ACTO

ASSOCIATION OF CLINICAL TRIALS ORGANIZATIONS

ACTO NEWSLETTER № 23

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CONTENTS

SUMMARY

In H1 2021 the Ministry of Health of the Russian Federation issued 330 approvals for conducting clinical trials, up 9.3% over the same period of 2020 with 302 approvals. Of 330 approvals, 153 were issued for international multicentre clinical trials (IMCTs), 15% more than in January-June 2020, when sponsors received 133 approvals for IMCTs. The number of approvals for conducting local trials of foreign sponsors increased by 10% (11 versus 10 approvals a year earlier). In January-June 2021 foreign sponsors received 15.6% fewer approvals for conducting bioequivalence studies than in the same period of 2020 (27 versus 32). The number of approvals issued to Russian sponsors for local trials also went down 10.7% (50 versus 56). On the contrary, the number of approvals for bioequivalence studies of Russian sponsors increased by 25.4%: 89 versus 71 in the first half of 2020.

Traditional survey of ACTO members once again provided insight into the practice of expert examination of planned trials. It showed that the share of applications for IMCTs with requests relating to completeness of documents, which had been demonstrating a downward trend for two years in a row, increased from 11.9% to 14.5% as compared to the 2020 survey data. The share of applications approved without comments after being reviewed by two expert bodies of the Ministry of Health of Russia (the Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products" (SCEEMP) and the Ethics Council) slightly increased, from 52.8% to 54.4%. This growth was ensured by the SCEEMP, the share of applications approved by its experts without comments increased from 67.1% in 2020 to 69.2% in 2021. On the contrary, the share of approvals without comments by the Ethics Council went down from 76.5% to 73.9%. The share of protocols, in which the age range of trial subjects was narrowed down, increased from 2.2% to 3.3% following both examinations. Most significant contribution to this growth was made by the SCEEMP: the share of such decisions of its experts increased from 1.3% to 2.7% of all applications reviewed. For the Ethics Council, on the contrary, there has been a reduction: 1.7% of applications with a narrowed down age range in 2020 and 0.5% based on the results of the 2021 survey.

Separate material analyzes how often the blinding method is used in the design of comparative trials in Russia. It considered protocols of the trials, approvals for which were obtained in 2020. The maximum share of protocols using the masking method falls on IMCTs (69.5% of all new studies). These are followed by local trials by Russian sponsors (49.6%). Blinding is least often used in the smallest group — local trials by foreign sponsors, most of which are carried out solely for the purpose of registration in Russia.

For technical reasons, this issue contains a section commonly featured in year-end newsletters: statistics on import of clinical trial medicinal products. As compared to 2019, the total cost of supplies in 2020 increased by 38.4% in ruble equivalent and by 23.6% in dollar equivalent and amounted to 22.5 billion and 0.3 billion, respectively. The growth rate in rubles for VAT amounted to 29.3%, for customs duties — 18.3%, for customs fees — 37%, and for VAT + customs duties + customs fees — 26.9%. These were the highest growth rates of the analyzed indicators in ruble equivalent since 2016.

One of the most significant events for the industry was cancellation of accreditation of medical organizations for the right to conduct clinical trials from 01 January 2021. An article on this topic highlights the challenges faced by the trials organizers after the entry into force of the regulation aimed at simplifying their work.

Traditionally, the issue includes material that helps to get an idea of activities of principal investigators based on the data from the corresponding register of the Ministry of Health. Several ratings have been compiled for the number of approvals as principal investigators, including separate ratings for specialists on oncology clinical trials and bioequivalence studies.

The issue ends with an appendix presenting a selection of tables and charts with descriptive statistics on IMCTs in the area of oncology and oncohaematology, approvals for which were issued by the Ministry of Health of Russia in 2020.

VOLUME AND DYNAMICS OF THE CLINICAL TRIALS MARKET

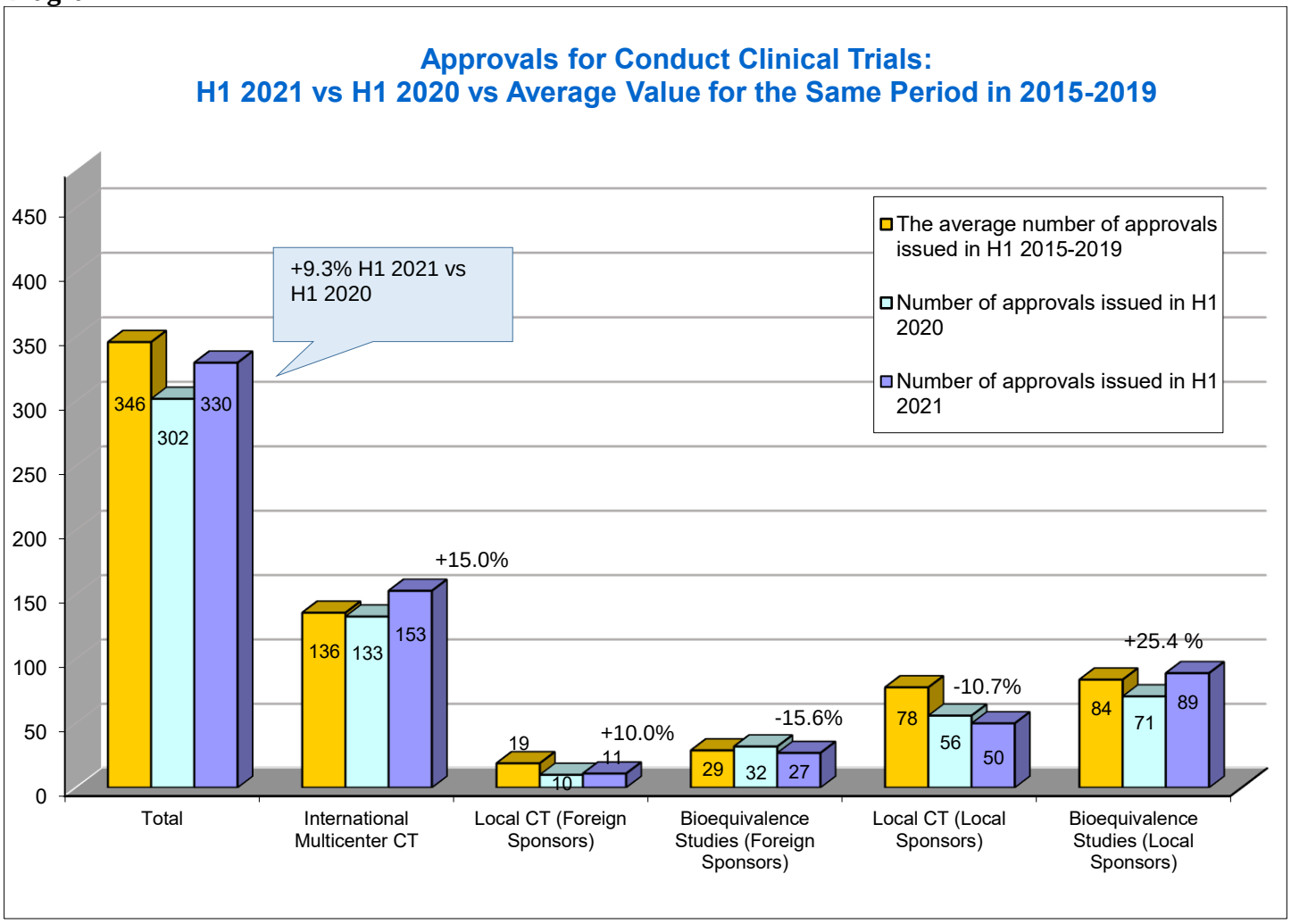
In H1 2021 the Ministry of Health of the Russian Federation has issued 330 approvals for conducting clinical trials (Diagram 1). This is 9.3% more than a year before: in January-June 2020 only 302 approvals were issued. Of 330 approvals issued in H1 2021, 23 (i.e. 7%) were issued for testing anti-Covid-19 drugs. For comparison, in the first half of 2020 there were 26 approvals or 8.6%.

To assess whether the indicators of 2021 have returned to the level of those recorded before the start of the novel coronavirus infection pandemic, it would be more correct to compare them with both the indicators of 2020, which was the year of the pandemic, and the arithmetic mean for the previous five years, i.e. 2015–2019. In 2015–2019 the average number of approvals issued in the first half of the year was 361, which is 8.6% more than in H1 2021. Thus, the total number of approvals issued for all types of clinical trials in the first half of 2021 lags behind the pre-crisis indicators.

The number of new approvals for international multicentre clinical trials (IMCTs) in the first half of 2021 was 153, which is 15% more than in January-June 2020 (133 IMCTs) and 11.8% more than the average number of approvals for IMCTs issued in January-June 2015–2019 (137 IMCTs).

The number of approvals for conducting local trials of foreign sponsors increased by 10% as compared to the first half of 2020: 11 versus 10. This is still significantly, by 58%, less than in 2015–2019, when an average of 26 approvals were issued per half year. The number of approvals issued to foreign sponsors for bioequivalence studies went down by 15.6% as compared to H1 2020. The decrease is even more noticeable in comparison with the average for January-June 2015–2019 — down 40%, 27 versus 45 approvals.

Diagram 1

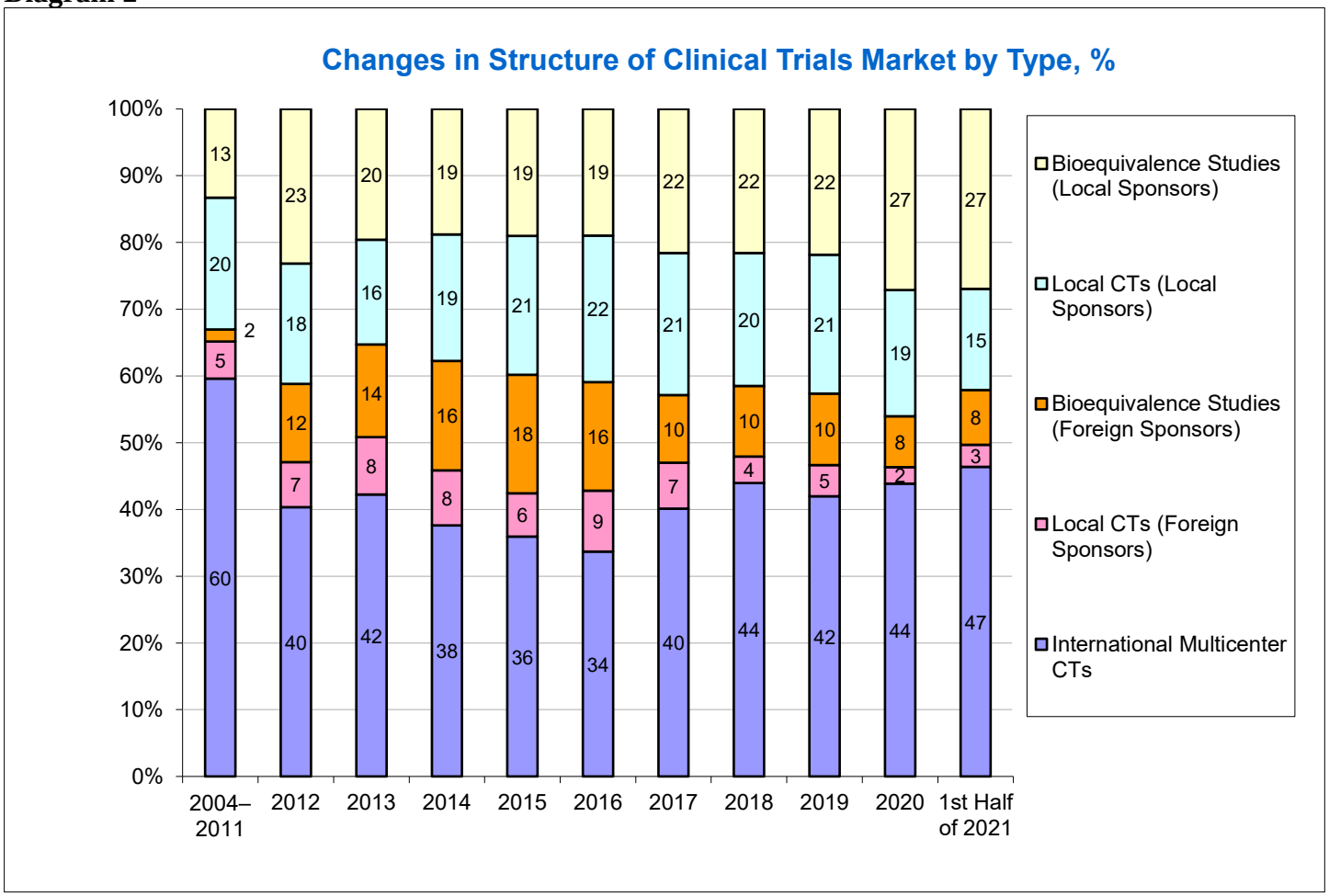


Data from www.grls.rosminzdrav.ru

The number of approvals issued to Russian sponsors for local trials decreased by 10.7% as compared to the first half of 2020 (50 versus 56 approvals) and by 34.2% as compared to the average for January-June 2015–2019 (76 approvals). The number of approvals for bioequivalence studies by Russian sponsors increased by 25.4% as compared to H1 2020 (89 versus 71) and by 14.1% as compared to the average for January-June 2015–2019 (78 approvals).

Changes in the market structure by type of clinical trials are shown in Diagram 2. The share of IMCTs in the first half of 2021 was higher than in entire 2020 and 2019: 47% versus 44% and 42%, respectively. This, actually, is the largest share of new IMCTs after 2011. The share of bioequivalence studies by Russian sponsors remained at the level of the year-end 2020 (27%), the highest for this type of studies. Local trials by Russian sponsors decreased to 15% — the absolute minimum since 2013. The share of bioequivalence studies by foreign sponsors remained at the level of 2020 (8%), the lowest since 2012. Local trials by foreign sponsors in H1 2021 amounted to 3% against 2% in 2020, which is also close to the minimum value for the entire time of our observations.

Diagram 2



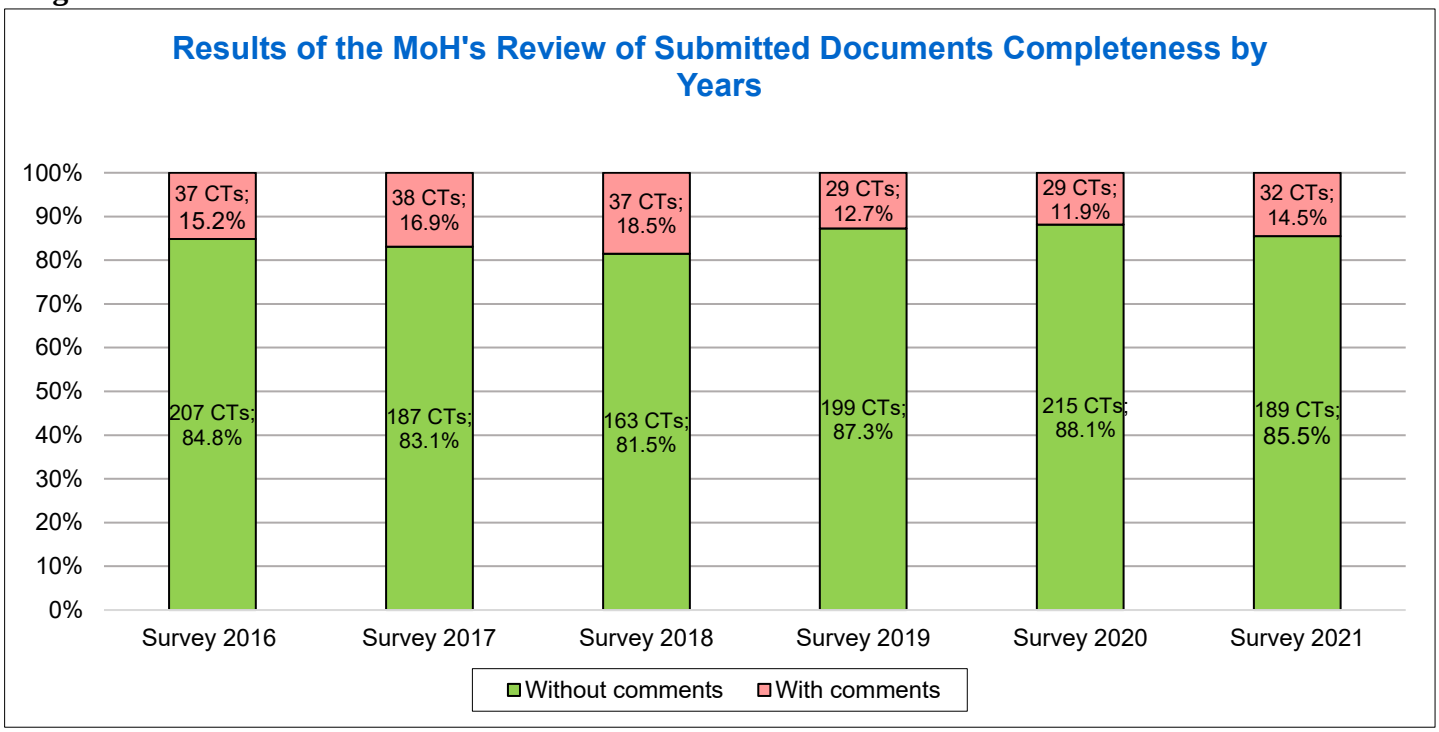
Data from www.grls.rosminzdrav.ru, www.roszdravnadzor.ru

EXPERT EXAMINATION OF PLANNED TRIALS

Every year ACTO conducts a survey among its members regarding practice of expert evaluation of documentation package submitted to the Ministry of Health of Russia together with an application for conducting a clinical trial. The survey, which included 23 pharmaceutical companies and contract research organizations, covers the results of review of initial applications for IMCTs from 01 July 2020 to 30 June 2021.

Diagram 3 shows the outcomes of checking the completeness of documents. Decreasing trend in the share of submissions, for which the applicants received requests from the Ministry of Health regarding completeness, noted in previous issues failed to hold out for three years in a row. According to the results of the latest survey, this share has stopped to decline and has grown from 11.9% to 14.5% over the past year. However, it still remained below the indicators of the 2016–2018 surveys.

Diagram 3



Data from www.grls.rosminzdrav.ru

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Diagram 4 shows the results of initial review of applications for conducting trials by each of the expert bodies of the Ministry of Health of Russia (the Federal State Budgetary Institution “Scientific Centre for Expert Evaluation of Medicinal Products” (hereinafter, the SCEEMP), and the Ethics Council) separately, as well as the overall result of review by both bodies.

As compared to the results of the previous survey, the share of applications approved without comments after passing both examinations slightly increased, from 52.8% a year earlier to 54.4%. This growth was ensured by only one of the expert bodies, the SCEEMP. The share of applications approved by its experts without comments increased from 67.1% in 2020 to 69.2% in 2021. On the contrary, the share of approvals without comments by the Ethics Council went down from 76.5% according to the 2020 survey to 73.9%.

The share of applications that received non-critical comments following both examinations decreased from 21.4% a year earlier to 15.3%. This was mainly due to the contribution of the SCEEMP. The share of non-critical comments from its experts decreased from 12.8% a year earlier to 8.1%, and from the Ethics Council — from 13.1% to 12.6%.

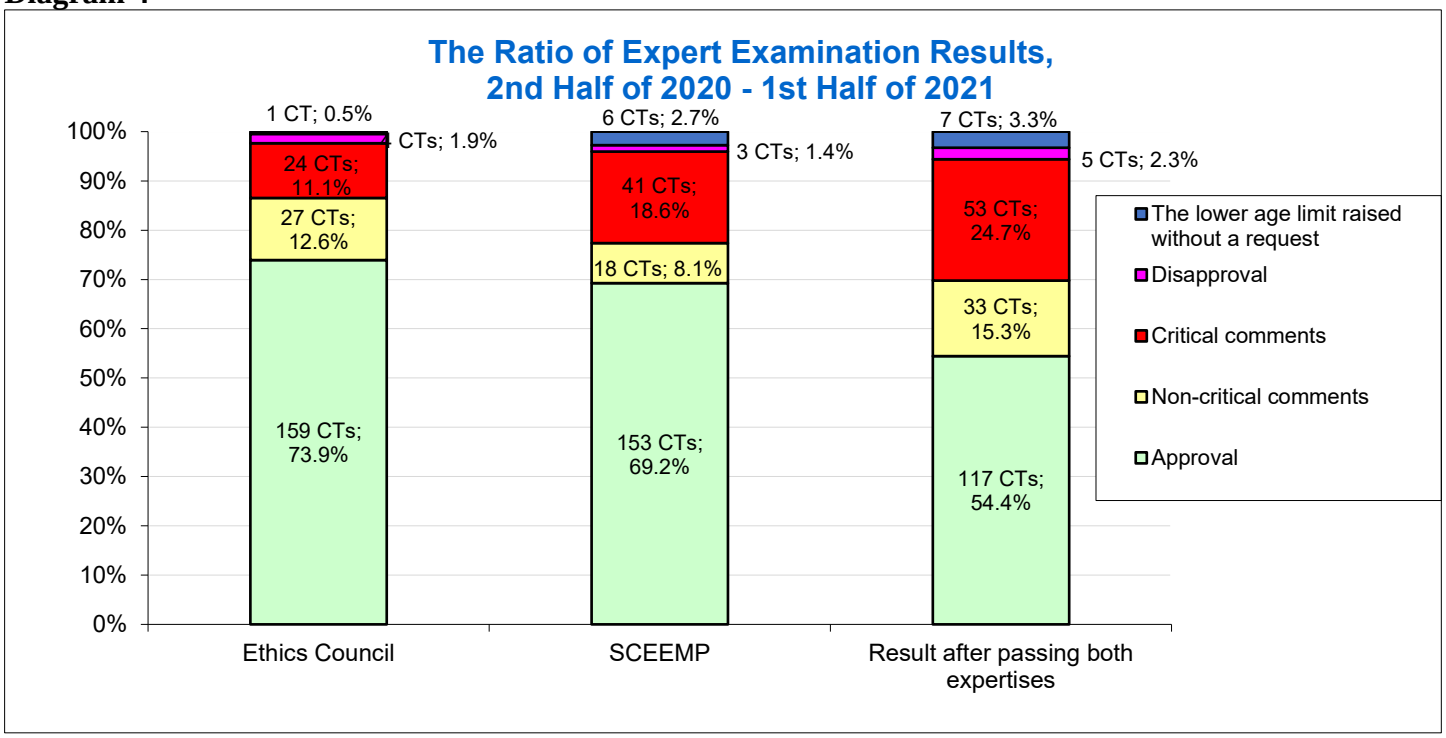
On the contrary, the share of applications that received critical comments increased noticeably, from 16.2% according to the 2020 survey to 24.7%. A larger share of initial submissions with critical comments was

recorded by ACTO only in the 2013 survey (35%), in 2014–2020 it did not exceed 22%. This growth is due entirely to the Ethics Council. The share of applications that received critical comments from its experts increased from 2.6% in 2020 to 11.1% in 2021. For comparison: the same share for the SCEEMP increased from 17.1% to 18.6%, which can be considered a minor fluctuation.

The share of disapprovals after the initial submission by both bodies decreased from 7.4% a year earlier to 2.3%. Decrease in this share is also noted for the SCEEMP and the Ethics Council separately, from 1.7% to 1.4% for the former and from 6.1% to 1.9% for the latter.

The share of IMCTs, in which the regulator reduced the age range of trial subjects without consulting the applicant, increased from 2.2% (five trials) in 2020 to 3.3% (seven trials) in 2021 based on the results of both examinations. This growth was ensured by the SCEEMP experts: in 2020 they reduced the age range in 1.3% of applications (three trials), and in 2021 — in 2.7% (six projects). For the Ethics Council, on the contrary, there has been a reduction: 1.7% of applications (four trials) with a reduced age range a year earlier and 0.5% (one trial) based on the results of the 2021 survey.

Diagram 4



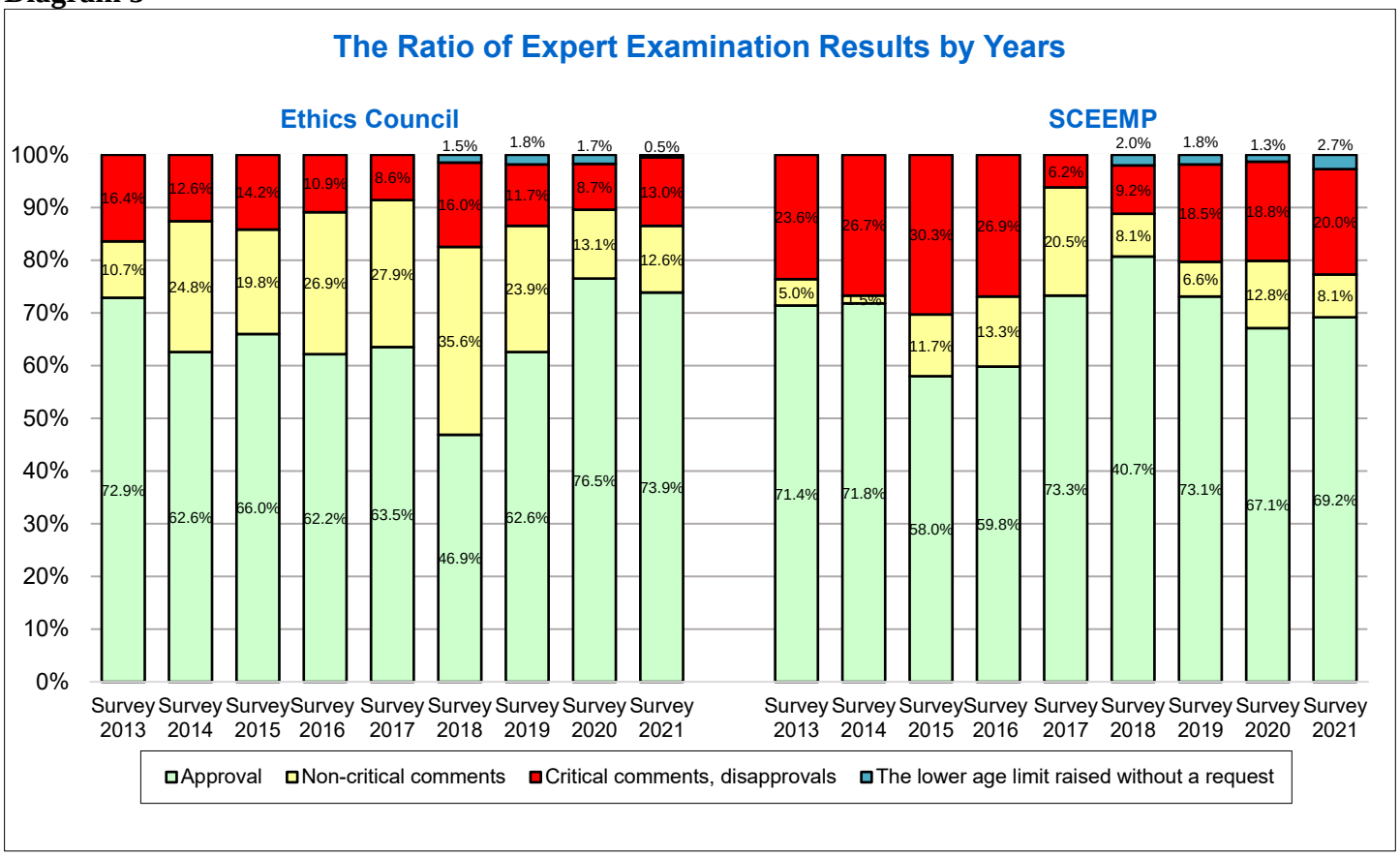
Data from poll of ACTO members

The dynamics of examination results separately for each expert body of the Ministry of Health from 2013 to 2021 is shown in Diagram 5. It can be observed that in 2019 and 2020 benevolence of the Ethics Council to applicants grew, but in 2021 it decreased again, which manifested in an increase in the share of approvals with critical comments and decrease in the share of approvals without comments. This might be a coincidence, however the noted breaking point coincided with the change of the management of the Ethics Council. In August 2020 Academician A. Chuchalin resigned from the position of chairman. Mass media linked his resignation to the scandal surrounding the accelerated development of anti-Covid vaccines[1]. Position of head of the Council was taken by the former deputy chairman A. Khokhlov.

Expert examination of the SCEEMP according to the 2021 survey demonstrates a contradictory tendency: on the one hand, the share of approvals without comments is growing, on the other — the share of applications, which received critical comments, is also growing. The diagram also shows an increase in the share of IMCTs, for which the SCEEMP experts narrowed down the age range of subjects.

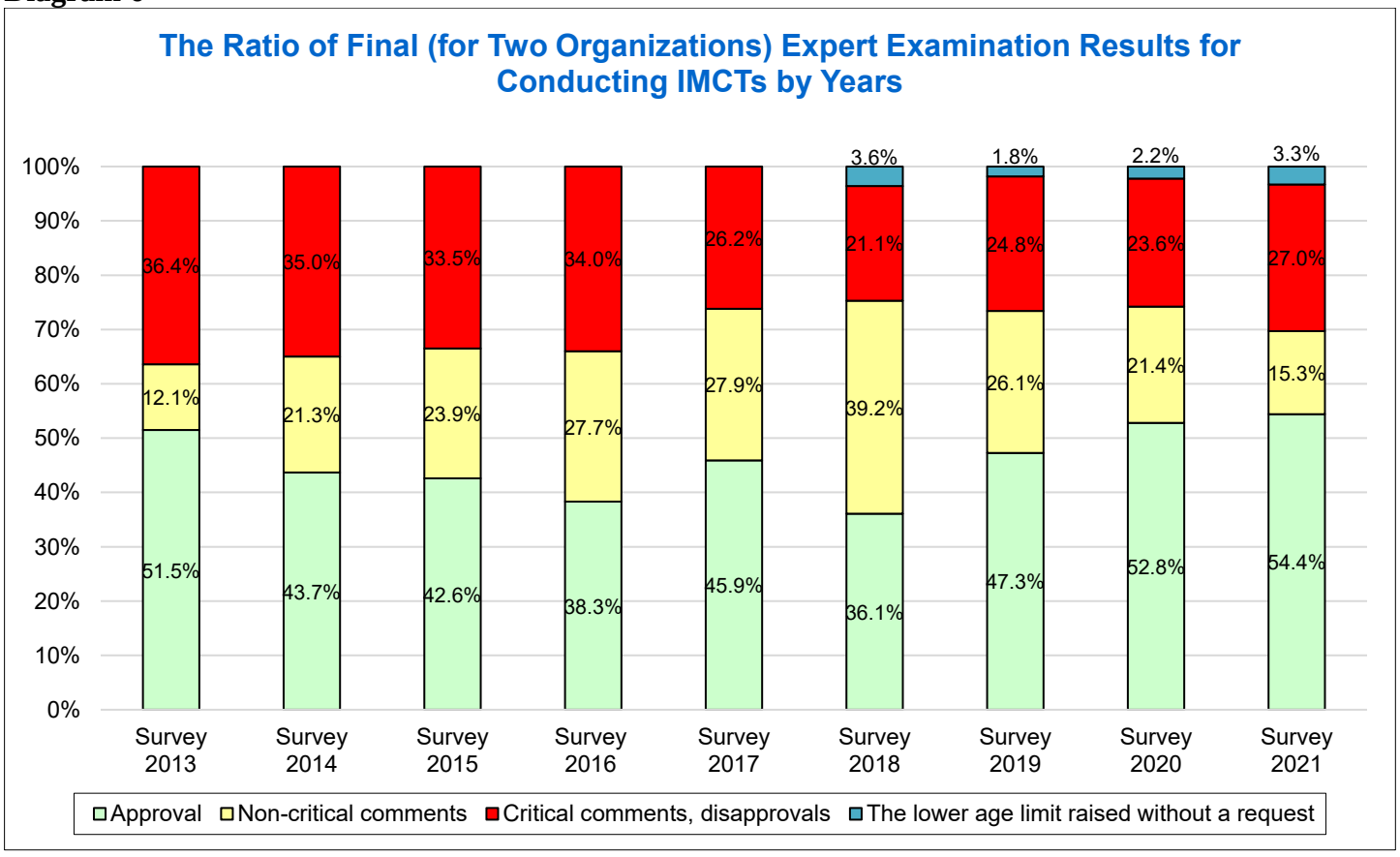
[1] https://pharmvestnik.ru/content/news/Aleksandr-Chuchalin-kritikovavshii-sroki-issledovaniya-vakciny-ot-COVID-19-pokinul-Sovet-po-etike.html

Diagram 5



Data from poll of ACTO members

Diagram 6



Data from poll of ACTO members

Consolidated view of the results of review of initial submissions by both expert bodies is shown in Diagram 6. It demonstrates the same contradictory trend as the SCEEMP examination (simultaneous growth of approvals without comments and approvals with critical remarks) and the same alarming rapid growth in the share of applications with a narrowed down age range.

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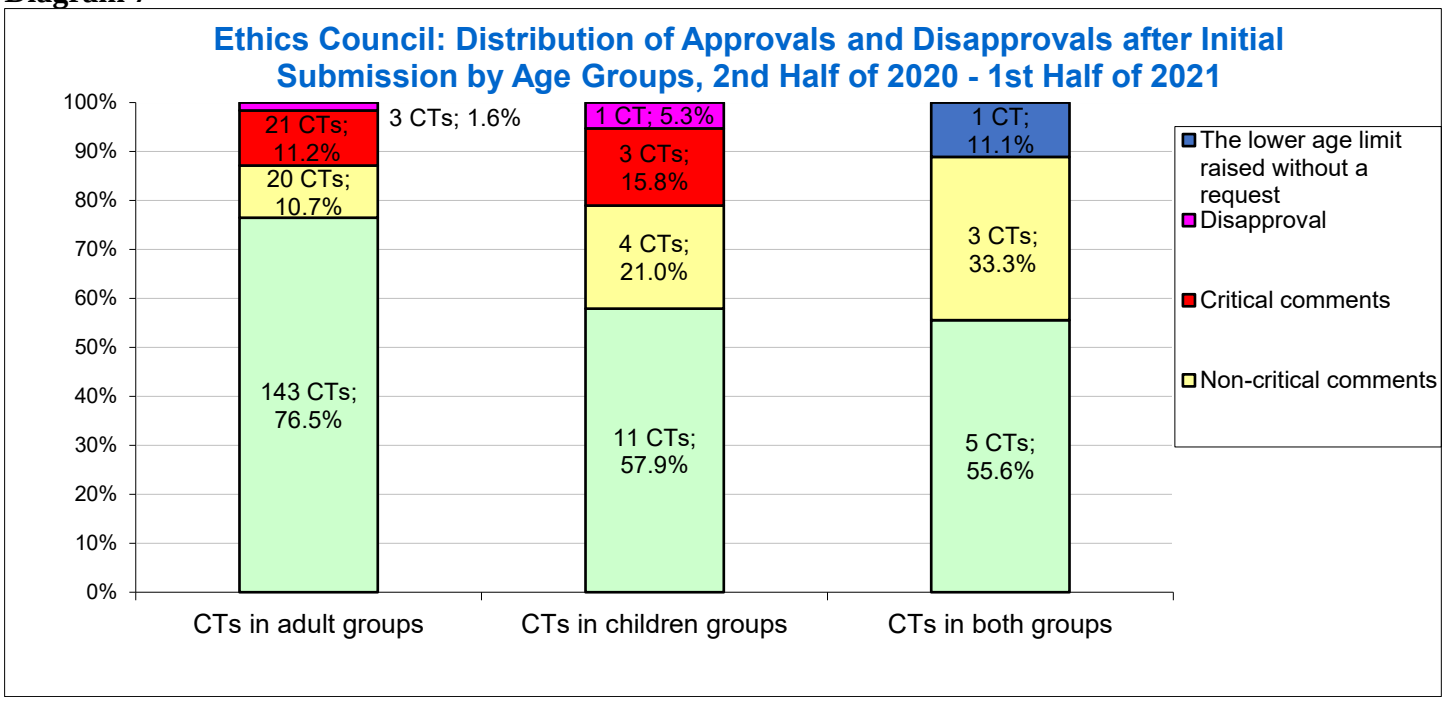
Traditionally, we separately analyze how the age of subjects of a planned trial affects the results of the initial review by the Ethics Council and the SCEEMP. To do so, we divide all applications for IMCTs into three categories: with the participation of adults, with the participation of pediatric population, and with the joint participation of both groups (adults and children). Results of examination by the Ethics Council for each of these categories separately are presented in Diagram 7.

For IMCTs with the participation of adults only, the share of approvals without comments is close to last year's (76.5% of protocols versus 77.8% in 2020). The share of submissions with non-critical comments slightly decreased (10.7% versus 15.3% in 2020). The share of applications that received critical comments went up from 2.1% to 11.2%. The share of disapprovals, on the contrary, decreased from 4.8% a year earlier to 1.6% following the 2021 survey.

Fewer and fewer reviews of exclusively pediatric protocols in the Ethics Council proceed without comments: the corresponding share decreased from 70.8% to 57.9%. On the contrary, the share of applications that received non-critical remarks increased from 4.2% to 21%, and those that received critical comments went up from the same 4.2% to 15.8%. This negative trend is somewhat mitigated by a decrease in the share of disapprovals from 12.5% a year earlier to 5.3% based on the results of the 2021 survey. There was no narrowing down of the age range of subjects of planned pediatric IMCTs by the Ethics Council experts in 2021 (a year earlier this figure was 8.3%).

Applications for IMCTs with a mixed, pediatric and adult population, reviewed by the Ethics Council experts also received comments more often than a year earlier. The share of approvals without comments decreased from 70.6% to 55.6%. The share of cases with non-critical remarks went up from 0 to 33%. However, there were no cases with critical remarks or disapprovals in this category (a year earlier, these shares were 5.9% and 11.8%, respectively). In one case (11.1% share) the Council experts cut the age range of IMCT subjects by raising the lower age limit in a trial of a drug against the novel coronavirus infection. A year earlier this share was almost the same, 11.8% (two trials).

Diagram 7



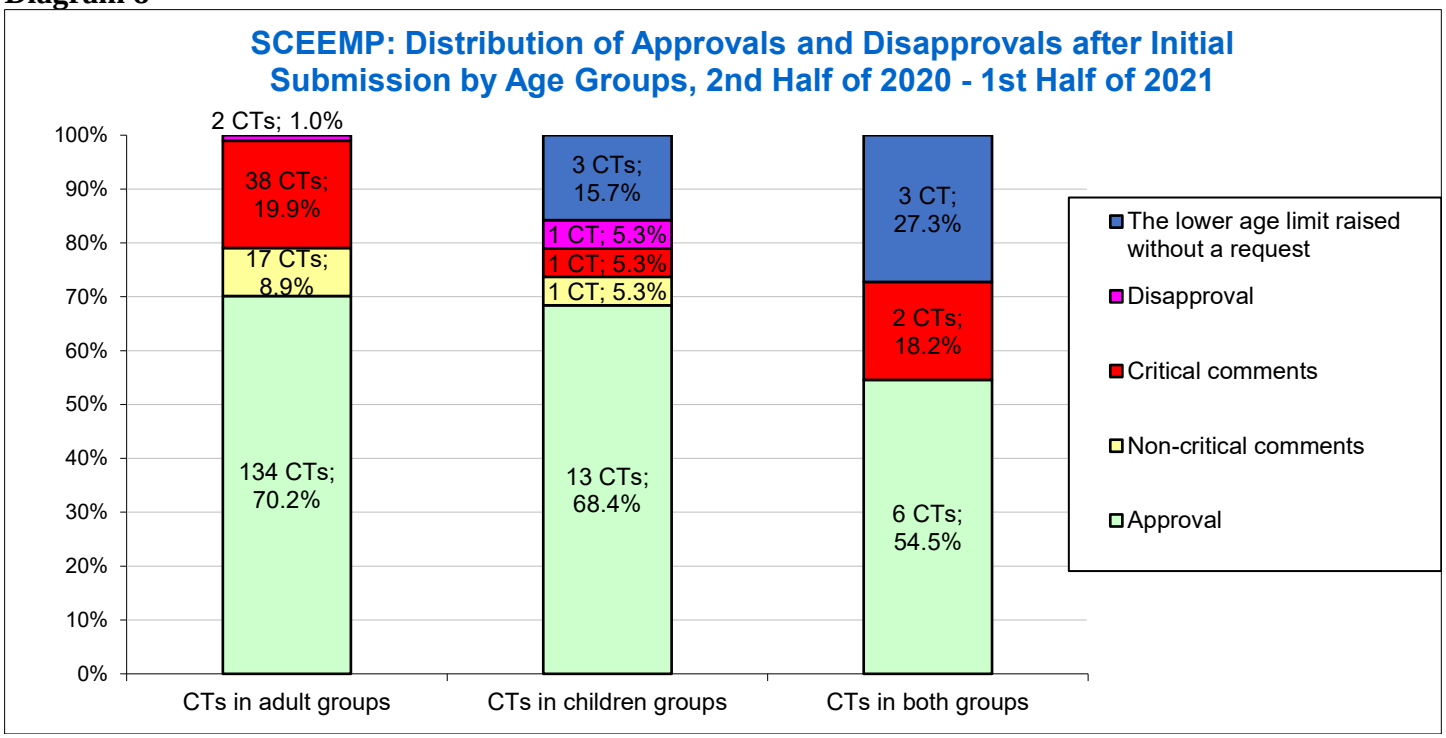
Data from poll of ACTO members

Diagram 8 shows the results of examination by the SCEEMP of IMCT protocols with the participation of different age groups.

For the exclusively adult population, as compared to the results of 2020, the share of approvals without comments slightly decreased, from 73.6% to 70.2%, the share of submissions with non-critical remarks — from 11.4% to 8.9%, and the share of disapprovals — from 2.1% to 1%. The share of reviews with critical comments went up from 13 to 19.9%.

In the category of pediatric protocols, the share of approvals without comments increased from 41.7% to 68.4%, however the share of IMCTs, for which the age range of subjects was narrowed down, also increased from 8.3% a year earlier (two trials) to 15.7% (three projects). Let's take a closer look at these three cases. Two of them pertain to neurology. The age group was narrowed down from 6-18 years old to 12-18 years old. The sponsor considered the issue of abandoning the trial in Russia due to the change in the age group, however decided to commence it. The third protocol provided for the participation of patients with an oncology disease — high-risk neuroblastoma. Initially it was supposed to enroll children >12 months of age, however in the issued approval the age range was reduced, it was allowed to enroll only children aged 3 and above. Neuroblastoma in childhood is, in fact, a congenital disease, since, according to experts, pathologic development of not yet mature nerve cells begins even before a child is born (embryonic tumor). In most children with this disease, it is detected before the age of 1 year. And high-risk neuroblastoma is a variant of the disease with a poor prognosis; despite the successful use of first-line combination therapy, the disease persists or progresses in about 50% of patients. Outcomes after relapse are generally unfavorable, and the 10-year overall survival rate is < 15%. The above mentioned study was designed to include patients with confirmed active disease after previous chemotherapy with a combination of drugs (≥2 agents, including an alkylating agent and a platinum-based compound). With this in mind, the decision of experts not to allow enrolment into the study of the youngest patients of those in whom the previous standard therapy turned to be ineffective, significantly reduces their chances for survival, and also seriously reduces the recruitment options, since the number of children with neuroblastoma aged three years and above cannot be high due to the specifics of the disease.

Diagram 8



Data from poll of ACTO members

Submissions with critical and non-critical remarks in the pediatric population amounted to 5.3% each in 2021 (33.3% and 16.7% a year earlier, respectively). In one case (5.3% share) the SCEEMP experts denied conducting of an IMCT after the review of a pediatric protocol; a year earlier our respondents did not report any SCEEMP's disapprovals of conducting a pediatric IMCT.

When reviewing applications for trials with the participation of mixed populations the SCEEMP experts made fewer comments in 2021 (18.2% share of critical comments versus 41.2% and 0 non-critical comments versus 23.5% a year earlier), but more often than a year earlier approved a project without comments (54.5% versus 29.4%) and more often narrowed down the age range (27.3% versus 5.9% of applications). Let's take a closer look at the three studies where the age range was narrowed down. These are protocols in the area of pulmonology, hematology and oncology. In all cases the trials were expected to include mixed groups, however the SCEEMP prohibited inclusion of patients under 18 years of age, limiting the recruitment to only adults.

In general, analyzing the results for two expert bodies the impression is that such an undesirable from the industry's point of view practice as cutting the age of trial subjects as compared to 2020 is becoming less common for the Ethics Council and, on the contrary, is starting to spread among the SCEEMP experts.

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This subsection contains description of the expert examination results depending on the therapeutic area of a trial applied for. Table 1 and Diagram 9 show the respective distribution for the Ethics Council. Table 2 and Diagram 10 — for the SCEEMP. It should also be mentioned that for the current survey we have introduced a new therapeutic area "Covid-19" separating it from the infectious diseases area, as was previously done for HIV, hepatitis C and tuberculosis.

The Ethics Council experts approved IMCT protocols for Covid-19 treatment and prevention drugs without comments less commonly than other protocols (share of 46.7%), which is somewhat unexpected given the urgent need for medicines against the disease that caused the pandemic and the widespread simplification and "cutting corners" in their development. This group of applications also had the largest share of critical comments. As disclosed in the messages of the ACTO members, a number of studies of anti-coronavirus drugs have not been launched in Russia both due to the long approval time and the need to finalize documentation packages with account for the comments made by the experts of the Ministry of Health (both the Ethics Council and the SCEEMP).

Protocols from another therapeutic area, immunology, 100% of which received approval from the Ethics Council without comments in 2020, in 2021 have only 50% share of approvals without comments. Although, this is the result of reviewing only six applications and the comments received were not critical. Dermatology (60%), neurology (63.2%) and rheumatology (63.6%) also had relatively low shares of approvals without comments. Over the period covered by the ACTO survey the Ethics Council experts were the most favorable to clinical trial protocols for medicines used in such therapeutic areas as pulmonology, endocrinology, nephrology, gynecology and hepatology, as well as protocols of the "other" category — all 100% of them were approved without comments (however, the number of protocols in the last three areas was insignificant, which means that it is too early to draw conclusions regarding the tendency based on the results obtained). Another trend is undoubtedly welcomed — the share of approvals without comments for oncological IMCTs continues to grow: 73.6% in 2021 versus 64% in 2020, 57% in 2019 and 32% in 2018.

Overall, in 2021 for all therapeutic areas, the share of applications approved after the initial review by the Ethics Council either exceeds or is close to 50%, which is slightly better than the results of the 2020 survey (when one therapeutic area had a share of approvals without comments of about 40%) and notably better than the results of 2019 (when six therapeutic areas had a share of approvals without comments of about 40% or less).

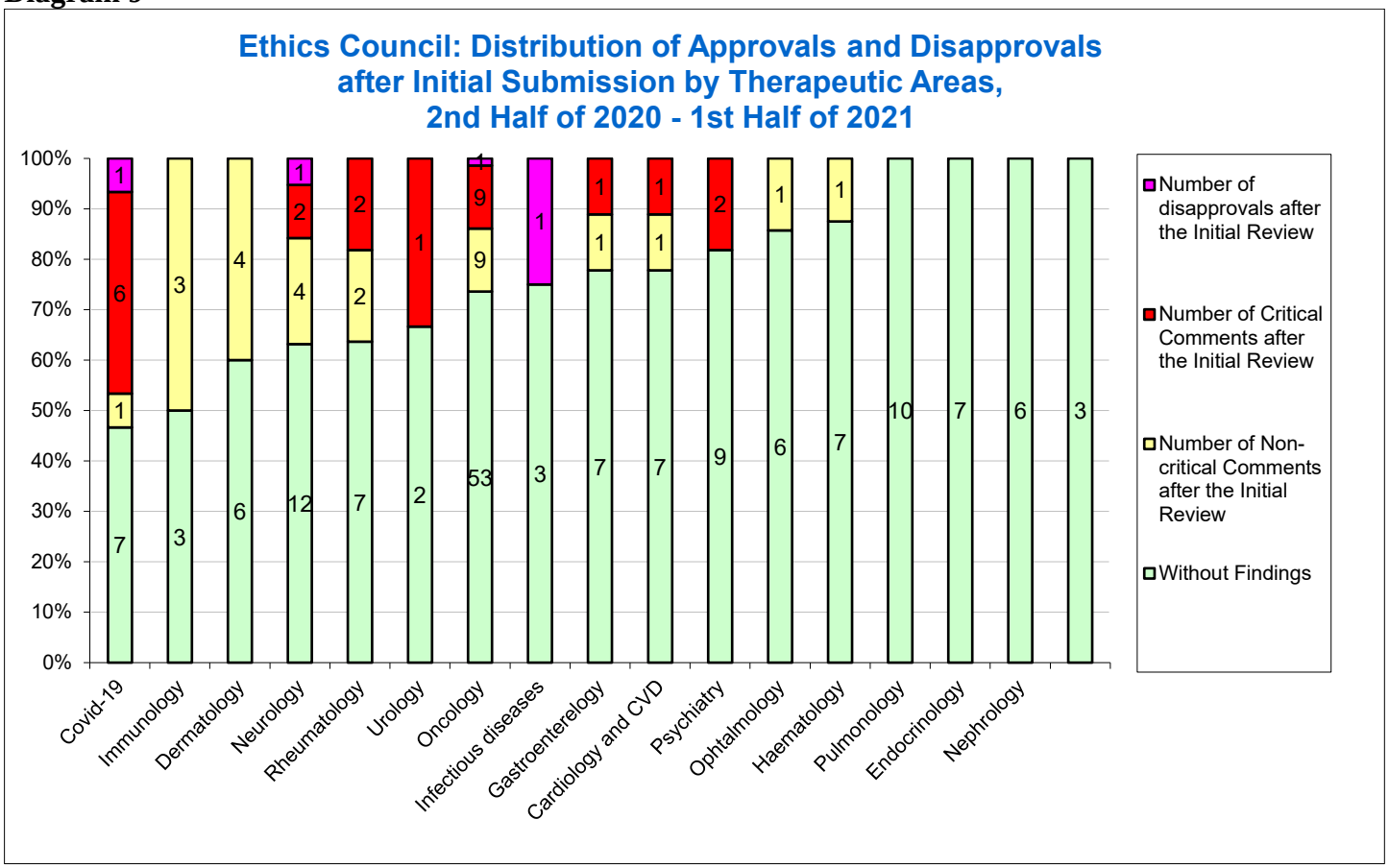
According to the results of the 2021 survey, the SCEEMP experts were least likely to approve without comments applications for IMCTs for medicines used for treatment of infectious diseases (the calculation did not include studies on Covid-19, there were also no studies on HIV, hepatitis C and tuberculosis) — 25% of approvals without comments, ophthalmology — 28.6%, urology and gynecology — 33.3% each. It may be noted here that ophthalmology and gynecology were also among the leaders of the anti-rating a year earlier. Covid-19 protocols were also reviewed by the SCEEMP quite critically — only 52.9% of approvals without comments. The maximum possible share of approvals without comments, 100%, was for IMCTs in the area of cardiology, endocrinology and hepatology.

Table 1

Ethics Council: Distribution of Approvals and Disapprovals by Therapeutic Areas									
Therapeutic Areas	**Total Number of Initial Submissions**	**Without Findings**	**Without Findings, % of Total**	**Number of Non-critical Comments after the Initial Review**	**Non-critical Comments after the Initial Review, % of Total**	**Number of Critical Comments after the Initial Review**	**Critical Comments after the Initial Review, % of Total**	**Number of Disapprovals after the Initial Review**	**Number of Disapprovals after the Initial Review, % of Total**
Oncology	72	53	73.6%	9	12.5%	9	12.5%	1	1.4%
Neurology	19	12	63.2%	4	21.1%	2	10.5%	1	5.3%
Covid-19	15	7	46.7%	1	6.7%	6	40.0%	1	6.7%
Rheumatology	11	7	63.6%	2	18.2%	2	18.2%	0	0.0%
Psychiatry	11	9	81.8%	0	0.0%	2	18.2%	0	0.0%
Dermatology	10	6	60.0%	4	40.0%	0	0.0%	0	0.0%
Pulmonology	10	10	100.0%	0	0.0%	0	0.0%	0	0.0%
Gastroenterelogy	9	7	77.8%	1	11.1%	1	11.1%	0	0.0%
Cardiology and Cardiovascular diseases	9	7	77.8%	1	11.1%	1	11.1%	0	0.0%
Haematology	8	7	87.5%	1	12.5%	0	0.0%	0	0.0%
Endocrinology	7	7	100.0%	0	0.0%	0	0.0%	0	0.0%
Ophtalmology	7	6	85.7%	1	14.3%	0	0.0%	0	0.0%
Immunology	6	3	50.0%	3	50.0%	0	0.0%	0	0.0%
Nephrology	6	6	100.0%	0	0.0%	0	0.0%	0	0.0%
Infectious diseases (except HIV/HCV/tuberculosis. Covid-19)	4	3	75.0%	0	0.0%	0	0.0%	1	25.0%
Urology	3	2	66.7%	0	0.0%	1	33.3%	0	0.0%
Obstetrics/Gynaecology	3	3	100.0%	0	0.0%	0	0.0%	0	0.0%
Hepatology	1	1	100.0%	0	0.0%	0	0.0%	0	0.0%
Other	4	4	100.0%	0	0.0%	0	0.0%	0	0.0%
Total	215	160	74.4%	27	12.6%	24	11.2%	4	1.9%

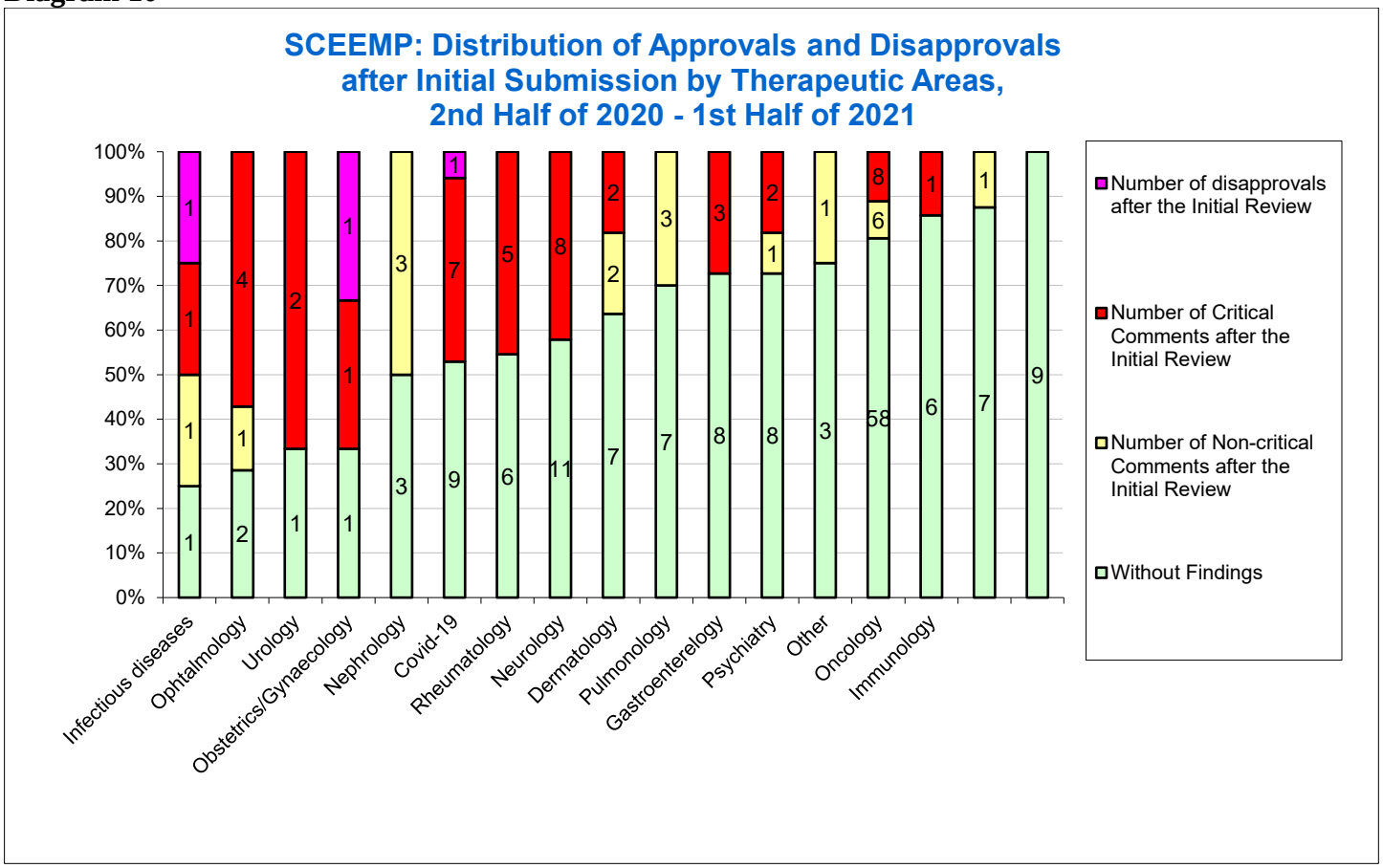
Data from poll of ACTO members

Diagram 9



Data from poll of ACTO members

Diagram 10



Data from poll of ACTO members

Table 2

SCEEMP: Distribution of Approvals and Disapprovals by Therapeutic Areas									
Therapeutic Areas	**Total Number of Initial Submissions**	**Without Findings**	**Without Findings, % of Total**	**Number of Non-critical Comments after the Initial Review**	**Non-critical Comments after the Initial Review, % of Total**	**Number of Critical Comments after the Initial Review**	**Critical Comments after the Initial Review, % of Total**	**Number of Disapprovals after the Initial Review**	**Number of Disapprovals after the Initial Review, % of Total**
Oncology	72	58	80.6%	6	8.3%	8	11.1%	0	0.0%
Neurology	19	11	57.9%	0	0.0%	8	42.1%	0	0.0%
Covid-19	17	9	52.9%	0	0.0%	7	41.2%	1	5.9%
Gastroenterelogy	11	8	72.7%	0	0.0%	3	27.3%	0	0.0%
Rheumatology	11	6	54.5%	0	0.0%	5	45.5%	0	0.0%
Psychiatry	11	8	72.7%	1	9.1%	2	18.2%	0	0.0%
Dermatology	11	7	63.6%	2	18.2%	2	18.2%	0	0.0%
Pulmonology	10	7	70.0%	3	30.0%	0	0.0%	0	0.0%
Cardiology and Cardiovascular diseases	9	9	100.0%	0	0.0%	0	0.0%	0	0.0%
Haematology	8	7	87.5%	1	12.5%	0	0.0%	0	0.0%
Endocrinology	7	7	100.0%	0	0.0%	0	0.0%	0	0.0%
Immunology	7	6	85.7%	0	0.0%	1	14.3%	0	0.0%
Ophtalmology	7	2	28.6%	1	14.3%	4	57.1%	0	0.0%
Nephrology	6	3	50.0%	3	50.0%	0	0.0%	0	0.0%
Infectious diseases (except HIV/HCV/tuberculosis. Covid-19)	4	1	25.0%	1	25.0%	1	25.0%	1	25.0%
Urology	3	1	33.3%	0	0.0%	2	66.7%	0	0.0%
Obstetrics/Gynaecology	3	1	33.3%	0	0.0%	1	33.3%	1	33.3%
Hepatology	1	1	100.0%	0	0.0%	0	0.0%	0	0.0%
Other	4	3	75.0%	1	25.0%	0	0.0%	0	0.0%
Total	221	155	70.1%	19	8.6%	44	19.9%	3	1.4%

Data from poll of ACTO members

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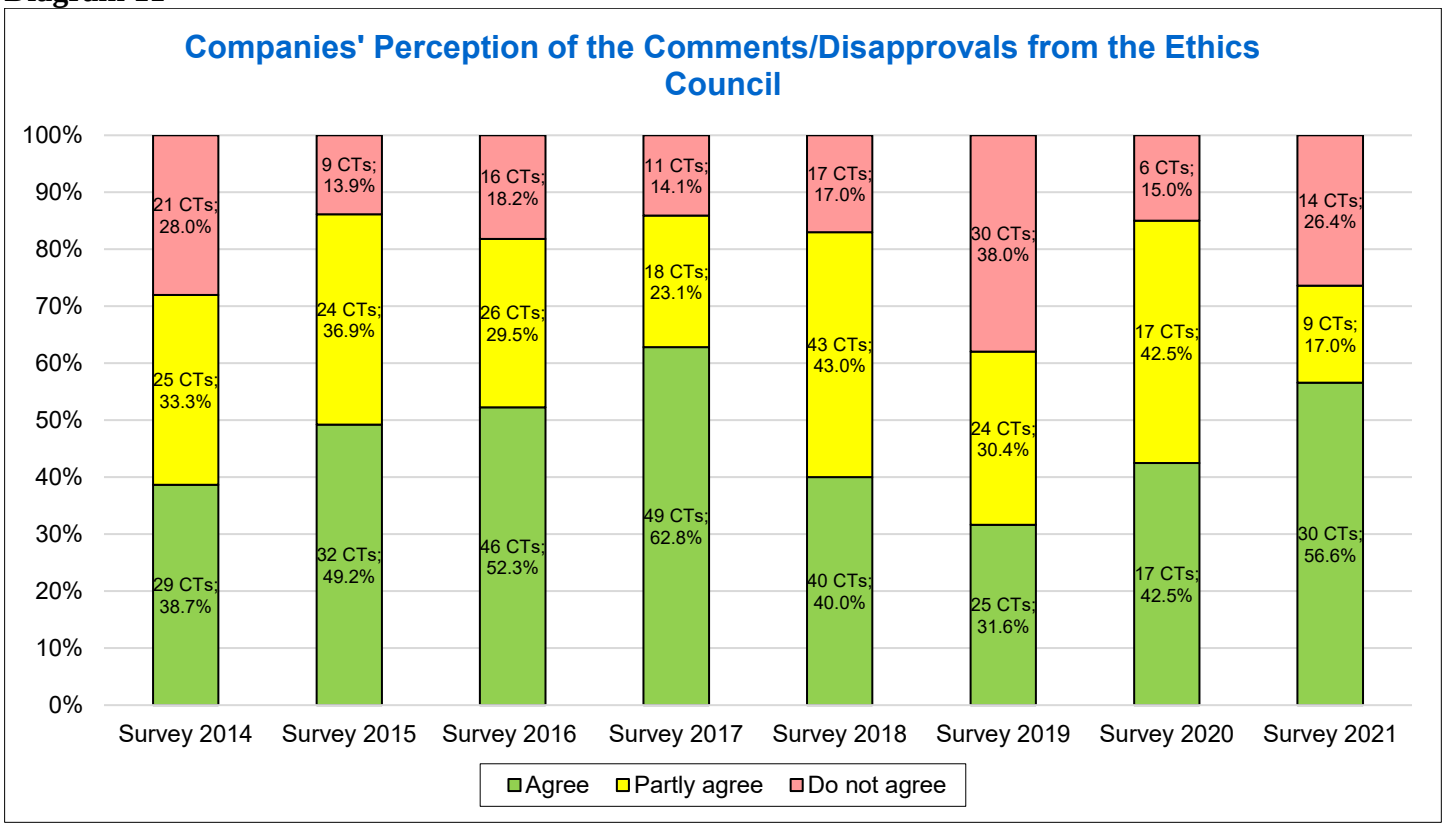
In our survey we also inquire what the applicants think of the comments made by the expert bodies, whether they consider them fair, whether they agree to modify documentation packages as proposed by the experts and how they react to the comments received in each specific case.

Diagram 11 shows how companies' perception of the expert examination of the Ethics Council changed from 2014 to 2021. It is apparent that, on the one hand, the level of agreement with the comments made continues to grow (56.6% versus 42.5% a year earlier), even if it has not yet reached its former maximum of 62.8% recorded in 2017. On the other hand, the level of explicit disagreement has also grown over the past year (26.4% versus 15% in 2020). The share of cases when respondents partially agreed is the lowest since 2014, i.e. according to the latest survey there is a certain polarization in the perception of comments from the Ethics Council in the industry.

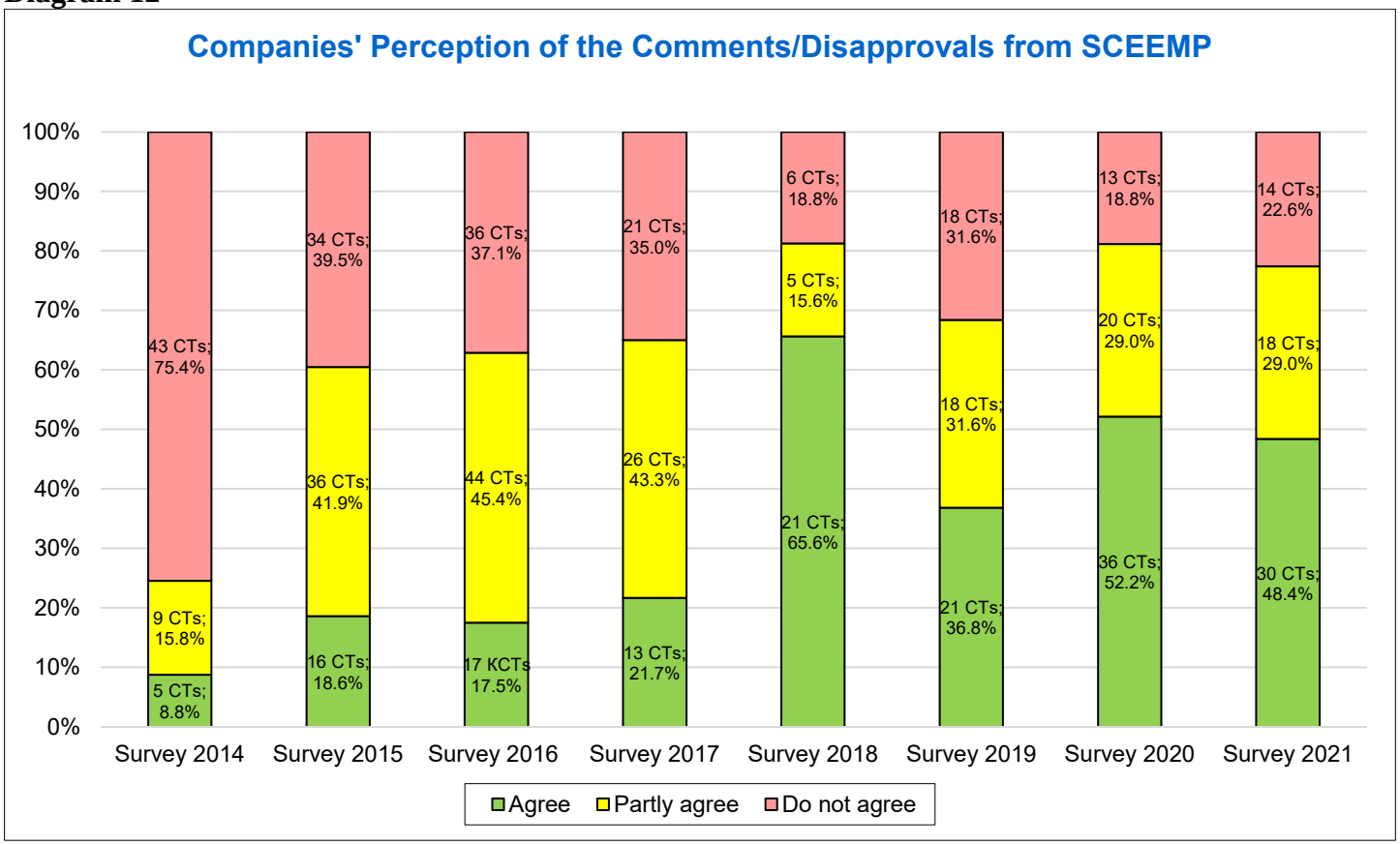
Diagram 11



Data from poll of ACTO members

When assessing the work of the SCEEMP experts the ACTO respondents were slightly more critical than in 2020. The level of agreement slightly decreased from 52.2% to 48.4%, while the level of explicit disagreement, on the contrary, increased from 18.8% to 22.6%. The share of "partly agree" answers remained at the level of 29%. In general, the results were close to last year's and, although they do not reach the maximum level of agreement with the SCEEMP's expert examination, which was observed in the 2018 survey, it is still noticeably better than the assessment of work of this expert body in the 2015–2017 surveys and especially 2014.

Diagram 12



Data from poll of ACTO members

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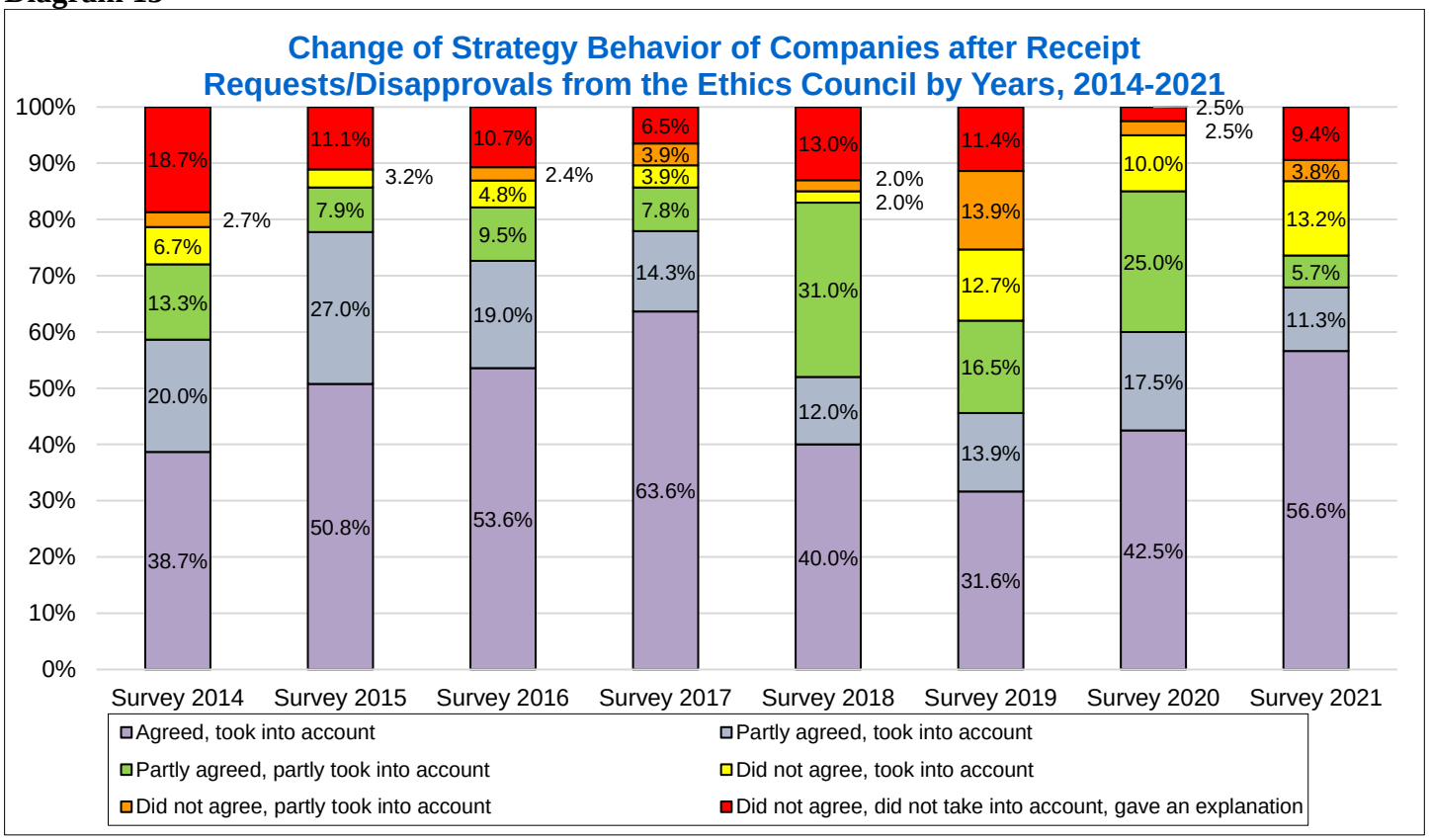
Diagram 13 shows, which strategy of responding to comments made by the Ethics Council experts was chosen by the applicants in 2004–2021. The share of answers "agreed, took into account" is growing for the second year in a row, from 31.6% in 2019 to 42.5% in 2020 and to 56.6% in 2021. However, the share of explicit disagreement has also significantly increased as compared to the previous survey: answers "did not agree, did not took into account, gave an explanation" increased from 2.5% in 2020 to 9.4% in 2021. The share of other answers suggesting disagreement also increased: from 2.5% up to 3.8% for "did not agree, partly took into account" and from 10% to 13.2% for "did not agree, took into account". However, the shares of answers "partly agreed, partly took into account" and "partly agreed, took into account" shrank to the minimum since 2014, 5.8% and 11.3% respectively — manifestation of the above-mentioned polarization in the evaluation of the Ethics Council examination by our respondents.

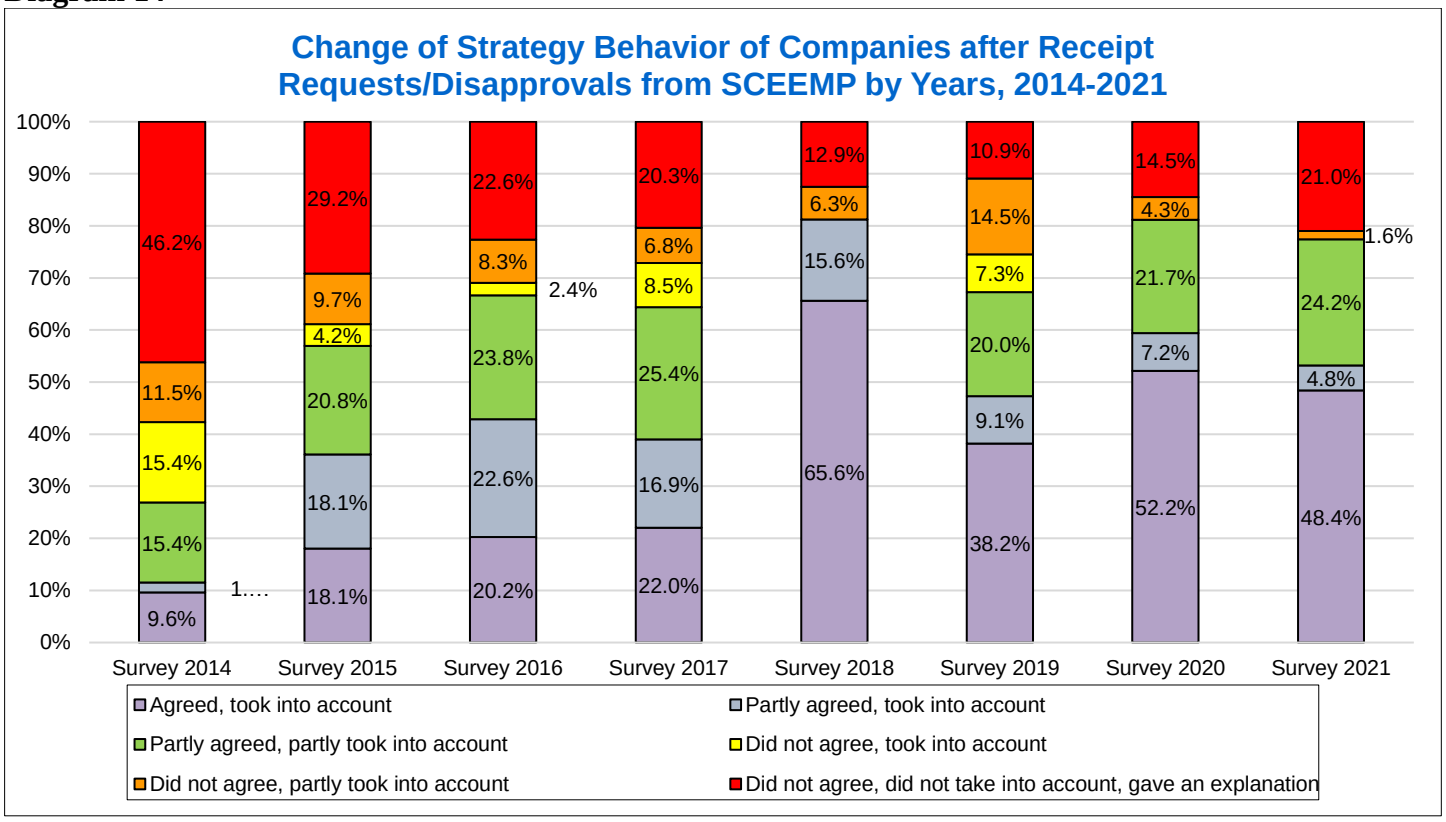
Diagram 14 allows to assess the changes in reaction to the comments of the SCEEMP over 2014–2021. The same growth of active disagreement with the examination can be observed here, which manifested itself in the evaluations. The share of answers "did not agree, did not took into account, gave an explanation" increased from 14.5% a year earlier to 21%. Answers "did not agree, partly took into account" were extremely rare in the 2021 survey, only 1.6% versus 2.5% a year earlier. The share of answers implying active agreement decreased: from 52.2% to 48.4% for "agreed, took into account", from 17.5% to 11.3% for "partly agreed, took into account", and only the share of answers "partly agreed, partly took into account", i.e. including an element of disagreement and a desire to prove oneself right, increased slightly, from 21.7% to 24.2%.

Diagram 13



Data from poll of ACTO members

Diagram 14

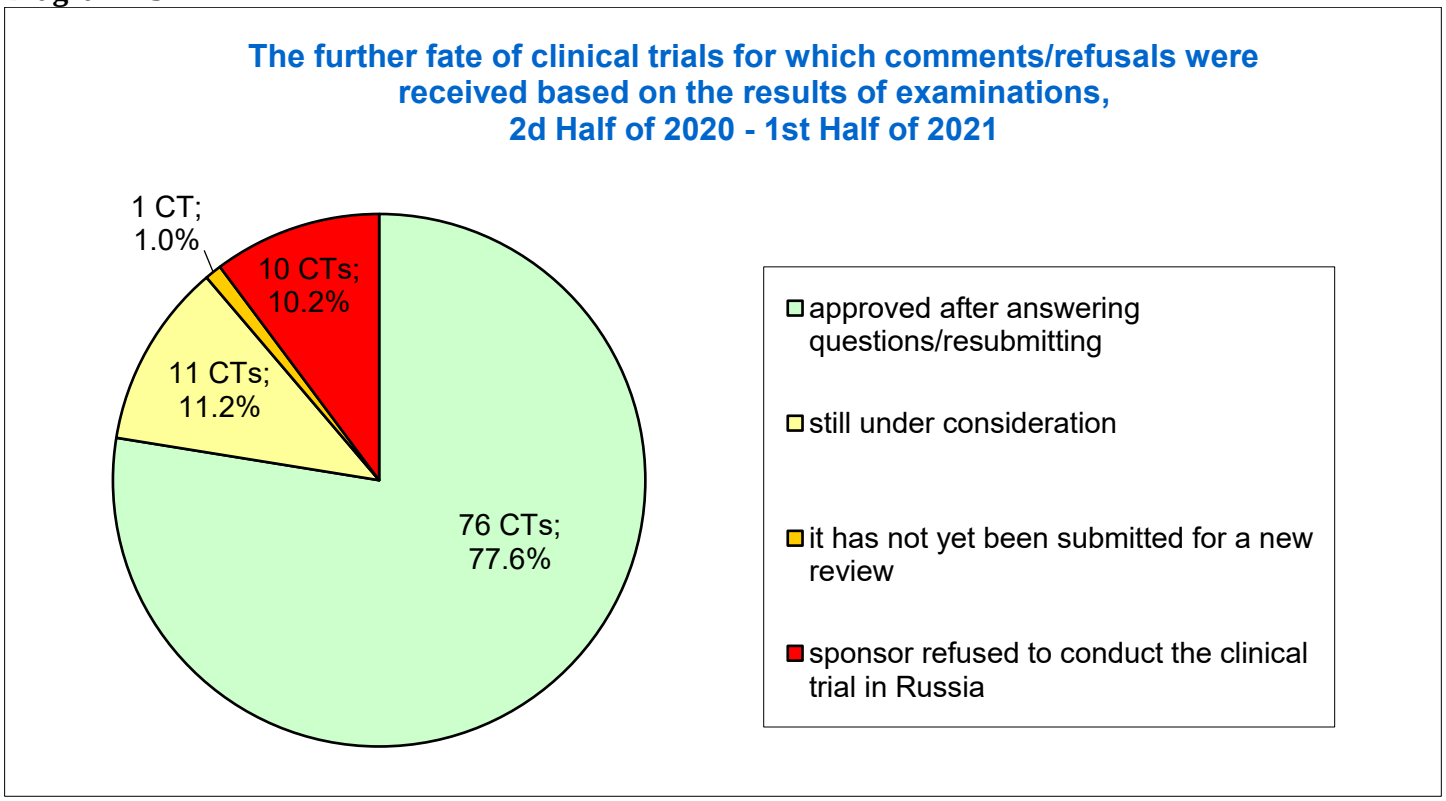


Data from poll of ACTO members

Up to 2017 the ACTO newsletter also contained statistics describing the further fate of the trials, which received comments and disapprovals after the initial review. Since these numbers were small and their ratio changed insignificantly from year to year, we stopped publishing such data. But since in the period from July 2020 to June 2021 sponsors more often than usual refused to conduct a trial in Russia following the results of the examination, we decided to present this information to the reader once again. It is shown in Diagram 15.

It is apparent that for the majority of IMCTs the comments made and disapprovals received did not become an insurmountable obstacle — 77.6% received approval upon subsequent submission or after responding to questions/comments of the experts. Another 11.2% of applications were pending at the end of the survey, and 1% were awaiting re-submission.

Diagram 15



Data from poll of ACTO members

However, we would like to note that in 10.2% of cases (which is as many as ten trials) the sponsor had to refuse to conduct the trial in Russia. Of these ten trials six (!) were for Covid-19 and one for each of oncology, obstetrics/gynecology, dermatology and cardiology. It is impossible to say unequivocally that it was the results of the examination that caused the sponsors to make such decision, however, according to the statements of the ACTO members, it was the negative examination and/or the long review time that had the main effect. Here are just a few of the respondents' comments:

– "Comment on the GMP [certificate], the sponsor refused to conduct the trial in Russia" (oncological protocol).

– "Recruitment period has ended" (Covid-19).

– "The sponsor refused after receiving the second comment from the SCEEMP. The sponsor confirmed in response to the first request that it would take the comments of the SCEEMP into account and update the necessary documents (Protocol), however the SCEEMP made a second comment — to provide exactly the updated protocol, although earlier this procedure with "sponsor commitment to update the document" was acceptable" (Covid-19).

– "Due to availability of vaccination the sponsor decided not to respond to the comments of the SCEEMP and excluded Russia, but it is impossible to say for sure, what had a greater influence" (Covid-19).

– “Ethics refused with the wording “there is no information on the results of using the drug in healthy volunteers and the rationale for the chosen dose” — this was at the height of the Covid-19 [pandemic]. The SCEEMP requested more than 10 items of additional clarifications on the dose and safety. After providing the information they denied us again, since [allegedly] the dose was not justified and the data of preclinical trials were not enough” (Covid-19).

– “Trial of a generic, a Phase I study report was requested, but the Sponsor failed to meet the deadline. The second request from the SCEEMP was received, but since the trial is competitive and recruitment in other countries went well, the Sponsor decided to refuse to participate in the Russian Federation” (dermatology).

– “The trial in Russia did not start due to the rapid rate of patient recruitment in the world” (cardiology).

APPLICATION OF THE MASKING METHOD IN CLINICAL TRIALS IN THE RUSSIAN FEDERATION

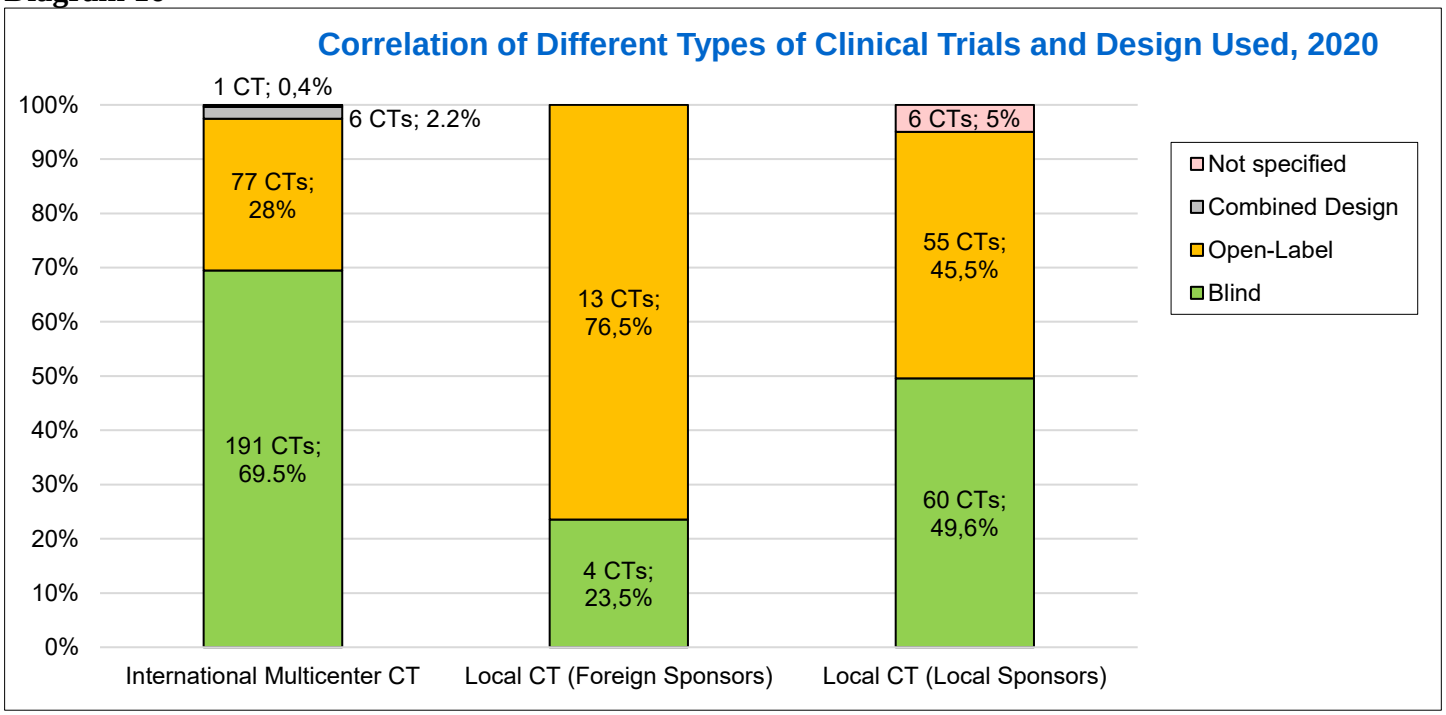
Diagram 16 shows the result of analysis of the practice of using the blind method in various types of trials, approvals for which were granted in 2020. For a more correct comparison, non-comparative trials were immediately excluded from the calculation. Whether the trial is comparative was assessed in accordance with the information about the protocol available for international projects — in international registries (clinicaltrials.gov and clinicaltrialsregister.eu), for Russian projects — focusing solely on the name of the protocol in the register of the Ministry of Health of Russia (grls.rosminzdrav.ru). The ratio of blind and open-label trials is shown separately for IMCTs, for local trials by foreign sponsors, and for local trials by Russian developers.

The share of comparative IMCTs using the blind method in 2020 was 69.5% (191 studies). In 2019 this indicator was 72.1% (186), and in 2018 — 76.3% (183). Based on the results of observations over a space of three years it would be premature to judge whether the figures reflect the actual downward tendency in the share of IMCT protocols with blinding or the changes are explained by random data fluctuations.

The share of blinding protocols in local trials by foreign sponsors amounted to 23.5% (four trials) at the end of 2020. In 2019 it was 26.7% (eight trials), and in 2018 — 40% (ten trials). For local trials by Russian sponsors, similar indicators are 49.6% (60 trials) in 2020, 60.6% (80 trials) in 2019, and 56% (42 trials) in 2018. It should be noted that the name of the six protocols for local trials by Russian sponsors in 2020 did not make it possible to conclusively establish whether their design provided for masking. In this regard the share of protocols using the blind method for this type of trials may actually turn out to be somewhat higher than shown in Diagram 16.

It would also be more correct to postpone conclusions regarding changes in the share of protocols with blinding in local trials over three years until a larger amount of data is accumulated. However, it may be noted that in 2018–2020 of the three types of comparative trials under consideration IMCTs consistently demonstrate the largest share of protocols using the blind method, the smallest share is accounted for by local trials of foreign sponsors. This seems logical, given that the purpose of the latter is most often satisfying the whims of the Russian regulator, rather than obtaining objective data.

Diagram 16



Data from www.grls.rosminzdrav.ru

IMPORT OF MEDICINAL PRODUCTS FOR CLINICAL TRIALS

Table 3 shows statistics for 2020 on import into the Russian Federation of medicinal products to be used for clinical trials including comparators and concomitant treatment.

As compared to 2019, the total value of shipments increased by 38.4% in ruble equivalent and by 23.6% in dollar equivalent. The growth rate in rubles for VAT amounted to 29.3%, for customs duties (CD) — 18.3%, for customs fees (CF) — 37%, and for VAT + CD + CF — 26.9%.

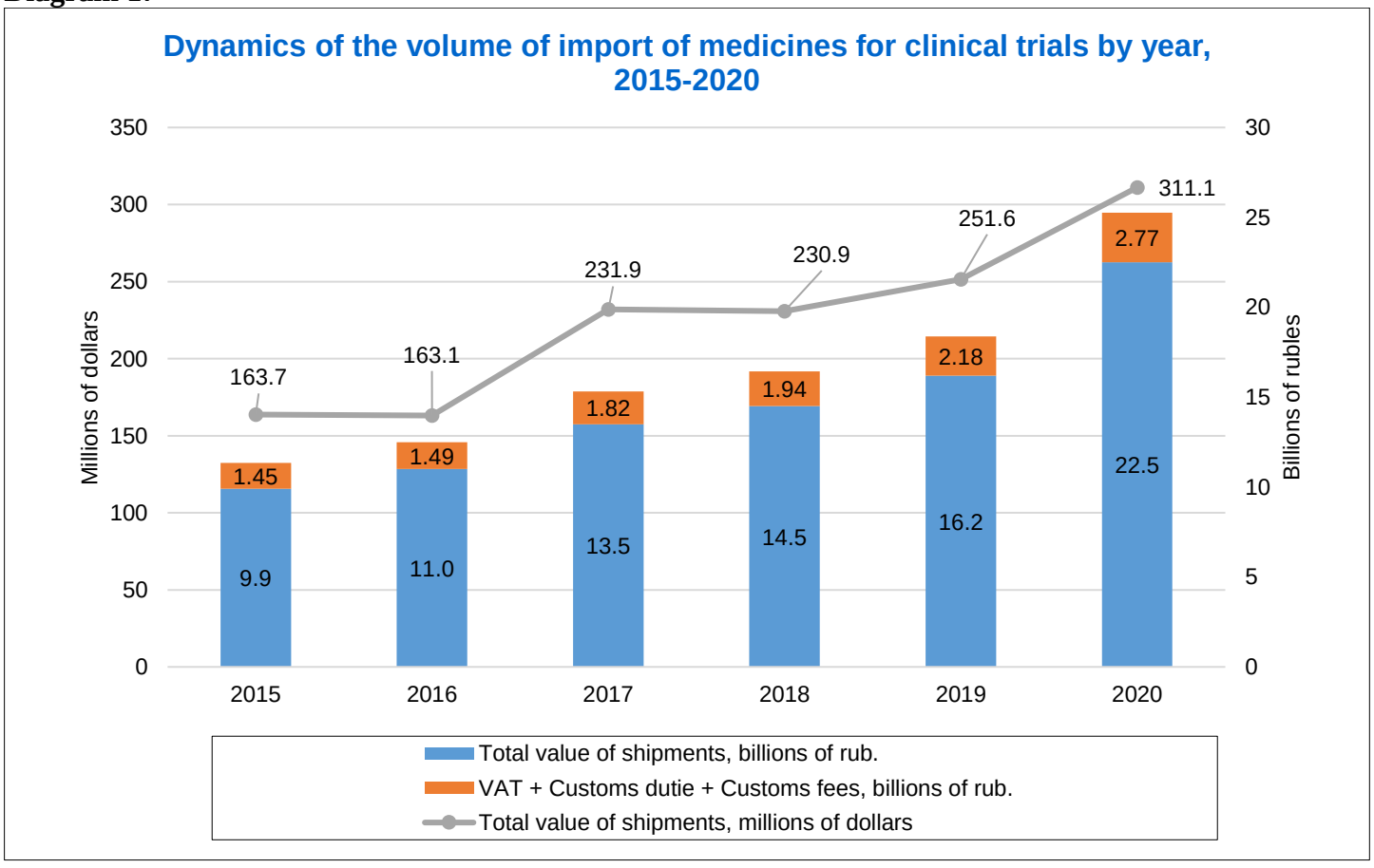
Table 3

Import of medicinal products to the Russian Federation for clinical trials, 2019-2020		
Parameter	**2019**	**2020**
Total value of shipments, rub.	16 241 047 409	22 474 751 823
Total value of shipments, $	251 611 534	311 102 610
VAT, rub.	1 672 642 159	2 162 501 228
Customs duties, rub.	489 490 838	579 223 861
Customs fees, rub.	18 654 524	25 561 402
VAT + Customs duties + Customs fees, rub.	2 180 787 522	2 767 286 491

Source: RNC Pharma

Diagram 17 shows the dynamics of the volume of imports of medicinal products for clinical trials into the Russian Federation since 2015. The graph shows that 2020 demonstrated the highest growth rate of the analyzed indicators in ruble equivalent for the entire observation period. In dollar equivalent, more intensive growth was recorded only in 2017, when it amounted to 42.2%. This is explained, apparently, by the fact that in 2017 for a number of economic reasons the exchange rate of ruble against dollar has stabilized and slightly increased.

Diagram 17



Source: RNC Pharma

Table 4 shows the top 10 leading manufacturers in terms of the volume of imported medicinal products. It should be noted that besides the manufacturers themselves trial medicines can be imported by both CROs involved in these trials and other pharmaceutical companies in order to use them as comparators or concomitant treatment for their research. In this regard, there is a separate column in Table 4 for the share of supplies that were made by the manufacturing company itself.

At the end of the year Amgen, Alexion Pharmaceuticals, Sanofi and Merck Group dropped out of the top 10 (seventh, eighth, ninth and tenth places in 2019). The vacated positions were taken by Astellas Pharma, AstraZeneca, Eli Lilly and AbbVie. The top part of the rating, aside from some reshuffles, did not undergo any significant changes as compared to 2019. It is worth noting the rise of Pfizer from the sixth to the third place and dropping of F. Hoffmann-La Roche from the fourth position a year earlier to the sixth place at the end of 2020.

Table 4

Top-10 pharmaceutical companies on import of medicinal products for clinical trials, 2020					
Ranking	**Company**	**Value of shipments, rub.**	**Number of shipments**	**Imported by the companies themselves, %**	**Ranking, 2018**
1	Merck & Co.	3 156 253 560	240	79.7%	2
2	Novartis	2 381 971 078	386	88.0%	1
3	Pfizer	2 138 075 631	170	56.4%	6
4	Johnson & Johnson	2 056 219 165	165	39.5%	3
5	BMS	1 946 880 028	247	32.5%	5
6	F. Hoffmann-La Roche	1 742 758 693	187	49.4%	4
7	Astellas Pharma	1 091 028 504	23	0.0%	16
8	AstraZeneca (incl. Acerta Pharma)	1 040 037 336	120	0.0%	AstraZeneca - 12; Acerta Pharma - 61
9	Eli Lilly	871 508 408	108	0.0%	11
10	AbbVie (incl. Allergan)	627 611 234	294	0.0%	AbbVie - 13; Allergan - 89

Source: RNC Pharma

CANCELING OF THE ACCREDITATION SYSTEM: PRACTICAL ASPECTS

...paved with good intentions.
Proverb

In 2019 the Russian government promised to make life easier for the business and, by launching the so-called "regulatory guillotine," abolish a number of regulatory acts and requirements set forth therein that are redundant, outdated and hindering development. Among others, Decree of the Government of the Russian Federation No. 683 dated 03 September 2010 that approved the procedure for mandatory accreditation of medical organizations for the right to conduct clinical trials was repealed from January 2021[2].

ACTO has always opposed the institution of accreditation considering it an excessive bureaucratic burden. A license for medical activities confirms that a clinic can carry out standard procedures required in clinical trials (taking samples, administering injections, dispensing drugs, etc.). CV of a Principal Investigator and his team members confirms their qualifications and ability to complete the tasks prescribed by the protocol. What the accreditation paper adds to this has always been a mystery to us. However, the accreditation had to be reissued from time to time (for example, in case of renaming, merging or otherwise reorganizing medical organizations, etc.) and renewed every five years. Considering all this, ACTO welcomed the decision to cancel the accreditation and notified its members and other interested parties about it beforehand in November 2020[3].

One might wonder, what can possibly go wrong?

The first signs appeared at the end of January 2021. ACTO members said that when submitting an application for a trial the system of the Ministry of Health still uses the database based on the register of accredited medical organizations. In practice, this meant that only the clinic that had already been included in the database (i.e. had accreditation before, this accreditation has not expired, the clinic has not changed its name, etc.) could be indicated as the trial site. Although the law allowed to add to the application trial sites in new medical organizations that had not previously had accreditation (as well as with expired accreditation or invalid due to a change in the clinic's details), the Ministry of Health did not create a technical possibility for this in advance.

At first, the department staff suggested the following workaround to the applicants: submit an application "as if" for accreditation of a clinic and attach a copy of the license for medical activities thereto (despite the fact that the license of a particular organization can be verified within the interdepartmental interaction between the Ministry of Health and Roszdravnadzor). Whether the documents must be submitted in paper or in electronic form, how long will it take to be entered into the register, what to do if a medical organization was reorganized in a previously approved trial, does this mean that the entire procedure with submission of documents "as if" for accreditation will have to be repeated again — all these questions and many more were left up in the air in January 2021 with no answers. As well as the question of how long the register of accredited medical organizations will exist after the cancellation of accreditation. Albeit under the new name "Information about organizations conducting clinical trials of medicinal product for human use".

Representatives of the industry understood and shared the desire of the Ministry of Health to keep the register in some form: it is much more convenient to select a clinic from a ready-made list saving time, minimizing typos, errors and duplication of information. However, the procedure for adding new organizations to the database was needed and needed "yesterday".

At the same time, in January 2021, the issue was raised at the meeting of the working group on implementation of the "regulatory guillotine" mechanism in the area of pharmaceuticals and medical devices.

[2] By Decree of the Government of the Russian Federation No. 855 dated 13 June 2020 certain regulatory acts of federal authorities were declared invalid from 01 January 2021, including Order of the Government of the Russian Federation No. 683 dated 03 September 2010 On Approval of the Rules of Accreditation of Healthcare Organizations for the Right to Carry Out Clinical Trials of Medicinal Products for Medical Use.

[3] "Information on cancellation of the system of accreditation of medical organizations for the right to conduct clinical trials" on ACTO's website.

The representative of the regulator proposed the following solution: it was promised to add a special form into the electronic system of the Ministry of Health by the end of February, which would allow the applicant to independently enter new medical organizations into the database and then select them when creating an application for a trial. Until the extended functionality starts working, it was proposed to submit applications for participation in a trial of medical organizations not listed in the registry in paper form.

However, it wasn't that simple. At first, some employees of the respective department of the Ministry of Health insisted that information about a new clinic should be submitted by a medical organization and not by a sponsor — in response to ACTO's complaints the head of the department promised to investigate the situation and raise the awareness among the executors. Then — already in March 2021 — it turned out that the Ministry of Health, instead of introducing a form that allows the applicant to enter medical organizations on its own, decided to combine its electronic system with the database of organizations licensed for medical activities, which is maintained by Roszdravnadzor. No clear timeframe was given for implementation of this ambitious idea. However, it was clear that before a brighter future, applicants would have to submit information about clinics that are not in the database on paper.

Moreover, the number of sites that are not in the database of the Ministry of Health should have increased like an avalanche throughout 2021: accreditation for a period of five years was introduced by Decree of the Government of 03 September 2010, most clinics obtained it in 2011 and renewed in 2016, which means that in 2021 these documents expired again, therefore making many medical organizations, even those included in the database, unavailable for selection when filling out an electronic application for a trial. The Ministry of Health also tried to deal with this problem manually: validity period of accreditation (which is, as a reminder, cancelled from 01 January 2021) for some medical centers in the database began to increase up to 2025 and even up to 2099. However, this could not resolve the issue of changing the name, address and other details, as well as entering new clinics.

In April 2021 new unpleasant details came to light. It turned out that the procedure for adding clinics that are not in the register in a trial actually is as follows: the organizer of a trial submits data about a clinic in paper form, waits for it to be handed over to the IT department and entered into the register, and only then gets the opportunity to submit an application for a trial or for amending the current protocol. The applicants wasted time because of this procedure not provided for in any regulations. In once such instance, patients already included in the trial had to be urgently transferred to another site. However, since the new site was not in the database, it took more than a month to resolve the urgent issue.

In May 2021, having concluded that it wasn't possible to solve the issue informally, ACTO sent an official letter to the Ministry of Health. The letter noted that the rights of trial organizers were violated, and the reason for this was the lack of a statutory possibility to submit information about medical organizations to the Ministry of Health, and that the legislation does not provide for preliminary submission of information about a clinic to enter it into the database. ACTO insisted that the functionality of the regulator's electronic system should be expanded.

In mid-June the issue seemed to get off the ground: a form allowing applicants to enter new medical organizations into the database appeared on the portal of the Ministry of Health. But, as expected, it wasn't that simple. It looks like the applicants were given the same form that was previously used by medical organizations requesting accreditation, and the content of the form remained unchanged. As a result, in addition to the standard information about the site provided for in clause 7 of part 2 of Article 39 of Federal Law No. 61 On Circulation of Medicines (name, form of incorporation, location and place of business, contact details), the trial organizers had to indicate information not provided for by laws and by-laws, in particular Taxpayer identification Number (INN) (including details of the document, i.e. the number of the form!), Primary State Registration Number (OGRN) (again, including the number of the form), information about the head of the organization (name, position), details of the license for medical activities, profile of medical activities, goals of clinical trials and even (we couldn't believe our eyes at first either) the type of accreditation, the one that has just been canceled. The system does not allow to form an application, if there are empty fields. According to ACTO members, even if the trial organizer has all the necessary information — which is by no means always the case and does not have to be like this — just filling out the form takes about 40 minutes of work of two employees of the applicant.

At the end of July 2021 — six months after the cancellation of accreditation for the right to conduct clinical trials — ACTO sent another letter to the Ministry of Health, where it insistently asked to bring the form allowing to enter information about a medical organization that is planned to be included in a trial into compliance with the requirements of the Federal of the Law On Circulation of Medicines and finally give an opportunity to no longer submit the same information about a clinic, which was previously required for accreditation. As of the beginning of September 2021, we were able to get only a verbal promise to remove unnecessary fields from the form from the Ministry of Health, however no specific deadlines were named.

Let's get back to the question, what could have gone wrong in a seemingly simple matter — cancellation of a clearly redundant requirement, such as accreditation of medical organizations for the right to conduct clinical trials? It seems that the entire tangle of difficulties, misunderstandings, mutual claims, hastily adopted half-measures and another difficulties in the "regulator-industry" relationship was due to the fact that implementation of an excellent initiative warmly approved by the industry — cancellation of accreditation — was not sufficiently thought out and prepared. And this, in turn, is most likely associated with another, much broader and systemic problem that ACTO has been trying to fix in recent years: the increasing weakening of contacts of the Ministry of Health with external players, including international pharmaceutical companies. The regulator's efforts to shield itself from feedback and the need to solve new problems that appear in the dialogue, to minimize the discussion of topical issues and to solve everything on its own without discussing it with the end consumers of services are becoming more and more intense. Naturally, such a position leads to emergence of "blind spots": problems that could have been identified and solved in advance in the course of discussion with the parties concerned, but about which the regulator, closed in on itself, simply did not have the opportunity to find out until they manifested in full strength.

RANKINGS OF PRINCIPAL INVESTIGATORS

Rankings presented below are based on the data from the Register of Principal Investigators of the Ministry of Health of the Russian Federation[4]. Since the register has been maintained since November 2010, the data below are for the period from November 2010 to July 2021, when the information was downloaded by ACTO. Please bear in mind that due to the technical features of a particular public database individual trials may disappear for a while and then appear again, so that statistical indicators are subject to some, albeit insignificant, fluctuations. In addition, the data obtained from the register contains duplicate entries (due to a typo in the first name, surname or date of birth, the same person may be entered in the register several times) and needs manual cleaning, which also leads to discrepancies between ACTO's statistics and automatic line counting in the register of the Ministry of Health.

Table 5 shows the overall ranking of principal investigators without division into specialties. Position therein depends on the number of appointments as Principal Investigator. The number of current protocols is displayed in a separate column. Due to the fact that ACTO now has the technical ability to assess, how many bioequivalence studies are carried out by a particular specialist, respective information is shown in a separate column of the table as a share of the total number of studies.

Obviously, the activity of investigators depends, among other things, on their specialization. Thus, oncology protocols often have a long observation period, so that the principal investigator may have a large number of formally active, but in fact background projects. Another group of protocols with distinctive features is bioequivalence studies, the specificity of which often allows to simultaneously work on a large number of projects. Therefore, in addition to the overall ranking, the following rankings are given:

- top 20 principal investigators for current studies in oncology (Table 6),
- top 20 specialists, with bioequivalence studies making up a considerable part of their projects in any period of their activity (Table 7),
- and top 50 principal investigators for current studies, excluding those specializing in oncology and bioequivalence studies (Table 8).

In addition to the rankings, the top 100 principal investigators were also distributed by cities of the Russian Federation (Diagram 18).

Table 5

TOP-100 of Principal Investigators by Total Number of Trials Conducted from November 2010 to H1 2021							
Ref. No.	**Principal investigator's full name**	**Total number of CTs**	**Number of ongoing CTs**	**Share of bioequivalence studies from the number of current CTs, %**	**Specialization**	**City**	**Ranking and Number of CTs in 2020**
1	Aleksandr Leonidovich Khokhlov	**543**	60	72%	infectious diseases, cardiology, clinical pharmacology, laboratory genetics, oncology, pulmonology, therapy	Yaroslavl	1 (504)
2	Sergey Mikhailovich Noskov	**291**	60	52%	cardiology, neurology, profpathology, rheumatology, clinical pharmacology, therapy	Yaroslavl	2 (256)

[4] http://grls.rosminzdrav.ru/CIExperts.aspx?moduleId=2

3	Alina Sergeevna Agafyina	**235**	88	0%	aviation and space medicine, cardiology, clinical pharmacology, infectious diseases, neurology, pulmonology, rheumatology, therapy	St. Petersburg	3 (203)
4	Anna Nikolaevna Galustyan	**198**	35	0%	allergology and immunology, infectious diseases, clinical pharmacology, oncology, health organization and public health, pediatrics, otorhinolaryngology, rheumatology, pulmonology, therapy	St. Petersburg	5 (191)
5	Olga Borisovna Yershova	**197**	39	0%	cardiology, rheumatology, clinical pharmacology, therapy	Yaroslavl	4 (192)
6	Ivan Gennadyevich Gordeev	**194**	49	0%	infectious diseases, cardiology, therapy	Moscow	6 (181)
7	Vladimir Ivanovich Vladimirov	**171**	64	0%	aviation and space medicine, oncology, urology	Pyatigorsk	7 (168)
8	Elena Anatolyevna Smolyarchuk	**166**	37	5%	obstetrics and gynecology, general medical practice (family medicine), rheumatology, clinical pharmacology, therapy, ophthalmology	Moscow	11 (154)
9	Olga Vilorovna Reshetko	**163**	51	0%	clinical pharmacology, psychiatry, rheumatology, therapy, pharmaceutical chemistry and pharmacognosy	Saratov	8 (157)
10	Konstantin Konstantinovich Laktionov	**161**	80	0%	oncology, surgery, thoracic surgery	Moscow	10 (155)
11	Yuri Grigoryevich Shvarts	**159**	44	0%	cardiology, nephrology, pulmonology, rheumatology, therapy, endocrinology	Saratov	13 (145)
12	Marina Leonidovna Stanislav	**157**	27	0%	radiology, rheumatology	Moscow	12 (151)
13	Konstantin Anatolyevich Zakharov	**154**	56	11%	infectious diseases, clinical pharmacology, general medical	St. Petersburg	22 (125)

					practice (family medicine), health organization and public health, therapy		
14	Mikhail Vladimirovich Dvorkin	**150**	102	1%	oncology, surgery	Omsk	16 (135)
15	Sergey Vladimirovich Orlov	**149**	65	0%	neurology, oncology	St. Petersburg	15 (143)
16	Artyom Yurievich Vorobyov	**146**	29	93%	neurology	MR, Serpukhov	21 (127)
17	Daniil Lyvovich Stroyakovsky	**145**	91	0%	neurology, oncology	Moscow	19 (128)
18	Natalya Vladimirovna Fadeeva	**139**	75	0%	oncology	Chelyabinsk	31 (114)
19	Vladimir Mikhailovich Moiseenko	**139**	74	0%	oncology	St. Petersburg	20 (127)
20	Guzel Zinnurovna Mukhametshina	**138**	62	0%	oncology	Kazan	18 (130)
21	Olga Leonidovna Barbarash	**138**	12	0%	cardiology, nephrology, pulmonology, rheumatology, therapy, endocrinology	Kemerovo	9 (157)
22	Vasily Ivanovich Trofimov	**137**	30	0%	allergology and immunology, gastroenterology, geriatrics, cardiology, pulmonology, therapy	St. Petersburg	17 (135)
23	Marina Nikolaevna Nechaeva	**135**	104	0%	oncology	Arkhangelsk	35 (109)
24	Aleksandr Yurievich Malygin	**135**	36	67%	anesthesiology-intensive care medicine, clinical pharmacology, neurology, ophthalmology, pulmonology, rheumatology	Yaroslavl	30 (115)
25	Sergey Yurievich Martsevich	**124**	4	0%	allergology and immunology, cardiology, clinical pharmacology, neurology, therapy, pharmaceutical chemistry and pharmacognosy	Moscow	23 (125)
26	Igor Dmitrievich Lifirenko	**123**	74	0%	oncology	Kursk	33 (111)
27	Oleg Aleksandrovich Gladkov	**123**	67	0%	oncology	Chelyabinsk	32 (114)
28	Viktor Vasilievich Shilov	**123**	3	67%	anesthesiology-intensive care medicine, infectious diseases, clinical pharmacology, therapy, toxicology, traumatology and orthopedics	St. Petersburg	24 (122)
29	Vladimir Valentinovich Yakusevich	**121**	30	0%	cardiology, clinical pharmacology,	Yaroslavl	28 (116)

					neurology, pulmonology, therapy		
30	Ivan Surenovich Sardanyan	**121**	20	70%	clinical pharmacology, oncology, healthcare organization and public health, pediatrics, pulmonology, rheumatology, therapy	St. Petersburg	29 (115)
31	Veronika Borisovna Popova	**118**	33	0%	rehabilitation medicine, clinical pharmacology, pulmonology, therapy, physiotherapy	St. Petersburg	36 (106)
32	Anton Sergeevich Yedin	**117**	23	0%	dermatovenerology, clinical pharmacology, health organization and public health, therapy	St. Petersburg	26 (116)
33	Marina Fedorovna Osipenko	**116**	49	0%	gastroenterology, clinical pharmacology, health organization and public health, pulmonology, therapy	Novosibirsk	34 (111)
34	Grigory Vladimirovich Rodoman	**115**	32	3%	clinical pharmacology, surgery, coloproctology	Moscow	37 (105)
35	Vladimir Ilyich Simanenkov	**115**	23	0%	gastroenterology, cardiology, clinical pharmacology, therapy, endocrinology	St. Petersburg	27 (116)
36	Natalya Nikolaevna Varnakova	**113**	22	91%	general medical practice (family medicine), therapy	Nizhny Novgorod	25 (117)
37	Nadezhda Vitalyevna Kovalenko	**105**	63	0%	oncology	Volgograd	41 (95)
38	Sergey Stepanovich Yakushin	**105**	32	0%	cardiology, nephrology, pulmonology, rheumatology, therapy	Ryazan	40 (97)
39	Nikolai Viktorovich Kislov	**102**	84	0%	oncology	Yaroslavl	75 (72)
40	Vasily Bogdanovich Vasilyuk	**102**	36	31%	infectious diseases, clinical pharmacology, general medical practice(family medicine), therapy, toxicology	St. Petersburg	72 (73)
41	Tatyana Alekseevna Raskina	**99**	22	0%	cardiology, rheumatology, therapy, endocrinology	Kemerovo	39 (98)

42	Rodion Aleksandrovich Oseshnyuk	**99**	6	33%	clinical pharmacology, neurology, therapy	St. Petersburg	38 (99)
43	Petr Aleksandrovich Chizhov	**98**	17	0%	cardiology, pulmonology, rheumatology, therapy, clinical pharmacology, surgery	Yaroslavl	46 (91)
44	Olga Petrovna Ukhanova	**97**	35	0%	allergology and immunology, otorhinolaryngology, pulmonology, therapy	Stavropol	42 (95)
45	Vladimir Vitalyevich Rafalsky	**96**	40	0%	allergology and immunology, gastroenterology, cardiology, clinical pharmacology, therapy	Kaliningrad	50 (87)
46	Olga Sergeevna Samoylova	**95**	55	0%	hematology, oncology	Nizhny Novgorod	49 (87)
47	Nina Alekseevna Karaseva	**94**	49	0%	oncology	St. Petersburg	43 (94)
48	Viktor Borisovich Shunkov	**94**	21	0%	clinical pharmacology, therapy, cardiology, oncology, rheumatology	St. Petersburg	55 (84)
49	Arkady Lyvovich Vertkin	**93**	7	0%	cardiology, clinical pharmacology, therapy	Moscow	45 (92)
50	Natalya Nikolaevna Maslova	**92**	35	0%	neurology	Smolensk	53 (85)
51	Elena Alekseevna Shumetova	**92**	10	0%	cardiology, therapy	Ivanovo	47 (91)
52	Elena Valentinovna Borodulina	**92**	3	67%	obstetrics and gynecology, clinical pharmacology, therapy	Tomsk	44 (93)
53	Dmitry Petrovich Udovitsa	**91**	27	0%	hematology, oncology	Sochi	14 (144)
54	Sergey Alekseevich Tyulyandin	**90**	25	0%	oncology, pulmonology	Moscow	52 (86)
55	Galina Lyvovna Ignatova	**90**	19	0%	allergology and immunology, pulmonology, therapy	Chelyabinsk	60 (79)
56	Andrey Petrovich Rebrov	**89**	20	0%	cardiology, rheumatology, pulmonology, therapy	Saratov	48 (88)
57	Evgeny Arsenyevich Gotovkin	**88**	40	0%	oncology, radiology	Ivanovo	58 (81)
58	Evgeny Valerievich Baskakov	**87**	23	100%	clinical pharmacology, health organization and public health, psychiatry, psychiatry-narcology	Yaroslavl	103 (65)
59	Sergey Valentinovich Cheporov	**87**	8	0%	oncology	Yaroslavl	51 (87)

60	Boris Yakovlevich Alekseev	**86**	58	0%	oncology, urology	Moscow	57 (81)
61	Zhanna Davidovna Kobalava	**86**	16	0%	cardiology, endocrinology, therapy	Moscow	54 (85)
62	Oleg Nikolaevich Lipatov	**84**	46	0%	oncology	Ufa	63 (76)
63	Natalya Petrovna Shilkina	**84**	16	0%	gastroenterology, rheumatology, cardiology, therapy	Yaroslavl	56 (83)
64	Svetlana Borisovna Yerofeeva	**83**	18	28%	cardiology, therapy, clinical pharmacology	Moscow	80 (70)
65	Aleksey Vladimirovich Smolin	**82**	62	0%	oncology, radiology	Moscow	66 (74)
66	Farit Akhatovich Khabirov	**82**	41	0%	neurology	Kazan	93 (68)
67	Rashida Vakhidovna Orlova	**81**	55	0%	oncology	St. Petersburg	140 (55)
68	Evgeniya Isaakovna Shmidt	**81**	23	0%	rheumatology	Moscow	59 (80)
69	Diana Nodarievna Alpenidze	**80**	13	0%	therapy, endocrinology	St. Petersburg	84 (69)
70	Gadel Maratovich Kamalov	**80**	10	40%	gastroenterology, cardiology, therapy	Kazan	65 (75)
71	Vsevolod Borisovich Matveev	**79**	55	0%	oncology, urology	Moscow	90 (68)
72	Ekaterina Yurievna Valuiskikh	**79**	51	0%	gastroenterology, therapy	Novosibirsk	81 (69)
73	Yuri Pavlovich Uspensky	**79**	38	0%	gastroenterology, infectious diseases, cardiology, pulmonology, therapy	St. Petersburg	76 (72)
74	Olga Viktorovna Bugrova	**79**	29	0%	cardiology, neurology, rheumatology, therapy	Orenburg	68 (74)
75	Natalya Grigoryevna Astafyeva	**79**	15	0%	allergology and immunology, pulmonology	Saratov	70 (74)
76	Olga Vladimirovna Vorobyova	**78**	30	0%	neurology	Moscow	96 (67)
77	Aleksandr Yurievich Vishnevsky	**78**	21	0%	anesthesiology-intensive care medicine, cardiology, therapy	St. Petersburg	71 (73)
78	Vadim Borisovich Shirinkin	**77**	35	0%	oncology, orthodontics	Orenburg	62 (76)
79	Natalya Nikolaevna Vezikova	**77**	20	0%	rheumatology, endocrinology, therapy	Petrozavodsk	69 (74)
80	Galina Aleksandrovna Chumakova	**77**	19	0%	gastroenterology, cardiology, therapy	Barnaul	64 (76)
81	Lyudmila Gennadyevna Lenskaya	**77**	10	0%	clinical pharmacology, oncology, healthcare organization and public health, pulmonology, rheumatology, therapy, surgery	Tomsk	74 (73)
82	Konstantin Dmitrievich Penkov	**76**	67	0%	oncology, clinical pharmacology,	St. Petersburg	160 (51)

					therapy, epidemiology		
83	Oleg Raisovich Ziganshin	**76**	33	0%	dermatovenerology, cosmetology, urology	Chelyabinsk	99 (66)
84	Aleksey Georgievich Manikhas	**76**	22	0%	oncology	St. Petersburg	61 (77)
85	Ildar Rishatovich Akhmetov	**76**	17	100%	anesthesiology-intensive care medicine, toxicology, clinical pharmacology	Moscow	78 (71)
86	Natalya Aleksandrovna Yeremina	**76**	16	0%	clinical pharmacology, therapy, gastroenterology, cardiology, neurosurgery, ophthalmology	Nizhny Novgorod	87 (69)
87	Aleksandr Valerievich Luft	**75**	48	0%	oncology, surgery, thoracic surgery	St. Petersburg	91 (68)
88	Aleksandr Voleslavovich Gordienko	**75**	33	0%	gastroenterology, cardiology, therapy	St. Petersburg	67 (74)
89	Natalya Evgenyevna Nikulenkova	**75**	22	0%	rheumatology	Vladimir	73 (73)
90	Nadezhda Vladimirovna Izmozherova	**75**	16	0%	cardiology, clinical pharmacology, rheumatology, therapy, pharmaceutical chemistry and pharmacognosy	Ekaterinburg	94 (68)
91	Svetlana Anatolyevna Protsenko	**74**	44	0%	oncology	St. Petersburg	77 (71)
92	Dmitry Vladimirovich Pokhabov	**74**	36	0%	neurology	Krasnoyarsk	111 (63)
93	Irinna Evgenievna Poverennova	**74**	32	0%	neurology, neurosurgery, oncology	Samara	110 (63)
94	Evgeny Ivanovich Kopyltsov	**73**	57	0%	oncology, urology	Omsk	114 (62)
95	Pavel Igorevich Skopin	**73**	50	0%	oncology	Saransk	121 (60)
96	Tatyana Ivanovna Martynenko	**73**	13	0%	pulmonology, therapy	Barnaul	104 (65)
97	Elena Vladimirovna Poddubskaya	**72**	57	0%	oncology	Moscow	126 (59)
98	Elena Pavlovna Ilivanova	**72**	23	0%	rheumatology	St. Petersburg	83 (69)
99	Leysan Ildarovna Myasoutova	**72**	13	0%	rheumatology, therapy	Kazan	86 (69)
100	Aleksandr Abramovich Myasnikov	**71**	45	0%	hematology, oncology	Petrozavodsk	143 (54)

Data from www.grls.rosminzdrav.ru

Table 6

Top-20 of Principal Investigators in Oncology by Number of Ongoing Trials						
Reference number	**Principal investigator's full name**	**Number of ongoing CTs**	**Total number of CTs**	**Specialization**	**City**	**Ranking and Number of CTs in 2020**
1	Marina Nikolaevna Nechaeva	**104**	135	oncology	Arkhangelsk	3 (86)
2	Mikhail Vladimirovich Dvorkin	**102**	150	oncology, surgery	Omsk	1 (104)
3	Daniil Lyvovich Stroyakovsky	**91**	145	oncology, neurology	Moscow	2 (87)
4	Nikolai Viktorovich Kislov	**84**	102	oncology	Yaroslavl	8 (61)
5	Konstantin Konstantinovich Laktionov	**80**	161	oncology, surgery, thoracic surgery	Moscow	4 (84)
6	Natalya Vladimirovna Fadeeva	**75**	139	oncology	Chelyabinsk	15 (48)
7	Vladimir Mikhailovich Moiseenko	**74**	139	oncology	St. Petersburg	23 (38)
8	Igor Dmitrievich Lifirenko	**74**	123	oncology	Kursk	6 (64)
9	Oleg Aleksandrovich Gladkov	**67**	123	oncology	Chelyabinsk	19 (42)
10	Konstantin Dmitrievich Penkov	**67**	76	oncology, clinical pharmacology, therapy, epidemiology	St. Petersburg	n/a*
11	Sergey Vladimirovich Orlov	**65**	149	neurology, oncology	St. Petersburg	7 (61)
12	Vladimir Ivanovich Vladimirov	**64**	171	aviation and space medicine, oncology, urology	Pyatigorsk	11 (57)
13	Nadezhda Vitalyevna Kovalenko	**63**	105	oncology	Volgograd	10 (58)
14	Guzel Zinnurovna Mukhametshina	**62**	138	oncology	Kazan	9 (59)
15	Aleksey Vladimirovich Smolin	**62**	82	oncology, radiology	Moscow	12 (57)
16	Boris Yakovlevich Alekseev	**58**	86	oncology, urology	Moscow	14 (55)
17	Evgeny Ivanovich Kopyltsov	**57**	73	oncology, urology	Omsk	n/a*
18	Elena Vladimirovna Poddubskaya	**57**	72	oncology	Moscow	n/a*
19	Olga Sergeevna Samoylova	**55**	95	hematology, oncology	Nizhny Novgorod	13 (55)
20	Rashida Vakhidovna Orlova	**55**	81	oncology	St. Petersburg	n/a*

*** Due to the technical limitations the ranking is calculated only for investigators who are in the top 100 by the total number of studies, therefore, ACTO does not have data on the number of current studies of specialists who were not included in the top 100 of 2020.**

Data from www.grls.rosminzdrav.ru

Table 7

Top-20 of Principal Investigators Including Those Specializing in Conducting Bioequivalence Studies by Number of Ongoing Trials							
Ref. No.	**Principal investigator's full name**	**Number of ongoing CTs**	**Share of bioequivalence studies from the number of current CTs, %**	**Total number of CTs**	**Share of bioequivalence studies from the total number of CTs, %**	**Specialization**	**City**
1	Aleksandr Leonidovich Khokhlov	**60**	72%	543	66%	infectious diseases, cardiology, clinical pharmacology, laboratory genetics, oncology, pulmonology, therapy	Yaroslavl
2	Sergey Mikhailovich Noskov	**60**	52%	291	59%	cardiology, neurology, profpathology, rheumatology, clinical pharmacology, therapy	Yaroslavl
3	Konstantin Anatolyevich Zakharov	**56**	11%	154	19%	infectious diseases, clinical pharmacology, general medical practice (family medicine), health organization and public health, therapy	St. Petersburg
4	Elena Anatolyevna Smolyarchuk	**37**	5%	166	30%	obstetrics and gynecology, general medical practice (family medicine), rheumatology, clinical pharmacology, therapy, ophthalmology	Moscow
5	Aleksandr Yurievich Malygin	**36**	67%	135	31%	anesthesiology-intensive care medicine, clinical pharmacology, neurology, ophthalmology, pulmonology, rheumatology	Yaroslavl
6	Vasily Bogdanovich Vasilyuk	**36**	31%	102	32%	infectious diseases, clinical pharmacology, general medical practice(family medicine), therapy, toxicology	St. Petersburg
7	Anna Nikolaevna Galustyan	**35**	0%	198	22%	allergology and immunology, infectious diseases, clinical pharmacology, oncology, health	St. Petersburg

						organization and public health, pediatrics, otorhinolaryngology, rheumatology, pulmonology, therapy	
8	Artyom Yurievich Vorobyov	**29**	93%	146	95%	neurology	MR, Serpukhov
9	Evgeny Valerievich Baskakov	**23**	100%	87	85%	clinical pharmacology, health organization and public health, psychiatry, psychiatry-narcology	Yaroslavl
10	Natalya Nikolaevna Varnakova	**22**	91%	113	95%	general medical practice (family medicine), therapy	Nizhny Novgorod
11	Ivan Surenovich Sardanyan	**20**	70%	121	60%	clinical pharmacology, oncology, healthcare organization and public health, pediatrics, pulmonology, rheumatology, therapy	St. Petersburg
12	Svetlana Borisovna Yerofeeva	**18**	28%	83	36%	cardiology, therapy, clinical pharmacology	Moscow
13	Ildar Rishatovich Akhmetov	**17**	100%	76	88%	anesthesiology-intensive care medicine, toxicology, clinical pharmacology	Moscow
14	Elena Alekseevna Shumetova	**10**	0%	92	58%	cardiology, therapy	Ivanovo
15	Gadel Maratovich Kamalov	**10**	40%	80	68%	gastroenterology, cardiology, therapy	Kazan
16	Arkady Lyvovich Vertkin	**7**	0%	93	62%	cardiology, clinical pharmacology, therapy	Moscow
17	Rodion Aleksandrovich Oseshnyuk	**6**	33%	99	63%	clinical pharmacology, neurology, therapy	St. Petersburg
18	Sergey Yurievich Martsevich	**4**	0%	124	45%	allergology and immunology, cardiology, clinical pharmacology, neurology, therapy, pharmaceutical chemistry and pharmacognosy	Moscow
19	Viktor Vasilievich Shilov	**3**	67%	123	75%	anesthesiology-intensive care medicine, infectious diseases, clinical pharmacology, therapy, toxicology, traumatology and orthopedics	St. Petersburg

20	Elena Valentinovna Borodulina	**3**	67%	92	83%	obstetrics and gynecology, clinical pharmacology, therapy	Tomsk

Data from www.grls.rosminzdrav.ru

Table 8

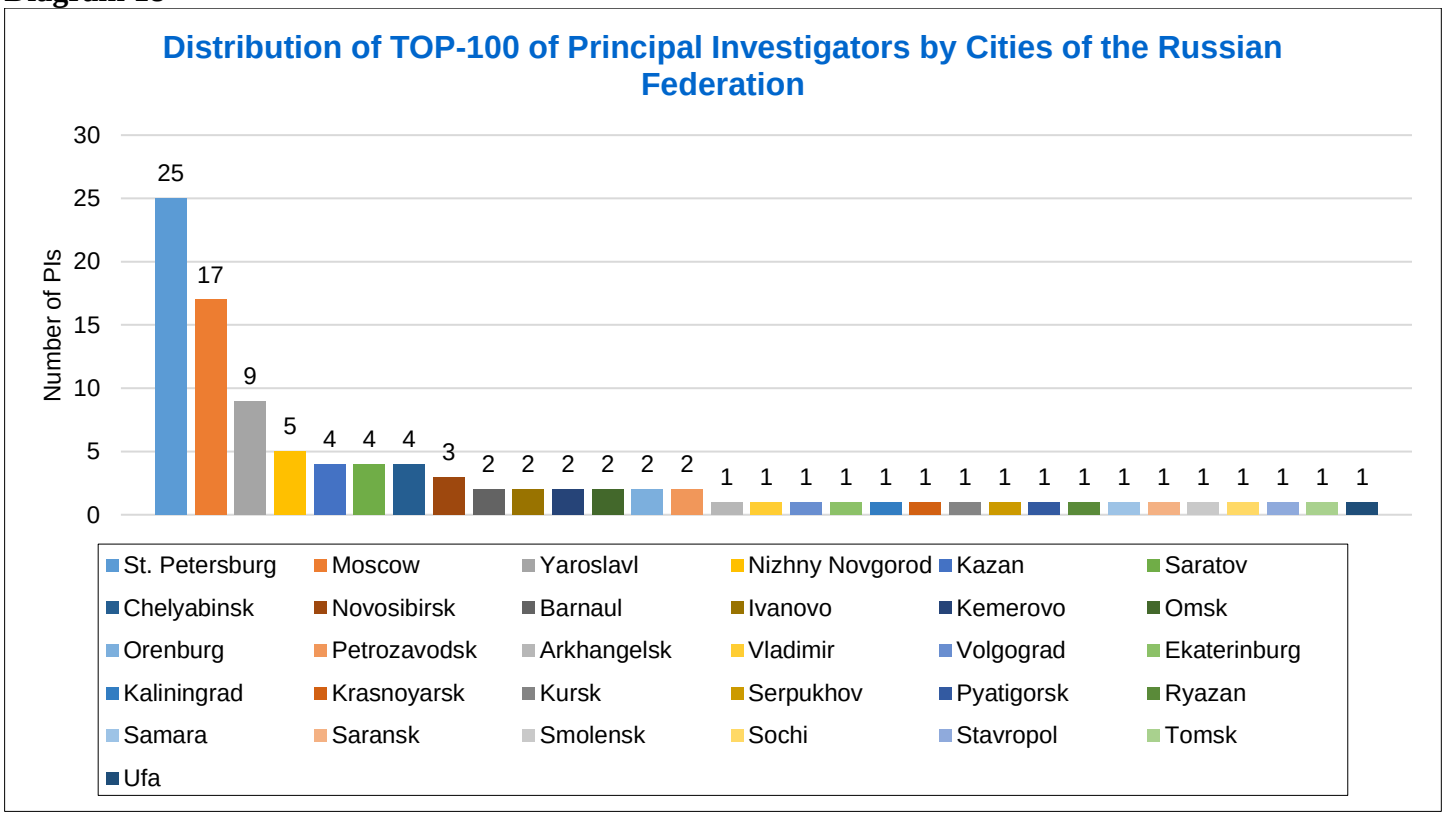
Top-50 of Principal Investigators (Excluding Oncologists and Specialists Engaged in Conducting Bioequivalence Studies) by Number of Ongoing Trials					
Reference number	**Principal investigator's full name**	**Number of ongoing CTs**	**Total number of CTs**	**Specialization**	**City**
1	Alina Sergeevna Agafyina	**88**	235	aviation and space medicine, cardiology, clinical pharmacology, infectious diseases, neurology, pulmonology, rheumatology, therapy	St. Petersburg
2	Olga Vilorovna Reshetko	**51**	163	clinical pharmacology, psychiatry, rheumatology, therapy, pharmaceutical chemistry and pharmacognosy	Saratov
3	Ekaterina Yurievna Valuiskikh	**51**	79	gastroenterology, therapy	Novosibirsk
4	Ivan Gennadyevich Gordeev	**49**	194	infectious diseases, cardiology, therapy	Moscow
5	Marina Fedorovna Osipenko	**49**	116	gastroenterology, clinical pharmacology, health organization and public health, pulmonology, therapy	Novosibirsk
6	Yuri Grigoryevich Shvarts	**44**	159	cardiology, nephrology, pulmonology, rheumatology, therapy, endocrinology	Saratov
7	Farit Akhatovich Khabirov	**41**	82	neurology	Kazan
8	Vladimir Vitalyevich Rafalsky	**40**	96	allergology and immunology, gastroenterology, cardiology, clinical pharmacology, therapy	Kaliningrad
9	Olga Borisovna Yershova	**39**	197	cardiology, rheumatology, clinical pharmacology, therapy	Yaroslavl
10	Yuri Pavlovich Uspensky	**38**	79	gastroenterology, infectious diseases, cardiology, pulmonology, therapy	St. Petersburg
11	Dmitry Vladimirovich Pokhabov	**36**	74	neurology	Krasnoyarsk
12	Olga Petrovna Ukhanova	**35**	97	allergology and immunology, otorhinolaryngology, pulmonology, therapy	Stavropol
13	Natalya Nikolaevna Maslova	**35**	92	neurology	Smolensk
14	Igor Gennadievich Bakulin	**34**	70	gastroenterology, infectious diseases, therapy	St. Petersburg
15	Veronika Borisovna Popova	**33**	118	rehabilitation medicine, clinical pharmacology, pulmonology, therapy, physiotherapy	St. Petersburg
16	Oleg Raisovich Ziganshin	**33**	76	dermatovenerology, cosmetology, urology	Chelyabinsk
17	Aleksandr Voleslavovich Gordienko	**33**	75	gastroenterology, cardiology, therapy	St. Petersburg
18	Grigory Vladimirovich Rodoman	**32**	115	clinical pharmacology, surgery, coloproctology	Moscow
19	Sergey Stepanovich Yakushin	**32**	105	cardiology, nephrology, pulmonology, rheumatology, therapy	Ryazan

20	Vasily Ivanovich Trofimov	**30**	137	allergology and immunology, gastroenterology, geriatrics, cardiology, pulmonology, therapy	St. Petersburg
21	Vladimir Valentinovich Yakusevich	**30**	121	cardiology, clinical pharmacology, neurology, pulmonology, therapy	Yaroslavl
22	Olga Vladimirovna Vorobyova	**30**	78	neurology	Moscow
23	Olga Viktorovna Bugrova	**29**	79	cardiology, neurology, rheumatology, therapy	Orenburg
24	Olga Polikarpovna Alekseeva	**29**	71	gastroenterology, therapy	Nizhny Novgorod
25	Marina Leonidovna Stanislav	**27**	157	radiology, rheumatology	Moscow
26	Anton Sergeevich Yedin	**23**	117	dermatovenerology, clinical pharmacology, health organization and public health, therapy	St. Petersburg
27	Vladimir Ilyich Simanenkov	**23**	115	gastroenterology, cardiology, clinical pharmacology, therapy, endocrinology	St. Petersburg
28	Evgeniya Isaakovna Shmidt	**23**	81	rheumatology	Moscow
29	Elena Pavlovna Ilivanova	**23**	72	rheumatology	St. Petersburg
30	Tatyana Alekseevna Raskina	**22**	99	cardiology, rheumatology, therapy, endocrinology	Kemerovo
31	Natalya Evgenyevna Nikulenkova	**22**	75	rheumatology	Vladimir
32	Viktor Borisovich Shunkov	**21**	94	clinical pharmacology, therapy, cardiology, oncology, rheumatology	St. Petersburg
33	Aleksandr Yurievich Vishnevsky	**21**	78	anesthesiology-intensive care medicine, cardiology, therapy	St. Petersburg
34	Andrey Petrovich Rebrov	**20**	89	cardiology, rheumatology, pulmonology, therapy	Saratov
35	Natalya Nikolaevna Vezikova	**20**	77	rheumatology, endocrinology, therapy	Petrozavodsk
36	Galina Lyvovna Ignatova	**19**	90	allergology and immunology, pulmonology, therapy	Chelyabinsk
37	Galina Aleksandrovna Chumakova	**19**	77	gastroenterology, cardiology, therapy	Barnaul
38	Viktor Avenirovich Kostenko	**19**	70	cardiology, otorhinolaryngology, therapy	St. Petersburg
39	Petr Aleksandrovich Chizhov	**17**	98	cardiology, pulmonology, rheumatology, therapy, clinical pharmacology, surgery	Yaroslavl
40	Zhanna Davidovna Kobalava	**16**	86	cardiology, endocrinology, therapy	Moscow
41	Natalya Petrovna Shilkina	**16**	84	gastroenterology, rheumatology, cardiology, therapy	Yaroslavl
42	Natalya Aleksandrovna Yeremina	**16**	76	clinical pharmacology, therapy, gastroenterology, cardiology, neurosurgery, ophthalmology	Nizhny Novgorod
43	Nadezhda Vladimirovna Izmozherova	**16**	75	cardiology, clinical pharmacology, rheumatology, therapy, pharmaceutical chemistry and pharmacognosy	Ekaterinburg
44	Natalya Grigoryevna Astafyeva	**15**	79	allergology and immunology, pulmonology	Saratov
45	Diana Nodarievna Alpenidze	**13**	80	therapy, endocrinology	St. Petersburg
46	Tatyana Ivanovna Martynenko	**13**	73	pulmonology, therapy	Barnaul
47	Leysan Ildarovna Myasoutova	**13**	72	rheumatology, therapy	Kazan

48	Lyubov Anatolyevna Shpagina	**13**	70	hematology, cardiology, pulmonology, clinical pharmacology, therapy, health organization and public health, profpathology, traumatology and orthopedics	Novosibirsk
49	Olga Leonidovna Barbarash	**12**	138	cardiology, nephrology, pulmonology, rheumatology, therapy, endocrinology	Kemerovo
50	Lyudmila Gennadyevna Lenskaya	**10**	77	clinical pharmacology, oncology, healthcare organization and public health, pulmonology, rheumatology, therapy, surgery	Tomsk

Data from www.grls.rosminzdrav.ru

Diagram 18



Data from www.grls.rosminzdrav.ru

Annex

IMCT STATISTICS FOR ONCOLOGY AND ONCOHAEMATOLOGY, 2020

Table 9

Distribution of IMCTs by Therapeutic Areas, 2020			
Therapeutic area	**Number of IMCTs**	**Share (%)**	**The number of planned participants**
Oncology	95	29.5%	6 494
Neurology	32	9.9%	2 573
COVID-19	31	9.6%	12 710
Gastroenterology/Coloproctology	21	6.5%	1 275
Oncohaematology	20	6.2%	900
Cardiology and CVD	14	4.3%	2 178
Rheumatology	13	4.0%	994
Dermatology	12	3.7%	657
Endocrinology	11	3.4%	1 575
Haematology	10	3.1%	168
Ophthalmology	10	3.1%	533
Psychiatry	10	3.1%	1 160
Pulmonology	10	3.1%	1 114
Infectious Diseases (except HIV/HCV/tuberculosis, COVID-19)	8	2.5%	482
HIV	5	1.6%	245
Nephrology	5	1.6%	232
Gynecology	3	0.9%	330
Otorhinolaryngology	3	0.9%	301
Allergology	2	0.6%	70
Immunology/Transplantology	2	0.6%	45
Anesthesiology	1	0.3%	40
Hepatology	1	0.3%	50
Cosmetology	1	0.3%	74
Urology	1	0.3%	30
Surgery/Orthopedics	1	0.3%	100
TOTAL	322	100.0%	34330

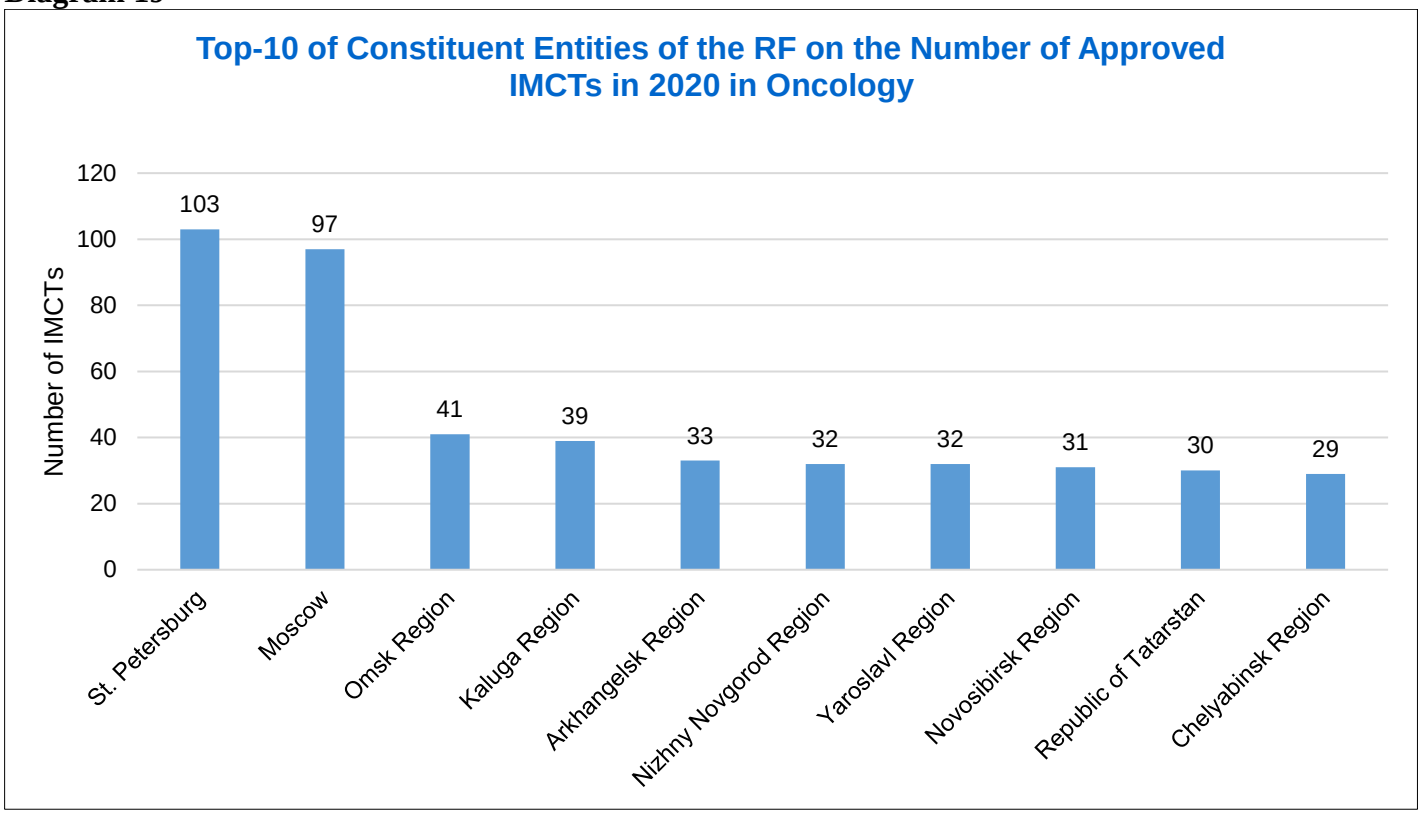
Data from www.grls.rosminzdrav.ru

Table 10

IMCT Distribution in Oncology and Oncohaematology, 2020			
No.	**Disease type**	**Number of IMCTs**	**Claimed number of subjects**
1	Lung and pleural cavity tumours	24	1 654
2	Breast tumour	18	1 185
3	Leukemia (incl. acute leukaemia and neutropaenia, acute myeloid leukemia, myelodysplastic syndrome, myelomonocytic leukaemia, lymphocytic leukemia, myelofibrosis, plasma cell dyscrasia)	14	687
4	Gastrointestinal tumours	11	1 045
5	Tumours without known localisation	9	366
6	Female reproductive system tumours	7	523
7	Kidney and genitourinary system tumors	7	354
8	Head and neck tumours	6	502
9	Prostate tumour	5	448
10	Liver tumours and biliary tract cancer	5	275
11	Multiple myeloma	4	176
12	Lymphoma	2	37
13	Melanoma	1	78
14	Neuroblastoma	1	34
15	Thyroid tumors	1	30
	TOTAL	115	7394

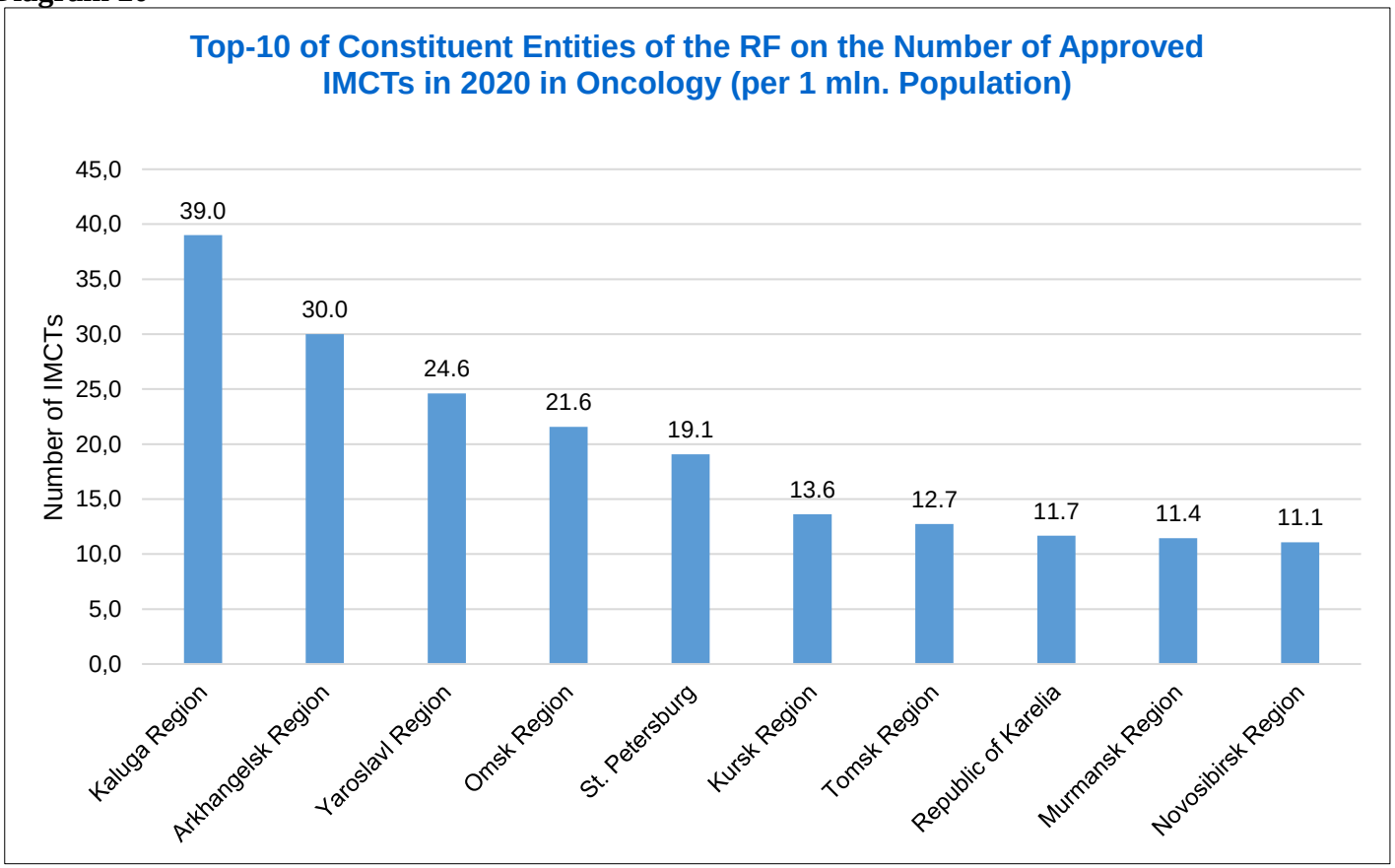
Data from www.grls.rosminzdrav.ru

Diagram 19



Data from www.grls.rosminzdrav.ru

Diagram 20



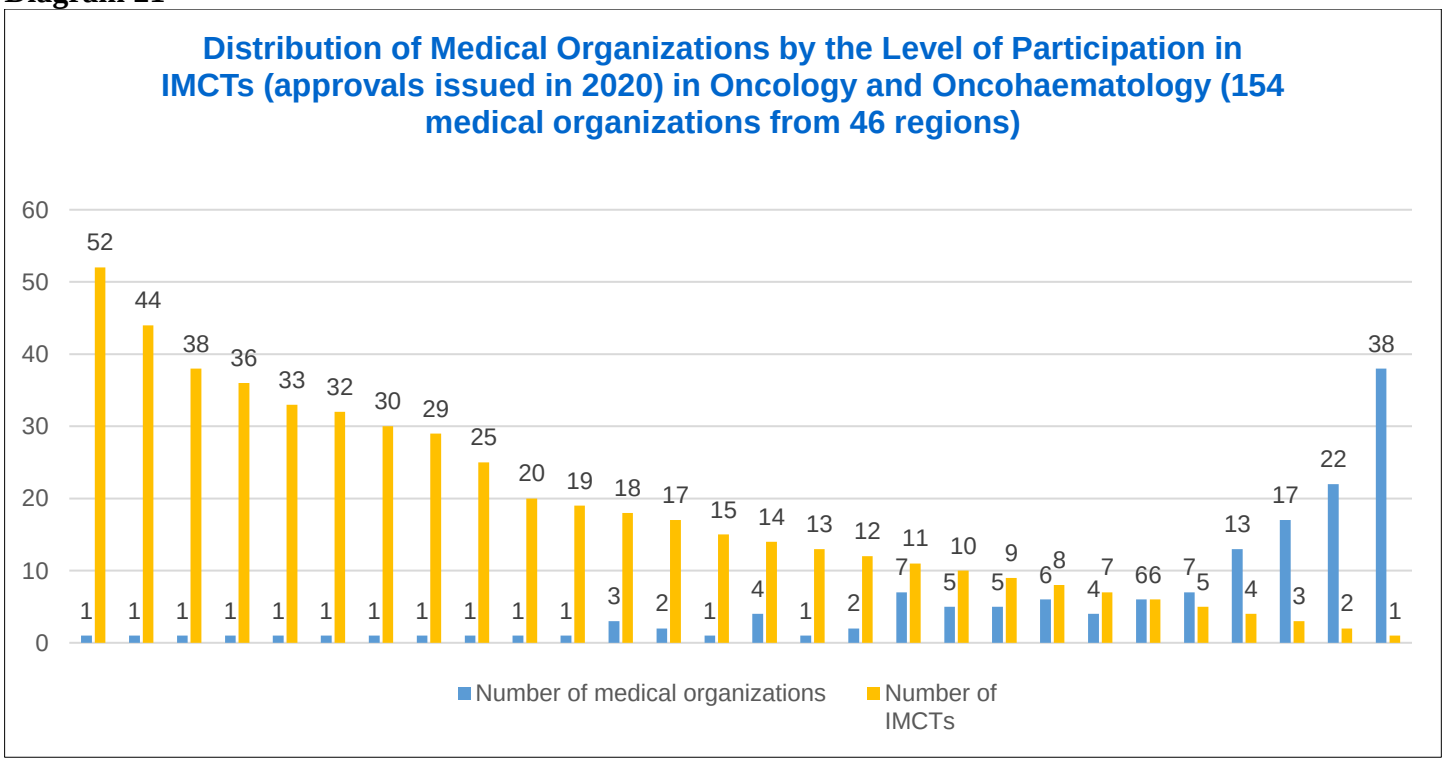
Data from www.grls.rosminzdrav.ru

Table 11

Ranking of Medical Organizations on the Activity of Participation in IMCTs in Oncology and Oncohaemotology Approved in 2020			
Place in ranking	**Name of medical organization**	**Number of IMCTs approved in 2020 with participation of this medical organization**	**Number of centres approved in 2020 for conducting IMCTs**
1	N. N. Blokhin Russian Cancer Research Centre, Russian Ministry of Health, Moscow	52	55
2	N.N. Petrov National Medicine Research Center of Oncology, Russian Ministry of Health, St. Petersburg	44	45
3	St. Petersburg Clinical Scientific and Practical Center for Specialized Types of Medical Care (Oncological), St. Petersburg	38	38
4	Clinical Oncological Dispensary, Omsk	36	36
5	National Medical Research Radiological Centre, Obninsk	33	39
6	Arkhangelsk Clinical Oncological Dispensary, Arkhangelsk	32	32
7	Regional Clinical Oncological Hospital, Yaroslavl	30	30
8	Republican Clinical Oncological Dispensary, Kazan	29	30
9	I. P. Pavlov First St. Petersburg State medical University, Russian Ministry of Health, St. Petersburg	25	25
10	Regional Clinical Center of Oncology and Nuclear Medicine, Chelyabinsk	20	20

Data from www.grls.rosminzdrav.ru

Diagram 21



Data from www.grls.rosminzdrav.ru