagram 10



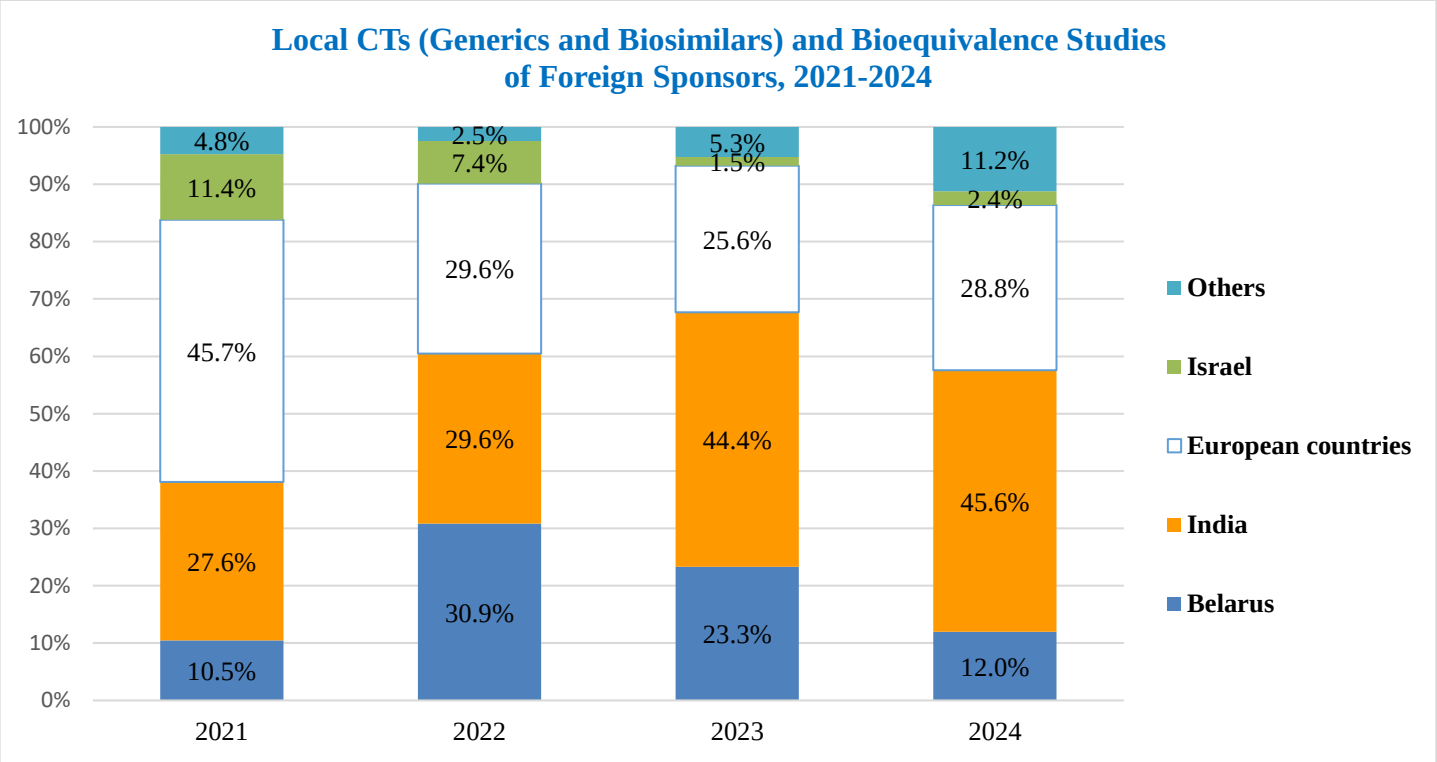
Data from www.grls.rosminzdrav.ru

In 2024, nearly half of approvals of this type of trials were issued by the Ministry of Health to companies from India: 57 out of 125, 45.6%. The share of this country has grown in recent years: in 2023, it was 44.4%, in 2022 – 29.6%. The share of approvals for sponsors from Belarus, on the contrary, has decreased over three years: 12.0% (15 trials) in 2024 vs 23.3% in 2023 and 30.9% in 2022.

European countries accounted for a total of 36 approvals or 28.8%, slightly more than in 2023 (25.6%). Among EU members, the most approvals in 2024 are held by Hungarian companies (seven, six of which belong to Gedeon Richter) and Slovenian companies (five, four of which belong to KRKA). Three approvals each are held by sponsors from Greece, Latvia, Malta, Poland, Croatia; two each by Spain and the Czech Republic; and one each from Austria, France, and the Netherlands. Among other countries, Turkish companies hold four approvals; Iranian and Israeli companies hold three each; Uzbek and South Korean sponsors hold two each; and Armenian, Chinese, and Singaporean sponsors hold one each.

Diagram 11 shows the strengthening of the position of Indian sponsors in the Russian market and changes in the shares of companies from other countries since 2021.

Diagram 11



Data from www.grls.rosminzdrav.ru

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In 2024, the number of local trials of reproduced domestically manufactured drugs decreased by 23.3% compared to 2023 (412 approvals compared to 537). The top five leaders among therapeutic areas remained the same as in the previous year, with no changes even in their order, though the number of protocols in each area decreased. The highest indicator was observed in cardiology and cardiovascular diseases[6] – 71 approvals (122 in the previous year). Next were endocrinology (48 protocols in 2024, 60 in 2023), oncology (47 and 52 respectively), infectious diseases[7] (30 and 42), and neurology (27 and 40).

Table 4

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars), Conducted by Local Sponsors, 2024			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Cardiology and CVD/Surgery/Intensive care	71	17.2%	3 231
Endocrinology	48	11.7%	3 020
Oncology	47	11.4%	4 119
Infectious Diseases (except HIV/HCV/tuberculosis)	30	7.3%	1 978
Neurology	27	6.6%	1 999
Analgesic and NSAIDs	24	5.8%	1 496
Gastroenterology/Coloproctology	22	5.3%	2 042
HIV/HCV/Tuberculosis	18	4.4%	1 044
Rheumatology	13	3.2%	1 328
Not identified	13	3.2%	743
Hepatology	12	2.9%	666
Haematology	11	2.7%	1 002

[6] We remind you that the decision to supplement the designation of the area with surgery and intensive care was made due to the high demand for anticoagulants, which are widely used.
[7] Tuberculosis, HIV, and hepatitis C were considered separately.

Allergology	11	2.7%	934
Dermatology	8	1.9%	1 549
Pulmonology	8	1.9%	1 018
Psychiatry	7	1.7%	366
Obstetrics and gynecology	7	1.7%	303
Immunology	5	1.2%	719
Urology	5	1.2%	352
Oncohaematology	5	1.2%	347
Transplantology/Immunology	5	1.2%	325
Otorhinolaryngology	5	1.2%	778
Antimicrobial agent for external use	2	0.5%	866
Phlebology	2	0.5%	92
Dentistry	1	0.2%	237
Narcology	1	0.2%	110
Parasitology	1	0.2%	52
Other	1	0.2%	50
Toxicology/Pulmonology	1	0.2%	42
Local anesthetic	1	0.2%	30
TOTAL	412	100.0%	30 838

Data from www.grls.rosminzdrav.ru

The most significant decrease in the number of trials, apart from the aforementioned major areas, was observed in the area combining HIV, hepatitis C, and tuberculosis (18 studies compared to 29 in the previous year). A noticeable increase compared to 2023 was shown by analgesics and non-steroidal anti-inflammatory drugs (24 protocols vs 16), allergology (11 protocols vs four), and hepatology (12 protocols vs six).

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In 2024, the top part of the list of drugs most popular in clinical trials for generics and biosimilars underwent significant updates (Table 5). Of the molecules included in the top 10 in 2023, only five retained their positions in 2024: rivaroxaban (the total number of bioequivalence studies involving it dropped from 31 the previous year to nine), apixaban (eight projects vs 16 in 2023), valsartan (nine vs 14), indapamide (nine vs 12) and metformin (eight vs 18)[8].

Vildagliptin, dapagliflozin, perindopril, sitagliptin and tamsulosin dropped out of the top 10 leaders. Joining the top 10 to replace the outgoing ones were ibuprofen and estradiol (12 studies each, both as monotherapy and in combination drugs), dydrogesterone and paracetamol (nine protocols each, separately and in combinations), as well as ademetionine (eight). Noteworthy is the shift in therapeutic areas: whereas in 2023 the top 10 was dominated by substances used in the production of drugs for cardiovascular diseases and diabetes, in 2024 the list expanded. Largely due to Russian companies' interest in ibuprofen and paracetamol, analgesics and non-steroidal anti-inflammatory drugs emerged as leaders. Interest in ademetionine, used in hepatology, is also exclusively of domestic origin. However, the inclusion of 5 substances used in gynaecology in Table 5 is thanks to foreign sponsors.

Table 5

Most Requested INN Used in Clinical Trials of Generics and Biosimilars in 2024				
Substance	**Number of CTs of foreign generics**	**Number of CTs of local generics**	**All clinical trials to a given INN**	**Therapeutic Area**
Ibuprofen (separately and in fixed combinations)	2	10	12	Analgesic and NSAIDs
Estradiol (separately and in fixed combinations)	11	1	12	Gynecology
Valsartan (separately and in fixed combinations)	7	2	9	Cardiology and CVD

[8] For the consistent popularity of rivaroxaban, metformin, vildagliptin and apixaban among generic drug manufacturers in Russia in recent years, see issue of the ACTO Newsletter No. 28 summarising the results of 2023.

Didrogesterone (separately and in fixed combinations)	7	2	9	Gynecology
Indapamide (separately and in fixed combination)	5	4	9	Cardiology and CVD
Paracetamol (in fixed combinations)	1	8	9	Analgesic and NSAIDs, infectious diseases
Rivaroxaban	2	7	9	Cardiology and CVD, surgery, covid-19
Ademethionine	0	8	8	Hepatology
Apixaban	3	5	8	Cardiology and CVD, perhaps covid-19
Metformin (separately and in fixed combinations)	6	2	8	Endocrinology, perhaps covid-19
Amlodipin (separately and in fixed combinations)	5	2	7	Cardiology and CVD
Perindopril (separately and in fixed combination)	4	3	7	Cardiology and CVD
Semaglutide	2	5	7	Endocrinology
Ticagrelor	2	5	7	Cardiology and CVD
Fluticasone (separately and in fixed combination)	2	4	6	Pulmonology, allergology
Empagliflozin (separately and in fixed combination)	3	3	6	Endocrinology
Dapagliflozin (separately and in fixed combinations)	3	2	5	Endocrinology
Linagliptin	1	4	5	Endocrinology
Nimesulide	3	2	5	Analgesic and NSAIDs
Pentoxifylline	0	5	5	Cardiology and CVD
Raltegravirир	1	4	5	HIV
Tacrolimus	0	5	5	Immunology, transplantology
Umifenovir	0	5	5	Infectious diseases
Ezetimibe (separately and in fixed combinations)	4	1	5	Cardiology and CVD
Esomeprazole	4	1	5	Gastroenterology
Eltrombopag	1	4	5	Haematology

Data from www.grls.rosminzdrav.ru

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In recent years, among companies conducting research on reproduced drugs in Russia, an alarming practice has begun to spread: sponsors do not indicate the reference drug in the title of the comparative study protocol. Instead of naming the comparator, such protocols may use the phrase «*in comparison with the reference drug*» without further specification. There are also titles in the format «*a bioequivalence study of a given drug involving healthy volunteers*», where the comparator is not mentioned even in general terms. We first wrote about this practice in the newsletter summarising 2023[9] and, unfortunately, it must be stated that in 2024 it has become even more widespread.

Diagram 12 illustrates this process: it shows the number of such protocols from 2021–2024. The growth, as can be seen, is impressive: from two protocols[10] in 2021 to 124 in 2024. In 2021, the issue affected 0.5% of comparative trials of generics/biosimilars, in 2022 – already 8%; in 2023 – 15%, and by the end of 2024, the reference drug is not named in 24% of protocols where such mentioning should be.

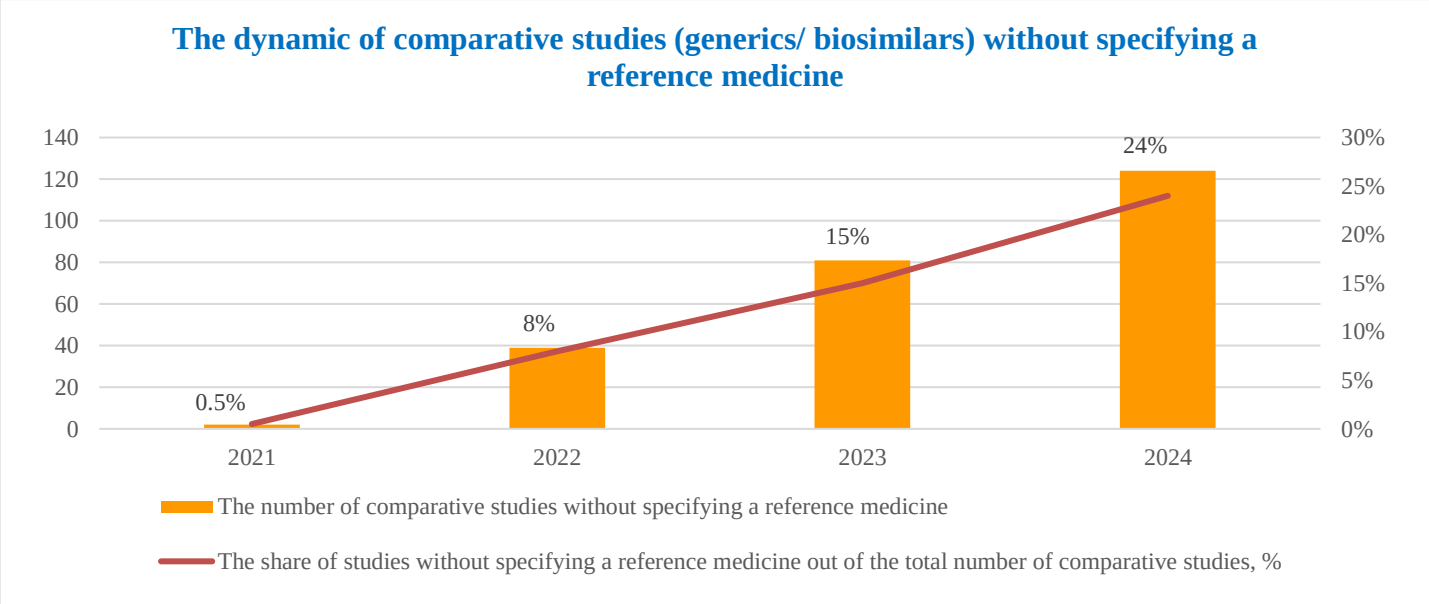
The reader may argue that the title of the protocol is not subject to the applicable legislation, and thus no violation can be claimed. A breach of the law – no, it is not. But there is also such a concept as the custom of

[9] See ACTO Newsletter No. 28.

[10] The Moscow Endocrine Plant conducted the *Open Randomised Crossover Two-Period Bioequivalence Study of the MZ-04/2020 Drug and the Reference Drug in Healthy Volunteers Following a Single Dose of Each Drug on an Empty Stomach*, while Binergia conducted the *Open Randomised Crossover Comparative Study of Pharmacodynamics (Pharmacodynamic Equivalence), Safety and Tolerability of Nadroparin Calcium, Solution for Injection, 9,500 IU Anti-Xa/ml (Binergia, Russia), Following Single Subcutaneous and Intravenous Administration in Healthy Volunteers*.

business practice. And we see that this custom is changing, and not for the better. Yes, an expert sees the protocol and can understand which reference is being discussed. But the end consumer, society as a whole, constrained by the limitations of the registry of approved studies, where essentially only the protocol's name is informative, cannot. Moreover, the rules of logic and the Russian language are violated in the construction «*bioequivalence study of drug N involving healthy volunteers*»: one cannot be equivalent in a vacuum, equivalence is only possible in relation to a specific standard. Therefore, we cannot call such practice conscientious, with all due respect to its adherents.

Diagram 12



Data from www.grls.rosminzdrav.ru

Table 6 lists sponsors whose protocol names did not indicate the reference drug, ranked by the total number of such cases over four years, 2021–2024. Additionally, the share of such trials in the total number of comparative trials of generics/biosimilars of the company for a given year is indicated in brackets. If a company conducted comparative trials and used the names of reference drugs in its protocols, the corresponding column contains «0». If the company did not have comparative trials of generics/biosimilars in the corresponding year, «n/a» is indicated.

It is evident that the list expands each year: two companies in 2021, five in 2022, 16 in 2023, and 29 in 2024 – the rate of growth resembles an epidemic. Sponsors are showing enthusiasm, and not only Russian ones: in addition to India, China, and Iran, the list includes companies from Bulgaria (Vetprom), Latvia (Olainfarm), the Netherlands (Synton B.V.), Poland (Polpharma), Croatia (Belupo), and South Korea (Korea Arlico Pharma Co.).

Table 6

Company	The number of comparative studies of generics/biosimilars without specifying a reference medicine (the share of such studies out of the total number of comparative studies of generics/biosimilars of a particular company for a given year is indicated in parentheses)				
	Total	2024	2023	2022	2021
Promomed Rus (incl. Biokhimik), Russia	71	14 (100%)	25 (100%)	32 (71.1%)	0
Pharmasyntez, Russia	60	32 (88.9%)	27 (71.1%)	1 (3.1%)	0
Pharmstandard-Leksredstva, Russia	22	10 (100%)	9 (64.3%)	3 (37.5%)	0
PSK Pharma, Russia	15	13 (86.7%)	2 (40%)	0	0
Akrikhin, Russia	7	7 (100%)	0	n/a	0
Tula Pharmaceutical Factory, Russia	6	2 (33.3%)	4 (33.3%)	0	n/a

Advanced Pharma, Russia	6	4 (100%)	2 (20%)	0	0
Izvarino Pharma (incl. Nanopharma Development), Russia	5	5 (33.3%)	0	0	0
Binnopharm Group, Russia	4	4 (40%)	0	0	n/a
PIQ-Pharma, Russia	4	1 (33.3%)	1 (50%)	2 (66.7%)	n/a
Emcure Pharmaceuticals, India	4	2 (33.3%)	1 (33.3%)	1 (100%)	0
Akums Drugs, India	3	3 (100%)	n/a	n/a	n/a
Biocad, Russia	3	3 (100%)	0	0	0
OTCPharm, Russia	3	3 (75%)	n/a	0	n/a
Polpharma, Poland	3	3 (100%)	n/a	0	0
ChemRar Pharma, Russia	3	2 (100%)	1 (33.3%)	0	0
AryoGenPharmed, Iran	2	n/a	2 (100%)	n/a	n/a
Geropharm, Russia	2	2 (33.3%)	0	0	0
Protek (incl. Rafarma, Sotex PharmFirm), Russia	2	1 (100%)	1 (9.1%)	0	0
Concern MIR, Russia	2	0	2 (25%)	n/a	n/a
Korea Arlico Pharm, Republic of Korea	2	2 (100%)	n/a	n/a	n/a
Rubikon, Belarus	2	2 (66.7%)	0	0	0
Bright Way Group (incl. Velpharm, Velpharm-M), Russia	1	1 (2.9%)	0	0	0
Aizant (Basis-Metigrins), Russia	1	n/a	1 (100%)	n/a	n/a
Belupo, Croatia	1	1 (33.3%)	n/a	n/a	0
Vetprom, Bulgaria	1	n/a	1 (100%)	n/a	n/a
Binergia, Russia	1	n/a	n/a	n/a	1 (20%)
Intas Pharmaceuticals, India	1	1 (25%)	n/a	n/a	n/a
Inteltreyd, Russia	1	n/a	1 (100%)	n/a	n/a
Ipca Laboratories, India	1	1 (100%)	n/a	n/a	n/a
Mabwell (Shanghai) Bioscience, China	1	1 (100%)	n/a	n/a	n/a
Moscow Endocrine Plant, Russia	1	0	0	0	1 (5.9%)
Olainfarm, Latvia	1	1 (100%)	n/a	n/a	n/a
CinnaGen, Iran	1	1 (33.3%)	n/a	n/a	n/a
Synthon B.V., Netherlands	1	1 (100%)	n/a	n/a	n/a
Pharmproject, Russia	1	0	1 (10%)	0	0
RV Lifesciences, India	1	1 (100%)	n/a	n/a	n/a

Data from www.grls.rosminzdrav.ru

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Table 7 presents the distribution by therapeutic areas for local trials of original medicines by foreign sponsors. Their total number nearly doubled in a year, with 11 approvals vs six in 2023.

Table 7

Distribution of Local CTs of Brand Name Drugs of Foreign Sponsors, 2024			
Therapeutic Area	**Number of CTs**	**Number of planned participants**	**Country of Sponsor**
Infectious Diseases (vaccines)	4	620	Great Britain, China, Cuba, Republic of Korea
Oncology	3	235	Great Britain
Gynecology	2	310	Belgium, Bulgaria
Immunology	1	30	Belarus
Cosmetology	1	16	Belarus
TOTAL	11	1 211	

Data from www.grls.rosminzdrav.ru

Most were vaccines: against respiratory syncytial and metapneumovirus (AstraZeneca, United Kingdom), meningococcal infection (Instituto Finlay de Vacunas, Cuba), and chickenpox (GK Biopharma from South Korea and Changchun BCHT Biotechnology from China).

AstraZeneca has initiated three oncology trials, which feature volrustomig, AZD0901, and a combination of durvalumab and oleclumab in their protocols.

In the field of gynaecology, the Belgian company Besins Healthcare has received an approval to study a combination of progesterone and estradiol, while the Bulgarian company Zentiva Pivot EOOD has received an approval for its estradiol. Two sponsors from Belarus, Daliopharma and Cosmo Science, plan to study their own immunoglobulin and botulinum toxin type A, respectively.

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The distribution of local tials of original medicines by Russian sponsors across therapeutic areas is presented in Table 8. In total, we counted 51 such protocols, which is 24% fewer than in 2023 (67 protocols) and 46% fewer than in 2022 (94 protocols). However, it must be noted that due to issues with insufficient information, we could not identify eight studies by domestic sponsors, and it is quite possible that there are original developments among them. Even taking this into account, it is clear that over the past two years the activity of domestic manufacturers in seeking new medicines has declined.

Table 8

Distribution of Local CTs of Brand Name Drugs (Including Biological Products) of Local Sponsors, 2024			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Infectious Diseases (except HIV/HCV/tuberculosis)	16	31.4%	8 332
Neurology	8	15.7%	1 355
Urology	6	11.8%	1 086
Cardiology and CVD	4	7.8%	2 046
Oncology	3	5.9%	164
Orthopedics	2	3.9%	520
Pulmonology	2	3.9%	331
Obstetrics and gynecology	2	3.9%	204
Oncohaematology	2	3.9%	120
Phlebology	1	2.0%	230
Allergology	1	2.0%	188
Traumatology/Surgery	1	2.0%	100
Endocrinology	1	2.0%	60
Haematology	1	2.0%	30
Phthisiology	1	2.0%	25
TOTAL	51	100.0%	14 791

Data from www.grls.rosminzdrav.ru

The largest area, as in 2023, was infectious diseases (excluding HIV, hepatitis C, and tuberculosis, but including Covid-19), which accounted for 16 protocols (13 the previous year). Eleven out of the 16 studies focus on vaccines. Four approvals were granted to the N.F. Gamaleya National Research Centre for Epidemiology and Microbiology, whose protocols study vaccines against pertussis, rotavirus, and Covid-19 (two studies). The Saint Petersburg Research Institute of Vaccines and Serums received two approvals to study vaccines: for the prevention of pneumococcal and meningococcal infections. Gritvak also works on a pneumococcal vaccine. Nacimbio and Fort LLC received an approval to study vaccines for flu prevention, Microgen – for tick-borne encephalitis, and Nanolek – for a vaccine against the human papillomavirus.

Among other drugs studied in the field of infectious diseases, the registry included two flu treatments called AV5124 (Pharmasyntez) and JCBC00101 (Promomed Rus.), "heavy-chain humanised monoclonal antibodies specific to botulinum toxin serotype A" (developed by the N.F. Gamaleya National Research Centre for Epidemiology and Microbiology), as well as Ingavirin Forte from Valenta and Rafamin from Materia Medica Holding NPF.

The second most popular therapeutic area for original drug developers in 2024 was neurology, with eight approvals (seven the previous year). Innopharm is studying botulinum toxin type A for arm spasticity after an ischaemic stroke and for children with cerebral palsy with upper limb spasticity (two protocols). Geropharm is researching bovine brain polypeptides (with no specified animal species) in patients with mild cognitive impairments and in children aged 2–5 years with specific speech development disorders (also two protocols). InertGas Service – combinations of oxygen with argon and oxygen with krypton on healthy volunteers; Ellara – nasal spray dicholine succinate in a placebo-controlled study in patients with ischemic stroke during the early recovery period; and the V.P. Serbsky National Medical Research Centre – 'olfactory mucosa ensheathing cells for autologous use' in patients with post-traumatic spinal cord cysts. We have no other domestic innovations in neurology to offer you.

In third place is urology with six approvals (there were three in 2023). Here, perhaps the most interesting development is by Lomonosov Moscow State University (a human mesenchymal stromal cell secret for severe spermatogenesis disorders). The other approval went to NextGen for the study of 'plasmid DNA' in painful bladder syndrome; to PharmEnterprises for the investigation of HC243 for chronic cystitis; to Yurspharm for testing 'somatostatin-containing genetically engineered protein' in men with oligozoospermia (the same drug is also being studied by the company in gynaecology, in women with infertility associated with ovarian dysfunction); to the N.F. Gamaleya Research Centre for the study of its fluorothiazinone in chronic bacterial cystitis; and to LLC Novoprost for the investigation of prostate extract (source unspecified) in chronic abacterial prostatitis.

PARTICIPATION OF MEDICAL ORGANIZATIONS IN BIOEQUIVALENCE STUDIES

Table 9 lists the medical organisations that most frequently conducted bioequivalence studies in 2024. The majority of them, 12 clinics, were also in the top 15 based on the results of 2023.

Table 9

Top-15 medical organizations on the activity of participation in bioequivalence studies (approvals issued in 2024)					
Place in ranking	**Name of medical organization**	**Total number of bioequivalence studies**	**Number of bioequivalence studies conducted by local sponsors**	**Number of bioequivalence studies conducted by foreign sponsors**	**Number of bioequivalence studies and sites ranking on approvals issued in 2023**
1	Clinical Hospital № 9, Yaroslavl	56	44	12	64 (1)
2–3	Cardiology Dispensary, Ivanovo	36	23	13	30 (6)
2–3	Eco-Safety Research Center, St. Petersburg	36	22	14	19 (17)
4	Miramed, Maykop	32	32	–	21 (14)
5	Clinical Hospital № 3, Yaroslavl	30	30	–	52 (2)
6	Yaroslavl Regional Clinical Narcological Hospital, Yaroslavl	29	17	12	43 (3)
7	Rostov Central District Hospital, Yaroslavl region, Rostov	24	22	2	31 (5)
8–9	National Scientific Center for Research and Pharmacovigilance, Saransk	20	19	1	26 (7–8)
8–9	X7 Clinical Research, St. Petersburg	20	13	7	23 (9–11)
10	Medical Technologies Maly, St. Petersburg	19	11	8	4 (24–26)
11	Clinical Hospital № 2, Yaroslavl	18	17	1	26 (7–8)
12	Clinical Hospital "RZD-Medicine", Yaroslavl	17	13	4	12 (21)
13–14	Ligand Research, Moscow	16	8	8	36 (4)
13–14	Certa Clinic, Moscow	16	11	5	22 (12–13)
15	Tomsk National Research Medical Center of the Russian Academy of Sciences, Tomsk	14	9	5	23 (9–11)

Data from www.grls.rosminzdrav.ru

The North-West Scientific Centre for Hygiene and Public Health, Saint Petersburg (three studies vs 23 in 2023), Research Lab, Moscow (seven vs 22), and Bessalar, Moscow (six vs 20), which occupied positions 9–11, 12–13, and 15–16 respectively in 2023, are no longer among the leaders. They were replaced by the Eco-Safety Research Centre, Saint Petersburg (36 studies vs 19 the year before), Medical Technologies Maly, Saint Petersburg (19 vs four), and the RZD-Medicine hospital in Yaroslavl (17 vs 12), which in 2024 ranked 2nd–3rd, 10th, and 12th respectively. Apart from the Eco-Safety Centre, which rose from 17th to 2nd–3rd place over the year, a significant improvement was demonstrated by Miramed from Adygea, climbing from 14th to 4th place. Ligand Research from Moscow, on the other hand, experienced a significant decline: from 4th to 13th–14th place. The number of studies vs the previous year decreased in 11 out of the top 15 clinics as the bioequivalence research sector contracted.

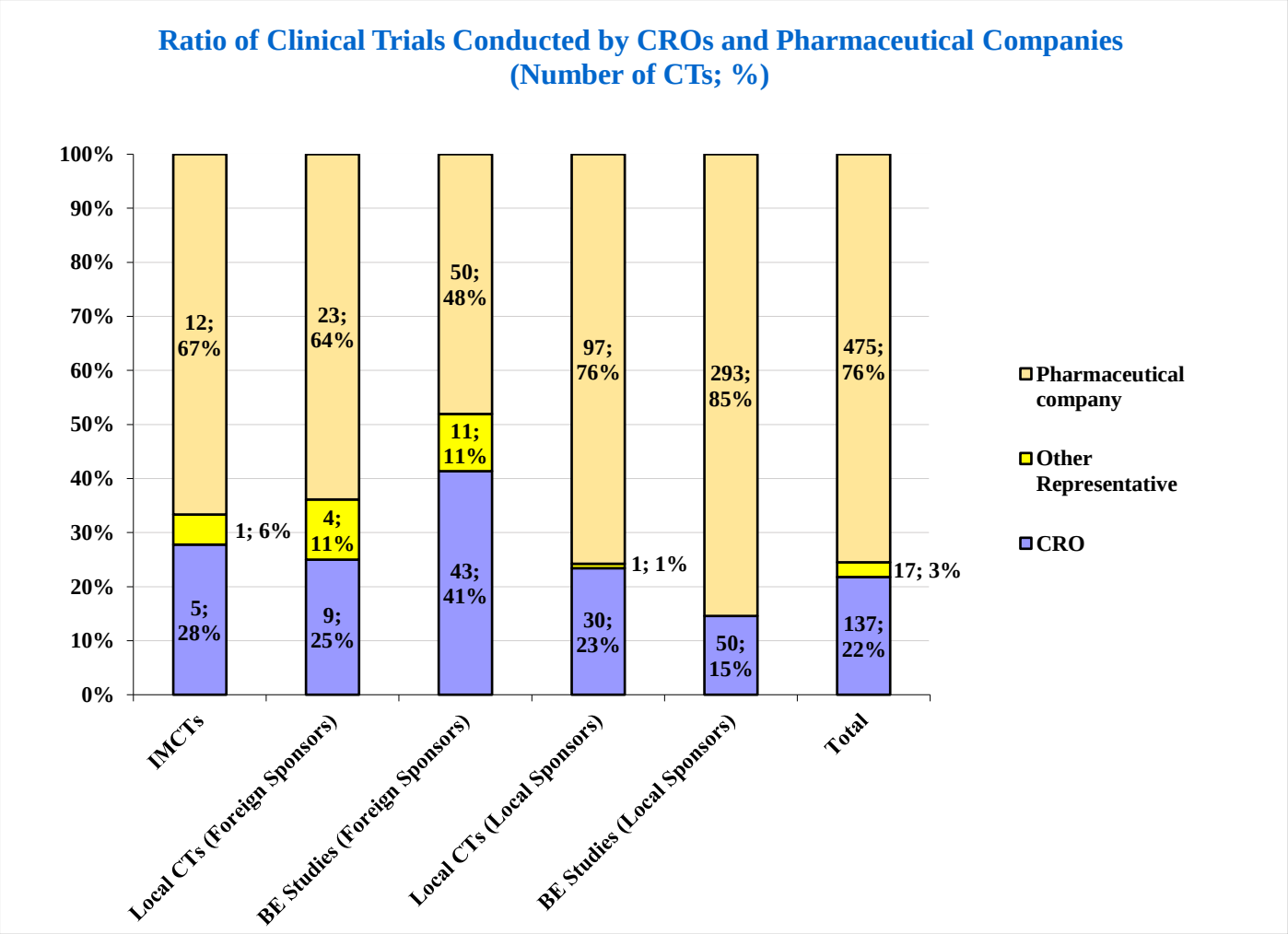
MAIN PLAYERS OF THE RUSSIAN CLINICAL TRIALS MARKET – 2024

This section provides statistics on the main participants in the Russian clinical trials market in 2024. It focuses primarily on sponsors and contract research organisations (CROs), but also mentions "other representatives" – legal entities that can assist in bringing a drug to market but do not specialise exclusively in the field of clinical trials.

Sponsors and CROs, general structural distribution

Diagram 13 illustrates the distribution of trials that sponsors, according to their submissions to the Ministry of Health, planned to conduct independently versus those intended to be conducted with the involvement of CROs. The presented data does not fully reflect the actual situation, as sponsors may choose not to mention a contract research organisation in their application, even if they intend to work with one. Nevertheless, this information provides a general understanding of the market structure and the role of CROs in clinical trials.

Diagram 13

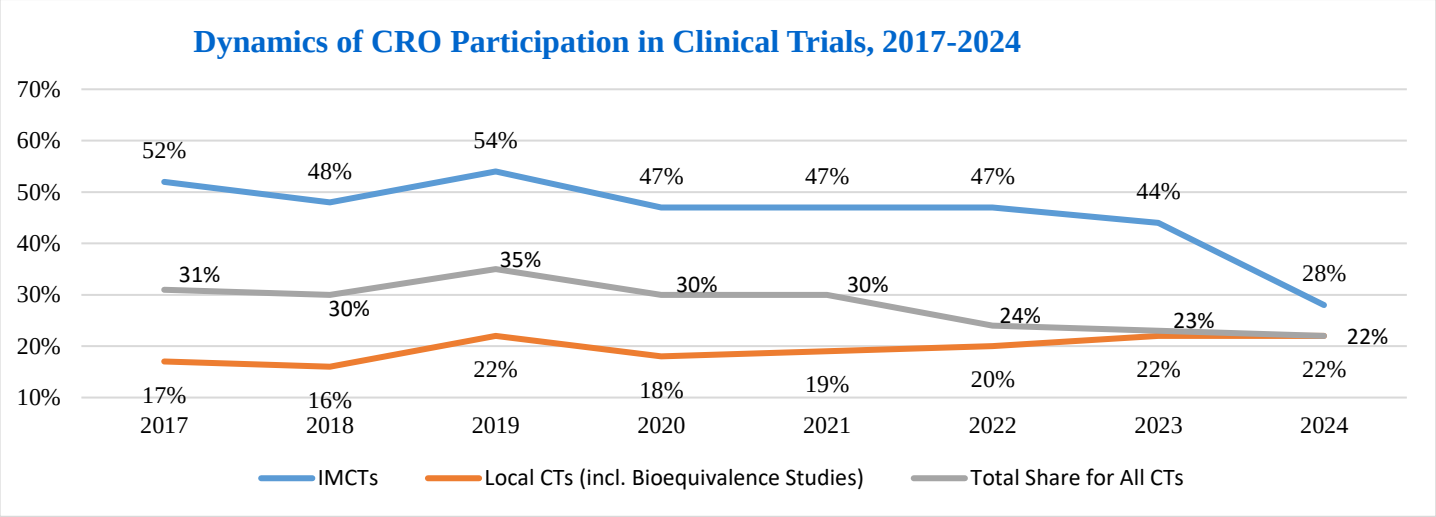


Data from www.grls.rosminzdrav.ru

Diagram 14 shows how the share of trials involving CROs changed between 2017–2024. It is evident that until 2022, contract research organisations participated, according to sponsors' applications, in approximately 30% of trials, while for the largest market sector at the time, IMCTs, this share was closer to 50%. With the departure of IMCTs following the onset of the war, the share of trials involving CROs began to decline and approached 20%. In 2024, more than half of all new IMCTs were initiated by Russian companies, and none of

them indicated in their applications that they planned to engage CROs. As a result, their share even in IMCTs fell to 28%.

Diagram 14



Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, sponsors

Table 10 provides a list of companies that received approvals for IMCTs in 2024. Although the total number of IMCT approvals in 2024 remained the same as in 2023. (18 new projects), the number of sponsors decreased. As of the end of 2023, there were 14 companies initiating IMCTs, while in 2024, there were only ten. Three of these ten companies are Russian, and collectively they initiated 10 out of the 18 IMCTs. The highest number of approvals belongs to Biocad – five, followed by Generium with three, and R-Pharm with two.

Table 10

Pharmaceutical Companies on Approvals for International Multicenter CTs, 2024					
No.	**Company (including separate companies, associated in group of companies, as well as independent divisions of the company)**	**Total**	**Conducted by themselves**	**Conducted by CRO**	**Number of IMCTs in 2023**
1	Biocad	5	5	–	2 CTs
2	Generium	3	3	–	n/a
3	AstraZeneca AB	2	1	1	1 CT
4	R-Pharm International	2	2	–	n/a
5	Altos	1	–	1	n/a
6	Ascentage Pharma Group	1	–	1	2 CTs
7	CinnaGen	1	–	1	n/a
8	Dr. REDDY's Lab.	1	–	1	1 CT
9	GSK	1	1	–	n/a
10	Oncotelic	1	–	1	n/a

Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, CROs

Contract research organisations planned to be involved in conducting IMCTs in 2024 are listed in Table 11. In a similar table summarising the results of the previous year, there were five CROs mentioned in a total of eight clinical trial approvals. In 2024, there are four CROs, and the total number of approvals involving them is five. Two trials for K-Research (Cromos Pharma) (conducted for Oncotelic and Ascentage Pharma from the USA), one for OCT (for Dr. REDDY's Lab, India), Parexel (AstraZeneca, United Kingdom), and Medical Innovations and Technologies (CinnaGen, Iran).

Table 11

CROs on Approvals for International Multicenter CTs, 2024				
No.	**Company**	**Number of IMCTs**	**Number of Sponsors**	**Number of IMCTs in 2023**
1	Cromos Pharma (K-Research)	2	2	2 CTs
2	OCT	1	1	n/a
3	Parexel	1	1	1 CT
4	Medical Innovations and Technologies	1	1	n/a

Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, foreign sponsors

Table 12 contains foreign sponsors who initiated the largest number of local trials (including bioequivalence studies) in Russia.

Mylan Laboratories ranks first with ten approvals, compared to seven projects and sixth place the previous year. Hetero Labs and Jodas Expoim shared 2nd–3rd place in 2024, each with eight new projects. At the same time, Hetero Labs dropped from first place (15 approvals in 2023), while Jodas Expoim rose from ninth place (five approvals in 2023). Rubikon (ten approvals and second place in 2023) and Sandoz (nine trials and third place in 2023) left the top ten, with both companies receiving only three approvals in 2024, placing them 12th–20th. Lekpharm received no approvals in 2024, although it ranked 4th–5th in 2023 with eight studies.

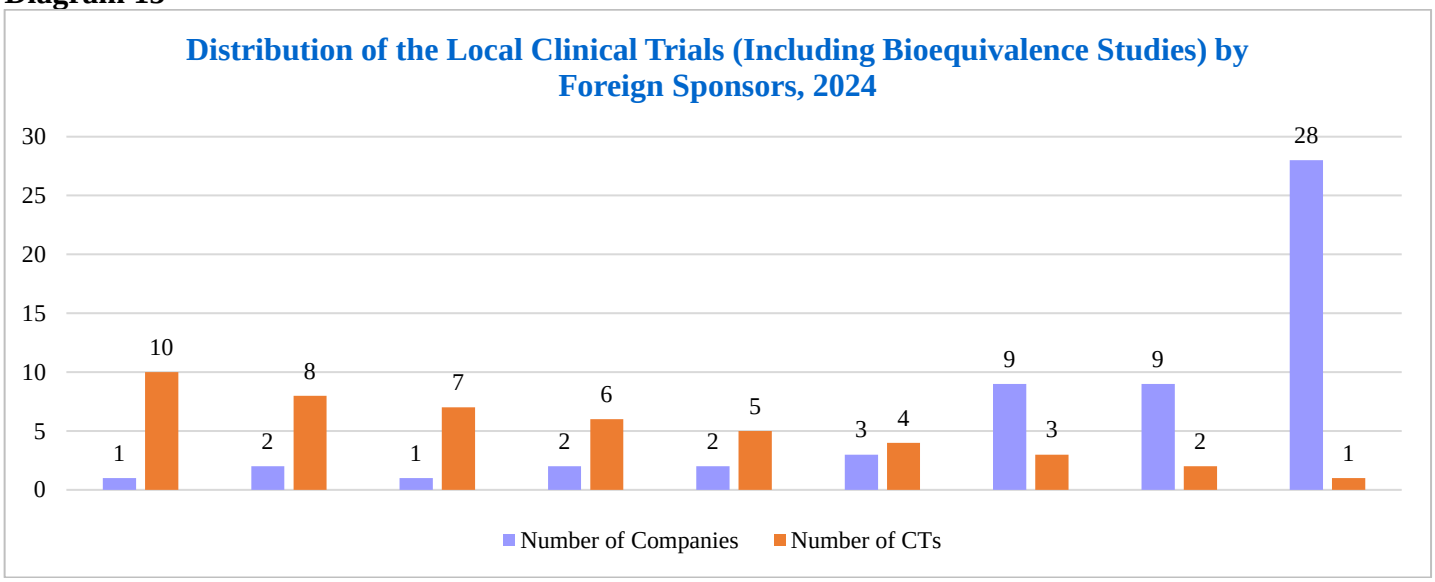
Table 12

Ranking of Foreign Sponsors on Approvals for Local CTs and Bioequivalence Studies, 2024					
Ranking in 2024	**Company**	**Total**	**Conducted by themselves**	**Conducted by CROs/other representatives**	**Number of CTs; Ranking in 2023**
1	Mylan Laboratories	10	10	–	7 CTs; 6
2–3	Hetero Labs	8	8	–	15 CTs; 1
2–3	Jodas Expoim	8	1	7	5 CTs; 9
4	Gedeon Richter	7	–	7	6 CTs; 7-8
5–6	Dr. REDDY's Lab.	6	5	1	8 CTs; 4-5
5–6	Emcure Pharmaceuticals	6	–	6	3 CTs; 13-16
7–8	KRKA	5	5	–	4 CTs; 10-12
7–8	Sun Pharma	5	5	–	6 CTs; 7-8
9–11	AstraZeneca AB	4	4	–	3 CTs; 13-16
9–11	Intas Pharmaceuticals	4	4	–	n/a
9–11	Pharmtechnology	4	–	4	4 CTs; 10-12

Data from www.grls.rosminzdrav.ru

The distribution of local trials and bioequivalence studies approved in 2024 among foreign sponsors is presented in Diagram 15. The total number of sponsors in this category in 2024 reached 57, exceeding the figure of the previous year (49 companies). The companies listed above with four or more approvals account for 48% (67 out of 140) of all new trials of the specified types.

Diagram 15



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, domestic sponsors

Table 13 presents the Russian manufacturers that obtained the highest number of approvals for conducting local trials (including bioequivalence studies) in 2024.

Pharmasyntez leads with 43 new studies, followed by Bright Way Group with 35, and RIF completes the top three with 24 approvals. Rif experienced the most significant rise in the rankings over the year: in 2023, the company conducted only five studies and was ranked in the third decade. Another player that significantly improved its performance is PSK Pharma, which also had just five approvals and a spot in the third decade in 2023, but in 2024, with 15 studies, it climbed to the 6th–7th positions. PPC RENEWAL suffered a significant drop in the rankings, landing in the 8th–10th positions with 13 new projects, whereas the previous year it topped the table with 45 approvals. Binnopharm Group also experienced a noticeable decline, falling from sixth to the 14th–15th positions (26 studies in 2023 and only ten in 2024).

Table 13

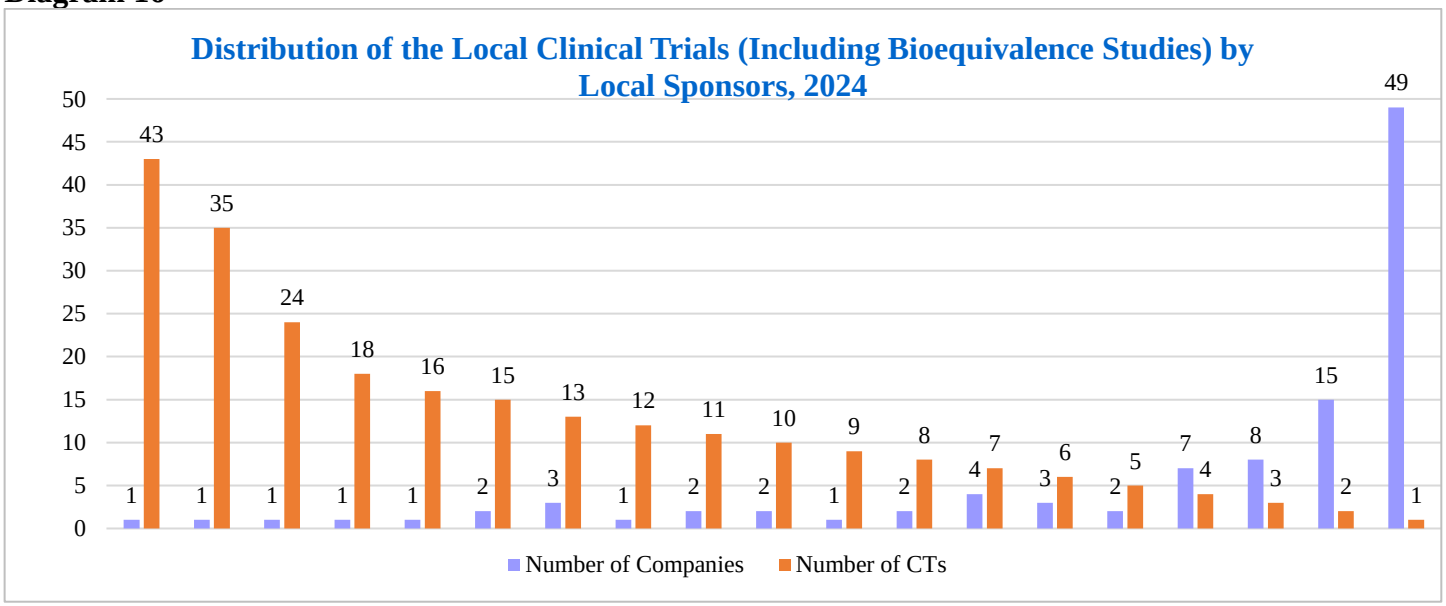
Top-15 Leading Local Sponsors on Approvals for Local Clinical Trials and Bioequivalence Studies, 2024					
Ranking in 2024	**Company**	**Total**	**Conducted by themselves**	**Conducted by CRO**	**Number of CTs; Ranking in 2023**
1	Pharmasyntez (incl. Pharmasyntez-Tyumen, Pharmasyntez-Nord)	43	43	–	39 CTs; 2
2	Bright Way Group (incl. Velpharm)	35	35	–	22 CTs; 7
3	Rif	24	24	–	5 CTs; 31-36
4	Amedart	18	18	–	34 CTs; 3
5	Promomed Rus	16	16	–	32 CTs; 4
6–7	Izvarino Pharma (incl. Nanopharma Development)	15	–	15	20 CTs; 8-9
6–7	PSK Pharma	15	15	–	5 CTs; 31-36
8–10	Atoll	13	13	–	13 CTs; 13
8–10	Solopharm	13	12	1	18 CTs; 10

8–10	Renewal	13	13	–	45 CTs; 1
11	R-Pharm	12	12	–	27 CTs; 5
12–13	Geropharm	11	10	1	20 CTs; 8-9
12–13	Pharmstandard (incl. Pharmstandard-Leksredstva, Pharmstandard-UfaVita)	11	11	–	14 CTs; 12
14–15	ABBA РУС	10	10	–	16 CTs; 11
14–15	Binnopharm Group (incl. Sintez)	10	10	–	26 CTs; 6

Data from www.grls.rosminzdrav.ru

Diagram 16 shows the distribution of trials among Russian sponsors. In 2024, a total of 106 Russian companies received approvals for local trials, including bioequivalence studies, seven more than the previous year. Fifteen companies that received 10 or more approvals initiated 55% (259 out of 471) of all new trials of these types over the year.

Diagram 16



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, CROs

Table 14 presents the top 10 CROs by the number of approvals for local trials, including bioequivalence studies, for 2024.

The National Scientific Centre for Research and Pharmacovigilance leads with 19 approvals. It is followed by Probiotech with 18 and AX Clinical Trials with 14 trials. Vs 2023, Synergy showed the most notable improvement: fourth place and ten approved projects, although a year earlier it had only one new study and ranked in the second ten. Falling out of the Top 10 were MDA (eleventh place with five approvals in 2024 compared to third place with 13 a year earlier), M VED (ranked in the second ten with one approval in 2024 compared to being in 4th–5th place with ten in 2023), and Excellence Research and Development (ranked 12th–15th with three approvals compared to 6th–7th place with nine a year earlier).

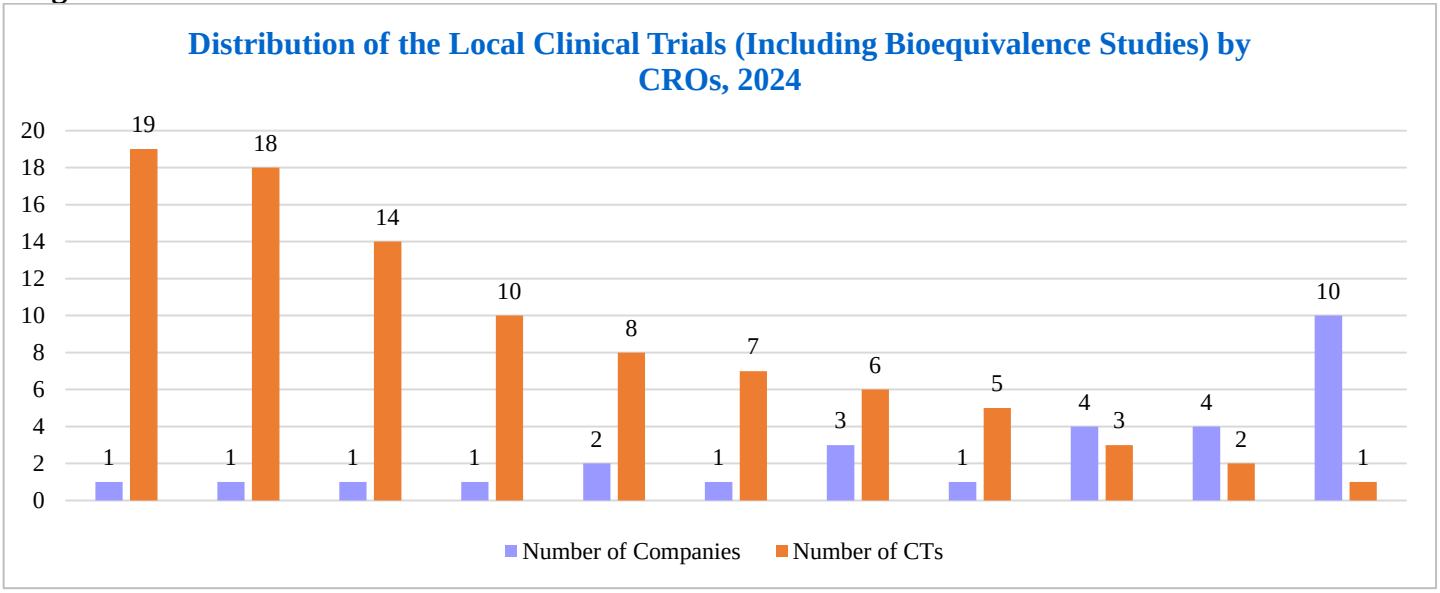
Table 14

Top-10 CROs Involved in the Local CTs and Bioequivalence Studies (on Approvals Issued in 2024)						
Ranking in 2024	**Company**	**Total number of local CTs**	**Number of CTs of foreign sponsors**	**Number of CTs of local sponsors**	**Number of sponsors**	**Number of CTs; Ranking in 2023**
1	National Scientific Center for Research and Pharmacovigilance	19	1	18	9	22 CTs; 2
2	Probiotech	18	2	16	3	30 CTs; 1
3	AX Clinical Trials and Consulting	14	10	4	7	9 CTs; 6-7
4	Synergy	10	6	4	5	1 CT; 23-28
5–6	IPHARMA	8	1	7	8	5 CTs; 10-11
5–6	Vita Aeterna	8	5	3	3	4 CTs; 12-13
7	OCT	7	4	3	5	7 CTs; 8-9
8–10	Ligand Research	6	1	5	4	7 CTs; 8-9
8–10	Eco-Safety Research Center	6	5	1	4	2 CTs; 18-22
8–10	X7 Research	6	1	5	4	10 CTs; 4-5

Data from www.grls.rosminzdrav.ru

Diagram 17 shows the distribution of approvals for local trials and bioequivalence studies across contract research organisations. In total, 29 CROs were planned to be involved in these types of studies in 2024, one more company than in 2023. Ten companies with the highest number of approvals (six or more) account for 75% (102 out of 137) of all new trials of these types.

Diagram 17



Data from www.grls.rosminzdrav.ru

CLINICAL TRIALS IN THE NEIGHBOR COUNTRIES OF THE RUSSIAN FEDERATION

In 2022, when it became clear that international clinical trials were withdrawing from the Russian market, we began to more actively monitor the situation in post-Soviet countries and publish our observations in a separate section of our publication[11]. We wanted to understand whether the war would affect the situation with clinical trials not only in the directly involved countries (primarily Russia and Ukraine, but it is probably quite safe to include Belarus here as well) but also in other post-Soviet countries. Will neighbouring states historically connected with Russia benefit from the outflow of international projects from Russia, and if so, which ones. The source of information for us is the ClinicalTrials.gov registry, probably the most comprehensive database of ongoing research worldwide.

Table 15 presents information on the clinical trial landscape in 14 countries as of mid-February 2025: the number of active interventional trials, the country's share in the global market, population size, and the number of trials per million residents. The ranking for the last indicator is also provided separately in Diagram 18 for easier visualisation.

Table 15

The activity of clinical trial markets in the neighboring countries of the Russian Federation as of 02/17/2025 (data for 02/06/2024 are also given in parentheses)

Region	Number of active interventional CTs	Share in the global CT market	Population, mln	Number of CTs, per million population
In the world	84 085 (80 639)			
Russia	824 (997)	0.98 (1.24)	146	5.6
Ukraine	319 (406)	0.38 (0.50)	30	10.6
Georgia	235* (224)	0.28 (0.28)	3.7	63.5
Lithuania	215 (230)	0.26 (0.29)	2.9	74.1
Estonia	143 (159)	0.16 (0.20)	1.4	102.1
Latvia	137 (155)	0.16 (0.19)	1.9	72.1
Moldova	70 (71)	0.08 (0.09)	2.4	29.2
Belarus	49 (71)	0.06 (0.09)	9.2	5.3
Kazakhstan	30 (22)	0.04 (0.03)	20.3	1.5
Armenia	23 (17)	0.03 (0.02)	3	7.7
Uzbekistan	18 (9)	0.021 (0.011)	37.5	0.5
Kyrgyzstan	13 (9)	0.015 (0.011)	7.3	1.8
Azerbaijan	3 (2)	0.004 (0.003)	10.2	0.3
Tadjikistan	2 (2)	0.002 (0.003)	10.3	0.2

Data from www.clinicaltrials.gov; data from official statistical agencies of the countries available as of mid-February 2025

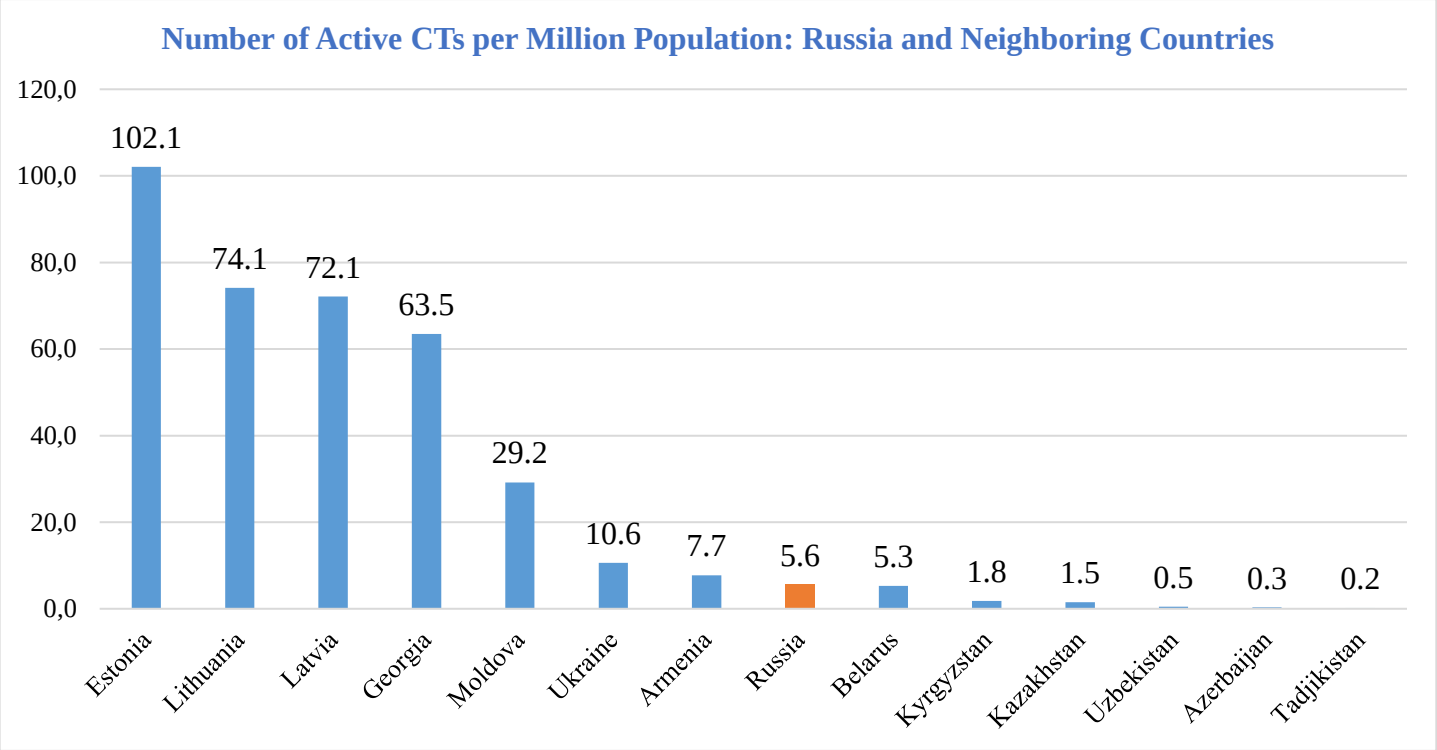
* In Georgia, only trials conducted in Tbilisi were taken into account, as changes in the search interface of the ClinicalTrials.gov database made it impossible to distinguish trials conducted in Georgia from those conducted in the state of Georgia, USA. We could not find any trials conducted in Georgia that did not have centres in Tbilisi. Therefore, we considered this new search method sufficiently accurate.

Globally, from February 2024 to February 2025, the total number of active interventional trials increased by 4% (84,085 vs 80,639). At the same time, their number continued to decline in Russia (824 vs 997, -17%), Ukraine (319 vs 406, -21%) and Belarus (49 vs 71, -31%). The Baltic States also recorded a decline, though not as significant: Latvia by 12% (137 projects vs 155 year-on-year), Estonia by 10% (143 vs 159), and Lithuania by 7% (215 vs 230). In Moldova, the figure formally decreased, but by only one project (70 vs 71). Growth was observed in Georgia (235 active projects vs 224 a year earlier, 5%), Armenia (23 vs 17, 35%), and Kazakhstan (30 vs 22, 36%). In Uzbekistan, the number of active trials doubled over the year, rising to 18 from nine.

[11] See the ACTO Newsletters No. 25, 26, 28.

Kyrgyzstan lags behind with only 13 vs nine. Azerbaijan reported three projects vs two a year earlier, while Tajikistan's figure remained unchanged at two active trials.

Diagram 18



Data from www.clinicaltrials.gov

In terms of interventional trials per million inhabitants, the Baltic States lead: 102.1 in Estonia, 74.1 in Lithuania, and 72.1 in Latvia. In February 2024, the indicators for these three countries were higher (113.6 in Estonia, 81.6 in Lithuania, and 79.3 in Latvia). However, Georgia's results increased (63.5 vs 60.5), narrowing its gap with the Baltic States. Moldova lags behind the Baltic states more significantly, and the growth in the relative number of studies is slower (29.2 vs 28.4). In other countries, the number of trials per million population is low, showing either very modest growth (Kazakhstan, Armenia, Uzbekistan, Kyrgyzstan, Azerbaijan) or a decline (Russia, Ukraine, Belarus).

Table 16 demonstrates how the number of active clinical trials has changed across various countries over the period from July 2022 to February 2025 (the dates of the first and last data collection points). The comparison is complicated by the fact that market sizes in the countries of interest vary greatly in scale. To make the comparison more accurate, both absolute and relative changes are provided for each market (colour scales simplify interpretation of the indicators), and the countries are divided into two groups: those with more than 20 trials as of mid-2022, and those with fewer.

Among relatively large markets, only Georgia has shown growth in all parameters from July 2022 to February 2025: an increase of 40 active trials, up 20.5% over 2.5 years, with 235 vs 195.

In Russia, Ukraine and Belarus, i.e., countries involved in the military-political crisis in the region, the number of trials has sharply decreased by more than 40%. In the same group, Latvia and Estonia also show a decline, though to a lesser extent: by 20.3% and 17.3% or by 35 and 30 trials, respectively. Lithuania, Moldova and Kazakhstan can be grouped as countries whose results fluctuate around the baseline but show almost no changes.

In the group of smaller markets, the scale of growth is largely determined by the size of the baseline, making it clear that any far-reaching conclusions based on these indicators are premature.

Table 16

Dynamics of the Number of Active CTs by Country				
Region	**Number of active interventional CTs for July 2022**	**Number of active interventional CTs for February 2025**	**Absolute change**	**Relative change**
In the world	77 750	84 085	+6 335	+8.1%
Group 1	*Countries with more than 20 active CTs in mid-2022*			
Russia	1 400	824	–576	–41.1%
Ukraine	595	319	–276	–46.4%
Belarus	90	49	–41	–45.6%
Latvia	172	137	–35	–20.3%
Estonia	173	143	–30	–17.3%
Lithuania	223	215	–8	–3.6%
Moldova	69	70	+1	+1.4%
Kazakhstan	28	30	+2	+6.7%
Georgia	195	235	+40	+20.5%
Group 2	*Countries with less than 20 active CTs in mid-2022*			
Kyrgyzstan	6	13	+7	+116.7%
Uzbekistan	10	18	+8	+80.0%
Armenia	16	23	+7	+43.8%
Tadjikistan	1	2	+1	+100.0%
Azerbaijan	3	3	0	0.0%

Data from www.clinicaltrials.gov

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The newsletter concludes with more detailed information on each country. The dynamics for the 'study start' parameter are shown for interventional trials from the ClinicalTrials.gov database for each year.[12] Additionally, there is a breakdown of trials for 2024 by types of interventions: ClinicalTrials.gov contains information on studies not only of medicinal products but also medical devices, diagnostic tests, surgical procedures, dietary supplements, nutritional regimes, etc. For trials of medicinal products, additional details clarify how many were local and how many were international, how many were initiated by pharmaceutical companies, and how many by academic institutions or individual investigators. A separate table is provided with the sponsors of medicinal product studies for 2024.

It is worth noting that international studies dominate in the Baltic states, Moldova, Ukraine and Georgia. This time, technically, Armenia can also be included, although the number of studies there is very small. In Belarus and Kazakhstan in 2024, academic projects take the lead, while in Kyrgyzstan only academic projects are represented.

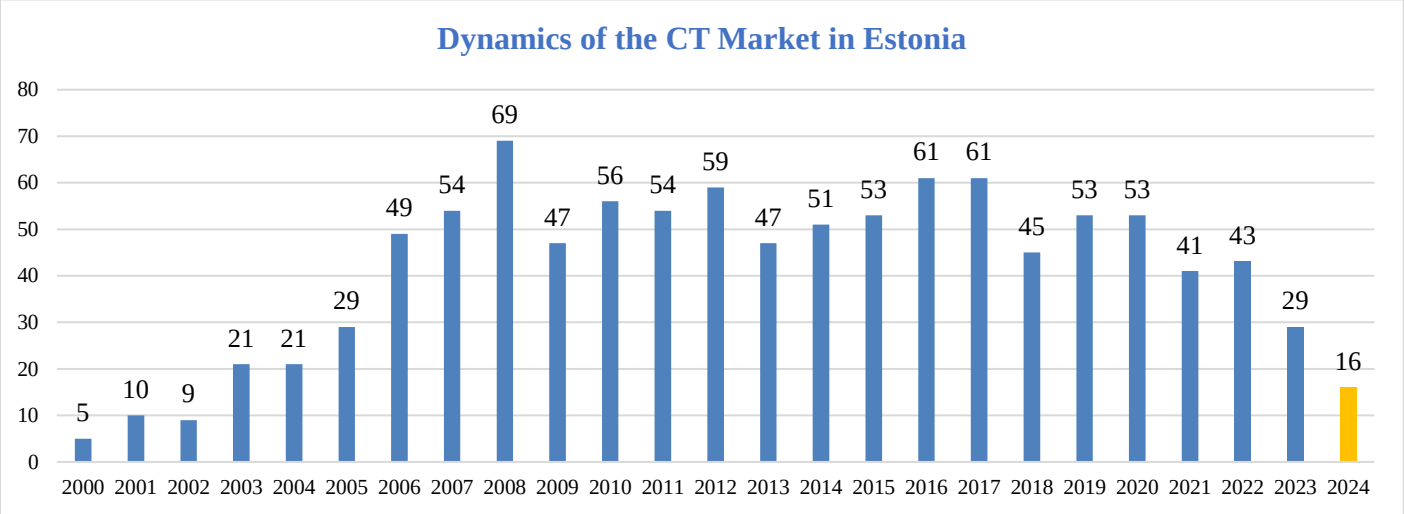
For Russia, an additional chart is provided showing discrepancies for 2024 between information on ClinicalTrials.gov and the register of clinical trials approved by the Ministry of Health of Russia. The fact is that some interventional drug trials are listed on ClinicalTrials.gov as having started in Russia in 2024, but the Ministry of Health has not issued approvals for their conduct. This was the case for 29 out of 52 trials (56%). The

[12] Previously, we used the "first posted" indicator; however, we noticed that some sponsors (primarily small, often non-commercial players) enter data retroactively, causing a study to appear in the database several years later. To more accurately link studies to their start year, we began using the "Study start" parameter.

majority of these, 23, are categorised as academic/investigator-initiated trials. There are a total of 26 academic protocols, and approvals from the Ministry of Health were granted only for work on three of them. Of the remaining six not included in the national register, four are international academic projects, while the other two are local studies.

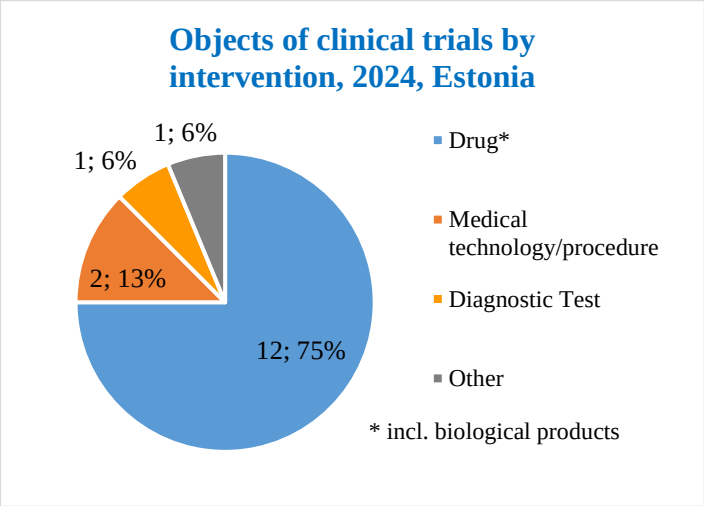
Readers are invited to delve into further details of the situation in each country independently.

Diagram 19



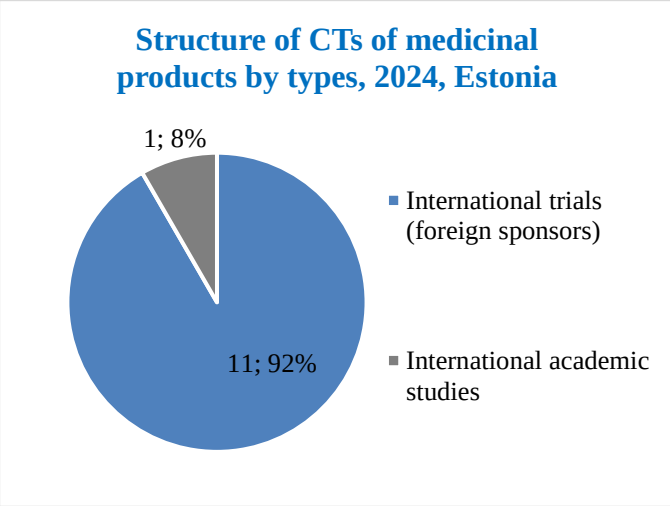
Data from www.clinicaltrials.gov

Diagram 20



Data from www.clinicaltrials.gov

Diagram 21



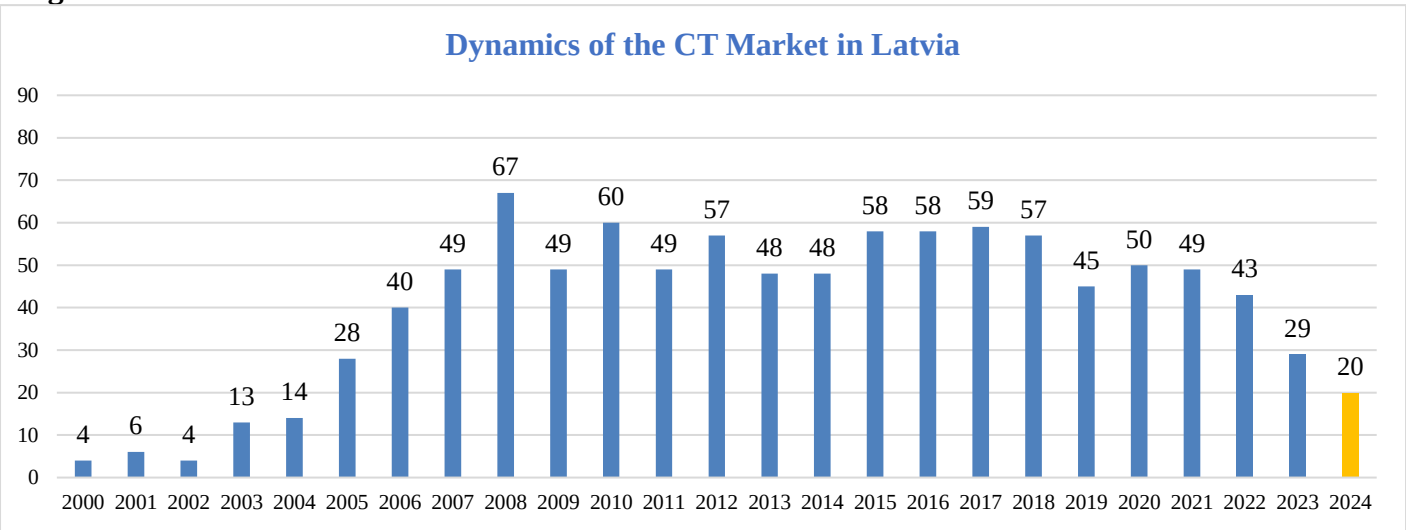
Data from www.clinicaltrials.gov

Table 17

Sponsors, 2024, Estonia	Total	Number of IMCTs	Number of International academic studies
AbbVie	2	2	–
GlaxoSmithKline	2	2	–
Sanofi	2	2	–
Angitia Biopharmaceuticals	1	1	–
Argenx	1	1	–
Boehringer Ingelheim	1	1	–
Intercept Pharmaceuticals	1	1	–
ModernaTX, Inc.	1	1	–
North Estonia Medical Centre	1	–	1
Total number of sponsors is 10	12	11	1

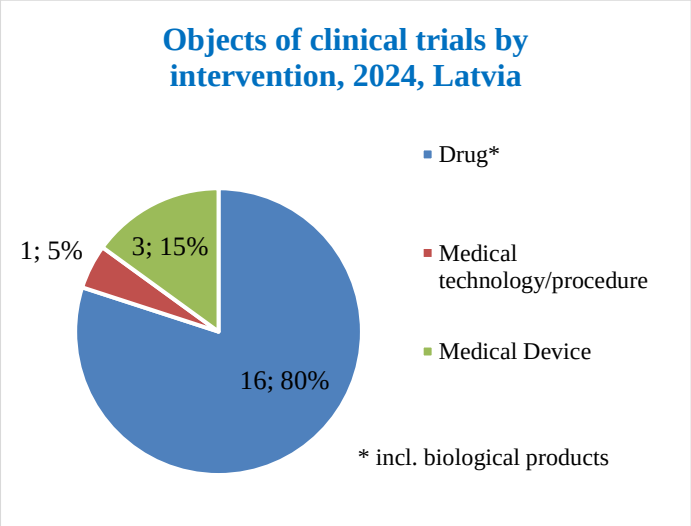
Data from www.clinicaltrials.gov

Diagram 22



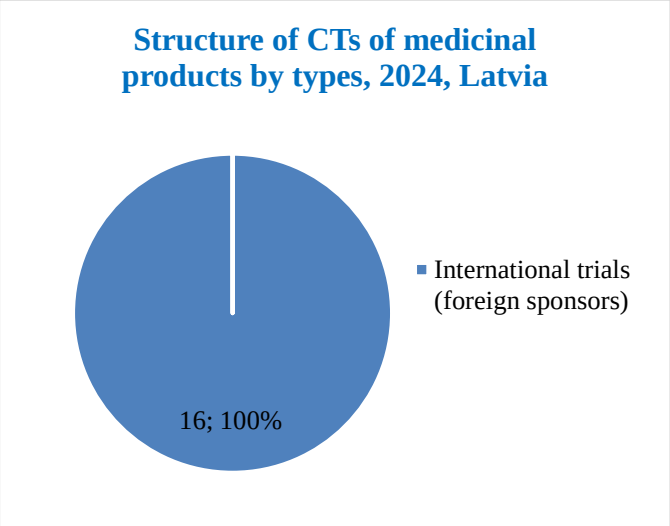
Data from www.clinicaltrials.gov

Diagram 23



Data from www.clinicaltrials.gov

Diagram 24



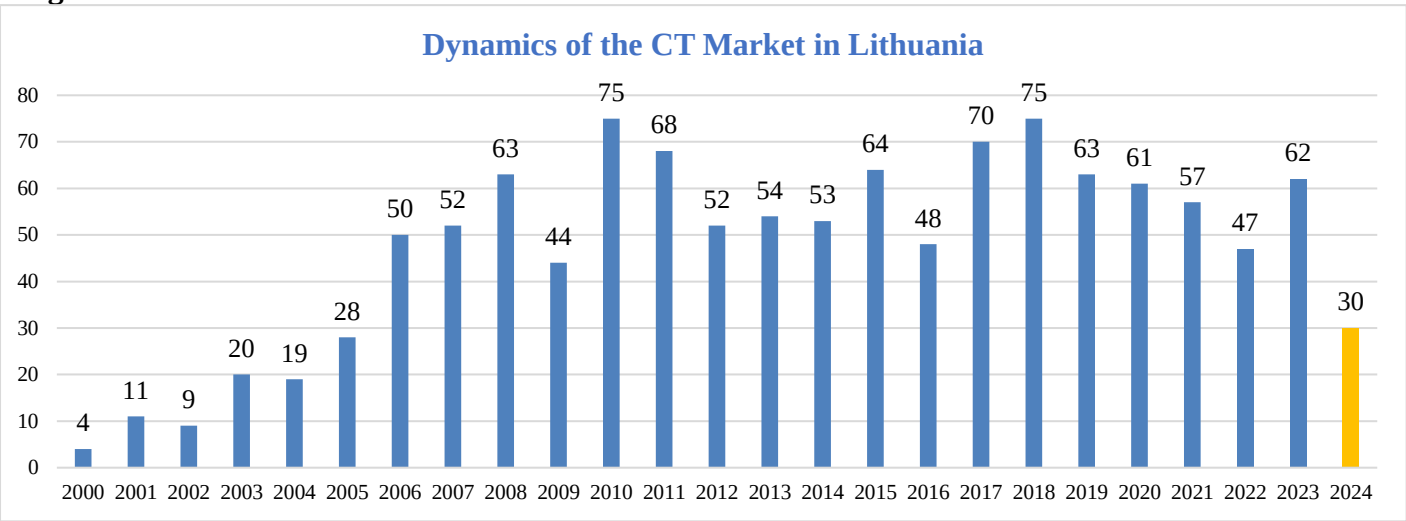
Data from www.clinicaltrials.gov

Table 18

Sponsors, 2024, Latvia	Total	Number of IMCTs
AbbVie	2	2
Eli Lilly and Company	2	2
Longboard Pharmaceuticals	2	2
Alvotech Swiss AG	1	1
Amgen	1	1
Argenx	1	1
Arrowhead Pharmaceuticals	1	1
EyeBiotech Ltd.	1	1
GB002, Inc.	1	1
Morphic Therapeutic, Inc	1	1
Regeneron Pharmaceuticals	1	1
Sanofi	1	1
Takeda	1	1
Total number of sponsors is 13	16	16

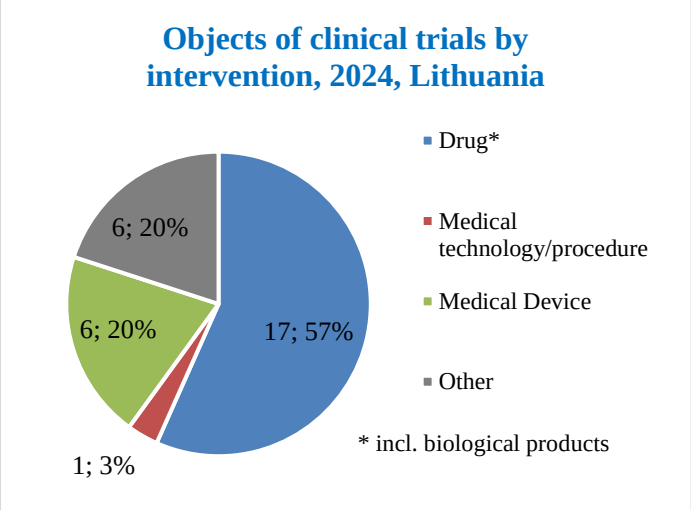
Data from www.clinicaltrials.gov

Diagram 25



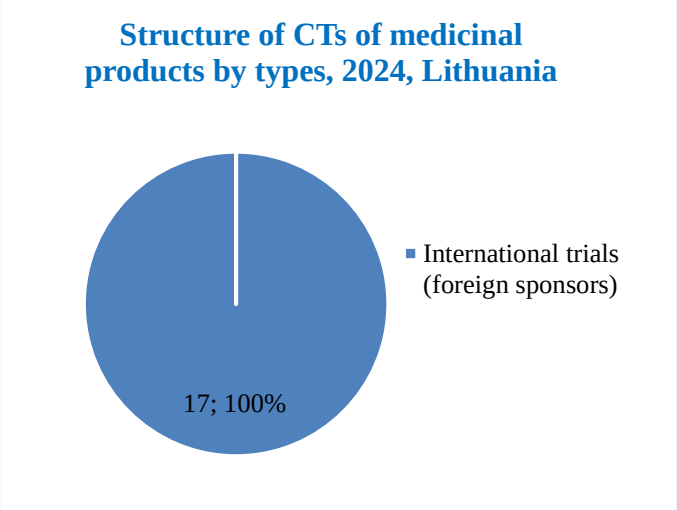
Data from www.clinicaltrials.gov

Diagram 26



Data from www.clinicaltrials.gov

Diagram 27



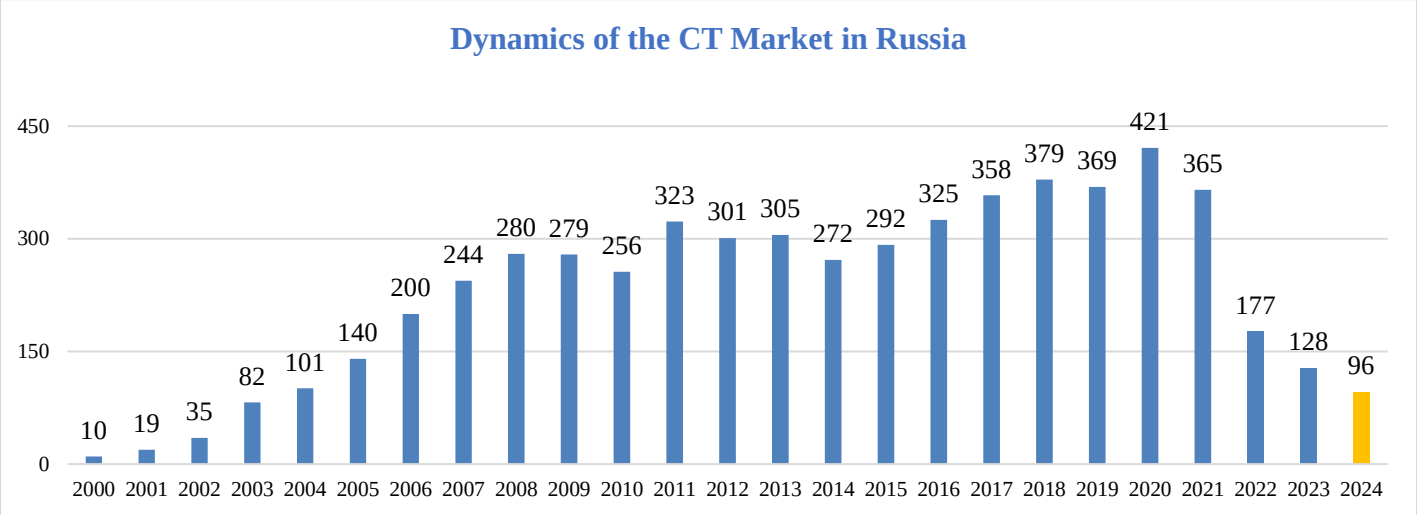
Data from www.clinicaltrials.gov

Table 19

Sponsors, 2024, Lithuania	Total	Number of IMCTs
AbbVie	2	2
Sanofi	2	2
Arrowhead Pharmaceuticals	1	1
Astellas Pharma Global Development, Inc.	1	1
Boehringer Ingelheim	1	1
Cynata Therapeutics Limited	1	1
Eli Lilly and Company	1	1
GB002, Inc.	1	1
H. Lundbeck A/S	1	1
Intercept Pharmaceuticals	1	1
Marinus Pharmaceuticals	1	1
NEC Bio B.V	1	1
Octapharma	1	1
Omeros Corporation	1	1
Regeneron Pharmaceuticals	1	1
Total number of sponsors is 15	17	17

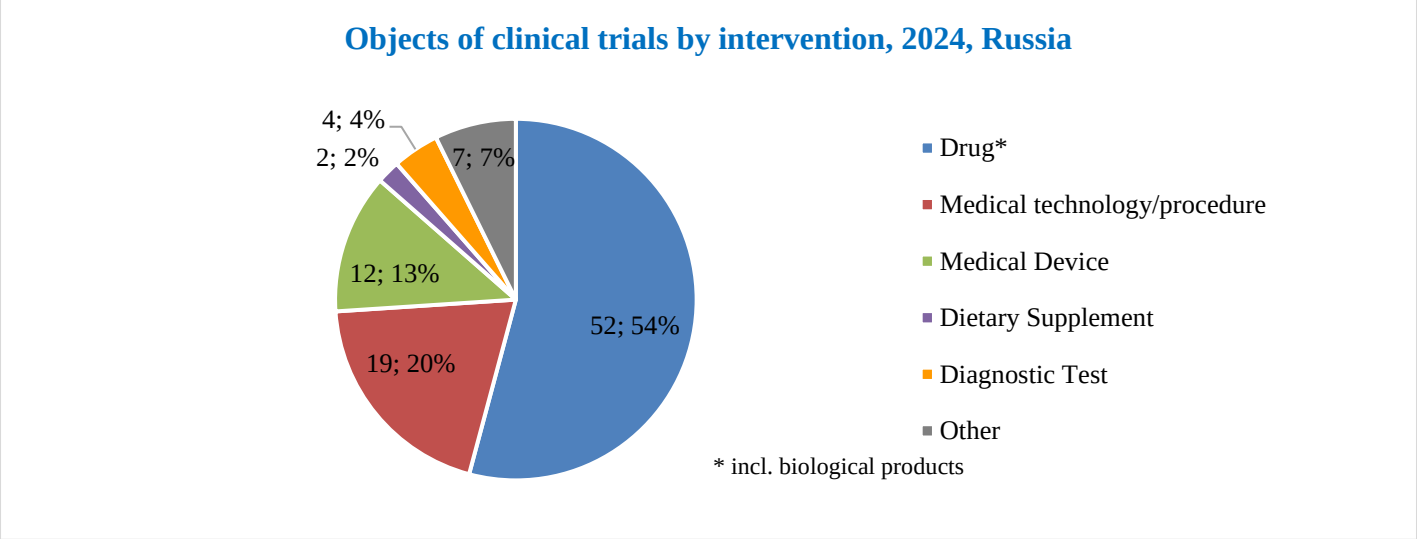
Data from www.clinicaltrials.gov

Diagram 28



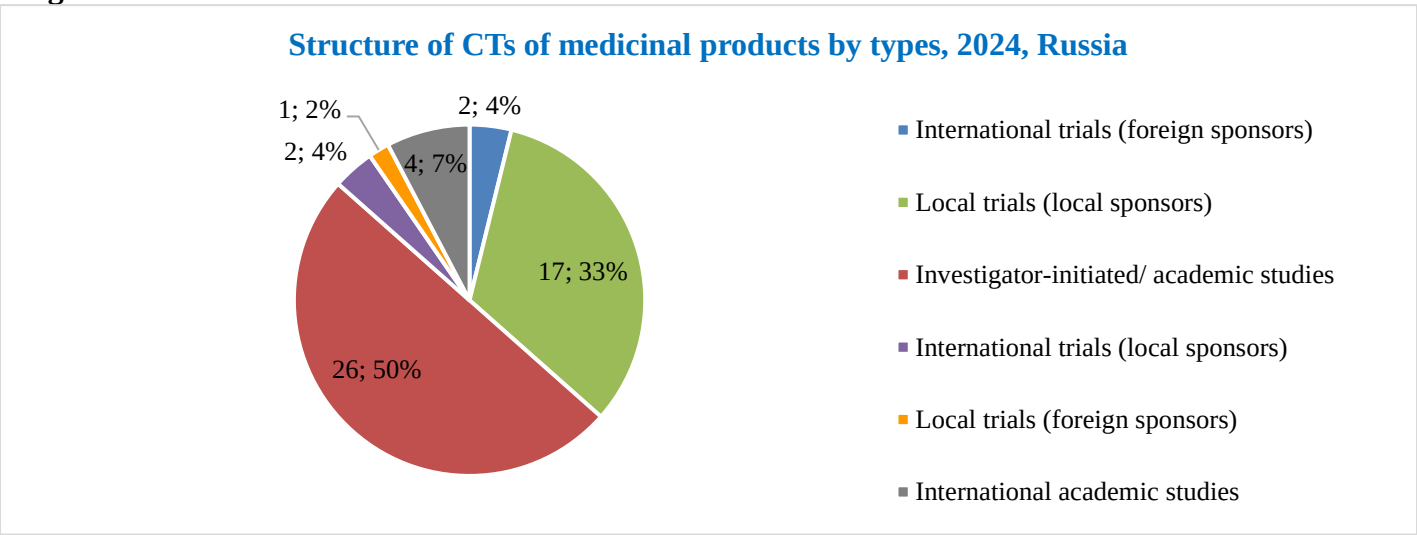
Data from www.clinicaltrials.gov

Diagram 29



Data from www.clinicaltrials.gov

Diagram 30



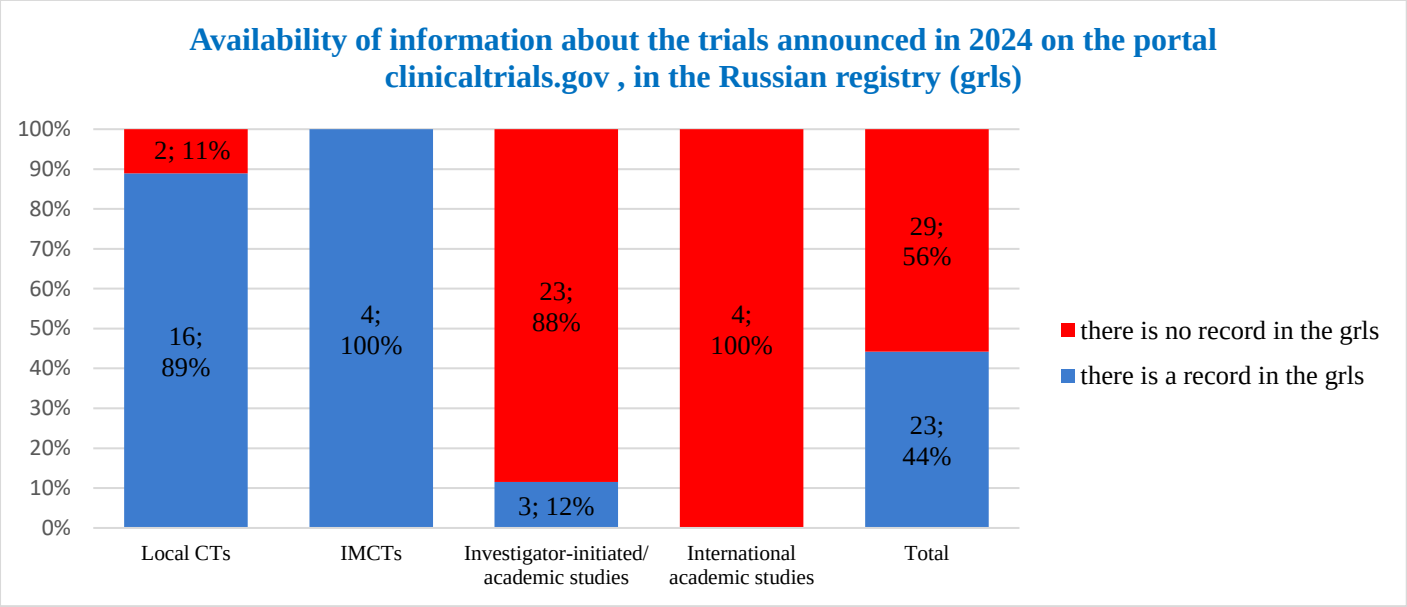
Data from www.clinicaltrials.gov

Table 20

Sponsors, 2024, Russia	Total	Number of local trials	Number of IMCTs	Number of investigator-initiated/ academic studies	Number of international academic studies
Valenta Pharm JSC	7	7	–	–	–
Biocad	5	4	1	–	–
St. Petersburg State Pavlov Medical University	4	–	–	3	1
Tomsk National Research Medical Center of the Russian Academy of Sciences	4	–	–	4	–
National Medical Research Center for Cardiology, Ministry of Health of Russian Federation	3	–	–	3	–
Saint Petersburg State University, Russia	3	–	–	3	–
AstraZeneca	2	1	1	–	–
I.M. Sechenov First Moscow State Medical University	2	–	–	2	–
Pirogov Russian National Research Medical University	2	–	–	2	–
Shenzhen Geno-Immune Medical Institute	2	–	–	–	2
Amur State Medical Academy	1	–	–	1	–
AO GENERIUM	1	1	–	–	–
Avva Rus, JSC	1	–	1	–	–
City Clinical Oncology Hospital No 1	1	–	–	1	–
Federal Research Institute of Pediatric Hematology, Oncology and Immunology	1	–	–	1	–
Federal State Budget Institution Research Center for Obstetrics, Gynecology and Perinatology Ministry of Healthcare	1	–	–	1	–
Federal State Budgetary Institution, V. A. Almazov Federal North-West Medical Research Centre, of the Ministry of Health	1	–	–	1	–
GlaxoSmithKline	1	–	1	–	–
Institute for Atherosclerosis Research, Russia	1	–	–	1	–
Materia Medica Holding	1	1	–	–	–
N.N. Petrov National Medical Research Center of Oncology	1	–	–	1	–
National Research Center for Hematology	1	–	–	1	–
Petrovsky National Research Centre of Surgery	1	–	–	1	–
PHARMENTERPRISES LLC	1	1	–	–	–
Pharmtechnology LLC	1	1	–	–	–
S.LAB (SOLOWAYS)	1	1	–	–	–
Supergene, LLC	1	1	–	–	–
Xijing Hospital	1	–	–	–	1
Total number of sponsors is 28	52	18	4	26	4

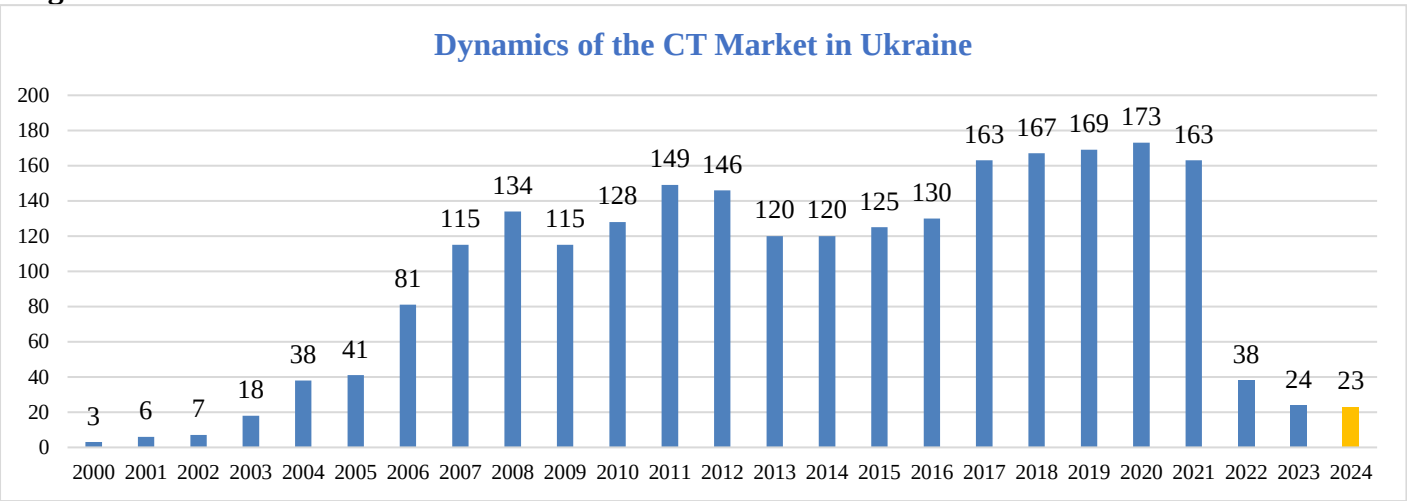
Data from www.clinicaltrials.gov

Diagram 31



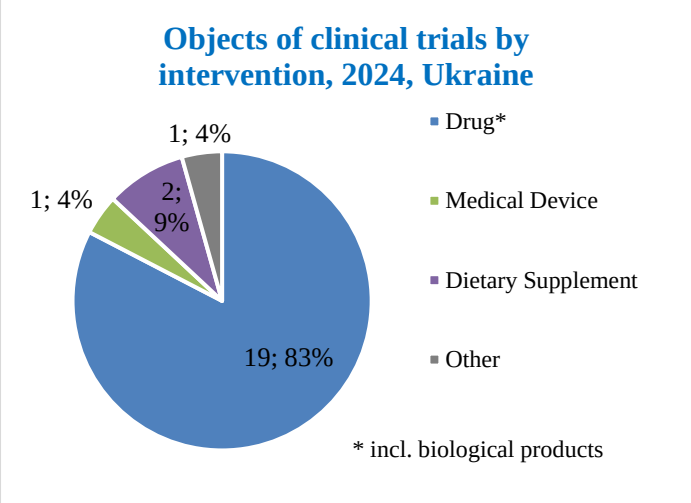
Data from www.clinicaltrials.gov, www.grls.rosminzdrav.ru

Diagram 32



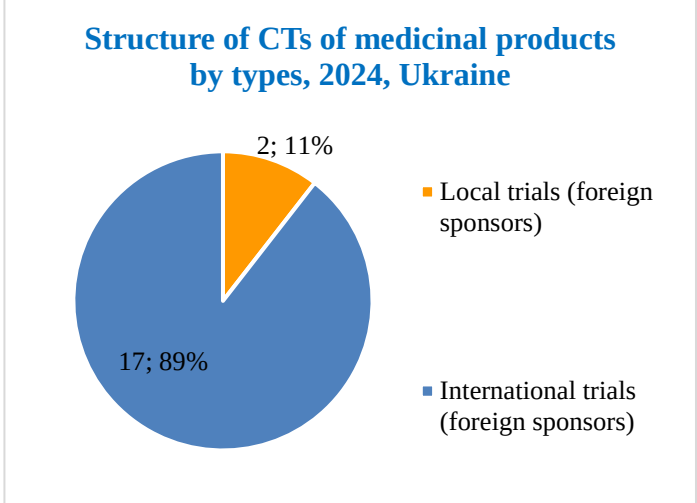
Data from www.clinicaltrials.gov

Diagram 33



Data from www.clinicaltrials.gov

Diagram 34



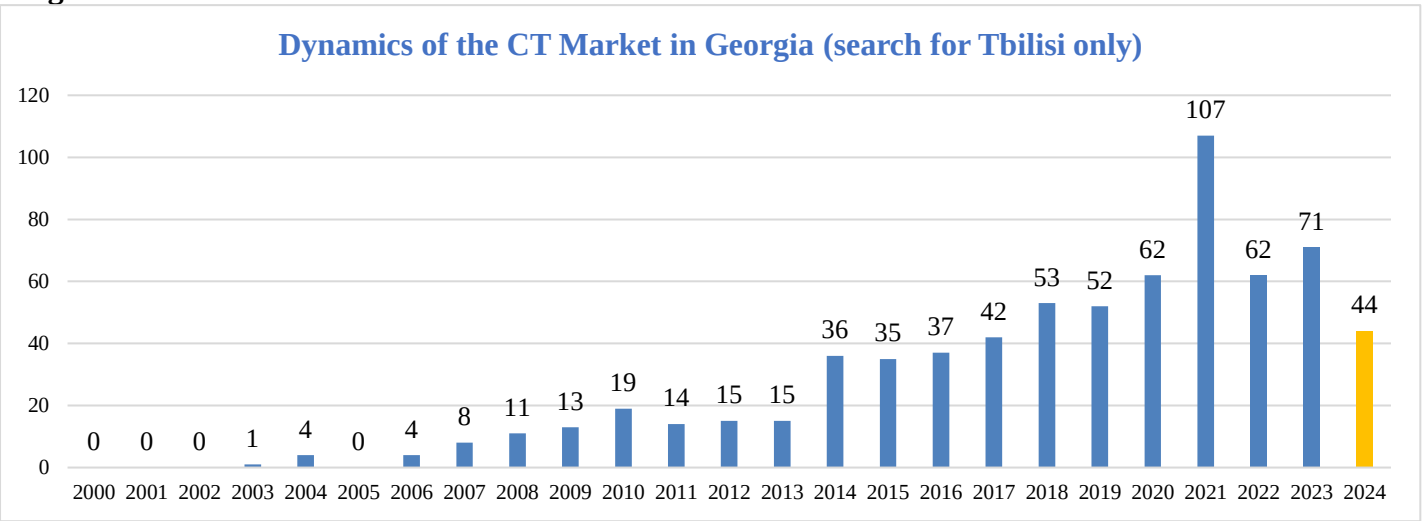
Data from www.clinicaltrials.gov

Table 21

Sponsors, 2024, Ukraine	Total	Number of IMCTs	Number of local trials
AstraZeneca	5	5	–
Merck Sharp & Dohme LLC	3	3	–
Alvotech Swiss AG	1	1	–
Bayer	1	1	–
Eli Lilly and Company	1	1	–
Formycon AG	1	1	–
Janssen Research & Development, LLC	1	1	–
Octapharma	1	1	–
Omeros Corporation	1	1	–
Sanofi	1	1	–
Thirty Respiratory Limited	1	–	1
Vector Vitale LLC	1	–	1
X4 Pharmaceuticals	1	1	–
Total number of sponsors is 13	19	17	2

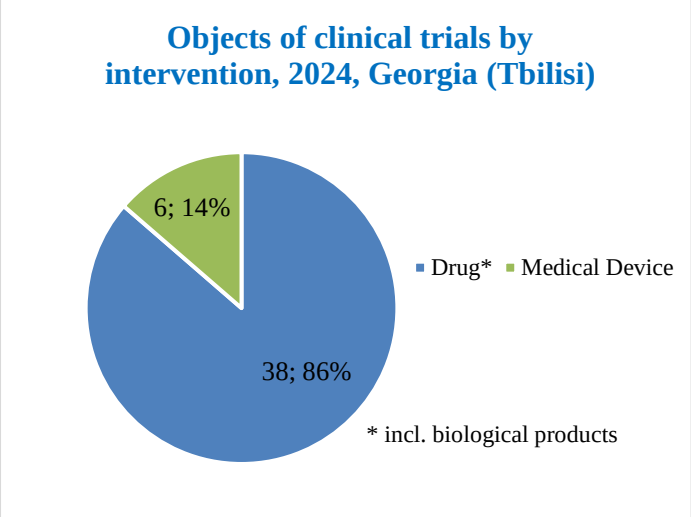
Data from www.clinicaltrials.gov

Diagram 35



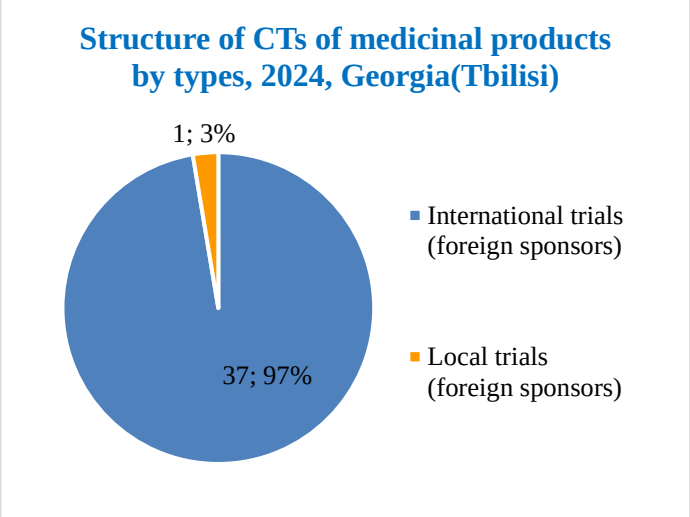
Data from www.clinicaltrials.gov

Diagram 36



Data from www.clinicaltrials.gov

Diagram 37



Data from www.clinicaltrials.gov

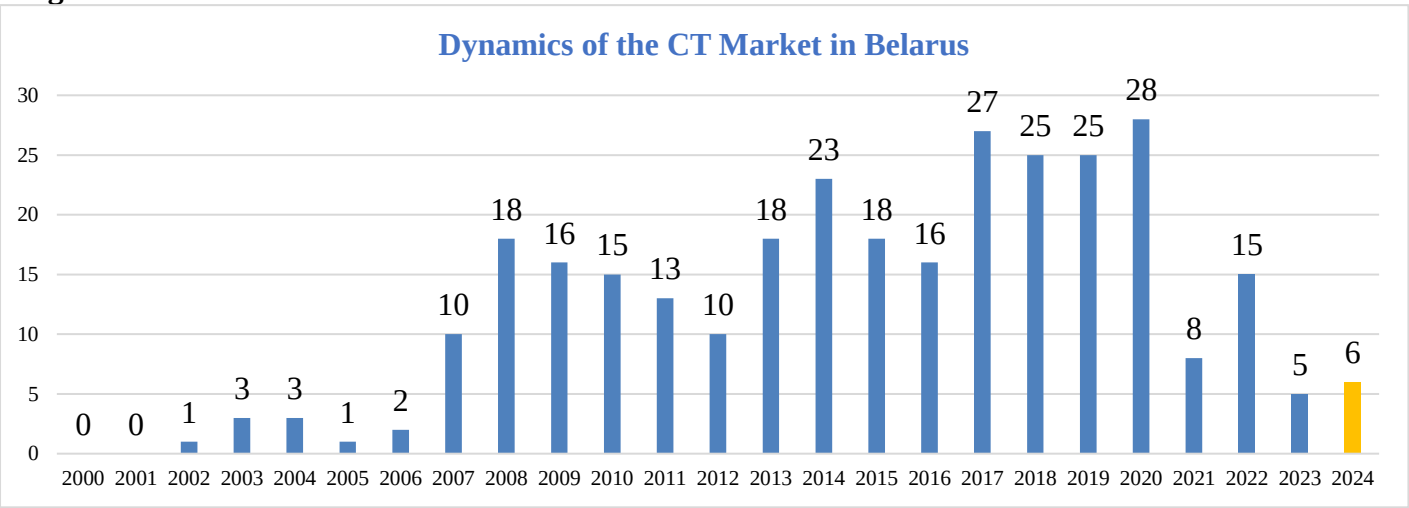
Table 22

Sponsors, 2024, Georgia	Total	Number of IMCTs	Number of local trials
Boehringer Ingelheim	3	3	–
Amgen	2	2	–
Argenx	2	2	–
H. Lundbeck A/S	2	2	–
Regeneron Pharmaceuticals	2	2	–
Sandoz	2	1	1
Alvotech Swiss AG	1	1	–
ApcinteX Ltd	1	1	–
Arbutus Biopharma Corporation	1	1	–
AstraZeneca	1	1	–
BicycleTx Limited	1	1	–
Cardurion Pharmaceuticals, Inc.	1	1	–
Formycon AG	1	1	–
Genexine, Inc.	1	1	–
Gilead Sciences	1	1	–
Idorsia Pharmaceuticals Ltd.	1	1	–
Jiangsu Atom Bioscience and Pharmaceutical Co., Ltd.	1	1	–

Kartos Therapeutics, Inc.	1	1	–
mAbxience Research S.L.	1	1	–
Merck Healthcare KGaA	1	1	–
Merck Sharp & Dohme LLC	1	1	–
ModernaTX, Inc.	1	1	–
Morphic Therapeutic, Inc	1	1	–
NMD Pharma A/S	1	1	–
Rezolute	1	1	–
Samsung Bioepis Co., Ltd.	1	1	–
Sanofi	1	1	–
Tectonic Therapeutic	1	1	–
UCB Biopharma SRL	1	1	–
Vedanta Biosciences, Inc.	1	1	–
X4 Pharmaceuticals	1	1	–
Total number of sponsors is 31	38	37	1

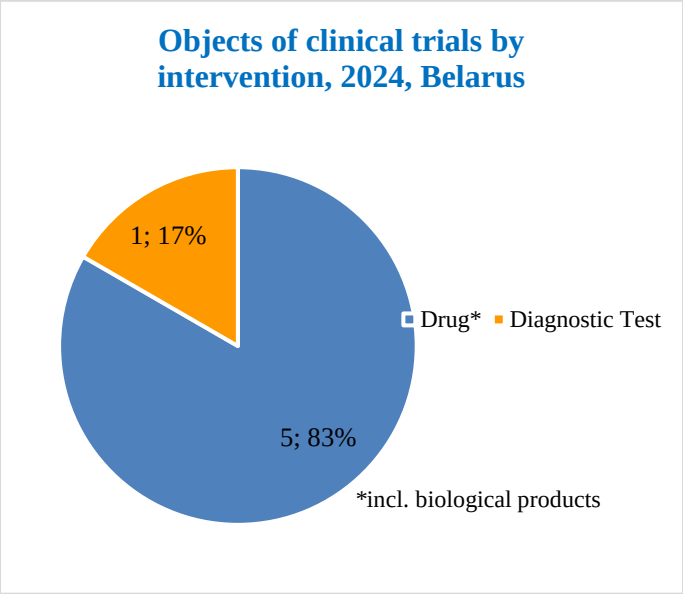
Data from www.clinicaltrials.gov

Diagram 38



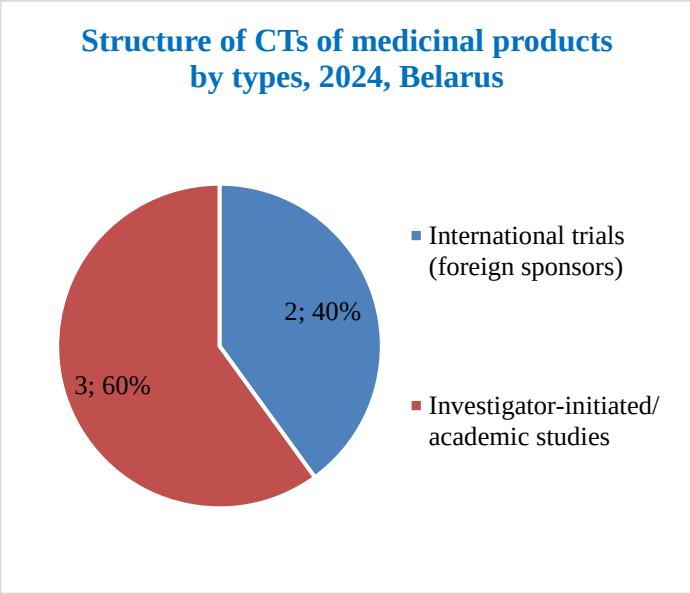
Data from www.clinicaltrials.gov

Diagram 39



Data from www.clinicaltrials.gov

Diagram 40



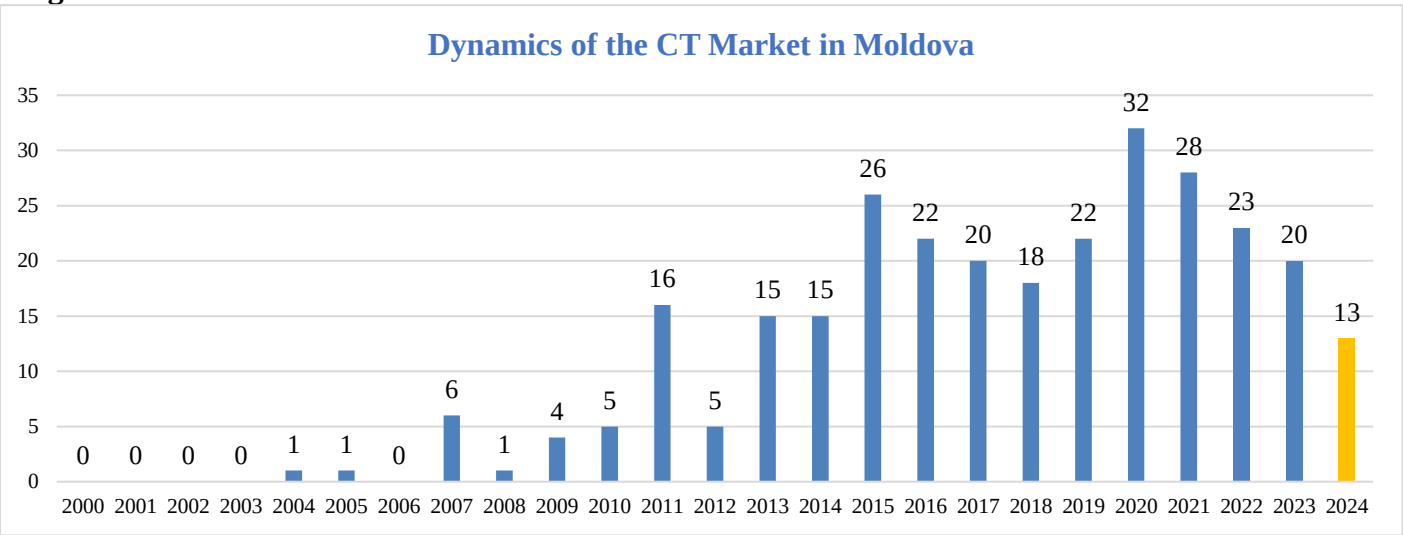
Data from www.clinicaltrials.gov

Table 23

Sponsors, 2024, Belarus	Total	Number of IMCTs	Sponsors, 2024, Belarus
Research Institute for Physical Chemical Problems of the Belarusian State University	2	–	2
AVVA Pharmaceuticals Ltd.	1	1	–
Biocad	1	1	–
Vitebsk Regional Clinical Cancer Centre	1	–	1
Total number of sponsors is 4	5	2	3

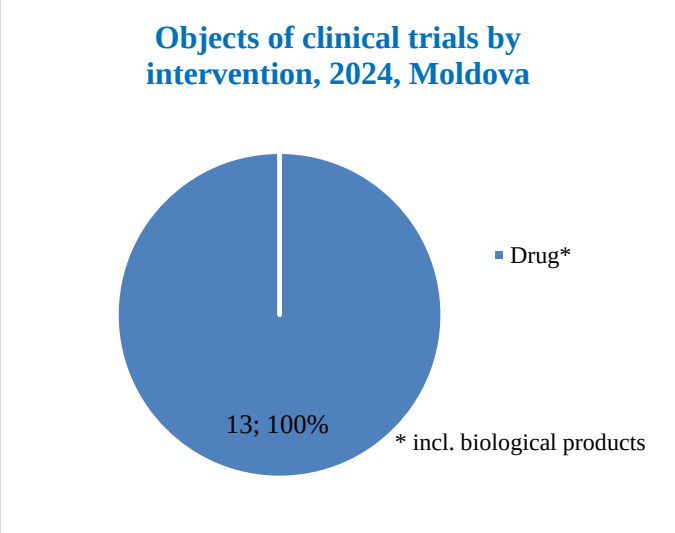
Data from www.clinicaltrials.gov

Diagram 41



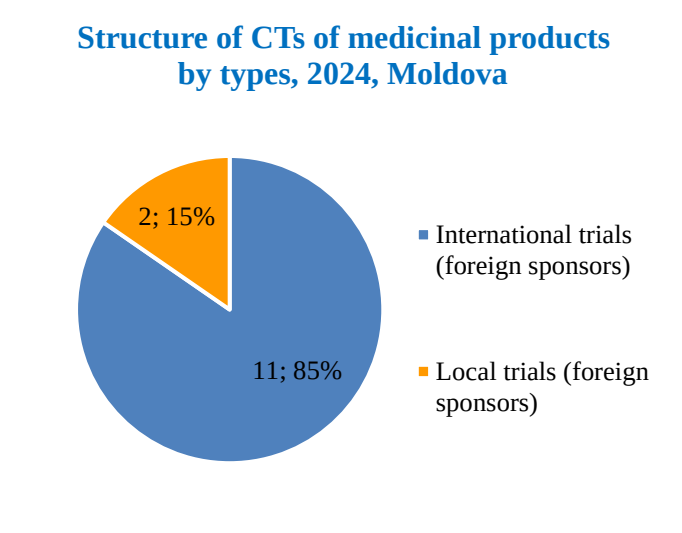
Data from www.clinicaltrials.gov

Diagram 42



Data from www.clinicaltrials.gov

Diagram 43



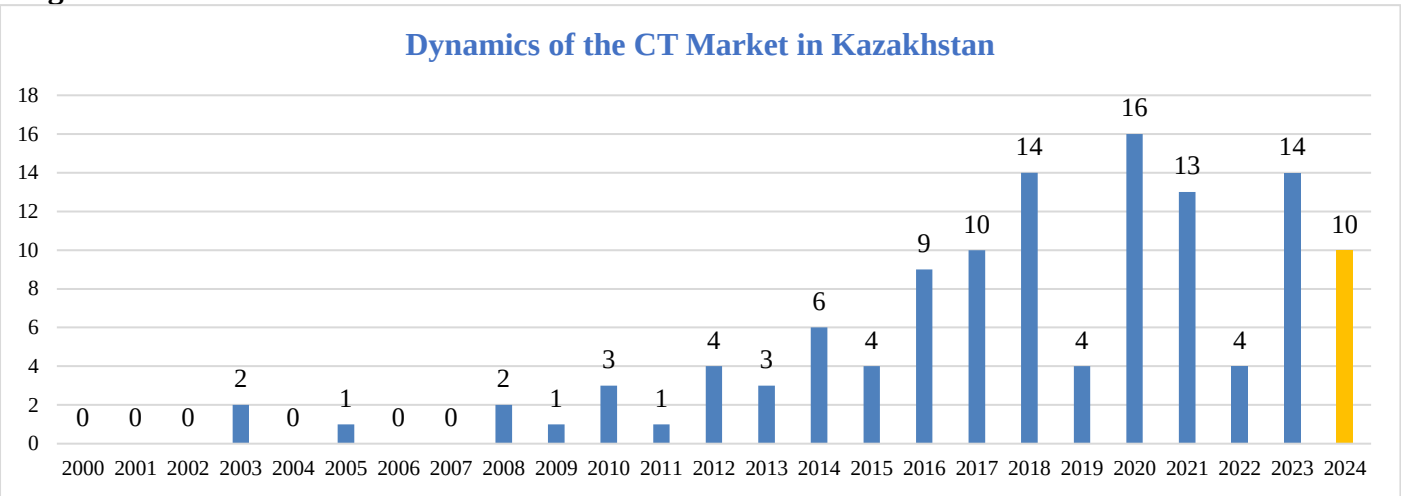
Data from www.clinicaltrials.gov

Table 24

Sponsors, 2024, Moldova	Total	Number of IMCTs	Number of local trials
mAbxience Research S.L	2	1	1
ApcinteX Ltd	1	1	–
Assembly Biosciences	1	1	–
BeiGene	1	1	–
Formycon AG	1	1	–
Gilead Sciences	1	1	–
Hummingbird Bioscience	1	1	–
Janssen Research & Development, LLC	1	1	–
Precision BioSciences, Inc.	1	1	–
Regeneron Pharmaceuticals	1	1	–
Syqe Medical	1	–	1
Tectonic Therapeutic	1	1	–
Total number of sponsors is 12	13	11	2

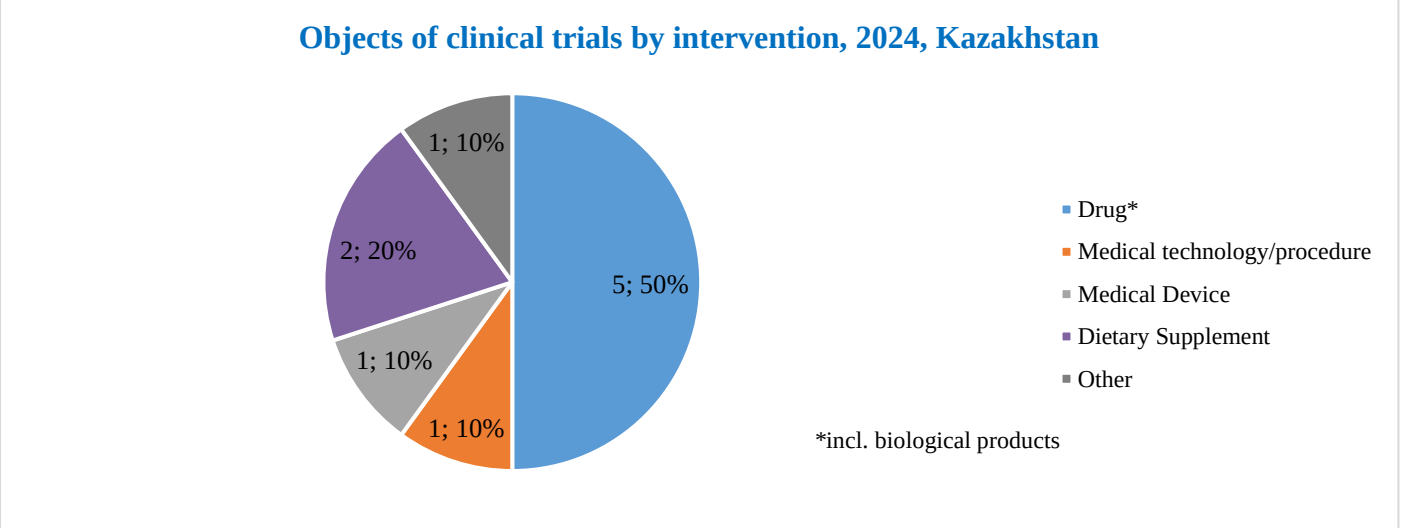
Data from www.clinicaltrials.gov

Diagram 44



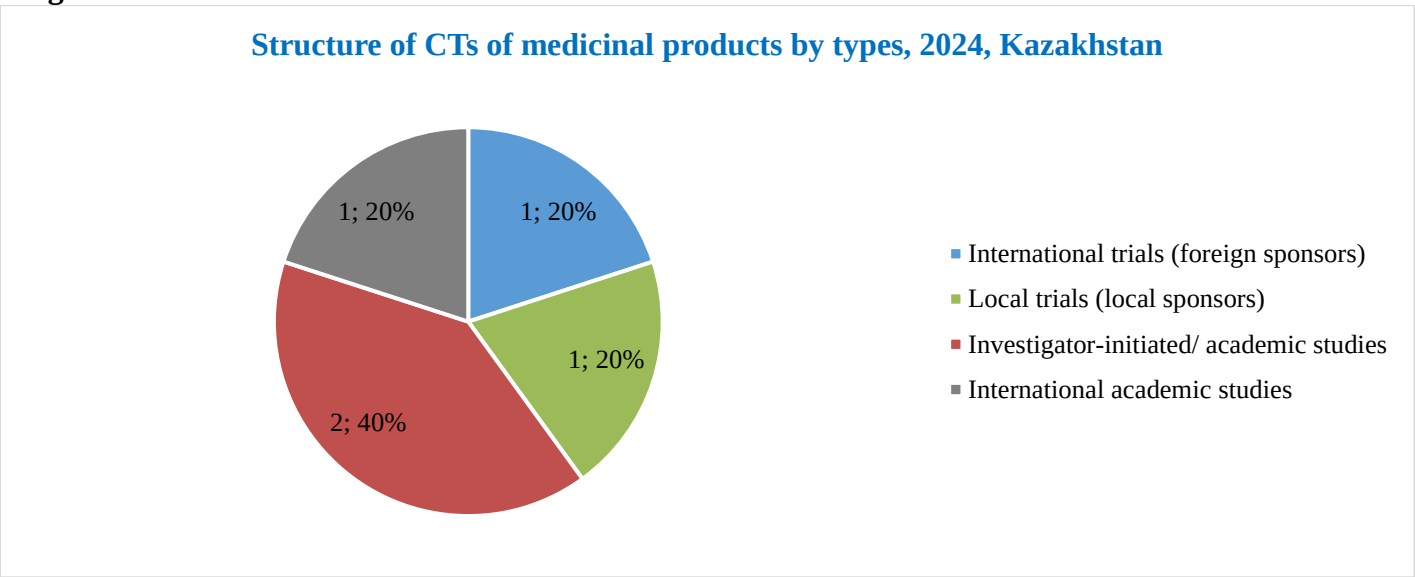
Data from www.clinicaltrials.gov

Diagram 45



Data from www.clinicaltrials.gov

Diagram 46



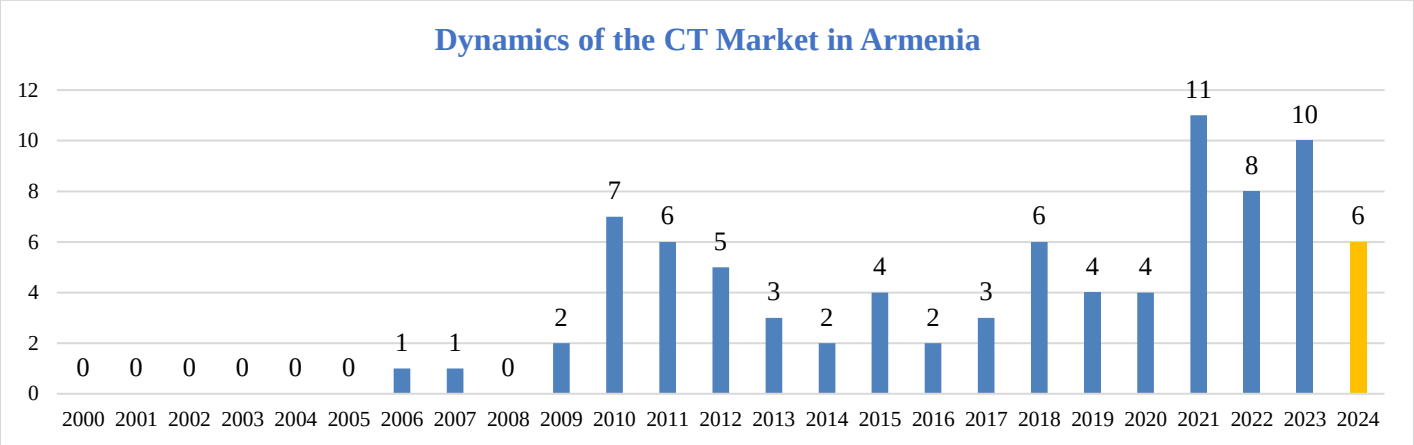
Data from www.clinicaltrials.gov

Table 25

Sponsors, 2024, Kazakhstan	Total	Number of IMCTs	Number of local trials	Number of investigator-initiated/ academic studies	Number of international academic studies
Industrial Microbiology LLP	1	–	1	–	–
Kazakhstan's Medical University "KSPH"	1	–	–	1	
Morphic Therapeutic, Inc	1	1	–	–	–
Ralf Rothoerl	1	–	–	1	
St. Petersburg State Pavlov Medical University	1	–	–	–	1
Total number of sponsors is 5	5	1	1	2	1

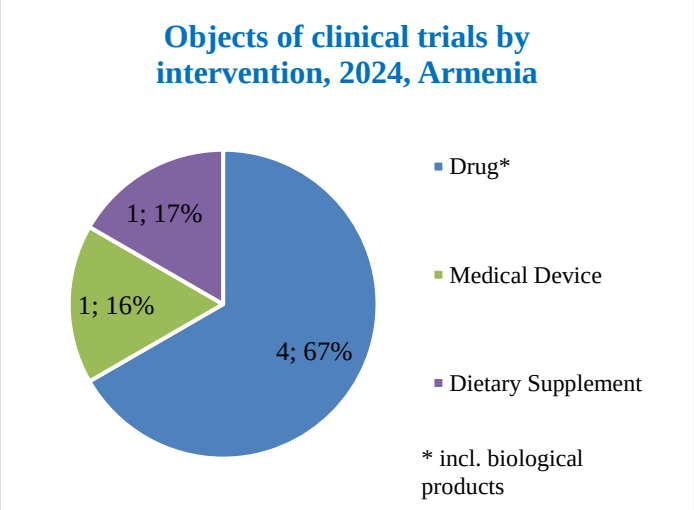
Data from www.clinicaltrials.gov

Diagram 47



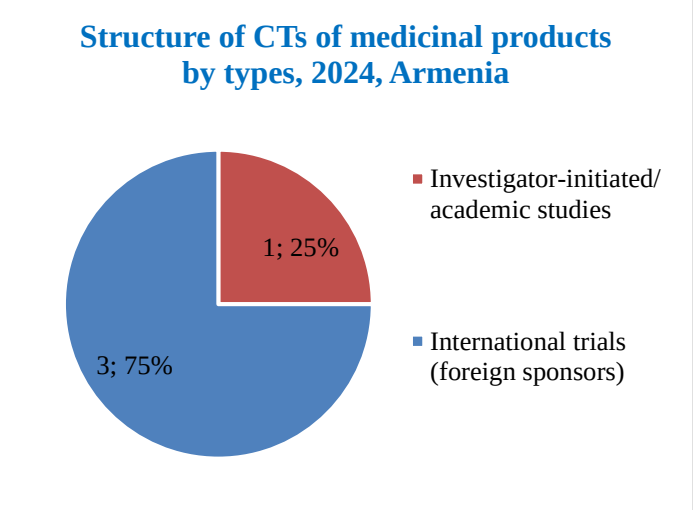
Data from www.clinicaltrials.gov

Diagram 48



Data from www.clinicaltrials.gov

Diagram 49



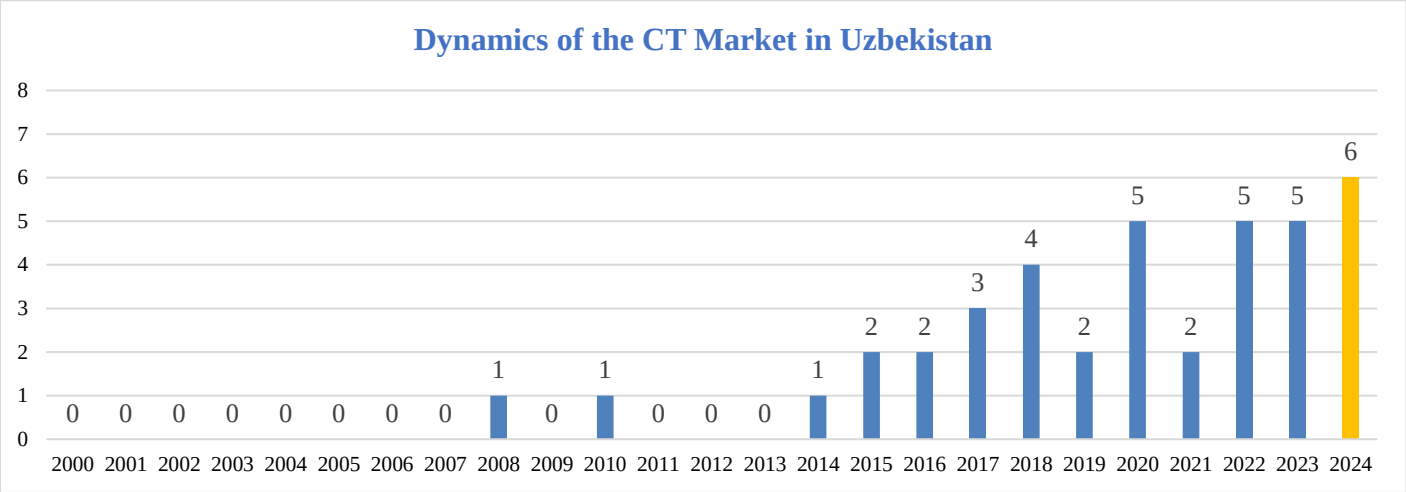
Data from www.clinicaltrials.gov

Table 26

Sponsors, 2024, Armenia	Total	Number of IMCTs	Sponsors, 2024, Armenia
Abbott	1	1	–
Immune Oncology Research Institute	1	–	1
Octapharma	1	1	–
Tectonic Therapeutic	1	1	–
Total number of sponsors is 4	4	3	1

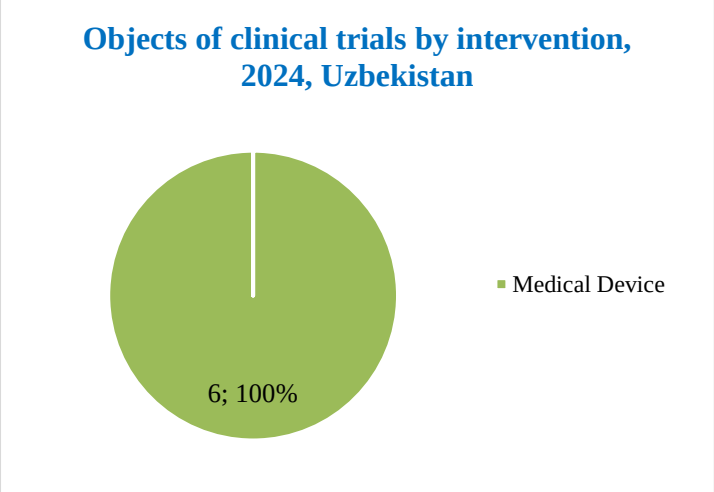
Data from www.clinicaltrials.gov

Diagram 50



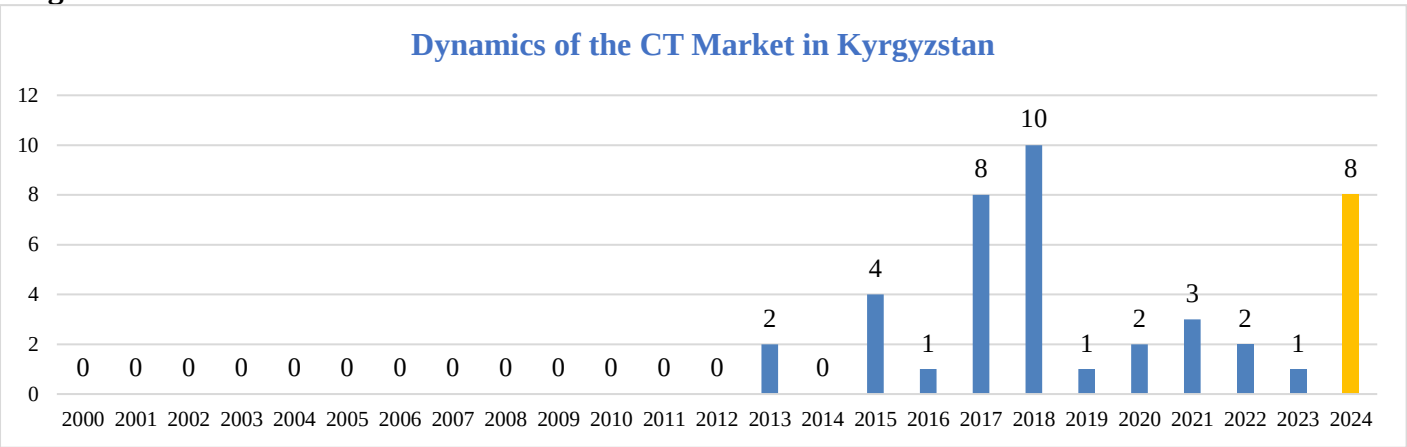
Data from www.clinicaltrials.gov

Diagram 51



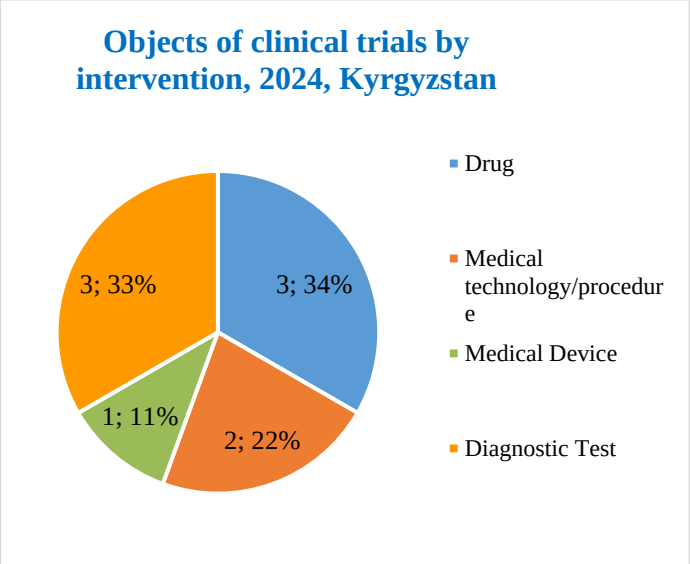
Data from www.clinicaltrials.gov

Diagram 52



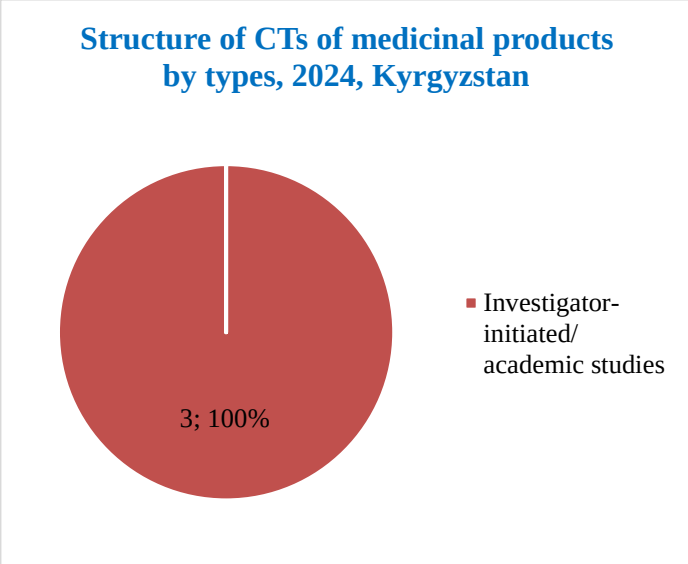
Data from www.clinicaltrials.gov

Diagram 53



Data from www.clinicaltrials.gov

Diagram 54



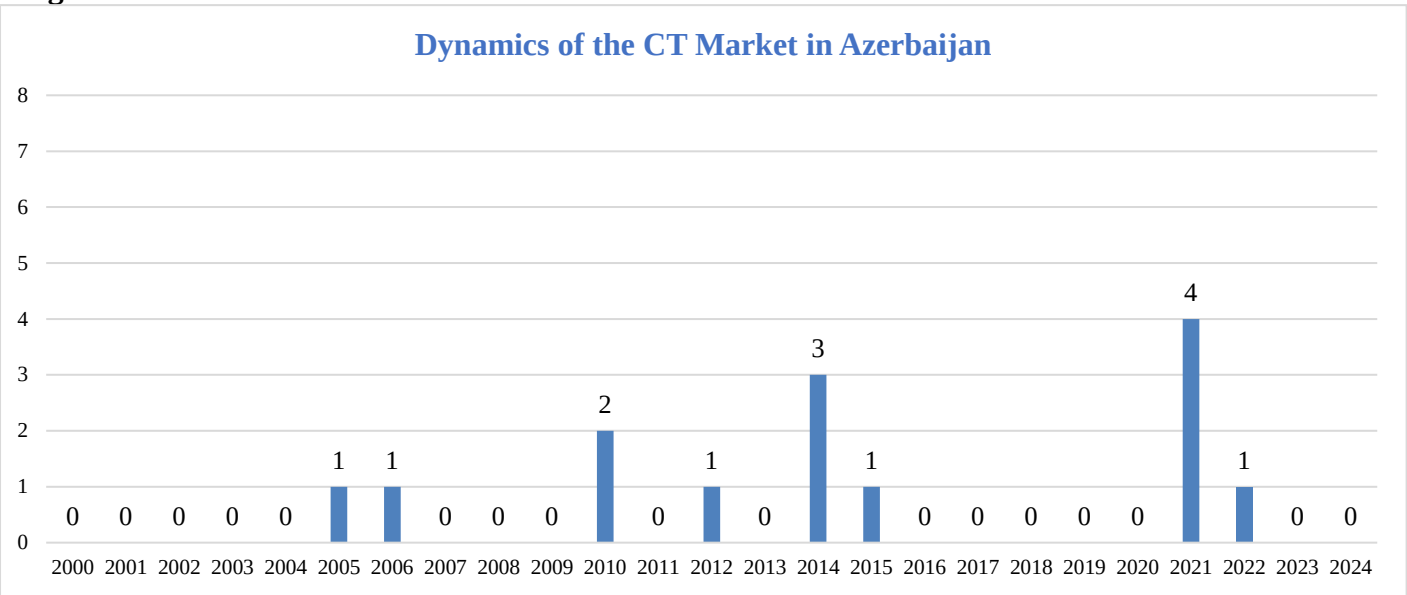
Data from www.clinicaltrials.gov

Table 27

Sponsors, 2024, Kyrgyzstan	Total	Number of investigator-initiated/ academic studies
University of Zurich	3	3

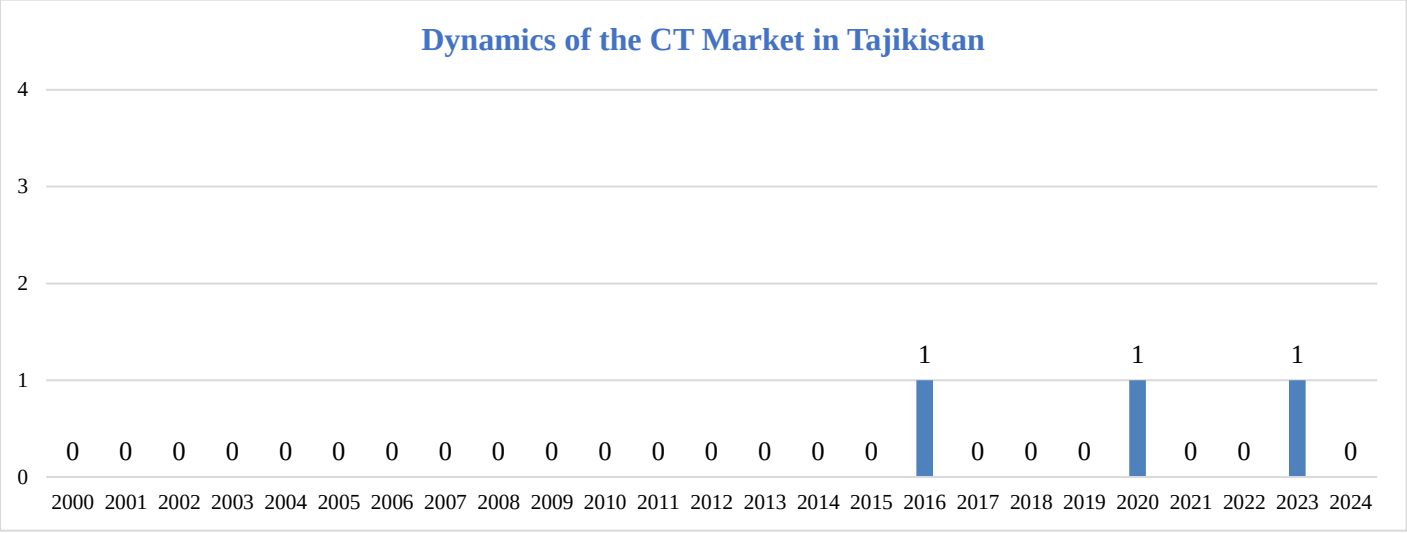
Data from www.clinicaltrials.gov

Diagram 55



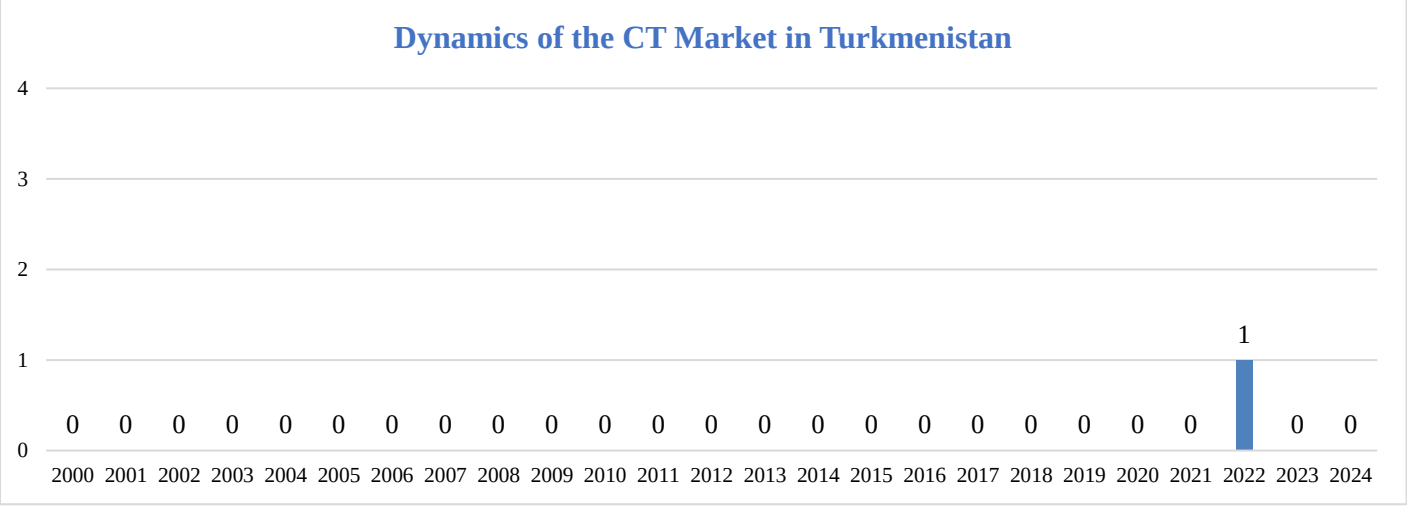
Data from www.clinicaltrials.gov

Diagram 56



Data from www.clinicaltrials.gov

Diagram 57



Data from www.clinicaltrials.gov

MAKE WAY FOR ELECTRONIC CONSENT! OR DIGITALISATION OF THE ENTIRE COUNTRY 2.0

In the previous issue of the newsletter[13] we described a problem posing a threat to the entire clinical trials market in Russia: according to the amendments adopted to the law "On Circulation of Medicines", obtaining informed consent from clinical trial participants must be carried out in electronic format "using an enhanced qualified or a simple electronic signature through the use of a unified identification and authentication system". Initially, the changes were to come into force on 1 January 2025. Our considerations regarding the purpose of this measure and its threats to the clinical trials market are outlined in detail in the mentioned publication. We would like to provide an update as of today.

It should be noted that throughout 2024, a number of meetings took place between the industry and representatives of the Ministry of Health and the Ministry of Digital Development of Russia to understand how officials envisaged the establishment of the new system for obtaining informed consent. During the discussions, it became clear that: a) none of the mentioned agencies intended to take responsibility for creating or overseeing the system; b) the Ministry of Digital Development (as the agency responsible for the advancement of information technologies) did not support the bill in its adopted form and considered the initiative to introduce an alternative-free electronic signature, certified in the Unified Identification and Authentication System (UIAS)[14], premature and impractical; c) the Ministry of Health, while on the one hand disassociating itself from authorship of the amendments, on the other hand acted as their sole defender, showing significant indifference to the specifics of how the system should be built. No arguments, apart from the repeated mantra of “digitalisation is our future” and therefore the industry must find ways to implement the law, could be obtained from the agency.

By the end of 2024, tensions were rising. The industry could not understand how the requirements of the law could be fulfilled and a functional system built without causing significant damage to clinical trial recruitment. A few service companies specialising in information technologies in healthcare have stated they do not see any issues with the technical implementation of the innovation. But this was somewhat disingenuous. In the proposed scenarios, one of the key 'laws'—the necessity of integration with the UIAS—remained unachievable. Moreover, the Ministry of Digital Development was in no hurry to allow an unclear and entirely uninteresting industry, also associated with 'experiments on humans,' into the state system.

In September 2024, five business associations[15]submitted a joint appeal to the Government of the Russian Federation concerning the practical implementation of the new procedure for obtaining informed consent from participants in clinical trials. On 25 October, a meeting of the Committee for the Development of the Pharmaceutical Industry of Business Russia was held, where the same issue was discussed. Representatives of the Ministry of Digital Development, present at the meeting, once again criticised the Ministry of Health's approach and reaffirmed their position on the impracticality of implementing the innovation at the current time. Representatives of the Ministry of Health stated that they are working on the possibility of postponing the implementation of the norm. On 29 October, the associations received a response from the Ministry of Health of Russia, in which the agency confirmed what had already been mentioned at the above-mentioned meeting: the possibility of postponing the implementation of the new requirements is being considered.

On 17 December 2024, the State Duma adopted the law 'On Amendments to Certain Legislative Acts of the Russian Federation.' Article 32 of the said law introduced amendments to the law On Circulation of Medicines, including the postponement of the transition to the electronic format for obtaining informed consent to 1 January 2026. The industry has been granted a one-year reprieve. However, officials did not forget their own interests. The same amendment changed the effective date of the provision on the transition to electronic

[13] See ACTO Newsletter No. 29.

[14] The Federal State Information System “Unified Identification and Authentication System in the Infrastructure Providing Information and Technological Interaction of Information Systems Used for the Provision of State and Municipal Services in Electronic Form”.

[15]The Association of Russian Pharmaceutical Manufacturers (ARPM), the Association of International Pharmaceutical Manufacturers (AIPM), the Association of Pharmaceutical Manufacturers of the Eurasian Economic Union (APMEEU), the Association of Pharmaceutical Companies 'Pharmaceutical Innovations' (Inpharma), and ACTO.

communication between the Ministry of Health and applicants when submitting documents for registration, obtaining approvals for clinical trials, and other licensing functions performed by the ministry in the field of circulation of medicines.

So, a postponement has been obtained. But this does not mean the sentence has been overturned. The year 2025 has arrived, but it has brought no clarity on how to build a system without delivering a devastating blow to an already struggling industry. Apparently, discussions will continue. Ideally, the law needs to be amended. An alternative approach needs to be outlined, allowing the use of both electronic and paper formats of informed consent, while also excluding the requirement to link the process to the state UIAS system. An approach logical from the perspective of common sense, but not necessarily from that of officials. The Ministry of Health is clearly uneasy at the thought of having to go to the Government and admit incompetence, that something incorrect was written into the law. It is much easier to pressure the industry. And the consequences in the form of complicating and increasing the cost of processes, reducing enrolment, slowing both clinical trials and subsequent registration? If they do occur, it will be later. Others may already have to take responsibility for them, if any responsibility is required at all...

But there is good news as well. And it has come from an international platform.

Undoubtedly, technical progress in the world does not stand still. The development of technologies, including digital ones, does not bypass the field of clinical research. We have observed practical steps towards the implementation of electronic informed consent forms (eICF) over the past ten years, and it was arguably the Covid-19 pandemic that gave the most significant impetus to the widespread adoption of this approach. The evolution of processes could not but be reflected in regulatory frameworks. And so, on 6 January 2025, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) approved the third revision of the Good Clinical Practice (GCP) guideline – E6(R3). And in this new guideline, in section 2.8.1., we find the following text: «*varied approaches (e.g., text, images, videos and other interactive methods) may be used in the informed consent process, including for providing information to the participant. When developing informed consent materials and processes, the characteristics of the potential trial population (e.g., participants may lack familiarity with computerised systems) and the suitability of the method of obtaining consent must be taken into account. If computerised systems are used to obtain informed consent, trial participants may be given the option of using paper-based documents as an alternative "*. However, our Russian law does not offer a choice, mandating the exclusive use of the electronic format. In doing so, it contradicts the international approach.

When was this an issue? As we know, Russia often has its own development path, and international norms, undoubtedly, do not guide us. Although, admittedly, it is necessary to glance at our closest neighbours. The matter is that compliance with ICH GCP is mandatory for international sponsors. And if a country plans to participate in international trials, it must declare the application of internationally recognised standards. This is precisely why the Eurasian Economic Union (EAEU) has adopted guidelines on good clinical practice similar to ICH GCP.

However, within the EAEU, only the first edition of this document is currently in force; it was only at the beginning of 2025 that the second edition of the document was adopted at the level of the working group tasked with forming common approaches to the regulation of the circulation of medicinal products within the EAEU. However, it has not yet been approved by the EEC Council's decision, but it is likely to happen in the near future. The visible lag in implementing international standards has nevertheless been noted by participants, and the working group has already initiated the development of the third revision based on E6(R3). Here, we believe, the Russian Ministry of Health will have to make a decision: either actively insist on implementing its own approach, explaining and somehow justifying its position to allied countries, or take active steps to amend Russian legislation.