ACTO

ASSOCIATION OF CLINICAL TRIALS ORGANIZATIONS

ACTO NEWSLETTER № 28

Summary of 2023 results

MOSCOW 2023

CONTENTS

This issue of the newsletter comes out two years after the start of the full-on military conflict between Russia and Ukraine. Throughout this entire time we watched in real time the collapse of what had been created in Russia with so much pain and effort in all the previous years since the late nineties — the industry of civilized international clinical trials meeting the high standards.

It was then, in the late nineties, even before the adoption of the law "On Medicines", that the largest Western companies, cautiously at first, then with more confidence, began to come to Russia with their international projects. There is still a common myth among the general public that Big Pharma is using developing countries as testing grounds. However, our readers are a professional audience who understand full well that a country's active participation in IMCTs is an indicator of a high level of healthcare development. And then, at the very beginning of the trials market in Russia, we were granted the honor and trust along with other countries to become participants in the process of developing the newest products of the global pharmaceutical giants. It was Western companies that brought the culture of modern human subject research to our country, which allows this process to be carried out with minimal risk both for trial subjects and for the future mass consumer of medicines. They introduced us to GCP and the Declaration of Helsinki, helped us to form a professional community and consolidate its commitment to the principles of evidence-based medicine, and taught many of its representatives logic and skills to identify cause-effect relations.

Coming of international clinical trials to our country stimulated the development of this area in the domestic industry. Although not all local manufacturers needed this, with an example of how processes should be carried out before their eyes, many were forced to follow suit to "comply". A number of them have made remarkable progress in that, which made it possible for them to be taken seriously.

At the same time, the industry of contract research organizations, logistics and IT companies accompanying the process has also been developing in the country. Over the years a significant number of professional teams and business units have been formed and found their feet, some of which subsequently merged with larger international companies, while others were able to enter the international market and become its full-fledged independent participants.

And then two years ago all hopes for further development of the IMCT industry in the country collapsed overnight. With the start of a full-on war representatives of Big Pharma, one after another, began to refuse to place new projects, or even completely leave Russia with their R&D departments. To the credit of the companies that have wound down their business in the country, so far only BMS has left "on bad terms", essentially abandoning its patients to their fate and cutting off their access to current therapy. The rest tried to deal with the situation in a more civilized manner; even when leaving they considered it necessary to fulfill their obligations to patients and handed over unfinished projects to the remaining market players.

The process of collapse of the IMCT industry in Russia was predictable and logical at this conjuncture, but no less painful for its participants. Some didn't want to believe, clutching at the hope that it would soon be over and resume its normal course. Some jumped at the available relocation offer and left the country. Some were forced to leave amid personnel cuts trying to find a job in the domestic industry or get back into medicine. Some continue to stay on the job going through with the studies in progress or trying to convince Western colleagues to bring at least some new projects to Russia. In any case, these past two years allow us to acknowledge the deepest crisis of the IMCT industry in Russia. Any positive developments will require considerable changes in the conditions and a lot of time...

But enough about ourselves. The reader may say that although international projects have left the country, the market continues to exist thanks to domestic companies since there's nothing stopping them from moving on. Besides, there's India and there's China, they will surely "save us". But just how well other players will actually be able to replace what was lost, we will be able to see in the not so distant future. Although there is serious skepticism in this regard. A stand-in always differs from the original, and the growing number of bioequivalence studies cannot possibly compensate for the loss of international programs of the leading pharmaceutical manufacturers. However, as we've already said — the future will tell.

In the meantime, we continue to observe and record how the clinical trials market in Russia is transforming under the influence of geopolitical factors.

SUMMARY

In 2023 the Ministry of Health of the Russian Federation has issued 761 approvals for conducting clinical trials. This is slightly more than in 2022 (740 approvals, +2.8%), but less than in 2021 (908 approvals, -16.2%). However, behind the minor fluctuations in the total number of approvals lie global structural changes in the market.

For two years new international projects have almost completely stopped coming to Russia. Only 18 approvals for conducting international multicentre clinical trials (IMCTs) were issued in 2023, of which two projects belonged to a domestic sponsor. Reduction in the number of new IMCTs was –85.5% of the 2022 figure (124 approvals) and –95.1% of the 2021 figure (367 approvals). As a result, the share of IMCTs decreased to 2.4% in the total number of trials, although it constituted 40% of the market before 2022 and 60% before 2012.

The drop in the number of international projects is accompanied by a rapid increase in the number of bioequivalence studies by Russian sponsors: 473 approvals in 2023, +28.9% as compared to 2022 (367 approvals) and +66.0% to the 2021 figure (285). That is a record in the entire history of the Russian market. As a result, the share of bioequivalence studies of domestic generics amounted to 62.2% of the total number of trials.

The share of bioequivalence studies conducted by foreign sponsors has also increased: 122 approvals as against 71 (+71.8%) in 2022 and 87 (+40.2%) in 2021.As a result, the share of this type of trials has reached 16% of the total number of trials approved in 2023. The number of approvals for local trials of therapeutic efficacy and safety of foreign sponsors remained almost unchanged year-on-year, 17 approvals in 2023 as against 16 in 2022, and amounted to less than half of the same figure in 2021 (36 approvals). The number of approvals for local trials by Russian sponsors dropped slightly below the 2021 level after a brief burst a year earlier: 131 approvals in 2023, 162 (–19.1%) in 2022 and 133 (–1.5%) in 2021.

In 2023, two-thirds of trials of generics and biosimilars initiated in the territory of Russia by foreign sponsors belonged to companies from India (59 protocols, 44% of the total number) and Belarus (31 trials, 23%). European countries (including those outside the European Union) accounted for a total of 34 approvals (26% of the total). For the first time in three years of observation the list of sponsors of studies of generics and biosimilars included Iran with three protocols (2%). Israel and China have two approvals each, Turkey and Armenia have one each. Based on data for 2021–2023 there is a decline in the share of European companies, as well as an increase in the activity of manufacturers from India and Belarus.

The most popular molecules among manufacturers of generic drugs in 2023 were rivaroxaban (seven approvals obtained by foreign companies and 24 — by Russian companies), metformin separately and in combination (ten and eight approvals, respectively), vildagliptin separately and in combination (five and twelve).

In addition to the figures described above this issue of the bulletin presents data on the activity of medical institutions and principal investigators in bioequivalence studies, statistics on the main groups of players of the Russian market (sponsors and contract research organizations) for various types of trials, as well as an overview of the situation in the markets of neighboring countries of the Russian Federation.

In addition, in this issue the reader will find a description of the practice of making backdated entries of new trials in the Ministry of Health register, as well as statistics of cases when the protocol names of comparative trials of generics did not contain the name of the reference drug.

VOLUME AND DYNAMICS OF THE RUSSIAN CLINICAL TRIALS MARKET

Last year the Russian clinical trials market continued to be influenced by the same factors that reformatted its landscape in 2022.The onset of military activities and the resulting breakdown in international ties caused a radical reduction in the number of new international multicentre clinical trials (IMCTs). At the same time, the number of bioequivalence studies conducted by Russian sponsors increased. The same processes were observed in 2023.

A year ago we recorded a reduction in the total number of approvals issued for conducting clinical trials by 18.5%: from 908 in 2021 to 740 in 2022. If we compare the 2023 figure with the previous year (Table 1), then formally it increased by 2.8% (761 approvals against 740). However, this is still 16.2% lower than in pre-war 2021.

Table 1

Approvals for Conduct Clinical Trials: 2023 vs 2022						
Year	**Total**	**International Multicenter CTs**	**Local CTs (Foreign Sponsors)**	**Bioequivalence Studies (Foreign Sponsors)**	**Local CTs (Local Sponsors)**	**Bioequivalence Studies (Local Sponsors)**
2023	761	18	17	122	131	473
2022	740	124	16	71	162	367
2021	908	367	36	87	133	285
2023 vs 2022, %	2.8%	-85.5%	6.3%	71.8%	-19.1%	28.9%
2023 vs 2021, %	-16.2%	-95.1%	-52.8%	40.2%	-1.5%	66.0%

Data from www.grls.rosminzdrav.ru

The number of approvals issued for IMCTs continued its rapid decline having pretty much reached the ground: 367 approvals in 2021, 124[1] in 2022 and only 18 in 2023 (a decrease by 85.5% year-on-year and by 95.1% as compared to 2021).

To be fair, a remark is needed here: the number of IMCTs in the ACTO newsletter does not match the number of IMCTs in the Ministry of Health register of approved trials. Over the past year 31 trials were listed as IMCTs in the register. Our statistics include only those trials, international status of which we can confirm from other sources[2]. Typically these include databases such as ClinicalTrials.gov and the EU Clinical Trials Register, and starting from the second half of 2023 we also began to check trials in the Indian registry CTRI.NIC.in.

The number of approvals for local trials of therapeutic efficacy and safety of foreign sponsors remained almost unchanged year-on-year (17 approvals in 2023 as against 16 in 2022), which amounts to less than half of the same figure in 2021 (36 approvals). However, the number of bioequivalence studies of foreign generics

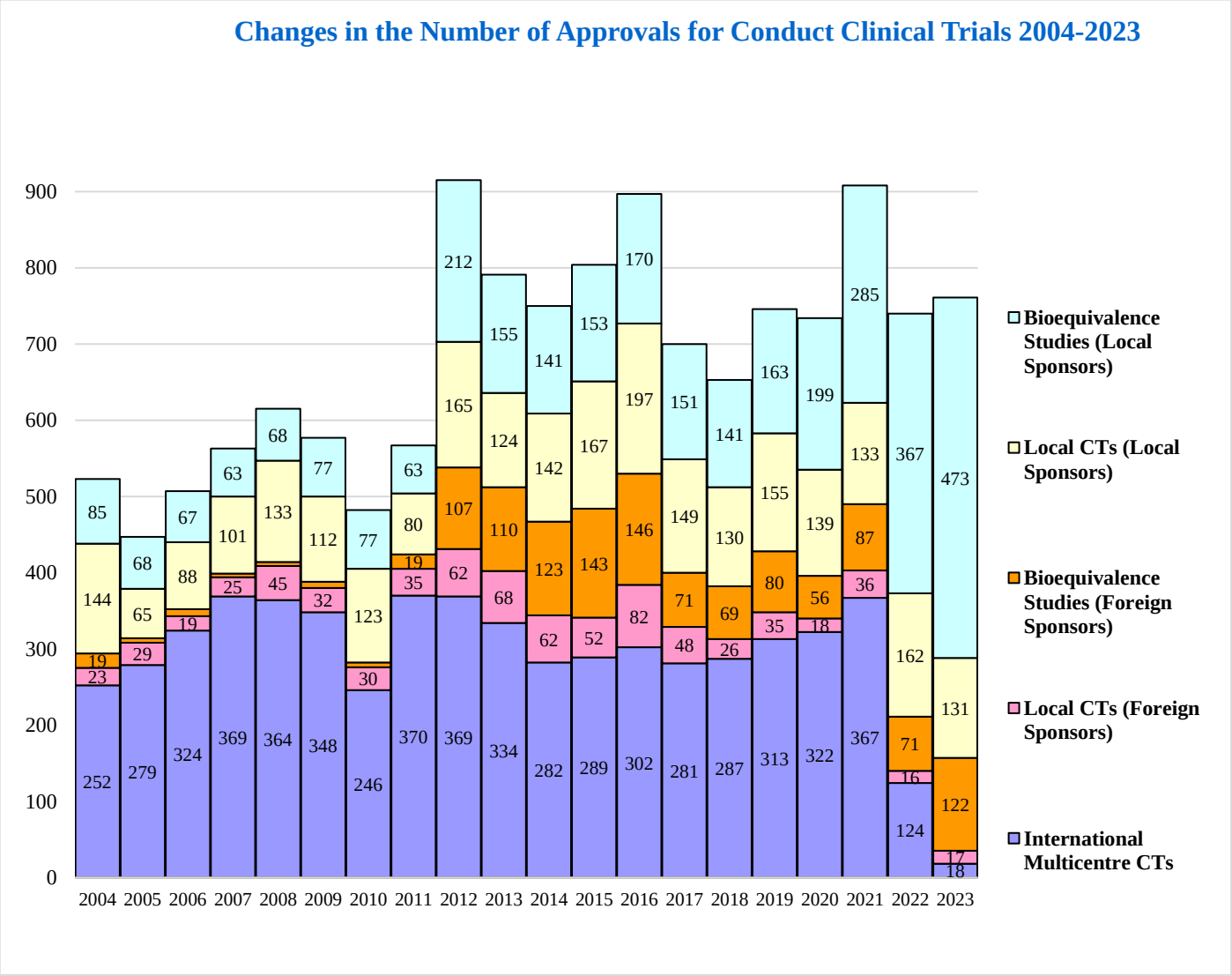
[1] A significant part of trials approved in 2022 never really got started — see ACTO Newsletter No. 26 for more details.
[2] For more detailed explanation and rationale of our classification approach, see pages 4-5 of ACTO Newsletter No. 27.

exceeded the pre-war level: 87 approvals at the end of 2021, 71 in 2022 and 122 in 2023, i.e. 71.8% more than in 2022 and 40.2% more than in 2021.

The number of approvals for local trials by Russian sponsors in 2023 almost returned to the 2021 level after a brief burst a year earlier: 133 approvals in 2021, 162 in 2022 and 131 in 2023.These figures, however, remain within the usual range of fluctuations for this type of trials (see diagrams 1 and 4 below). But the number of bioequivalence studies conducted by Russian sponsors continued to grow without losing momentum: 285 approvals in 2021, 367 in 2022 (+28.8% YoY) and 473 in 2023 (+28.9% YoY). Which ultimately resulted in a 66% increase as compared to the pre-war period.

Diagram 1 shows the dynamics of the same figures in a more distant retrospective. What catches the eye is the abnormally low number of approvals for IMCTs in 2023 and the fivefold increase in the number of approvals for bioequivalence studies by Russian sponsors over the past 20 years. One can also note the sensitivity to crises of local trials by foreign sponsors: their minimum values (16–18 approvals) occurred during the 2020 pandemic and the 2022–2023 military years.

Diagram 1

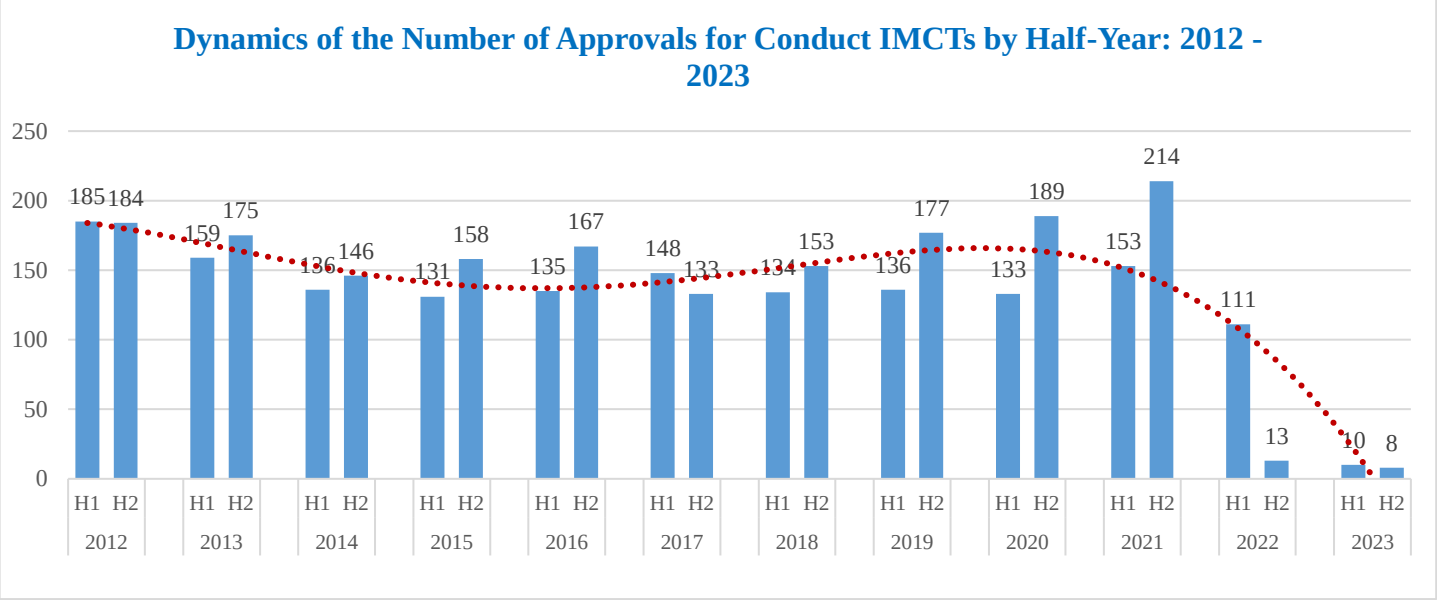


Data from www.grls.rosminzdrav.ru

Diagrams 2–6 show the dynamics over the past 12 years for each type of trials separately. Semi-annual indicators are supplemented with a polynomial trend line, smoothing out random fluctuations.

Diagram 2 clearly reflects the turning point of 2022 and the subsequent drastic collapse in the number of approvals for IMCTs.

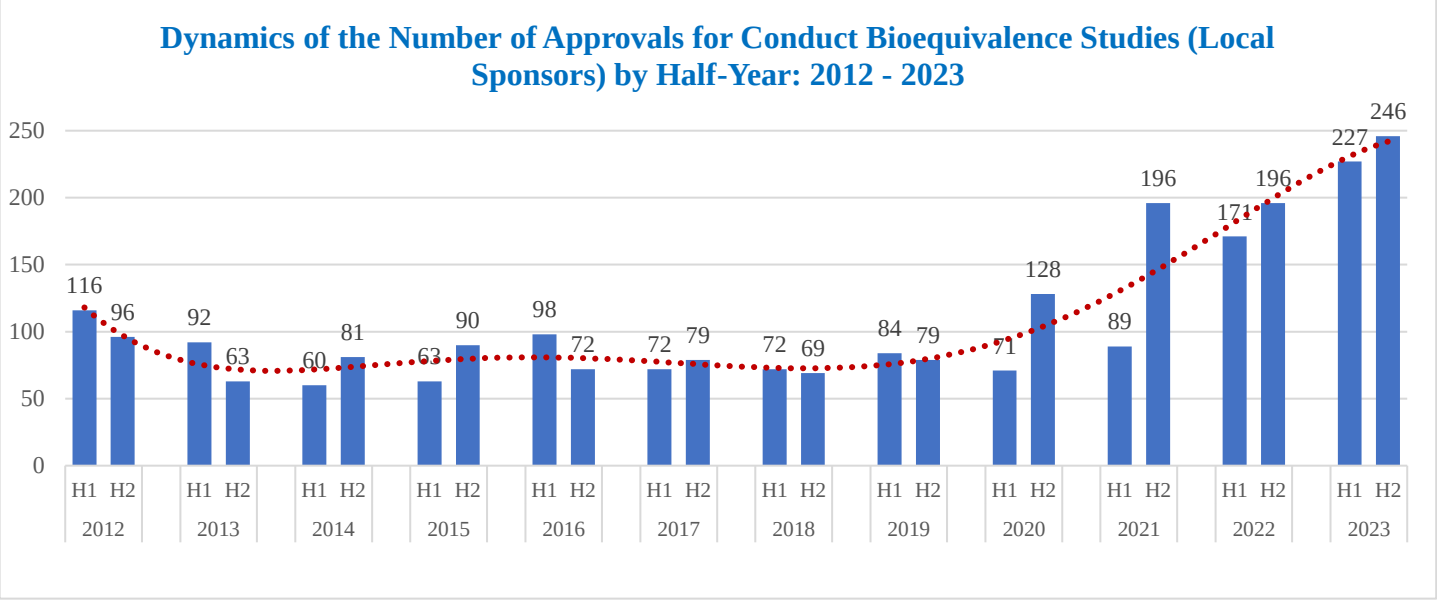
Diagram 2



Data from www.grls.rosminzdrav.ru

Data from bioequivalence studies of Russian sponsors (Diagram 3) show that for these trials 2020 was the year of change in dynamics; it was then in the second half of the year that the first signs of growth were registered. And if the pandemic clearly served as a booster in 2020, then later the decisive factor, apparently, was the dramatic strengthening of the policy towards import substitution.

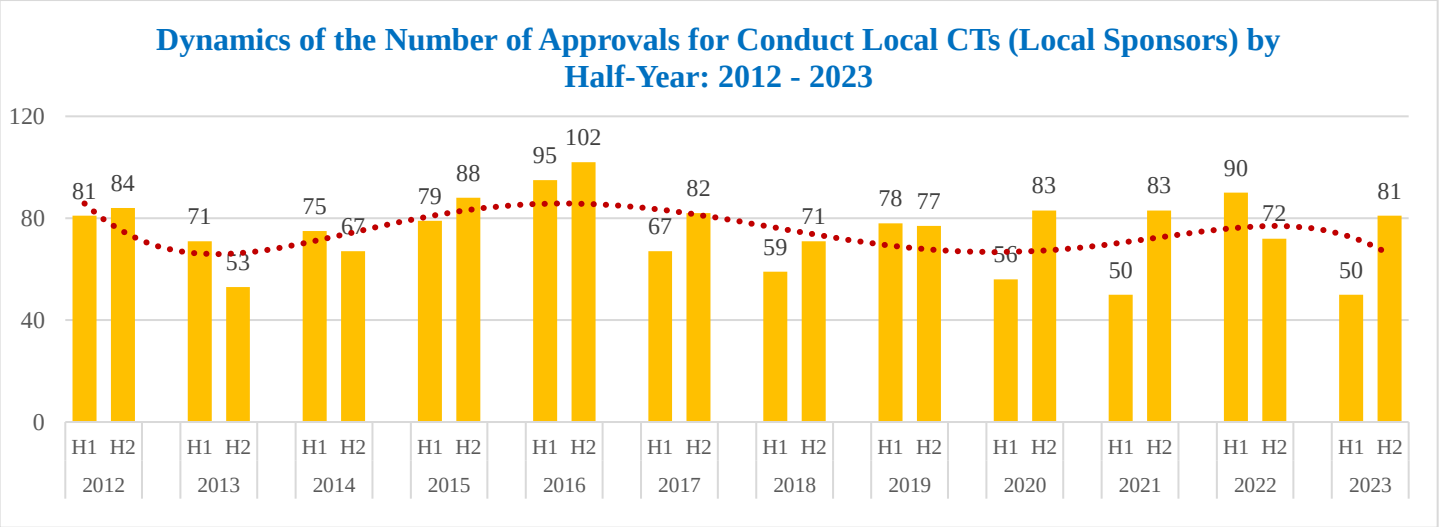
Diagram 3



Data from www.grls.rosminzdrav.ru

In contrast to bioequivalence studies, other types of local trials of Russian manufacturers show no growth dynamics; one can even discern some downward trend (Diagram 4). It is not entirely clear, why the factor of the need to increase domestic production has not yet have any effect here. This is probably due to the fact that organizing and conducting such trials require more resources than bioequivalence studies, not to mention the tasks of setting up production that is more complex than for tablet forms of generics.

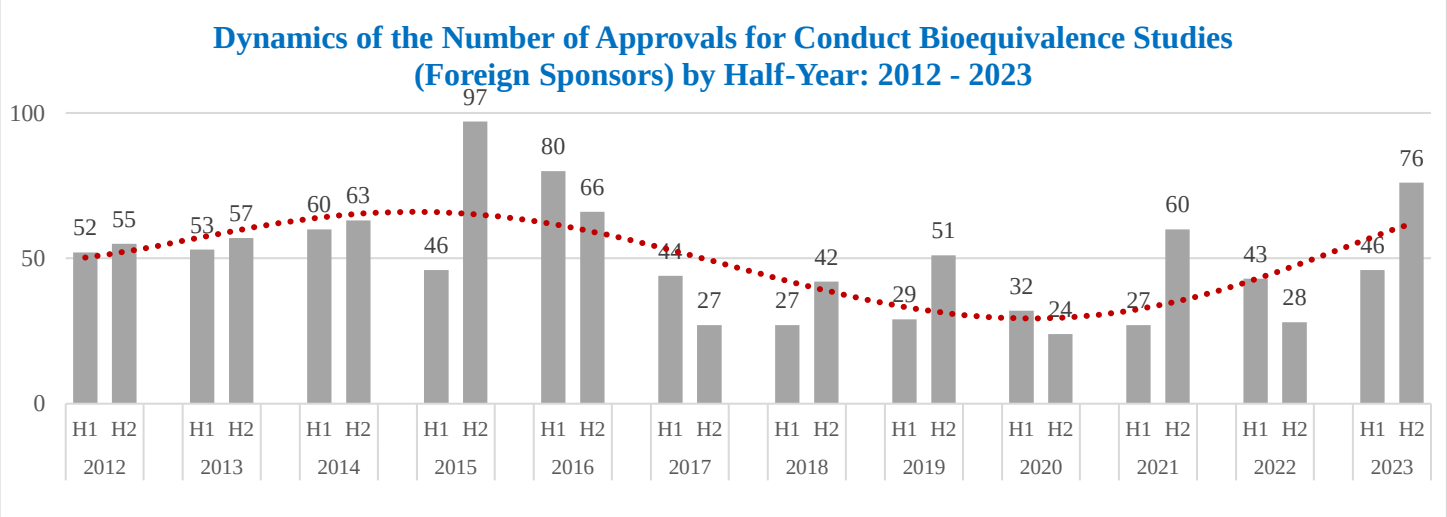
Diagram 4



Data from www.grls.rosminzdrav.ru

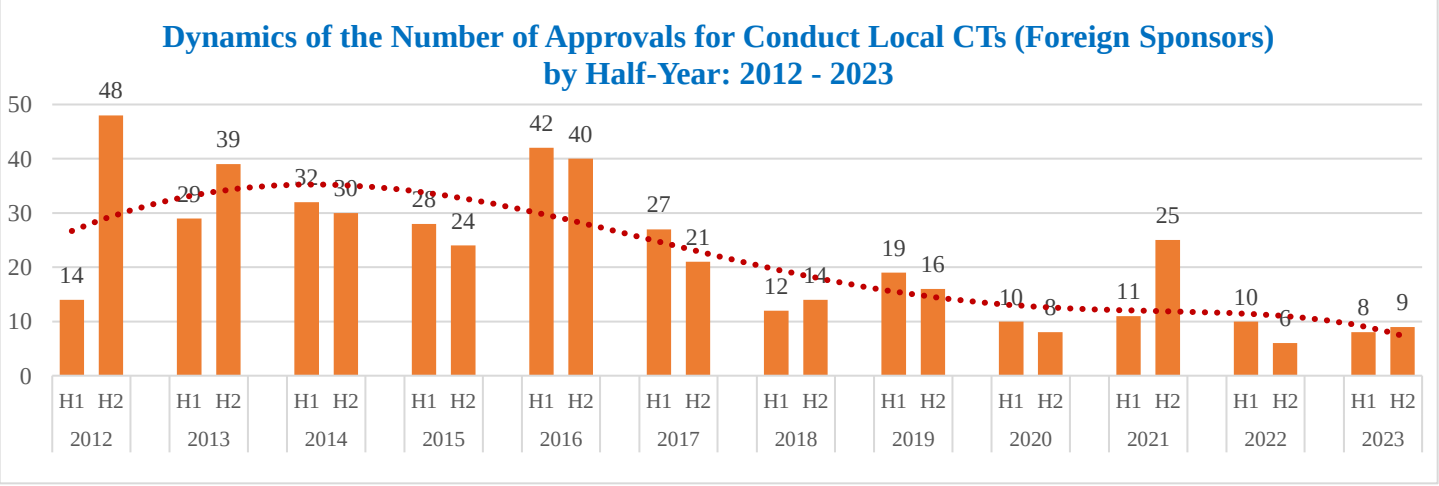
The number of bioequivalence studies of foreign generics has also been increasing in recent years (Diagram 5), however, the growth rate is far behind that of their Russian competitors.

Diagram 5



Data from www.grls.rosminzdrav.ru

Diagram 6



Data from www.grls.rosminzdrav.ru

The dynamics of the number of other local trials of foreign sponsors (Diagram 6) in recent years has been predominantly negative, although smooth without prominent changes in trend. There are still changes within this category of trials; more details on that are provided in the section on therapeutics areas, where, among other things, the geographic distribution of sponsors conducting local trials in Russia is analyzed.

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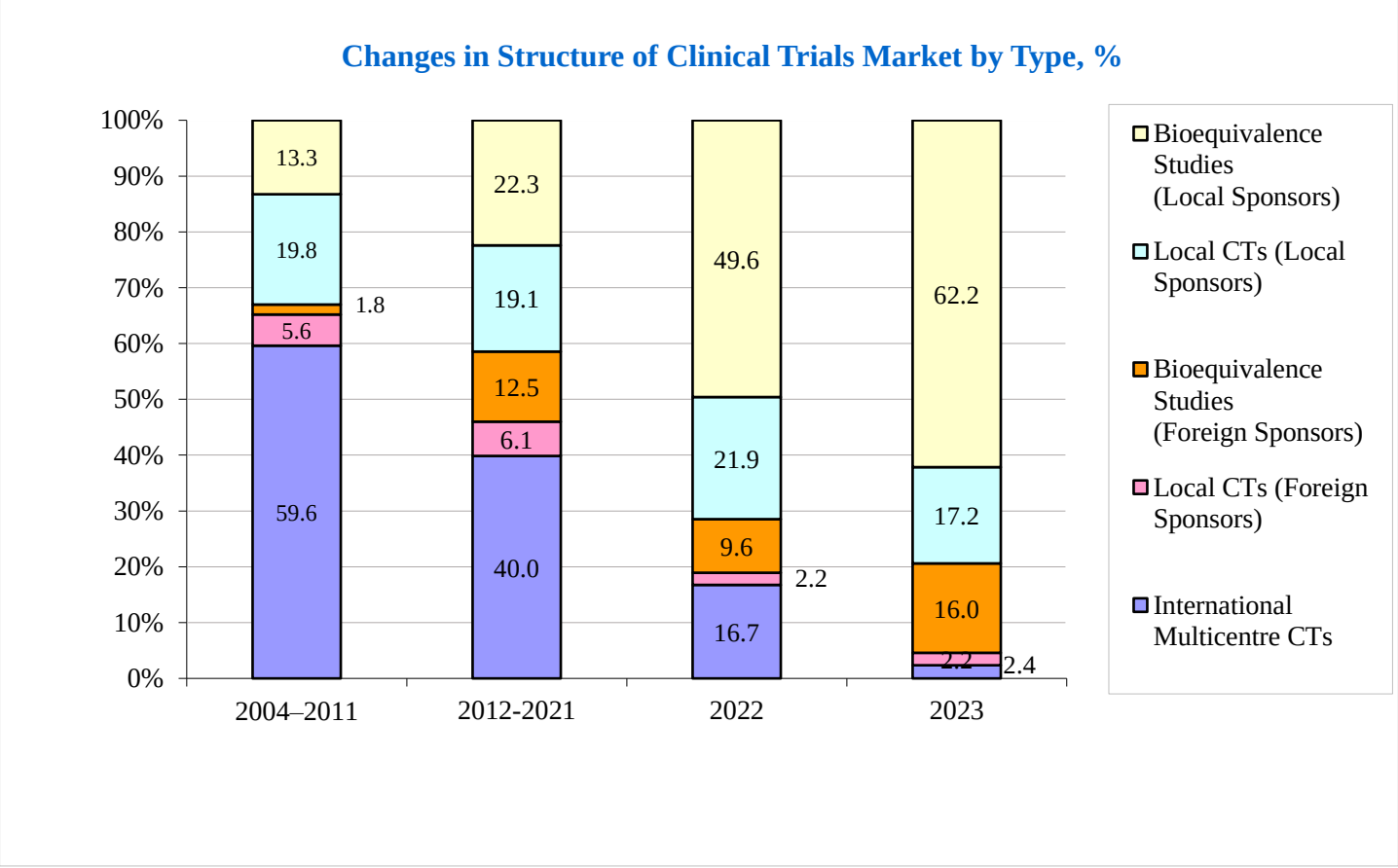
Diagram 7 shows how the share ratio of different types of trials changed from the beginning of observations in 2004 up to 2023. Over these 20 years the market landscape has changed significantly twice: after the adoption of the law “On the Circulation of Medicines” and after the entry of the Russian armed forces into the territory of Ukraine in February 2022.The period before the legislative reform in the diagram corresponds to 2004–2011, after the reform — 2012–2021.Within these periods indicators of each type of trials were relatively stable. The latest period in the market history associated with the geopolitical crisis is presented separately for 2022 and 2023.

Diagram 7



Data from www.grls.rosminzdrav.ru

The main differences between the pre- and post-reform periods are that after the adoption of the law “On the Circulation of Medicines” the number of applications submitted for local trials and bioequivalence studies increased significantly (see also Diagram 1). The number of approvals for IMCTs did not decrease, however due to the increase in the number of approvals for other types the share of IMCTs in the total volume decreased.

The turning point of 2022 is characterized primarily by a sharp drop in the number of approvals for IMCTs, which set an anti-record in 2023 with a share of 2.4%, and a not so sharp, but still a decrease — for local trials of foreign sponsors with a share of 2.2%. The second characteristic feature of this period is the increase in the number of approved bioequivalence studies by Russian sponsors, which are breaking records both in absolute numbers (473 approvals) and in relative terms (62.2%). Only IMCTs in certain years managed to achieve a share

of more than 60%, but this took place before the legislative reform, i.e. more than ten years ago. And this is the first time when the number of more than 400 approvals is recorded for one type of trials.

It is perhaps worth noting, that looking at Diagram 7 our readers may get the impression of a more gradual reduction in the share of IMCTs, than how it actually happened: from 40% in the pre-war period to 16.7% in 2022 and 2.2% in 2023. But if we consider the fact, that the diagram is based on the number of approvals issued, not projects that have actually started, and that many of the 2022 approvals were issued based on applications submitted before the onset of military activities, it becomes clear that in reality the drop was dramatic.

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In conclusion of the first section we would like to talk about the increasing **practice of making backdated entries of approved trials in the Ministry of Health register.** We have been observing how the register of approved trials is maintained since its creation in 2010. Naturally, some entries may sometimes have inaccuracies, typos, and minor errors. As a rule, we do not pay attention to this unless the problem becomes systemic. However, what we observed in 2023 was far from an isolated incident.

According to the "Procedure for maintaining, publishing and posting on the official Internet website of the Ministry of Health register of approved clinical trials of medicinal products for medical use" approved by Order of the Ministry of Health of Russia of 26 August 2010 No. 754n, "register entries shall be made in the register within a period not exceeding one working day from the date of the decision to issue an approval for conducting a clinical trial of a medicinal product for medical use".

In previous years this was generally the case, with rare exceptions. However, in 2023 we began to regularly notice gaps in the numbering of issued approvals: a study would appear in the register with approval number 309, then with number 311, then 312 and so on, but there would be no entry with number 310. It would eventually appear, but later, after two weeks. The delay period varied from three days to three months and averaged 22 days. It should however be noted that there could be a slight delay before we detected some of the backdated trials. Moreover, it was not always easy to detect those: for example, a bioequivalence study of linagliptin by the Russian company Pharmstandard-Leksredstva with approval number 374 appeared in the register in the second half of the year with 27 *June* indicated as the date of issue of the approval, although approvals for trials with numbers 373 and 375 were dated 17 and 18 *July*, respectively. To catch the moment when this trial appeared in the database we had to constantly monitor the seemingly long-closed June.

In total, we counted 35 backdated trials entered in the Ministry of Health register in 2023, 4.6% of the total number of approvals issued during the year, which is quite a lot. The first omissions started to appear in mid-June. In total, there were five approvals entered into the register late in June, ten in July, nine in August, six in September, four in October and one in November.

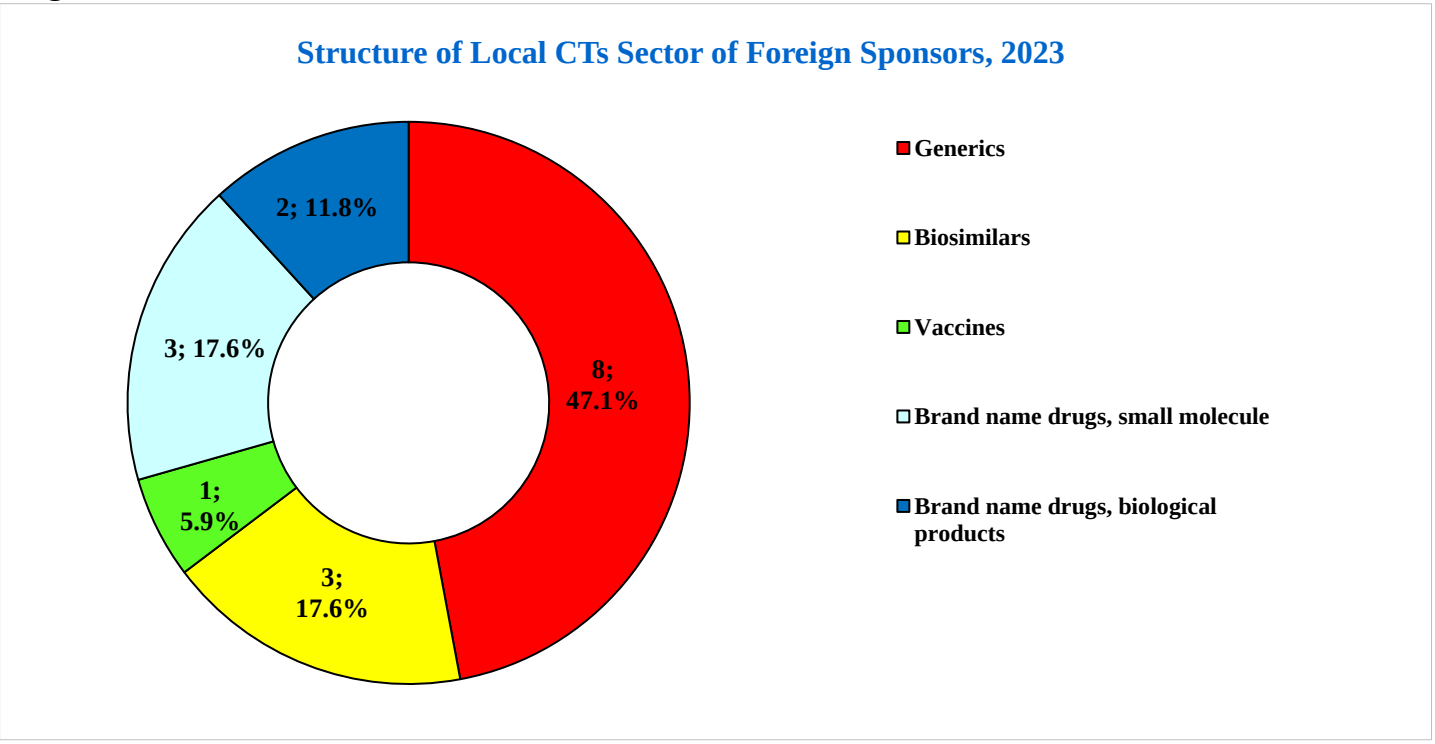
We were not able to identify any dependency on the characteristics of the trials themselves (their type, therapeutic focus, sponsor).

STRUCTURE OF THE MARKET FOR LOCAL TRIALS

Diagrams 8 and 9 show, which types of drugs were tested in local trials of therapeutic efficacy and safety by foreign and Russian sponsors, respectively. When reading these diagrams keep in mind that unless specifically stated, local trials were considered without regard to bioequivalence studies.

Eight out of 17 approvals for local trials by foreign sponsors (Diagram 8) were for generics, three for biosimilars. Another three protocols featured original small molecules, and two included original biological preparations. One approval was issued for a trial of a vaccine to prevent meningococcal infections.

Diagram 8

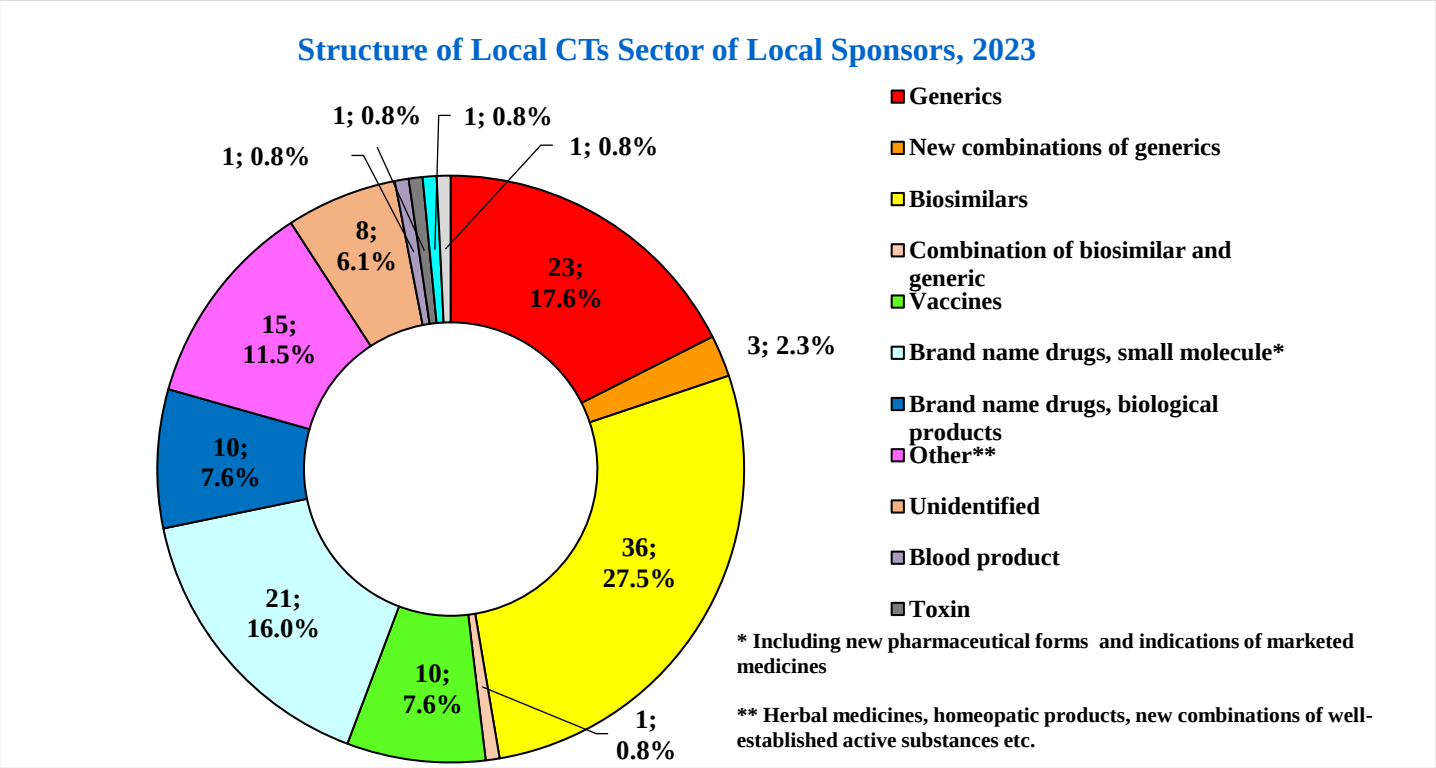


Data from www.grls.rosminzdrav.ru

The first thing that catches the eye when looking at the distribution structure by type of local trials by Russian sponsors in 2023 is an unusually large share of biosimilar trials (Diagram 9). They accounted for 27.5% of approvals for this group of trials (36 out of 131), and this is a serious claim from domestic manufacturers. Previously, the maximum share of biosimilars was recorded in 2018 — 14.6% (19 approvals out of 130). Now this number has almost doubled. Moreover, 64% of all biosimilars (23 out of 36 protocols) were for monoclonal antibodies (three — adalimumab, two for each of bevacizumab, natalizumab, pembrolizumab, rituximab, daratumumab, pertuzumab, omalizumab and denosumab, and one for each of ustekinumab, eculizumab, canakinumab and trastuzumab). Of the remaining 13 protocols three were dealing with biosimilars of romiplostim, three involved various insulins, four — interferons, plus one for each of semaglutide and galsulfase equivalents.

Perhaps it is worth naming companies that have been active in creating biosimilars. These are Generium (seven protocols), Geropharm (six), Mabscale (four). Binnopharm, Grotex, R-Pharm, Pharmasintez-Nord and Firn M had three trials of biosimilars each. The latter specializes mainly in interferons. Two approvals were issued to Biocad (another one of its trials of the biosimilar nivolumab was classified by us as an IMCT, since it is also being conducted in Belarus). Finally, one protocol was registered for each of Promomed and Lekko.

Diagram 9



Data from www.grls.rosminzdrav.ru

Among the remaining local trials 26 approvals (19.9%) featured generics and their combinations, 21 (16.0%) were issued for original small molecules, ten (7.6%) for each of original biological preparations and vaccines that we single out as a separate group. A biosimilar and generic combination, a blood product, a medical gas, a toxin, and a contrast agent were featured in one protocol each. Fifteen trials (11.5%) were classified as “other”, where we include herbal or animal products and homeopathic medicines.

Finally, eight protocols (6.1%) included substances that could not be referred to any group due to the lack of information in open sources. Half of those were claimed by the same sponsor, Promomed Rus. Instead of the names of investigational products the company indicated only their codes, data about which were not publish by it anywhere, so even the therapeutics area declared by the sponsor could not be independently confirmed.

STRUCTURE OF THE CLINICAL TRIALS MARKET BY THERAPEUTICS AREAS

We traditionally begin market analysis by therapeutics area with IMCTs. Their number in Russia has decreased so much that it is possible to talk about each one of them individually.

The largest number of approvals, eight, were issued for IMCTs in the area of oncology. Four of these sponsored by Roche (two), AstraZeneca and Pfizer are protocols involving subjects of previously completed trials who continue therapy with the same investigational product (sponsors call them “extension study”, “rollover study”, “treatment extension”, “continued access”). All four were supposed to include only 12 subjects in total.

Another two approvals were obtained by the American company Agenus for full-scale phase II studies of botensilimab (treatment of advanced melanoma) and a combination of botensilimab and balstilimab (colorectal cancer), which declared its intention to involve 80 and 90 Russian patients in these projects. Another two trials, both for skin melanoma, were organized by the Russian company Biocad and are aimed at studying a fixed combination of the original domestic monoclonal antibodies nurulimab and prolgolimab (684 subjects were enrolled), as well as the biosimilar nivolumab (300 patients). Technically they meet the criteria for being classified as IMCT: the sponsor positions them as international, information about them is posted in ClinicalTrials.gov, and geographical spread of conducting thereof covers several countries. In the case of these two particular protocols, “several” means literally two, and quite closely integrated ones at that: the Russian Federation and the Republic of Belarus.

Table 2

Distribution of International Multicenter CTs by Therapeutic Areas, 2023				
Therapeutic Area	**Number of IMCTs**	**Share (%)**	**The number of planned participants**	**Comment**
Oncology	8	44.4%	1 166	4 – extension studies, 4 – clinical trials with the recruitment of new participants
Oncohaematology	5	27.8%	180	2 – extension studies, 2 – clinical trials with the recruitment of new participants, 1 – the sponsor refused to start in Russia
Ophthalmology	1	5.6%	200	clinical trial with the recruitment of new participants
Gastroenterology	1	5.6%	100	clinical trial with the recruitment of new participants
HIV	1	5.6%	39	extension study
Cosmetology	1	5.6%	10	clinical trial with the recruitment of new participants
Neurology	1	5.6%	4	clinical trial with the recruitment of new participants
TOTAL	18	100.0%	1 699	

Data from www.grls.rosminzdrav.ru

Another five approvals were issued for trials in the related area — oncohematology. For one of them, pediatric phase Ib trial, the application was submitted before February 2022, however regulatory review was delayed and approval was issued only in February 2023. By that time the sponsor (AbbVie) refused to conduct the trial in Russia. Another two are extension studies by Sanofi and Janssen, where it was planned to include one and 24 subjects of previous studies. Finally, two new trials by Ascentage Pharma Group, US, aimed at researching olverembatinib in acute lymphoblastic leukemia and lisaphtoclax in chronic lymphocytic leukemia/lymphoma, were planned to enroll 20 and 125 patients, respectively.

One approval was issued for each of HIV, gastroenterology, neurology, ophthalmology and cosmetology. MSD’s protocol for HIV positive patients was a study designed to include 39 subjects of the company’s previous programs. Remaining protocols involved recruitment of new patients. Dr.Reddy’s Laboratories sponsored a trial

of tegoprazan in patients with erosive gastroesophageal reflux disease. Another Indian sponsor, CuraTeQ Biologics, announced a trial of a ranibizumab biosimilar in macular degeneration of the retina. Ferrer Internacional, Spain, has planned to study edaravone in ALS. And Korean Protox — a trial of a botulinum toxin preparation for wrinkle correction.

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Table 3 shows the distribution by therapeutics area of local trials and bioequivalence studies of generics and biosimilars by foreign sponsors. The total number of these trials increased by 64% over the year (133 approvals in 2023 as against 81 in 2022).

Cardiology and CVD (due to the presence of relevant drugs in recent years, we have combined this area with surgery and intensive care) ranks at the top with 49 trials versus 30 a year earlier. Second place goes to endocrinology: 17 studies vs eight in 2022. Third place was shared by neurology and urology, with nine protocols each. The number of neurological trials was the same as in 2022. And urology has improved; a year earlier there was only one urological protocol.

Table 3

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars) of Foreign Sponsors, 2023			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Cardiology and CVD/Surgery/Intensive care	49	36.8%	2 907
Endocrinology	17	12.8%	852
Neurology	9	6.8%	645
Urology	9	6.8%	559
Infectious Diseases (except HIV/HCV/tuberculosis, COVID-19)	7	5.3%	462
Haematology	6	4.5%	457
Analgesic and NSAIDs	6	4.5%	425
Oncology	6	4.5%	287
Rheumatology	5	3.8%	252
Dermatology	4	3.0%	644
Gastroenterology	3	2.3%	290
Ophthalmology	2	1.5%	280
Pulmonology	1	0.8%	44
Psychiatry	2	1.5%	153
Hepatology	2	1.5%	102
Obstetrics and gynecology	2	1.5%	64
Phlebology	1	0.8%	70
Oncohaematology	1	0.8%	50
HIV	1	0.8%	40
TOTAL	133	100.0%	8583

Data from www.grls.rosminzdrav.ru

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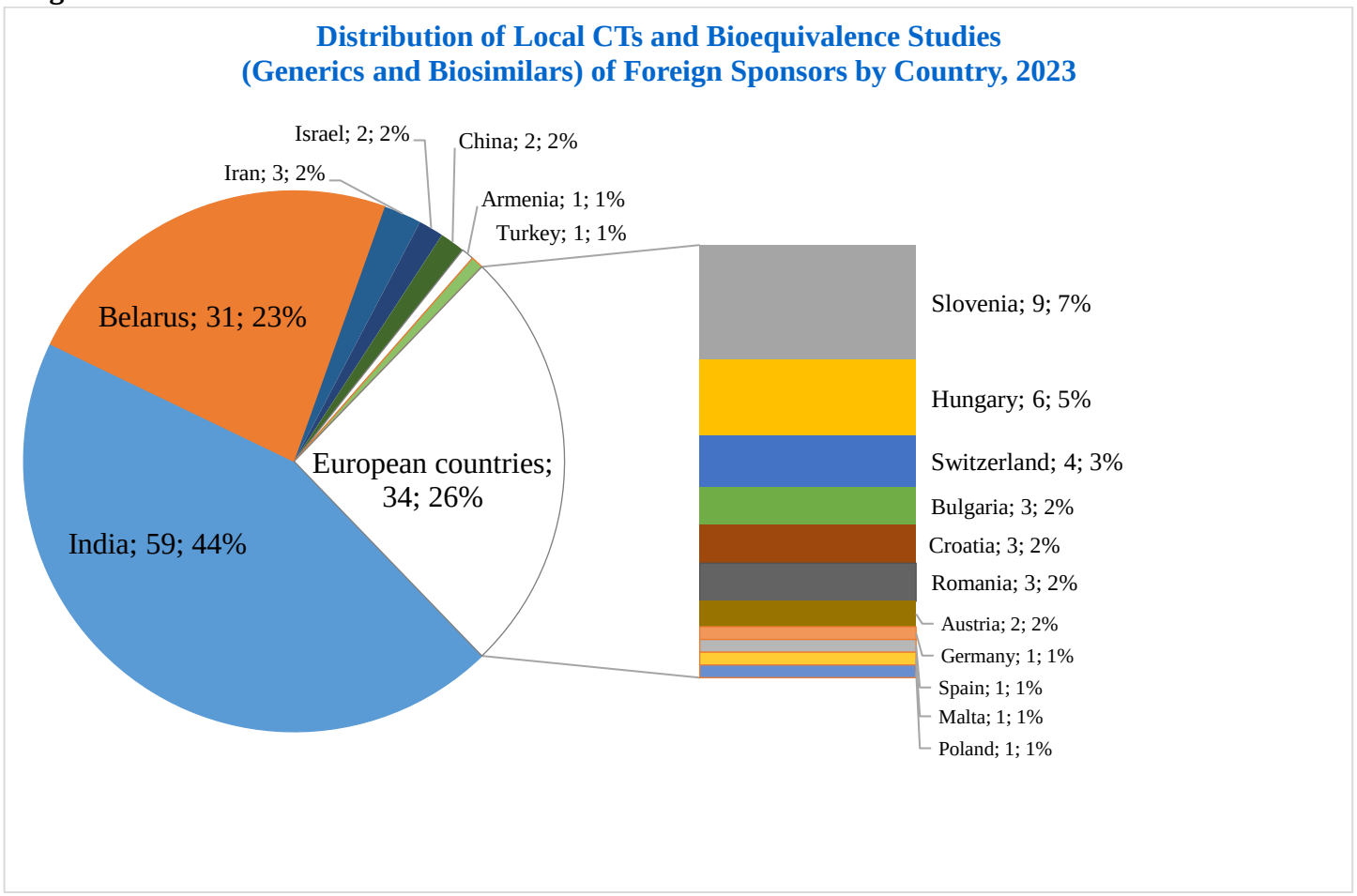
Starting from 2022 we are analyzing the countries of origin of sponsors who want to register their generics and biosimilars in Russia (Diagrams 10 and 11).

Two-thirds of local trials of this kind in 2023 were conducted by manufacturers from India (59 protocols, 44% of the total number) and Belarus (31 trials, 23%). European countries (including those outside the European Union) accounted for a total of 34 approvals (26% of the total).

Diagram 10



Data from www.grls.rosminzdrav.ru

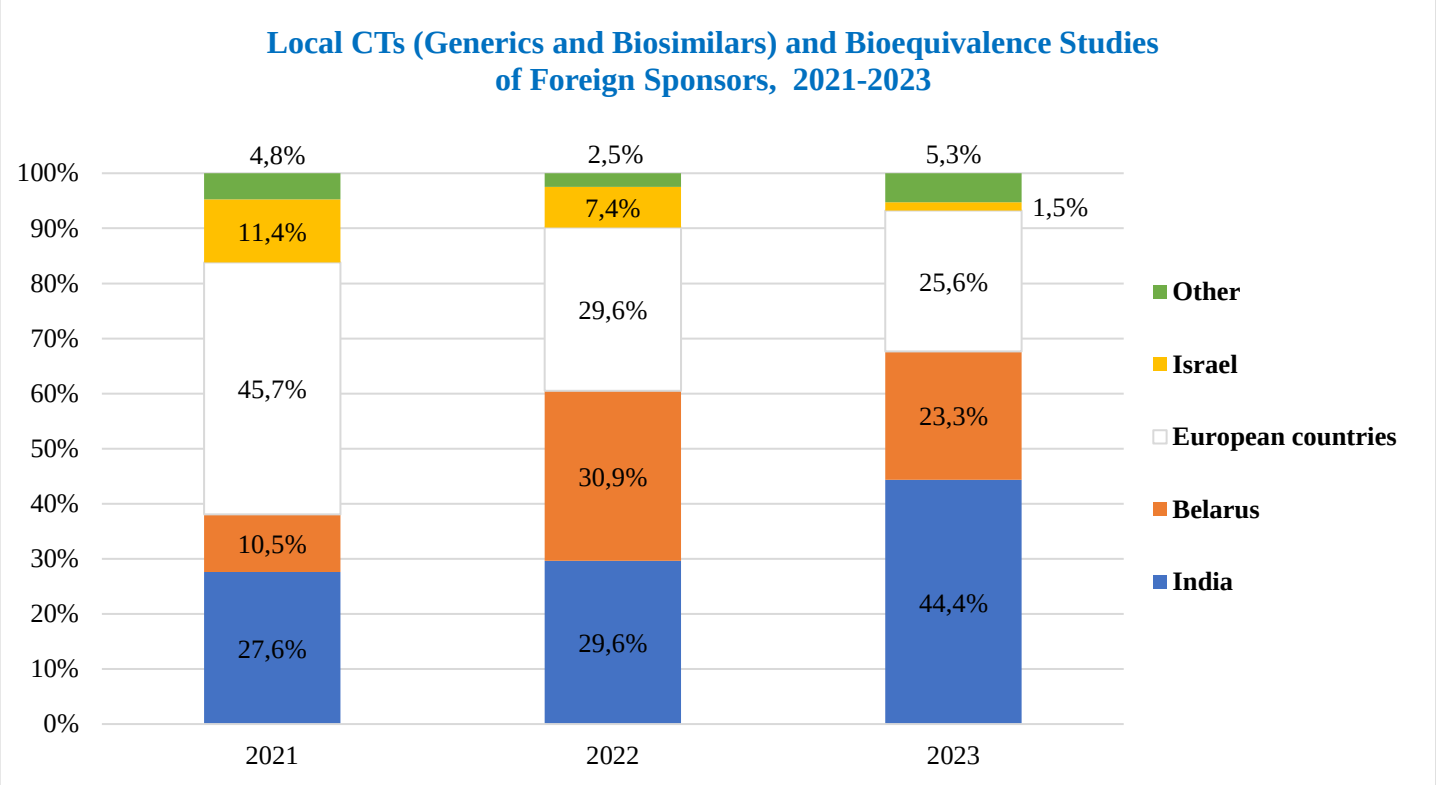
Among European countries the largest number of approvals — nine — were issued to sponsors from Slovenia (five to Sandoz, including Lek, another four to KRKA), six to Hungarian Gedeon Richter, two to each of the Swiss branches of Sandoz and Chemo. Three approvals were issued to Bulgarian manufacturers (two to Alvogen Pharma Trading Europe EOOD, one to Vetprom), three to Croatian Belupo and three to sponsors from Romania (two to Rompharm Company and one to Hiperion). Austrian Sandoz got two approvals. German Stada Arzneimittel, Spanish Galenicum Health, Polish Polpharma and Maltese Combino Pharm obtained one each.

For the first time in three years of observation the list of sponsors of studies of generics and biosimilars included Iran with three approvals, two of which were issued to AryoGen Pharmed and one to Cinnagen Co. Israel (Teva) and China (Tonghua Anrate Biopharmaceutical Co. and Bio-Thera Solutions) have two approvals each, and Turkey (World Medicine Ilac San. Ve Tic.) and Armenia (Russian Altayvitamin commissioned by GIGA FARM from Armenia announced a study of vitamin D) have one each.

Diagram 11 shows how the share of foreign sponsors from different regions of the world in trials of generics changed over three years of observation. It can be observed that with the beginning of the war the share of European companies started to decrease: 45.7% in 2021, 29.6% in 2022 and 25.6% in 2023. The share of Israeli Teva also dropped: 11.4% in 2021, 7.4% in 2022 and only 1.5% in 2023. The share and composition of manufacturers from “other countries” fluctuates: 4.8% in 2021 (sponsors from the USA, South Korea, Turkey), 2.5% in 2022 (USA and South Korea) and 5.3% in 2023 (Iran, China, Armenia, Turkey). Since the beginning of

2022 the share of manufacturers from India has increased (27.6% in 2021, 29.6% in 2022 and 44.4% in 2023), the same can be said about manufacturers from Belarus, although their growth was less consistent, but still pretty noticeable compared to pre-war 2021 (10.5% in 2021, 30.9% in 2022 and 23.3% in 2023).

Diagram 11



Data from www.grls.rosminzdrav.ru

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Table 4 shows the distribution by therapeutics areas for the local trials of domestically produced generics and biosimilars. As compared to 2022, the number of such trials increased by 23.5% (537 approvals vs 435).

Products used in cardiology and CVD/surgery/intensive care still remain the most popular both among the Russian and foreign generic manufacturers — 122 approvals. These are followed by therapeutics areas, such as endocrinology (60 protocols) and oncology (52), infectious diseases, excluding HIV/HCV/TB and Covid-19 (42 approvals), and neurology (40).

The most growth as compared to 2022 was shown by endocrinology (60 protocols vs 35), infectious diseases (42 vs 25), and gastroenterology/coloproctology (32 protocols vs 16 a year earlier). The number of trials of generics and biosimilars against Covid-19 decreased the most: three trials as against 22 a year before.

Table 4

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars), Conducted by Local Sponsors, 2023			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Cardiology and CVD/Surgery/Intensive care	122	22.7%	6 026
Endocrinology	60	11.2%	3 742

Oncology	52	9.7%	5 279
Infectious Diseases (except HIV/HCV/tuberculosis, COVID-19)	42	7.8%	2 744
Neurology	40	7.4%	2 964
Gastroenterology/Coloproctology	32	6.0%	1 978
HIV/HCV/Tuberculosis	29	5.4%	1 639
Rheumatology	21	3.9%	1 980
Analgesic and NSAIDs	16	3.0%	706
Oncohaematology	14	2.6%	1 614
Obstetrics and gynecology	14	2.6%	634
Haematology	13	2.4%	757
Urology	13	2.4%	618
Psychiatry	13	2.4%	480
Immunology	7	1.3%	330
Hepatology	6	1.1%	794
Pulmonology	6	1.1%	651
Dermatology	5	0.9%	1 664
Otorhinolaryngology	5	0.9%	423
Transplantology	4	0.7%	320
Phlebology	4	0.7%	208
Allergology	4	0.7%	129
Covid-19	3	0.6%	444
Parasitology	3	0.6%	88
Surgery	2	0.4%	130
Nephrology	2	0.4%	96
Anesthesiology	1	0.2%	80
Dentistry	1	0.2%	42
Ophthalmology	1	0.2%	36
Not identified	1	0.2%	86
Other	1	0.2%	20
TOTAL	537	100.0%	36 702

Data from www.grls.rosminzdrav.ru

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Table 5 shows the most popular molecules among generic manufacturers in 2023.

Table 5

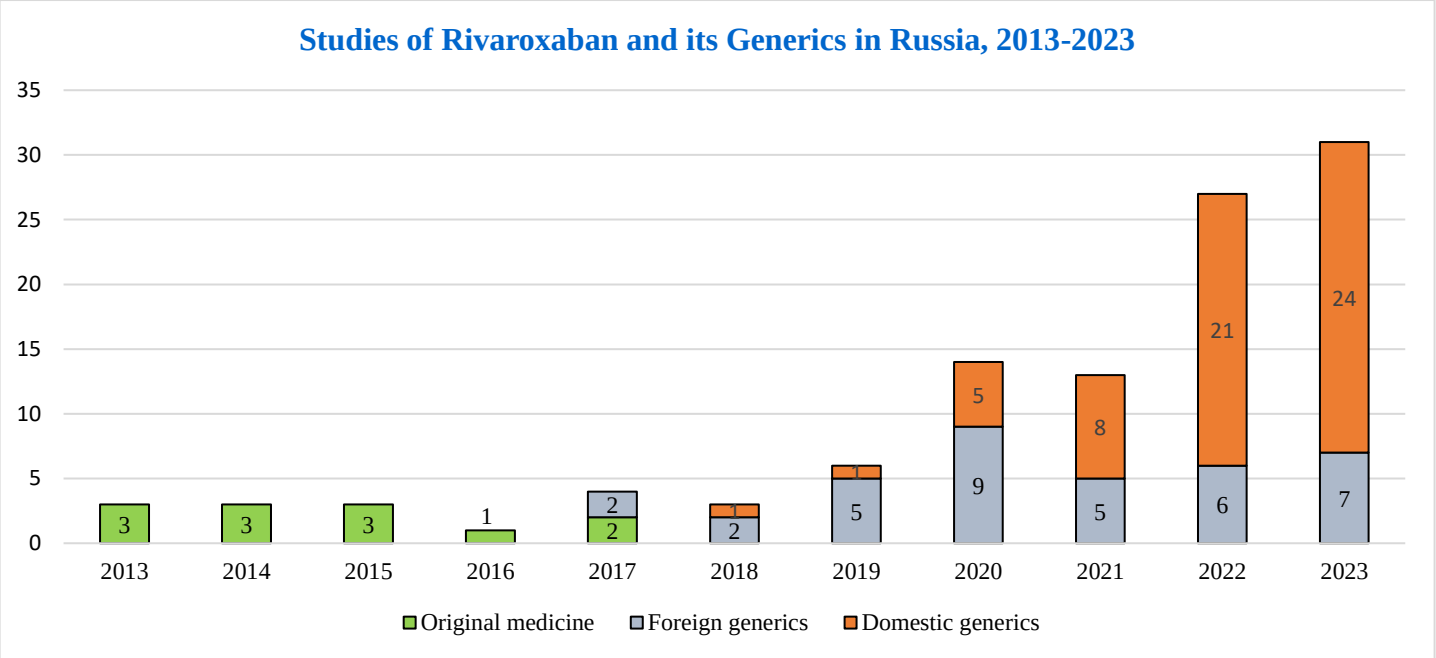
Most Requested INN Used in Clinical Trials of Generics and Biosimilars in 2023				
Substance	**Number of CTs of foreign generics**	**Number of CTs of local generics**	**All clinical trials to a given INN**	**Therapeutic Area**
Rivaroxaban	7	24	31	Cardiology and CVD, surgery, covid-19

Metformin (separately and in fixed combinations)	10	8	18	Endocrinology, perhaps covid-19
Vildagliptin (separately and in fixed combinations)	5	12	17	Endocrinology, perhaps covid-19
Apixaban	11	5	16	Cardiology and CVD, perhaps covid-19
Valsartan (separately and in fixed combinations)	8	6	14	Cardiology and CVD
Indapamide (in fixed combination)	6	6	12	Cardiology and CVD
Dapagliflozin (separately and in fixed combinations)	2	9	11	Endocrinology
Perindopril (separately and in fixed combination)	3	8	11	Cardiology and CVD
Sitagliptin (separately and in fixed combinations)	6	5	11	Endocrinology, perhaps covid-19
Tamsulosin (separately and in fixed combinations)	7	4	11	Urology
Amlodipin (in fixed combinations)	5	5	10	Cardiology and CVD
Ticagrelor	2	7	9	Cardiology and CVD
Amoxicillin (separately and in fixed combinations)	–	8	8	Infectious diseases
Dutasteride (in fixed combination)	7	1	8	Urology
Deferasirox	1	6	7	Haematology
Telmisartan (separately and in fixed combinations)	2	5	7	Cardiology and CVD
Empagliflozin	1	6	7	Endocrinology
Hydrochlorothiazide (in fixed combinations)	1	5	6	Cardiology and CVD
Dolutegravir	1	5	6	HIV
Clavulanic acid (in fixed combinations)	–	6	6	Infectious diseases
Metoprolol	–	6	6	Cardiology and CVD
Sacubitril (in fixed combinations)	4	2	6	Cardiology and CVD
Sofosbuvir (separately and in fixed combinations)	–	6	6	HCV
Axitinib	–	5	5	Oncology
Dabigatran Etexilate	1	4	5	Cardiology and CVD, surgery
Didrogesterone (separately and in fixed combinations)	1	4	5	Gynecology
Paracetamol (separately and in fixed combinations)	–	5	5	Analgesic and NSAIDs, infectious diseases
Tadalafil	–	5	5	Urology, cardiology and CVD
Torasemide (separately and in fixed combinations)	2	3	5	Cardiology and CVD, nephrology

Data from www.grls.rosminzdrav.ru

For the fourth year in a row the antithrombotic drug rivaroxaban leads the ranking: 31 bioequivalence studies in 2023, of which 24 were initiated by domestic sponsors. Most likely, the Covid-19 pandemic served as a booster for such popularity of the drug. However, even after it was over, interest in this drug is still growing. This is primarily thanks to the Russian manufacturers: in 2022 Russian companies initiated 21 out of 27 trials of generics of rivaroxaban, in 2021 — eight out of 13. In 2020 the leadership was ensured by foreign sponsors: they owned nine out of 14 protocols (Diagram 12). At the beginning of April 2024, the State Register of Medicines already lists 18 manufacturers of generic drugs with the INN rivaroxaban, ten of which are domestic. The first four generics were registered in 2022, nine in 2023, five in the first quarter of 2024. And, judging by the ongoing activity in conducting bioequivalence studies, another three dozen manufacturers would also like to be added to this list.

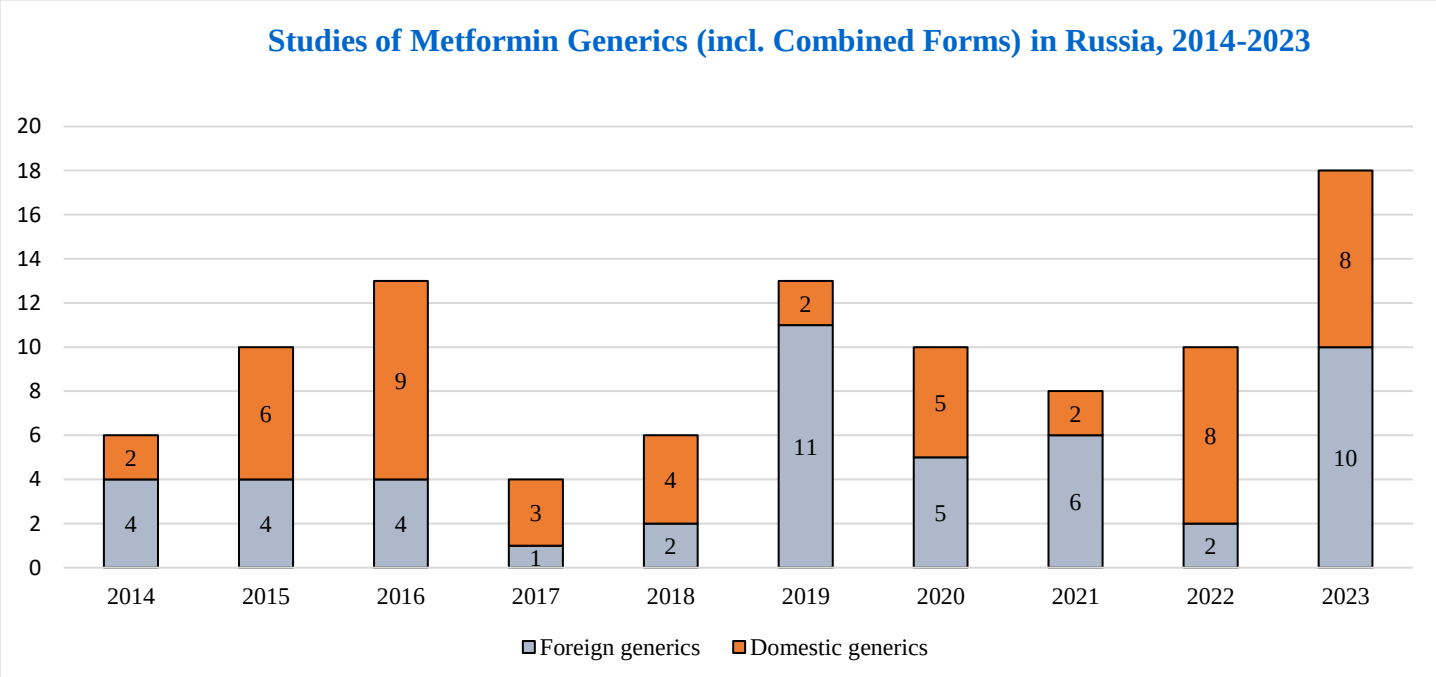
Diagram 12



Data from www.grls.rosminzdrav.ru

Second place in the 2023 ranking was taken by metformin, a hypoglycemic drug that has been in vogue for a long time now. The drug has consistently appeared on the list of the most popular molecules since the very first years of our observations and continues to remain in steady demand among both Russian and foreign manufacturers of generic drugs (Diagram 13). The pandemic also supported interest in the drug, since metformin was used both in therapy for Covid-19 and to reduce the likelihood of developing the post-Covid-19 syndrome. As of 2024 marketing authorizations for mono- and combination drugs with this INN are held by almost fifty manufacturers, more than half of which are Russian.

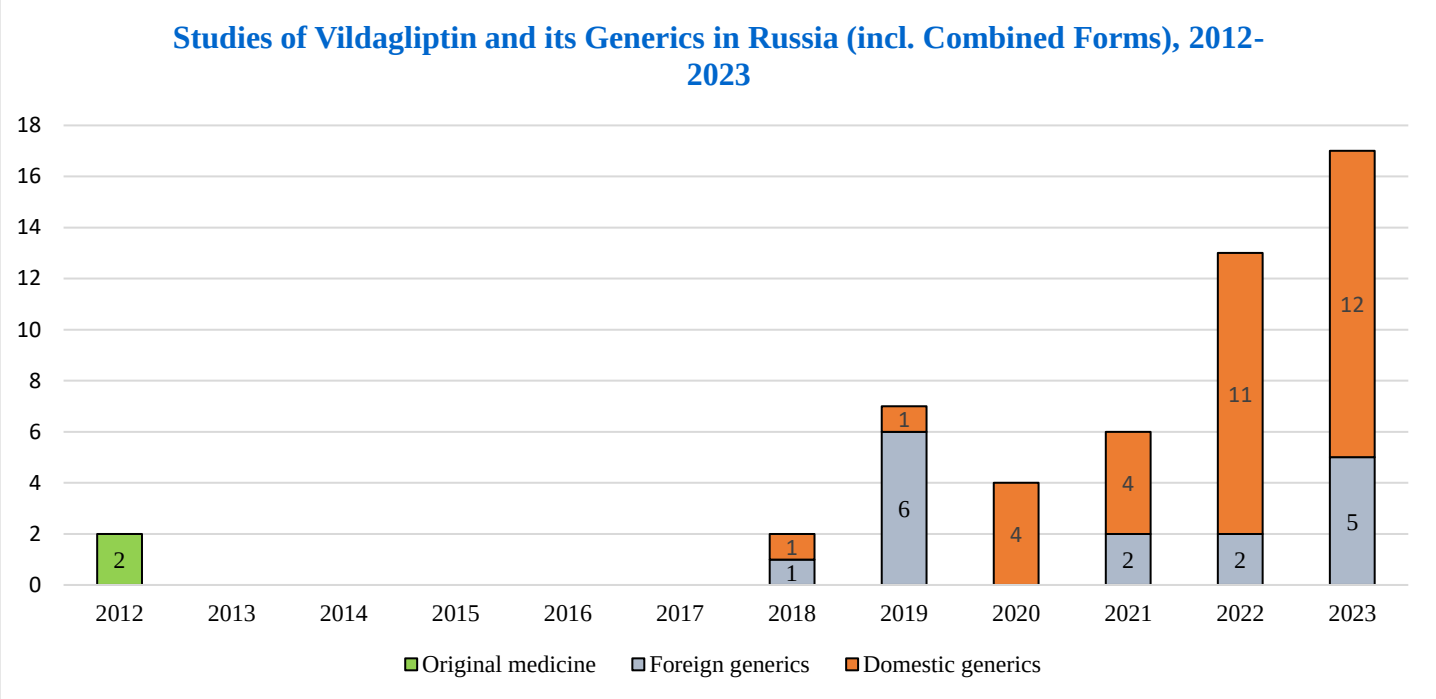
Diagram 13



Data from www.grls.rosminzdrav.ru

In third place is another hypoglycemic substance, vildagliptin, used both independently and in combination with metformin. Like its older brother, the drug was used with some success during the pandemic. According to the register at the beginning of April 2024 marketing authorizations for generics of vildagliptin are held by three foreign and 12 Russian companies. And, judging by the growing number of bioequivalence studies, their number will only increase. Diagram 14 shows how the number of trials of generics of vildagliptin has been growing since 2018.

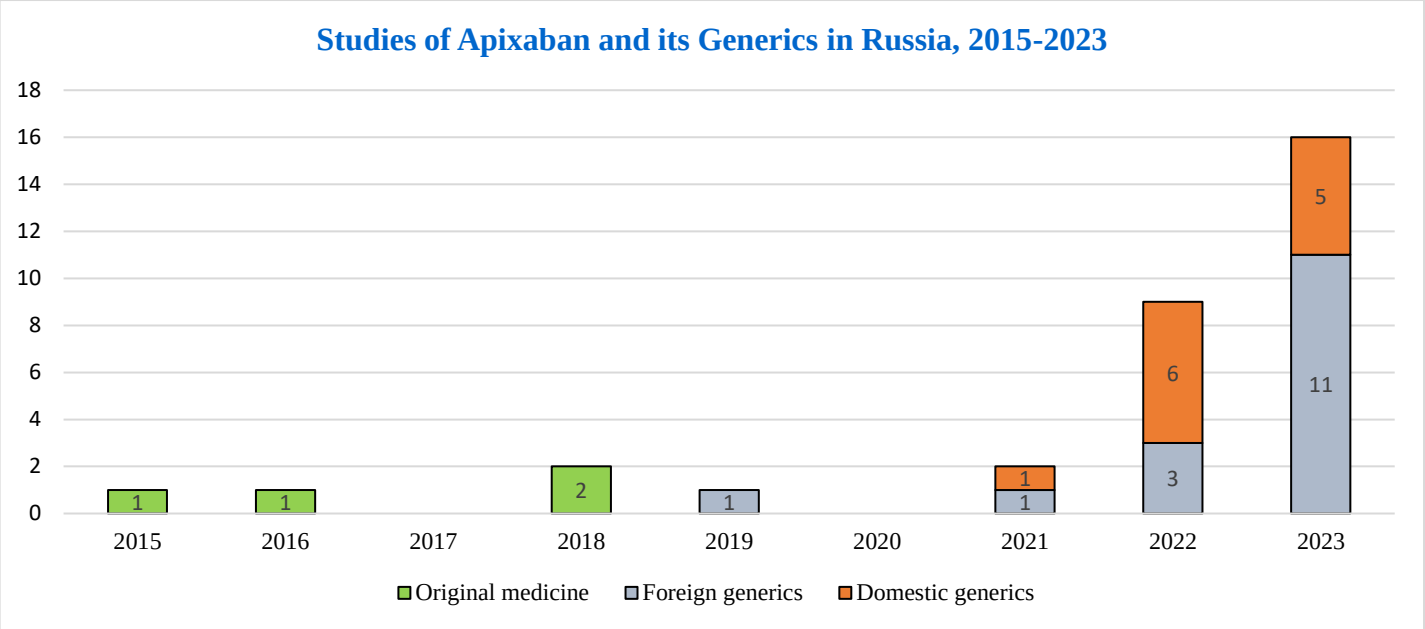
Diagram 14



Data from www.grls.rosminzdrav.ru

Finally, the last drug, which we would also like to briefly dwell upon when commenting on the list of the most popular drugs for copying, is the anticoagulant apixaban, a blockbuster created by the alliance of BMS and Pfizer. The same way as with the top three drugs, the well-deserved interest in apixaban was fueled by the Covid-19 pandemic. According to the PharmaTrend study (IQVIA Rx Awards), Pfizer's Eliquis (apixaban) was recognized as the best prescription brand in Russia in 2020 demonstrating the largest increase in sales in absolute figures among prescription drugs. As can be seen from the register of registered medicines of the Ministry of Health, five generics of apixaban were registered in Russia in 2023 (three from Russian manufacturers, two from foreign manufacturers). Another marketing authorization for a generic of apixaban was issued to a Russian manufacturer at the end of March of this year. The patent for the original drug has not yet expired, therefore copies, even if registered, cannot yet be sold. However, as you might guess from Diagram 15, the number of those who want to enter the market is only increasing.

Diagram 15



Data from www.grls.rosminzdrav.ru

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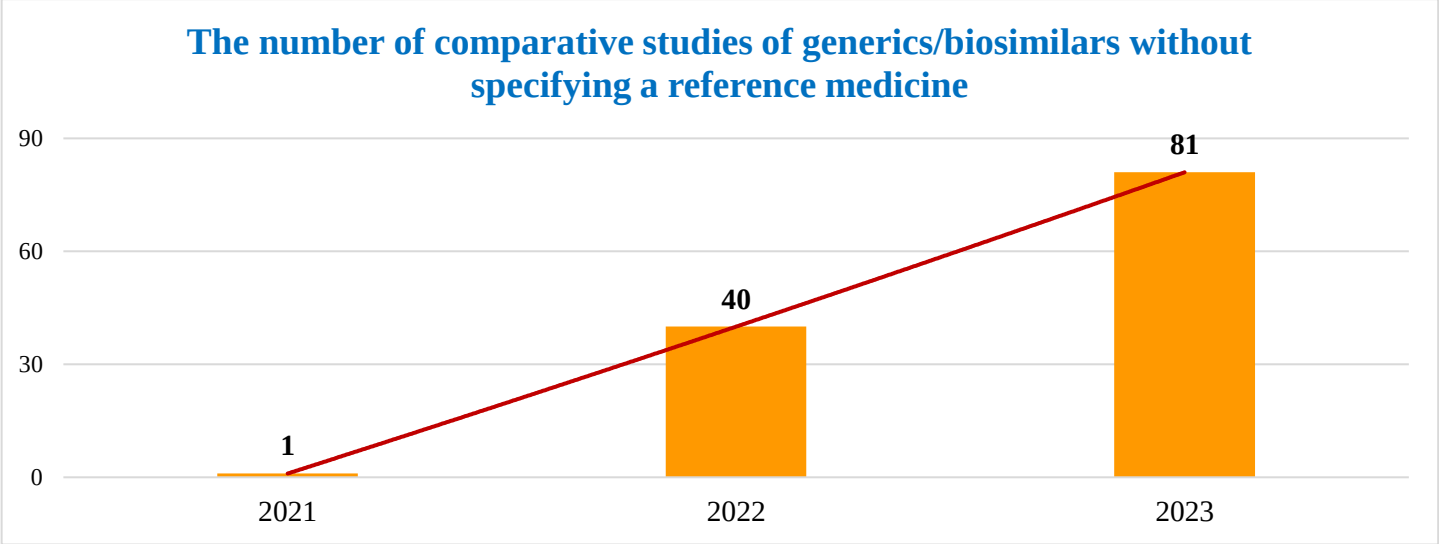
Speaking of generics, we would also like to talk about another problem that we encountered when analyzing data for 2023, specifically — the spread of the tendency among certain generic manufacturers **to not specify the reference drug in the title of the protocol for a comparative study of a generic**. Usually, this is the case for bioequivalence studies. However, there have also been isolated cases of local trials of therapeutic efficacy and safety, the purpose of which was clearly to register a generic based on its comparison with the original drug. Names of such protocols appear as follows: "comparative study of pharmacokinetics of drug A *(name of the drug)* in comparison with the reference drug *(in this exact generalized formulation, without the name, indication of the manufacturer or other identifying features)*" or even "comparative study of bioequivalence of drug A (*name of the drug*) with the participation of healthy volunteers *(that's about it, no mention of the reference drug)"*. That is, the comparison drug is either not mentioned at all, or it is indicated that there is one per se, but the sponsor does not consider it necessary to specify, which one it is.

On the one hand, we are not aware of any requirements that would strictly regulate the name of study protocols. On the other hand, there is clearly a problem with logic here. It is illogical and, generally, not entirely correct to talk about the equivalent/equivalence of anything (and in our case, about the "biological equivalence" of one drug to another) without naming the actual reference substance. Such a trick on the part of the manufacturer of a generic drug can hardly be called good practice. Ultimately, behind it there is an intention to hide information. From whom? From "competitors" represented by the manufacturer of the original drug or other generic manufacturers? From the end consumer? Considering the rather flawed nature of the Russian register, which can provide very little significant information as it is (and one can only learn about the comparator from the name of the protocol), the spread of such a practice appears to be clearly against the public interests.

We first noticed this practice back in 2022, however at that time, either due to other priorities, or because it was not so obvious and seemed like an isolated even, we did not give it due attention. Unfortunately, the 2023 results show that the practice has exploded and is threatening to gain a foothold. Having retrospectively reviewed the register of issued approvals for the past three years we present our findings to the reader. The dynamics over the past three years is presented in Diagram 16.

Diagram 16



Data from www.grls.rosminzdrav.ru

In 2021 there was only one protocol without specifying a reference drug (Table 6). Its sponsor is the Moscow Endocrine Plant, which conducted a "study of bioequivalence of the drug MZ-04/2020 and the comparator"[3]. We were not able to find out from open sources, what exactly the substance MZ-04/2020 is and what the comparator drug was.

Table 6

Company	The number of comparative studies of generics/biosimilars without specifying a reference medicine			
	Total	2021	2022	2023
Promomed Rus	**56**	–	31	25
Pharmasyntez	**28**	–	1	27
Pharmstandard-Leksredstva	**12**	–	3	9
Tula Pharmaceutical Factory	**4**	–	–	4
PIQ-Pharma	**3**	–	2	1
Advanced Pharma	**2**	–	–	2
Concern MIR	**2**	–	–	2
PSK Pharma	**2**	–	–	2
AryoGen Pharmed, Iran	**2**	–	–	2
Emcure Pharmaceuticals Limited, India	**2**	–	1	1
Protek	**1**	–	–	1
Pharmproject	**1**	–	–	1
ChemRar Pharma	**1**	–	–	1
Aizant Drug Research Solutions Pvt. Ltd. (Basis-Metigreens)	**1**	–	–	1
Inteltreyd	**1**	–	–	1
Vetprom, Bulgaria	**1**	–	–	1
Valenta Pharm	**1**	–	1	–
Biokhimik	**1**	–	1	–
Moscow Endocrine Plant	**1**	1	–	–

Data from www.grls.rosminzdrav.ru

[3] RCT No. 439 dated 10 August 2021, protocol No. MZ-BE-04/21 "Open randomized cross-over two-period study of bioequivalence of the drug MZ-04/2020 and the comparator drug in healthy volunteers after a single dose of each drug on an empty stomach".

In 2022 we have counted as many as 40 such protocols. Chronologically, the first one was PIQ-PHARMA, which in March 2022 obtained an approval to compare Covasis® with Vasobral® and shortly after, in April, two approvals to compare Elkar® (levocarnitine) "with the reference drug"[4] without further specification. Then other sponsors got in on the act, Promomed Rus stood out the most. In 2022 it obtained 52 approvals for new trials in total, of which 44 involved comparison with a reference drug, and in just 13 of them the drug was actually specified. Thus, out of 40 protocols in 2022 without specifying a reference drug 31 belong to Promomed Rus (Table 6).

It can be easily observed through the Ministry of Health database, how the new practice has been consolidating in the company: before the end of June 2022 all protocols with reference drugs contain their names, from the beginning of July until 20 August both variants can be found (five protocols with specification of the reference and seven without), after 20 August not a single Promomed Rus protocol with reference drugs contains their names. Here is one example from this period: "Open randomized cross-over comparative study of pharmacokinetics and bioequivalence of the drug XTBC01801 (PROMOMED RUS LLC, Russia) with the participation of healthy volunteers". Biological equivalent of what drug exactly XTBC01801 is supposed to be remains unknown, and information about XTBC01801 cannot be found in open sources either.

Other companies that have protocols without mentioning a reference drug in 2022 couldn't reach Promomed Rus in scope:

— Pharmstandard-Leksredstva obtained six approvals for trials involving assessment of the drug equivalence during the year, three of them named the reference drug and three did not,

— PIQ-PHARMA had only three trials of this specific kind during the year, two of them did not contain a reference,

— Emcure Pharmaceuticals Ltd. obtained one approval, comparator drug was not named in the protocol,

— Pharmasyntez obtained 35 approvals in total in 2022, of which 32 were supposed to name the comparator and in 31 of them it was actually named.

Pharmasyntez obtained its only approval for a bioequivalence study without a reference in 2022 at the end of November. And in 2023 it took this practice to the assembly line: out of 38 protocols where it would be logical to specify a comparator, it wasn't named in 27. Promomed Rus remained true to itself: out of 25 protocols in 2023 that require speciation of a reference this sponsor does not have a single protocol that specifies the reference. Pharmstandard-Leksredstva, half of the bioequivalence studies of which in 2022 did not specify the reference drug, began to do this more often: in 2023 there were nine protocols like that out of 13. In 2023 PIQ-PHARMA obtained only two approvals for bioequivalence studies, one of them specifies the reference, the other does not; Emcure Pharmaceuticals had three studies, one of them is without the reference, i.e., in these companies the practice of omitting the comparator drug, on the one hand, is present, but on the other hand, it has not become the baseline.

It is alarming that the list of sponsors that do not specify reference drugs has expanded. In 2023 it was supplemented by PSK Pharma (two protocols without a reference out of five where it should be specified, i.e. 40%), Tula Pharmaceutical Factory (four out of 12, that's 33%), ChemRar Pharma (one out of three, also 33%), Concern MIR (two out of eight, 25%), Advance Pharmaceuticals (two out of ten, 20%), Pharmproject (one out of ten, 10%), Protek (one out of 11, that's 9.1%), as well as Aizant Drug Research Solutions Private Limited,

[4] RCT No. 289 dated 20 April 2022, protocol No. LEV-BE-PEL-2021 "Open randomized two-stage cross-over study of comparative pharmacokinetics and bioequivalence of the drug Elkar®, effervescent granules for the preparation of solution for oral administration, 1000 mg (PIQ-PHARMA LLC, Russia) in comparison with the reference drug, after a single oral dose of 2 g on an empty stomach in adult healthy male and female volunteers".
RCT No. 296 dated 21 April 2022, protocol No. LEV-BE-SOL-2021 "Open randomized two-stage cross-over study of comparative pharmacokinetics (bioequivalence) of the drug Elkar® (levocarnitine), oral solution 300 mg/ml (PIQ-PHARMA LLC, Russia) in comparison with the reference drug in two groups of healthy volunteers after a single oral dose of 2 g on an empty stomach".

Inteltrade and Vetprom (one out of one for all three companies) and ArioGen Pharmed (two out of two). By the end of 2024 we will be able to assess whether the practice of concealing references will take hold in these companies and whether the list of such companies will expand. But, of course, with much greater pleasure we would observe the reverse processes.

To complete the picture, it should be added that most sponsors still specify reference drugs in the names of those protocols where this is logically necessary. Thus, in 2023 Renewal has got 45 approvals for trials that require specification of a reference drug, Amedart — 34, R-Pharm — 27, Binnopharm Group — 26, and in all their protocols, without exception, the comparator was specified, the same goes for three dozen other sponsors with fewer approvals.

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Table 7 shows the distribution by therapeutics area of local trials of original medications by foreign sponsors. The total number remained at the 2022 level, six approvals, one in each therapeutics area. British AstraZeneca tested the monoclonal antibody AZD3152 as a means of pre-exposure prophylaxis for Covid-19, a combination of ceralasertib and durvalumab in patients with lung cancer, as well as budesonide with albuterol sulfate for the prevention of bronchospasm. Belgian Besins Healthcare studied its estradiol in estrogen deficiency, Serum Institute of India — vaccine for the prevention of meningococcal infections, and Indian Wockhardt Bio — levonadifloxacin in acute bacterial infection of skin and soft tissues.

Table 7

Distribution of Local CTs of Brand Name Drugs of Foreign Sponsors, 2023			
Терапевтическая область	**Число КИ**	**Планируемое число участников**	**Страна разработчика**
Covid-19	1	130	Great Britain
Oncology	1	55	Great Britain
Pulmonology	1	120	Great Britain
Gynecology	1	332	Belgium
Infectious diseases (vaccine for the prevention of meningococcal infections)	1	80	India
Surgery	1	380	Switzerland
TOTAL	6	1 097	

Data from www.grls.rosminzdrav.ru

Table 8 shows similar distribution for Russian developers of original drugs. Here, the total number of trial approvals is 67, 29% less than a year earlier with 94 approvals.

Table 8

Distribution of Local CTs of Brand Name Drugs (Including Biological Products)			
Therapeutic Area	**Number of CTs**	**Share (%)**	**Number of planned participants**
Infectious Diseases (except HIV/HCV/tuberculosis, COVID-19)	8	11.9%	2 040
Oncology	8	11.9%	975
Neurology	7	10.4%	378
Covid-19	5	7.5%	820

Cardiology and CVD	4	6.0%	780
Pulmonology	4	6.0%	705
Gastroenterology	4	6.0%	389
Rheumatology	3	4.5%	1 212
Urology	3	4.5%	1 012
Phthisiology	3	4.5%	820
Psychiatry	3	4.5%	648
Haematology	3	4.5%	149
Intensive Care/Anesthesiology	3	4.5%	134
Dermatology	2	3.0%	492
Otorhinolaryngology	2	3.0%	440
Endocrinology	2	3.0%	110
Nephrology	1	1.5%	210
Not identified	1	1.5%	94
Oncohaematology	1	1.5%	45
TOTAL	67	100.0%	11 453

Data from www.grls.rosminzdrav.ru

First place in this distribution in 2020–2022 was occupied by Covid-19, and in earlier years by infectious diseases. At the end of 2023 infectious diseases (excluding HIV/HHV/TB and Covid-19) regained first place sharing it with oncology (eight approvals each). Before the pandemic there always remained a significant gap between infectious diseases and oncology, which often took second place.

Of the eight trials of agents to combat infectious diseases four were announced by Gamaleya National Center of Epidemiology and Microbiology (vaccines for the prevention of influenza and rotavirus infection, a drug based on monoclonal antibodies for the treatment of influenza and a combination of sodium polyprenyl phosphate/phytosterol). The remaining four trials were initiated by: Smorodintsev Research Institute of Influenza (vector vaccine for the prevention of respiratory syncytial viral infection in the elderly), Saint Petersburg Scientific Research Institute of Vaccines and Serums (vaccine for the prevention of pneumococcal infections), Medsintez plant (Triazavirin® for ARVI in children) and Valenta Pharmaceuticals (Ingavirin® for ARVI in children).

Of the eight approvals for trials of oncology drugs shown in Table 8, Biocad obtained two: BCD-245, an anti-GD2 monoclonal antibody being studied in combination with chemotherapy in relapsed/refractory neuroblastoma (Phase II-III) and BCD-236, a Phase I development being studied in "subjects with malignancies". Newvac is conducting a phase III study of Quisinostat, a product originally developed by Janssen Pharmaceuticals, in combination with other chemotherapy for ovarian cancer, peritoneal carcinoma, or fallopian tube carcinoma. Life Sciences OHFC obtained an approval to study the contrast agent indocyanine green in the detection of sentinel lymph nodes. The Federal State Budgetary Institution Russian Scientific Center for X-Ray Radiology of the Russian Ministry of Health is studying a peptide inhibitor of RAS-GTPase for the treatment of patients diagnosed with gastrointestinal tumors.

Promomed Rus LLC announced for study in Phase I something unidentifiable under the code LOFB07801. It is planned to evaluate pharmacokinetic profile, safety, tolerability, immunogenicity *(biological drug?)* and provide a preliminary assessment of the effectiveness of the drug LOFB07801 in patients with malignant neoplasms of various locations.

Siberian State Medical University conducted a Phase I study of a drug called Polistan (no INN) in healthy volunteers. It is stated on the university's website that this is "a new injectable drug to increase the effectiveness and reduce the toxic effects of chemotherapy for solid tumors". We couldn't find any other details that would give us an understanding of what exactly is being studied here.

Finally, Saratov State Medical University named after V. I. Razumovsky conducted a “Pilot open-label phase I clinical trial to evaluate the safety of a single use of tablets based on the extract of *Gratiola officinalis* in patients with stage III–IV genitourinary cancer”. As it is said on Russian Wikipedia, *Gratiola officinalis* is “a perennial plant 15–60 cm high, which due to its poisonous properties is used in folk medicine”. Apparently, at stage III-IV cancer it won’t hurt either.

This detailed transcript is intended to give readers an idea of how diverse and creative domestic developers are in their approach to such a complex and knowledge-intensive therapeutics area as oncology.

PARTICIPATION OF MEDICAL ORGANIZATIONS AND PRINCIPAL INVESTIGATORS IN BIOEQUIVALENCE STUDIES

Table 9 lists medical organizations that were most often involved in bioequivalence studies last year. Majority of them, 16 out of 20, appeared in a similar ranking at the end of 2022.

Table 9

Top-20 medical organizations on the activity of participation in bioequivalence studies (approvals issued in 2023)					
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 2022**
1	Clinical Hospital No. 9, Yaroslavl	64	51	13	20 (10–11)
2	Clinical Hospital No. 3, Yaroslavl	52	48	4	55 (1)
3	Yaroslavl Regional Clinical Narcological Hospital, Yaroslavl	43	33	10	32 (3–4)
4	Ligand Research, Moscow	36	11	25	18 (13–14)
5	Rostov Central District Hospital, Yaroslavl region, Rostov	31	30	1	30 (5)
6	Cardiology Dispensary, Ivanovo	30	21	9	32 (3–4)
7–8	Clinical Hospital No. 2, Yaroslavl	26	21	5	20 (10–11)
7–8	National Scientific Center for Research and Pharmacovigilance, Saransk	26	25	1	n/a
9–11	X7 Clinical Research, St. Petersburg	23	9	14	22 (7)
9–11	North-West Public Health Research Center, St. Petersburg	23	22	1	4 (21)
9–11	Tomsk National Research Medical Center of the Russian Academy of Sciences, Tomsk	23	19	4	8 (15–16)
12–13	Research Lab, Moscow	22	22	–	n/a
12–13	Certa Clinic, Moscow	22	16	6	5 (18–20)
14	Miramed, Maykop	21	21	–	n/a
15–16	Bessalar clinic, Moscow	20	18	2	21 (8–9)
15–16	N.P. Bekhtereva Institute of Human Brain of the Russian Academy of Sciences, Saint Petersburg	20	20	–	19 (12)
17	Eco-Safety Research Center, St. Petersburg	19	17	2	38 (2)
18	I. M. Sechenov First Moscow State Medical University, Russian Ministry of Health, Moscow	18	12	6	21 (8–9)
19	Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency, Moscow	17	8	9	18 (13–14)
20	Professorial Clinic, Perm	14	10	4	5 (18–20)

Data from www.grls.rosminzdrav.ru

Of organizations that were not included in the top 20 of the previous year, the National Scientific Center for Research and Pharmacovigilance, which changed its registration from Kazan to Saransk during the year, was the most notable this time. It shared 7th and 8th places with Clinical Hospital No. 2, Yaroslavl (26 protocols each). Other three newcomers were less active: (1) North-West Public Health Research Center with 23 trials that shared places 9–11 with the St. Petersburg clinic X7 Clinical Research and Tomsk National Research Medical Center of the Russian Academy of Sciences, (2) Miramed clinic, Adygea, placed 14th with 21 protocols and (3) Research Lab, Moscow, with 22 new trials that shared lines 12–13 of the rating with Serta Clinic, also Moscow.

Among the leaders, the most growth in activity as compared to 2022 was shown by the Yaroslavl Regional Clinical Hospital No. 9 (64 trials vs 20 a year earlier), the St. Petersburg North-West Public Health Research Center (23 protocols vs four) and the Moscow Ligand Research (36 vs 18 in 2022).

Eco-Safety Research Center, St. Petersburg, remained in the top twenty of the most active organizations, although noticeably dropped in the ranking (from second place to 17th with 19 protocols vs 38 a year earlier). Remaining clinics, activity of which decreased compared to 2022, lost no more than three protocols.

One can also note traditionally high results of clinics in Yaroslavl region. At the end of 2023 six of them were listed in the top twenty. It is not surprising that the 2023 ranking of principal investigators (Table 10) included four representatives of Yaroslavl, three of which "made the podium".

Table 10

Top-10 Principal Investigators by Number of New Trials in 2023 (PIs with the number of new projects of 25 or more are presented)					
Reference number	**Principal investigator's full name**	**Number of CTs in 2023**	**Total number of CTs (as of March 2024)**	**Specialization**	**City**
1	Anna Vladimirovna Snegireva	**66**	103	clinical pharmacology, therapy	Yaroslavl
2	Sergey Mikhailovich Noskov	**55**	445	cardiology, neurology, profpathology, rheumatology, clinical pharmacology, therapy	Yaroslavl
3	Aleksandr Yurievich Malygin	**41**	235	anesthesiology-intensive care medicine, clinical pharmacology, neurology, ophthalmology, pulmonology, rheumatology	Yaroslavl
4	Irina Sergeevna Rodyukova	**33**	110	cardiology, clinical pharmacology, therapy	Moscow
5	Elena Anatolyevna Smolyarchuk	**32**	244	obstetrics and gynecology, general medical practice (family medicine), rheumatology, clinical pharmacology, therapy, ophthalmology	Moscow
6	Ivan Surenovich Sardanyan	**30**	201	clinical pharmacology, oncology, healthcare organization and public health, pediatrics, pulmonology, rheumatology, therapy	St. Petersburg
7	Evgeny Valerievich Baskakov	**29**	155	clinical pharmacology, health organization and public health, psychiatry, psychiatry-narcology	Yaroslavl
8	Olga Anatolyevna Belova	**28**	128	cardiology, therapy, healthcare organization and public health	Ivanovo
9	Elena Sergeevna Shalukho	**26**	68	occupational pathology, therapy	St. Petersburg
10	Evgeniya Valeryevna Tavlueva	**25**	33	cardiology	Moscow

Data from www.grls.rosminzdrav.ru

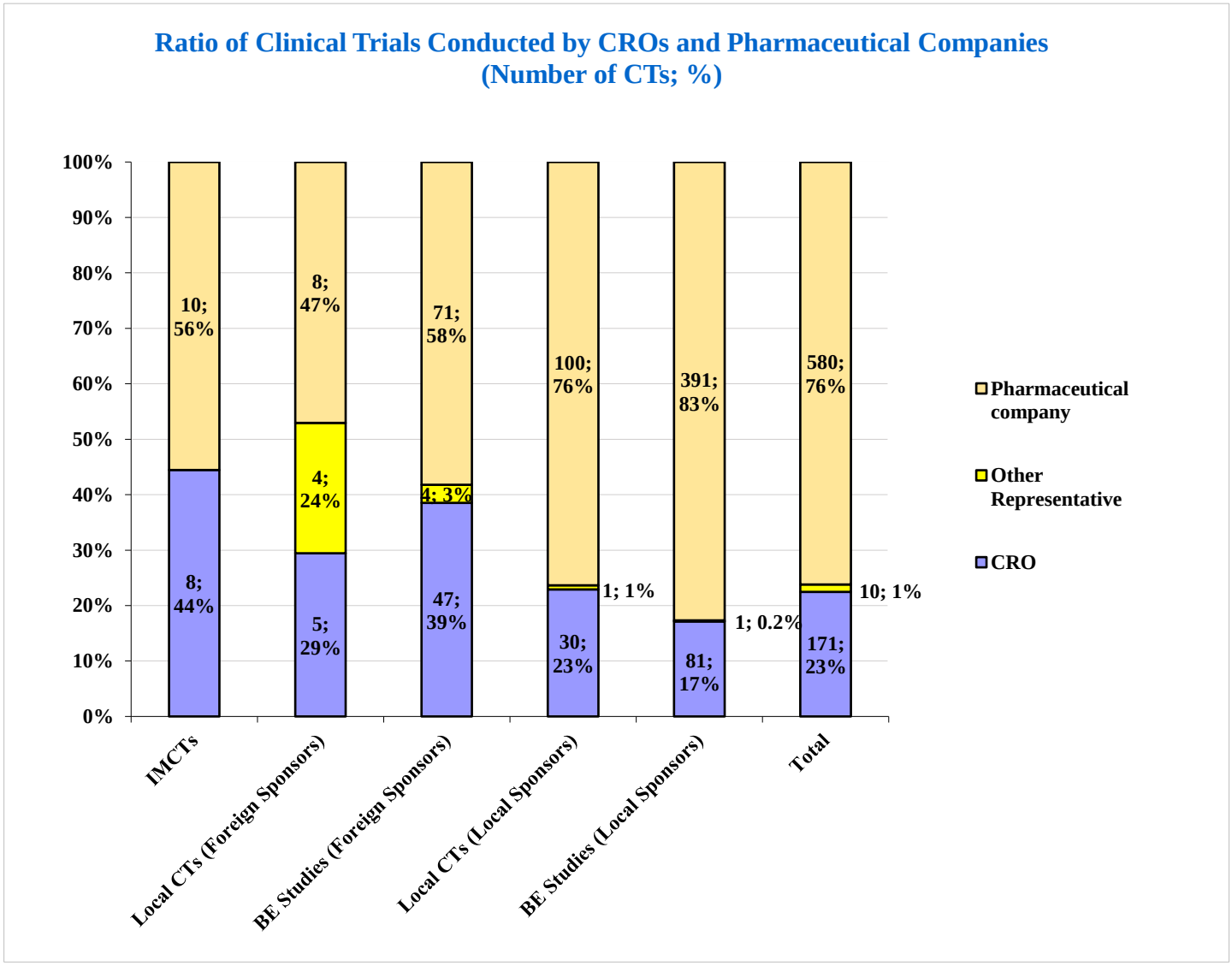
MAIN PLAYERS OF THE RUSSIAN CLINICAL TRIALS MARKET — 2023

Below are statistics on the main players of the Russian clinical trials market for 2023, separately for sponsors and contract research organizations (CROs). Diagram 17 also contains “other representatives” — legal entities that provide certain types of services for the distribution or introduction of a drug to the Russian market, but do not provide a full range of CRO services.

Sponsors and CROs, general structural distribution

Diagram 17 shows the share ratio of trials, which, according to applications submitted to the Ministry of Health, were planned by sponsors to be conducted independently or with the involvement of a CRO. The statistics we present never fully correspond to the actual state of things, since sponsors do not always indicate in the application the fact of involvement of a contract research organization. However, it helps to get a general sense of the situation.

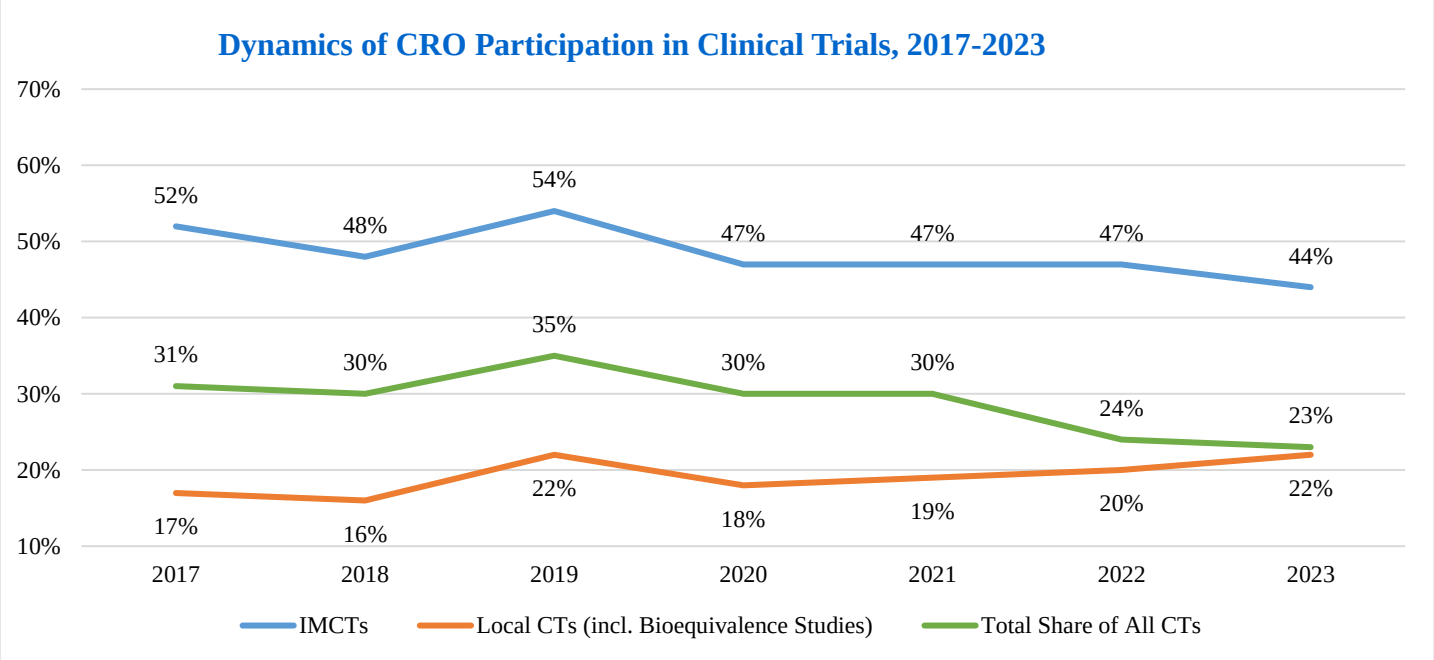
Diagram 17



Data from www.grls.rosminzdrav.ru

Diagram 18 shows how the share of CRO participation in clinical trials has changed since 2017. Since in practice specialization of CROs is of importance, data are presented separately for IMCTs and for local trials (including bioequivalence studies), and the aggregate for all trials is also given. It can be observed that the share of CRO participation in the total number of trials ranged from 30% to 35% for all five pre-war years, and starting from 2022 it went down dropping first to 24% and last year to 23%. At the same time the share of participation of contract organizations in local trials has been growing over the past four years from 18% in 2020 to 22% in 2023. It is clear that reduction in the total share was primarily due to the situation with IMCTs. And the reason lies not so much in the change in involvement of CROs in IMCTs (although it also decreased in 2023 by 3 percentage points as compared to the previous three years), but rather in the sharp reduction in the number of international projects: historically, the share of CRO engagement was higher for IMCTs in particular.

Diagram 18



Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, sponsors

In this section we traditionally publish the top of leaders by the number of approvals for IMCTs per year. However, in 2023 there were only 14 sponsors of international trials, and all of them were included in the ranking (Table 11).

Of the companies whose names we used to see in the top, when it still made sense to mark out leaders, only F. Hoffmann-La Roche, AbbVie, AstraZeneca, Janssen Pharmaceutica, Merck & Co., Pfizer and Sanofi remained in the table. The first one of those named above has two approvals, the rest have one each. Almost all of them are special protocols for a very small number of participants of previously completed IMCTs (five out of eight protocols have five or fewer subjects). The only exception is AbbVie, which obtained approval in early 2023 for an application submitted a year earlier, even before the start of the war, and canceled the start of this IMCT in Russia, so the company is included in the list only formally.

Sponsors of trials involving recruitment of new patients in 2023 were Agenus and Ascentage Pharma Group (USA), Biocad (Russia), CuraTeQ Biologics and Dr. REDDY's Lab. (India), Ferrer Internacional (Spain) and Protox (South Korea). The American and Russian companies have two approvals each, the rest have one.

Table 11

Pharmaceutical Companies on Approvals for International Multicenter CTs, 2023					
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; Ranking in 2022**
1	Agenus	2	–	2	n/a
2	Ascentage Pharma Group	2	–	2	1 CT; 19–58
3	F. Hoffmann-La Roche	2	2	–	10 CTs; 3
4	Biocad	2	2	–	n/a
5	AbbVie	1	1	–	5 CTs; 7
6	AstraZeneca AB	1	–	1	7 CTs; 4
7	CuraTeQ Biologics	1		1	n/a
8	Dr. REDDY's Lab.	1	1	–	n/a
9	Ferrer Internacional	1	–	1	1 CT; 19–58
10	Janssen Pharmaceutica	1	1	–	6 CTs; 5–6
11	Merck & Co.	1	1	–	11 CTs; 2
12	Pfizer	1	1	–	1 CT; 19–58
13	Protox	1	–	1	n/a
14	Sanofi	1	1	–	2 CTs; 11–18

Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, CROs

Table 12 lists contract research organizations, which sponsors planned to involve in conducting IMCTs in 2023. As in the case of sponsors, since there were too few approvals for international projects, all participating CROs ended up being presented in the table. Three CROs were mentioned in applications for two new IMCTs, two in one application.

Of the leaders of the pre-war years Parexel is left with one protocol for subjects of previously completed AstraZeneca trials. Cromos Pharma was placed 5th-6th in the respective table at the end of 2022 with four approvals, in 2023 there were only two approvals, both with the sponsor Ascentage Pharma Group, USA. Atlant Clinical (CRO belongs to the sponsor itself, Agenus, USA) and Accell Clinical Research (sponsors — Ferrer Internacional, Spain, and CuraTeQ Biologics, India) have two approvals each. Another approval was issued to Regapharm, sponsor Protox, South Korea.

Table 12

CROs on Approvals for International Multicenter CTs, 2023				
No.	**Company**	**Number of IMCTs**	**Number of Sponsors**	**Number of IMCTs; Ranking in 2022**
1	Accell Clinical Research	2	2	1 CT; 13–20
2	Atlant Clinical	2	1	n/a
3	Cromos Pharma (K-Research)	2	1	4 CTs; 5–6
4	Parexel	1	1	5 CTs; 3–4
5	Regapharm	1	1	n/a

Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, foreign sponsors

The top foreign sponsors that initiated local trials in Russia, including bioequivalence studies, are presented in Table 13.

Hetero Labs tops the list with 15 approvals. The company had already taken the top spot in 2018 and 2019, and generally makes the list of leaders more often than not. It is followed by Rubikon with ten approvals. This company from Belarus was included in the corresponding table for the first time at the end of 2022. Sandoz is in third place with nine protocols. Places 4–5 were shared by the top regular Dr. REDDY's Lab. and Lekpharm, another company from Belarus, who also ranked in the top for the first time in 2022. Mylan Laboratories holds sixth place with seven approvals. Places 7–8 (six approvals each) are held by Gedeon Richter and Sun Pharma. Jodas Expoim ranks ninth with five approvals. Lines 10 to 12 are shared by three companies (all with four approvals each): KRKA, Micro Labs and Pharmtechnology.

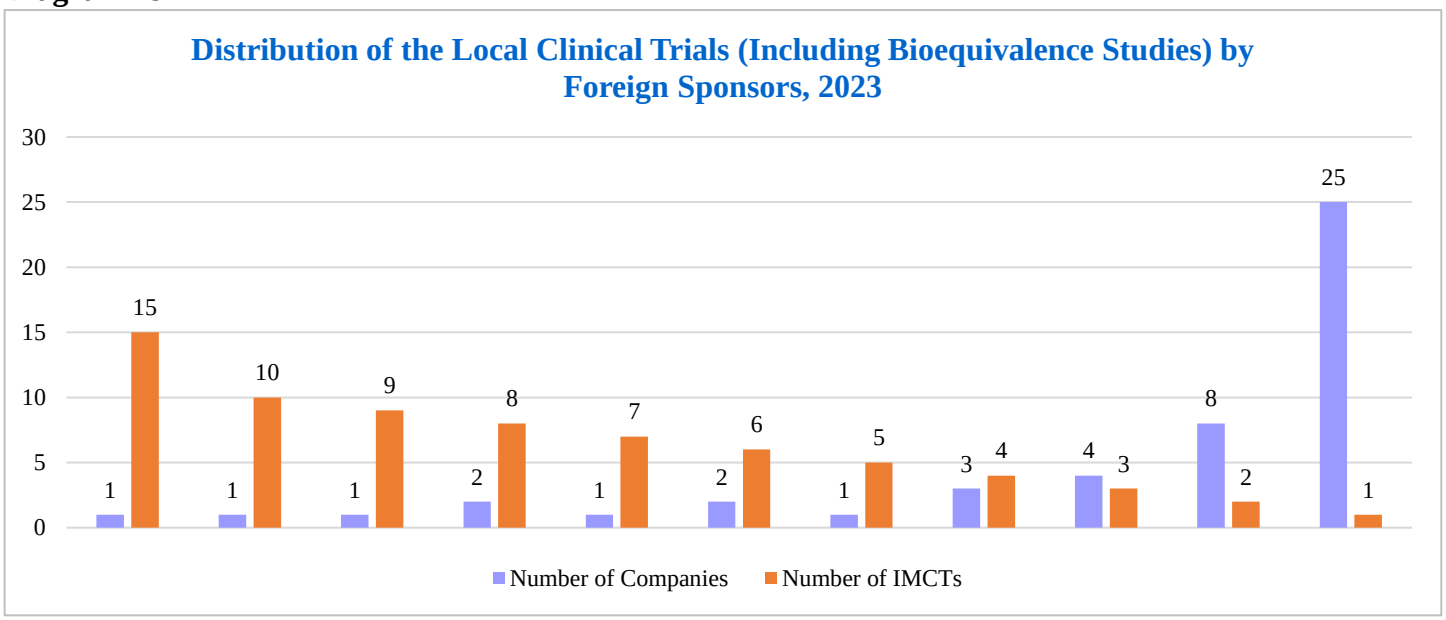
Table 13

Ranking of Foreign Sponsors on Approvals for Local CTs and Bioequivalence Studies, 2023					
Ranking in 2023	**Company**	**Total**	**Conducted by themselves**	**Conducted by CROs/other representatives**	**Number of CTs; Ranking in 2022**
1	Hetero Labs	15	15	–	2 CTs; 12–20
2	Rubikon	10	1	9	5 CTs; 6
3	Sandoz (incl. Lek d.d.)	9	9	–	7 CTs; 1–2
4–5	Dr. REDDY's Lab.	8	7	1	6 CTs; 3–5
4–5	Lekpharm	8	–	8	6 CTs; 3–5
6	Mylan Laboratories	7	7	–	2 CTs; 12–20
7–8	Gedeon Richter	6	–	6	2 CTs; 12–20
7–8	Sun Pharma	6	6	–	4 CTs; 7–9
9	Jodas Expoim	5	3	2	1 CT; 21–34
10–12	KRKA	4	4	–	4 CTs; 7–9
10–12	Micro Labs	4	1	3	n/a
10–12	Pharmtechnology	4	–	4	4 CTs; 7–9

Data from www.grls.rosminzdrav.ru

Diagram 19 shows the distribution of local trials and bioequivalence studies approved in 2023 among foreign sponsors. 25 companies obtained one approval each, eight obtained two each, four — three each, three — four each, two — six each, and another two obtained eight each. Another five companies obtained five, seven, nine, ten and fifteen approvals respectively. The total number of sponsors in this category in 2023 was 49, which is higher than the previous year (34 companies). For details of their geographical distribution, see the section on therapeutics areas.

Diagram 19



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, domestic sponsors

Table 14 shows the top Russian manufacturers leading by the number of approvals obtained in 2023 for local trials including bioequivalence studies.

As can be seen from the table, the top three included Renewal with 45, Pharmasyntez with 39 and Amedart with 34 approvals, respectively. Information regarding the change in activity as compared to the previous year may be more interesting (presented in the last column of the table). The most growth in activity was shown by Amedart (34 studies vs two in 2022), Binnopharm Group (26 vs four) and Renewal (45 vs 27). Of the last year's leaders, only one company's activity decreased: in 2022 Promomed Rus ranked first with 53 approvals, and in 2023 it placed 4th with 32.

Table 14

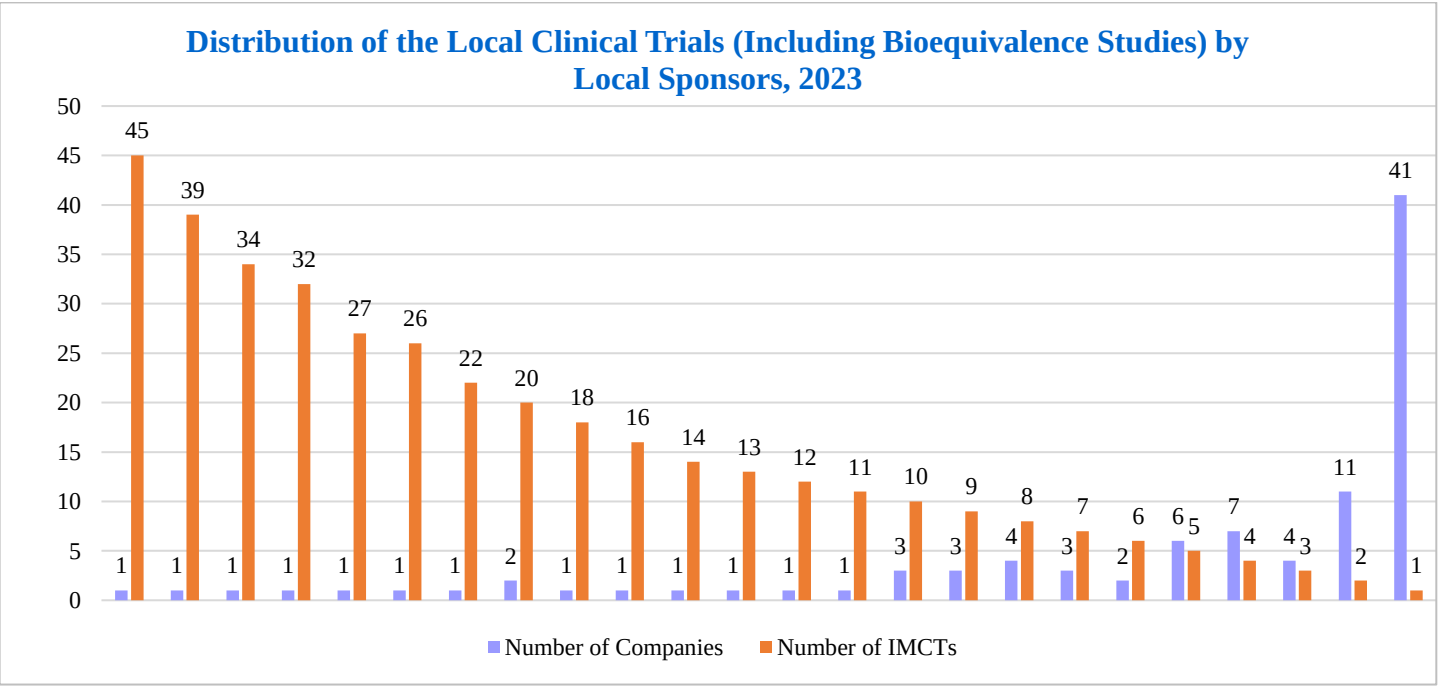
Top-15 Leading Local Sponsors on Approvals for Local Clinical Trials and Bioequivalence Studies, 2023					
Ranking in 2023	**Company**	**Total**	**Conducted by themselves**	**Conducted by CRO**	**Number of CTs; Ranking in 2022**
1	Renewal	45	45	–	27 CTs; 3
2	Pharmasyntez (incl. Pharmasyntez-Tyumen, Pharmasyntez-Nord, Pharmasyntez-Kaluga)	39	39	–	37 CTs; 2
3	Amedart	34	34	–	2 CTs; 43–63
4	Promomed Rus	32	32	–	53 CTs; 1
5	R-Pharm	27	27	–	19 CTs; 5
6	Binnopharm Group	26	26	–	4 CTs; 29–35
7	Bright Way Group (incl. Velpharm)	22	22	–	17 CTs; 7–8
8–9	Geropharm	20	20	–	6 CTs; 23–25
8–9	Izvarino Pharma (incl. Nanopharma Development)	20	–	20	11 CTs; 11–15
10	Solopharm	18	18	–	18 CTs; 6

11	AVVA RUS	16	16	–	11 CTs; 11–15
12	Pharmstandard (incl. Phs-Leksredstva, Lekko)	14	14	–	8 CTs; 20
13	Atoll	13	12	1	6 CTs; 23–25
14	Tula Pharmaceutical Factory	12	–	12	1 CT; 64–117
15	Protek (incl. Rafarma, Protek-SVM)	11	6	5	4 CTs; 29–35

Data from www.grls.rosminzdrav.ru

Distribution of new trials by Russian sponsors is shown in Diagram 20. In 2023 a total of 99 Russian companies obtained approvals to conduct bioequivalence studies and other types of local trials, which is less than a year earlier, when there were 117 of them.

Diagram 20



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, CROs

Table 15 shows the 2023 top CROs leading by the number of approvals for local trials, including bioequivalence studies.

The first three lines are occupied by Probiotech with 30, the National Scientific Center for Research and Pharmacovigilance with 22 and MDA with 13 new trials. The National Scientific Center for Research and Pharmacovigilance made it into the top CROs for the first time ever, as did two other companies, M VED (ten trials, places 4–5) and AX Clinical Trials and Consulting (nine, places 6–7). Of those who remained in the top since the previous year, OCT Rus increased its activity the most: in 2022, it obtained two approvals and shared lines 13–17 of the rating with other companies; in 2023 it announced seven trials ranking 8–9. iPharma has reduced its activity more than other leaders: five approvals in 2023 vs 11 a year earlier, occupying places 10–11 vs third.

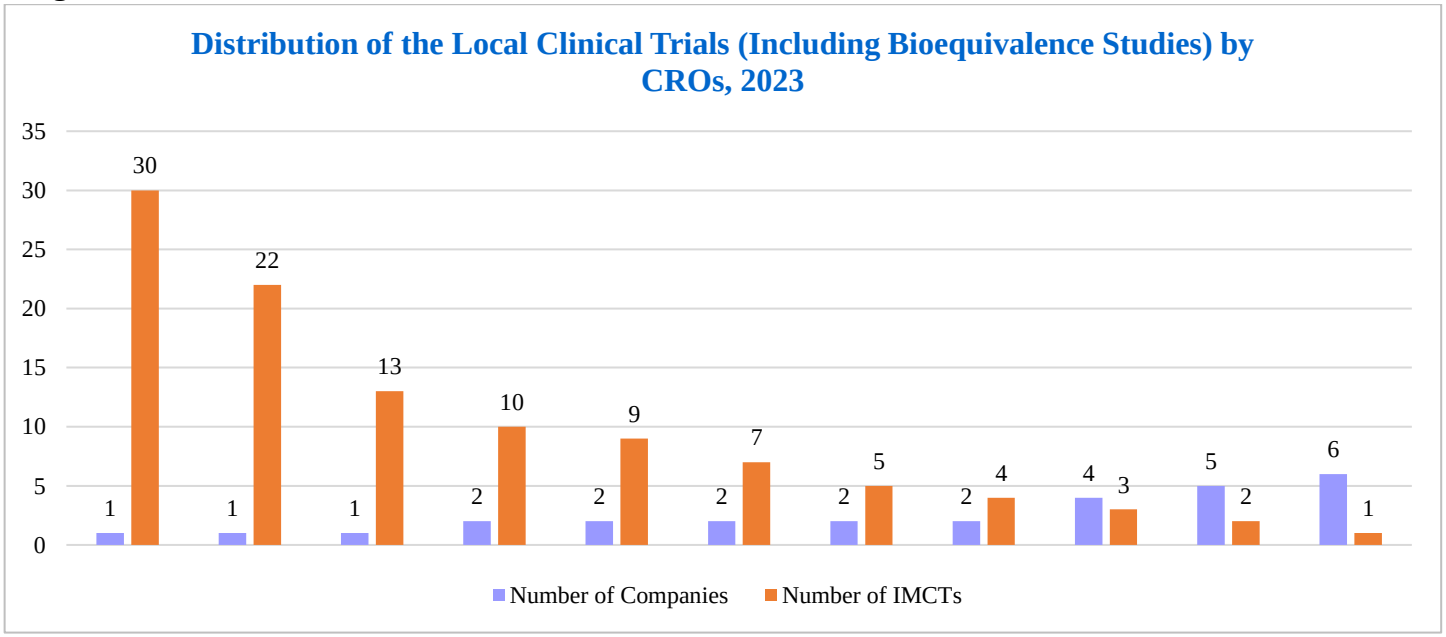
Table 15

Ranking of CROs Involved in the Local CTs and Bioequivalence Studies (on Approvals Issued in 2023)						
Ranking in 2023	**Company**	**Total number of local CTs, 2022**	**Number of CTs of foreign sponsors**	**Number of CTs of local sponsors**	**Number of sponsors**	**Number of CTs; Ranking in 2022**
1	Probiotech	30	7	23	6	28 CTs; 1
2	National Scientific Center for Research and Pharmacovigilance	22	1	21	4	n/a
3	Medical Development Agency (MDA)	13	3	10	6	14 CTs; 2
4–5	X7 Research	10	6	4	8	8 CTs; 4–5
4–5	M VED	10	1	9	3	n/a
6–7	AX Clinical Trials and Consulting	9	8	1	6	n/a
6–7	Accellena Research and Development	9	–	9	4	7 CTs; 6–8
8–9	Ligand Research	7	4	3	5	7 CTs; 6–8
8–9	OCT	7	6	1	3	2 CTs; 13–17
10–11	Innovative Pharmacology Research (IPHAR)	5	–	5	4	2 CTs; 13–17
10–11	IPHARMA	5	–	5	4	11 CTs; 3

Data from www.grls.rosminzdrav.ru

Diagram 21 shows the distribution of local trials and bioequivalence studies by contract research organization. In 2023 a total of 28 CROs were planned to be involved in these types of trials, four more than in 2022.

Diagram 21



Data from www.grls.rosminzdrav.ru

CLINICAL TRIALS
IN THE NEIGHBOR COUNTRIES OF THE RUSSIAN FEDERATION

From mid-2022 we began publishing an overview of the situation with clinical trials in the markets of countries with a common Soviet past in our ACTO newsletters. And we let readers make their own conclusions about the development of industry in each of these countries separately and the connection of this parameter with the course of the country's direction chosen after the collapse of the USSR.

Table 16 shows the number of active interventional trials, the country's share in the global market, the total population, and the number of trials per million for each country, according to clinicaltrials.gov. For the sake of clarity, ranking by the number of active trials per 1 million people is also shown separately in Diagram 22.

Table 16

The activity of clinical trial markets in the neighboring countries of the Russian Federation as of 02/06/2024 (data for 02/13/2023 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	**80 639** (78 014)			
Russia	**997** (1 264)	**1.24** (1.62)	**146.2**	**6.8**
Ukraine	**406** (517)	**0.50** (0.66)	**31**	**13.1**
Lithuania	**230** (218)	**0.29** (0.28)	**2.9**	**79.3**
Georgia	**224** (198)	**0.28** (0.25)	**3.7**	**60.5**
Estonia	**159** (164)	**0.20** (0.21)	**1.4**	**113.6**
Latvia	**155** (164)	**0.19** (0.21)	**1.9**	**81.6**
Belarus	**71** (82)	**0.09** (0.11)	**9.2**	**7.7**
Moldova	**71** (61)	**0.09** (0.08)	**2.5**	**28.4**
Kazakhstan	**22** (25)	**0.03** (0.03)	**20**	**1.1**
Armenia	**17** (16)	**0.02** (0.02)	**3**	**5.7**
Uzbekistan	**9** (10)	**0.011** (0.013)	**36.8**	**0.3**
Kyrgyzstan	**9** (10)	**0.011** (0.013)	**7.1**	**1.3**
Azerbaijan	**2** (3)	**0.003** (0.004)	**10.1**	**0.2**
Tadjikistan	**2** (2)	**0.003** (0.003)	**10.1**	**0.2**

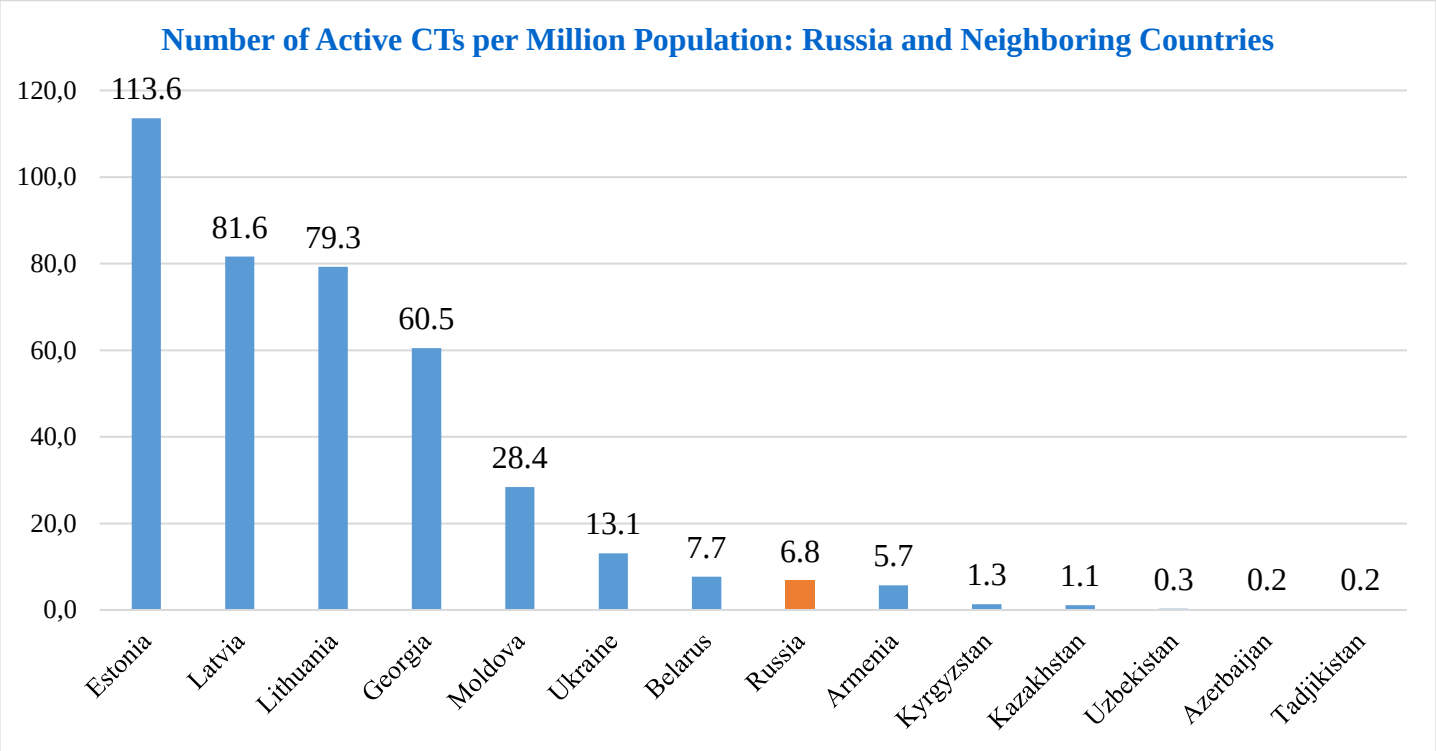
Data from www.clinicaltrials.gov; data from official statistical agencies of the countries available at the beginning of 2024

Over the past year (both times the indicators were taken in February), the total number of active interventional trials has increased in Moldova (+16.4%, 71 studies vs 61 in 2023), Georgia (+13.1%, 224 vs 198), Armenia (+6.3%, although here account must be taken of the low base effect: 17 vs 16) and Lithuania (+5.5%, 230 vs 218). It decreased in Ukraine (-21.5%, 406 studies vs 517 a year earlier), Russia (-21.1%, 997 vs 1264), Belarus (-13.4%, 71 vs 82), Kazakhstan (-12%, here also consideration must be given to the low base effect: 22 studies vs 25), Latvia (-5.5%, 155 vs 164), and Estonia (-3%, 159 vs 164). Due to the small number of trials in general, there is no point in specifying the rate of reduction in Uzbekistan and Kyrgyzstan (nine vs ten in both cases), and in Azerbaijan (two vs three). In Tajikistan, the indicator remained the same — two active intervention trials.

The Baltic countries integrated into the legal, logistics and other systems of the European Union are leading in terms of the number of intervention trials per 1 million people (Diagram 22 and the right column of Table 16). In Estonia, as of February 2024, there were 113.6 trials per 1 million people, 81.6 in Latvia and 79.3 in Lithuania. Of the rest, Georgia was the closest to the Baltic countries with 60.5 intervention trials per 1 million

people. Georgia is followed by Moldova with half the number — 28.4 trials per 1 million, behind which there is Ukraine also with almost half the number — 13.1 trials. Russia is only eighth in this ranking (6.8) having decreased its last year result by 20.1% and losing to Belarus (a year earlier, both countries had a rate of 8.6 trials per 1 million people).

Diagram 22

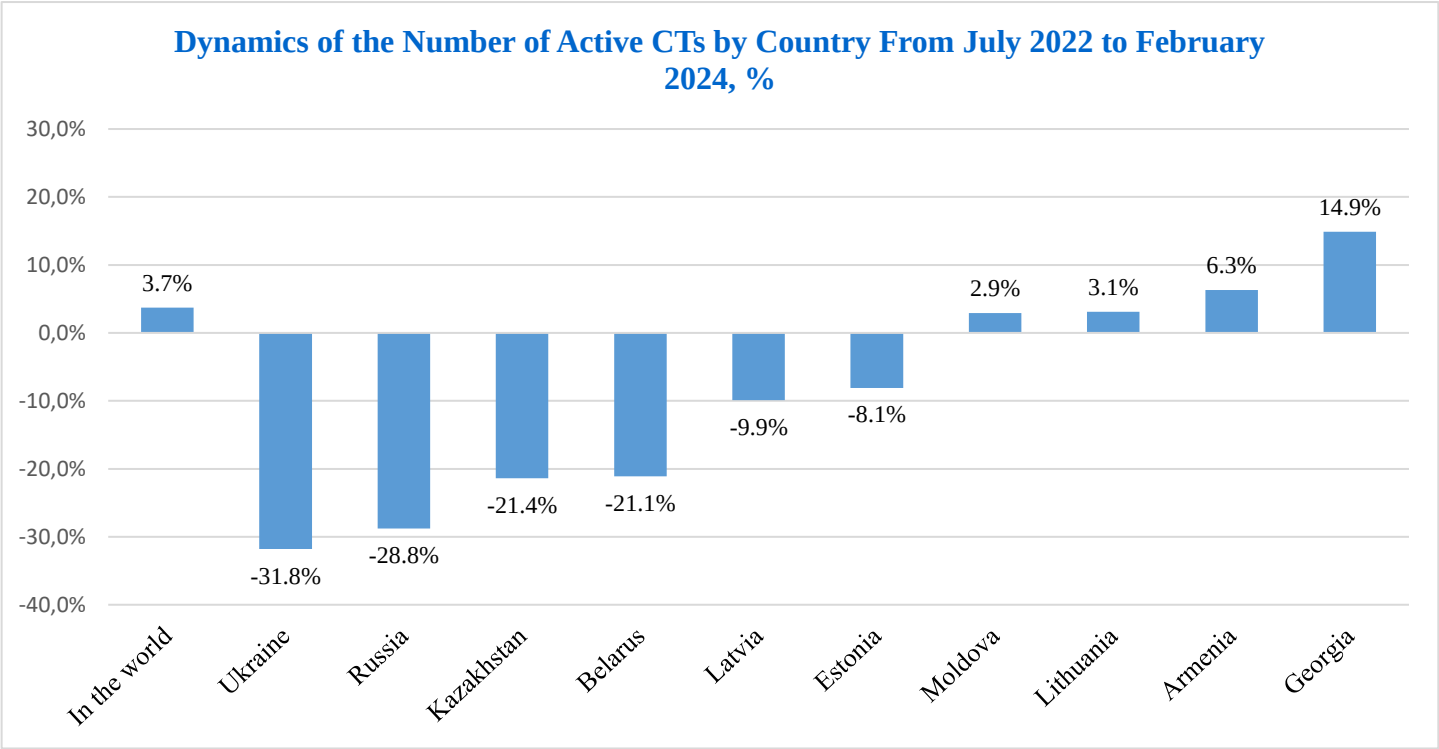


Data from www.clinicaltrials.gov

Let's try to assess how the clinical trials markets in the countries reviewed have changed since the beginning of the war. The first data, with which we can make a comparison, were collected only in July 2022.However, we believe that they are close to pre-war levels due to the market rigidity: over a period of several months its transformation could not have a noticeable impact on the statistics. Diagram 23 shows the change in the number of active intervention trials from July 2022 to February 2024.To avoid distracting the reader's attention by the low base effect, data is presented only for those countries with more than ten studies. Thus, Azerbaijan, Kyrgyzstan, Tajikistan and Uzbekistan are excluded from the comparison.

It is clearly visible, just how significantly the number of active trials dropped in Ukraine (-31.8%, 406 trials in February of this year vs 595 in July 2022). Russia is not doing much better with a reduction of -28.8%, but let's not forget that in absolute terms the number of trials in Russia was initially 2.4 times greater than in Ukraine (1,400 in the summer of 2022 and 997 in February 2024). Despite the completely different political and economic situation and opportunities the results of Kazakhstan and Belarus were similar. For the former the reduction was -21.4% (22 vs 28), for the latter — -21.1% (71 vs 90). And unlike Belarus, where the reasons for the reduction are clear, the dynamics of Kazakhstan are more difficult to explain. Market volumes also decreased in Latvia (-9.9%, 155 vs 172 studies) and Estonia (-8.1%, 159 vs 173). Stability and growth, although slightly noticeable, at the level of statistical error, was demonstrated by the markets of Moldova (growth +2.9%, 71 active trials vs 69 in July 2022), Lithuania (+3.1%, 230 projects vs 223), as well as Armenia (17 active trials vs 16, which due to the low base showed an increase of +6.3%). A truly significant increase is demonstrated by Georgia, which added 14.9% increasing the number from 195 active intervention trials to 224.

Diagram 23



Data from www.clinicaltrials.gov

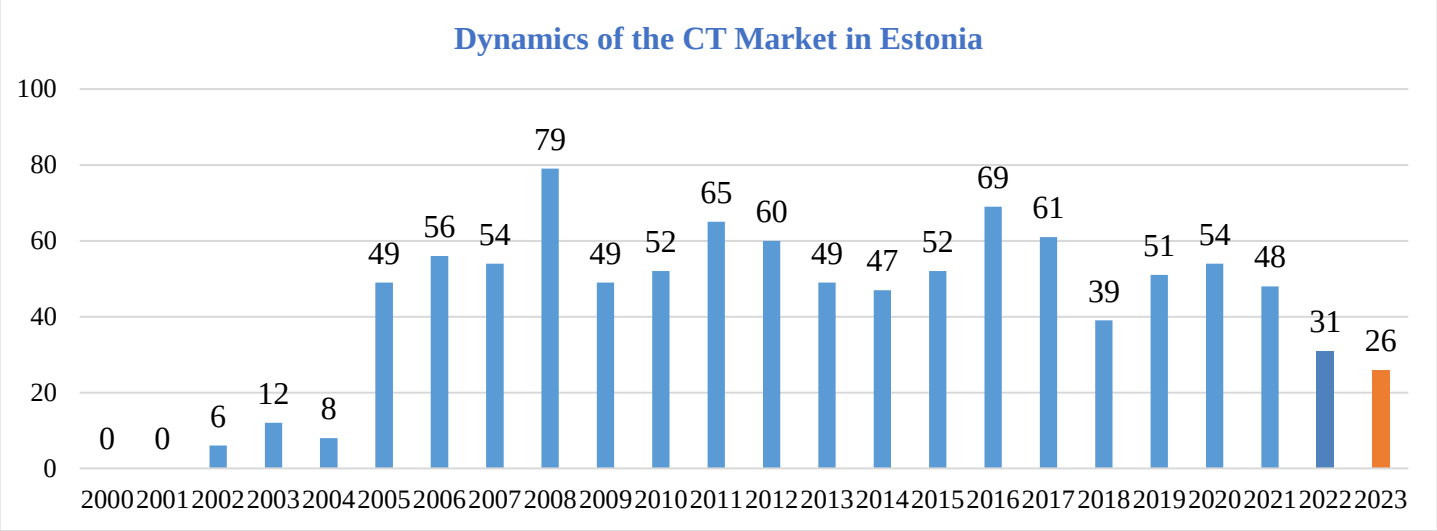
Below is information on the dynamics of the clinical trials market according to clinicaltrials.gov in each of the countries under review for the period from 2000 to 2023.It should however be noted that data for the previous year does not appear in the database immediately; this time we collected the data in February 2024, and this is clearly not the final result. In addition, for reasons unknown to us, the database numbers for recent years (usually 3-5 years) are slightly adjusted for one or two trials. As a result, we also adjust the statistics presented, therefore the careful reader may notice that figures for previous years slightly differ (usually upwards) from those that were present in previous issues of our newsletters.

In addition to the market dynamics for each country, which we present yet again, this issue also contains more detailed data on the specific trials behind the figures presented. We were prompted to do this by a striking difference in the data: only 18 approvals for IMCTs in Russia in 2023 (since IMCTs specifically are reflected in the clinicaltrials.gov database in the first place) and 145 new trials according to the version of the said resource. And then it became evident that we need to take a closer look at the proposed data array. The fact is that clinicaltrials.gov, having begun its development with pharmaceuticals, with time began to include more and more data on trials of medical devices, diagnostic tests, surgical methods and procedures, dietary supplements, nutritional regimens, etc. And the statistics usually provided by us in our newsletters using the clinicaltrials.gov database as a source include all those trials. Unfortunately, functionality does not yet allow automatic sorting of only pharmaceuticals related data. We had to do it manually, but given the large amounts of information, we limited our sample to only 2023.

A diagram is provided for each country that shows exactly what types of interventions are planned in the trials over the past year. For example, in Estonia the total number of new trials in 2023 is 26 (Diagram 24), of which only 17 are trials of drugs, including vaccines and any other biological products (Diagram 25). We also assessed how many trials of medicinal products were local (limited to sites of a specific country) and how many were international, and how many of them were initiated by pharmaceutical companies and how many — by academic institutions or individual investigators. For Estonia the respective breakdown is shown in Diagram 26: of 17 trials of medicinal products 15 are international, one local and one academic.

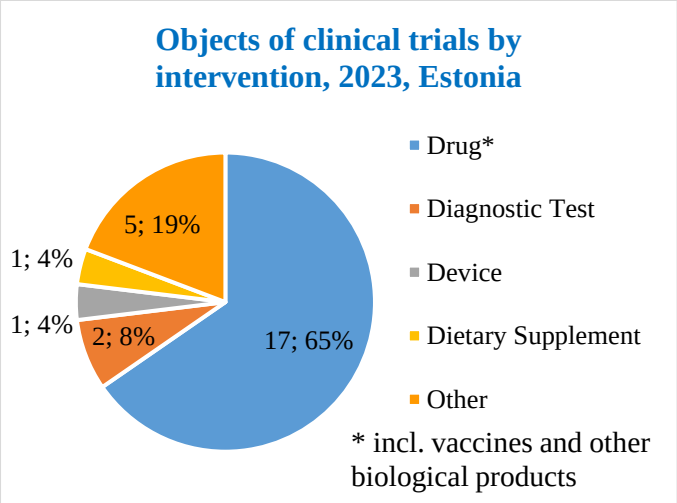
We invite readers to independently go through the information on specific countries. We will just share some of our observations. International trials of medicinal products are prevailing in the Baltic countries, Moldova and Georgia. Georgia was particularly impressive with the variety of international sponsors and the seriousness of projects. In Belarus international studies formally prevails, there are four of them out of six, however in reality they all have one sponsor — Russian company Biocad, and their geography is limited to the territories of Russia and Belarus, which makes their international status rather nominal. In Russia IMCTs in 2023 accounted for only 10% of new trials of medicines, while local (48%) and academic (36%) trials, including those initiated by specific investigators, prevailed. In Kazakhstan, the majority of new trials were also academic (87%), of which one was initiated by an investigator.

Diagram 24



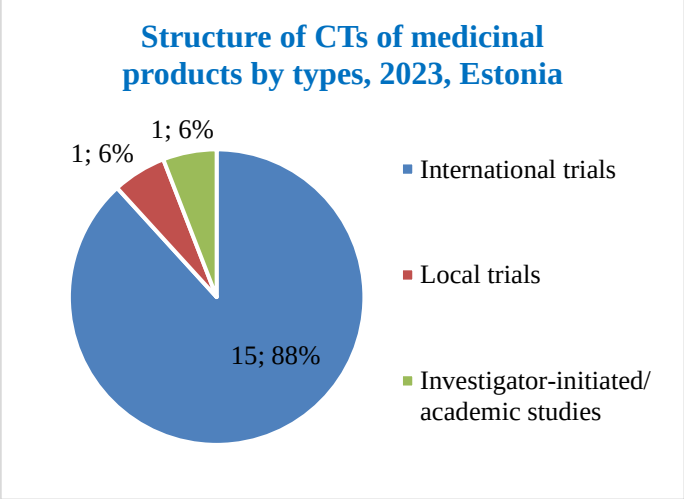
Data from www.clinicaltrials.gov

Diagram 25



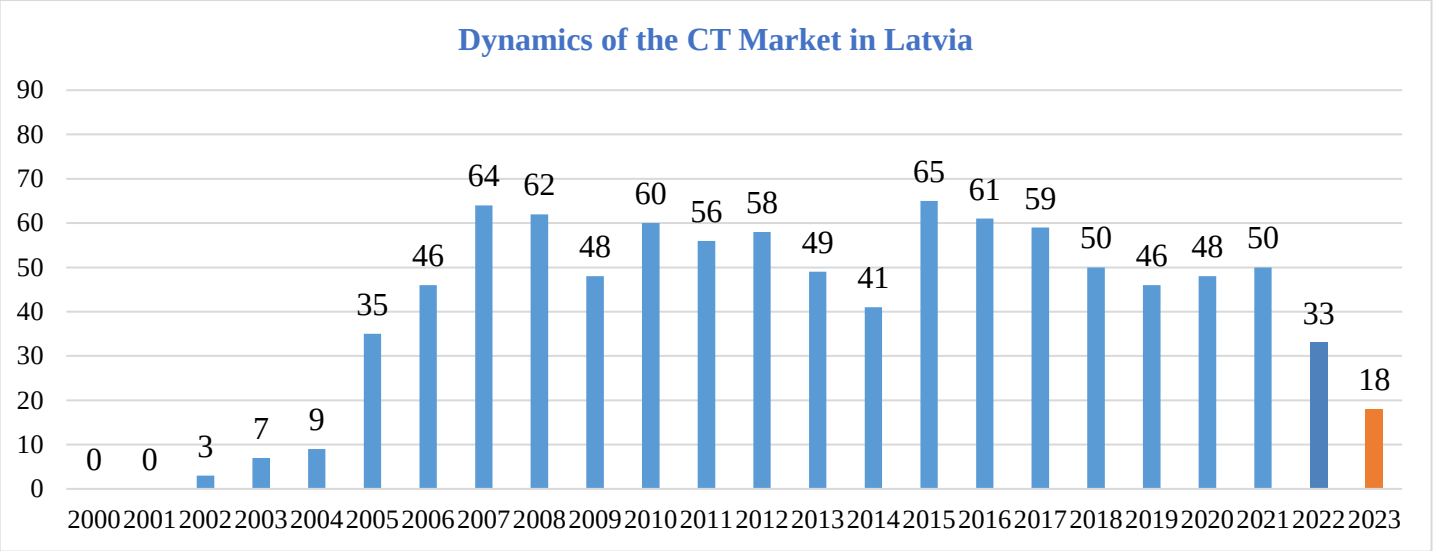
Data from www.clinicaltrials.gov

Diagram 26



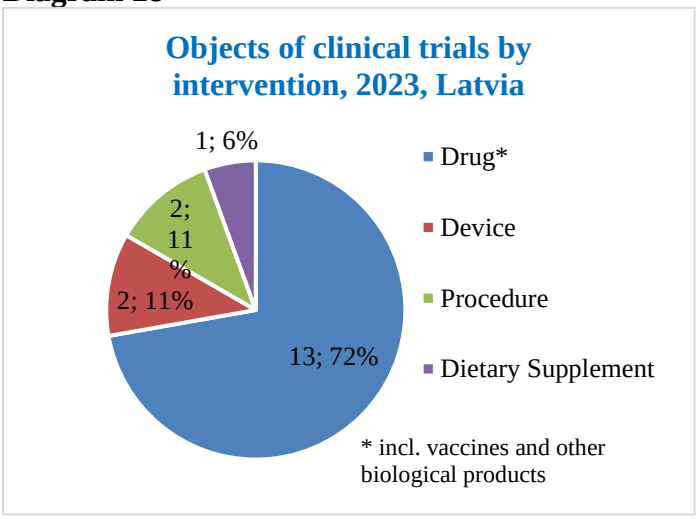
Data from www.clinicaltrials.gov

Diagram 27



Data from www.clinicaltrials.gov

Diagram 28



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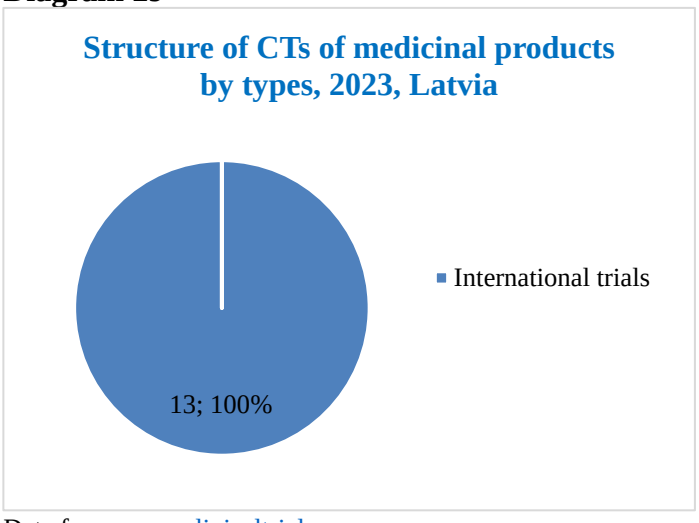

Data from www.clinicaltrials.gov

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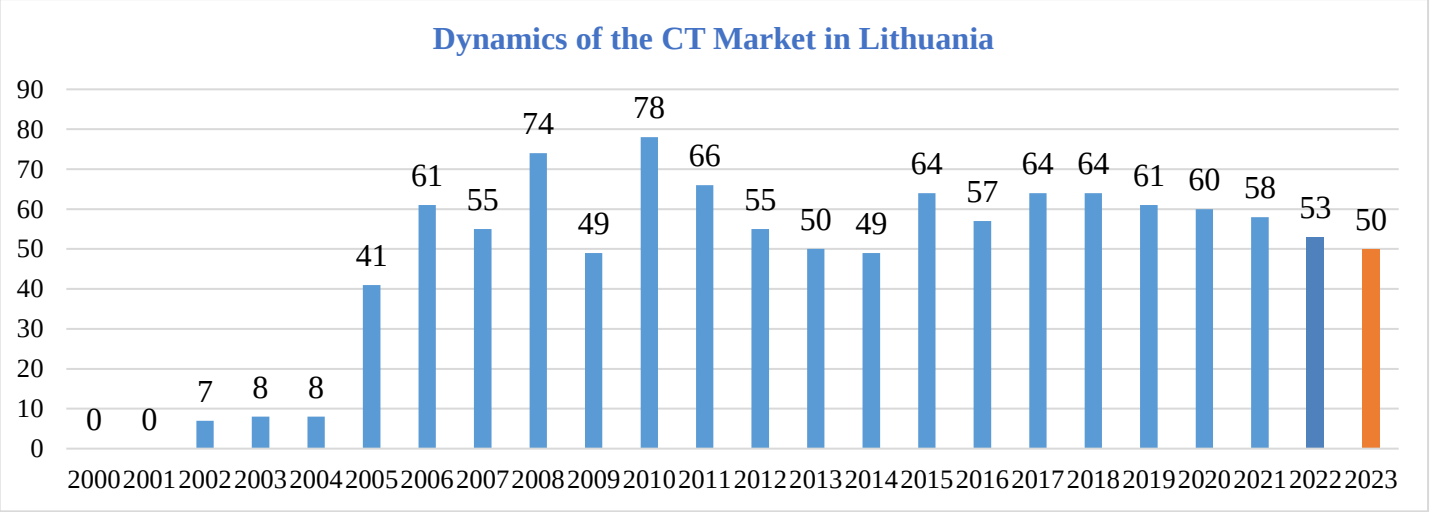

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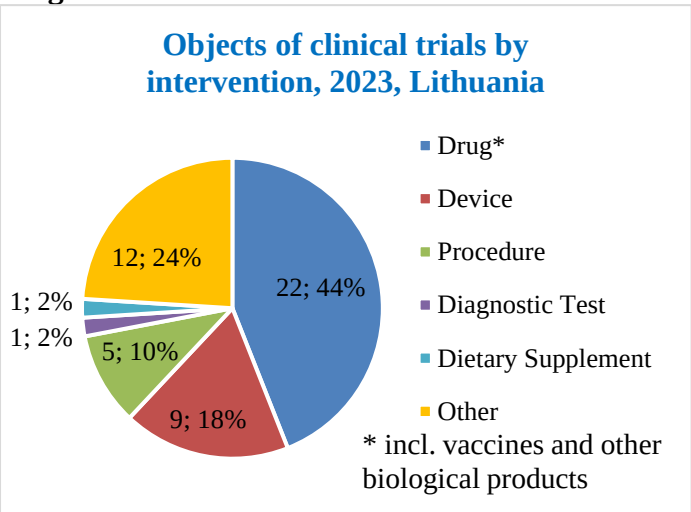
Diagram 31



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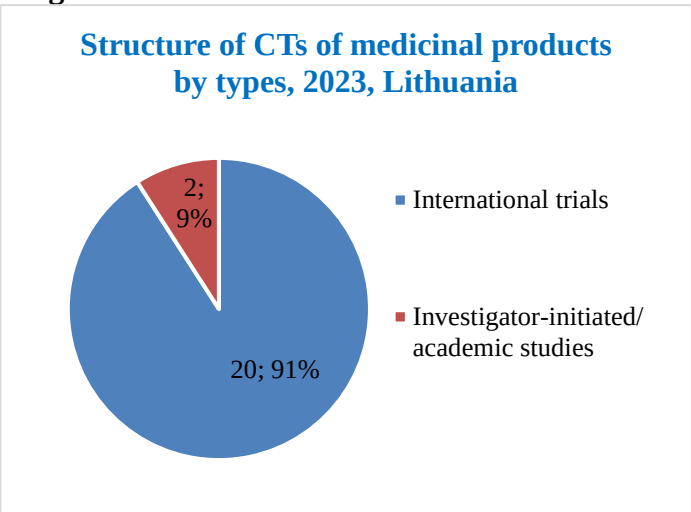

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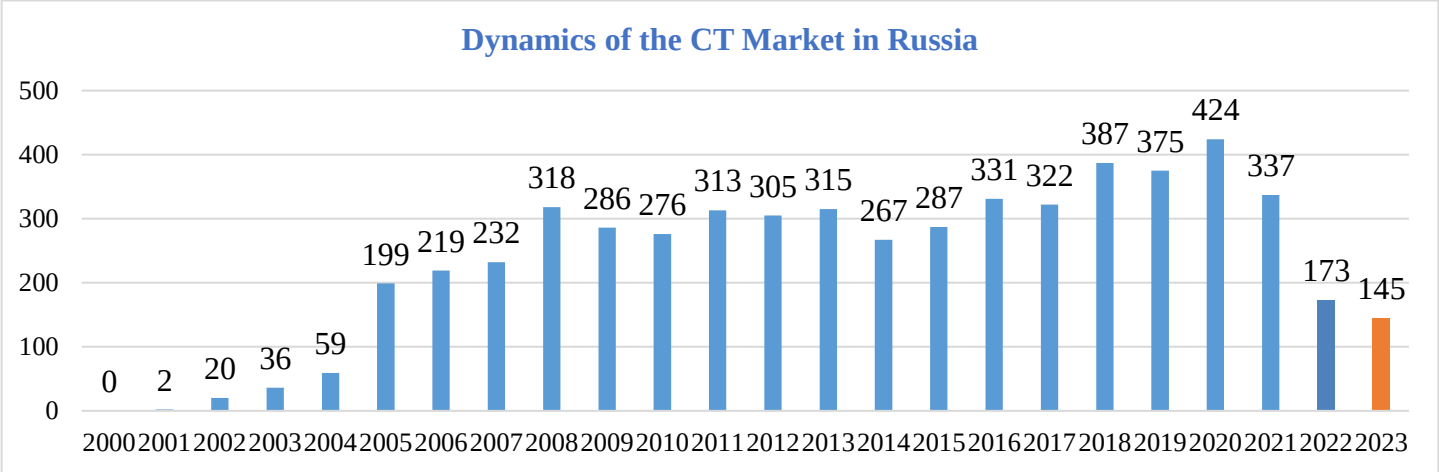
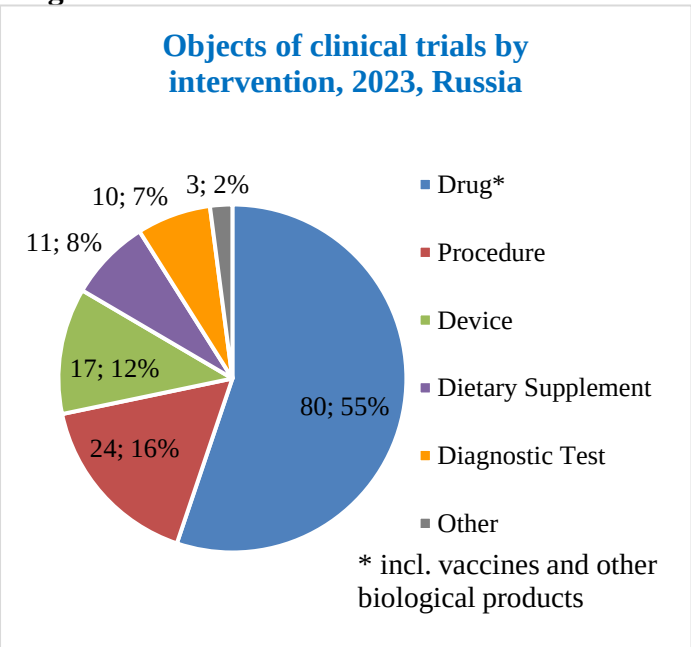
Diagram 33



Data from www.clinicaltrials.gov

Diagram 34



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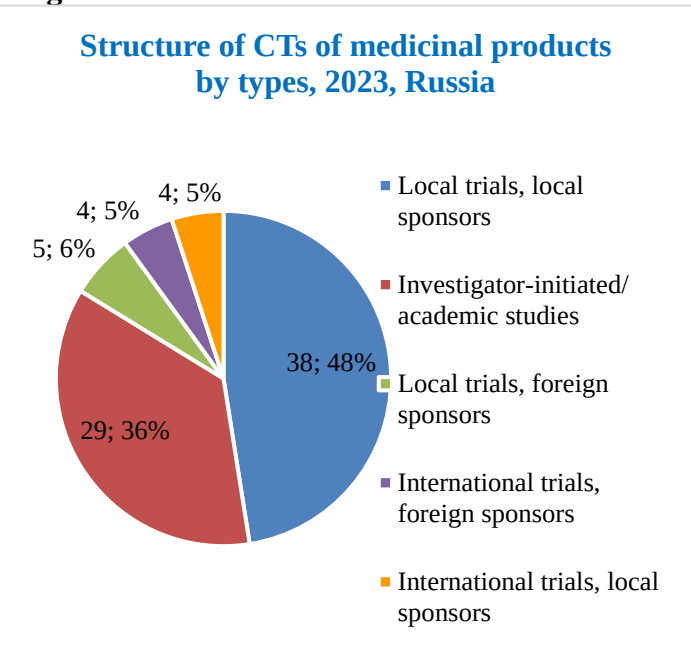

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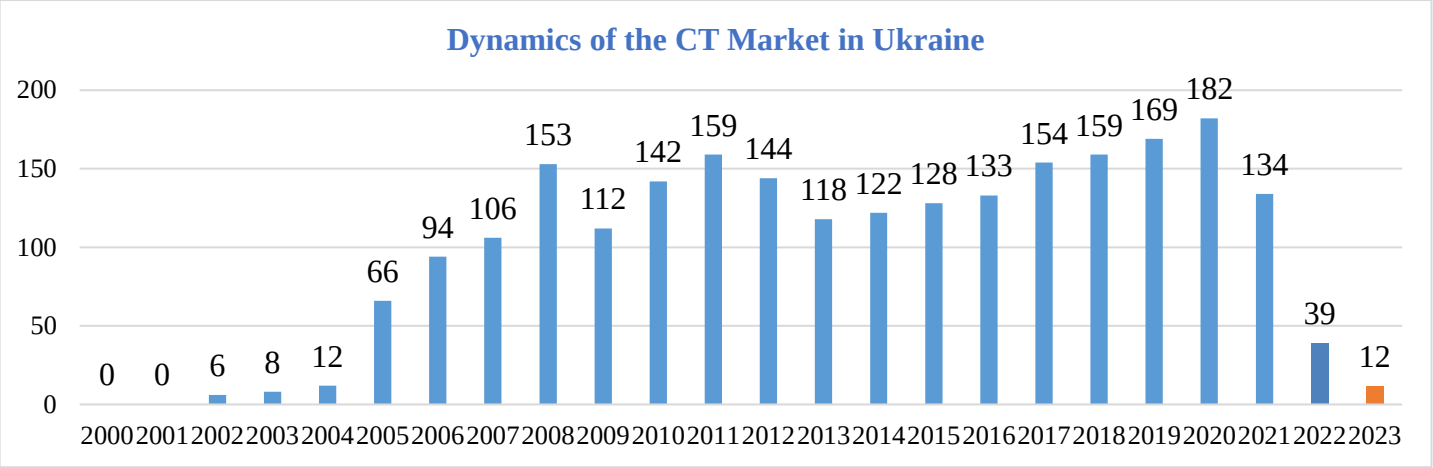

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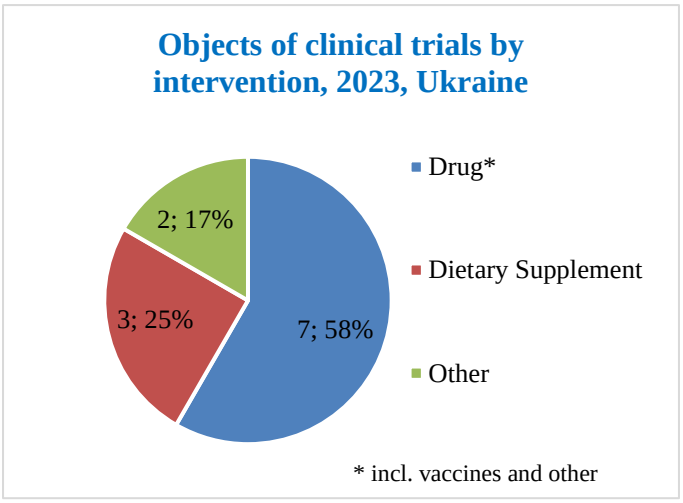

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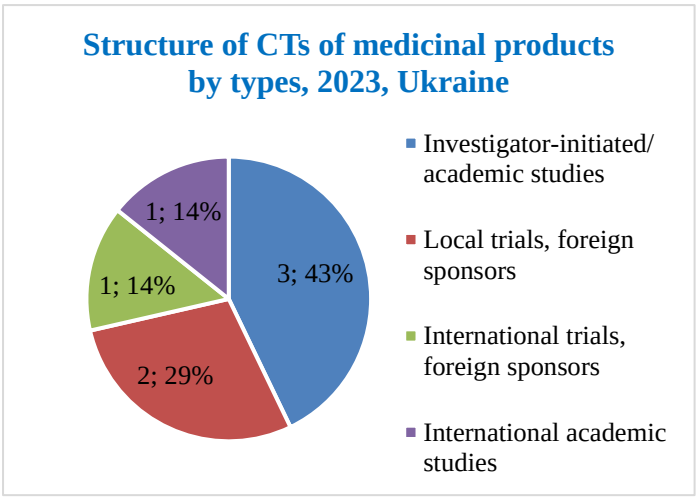

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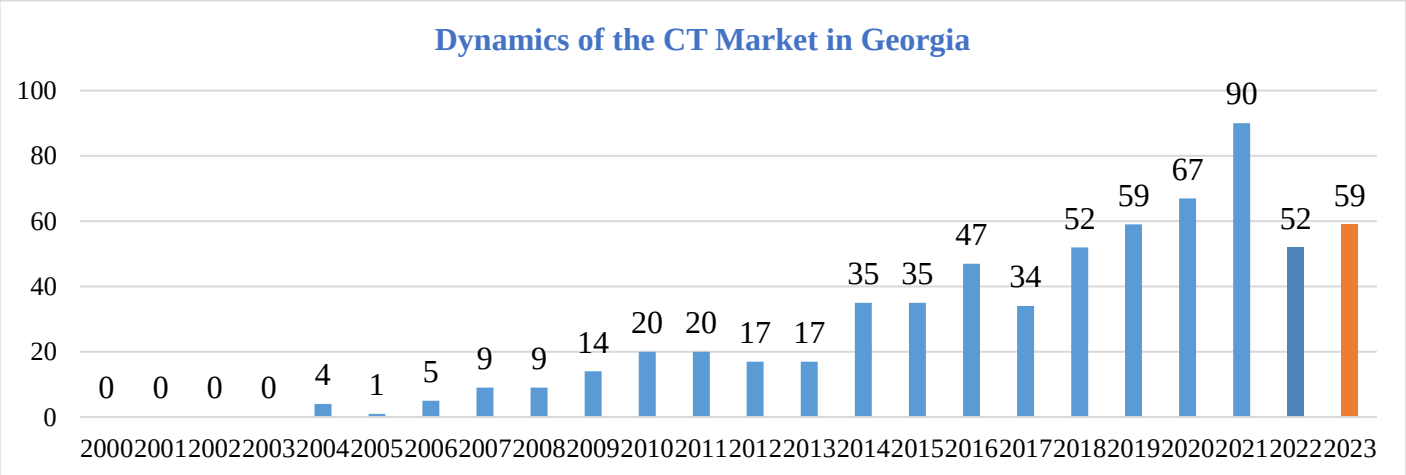

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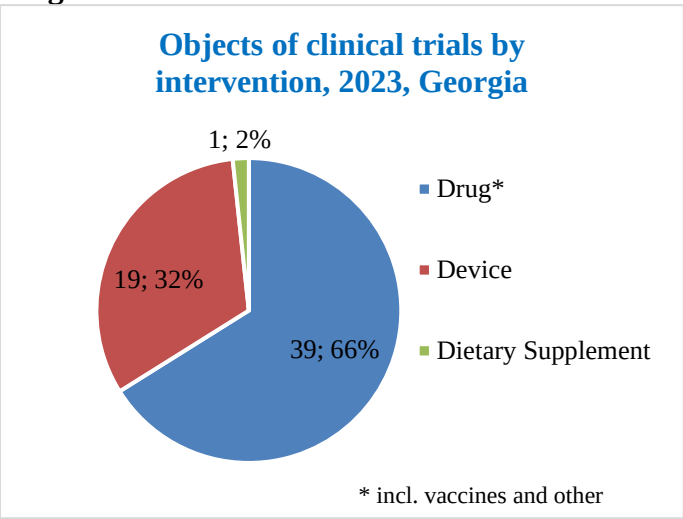

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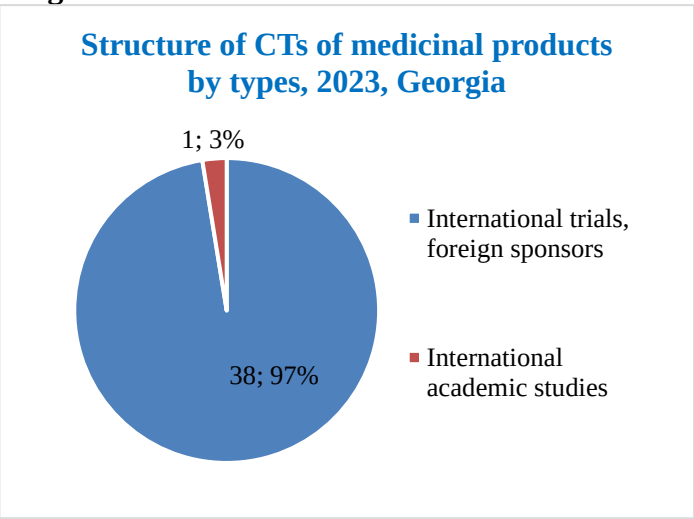

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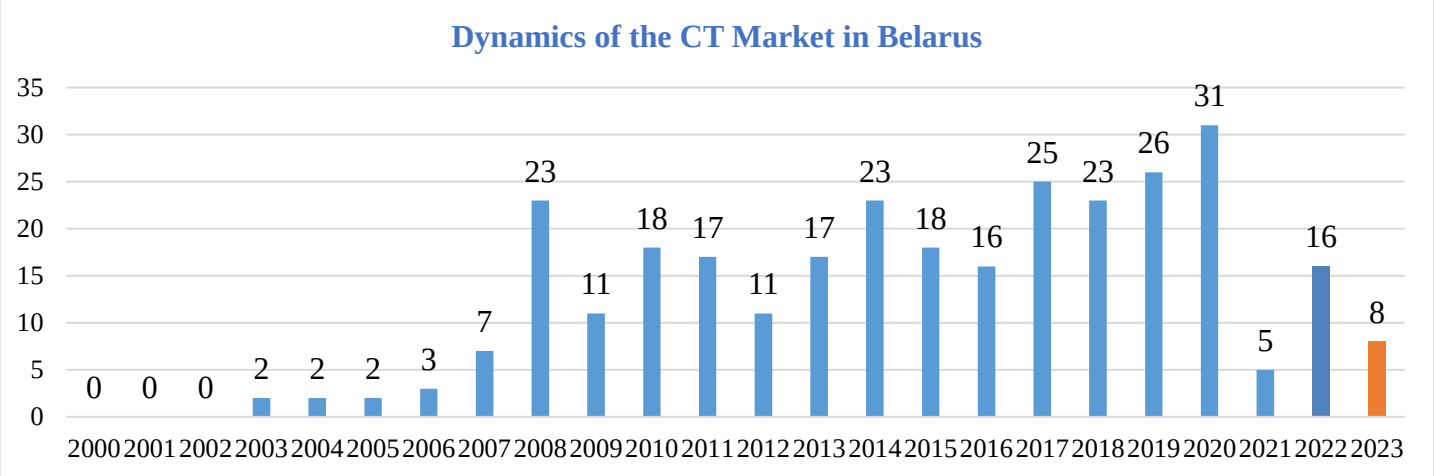

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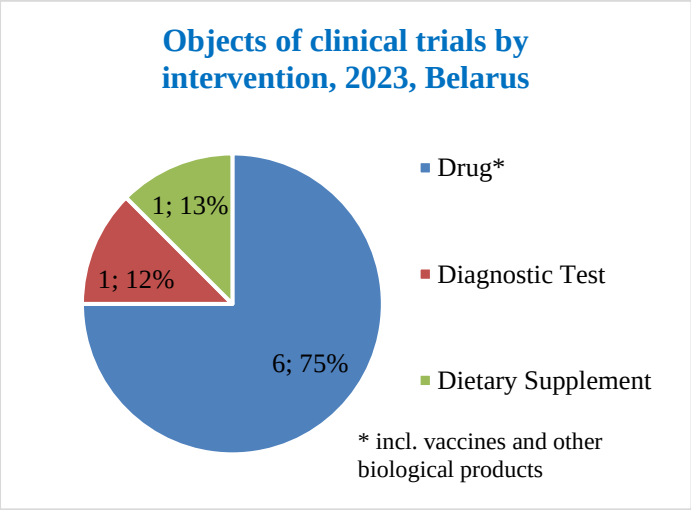

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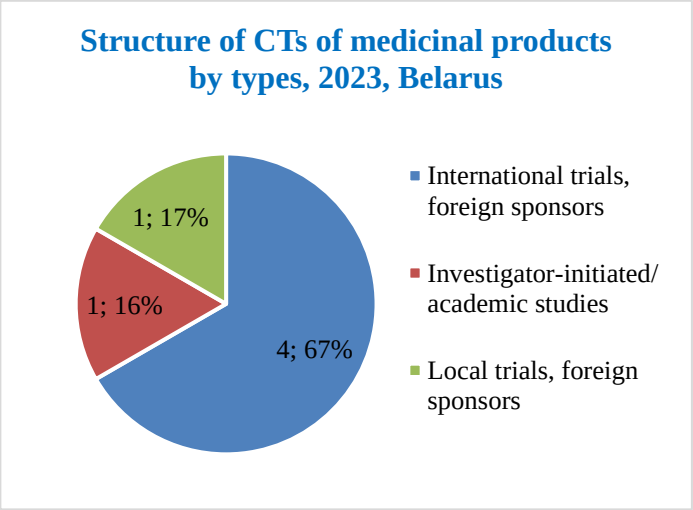

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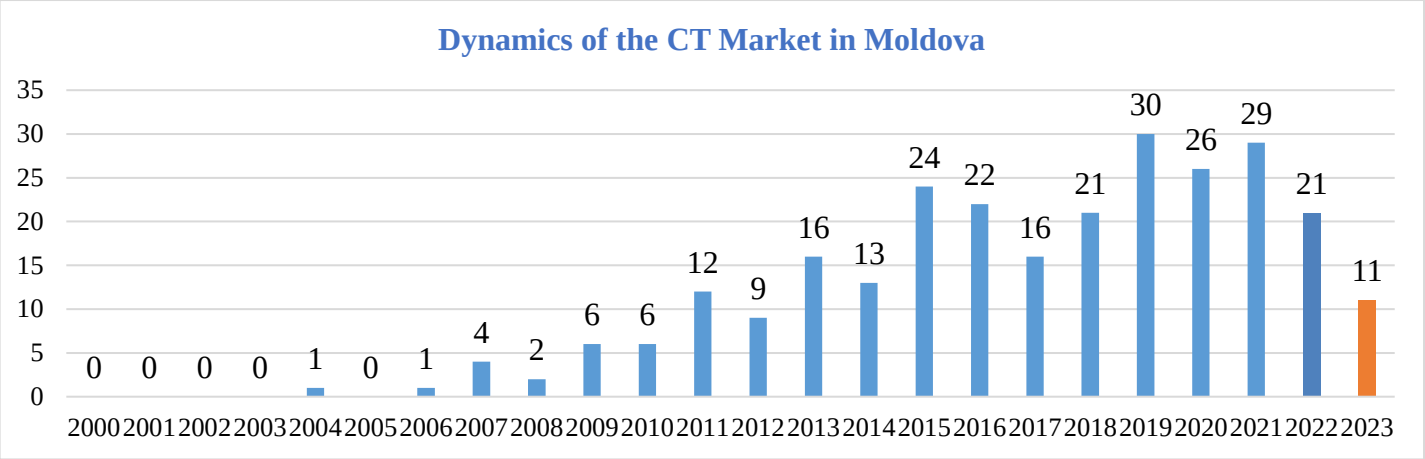

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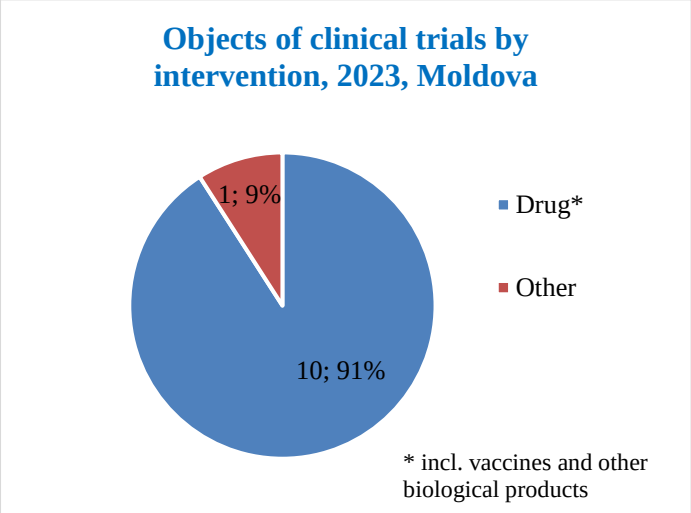

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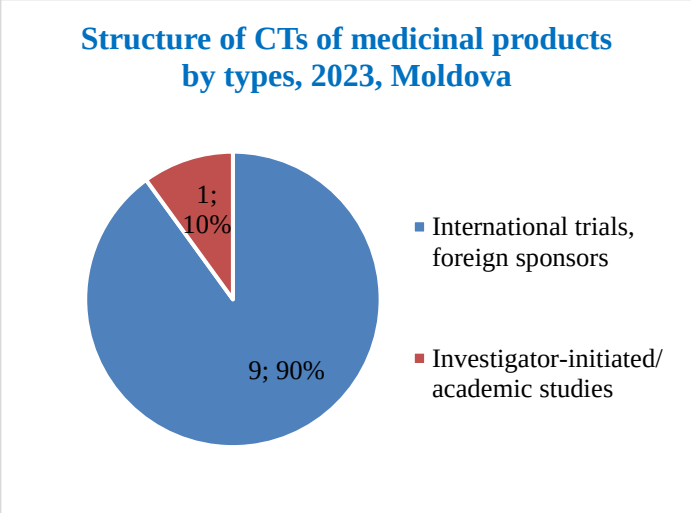

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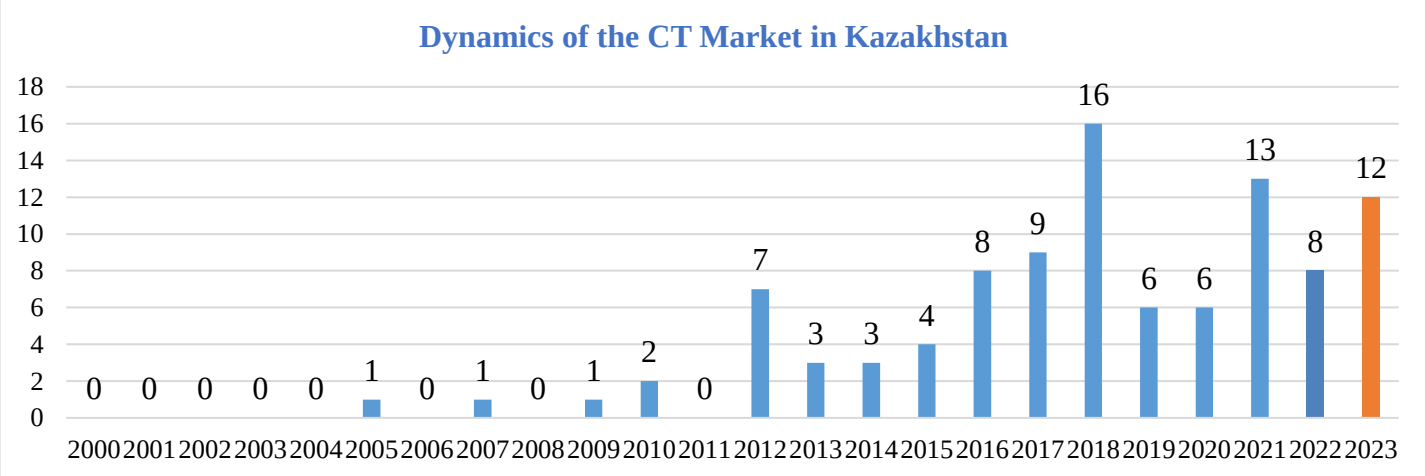

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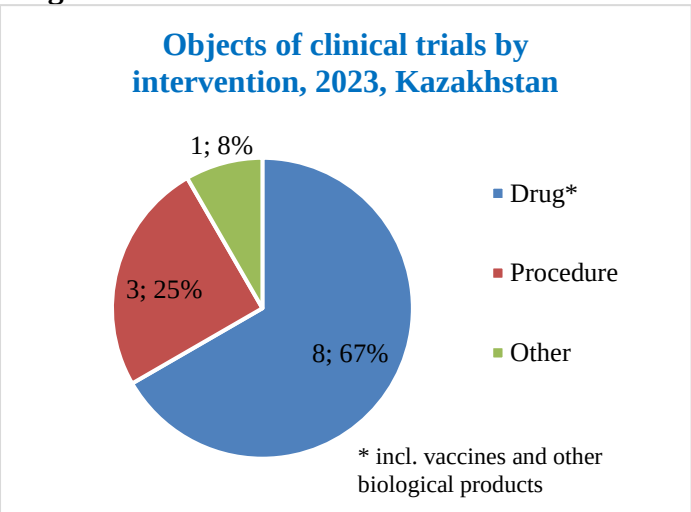

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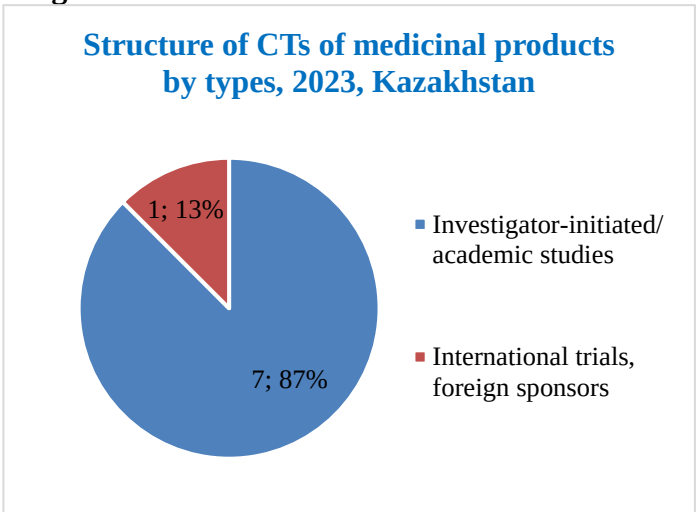

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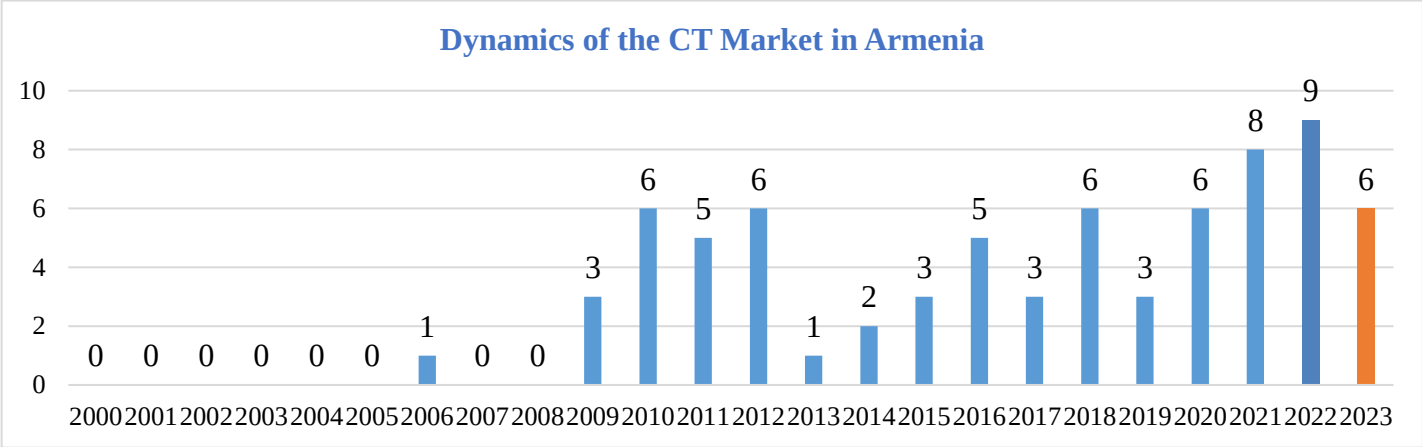

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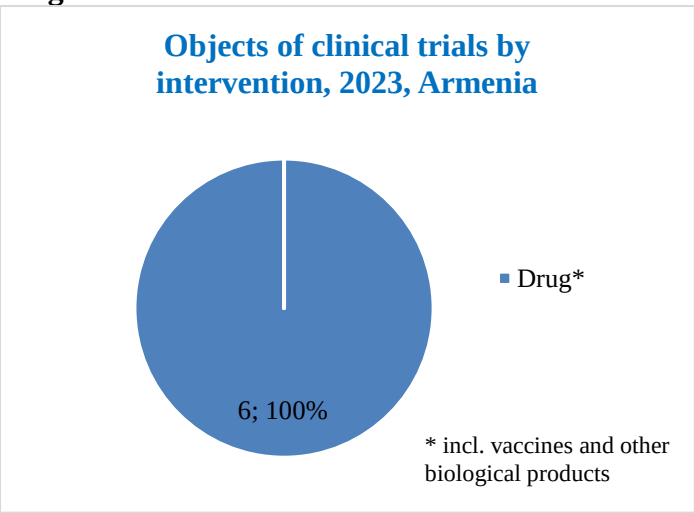

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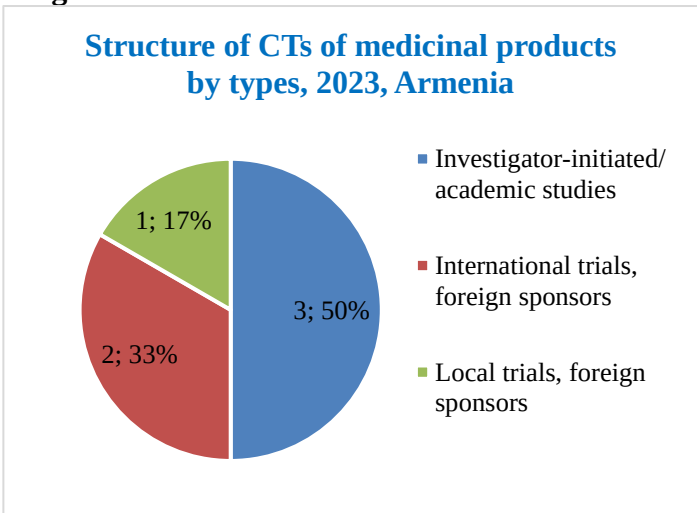

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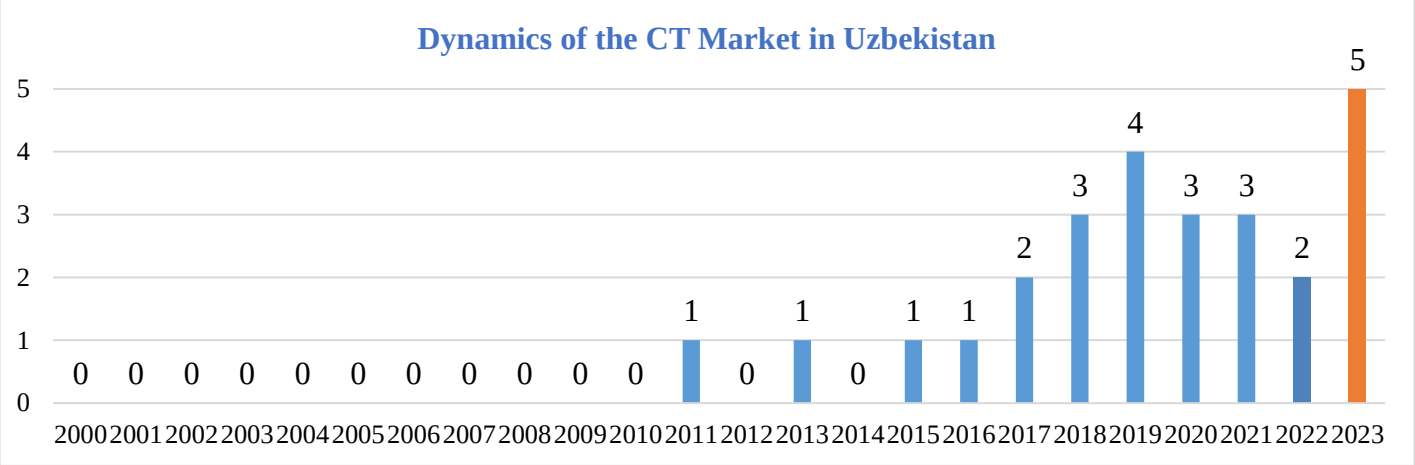

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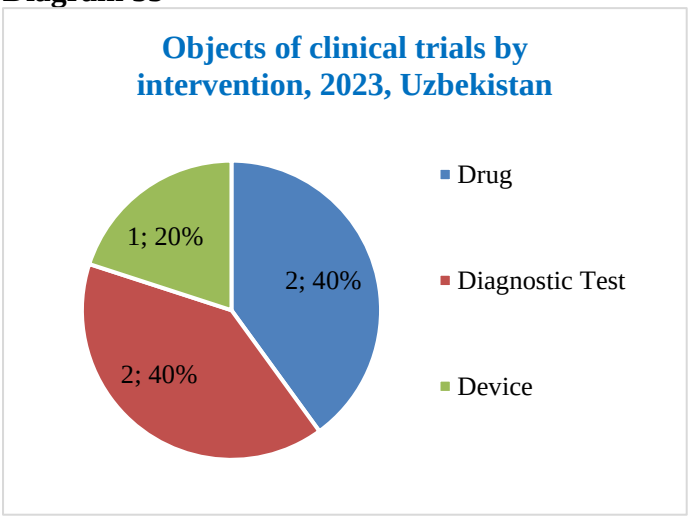

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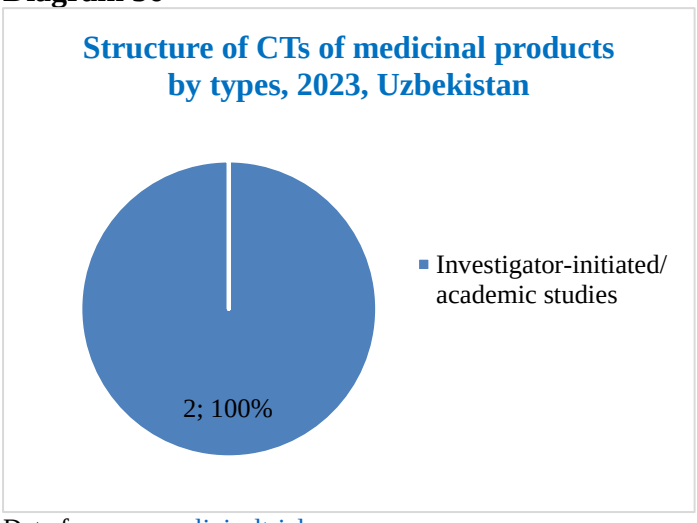

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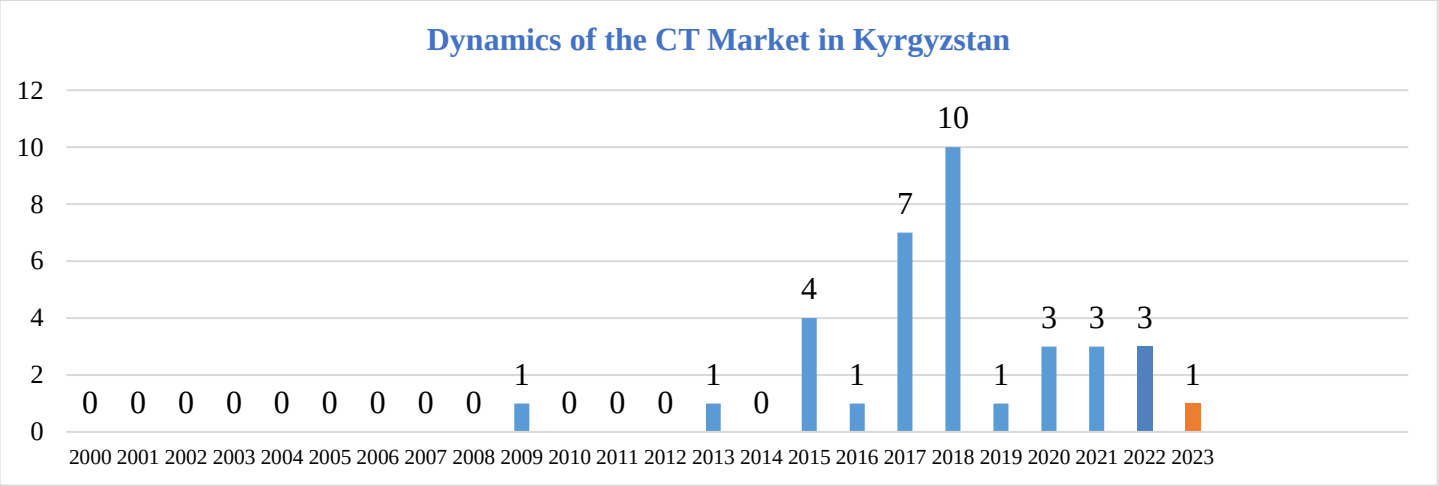

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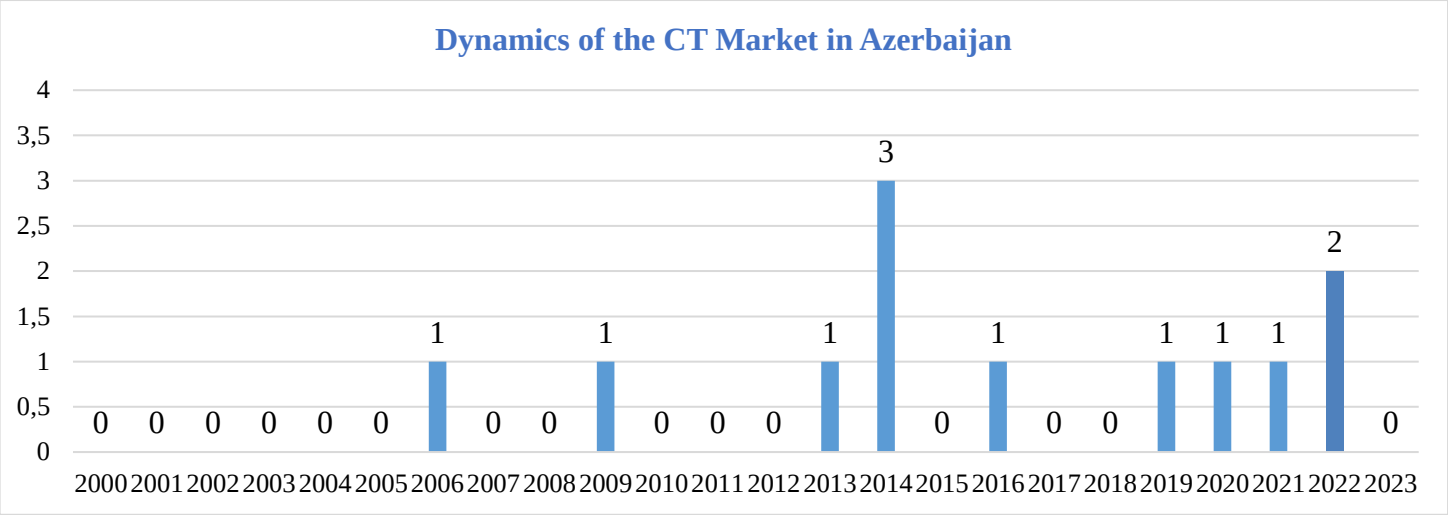

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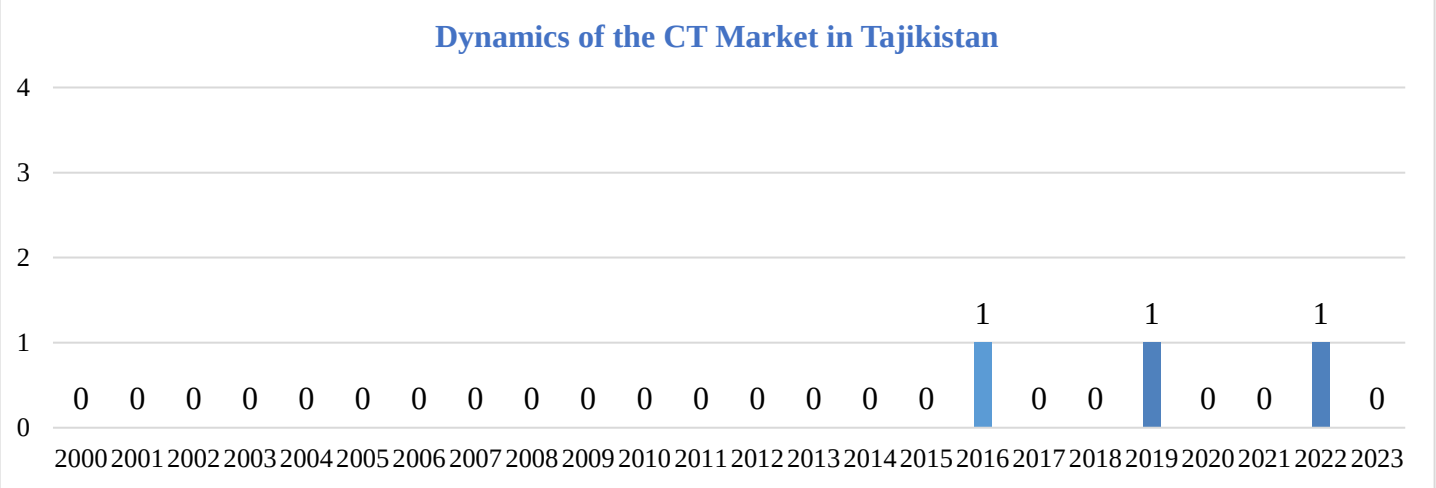

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