

ACTO

ASSOCIATION OF CLINICAL
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Summary of 2021 results

MOSCOW 2022

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This issue of ACTO Newsletter presents the results of 2021, which, as is now clear, was the last year when the familiar rules of the game that imply close ties with the global economy were applied both in the Russian clinical trials market and in the country in general. In 2022 these ties were broken, and although it is not yet possible to predict all the ramifications of Russia's international isolation for clinical trials, it is already obvious that the 2021 overview is a description of what is commonly referred to as "vanishing scenery". As such, we present it to our readers along with all the observations, which still seemed relevant during preparation of the text at the beginning of 2022, for example, statements regarding the success of the industry that can be found in several sections.

SUMMARY

The Newsletter opens with a description of the market volume. In 2021 the Ministry of Health of the Russian Federation issued a total of 908 approvals for conducting clinical trials, up 23.7% over 2020 with 734 approvals. In terms of the total number of new projects, 2021 was in the top three most successful years for the industry over the past decade along with 2012 and 2016, when 915 and 897 new trials were approved, respectively.

367 approvals were issued for conducting international multicentre clinical trials (IMCT), 14% more than in the previous year (322 approvals in 2020). The number of approvals for bioequivalence studies also increased: from 199 in 2020 to 285 in 2021 for Russian sponsors (43.2% increase) and from 56 to 87 for foreign ones (55.4% increase). The number of approvals for other local trials by foreign sponsors doubled over the year: from 18 in 2020 to 36 in 2021. Local trials by Russian sponsors, however, were the only type of trials, the number of approvals for which decreased: from 139 in 2020 to 133 at year-end 2021, i.e. by 4.3%.

Oncology studies, as in every recent year, accounted for the majority of new IMCTs; in 2021 their number stood at 108 protocols or 29.4% of all new international projects. Next is oncohaematology (subsection of oncology) with 37 IMCTs and a share of 10.1%, followed by neurology with 34 approvals and a share of 9.3%. As of year-end 2021 Covid-19 didn't make it into the top 5, although it remained in the top 10 placing eighth with 16 protocols and a share of 4.4%. However, Covid-19 ranks second among other therapeutic areas by the number of patients that were supposed to be enrolled in the trial — 7,273 participants, 5,800 of which for vaccine studies.

In the distribution of IMCTs across the territory of the Russian Federation, the first place was traditionally taken by the Central Federal District with 328 new international trials. It is followed by the North-Western Federal District with 310 projects. Third place was held by the Volga Federal District, where 228 IMCTs were announced. They are followed by the Siberian (194 new IMCTs), Ural (116), Southern (71), North Caucasian (63) and Far Eastern (5 new IMCTs) Federal Districts.

The timeframes for issuing approval documents in 2021 were affected by the introduction of electronic document management for two types of approvals: from 01 July 2021 for approvals for import/export of biosamples and from 01 September 2021 for approvals for import of medicinal products for clinical trials. This innovation resulted in a noticeable shortening of the timeframes. If before September 2021 it took, on average, 18 calendar days to obtain approvals for import of medicinal products, now it takes only eight. Before July 2021 approvals for import/export of biosamples were issued on average within 21 days, after — within 13 days. The average period for obtaining approvals, for which hard-copy document workflow remained, on the contrary, has increased: from 103 days in 2020 to 111 days in 2021 for approvals for conducting clinical trials, from 65 to 77 days for making changes in the protocol, and from 39 to 44 days for other submissions.

In addition to the above-mentioned topics the Newsletter presents the distribution of IMCTs by phase, statistics regarding activity of sponsors and contract research organizations in certain types of trials, assessment of participation of medical organizations in IMCTs and in bioequivalence studies, and detailed statistics on IMCTs dedicated to studying medicinal products used in oncology and oncohaematology in tables in the appendix.

VOLUME AND DYNAMICS OF THE CLINICAL TRIALS MARKET

Comparison of the results of 2021 with the results of 2020 and the preceding 2019 shows that the difficulties encountered by the industry after the start of the coronavirus pandemic have essentially been overcome. Even in 2020 the total number of approvals for clinical trials of all types in Russia decreased insignificantly (by 1.6% as compared to 2019), despite short-term lockdowns and inevitable stress due to the changing rules of the game. In 2021 the total number of approvals increased by 23.7% and amounted to 908 against 734 in 2020 (see Table 1). The results of 2021 exceed not only the figures of the challenging 2020, but also the rather calm 2019 (746 approvals) — by 21.7%.

The number of new approvals for international multicentre clinical trials (IMCTs) was the least subject to fluctuations: the Ministry of Health of the Russian Federation issued 367 of them in 2021 against 322 in 2020, i.e. 14% more. As compared to 2019 (313 approvals) the increase was 17.3%.

The number of approvals for bioequivalence studies also increased: from 199 in 2020 to 285 in 2021 for Russian sponsors (43.2% increase) and from 56 to 87 for foreign ones (55.4% increase). There has also been an increase as compared to 2019: by 74.8% for Russian and 8.7% for foreign sponsors.

The number of approvals for other local trials by foreign sponsors doubled over the year: from 18 in 2020 to 36 in 2021. There is little change from 2019. However the number of local trials by Russian sponsors decreased by 4.3%, from 139 in 2020 to 133 in 2021. As compared to 2019 the reduction is even more noticeable — by 14.2%, from 155 to 133. Thus, the only category of clinical trials in Russia, the number of new projects in which has decreased over the past two years, is local trials by Russian sponsors. However, if we look at the dynamics of this type of trials over a longer period of time (see Diagram 1), it can be seen that in certain previous years (for example, 2013, 2018) Russian sponsors obtained even fewer approvals for local trials.

Table 1

Approvals for Conduct Clinical Trials: 2021 vs 2020 & 2019						
Year	Total	International Multicenter CTs	Local CTs (Foreign Sponsors)	Bioequivalence Studies (Foreign Sponsors)	Local CTs (Local Sponsors)	Bioequivalence Studies (Local Sponsors)
2021	908	367	36	87	133	285
2020	734	322	18	56	139	199
2019	746	313	35	80	155	163
2021 г. vs 2020 г., %	23.7%	14.0%	100.0%	55.4%	-4.3%	43.2%
2021 г. vs 2019 г., %	21.7%	17.3%	2.9%	8.7%	-14.2%	74.8%

Data from www.grls.rosminzdrav.ru

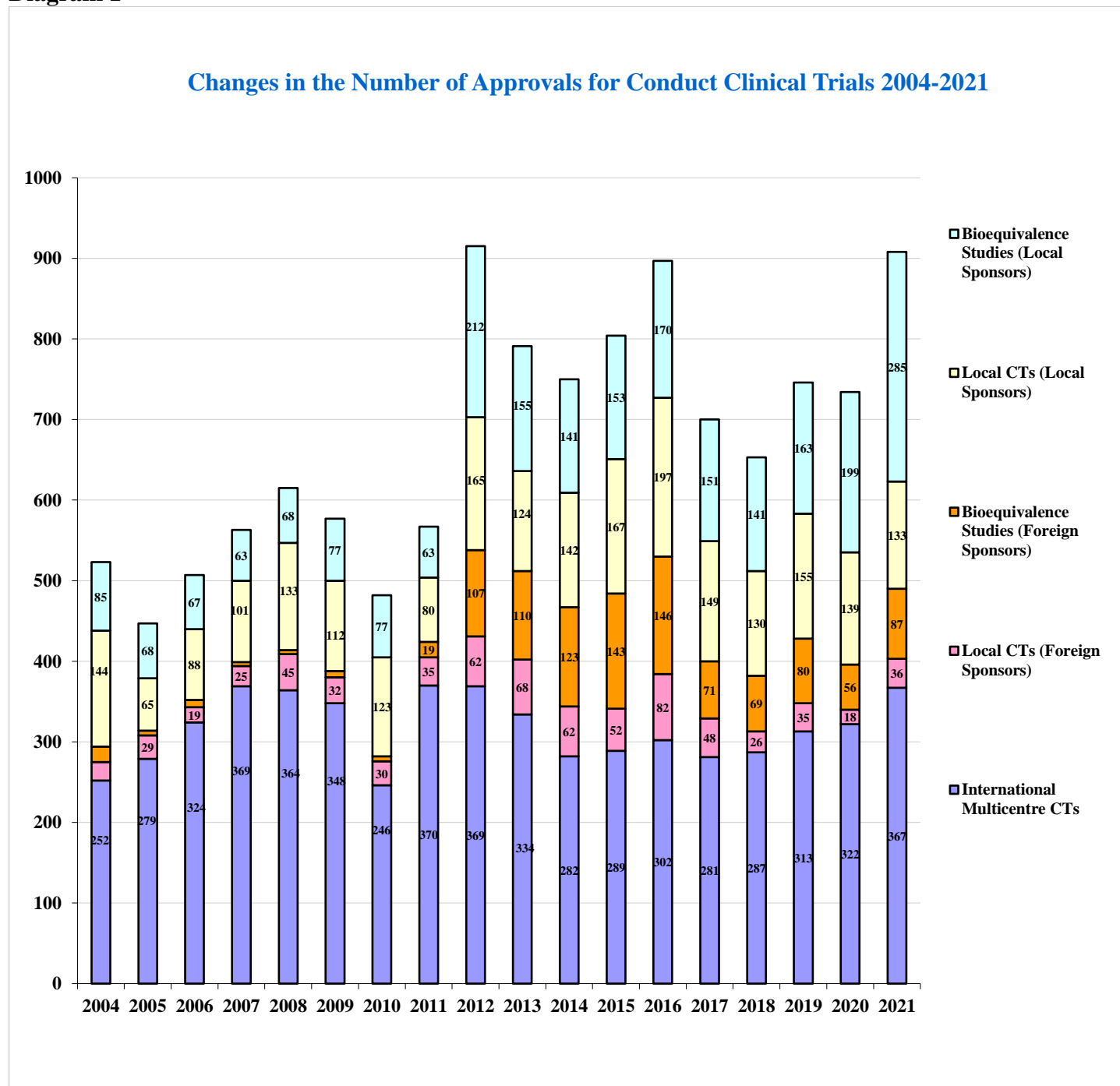
Diagram 1 shows, how the volume and structure of the clinical trials market in Russia has been changing since 2004. It can be seen that in terms of the total number of new projects (as a reminder, there are 908 of them) the past year entered the top three most successful years for the industry, along with 2012 and 2016, when 915 and 897 approvals were issued, respectively.

It can be observed that 2021 was one of the most successful years for international trials as well. The threshold of 360 approvals has only been crossed four times before: in 2007 (369 new IMCTs), in 2008 (364), in 2011 (370) and in 2012 (369). In other words, the result of 2021 is only three projects behind the best indicator over the years of ACTO's monitoring.

Bioequivalence studies by Russian sponsors in 2021 set an absolute record for the entire time of monitoring — 285 approvals. The previous best record was achieved in 2012, when the regulator issued 212 approvals for trials in this category.

As for other types of trials, 2021 went without surprises, the number of approvals for these projects remained within their usual range of fluctuations.

Diagram 1



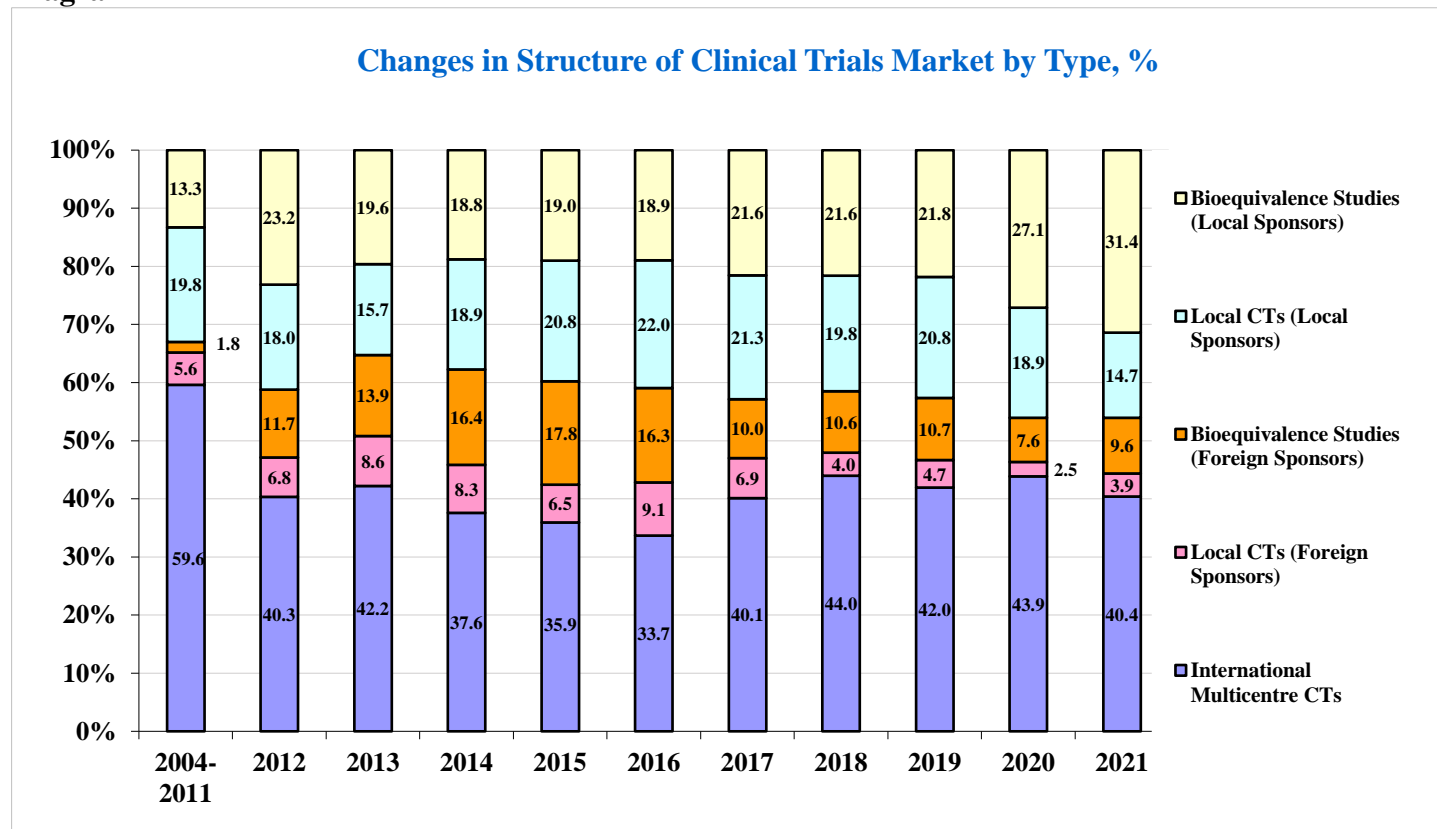
Data from www.grls.rosminzdrav.ru, www.roszdravnadzor.ru

STRUCTURE AND DYNAMICS OF THE CLINICAL TRIALS MARKET BY TYPE

Diagram 2 shows changes in the shares of different types of trials in the overall market structure.

As compared to 2020, the share of bioequivalence studies by Russian sponsors increased most noticeably, from 27.1% to a maximum value of 31.4% in 2021. The share of bioequivalence studies by foreign sponsors also increased, from 7.6% to 9.6%. In addition, the very small share of local trials by foreign sponsors in the total volume has become slightly larger: 3.9% against 2.5% in 2020. Shares of IMCTs, on the contrary, have decreased, from 43.9% in 2020 to 40.4% in 2021, as well as the share of local trials by Russian sponsors, from 18.9% a year earlier to 14.7% in 2021.

Diagram 2



Data from www.grls.rosminzdrav.ru, www.roszdravnadzor.ru

Diagram 3 shows the ratio between various groups of drugs, approvals for local trials of which were obtained by foreign sponsors during 2021 (excluding bioequivalence studies).

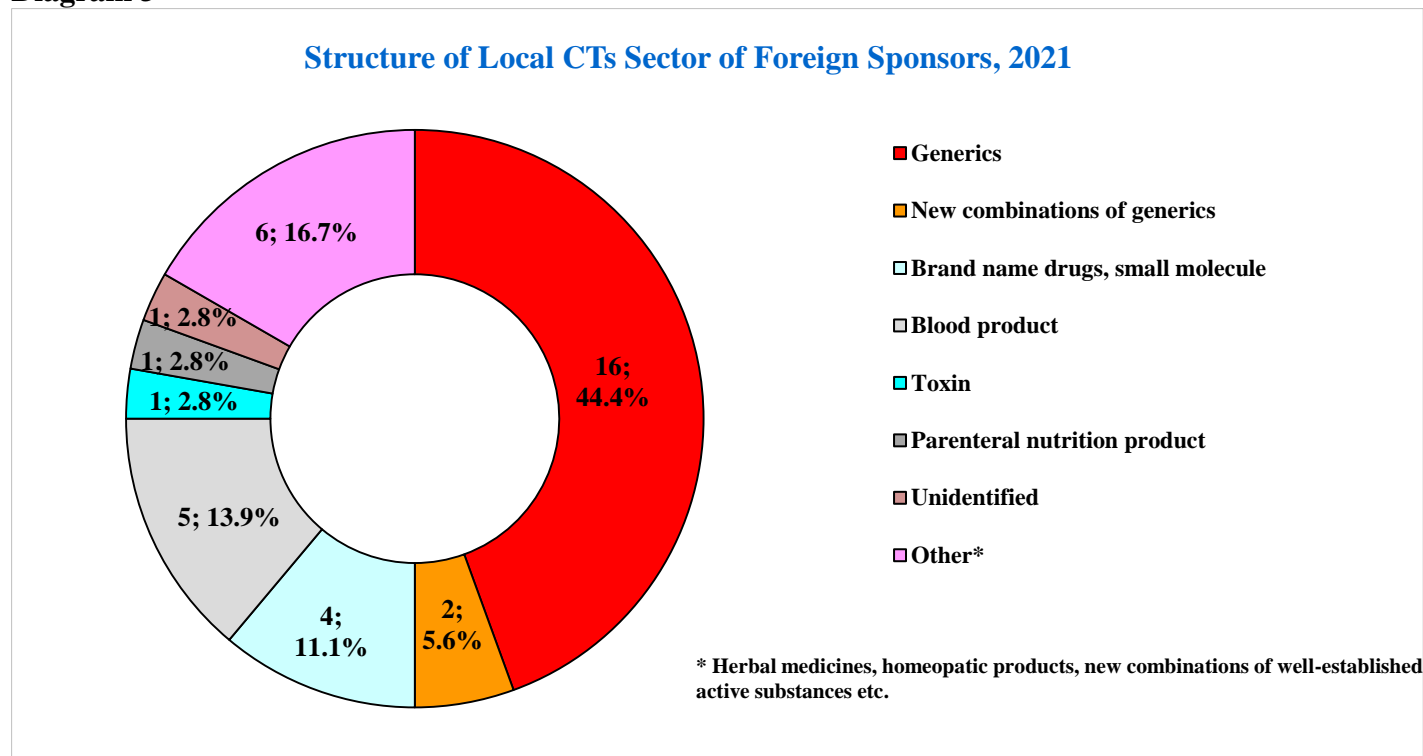
Generics traditionally are in the lead: 16 protocols and a share of 44.4%. They are followed by preparations of herbal or animal origin, homeopathic products, combinations of well-established substances, etc., grouped under the “Other” category in ACTO Newsletters, with a share of 16.7% (six new studies). Next are blood products (five studies) with a share of 5.6% and original small molecules (four projects, 11.1% share). Two approvals (5.6% share) were issued for new combinations of generics, one each (2.8% share) for a toxin, a parenteral nutrition product, and one other drug that could not be identified.

Diagram 4 shows the ratio between different groups of drugs in protocols of local trials by Russian sponsors (excluding bioequivalence studies), approvals for which were issued in 2021.

As usual, generics have the largest share: 27.8%, which corresponds to 37 trials. The second largest is the share of approvals for testing of original small molecules — 21.1%, which corresponds to 28 protocols. Slightly

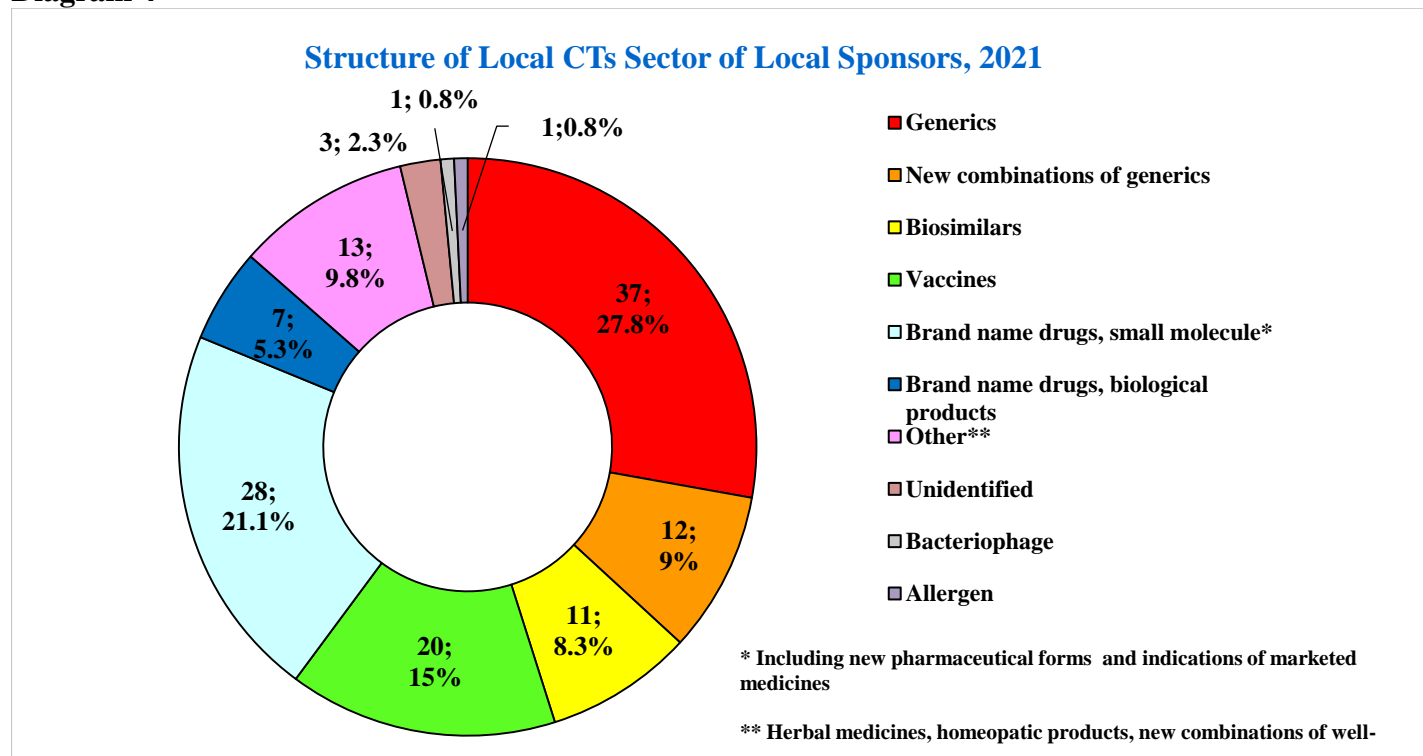
fewer, 15% (20 studies) is accounted for by vaccines. As in the previous years, a large share of approvals is attributed to the “Other” products (9.8%, 13 protocols), in which we include homeopathic products, products based on herbal and animal raw materials, and the like. New combinations of generics appeared in 12 approvals (9% share), biosimilars in 11 (8.3% share), original biological products — in seven (5.3% share). Russian sponsors obtained one approval (0.8% share) for local trials of bacteriophage and one for allergen. Another three active substances (2.3% of approvals) could not be identified.

Diagram 3



Data from www.grls.rosminzdrav.ru

Diagram 4



Data from www.grls.rosminzdrav.ru

STRUCTURE OF THE IMCT MARKET BY PHASE

Diagram 5 shows the distribution of IMCTs approved in 2021 by study phase.

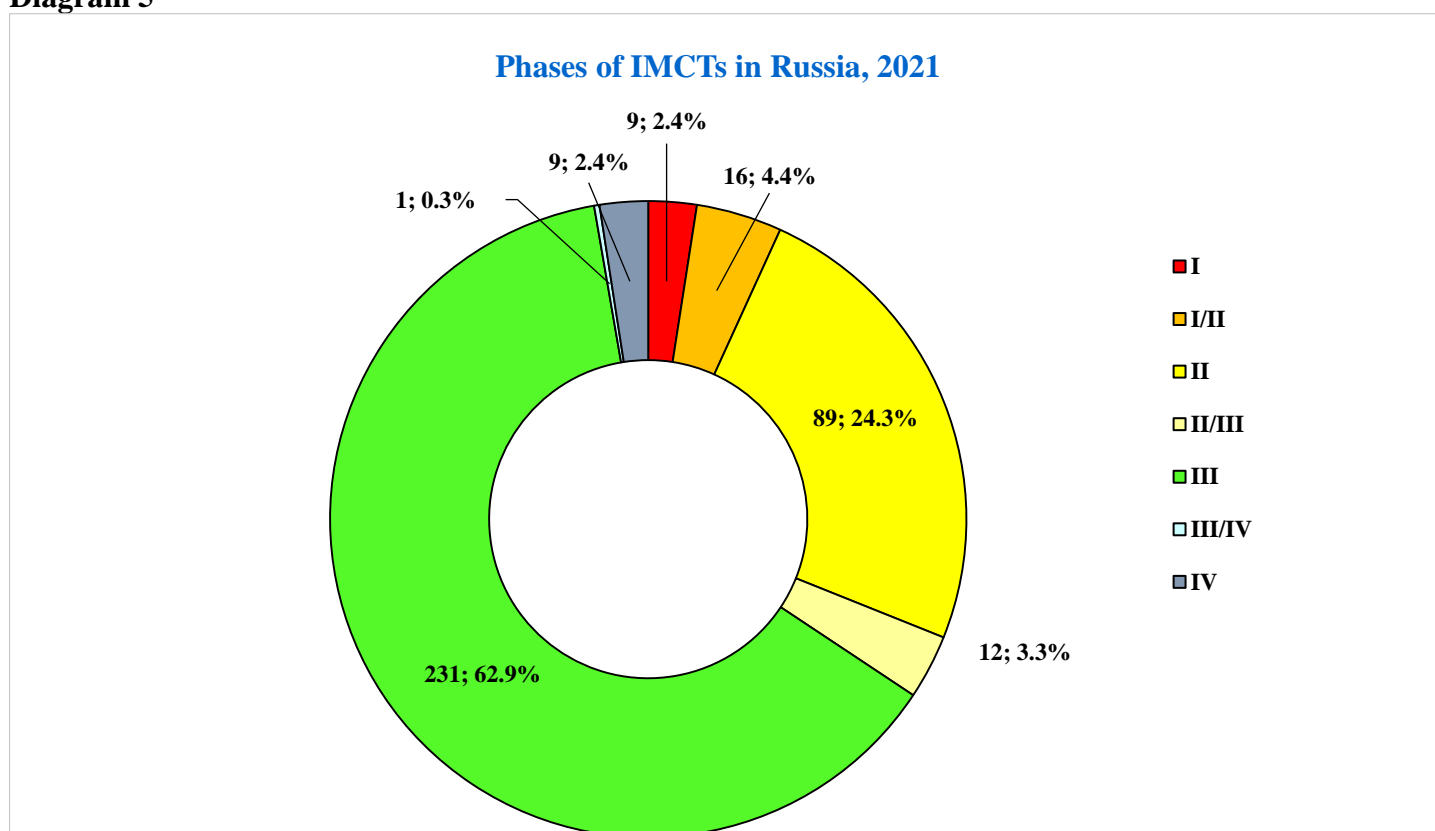
As always, the most approvals were issued for Phase III trials in 2021: 231 or 62.9%. Another protocol was for Phase III–IV, which corresponds to a share of 0.3%.

Phase II accounted for 89 approvals or 24.3%. Another 12 studies pertained to Phase II–III, corresponding to a share of 3.3%.

The share of Phase I protocols traditionally remains small. In 2021 it amounted to nine trials, or 2.4% of all approvals for IMCTs over a year. Eight out of nine protocols were for oncology, one for haematology. Phase I–II trials accounted for 16 protocols or 4.4% of new IMCTs.

The share of Phase IV by volume turned out to be equal to the share of Phase I — 2.4%, nine approvals as well.

Diagram 5



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

STRUCTURE OF THE CLINICAL TRIALS MARKET BY THERAPEUTIC AREAS

Table 2 shows the distribution of IMCTs approved in 2021 by therapeutic area. For a long time, oncology has been dominating this distribution, this time with 108 new protocols and a share of 29.4%. For the first time since we set oncohaematology apart from oncology as a separate category (i.e. since 2016), it managed to place second: 37 IMCTs and 10.1% at year-end 2021. Active growth of oncohaematological studies resulted in neurology, which ranked second in 2020 and 2019, dropping one position with 34 approvals and a share of 9.3% in 2021. Fourth place was taken by rheumatology with 28 new IMCTs and a 7.6% share. Gastroenterology ranked fifth with 22 IMCTs or 6% of all approvals.

Covid-19, which occupied the third line of the table in 2020, didn't make it into the top five in 2021, although it remained in the top 10 placing eighth with 16 protocols and a share of 4.4%. Worth noting is that Covid-19 ranks second among other therapeutic areas in terms of the number of patients that were supposed to be enrolled in the trial — 7,273 participants, 5,800 of which for vaccine studies.

Table 2

Distribution of International Multicenter CTs by Therapeutic Areas, 2021			
Therapeutic Area	Number of IMCTs	Share (%)	Planned number of participants
Oncology	108	29.4%	9 561
Oncohaematology	37	10.1%	968
Neurology	34	9.3%	2 708
Rheumatology	28	7.6%	2 349
Gastroenterology	22	6.0%	1 303
Pulmonology	19	5.2%	2 847
Cardiology and CVD/Vascular surgery	17	4.6%	4 490
Covid-19	16	4.4%	7 273
Haematology	12	3.3%	177
Endocrinology	11	3.0%	788
Ophthalmology	9	2.5%	994
Dermatology	8	2.2%	339
Allergology	7	1.9%	515
Psychiatry	7	1.9%	752
Hepatology	6	1.6%	825
Infectious Diseases (except HIV/HCV/tuberculosis, Covid-19)	6	1.6%	1 230
Nephrology	5	1.4%	592
Obstetrics and gynecology	3	0.8%	248
Otorhinolaryngology	3	0.8%	220
HIV	2	0.5%	115
Immunology	2	0.5%	28
Urology	2	0.5%	203
Maxillofacial surgery	1	0.3%	112
Cosmetology	1	0.3%	50
Phlebology	1	0.3%	320
TOTAL	367	100.0%	39 007

Data from www.grls.rosminzdrav.ru

Table 3 shows the distribution by therapeutic area of local trials of generics, as well as bioequivalence studies by foreign sponsors.

In terms of the number of new projects the leading area is “cardiology and CVD/vascular surgery” with 24 protocols and a 22.9% share of the total number of approvals in this category. The second place belongs to endocrinology with 11 studies and a share of 10.5%. Two categories, (1) analgesics and non-steroidal anti-inflammatory drugs and (2) psychiatry, ranked third with eight approvals and 7.6% each. Fifth place is held by infectious diseases (excluding HIV, hepatitis C, tuberculosis and Covid-19) with seven new studies and a share of 6.7%. Three therapeutic areas ranked sixth at the same time: pulmonology, neurology and HIV with six protocols and 5.7% each.

Covid-19 accounts for only one approval (1% share), however, it is important to note that drugs used in other therapeutic areas, specifically, cardiology and endocrinology, are also used for symptomatic treatment of coronavirus infection. Therefore, some of the new trials in these areas may be related to the desire of sponsors to further promote the drug on the market as part of complex therapy for Covid-19 as well. These drugs include, in particular, the anticoagulant Rivaroxaban and the glucose-lowering medicine Metformin, which appears in the protocols for treatment of Covid-19 patients with diabetes. The first drug accounted for five out of 24 cardiological protocols, the second — for six (including in combinations) out of 11 endocrinological protocols.

Table 3

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars) of Foreign Sponsors, 2021			
Therapeutic Area	Number of CTs	Share (%)	Planned number of participants
Cardiology and CVD/Vascular surgery	24	22.9%	1 922
Endocrinology	11	10.5%	560
Analgesics and NSAIDs	8	7.6%	1 637
Psychiatry	8	7.6%	659
Infectious Diseases (except HIV/HCV/tuberculosis, Covid-19)	7	6.7%	569
Pulmonology	6	5.7%	602
Neurology	6	5.7%	418
HIV	6	5.7%	290
Gastroenterology	5	4.8%	370
Ophthalmology	4	3.8%	614
Gynecology	4	3.8%	422
Rheumatology	4	3.8%	216
Dermatology	3	2.9%	645
Oncohaematology	3	2.9%	242
Urology	2	1.9%	70
Covid-19	1	1.0%	140
Oncology	1	1.0%	60
Anthelmintic medicine	1	1.0%	48
Allergology	1	1.0%	36
TOTAL	105	100.0%	9 520

Data from www.grls.rosminzdrav.ru

Table 4 shows the distribution by therapeutic area of local trials of generics and biosimilars, as well as bioequivalence studies, approvals for which were issued in 2021 to domestic sponsors. In this category of trials neurology is again in the lead in terms of the number of new projects, as in the previous three years. This time it got 56 approvals and a share of 16.2% of the total. The second place belongs to cardiology and cardiovascular diseases with 50 trials and a 14.5% share. The category “HIV/HCV and tuberculosis” ranks third with 28 protocols and a share of 8.1% (of which only two protocols tested anti-tuberculosis drugs and no one to treat hepatitis C). Infectious diseases (excluding HIV, HCV, tuberculosis and Covid-19) placed fourth accounting for 27 approvals and a share of 7.8%. Oncology fell behind just a bit: fifth place with 26 new studies and a 7.5% share.

Covid-19 only ranked 13th in Table 4 with eight new studies and a share of 2.3%. A year earlier it placed eighth with 11 studies and a share of 4.2%. But again, it must be noted that some of the drugs used in the complex therapy of Covid-19 (for example, anticoagulants) are included in the statistics of other therapeutic areas.

Table 4

Distribution of Local CTs and Bioequivalence Studies (Generics and Biosimilars), Conducted by Local Sponsors, 2021			
Therapeutic Area	Number of CTs	Share (%)	Planned number of participants
Neurology	56	16.2%	4 200
Cardiology and CVD	50	14.5%	2 181
HIV/HCV/Tuberculosis	28	8.1%	1 279
Infectious Diseases (except HIV/HCV/tuberculosis, Covid-19)	27	7.8%	1 207
Oncology	26	7.5%	2 324
Analgesics and NSAIDs	21	6.1%	680
Gastroenterology/Coloproctology	14	4.1%	1 053
Rheumatology	13	3.8%	1 385
Psychiatry	13	3.8%	754
Oncohaematology	12	3.5%	732
Endocrinology	11	3.2%	515
Haematology	9	2.6%	499
Covid-19	8	2.3%	1 748
Urology	7	2.0%	1 037
Pulmonology	6	1.7%	374
Transplantology/Immunology	5	1.4%	386
Obstetrics and gynecology	4	1.2%	722
Narcology	4	1.2%	280
Anaesthesiology	4	1.2%	259
Intensive Care	4	1.2%	200
Dermatology	3	0.9%	516
Immunology	3	0.9%	246
Allergology	3	0.9%	111
Otorhinolaryngology	2	0.6%	526
Ophthalmology	2	0.6%	150
Hepatology	2	0.6%	104
Parasitology	2	0.6%	80
Antinicotin therapy	2	0.6%	63
Surgery/Haematology	1	0.3%	196
Phlebology	1	0.3%	150
Coloproctology	1	0.3%	44
Nephrology	1	0.3%	30
TOTAL	345	100.0%	24 031

Data from www.grls.rosminzdrav.ru

Table 5 lists molecules that appeared most frequently in trial approvals for generics and biosimilars in 2021. The content of the table, among other factors, was obviously affected by the coronavirus pandemic. Interest of generic manufacturers in the anticoagulant Rivaroxaban (13 protocols), the glucose-lowering medicine Metformin (eight protocols), the antiviral drugs Ritonavir (seven) and Favipiravir (six) may be explained by the possibility to use these drugs as symptomatic treatment for Covid-19 as well. But, of course, the rating was formed under the influence of multiple reasons. For instance, Dabigatran (seven approvals for trials), on the one hand, is an anticoagulant and is included in the Covid-19 treatment protocols, and on the other hand, it belongs to popular drugs, patent protection of which will soon expire¹.

Table 5

Most Requested INN Used in Clinical Trials of Generics in 2021				
Substance	Number of CTs of foreign generics	Number of CTs of local generics	All clinical trials to a given INN	Therapeutic Area
Rivaroxaban	5	8	13	Cardiology and CVD, surgery, covid-19
Pirindopril (separately and in fixed combinations)	4	5	9	Cardiology and CVD
Metformin (separately and in fixed combinations)	6	2	8	Endocrinology, perhaps covid-19
Amlodipin (separately and in fixed combinations)	3	4	7	Cardiology and CVD
Dabigatran	4	3	7	Cardiology and CVD, surgery
Deferasirox	–	7	7	Haematology
Ibuprofen (separately and in fixed combinations)	2	5	7	Analgesic and NSAIDs
Ritonavir (separately and in fixed combinations)	2	5	7	HIV, perhaps covid-19
Vildagliptin (separately and in fixed combinations)	2	4	6	Endocrinology
Indapamide (in fixed combination)	3	3	6	Cardiology and CVD
Lamivudine (separately and in fixed combinations)	2	4	6	HIV
Lopinavir (in fixed combinations)	1	5	6	HIV, other infectious diseases, perhaps covid-19
Raltegravir	–	6	6	HIV
Favipiravir (separately and in fixed combinations)	–	6	6	Covid-19
Ethylmethylhydroxypyridine succinate	–	6	6	Neurology, ophthalmology
Dasatinib	2	3	5	Oncohaematology
Levofloxacin (separately and in fixed combinations)	2	3	5	Infectious diseases, ophthalmology
Melatonin (separately and in fixed combinations)	1	4	5	Neurology
Paliperidone	5	–	5	Psychiatry
Paracetamol (separately and in fixed combinations)	3	2	5	Analgesic and NSAIDs, infectious diseases
Sunitinib	–	5	5	Oncology
Tamsulosin (separately and in fixed combinations)	–	5	5	Urology
Valsartan (separately and in fixed combinations)	–	4	4	Cardiology and CVD
Candesartan (separately and in fixed combinations)	–	4	4	Cardiology and CVD
Oseltamivir	1	3	4	Infectious diseases
Pantoprazole	1	3	4	Gastroenterology
Sitagliptin (separately and in fixed combinations)	2	2	4	Endocrinology, perhaps covid-19
Tolperisone	1	3	4	Neurology
Etoricoxib	2	2	4	Rheumatology

Data from www.grls.rosminzdrav.ru

¹ “[Top drugs in danger of losing patent protection](#)”, Endpoints News, 09.02.2022.

Tables 6 and 7 show the distribution by therapeutic area of local trials of original medications by foreign and Russian sponsors, respectively. In both categories of sponsors, the top spots are held by drugs intended to combat the new coronavirus infection. In 2021 foreign sponsors showed as much interest in gastroenterology and haematology as in Covid-19 (three approvals in each of the said areas). Two protocols are oncohaematological, another seven therapeutic areas got one new trial each.

27 protocols of Russian sponsors were attributed to Covid-19. Testing of domestic vaccines provided this therapeutic area with a huge lead over the rest in terms of the planned number of enrolled patients. Covid-19 is followed by trials of drugs for treatment of infectious diseases (except for HIV, hepatitis C, tuberculosis and Covid-19) — 17 protocols. Further behind are neurology (six trials), oncology (four) and 11 other therapeutic areas with three or less new projects.

Table 6

Distribution of Local CTs of Brand Name Drugs of Foreign Sponsors, 2021		
Therapeutic Area	Number of CTs	Planned number of participants
Covid-19	3	674
Gastroenterology	3	390
Haematology	3	36
Oncohaematology	2	200
Gynecology	1	546
Neurology	1	364
Cosmetology	1	220
Infectious Diseases (except HIV/HCV/tuberculosis, Covid-19)	1	250
Rheumatology	1	120
Intensive Care	1	70
Immunology	1	45
TOTAL	18	2 915

Data from www.grls.rosminzdrav.ru

Table 7

Distribution of Local CTs of Brand Name Drugs (Including Biological Products) of Local Sponsors, 2021			
Therapeutic Area	Number of CTs	Share (%)	Planned number of participants
Covid-19	27	37.5%	47 906
Infectious Diseases (except HIV/HCV/tuberculosis, Covid-19)	17	23.6%	5 399
Neurology	6	8.3%	1 705
Oncology	4	5.6%	309
Cardiology and CVD	3	4.2%	439
HIV/Tuberculosis	2	2.8%	8 010
Gynecology	2	2.8%	1 116
Otorhinolaryngology	2	2.8%	488
Allergology	2	2.8%	475
Psychiatry	2	2.8%	215
Intensive Care	1	1.4%	176
Urology	1	1.4%	135
Immunology	1	1.4%	100
Pulmonology	1	1.4%	46
Dermatology	1	1.4%	20
TOTAL	72	100.0%	66 539

Data from www.grls.rosminzdrav.ru

DISTRIBUTION OF APPROVED IMCTs ACROSS RUSSIA

Table 8 shows the distribution of IMCTs across the territory of the Russian Federation².

The Central Federal District with 328 new international projects traditionally heads the list in terms of “the number of IMCTs per region”. As compared to 2020 it improved the result by 34 new projects. The maximum contribution to the growth of the region’s indicators was made by Moscow and Moscow Region. Moscow got 308 approvals in 2021, which is 34 new IMCTs more than a year earlier. Moscow Region got 56 approvals, 31 more than in 2020. Yaroslavl Region, although remaining active within the Central Federal District with 59 IMCT approvals in 2021, has lost quite a bit: 18 less than in 2020.

Second place in terms of “the number of IMCTs per region” belongs to the North-Western Federal District with 310 new international trials. In 2019 it managed to overtake the Central Federal District and top the ranking, however, even after returning to second place it continues to stay close to first place. In 2021 the North-Western Federal District improved its 2020 result by 23 IMCTs. The growth leaders within the North-Western Federal District over the past year are St. Petersburg with 303 studies (23 IMCTs more than in 2020) and Leningrad Region with 36 (14 more). Negative dynamics within the region was demonstrated by Arkhangelsk Region, where 34 new IMCTs were announced in 2021, which is 13 less than a year earlier.

The third place in terms of “the number of IMCTs per region” was held by the Volga Federal District, where 228 international trials were announced, which is 18 more than the result of 2020. The main contribution to the growth of the region was made by the Udmurt Republic with 25 projects (18 IMCTs more than a year earlier) and Penza Region with 20 (13 more). Kirov Region reduced its activity: 13 new IMCTs in 2021 against 25 in 2020.

Remaining places in the ranking in terms of “the number of IMCTs per region” were distributed as follows: fourth place belongs to the Siberian Federal District (194 new IMCTs, three more than in 2020), fifth place — Ural (116, three trials less), sixth — Southern (71, major reduction by 22 IMCTs), seventh — North Caucasian (63, an increase by 12 studies), and eighth — Far Eastern Federal District (five new IMCTs, three less than in 2020).

In terms of a rather conservative indicator “the number of IMCTs per million of population” the Russian regions were distributed traditionally. First place was taken by the North-Western Federal District, where 22.3 new IMCTs per million residents were announced (20.5 a year earlier). The second position belongs to the Siberian Federal District with a result of 11.4 (11.2 in 2020). The Ural Federal District ranked third with 9.4 (9.6 previously). Next are the Central Federal District (8.3 against 7.5 a year earlier) and the Volga Federal District (7.8 against 7.3 in 2020). The Southern Federal District placed sixth in 2020 with 5.6 IMCTs per million of population, however activity of the region decreased in 2021, and now it only came in seventh with a result of 4.3 giving place to the North Caucasian Federal District (6.3 in 2021 and 5.1 in 2020). The ranking is closed by the Far Eastern Federal District, activity of which reduced to 0.6 in 2021 against 1 IMCT per million of population a year earlier.

² See the calculation methodology in [ACTI Newsletter No. 12](#).

Table 8

Distribution of IMCTs approved in 2021 by regions of the RF									
Region	Number of IMCTs, per region	Number of IMCTs, per million population*	Number of health care organizations, which approved sites for IMCTs, per region	How many times medical organizations of the region were involved in IMCTs (number of open sites)	Region	Number of IMCTs, per region	Number of IMCTs, per million population*	Number of health care organizations, which approved sites for IMCTs, per region	How many times medical organizations of the region were involved in IMCTs (number of open sites)
Central Federal District	328	8.3	175	992 (1035)	North Caucasian Federal District	63	6.3	13	67
Moscow	308	24.3	108	672 (708)	Stavropol Territory	59	21.1	11	62
Yaroslavl Region	59	49.2	16	70	Kabardino-Balkarian Republic	3	3.3	1	3
Moscow Region	56	7.3	10	60	Republic Of North Ossetia – Alania	2	2.9	1	2
Kaluga Region	41	41.0	3	44 (49)	Siberian Federal District	194	11.4	67	374 (377)
Smolensk Region	34	37.8	6	35	Novosibirsk Region	86	30.7	25	102
Ryazan Region	29	26.4	4	32 (34)	Omsk Region	73	38.4	9	75
Ivanovo Region	21	21.0	4	21	Kemerovo Region	47	18.1	8	52 (53)
Kursk Region	16	14.5	4	16	Krasnoyarsk Territory	46	15.9	7	50
Voronezh Region	12	5.2	4	12	Tomsk Region	45	40.9	6	48 (50)
Tula Region	7	4.7	2	7	Altai Territory	43	18.7	10	44
Vladimir Region	6	4.6	3	6	Irkutsk Region	3	1.3	2	3
Kostroma Region	3	5.0	1	3	Ural Federal District	116	9.4	32	157
Tambov Region	3	3.0	1	3	Chelyabinsk Region	66	19.4	10	76
Lipetsk Region	3	2.7	3	3	Sverdlovsk Region	55	12.8	17	60
Tver Region	3	2.3	2	3	Tyumen Region	20	13.3	4	20
Belgorod Region	3	2.0	2	3	Khanty-Mansi Autonomous Area	1	0.6	1	1
Orlov Region	1	1.4	1	1	Volga Federal District	228	7.8	95	495 (505)
Bryansk Region	1	0.8	1	1	Republic of Tatarstan	102	26.2	16	116 (118)
Southern Federal District	71	4.3	24	95	Nizhny Novgorod Region	69	21.6	14	76 (77)
Rostov Region	38	9.0	11	43	Saratov Region	57	23.8	13	65 (71)
Krasnodar Territory	35	6.1	9	39	Samara Region	55	17.2	15	57 (58)
Volgograd Region	13	5.2	4	13	Republic of Bashkortostan	51	12.8	5	52
Northwestern Federal District	310	22.3	139	912 (940)	Udmurtian Republic	25	16.7	7	25
Saint-Petersburg	303	56.1	120	792 (820)	Penza Region	20	15.4	5	20
Leningrad Region	36	18.9	6	38	Ulyanovsk Region	18	15.0	2	18
Arkhangelsk Region	34	30.9	4	34	Republic of Mordovia	17	21.3	3	17
Republic of Karelia	21	34.4	1	21	Orenburg Region	17	8.9	4	17
Republic of Komi	7	8.8	2	7	Perm Territory	16	6.2	6	16
Novgorod Region	6	10.0	1	6	Kirov Region	13	10.0	4	13
Kaliningrad Region	6	6.0	2	6	Mari El Republic	3	4.3	1	3
Murmansk Region	4	5.7	1	4	Far Eastern Federal District	5	0.6	3	5
Pskov Region	2	3.3	1	2	Trans - Baikal Territory	3	2.7	1	3
Vologda Region	2	1.7	1	2	Republic of Buryatia	1	1.0	1	1
					Khabarovsk Territory	1	0.8	1	1

*We used data of Rosstat on the resident population of the region as of January 1, 2021

Diagram 6 represents grouping of the constituent entities of the Russian Federation depending on how many new international trials were planned to be launched there in 2021.

The “over 200 IMCTs” segment is traditionally occupied by two capitals, Moscow and St. Petersburg.

The “101–200 IMCTs” segment includes only one constituent entity, the Republic of Tatarstan.

Eleven constituent entities of the Russian Federation at year-end 2021 ended up in the “51–100 IMCTs” segment. Nine of them have remained there since last year, specifically, the Republic of Bashkortostan, Nizhny Novgorod Region, Novosibirsk Region, Omsk Region, Samara Region, Saratov Region, Sverdlovsk Region, Chelyabinsk Region and Yaroslavl Region. They were joined by Moscow Region and Stavropol Territory, which in 2020 were included in the segments with less activity. Tomsk Region and Krasnodar Territory, on the contrary, reduced their activity and left the segment.

Ten constituent entities comprise a group of regions, where 31 to 50 new IMCTs were announced. Since last year six regions have retained their place in the group: Altai and Krasnoyarsk Territories, Arkhangelsk, Kemerovo, Rostov and Smolensk Regions. Kaluga and Leningrad Regions increased their activity and thus earned their places in the group. Krasnodar Territory and Tomsk Region ended up there due to decrease in the number of new international projects as compared to 2020. Ryazan Region and Stavropol Territory left the group, the former dropped down to the segment with less activity, the latter made it into the more active group.

The next segment, “21–30 IMCTs”, includes four constituent entities of the Russian Federation: Ryazan Region, which has decreased its activity as compared to 2020, as well as the Republic of Karelia, Udmurt Republic and Ivanovo Region, activity of which, on the contrary, has increased. Composition of this segment has been completely renewed as compared to 2020: Moscow and Leningrad Regions left the segment due to increased activity, and Volgograd, Kirov and Tyumen Regions — due to its decrease.

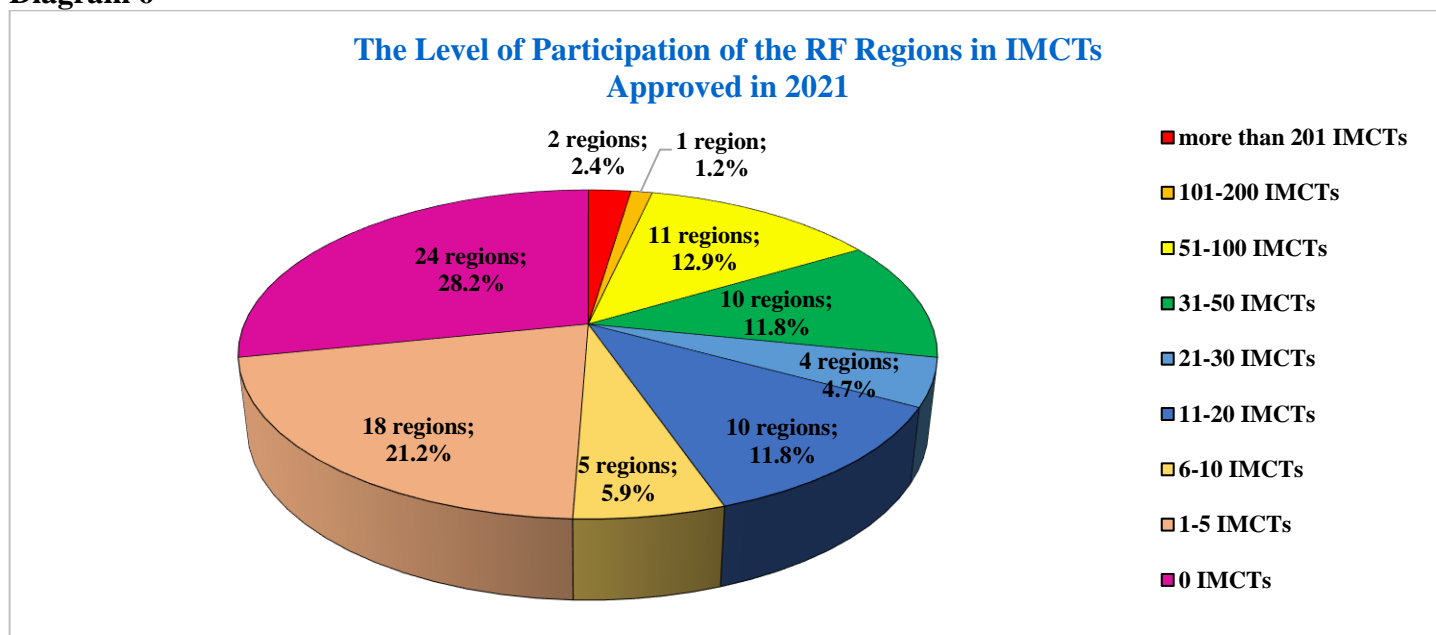
11 to 20 new international trials were announced in ten constituent entities of the Russian Federation. Four of them have retained their positions since last year: Kursk and Orenburg Regions, Perm Territory and the Republic of Mordovia. Due to increase in activity Voronezh, Penza and Ulyanovsk Regions joined the segment together with the regions with decreased activity: Volgograd, Kirov and Tyumen Regions. Ivanovo and Kaluga Regions left the segment having moved up into the category with higher activity, just like the Republic of Karelia, as well as Murmansk and Tver Regions, where the number of new projects decreased.

The “6–10 IMCTs” segment is represented by five constituent entities of the Russian Federation, four of which remained unchanged from last year: the Republic of Komi, Vladimir, Kaliningrad and Tula Regions. They were joined by Novgorod Region, activity of which has increased as compared to 2020. Voronezh, Penza, Ulyanovsk Regions and the Udmurt Republic left the segment (their activity has increased), as well as Irkutsk Region (decreased activity).

Among the 18 constituent entities of the Russian Federation with only 1–5 new IMCTs announced nine retained their positions from last year. These are Belgorod, Bryansk, Vologda, Kostroma, Lipetsk and Tambov Regions, as well as the Kabardino-Balkarian Republic, the Republic of Mari El and Trans-Baikal Territory. Due to decrease in the number of new IMCTs Irkutsk, Murmansk and Tver Regions joined the segment. In addition, in 2021 it included six regions where no new IMCTs were announced in 2020, these are Oryol and Pskov Regions, the Republic of Buryatia, the Republic of North Ossetia – Alania, Khabarovsk Territory and Khanty-Mansi Autonomous Area – Yugra.

24 constituent entities of the Russian Federation didn't plan to start any new IMCTs in 2021. In 2020, there were 28 of these.

Diagram 6



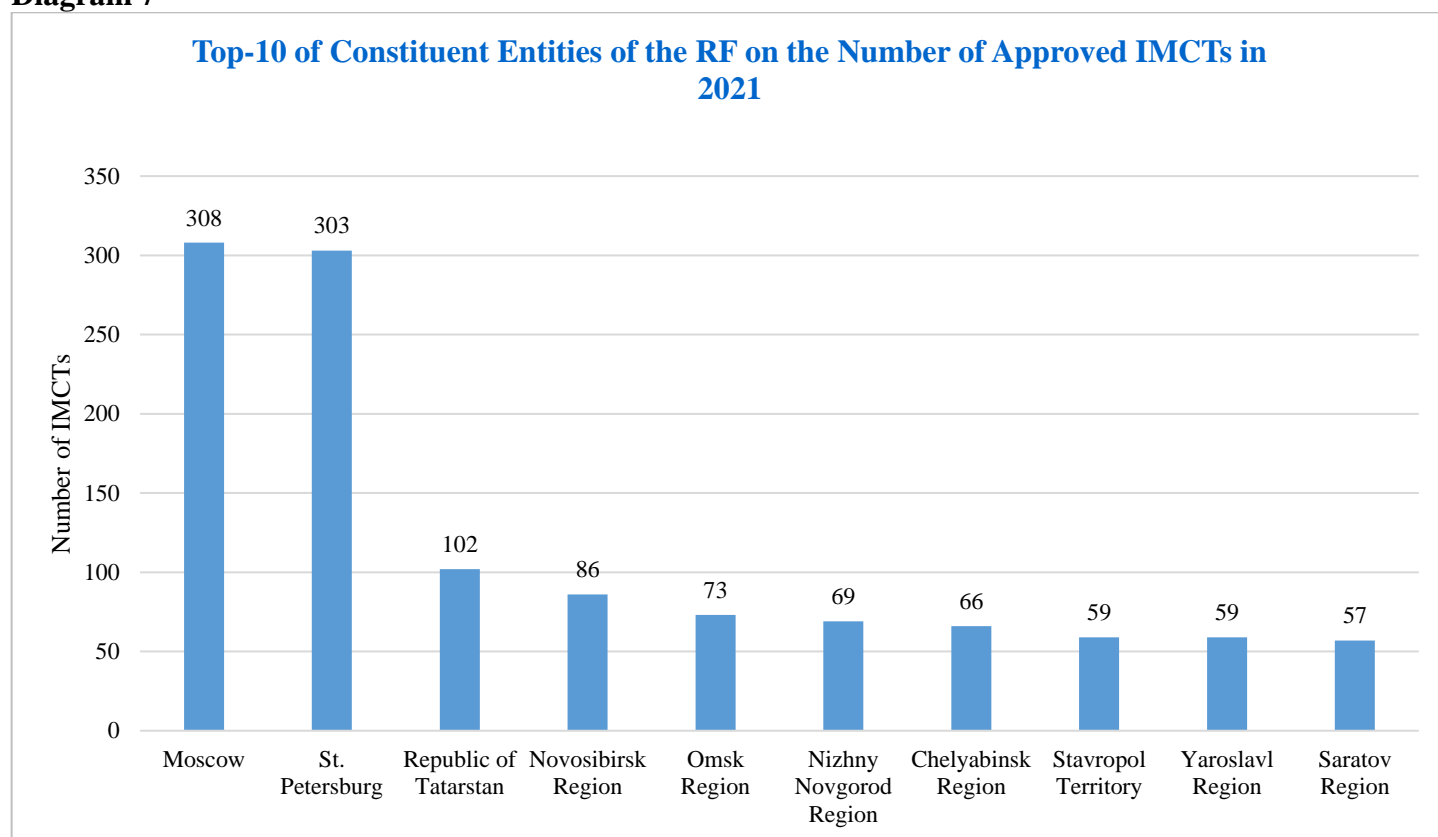
Data from www.grls.rosminzdrav.ru

Ten constituent entities of the Russian Federation leading by number of IMCTs approved in 2021, in absolute and relative figures, are shown in Diagrams 7 and 8.

Eight out of ten leaders in terms of the absolute number of new international projects confirmed their status and remained in the top 10. Traditional rotation of Moscow and St. Petersburg atop the ranking, which was interrupted in 2020, has resumed. This time Moscow took the lead with 308 new IMCTs. St. Petersburg is only five trials behind. Tatarstan placed third with a result of 102 IMCTs (101 a year earlier). Novosibirsk Region obtained fewer approvals than in 2020, 86 versus 96, but retained fourth place. Omsk Region is in fifth position with 73 IMCTs (65 and eighth place in 2020), Nizhny Novgorod Region is sixth with 69 (previously 66 and seventh place), next is Chelyabinsk Region with 66 (67 and sixth place a year earlier). They are followed by Stavropol Territory and Yaroslavl Region, both with 59 IMCTs. In 2020 Stavropol Territory was not presented in the top 10 and Yaroslavl Region was in fifth place with a result of 77 trials. The top ten in 2021 is closed by Saratov Region with 57 new international projects. It, too, was not presented in the top 10 a year earlier. Tomsk and Samara Regions, which ranked ninth and tenth in 2020, dropped out of the top ten.

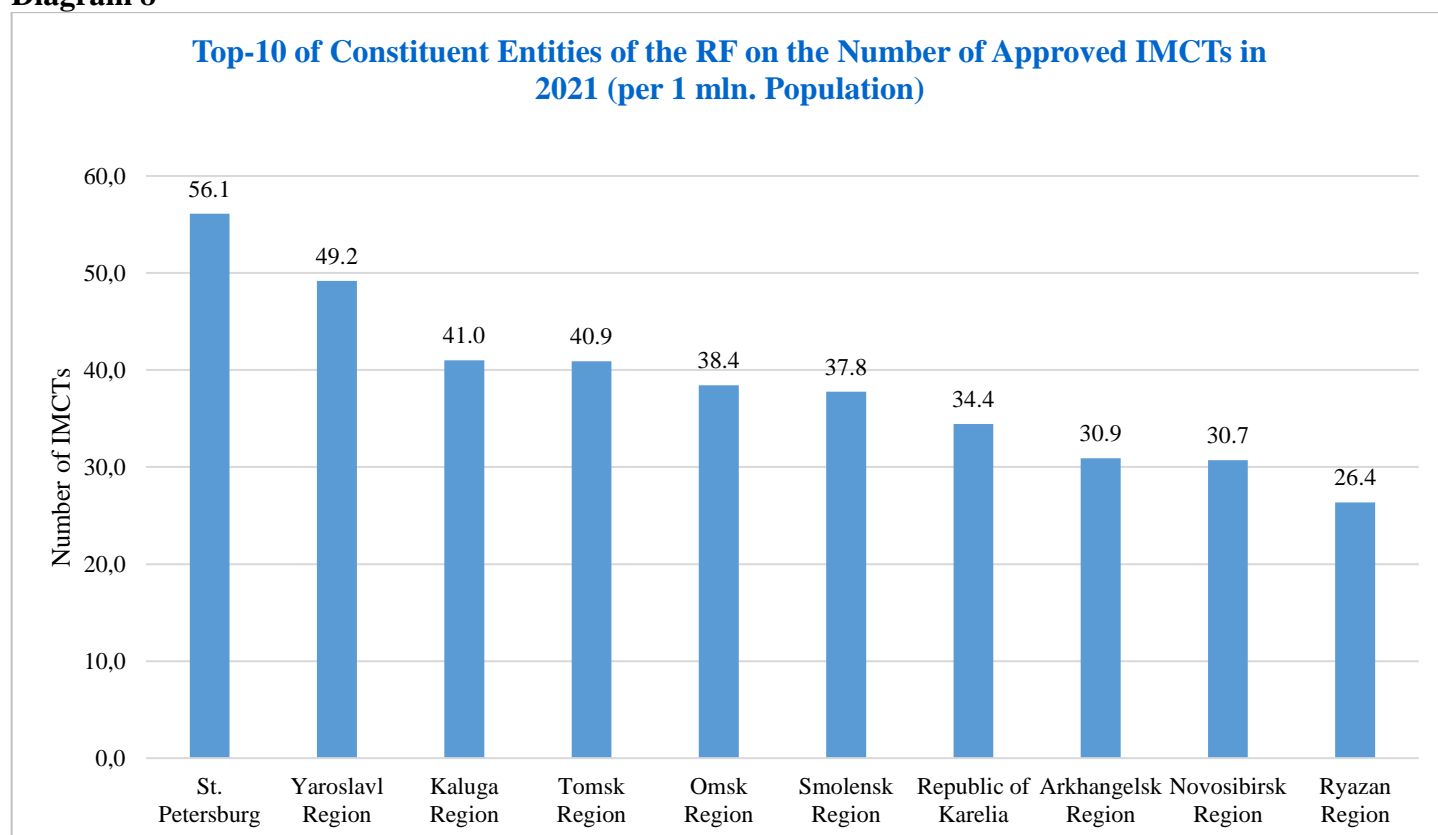
In terms of the number of IMCTs per million of population the changes in the top 10 are also small, but remarkable. Perhaps the most unexpected is that the leader is St. Petersburg and not Yaroslavl Region, as it has been throughout recent years. Its result in 2021 is 56.1 IMCTs per million residents (51.9 and third place in 2020). The change of leaders is not so much due to increase in activity in St. Petersburg, but to its decrease in Yaroslavl Region: the indicator of the latter dropped from 59.2 in 2020 to 49.2 in 2021. Third place in the top 10 with an indicator of 41.0 was taken by Kaluga Region not presented in the previous year's top ten. The Republic of Tatarstan, which ranked tenth in 2020, dropped out of the top 10. The rest of constituent entities of the Russian Federation remained on the leaderboard with five of them ranking lower than last year (Tomsk, Smolensk, Arkhangelsk, Novosibirsk and Ryazan Regions) and two — higher (Omsk Region and the Republic of Karelia).

Diagram 7



Data from www.grls.rosminzdrav.ru

Diagram 8



Data from www.grls.rosminzdrav.ru

The ranking of medical organizations that were most often involved in conducting new IMCTs under approvals in 2021 has undergone the following changes.

As many as twelve organizations retained their top 20 spots from the previous year:

- I. P. Pavlov First Saint Petersburg State Medical University ranked first again, despite slight reduction in activity from 71 to 69 new IMCTs;
- N. N. Blokhin Russian Cancer Research Center, Moscow — remained second having slightly increased the number of new IMCTs from 61 to 65;
- Omsk Clinical Oncological Dispensary moved up from sixth to third place due to increase in the number of new international trials from 37 in 2020 to 48 in 2021;
- Almazov National Medical Research Centre, St. Petersburg — fourth place with 47 IMCTs in 2021, eighth place and 33 IMCTs a year earlier;
- N. N. Petrov National Medicine Research Center of Oncology, St. Petersburg — dropped from third to fifth place, although the number of new IMCTs at the site increased slightly, from 44 to 46;
- I. M. Sechenov First Moscow State Medical University, Moscow — sixth place in 2021, down from fourth place in 2020, despite an increase in the number of new international trials from 39 to 45;
- St. Petersburg Clinical Scientific and Practical Center for Specialized Types of Medical Care (Oncological) — it is already a common case when the number of new projects grows from 38 to 45, however the place in the ranking drops from fifth to seventh;
- Saratov State Medical University named after V.I. Razumovsky — eighth place with 31 new IMCTs in 2021 against twelfth spot in the ranking with 26 IMCTs in 2020;
- Obninsk National Medical Research Radiological Centre — 12th place with 28 IMCTs in 2021 against seventh place with 34 IMCTs in 2020;
- Arkhangelsk Clinical Oncological Dispensary — 13–15th place with 25 new projects in 2021 against ninth place with 33 IMCTs in 2020;
- Kazan Republican Clinical Oncological Dispensary — 16–17th place with 26 IMCTs in 2021 against 11th spot with 30 IMCTs at year-end 2020;
- Medsi Group of Companies, Moscow — the only medical organization in the top 20 representing the non-governmental sector of the healthcare system, ranks 18th with 25 IMCTs, which is slightly worse than in 2020, when Medsi ranked 16th with 23 new projects.

Three organizations that were included in the top 20 of 2019 and returned to it after a temporary absence:

- Kazan State Medical University — tenth place with 29 trials in 2021, a year earlier — 27–28th place with 19 projects;
- Pirogov Russian National Research Medical University, Moscow — 19th place with 24 IMCTs, 37–41st place with 17 trials in 2020;
- North-Western State Medical University named after I.I. Mechnikov, St. Petersburg — 20th place with 24 projects in 2021, in 2020 — 42nd place with 16 IMCTs.

Five organizations were included in the top 20 by number of new IMCTs for the first time over the course of ACTO's monitoring.

- Botkin Hospital, Moscow — went up from 37–41st place straight to ninth having increased the number of new IMCTs from 17 to 31 as compared to 2020, i.e. almost twofold;
- Moscow City Oncological Hospital No. 62, Istra settlement, Moscow Region — moved up from 43–48th place to 11th, the number of new IMCTs increased from 15 in 2020 to 29;
- Republican Clinical Oncological Dispensary, Ufa — 13–15th place with 27 new projects in 2021, 27–28th place with 19 IMCTs a year earlier;
- The Loginov Moscow Clinical Scientific Center — 13–15th place as well with the same 27 IMCTs in 2021 against 49–53rd place with 14 projects in 2020;
- Ultrasound 4D Clinic, Pyatigorsk — 16–17th place with 26 IMCTs, 33–36th place with 18 projects a year earlier.

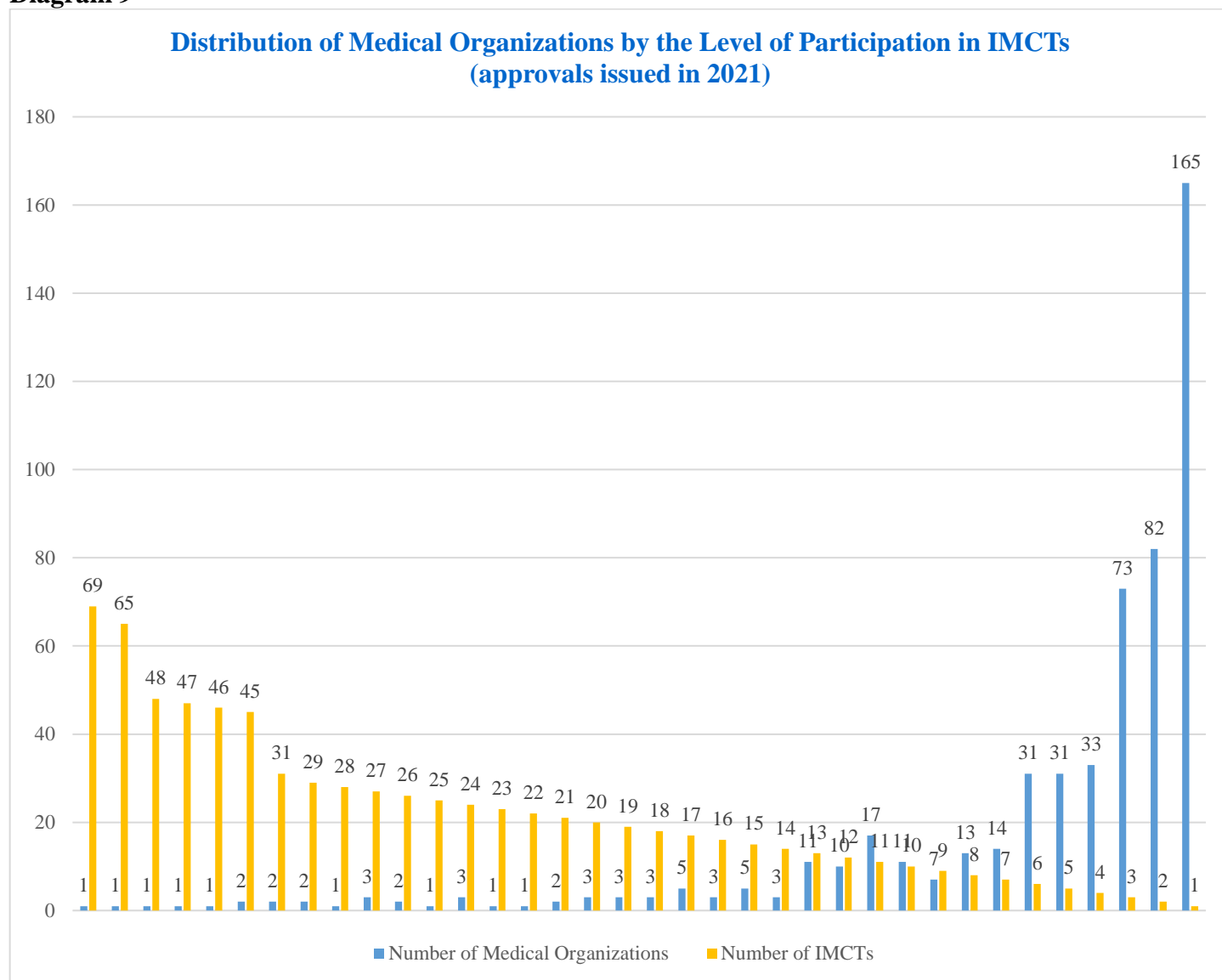
Table 9

Top-20 Medical Organizations on the Activity of Participation in IMCTs Approved in 2021				
Place in ranking	Name of medical organization	Number of IMCTs approved in 2021 with participation of this medical organization	Number of sites approved in 2021 for conducting IMCTs	Number of IMCTs and ranking of the sites (on approvals issued in 2020)
1	I. P. Pavlov First St. Petersburg State medical University, Russian Ministry of Health, St. Petersburg	69	73	71 (1)
2	N. N. Blokhin Russian Cancer Research Centre, Russian Ministry of Health, Moscow	65	66	61 (2)
3	Clinical Oncological Dispensary, Omsk	48	48	37 (6)
4	Almazov National Medical Research Centre, St. Petersburg	47	48	33 (8)
5	N.N. Petrov National Medicine Research Center of Oncology, Russian Ministry of Health, St. Petersburg	46	50	44 (3)
6	I. M. Sechenov First Moscow State Medical University, Russian Ministry of Health, Moscow	45	50	39 (4)
7	St. Petersburg Clinical Scientific and Practical Center for Specialized Types of Medical Care (Oncological), St. Petersburg	45	45	38 (5)
8	Saratov State Medical University named after V. I. Razumovsky, Russian Ministry of Health, Saratov	31	37	26 (12)
9	The Botkin Hospital, Moscow	31	33	17 (37–41)
10	Kazan State Medical University, Kazan	29	31	19 (27–28)
11	Moscow City Oncological Hospital No. 62, Moscow Department of Healthcare, Moscow region, Krasnogorsky district, Istra	29	29	15 (43–48)
12	National Medical Research Radiological Centre, Obninsk	28	33	34 (7)
13–15	Republican Clinical Oncological Dispensary, Ufa	27	27	19 (27–28)
13–15	Arkhangelsk Clinical Oncological Dispensary, Arkhangelsk	27	27	33 (9)
13–15	The Loginov Moscow Clinical Scientific Center, Moscow	27	27	14 (49–53)
16–17	Republican Clinical Oncological Dispensary, Kazan	26	26	30 (11)
16–17	Ultrasound 4D Clinic, Stavropol Territory, Pyatigorsk	26	26	18 (33–36)
18	Group of companies Medsi, Moscow	25	26	23 (16)
19	Pirogov Russian National Research Medical University, Moscow	24	26	17 (37–41)
20	North-Western State Medical University named after I.I. Mechnikov, St. Petersburg	24	25	16 (42)

Data from: www.grls.rosminzdrav.ru

Distribution of IMCTs approved in 2021 by medical organization is shown in Diagram 9. Nine clinics were planned to be involved in conducting more than 30 new IMCTs, 16 — in conducting 21 to 30 studies, 63 — 11 to 20 projects, 76 — six to ten studies, 137 — three to five, 82 organizations declared its participation in two IMCTs and 165 — in only one. In total, 548 institutions were involved in new international projects in 2021, which is six more than in the previous year.

Diagram 9



Data from www.grls.rosminzdrav.ru

We traditionally consider the two regions with the largest number of IMCTs separately and in more detail than the others. Tables 10 and 11 show the distribution of IMCTs by medical organizations of various departmental subordinations in Moscow and St. Petersburg.

In Moscow (Table 10) it was planned to involve 108 medical organizations in conducting new IMCTs during 2021, which is five more than in 2020. The number of sites approved during the year also increased: 708 in 2021 against 690 in 2020.

Clinics of the Ministry of Health of Russia retained their leadership in terms of the number of approved IMCT sites. This number increased from 270 in 2020 to 292 in 2021. The number of medical organizations where new sites were announced to open remained unchanged — 23 clinics.

Second place in terms of the number of approved sites is still occupied by medical organizations subordinated to the Department of Health of Moscow, although the main indicators have decreased compared to 2020: the number of new sites from 201 to 175, and the number of organizations involved from 33 to 31.

Third place in terms of the number of IMCT sites is taken by the non-governmental healthcare system, where both the number of new sites (102 in 2020 and 127 in 2021) and the number of clinics involved (25 in 2020 and 27 in 2021) have increased.

Fourth place is taken by clinics subordinated to federal authorities except for the Ministry of Health of Russia. Here, too, both the number of new sites and the number of involved clinics have increased (from 82 in 2020 to 88 in 2021, and from 17 in 2020 to 21 in 2021, respectively).

Fifth place is taken by medical organizations subordinated to the Ministry of Health of Moscow Region. In 2021 it was planned to open 21 new sites in these institution, a little less in 2020 — 19. The number of clinics involved in IMCTs has barely changed: four in 2021, three in 2020.

The lowest number of new sites announced in 2021 was demonstrated by clinics of the Russian Railways: five compared to 16 a year earlier. The number of clinics has not changed: two both in 2020 and 2021.

Beside the indicators discussed above we additionally calculate the coefficient designated as the activity coefficient. It expresses the ratio of the number of new sites to the number of organizations, i.e. it shows how many sites are opened on average in each clinic of the specified departmental subordination.

Table 10

The level of participation of healthcare organizations in Moscow in IMCTs depending on subordination						
Subordinated to	The number of medical organizations involved in new IMCTs		The number of sites approved for IMCTs		Activity Coefficient	
	2021	2020	2021	2020	2021	2020
Ministry of Healthcare of the Russian Federation	23	23	292	270	12.7	11.7
Moscow Department of Healthcare	31	33	175	201	5.6	6.1
Ministry of Healthcare of the Moscow region	4	3	21	19	5.3	6.3
Non-governmental health system	27	25	127	102	4.7	4.1
Federal bodies (except Ministry of Healthcare of the RF)	21	17	88	82	4.2	4.8
JSC "Russian Railways"	2	2	5	16	2.5	8.0
TOTAL	108	103	708	690	6.6	6.7

Data from www.grls.rosminzdrav.ru

In St. Petersburg (Table 11) the total number of medical organizations increased by just one as compared to 2020 and amounted to 120. The number of approved IMCT sites has increased from 744 to a record 820.

In St. Petersburg clinics subordinated to the St. Petersburg Healthcare Committee are still in the lead in terms of the number of approved sites, although this number has decreased: 268 in 2020 and 254 in 2021. The number of organizations involved has remained the same — 46 both in 2020 and 2021.

Second place is taken by clinics of the Ministry of Health of Russia, where the number of new sites has gone up from 215 in 2020 to 235 in 2021. Although the number of medical organizations remained at 11.

The non-governmental healthcare system placed third: 166 sites in 2020 and 218 in 2021. The number of medical organizations increased: 49 and 51 consecutively over the past two years.

Fourth place is taken by clinics subordinated to federal authorities except for the Ministry of Health of Russia. Here, in 2021, it was planned to open 73 new IMCT sites (68 in 2020) in ten medical organizations (11 in 2020).

They are followed by clinics of the Regional Healthcare Committee. Dynamics of the number of new sites: 18 in 2020 and 21 in 2021. All new sites were supposed to be opened in just one medical organization, the Leningrad Regional Clinical Hospital.

The ranking is closed by clinics of the Russian Railways: 19 sites against nine in 2020, all in the same clinic, Clinical Hospital RZD-Medicine.

Changes in the average number of sites that were planned to be opened in organizations of the specified departmental subordination over the year can be seen in the column “activity coefficient”.

Table 11

The level of participation of healthcare organizations in St. Petersburg in IMCTs depending on subordination						
Subordinated to	The number of medical organizations involved in new IMCTs		The number of sites approved for IMCTs		Activity Coefficient	
	2021	2020	2021	2020	2021	2020
Ministry of Healthcare of the Russian Federation	11	11	235	215	21.4	19.5
Committee of Health of the Leningrad Region	1	1	21	18	21.0	18.0
JSC "Russian Railways"	1	1	19	9	19.0	9.0
Federal bodies (except Ministry of Healthcare of the RF)	10	11	73	68	7.3	6.2
Health Committee of Saint-Petersburg	46	46	254	268	5.5	5.8
Non-governmental health system	51	49	218	166	4.3	3.4
TOTAL	120	119	820	744	6.8	6.3

Data from www.grls.rosminzdrav.ru

PARTICIPATION OF MEDICAL ORGANIZATIONS IN BIOEQUIVALENCE STUDIES

Table 12 presents medical organizations that were most actively involved in conducting bioequivalence studies according to the 2021 approvals.

13 of 15 clinics were included in a similar ranking for the previous year. Two newcomers, Rostov Central Regional Hospital (presented in the ranking for the first time over the entire period of monitoring) and Tomsk National Research Medical Center of the Russian Academy of Sciences, ranked 13–15th with ten new projects each.

Almost all medical organizations increased their activity, with two exceptions: Yaroslavl Clinical Hospital No. 3 received one project less than in 2020 (21 versus 22) and Medical Center Probiotech in Serpukhov — five less (20 versus 25).

The most noticeable increase in activity as compared to the previous year was demonstrated by “Ligand Research” (from six to 21 projects, 3.5 times more), Clinical Hospital “RZD-Medicine”, Yaroslavl (from 19 to 38, a two-fold increase) and the already mentioned Tomsk National Research Medical Center of the Russian Academy of Sciences (four against ten, a 2.5-fold increase).

Table 12

Top-15 medical organizations on the activity of participation in bioequivalence studies (approvals issued in 2021)					
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 2020
1	Clinical Hospital "RZD-Medicine", Yaroslavl	38	29	9	19 (5)
2	Clinical Hospital No. 2, Yaroslavl	31	26	5	18 (6)
3	Yaroslavl Regional Clinical Narcological Hospital, Yaroslavl	28	28	–	17 (7)
4	Eco-Safety Research Center, St. Petersburg	26	25	1	22 (2–3)
5	X7 Clinical Research, St. Petersburg	24	14	10	13 (8–9)
6–8	Clinical Hospital No. 3, Yaroslavl	21	19	2	22 (2–3)
6–8	Ligand Research, Moscow	21	1	20	6 (14–15)
6–8	Certa Clinic, Moscow	21	20	1	20 (4)
9	Medical Center Probiotech, Serpukhov	20	15	5	25 (1)
10	N.P. Bekhtereva Institute of Human Brain of the Russian Academy of Sciences, Saint Petersburg	19	7	12	12 (10)
11	Cardiology Dispensary, Ivanovo	17	11	6	13 (8–9)
12	North-West Public Health Research Center, St. Petersburg	13	13	–	10 (12)
13–15	Rostov Central Regional Hospital, Yaroslavl region, Rostov	10	10	–	n/a
13–15	Bessalar clinic, Moscow	10	9	1	8 (13)
13–15	Tomsk National Research Medical Center of the Russian Academy of Sciences, Tomsk	10	8	2	4 (17)

Data from www.grls.rosminzdrav.ru

MAIN PLAYERS ON THE RUSSIAN CLINICAL TRIALS MARKET – 2021

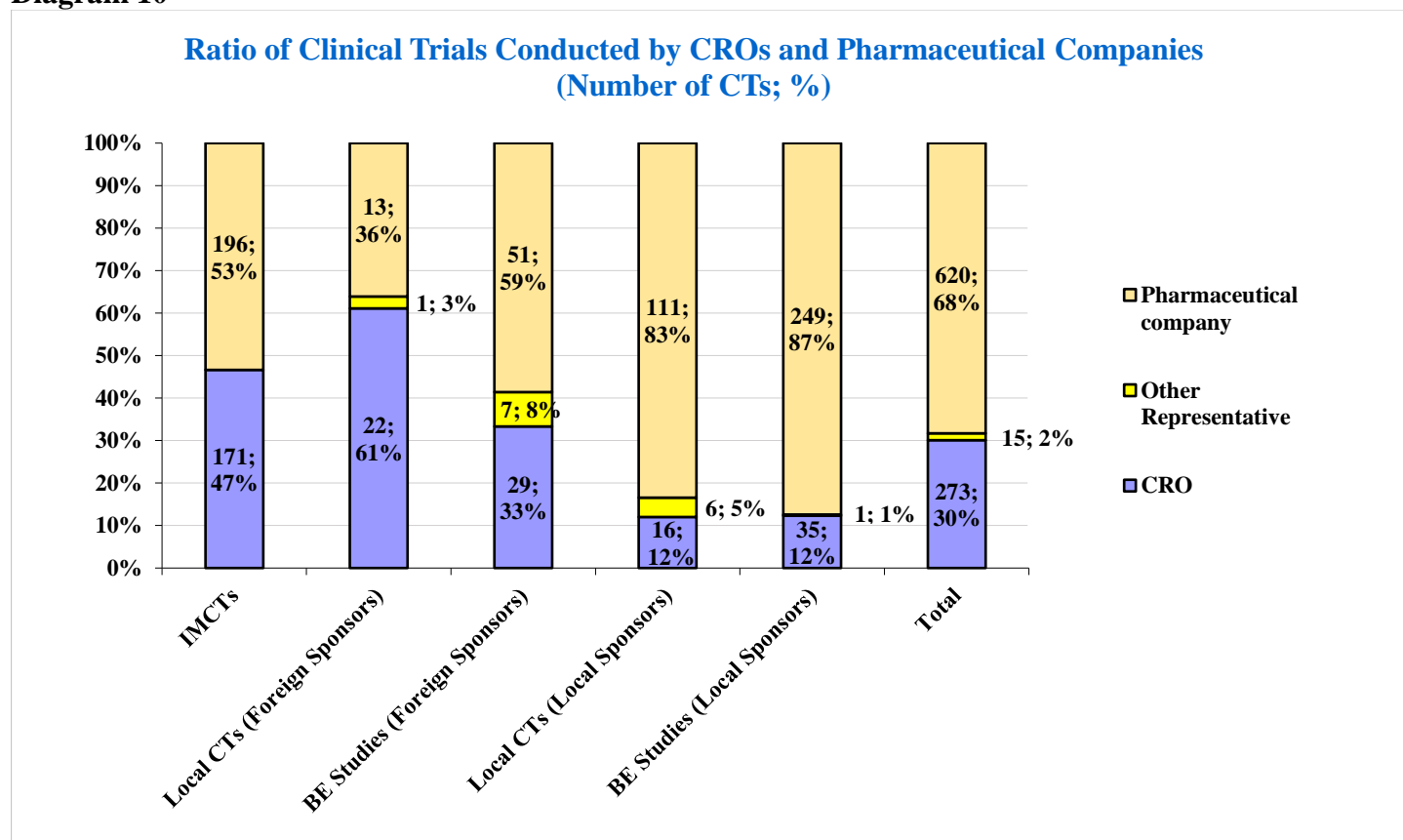
The principles that apply to the classification of the main market participants can be found in the corresponding sections of Newsletters No. [12](#) and [14](#).

Sponsors and CROs, general structural distribution

When preparing an application, a sponsor may indicate whether it plans to conduct the trial on its own or engage another organization to conduct it. This role can be taken by a contract research organization (CRO) or other organization, which is not specialized, but also provides services to pharmaceutical companies for introduction of products to the market. Sponsors do not always provide information on the engagement of an intermediary in the application, however, the information in the register of the Ministry of Health of Russia still provides some insight into the share of studies conducted by sponsors on their own (Diagram 10).

As compared to 2020, the shares of all types of trials conducted by sponsors by themselves (68%), with the help of CROs (30%) and other representative (2%) remained unchanged. For IMCTs the ratio of 53% (conducted by sponsors themselves) and 47% (with the involvement of CROs) is exactly the same as last year. Fluctuations and therefore differences from the results of 2020 are more noticeable in those types of trials, for which a small number of approvals is issued. CROs were involved in local trials by foreign sponsors under approvals issued in 2021 more often than a year earlier (61% against 44% in 2020). Involvement of CROs in bioequivalence studies by the same category of sponsors, on the contrary, was less common (33% against 48% a year earlier). As for approvals issued to Russian sponsors, the situation is reversed: as compared to the previous year, CROs were involved less frequently in local trials (12% against 13% in 2020) and more often in bioequivalence studies (12% against 9%).

Diagram 10



Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, sponsors

Table 13 shows top 10 sponsors that obtained the most approvals for IMCTs in 2021.

Nine out of ten companies were also included in the similar ranking of the previous year. The only exception is Novo Nordisk, which increased the number of approvals for the year from five to 12 and moved up from 14–15th to eighth place. AbbVie dropped out of the top 10: the number of approvals for IMCTs it obtained during the year remained unchanged (nine in both 2020 and 2021), but since other sponsors obtained more approvals, AbbVie went down from 8–9th to 11–12th place in the ranking.

Positions in the ranking were improved, as compared to the previous year, for Pfizer (up from 10–11th to seventh place, increase in the number of new IMCTs from eight to 13), Novartis (up from fourth to second place, number of approvals increased from 17 to 30) and AstraZeneca (up from second to first place, from 25 to 34 approvals).

Merck (an increase in the number of approvals from 23 to 26, third place), Janssen Pharmaceutica (an increase in the number of IMCTs from 16 to 17, fifth place) and Sanofi (from 13 to 15, sixth) remained in the same places.

Three companies went down in the ranking: F. Hoffmann-La Roche (from first to fourth place, 25 new IMCTs against 26 a year earlier), GSK (from 8–9th to 9–10th, ten approvals against nine) and Eli Lilly (from seventh to 9–10th, ten IMCTs against 11 in 2020).

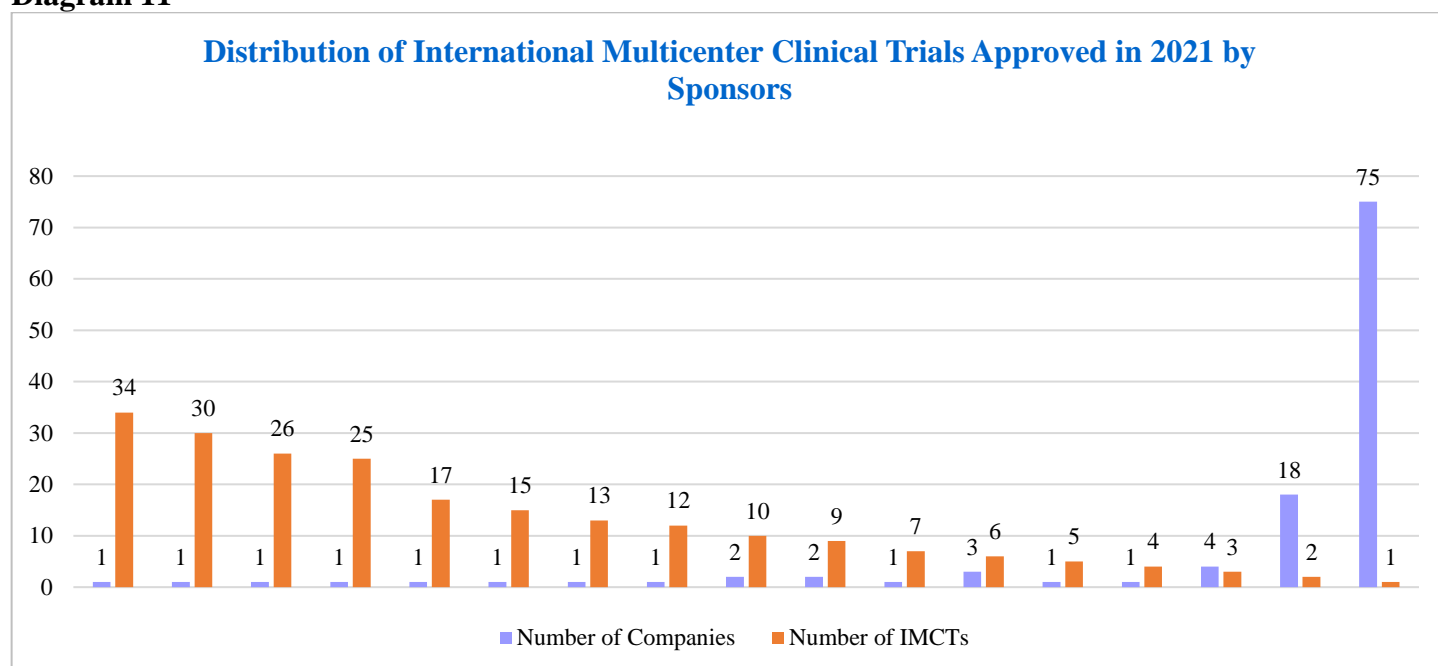
Table 13

Ranking of Leading Pharmaceutical Companies on Approvals for International Multicenter CTs, 2021					
Rating in 2021	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 2020
1	AstraZeneca AB	34	24	10	25 CTs; 2
2	Novartis (incl. Hexal, Lek Pharmaceuticals d.d.)	30	28	2	17 CTs; 4
3	Merck & Co.	26	26	–	23 CTs; 3
4	F. Hoffmann-La Roche (incl. Genentech)	25	25	–	26 CTs; 1
5	Janssen Pharmaceutica (incl. Actelion Pharmaceuticals)	17	12	5	16 CTs; 5
6	Sanofi	15	15	–	13 CTs; 6
7	Pfizer	13	13	–	8 CTs; 10–11
8	Novo Nordisk	12	12	–	5 CTs; 14–15
9–10	GSK (incl. ViiV Healthcare UK Limited)	10	7	3	9 CTs; 8–9

Data from www.grls.rosminzdrav.ru

Diagram 11 shows the distribution of approvals for IMCTs issued in 2021 by sponsors. Four companies obtained more than 20 approvals each, another four — 11 to 20 approvals, eight companies — six to ten approvals. 99 sponsors planned to launch five or less IMCTs, of which 75 companies have only one new project each. As compared to 2020, the total number of sponsors that obtained approvals to conduct IMCTs during the year decreased from 121 to 115.

Diagram 11



Data from www.grls.rosminzdrav.ru

International multicentre clinical trials, CROs

Table 14 shows CROs that were most often engaged by sponsors to conduct international projects according to IMCT approvals issued in 2021.

All of the companies listed in the table remained on the leaderboard from the previous year, except for ICON, which managed to push IPHARMA out of ninth place having increased the number of new IMCTs from four to six. PRA has gone up noticeably in the ranking: places 1–2 against 8–9 in 2020 and 22 approvals against five. IQVIA obtained 22 approvals, one third less than a year earlier, which resulted in it being unable to become an absolute leader as in previous years and sharing 1–2 lines with PRA.

The rest of the companies moved down in the ranking as compared to 2020: Parexel from second to third place, PPD from third to fourth, Syneos Health from fourth to fifth, PSI from fifth to eighth. As in the previous year, places 6–7 were shared by Medpace and Labcorp, formerly known as Covance.

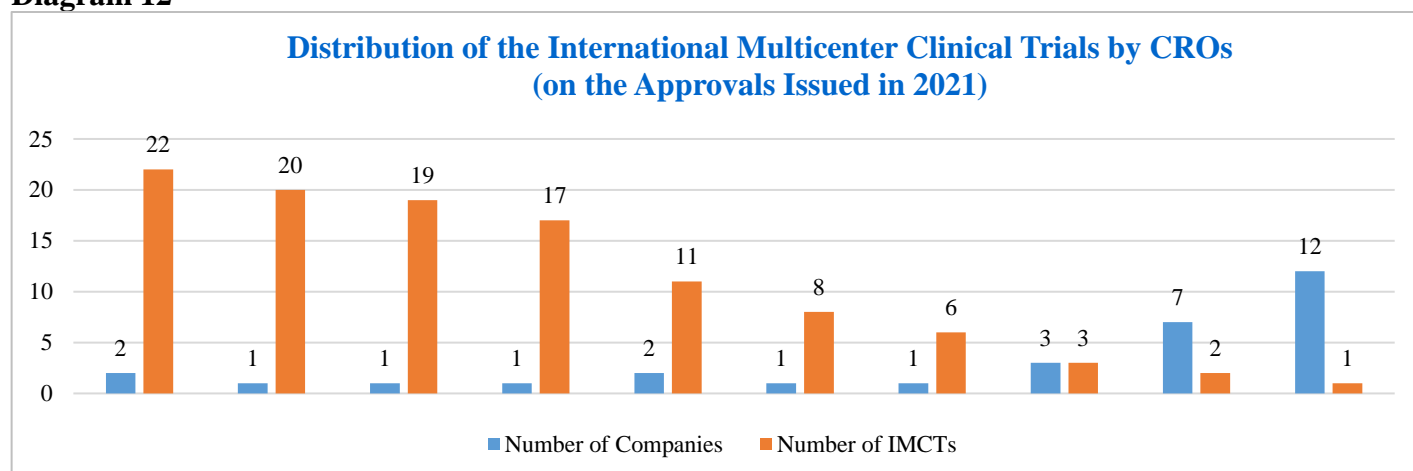
Table 14

Ranking of Leading CROs on Approvals for International Multicenter CTs, 2021				
Ranking in 2021	Company	Number of IMCTs	Number of Sponsors	Number of IMCTs; Ranking in 2020
1–2	IQVIA	22	15	33 CTs; 1
1–2	PRA Health Sciences	22	14	5 CTs; 8–9
3	Parexel	20	17	19 CTs; 2
4	PPD	19	10	14 CTs; 3
5	Syneos Health	17	13	12 CTs; 4
6–7	Labcorp (formerly Covance)	11	7	6 CTs; 6–7
6–7	Medpace	11	8	6 CTs; 6–7
8	PSI	8	8	8 CTs; 5
9	ICON	6	5	4 CTs; 10–11

Data from www.grls.rosminzdrav.ru

Diagram 12 shows the distribution of new IMCTs among contract research organizations. Seven CROs were planned to be engaged by sponsors to conduct more than ten new IMCTs, two — six to ten, and 22 — less than five. The total number of CROs involved in IMCTs under approvals in 2021 has not changed compared to 2020 — 31 organizations.

Diagram 12



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, foreign sponsors

Foreign sponsors that obtained most approvals for bioequivalence studies and local trials in 2021 are shown in Table 15.

Top 10 has been updated significantly. First place with 12 approvals is taken by Teva, which only made it into the top 20 in 2020. It is followed by Dr. REDDY's Lab with ten approvals (second place against 3–4th in 2020), Berlin-Chemie with seven (third place against 5–8th) and KRKA with six (sixth place against second).

Of the six companies with four approvals that shared place 5–10 in 2021, three were included in the previous year's top ten: Gedeon Richter, Hetero Labs and Novartis. The other three not presented in the top 10 in 2020 are Emcure Pharmaceuticals, Pharmland and Servier Laboratories.

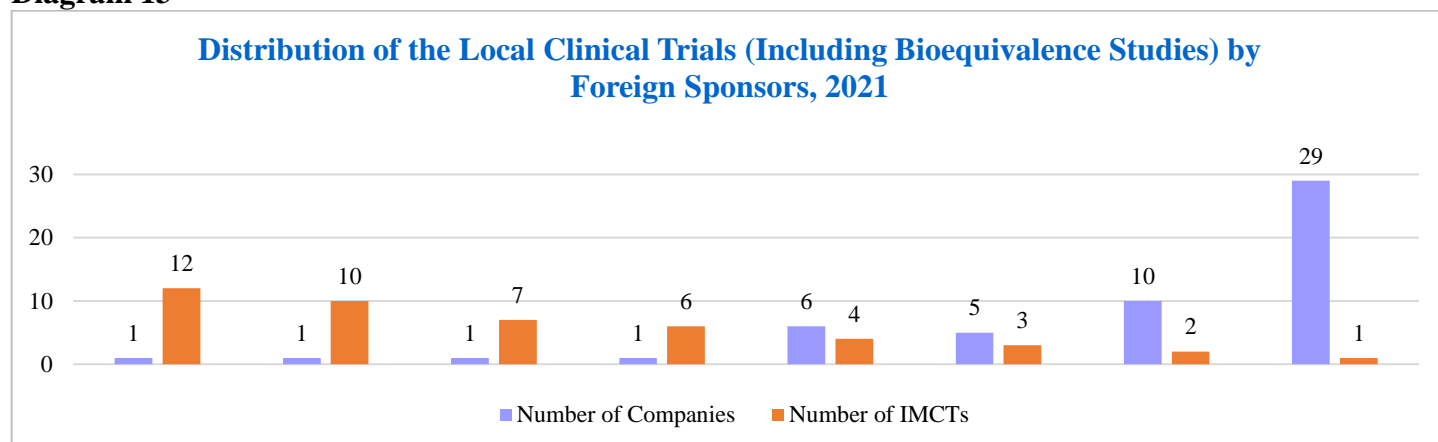
Table 15

Top-10 Foreign Sponsors on Approvals for Local CTs and Bioequivalence Studies, 2021					
Ranking in 2021	Company	Total	Conducted by themselves	Conducted by CROs/other representatives	Number of CTs; Ranking in 2020
1	Teva	12	12	–	2 CTs; 11–16
2	Dr. REDDY's Lab.	10	10	–	5 CTs; 3–4
3	Berlin-Chemie	7	–	7	4 CTs; 5–8
4	KRKA	6	6	–	6 CTs; 2
5–10	Emcure Pharmaceuticals	4	–	4	n/a
5–10	Gedeon Richter	4	–	4	5 CTs; 3–4
5–10	Hetero Labs	4	4	–	4 CTs; 5–8
5–10	Novartis (incl. Sandoz, Hexal)	4	4	–	2 CTs; 11–16
5–10	Pharmland	4	–	4	n/a
5–10	Servier Laboratories	4	4	–	n/a

Data from www.grls.rosminzdrav.ru

The distribution of new local trials and bioequivalence studies among foreign companies is shown in Diagram 13. The total number of sponsors in this category in 2021 improved to 54, a significant increase from the previous year's result, when only 33 companies obtained approvals for these types of studies.

Diagram 13



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, domestic sponsors

Table 16 contains information about Russian sponsors that obtained most approvals for bioequivalence studies and local trials in 2021.

Half of the companies remained in the top 10 from the previous year. Pharmasintez, the leader of 2021 (35 approvals) rose from fourth to first place over the year. Atoll, the 2020 number-one, moved down to place 9–10 with ten approvals. Promomed Rus (26 new protocols) and Canonpharma Production (28) swapped places and became the third and the second, respectively. Renewal (19 studies) moved up from fifth to fourth place.

Another five sponsors that made it into the top spots in the rating in 2021 were either in the top 30 or below in 2020, or had no approvals for studies at all. These are Moscow Endocrine Plant (18 protocols, fifth place), Valenta Pharm (16 studies, sixth place), Werteks (13 studies, seventh place), Bright Way Group (12 protocols, eighth place) and Izvarino Pharma (ten approvals, shared 9–10th lines of the rating with Atoll).

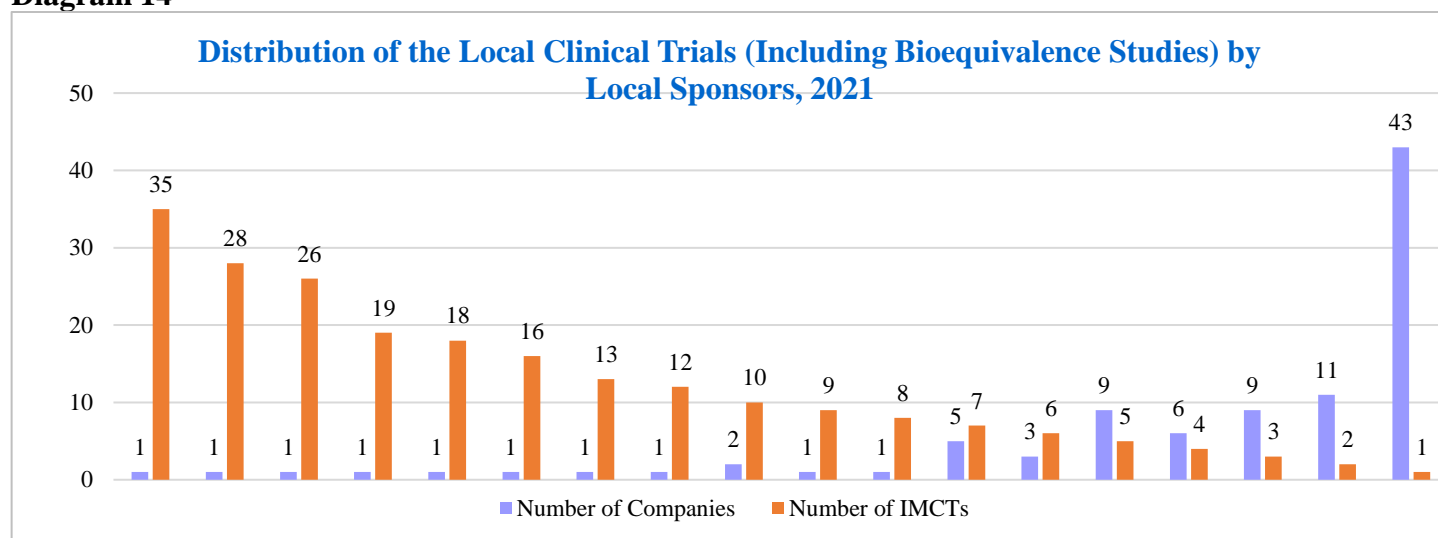
Table 16

Ranking of Leading Local Sponsors on Approvals for Local Clinical Trials and Bioequivalence Studies, 2021					
Ranking in 2021	Company	Total	Conducted by themselves	Conducted by CRO	Number of CTs; Ranking in 2020
1	Pharmasintez (incl. Pharmasintez-Nord, Pharmasintez-Tyumen)	35	35	–	15 CTs; 4
2	Canonpharma Production	28	28	–	16 CTs; 3
3	Promomed Rus	26	26	–	19 CTs; 2
4	Renewal	19	19	–	12 CTs; 5
5	Moscow Endocrine Plant	18	18	–	5 CTs; 19–23
6	Valenta Pharm	16	16	–	4 CTs; 24–29
7	Werteks	13	13	–	2 CTs; 36–51
8	Bright Way Group (incl. Velpharm)	12	12	–	4 CTs; 24–29
9–10	Atoll	10	10	–	22 CTs; 1
9–10	Izvarino Pharma (incl. Nanopharma Development)	10	–	10	n/a

Data from www.grls.rosminzdrav.ru

Diagram 14 shows the distribution of approvals for local trials and bioequivalence studies issued to domestic sponsors in 2021. Eight companies obtained more than ten approvals each, 12 — six to ten, 78 — five or less. The total number of Russian sponsors launching new projects has slightly decreased as compared to 2020, from 103 to 98.

Diagram 14



Data from www.grls.rosminzdrav.ru

Local trials and bioequivalence studies, CROs

Table 17 lists CROs that were most frequently engaged by sponsors to conduct bioequivalence studies and local trials in 2021. Six of them were in the lead in 2020 as well. Probiotech moved up to the first line from 3–4th place. ClinPharmDevelopment went up from fifth to second place. MDA and X7 Research moved up from 8–10th to 3rd and 4th places, respectively, while IPHAR moved up from the same 8–10th to 6–9th place in the ranking separating them from Accellena Research and Development (place 6–7 in 2020) and Expert Legal Center (previously placed 13–18th). Beside the latter ARS (fifth place against 11–12th a year earlier) and Atlant Clinical (placed 6–9th in 2021, in 2020 it didn't obtain approvals for this type of studies) also managed to make it into the top.

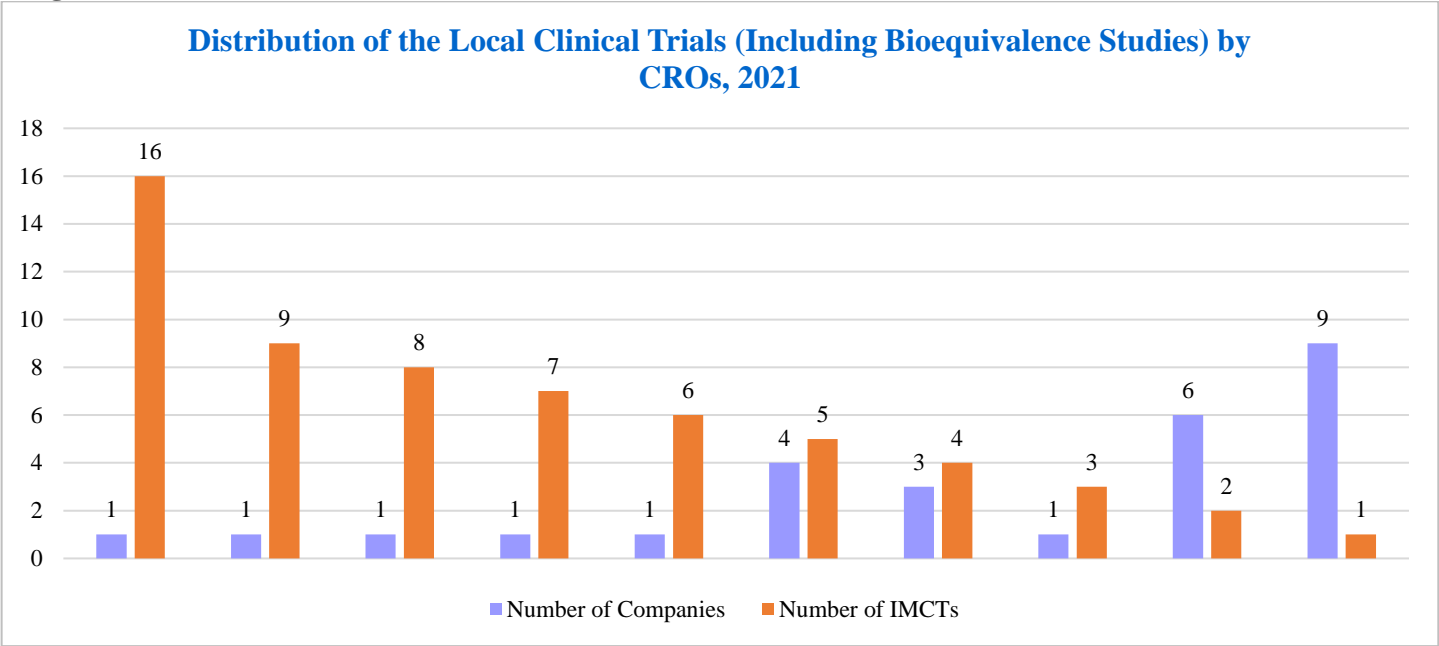
Table 17

Top-10 CROs Involved in the Local CTs and Bioequivalence Studies (on Approvals Issued in 2021)						
Ranking in 2021	Company	Number of CTs of foreign sponsors	Number of CTs of local sponsors	Total number of local CTs, 2021	Number of sponsors	Number of CTs; Ranking in 2020
1	Probiotech	5	11	16	5	8 CTs; 3–4
2	ClinPharmDevelopment	4	5	9	6	6 CTs; 5
3	Medical Development Agency (MDA)	—	8	8	3	3 CTs; 8–10
4	X7 Research	6	1	7	5	3 CTs; 8–10
5	ARS	6	—	6	3	2 CTs; 11–12
6–9	Atlant Clinical	3	2	5	5	n/a
6–9	Innovative Pharmacology Research (IPHAR)	5	—	5	2	3 CTs; 8–10
6–9	Accellena Research and Development	—	5	5	2	4 CTs; 6–7
6–9	Expert Legal Center	1	4	5	3	1 CT; 13–18

Data from www.grls.rosminzdrav.ru

Diagram 15 shows the distribution of local trials and bioequivalence studies by contract research organizations. The total number of CROs involved in such projects in 2021 was 28, 18 more than a year earlier.

Diagram 15



Data from www.grls.rosminzdrav.ru

TIMEFRAMES FOR OBTAINING APPROVALS

Analysis of the timeframes for issue of the main types of approvals by the Ministry of Health of Russia is based on the results of a survey of 28 pharmaceutical companies and contract research organizations that are members of ACTO and AIPM. The outcomes of consideration of all applications, decisions on which were made during 2021, were taken into account, even if the applications themselves were submitted before 01 January 2021. The methodology is described in more detail in earlier issues of ACTO Newsletters.

Before proceeding to the analysis of the results further clarification is needed. In 2021 the Ministry of Health began transition to electronic document management. Over time it should affect all types of approvals. Meanwhile, the transition has affected two administrative procedures: issue of approvals for import/export of biosamples (hard-copy document workflow was cancelled from 01 July 2021) and issue of approvals for import of medicinal products (transition to electronic interaction occurred on 01 September 2021). Since the timeframes for issue of approvals before and after the transition to electronic document management differ quite a bit, Table 18, which presents the overall results of the survey, shows them separately.

The transition to electronic document management helped to significantly accelerate obtaining of respective approvals. If before September 2021 it took, on average, 18 calendar days to obtain approvals for import of medicinal products, now it takes only eight (Table 18). Before July 2021 approvals for import/export of biosamples were issued on average within 21 days, after — within 13 days. The minimum timeframe for both categories of approvals was reduced from seven to one calendar day. During the period of ACTO's monitoring (since 2012) such high efficiency in issuing these types of approvals is recorded for the first time.

Table 18

Timeframes for Issuing Approvals, 2021				
Type of approval		2021	2020	2021 vs 2020, %
To Conduct Clinical Trials*		111	103	7.8%
To Import Medicines	before September 1, 2021	18	17 (no Electronic Document Flow system)	5.9%
	after September 1, 2021	8		-52.9%
To Import/Export Biosamples	before July 1, 2021	21	22 (no Electronic Document Flow system)	-4.5%
	after July 1, 2021	13		-40.9%
To Make Amendments to the Protocol		77	65	18.5%
Other Approvals**		44	39	12.8%

Data from timeframes monitoring of ACTO and AIPM

* For all applications, regardless of the availability of requests from expert organizations or the Ministry of Health. If there is a request, the response time is not excluded from the calculation;

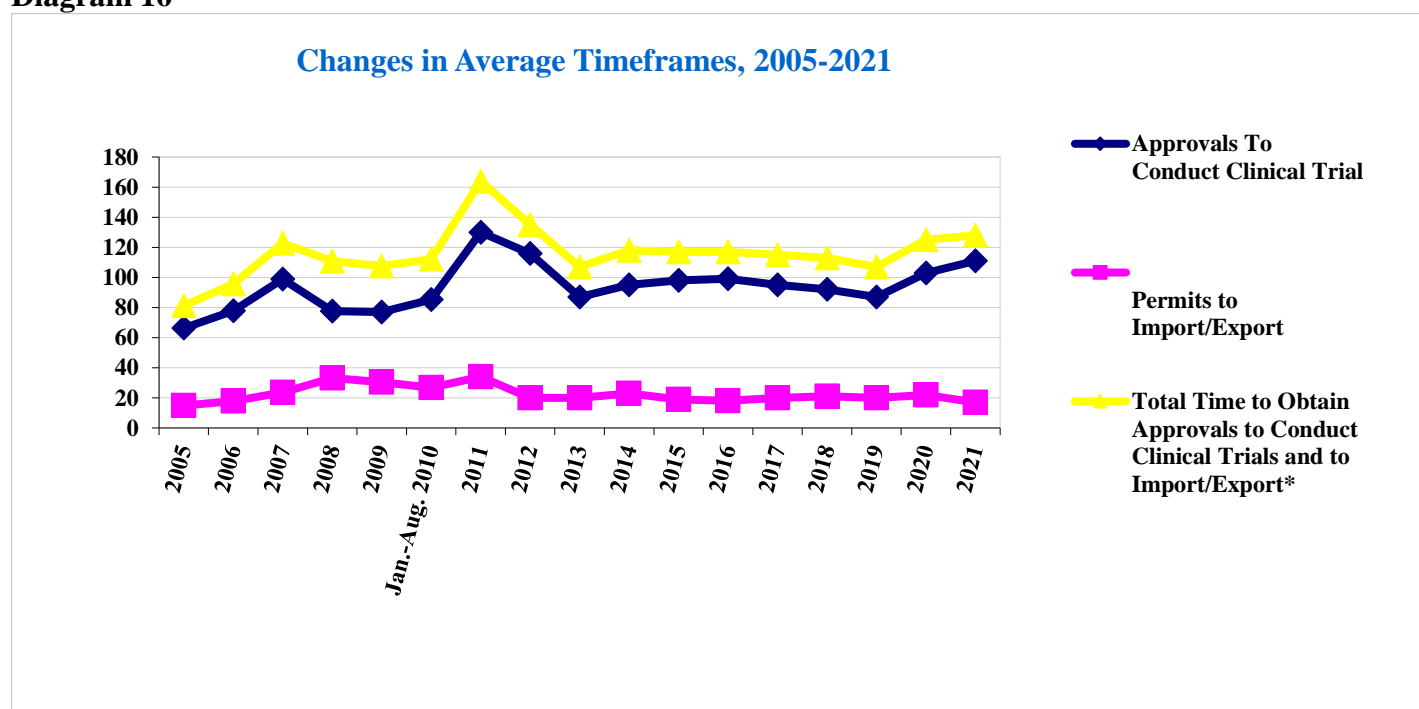
** In the absence of requests from expert organizations or the Ministry of Health;

The average period for issue of approvals for conducting clinical trials continued to grow in 2021: from 87 calendar days in 2019 to 103 calendar days in 2020 and 111 days in 2021. The average period for making amendments to the protocol was 77 days in 2021, which is significantly longer than in 2020 (65 days). Such a long period for making amendments became a separate target for criticism by the applicants in 2021. Industry associations, both ACTO and AIPM, even sent letters to the Ministry of Health specifically requesting to pay

attention to unacceptability of such a long processing of applications. There was no active reaction to the letters, the Ministry, as per usual in recent years, got off with run-around replies. In addition to those mentioned above, the average period for “other submissions” has also increased: 29 days in 2019, 39 in 2020 and 44 in 2021.

Diagram 16, which presents data since 2005, shows that in 2021 the increased timeframes for issue of approvals for conducting clinical trials cannot be compensated by the reduced timeframes for issue of approvals for import/export of biosamples in the second half of the year. While the negative trend persists, the “total time” indicator, which denotes the total time spent on obtaining minimum essential approvals required to launch a new trial, continues to grow: 107 days in 2019, 125 in 2020 and 128 in 2021.

Diagram 16



Data from timeframes monitoring of ACTO

In 2020 we recorded an increase in violations of timeframes for issue of all types of approval documents (with the exception of approvals for trials of anti-coronavirus drugs, which were processed as a priority, and timeframes for which were calculated separately³). In 2021 the situation improved noticeably only for those types of approvals that began to be issued in electronic form and only after transition to electronic document management.

The share of timely issued approvals for import of medicinal products in 2020 was only 15.9%. In 2021 it decreased even more — to 12.7%, however after the introduction of electronic form it reached an unprecedented level of 85.7%. In 2020 only 35% of all approvals for import/export of biosamples were issued in due time, in 2021 this share was 42.6% before the introduction and a whopping 88.5% after the introduction of electronic documents. As can be seen from the table, transition to electronic circulation not only significantly increased the share of approvals issued in due time, but also resulted in elimination of cases where processing time was more than twice as long.

³ Detailed timeframe monitoring data for 2020-2021 and earlier periods is provided in the [respective section of the ACTO website](#).

Unfortunately, the shares of other types of approvals issued in due time not yet affected by the reform have decreased even compared to the unsuccessful 2020: for conducting clinical trials — from 2.8% to 0.7%, for making amendments to the protocol — from 12.4% to 0.4%, for other submissions — from 47.1% to 19.6%. It was also noted for these three types of approvals that the share of cases, when approvals were issued with a less than 1.5-times delay, decreased while the share of 1.5–1.9-times delays increased, and for approvals to make amendments to the protocol delays as much as 2–2.9 times became more frequent.

Table 19

Violations of Timeframes, 2021 vs 2020 (Excluding Clinical Trials on COVID-19)								
Type of Approval		Approvals Issued on Time	Approvals Issued in Violation of Timeframes					
			Total	Less than in 1.5 times	In 1.5–1.9 times	In 2–2.9 times	In 3–3.9 times	In 4 times and more
To Conduct Clinical Trials*	2021	0.7%	99.3%	50.7%	47.2%	1.4%	~	~
	2020	2.8%	97.3%	71.6%	20.2%	5.5%	~	~
To Import Medicines	2021 (before the implementation of electronic document flow system)	12.7%	87.3%	47.2%	26.6%	11.7%	1.5%	0.3%
	2021 (after the implementation of electronic document flow system)	85.7%	14.3%	7.9%	6.4%	~	~	~
	2020	15.9%	84.1%	42.2%	28.6%	12.4%	0.7%	0.2%
To Import/Export Biosamples	2021 (before the implementation of electronic document flow system)	42.6%	57.4%	44.4%	11.7%	1.3%	~	~
	2021 (after the implementation of electronic document flow system)	88.5%	11.5%	8.8%	2.5%	~	0.2%	~
	2020	35.0%	65.0%	44.8%	16.1%	3.5%	0.5%	0.1%
To Make Amendments to the Protocol	2021	0.4%	99.6%	26.6%	62.8%	10.2%	~	~
	2020	12.4%	87.6%	48.5%	36.6%	2.5%	~	~
Other Approvals (to Prolong Clinical Trials, to Include New Sites, to Enroll Additional Patients, etc.)	2021	19.6%	80.4%	56.8%	20.8%	2.7%	0.1%	~
	2020	47.1%	52.9%	43.7%	7.1%	1.9%	0.2%	~

Data from timeframes monitoring of ACTO and AIPM

* For all applications, regardless of the availability of requests from expert organizations or the Ministry of Health.

IMCT STATISTICS FOR ONCOLOGY AND ONCOHAEMATOLOGY, 2021

Table 20

IMCT Distribution in Oncology and Oncohaematology, 2021			
No.	Disease type	Number of IMCTs	Claimed number of subjects
1	Lung and pleural cavity tumours	23	3 538
2	Leukemia (incl. acute leukaemia and neutropaenia, acute myeloid leukemia, myelodysplastic syndrome, myelomonocytic leukaemia, lymphocytic leukemia, myelofibrosis, plasma cell dyscrasia)	21	450
3	Breast tumour	19	1 895
4	Gastrointestinal tumours	13	625
5	Tumours without known localisation	12	432
6	Kidney and genitourinary system tumors	10	797
7	Female reproductive system tumours	10	606
8	Prostate tumour	9	1 137
9	Lymphoma	9	253
10	Multiple myeloma	5	210
11	Central nervous system tumor	5	195
12	Melanoma	3	194
13	Liver tumours and biliary tract cancer	3	115
14	Head and neck tumours	2	58
15	Thyroid tumors	1	24
	TOTAL	145	10529

Data from www.grls.rosminzdrav.ru

Diagram 17

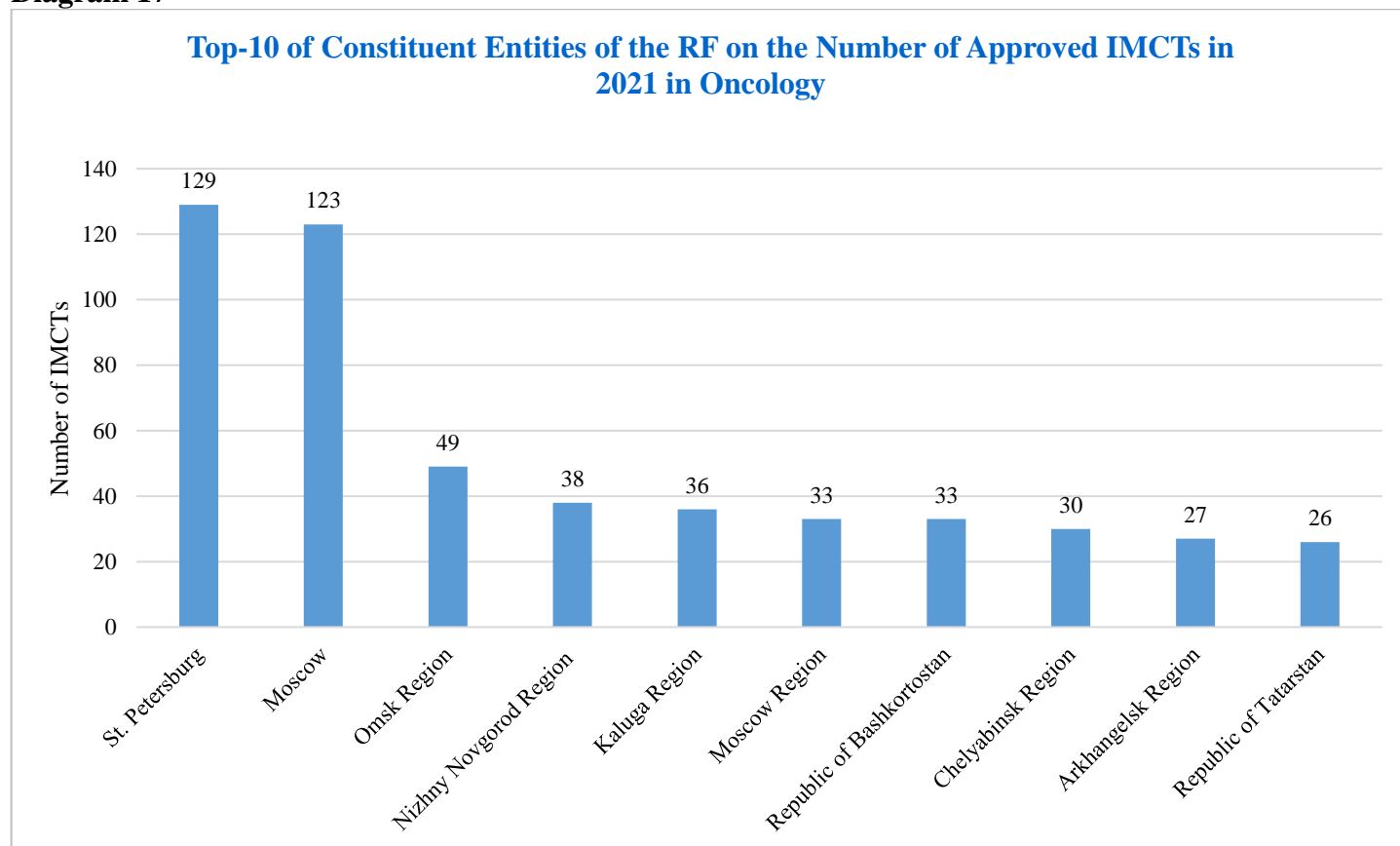
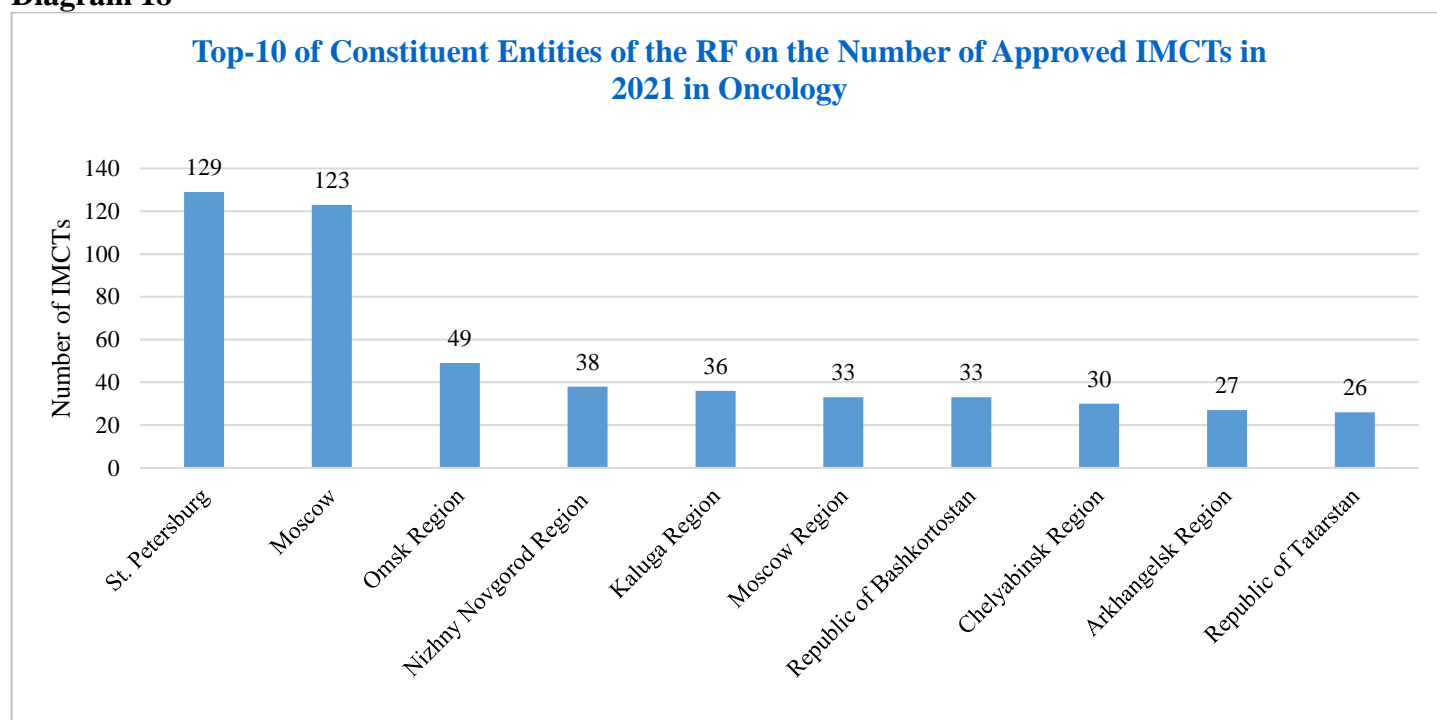
Data from www.grls.rosminzdrav.ru

Diagram 18



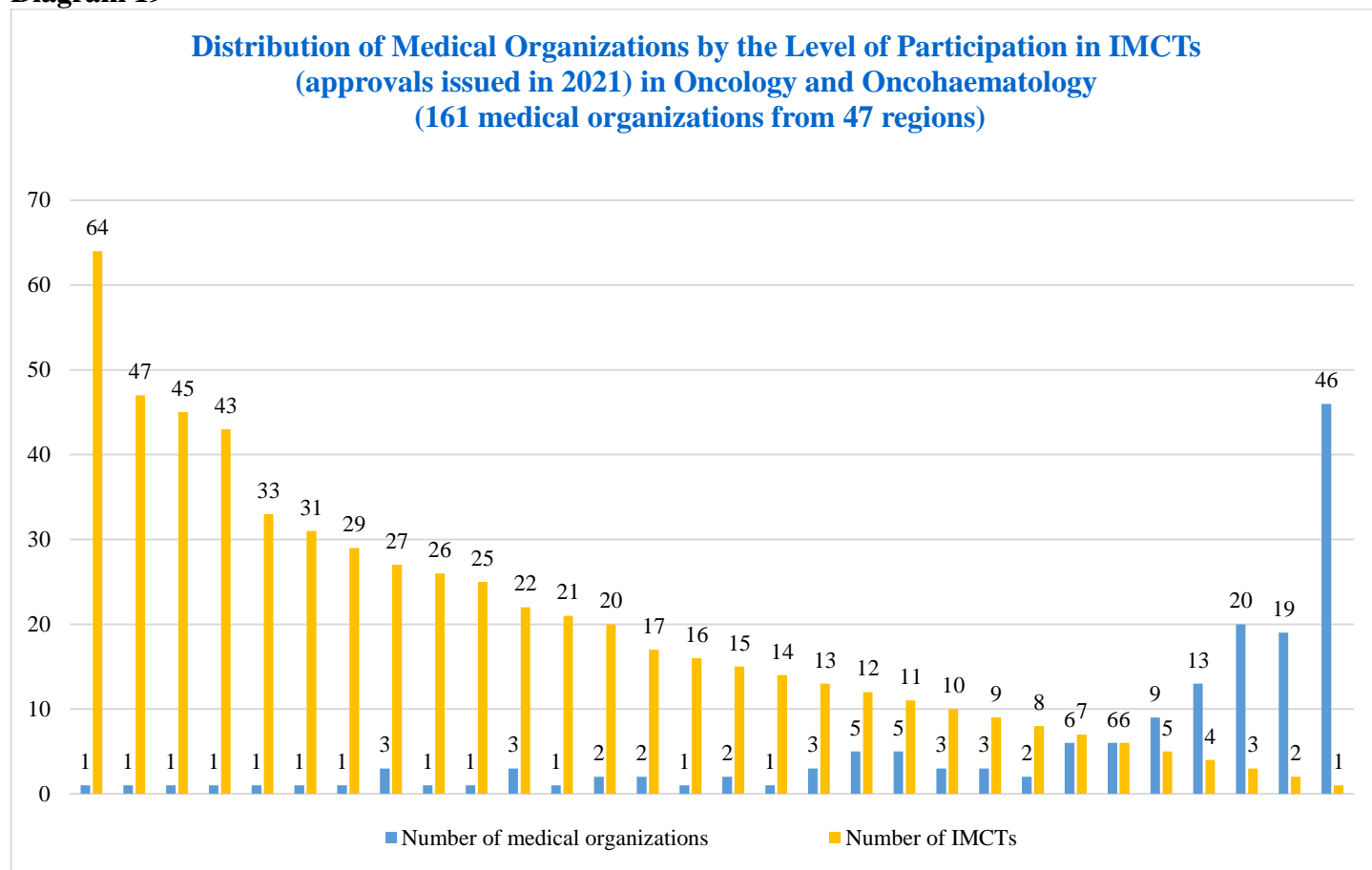
Data from www.grls.rosminzdrav.ru

Table 21

Ranking of Medical Organizations on the Activity of Participation in IMCTs in Oncology and Oncohaematology Approved in 2021			
Place in ranking	Name of medical organization	Number of IMCTs approved in 2021 with participation of this medical organization	Number of sites approved in 2021 for conducting IMCTs
1	N. N. Blokhin Russian Cancer Research Centre, Russian Ministry of Health, Moscow	64	65
2	Clinical Oncological Dispensary, Omsk	47	47
3	St. Petersburg Clinical Scientific and Practical Center for Specialized Types of Medical Care (Oncological), St. Petersburg	45	45
4	N.N. Petrov National Medicine Research Center of Oncology, Russian Ministry of Health, St. Petersburg	43	47
5	Almazov National Medical Research Centre, St. Petersburg	33	34
6	I. P. Pavlov First St. Petersburg State medical University, Russian Ministry of Health, St. Petersburg	31	32
7	Moscow City Oncological Hospital No. 62, Moscow Department of Healthcare, Moscow region, Krasnogorsky district, Istra	29	29
8	National Medical Research Radiological Centre, Obninsk	27	32
9	Arkhangelsk Clinical Oncological Dispensary, Arkhangelsk	27	27
10	Republican Clinical Oncological Dispensary, Ufa	27	27

Data from www.grls.rosminzdrav.ru

Diagram 19



Data from www.grls.rosminzdrav.ru