

Clinical Trials in Russia
Orange Paper
3rd Quarter 2017



© CRO Synergy Research Group
11, 4-Magistralnaya Ul., 123007 Moscow, Russia
www.synergycro.ru



Contents

Executive Summary – English	3
Executive Summary – Russian	4
Clinical Trials by Type and Manufacturing Country	5
Figure 1. Clinical Trials in Russia in Q3 2017	5
Figure 2. Clinical Trials by Type in Q3 2017	6
Figure 3. Russian vs International Sponsors in Q3 2017	6
Figure 4. Sponsors' Country of Origin for Q3 2017 Clinical Trials in Russia.....	7
All Clinical Trials by Phase	7
Figure 5. All Clinical Trials in Russia in Q3 2017 by Phase	8
Figure 6. Percentage Breakdown of Russian Clinical Trials by Phase	8
Figure 7. Number of Study Subjects in Q3 2017 by Study Phase	9
The Top Five: Sponsors, Sites and CROs.....	10
Table 1. Top-5 International Study Sponsors in Q3 2017	10
Table 2. Top-5 Russian Study Sponsors in Q3 2017.....	10
Table 3. Top-5 Russian Research Sites (BE and Phase I studies) in Q3 2017	10
Table 4. Top-5 Russian Research Sites (Phase II-IV studies) in Q3 2017	11
Table 5. Top-5 Russian Research Sites (all studies) in Q3 2017	11
Table 6. Top-CROs in Russia in Q3 2017	11
Therapeutic Areas of Russian Clinical Trials in Q3 2017	12
Figure 8. Clinical Trials in Russia in Q3 2017 by Therapeutic Area.....	12
Clinical Trials Results.....	12
Table 7. New Drugs Approved by FDA in Q3 2017 and Tested in Russian Sites	13
Table 8. New Drugs Approved by EMA in Q3 2017 and Tested in Russian Sites.....	13
About Synergy Research Group.....	14



Executive Summary – English

The Ministry of Health of the Russian Federation approved 158 new clinical trials of all types, including local and bioequivalence studies, during Q3 2017. This represents a 34% decrease over Q3 2016.

The main contribution to the total number of studies in Q3 2017 was made by multinational multi-center clinical trials (MMCT), the number of these studies being 65 and it is 27% less than in Q3 2016. The number of bioequivalence studies (BE) significantly decreased from 72 studies in Q3 2016 to 43 in Q3 2017, a 40% decrease from last year's figure. The number of local clinical trials (LCT) decreased from 80 in Q3 2016 to 50 in Q3 2017.

Clinical trials in Russia in Q3 2017 were sponsored by companies from 22 countries. Russian sponsors accounted for the largest number of trials (69) whilst American sponsors took the runners-up place with 30 new studies; they were followed by Indian and Swiss sponsors (11 trials each).

The number of Phase I clinical trials has decreased from 23 studies to 11 new studies in Q3 2017 (52% decrease). The number of Phase II trials (29 new studies) increased in comparison with Q3 2016 (23 studies). The number of Phase III trials decreased from 115 to 66 studies, 43% less than in Q3 2016. The number of Phase IV trials increased in comparison with Q3 2016 from eight to nine studies.

The number of subjects planned to be enrolled in Phase I-IV trials launched in Q3 2017 is 11,652, less than Q3 2016 figure, when 22,226 subjects were planned to be enrolled.

AbbVie Inc. is the leading sponsor of foreign pharmaceutical manufacturers in Q3 2017 by sponsoring seven new studies. They are followed by *Eli Lilly and Company* and *Novartis*, having five new studies each, albeit differentiated by the number of patients, and then closely followed by *Merck & Co.* and *AstraZeneca*, each with four new studies in Q3 2017, again differentiated by the number of patients.

Top five domestic pharmaceutical manufacturers by the number of new studies in Q3 2017 is headed by *Biocad* and *North Star*, each having six new trials and differentiated by the number of patients. They are followed by *Sotex* and *Pharmasyntez* with four new trials each. The top five is concluded by *Obnovlenie Pharmaceutical Company* having three new studies.

The top five Russian research sites (BE and Phase I studies) include: *Medical Center Probiotec* (7 new studies), *Clinical Hospital N2 of the Yaroslav Region* and *Ecosafety Ltd.* (six studies each), *Bioeq Ltd.* (five studies).

The top Russian research sites (Phase II-IV studies) include: *First Moscow State Medical University named after I.M. Sechenov* (13 new studies), *First St. Petersburg State Medical University named after I.P. Pavlov* and *Research Institute of Oncology named after N.N. Petrov* (11 studies each), *Russian Oncological Scientific Center named after N.N. Blokhin* (10 studies).

The top five CROs in Russia are: *OST RUS*, *PSI*, *Quintiles* and *Synergy Research Group* (three new studies each), and *iPharma* (two studies).

The top therapeutic areas were: Therapy (22 new studies), Oncology (21 studies), Infectious diseases (17 studies), Rheumatology (12 studies), Hematology (12 studies), Neurology (eight studies), Pediatrics (seven studies), Traumatology and orthopedics, Surgery and Endocrinology (six studies each).

The U.S. Center for Drug Evaluation and Research (CDER) of the FDA approved 41 new drugs during Q3 2017, and **10** of these were (or are being) studied in clinical trials conducted in Russia.

During Q3 2017, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 28 new drug applications¹. **Twenty** of the drugs which received positive opinions were (or are being) studied in clinical trials in Russia.

¹ Positive opinions on new generic, hybrid and biosimilar medicines are not included.



Executive Summary – Russian

В третьем квартале 2017 года Министерством здравоохранения Российской Федерации было выдано 158 разрешений на все виды клинических исследований (КИ), что на 34% меньше, чем за аналогичный период 2016 года.

При этом количество новых международных многоцентровых КИ, инициированных в третьем квартале 2017 года, составило 65, что на 27% меньше по сравнению с аналогичным периодом прошлого года. Количество исследований биоэквивалентности уменьшилось на 40% по сравнению с 2016 годом и составило 43 против 72. Количество локальных КИ, проводимых на территории России, значительно уменьшилось по сравнению с третьим кварталом 2016 года и составило 50 исследований против 80.

Спонсорами КИ, разрешенных к проведению в России в третьем квартале 2017 года, выступили компании из 22 стран. На первое место вышли российские производители с 69 КИ, за ними идут американские спонсоры с 30 КИ, Индия и Швейцария (11 КИ каждая).

В третьем квартале 2017 года было инициировано 11 новых КИ I фазы, что на 52% меньше, чем за тот же период 2016 года (23 КИ). Количество исследований II фазы (29 новых исследований) увеличилось по сравнению с третьим кварталом 2016 года (23 КИ). Количество КИ III фазы уменьшилось с 115 до 66, что на 43% меньше по сравнению с аналогичным периодом прошлого года. Количество исследований IV фазы увеличилось по сравнению с третьим кварталом 2016 года с восьми до девяти исследований.

Количество субъектов для участия в исследованиях I-IV фаз в третьем квартале 2017 года составило 11 652, что меньше, чем в третьем квартале 2016 года, когда планировалось участие 22 226 субъектов.

В третьем квартале 2017 года лидирующие позиции среди иностранных производителей по количеству новых исследований заняла компания *AbbVie Inc.* с семью новыми исследованиями. Далее следуют компании *Eli Lilly and Company* и *Novartis*, каждая с пятью новыми КИ, но с разным количеством пациентов, и *Merck & Co.* и *AstraZeneca*, каждая с четырьмя новыми КИ, но с разным количеством пациентов.

Список пяти лидирующих отечественных производителей по количеству новых исследований в третьем квартале 2017 года возглавили компании *Биокад* и *Северная Звезда* с шестью исследованиями каждая. Далее следуют компании *Сотекс* и *Фармасинтез* (по четыре новых КИ) и *ПФК Обновление* (три исследования).

В пятерку передовиков по исследованиям биоэквивалентности и I фазы в третьем квартале 2017 года вошли следующие центры: *Медицинский центр Пробиотек* (семь новых КИ), *Клиническая больница №2 Ярославской области* и *ООО «НИЦ Эко-безопасность»* (шесть новых КИ каждый), *ООО «БиоЭк»* (пять КИ).

Лидирующие центры по исследованиям II-IV фаз: *Первый Московский государственный медицинский университет имени И.М. Сеченова* (13 новых исследований), *Первый Санкт-Петербургский государственный медицинский университет имени академика И.П. Павлова* и *Научно-исследовательский институт онкологии имени профессора Н.Н. Петрова* (по 11 КИ каждый), *Российский онкологический научный центр имени Н.Н. Блохина* (десять новых исследований).

Пятерка лидеров среди КИО в России: *ОСТ*, *Quintiles*, *PSI* и *Synergy Research Group* (по три новых КИ), и *ИФАРМА* (два КИ).

Наибольшее количество исследований проведено в следующих областях: общая терапия – 22, онкология – 21, инфекционные болезни – 17, ревматология – 12, гематология – 12, неврология – восемь, педиатрия – семь новых КИ.

FDA одобрен в третьем квартале 2017 года 41 новый лекарственный препарат, по 10 из которых в России проводились (или проводятся) КИ. ЕМА одобрено в третьем квартале 2017 года 28 новых лекарственных препаратов, по 20 из которых в России проводились (или проводятся) КИ.



Clinical Trials by Type and Manufacturing Country

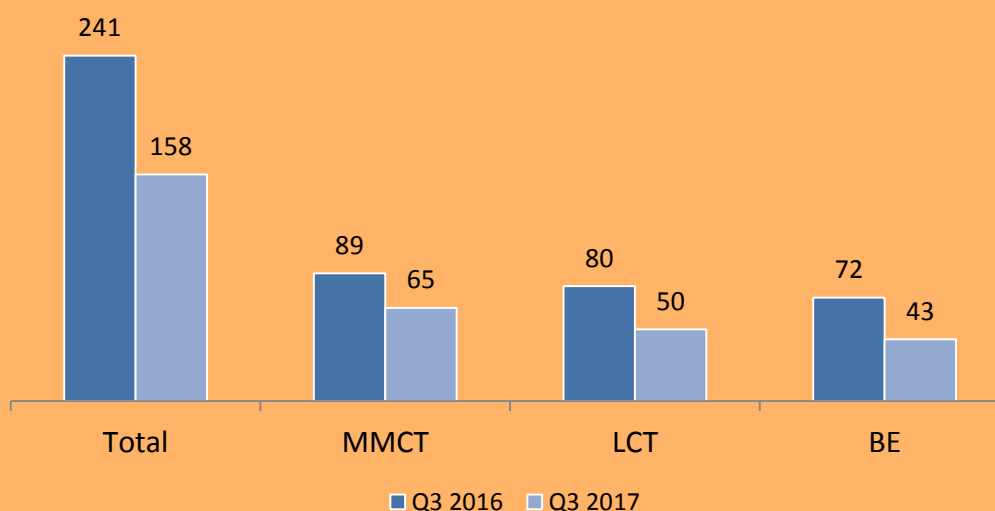
The Russian MoH approved 158 new clinical trials of all types including local and bioequivalence studies during Q3 2017, demonstrating a 34% decrease in comparison with the same period last year.

As shown in **Figure 1**, the main contribution to the total number of studies was made by multinational multi-center clinical trials (MMCT); the number of these studies decreased from 89 studies in Q3 2016 to 65 in Q3 2017, representing a 27% decrease from last year's figure.

The number of bioequivalence studies (BE) significantly decreased from 72 studies in Q3 2016 to 43 in Q3 2017, representing a 40% decrease from last year's figure.

The number of local clinical trials (LCT) decreased from 80 in Q3 2016 to 50 in Q3 2017, representing a 38% decrease from last year's figure.

Figure 1. Clinical Trials in Russia in Q3 2017



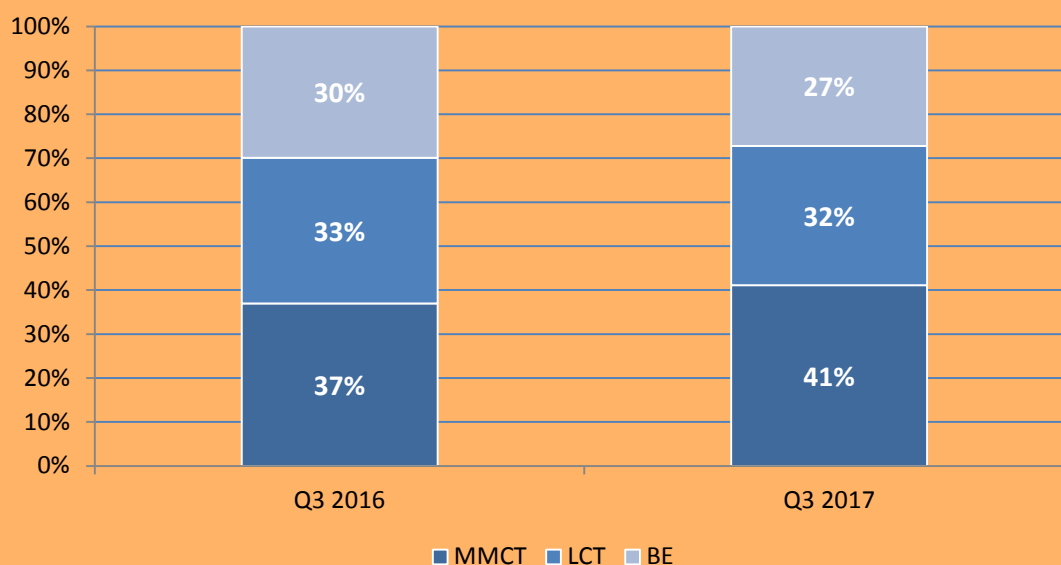
The percentage change between different study types (multinational multi-center clinical trials, local clinical trials and bioequivalence studies) since last year are shown in **Figure 2**.

The share of bioequivalence studies decreased from 30% to 27% of the total number of clinical trials approved in Q3 2017.

The share of the local clinical trials was almost identical, 33% in Q3 2016, compared to 32% in Q3 2017, and the share of multinational multi-center clinical trials was 41% of the total number of trials approved during Q3 2017 (37% in Q3 2016).

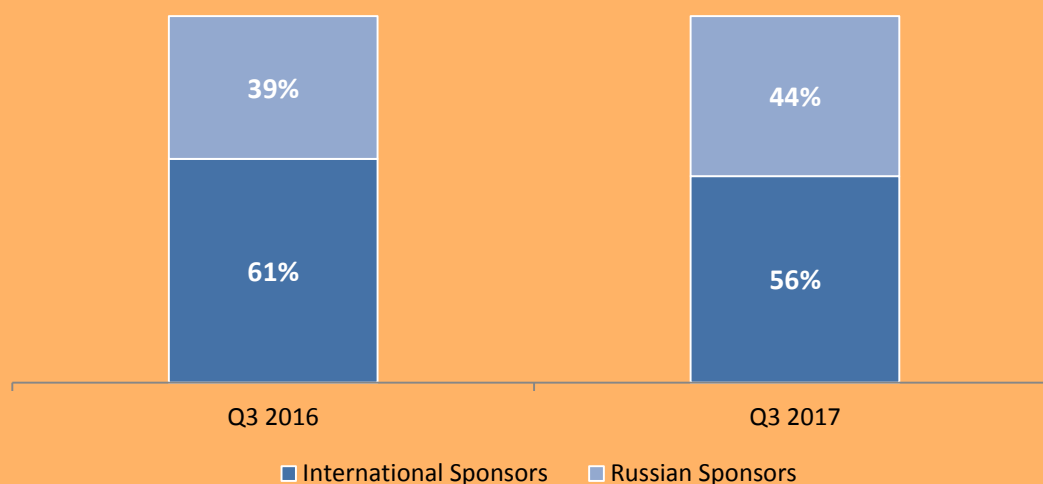


Figure 2. Clinical Trials by Type in Q3 2017



The geographic origins of sponsors changed in comparison with last year. 56% of the total number of new studies in Q3 2017 were sponsored by foreign companies which received 89 study approvals (61% in Q3 2016). The share of studies of local manufacturers increased from 39% in Q3 2016 to 44% in Q3 2017, and amounted to 69 studies (**Figure 3**).

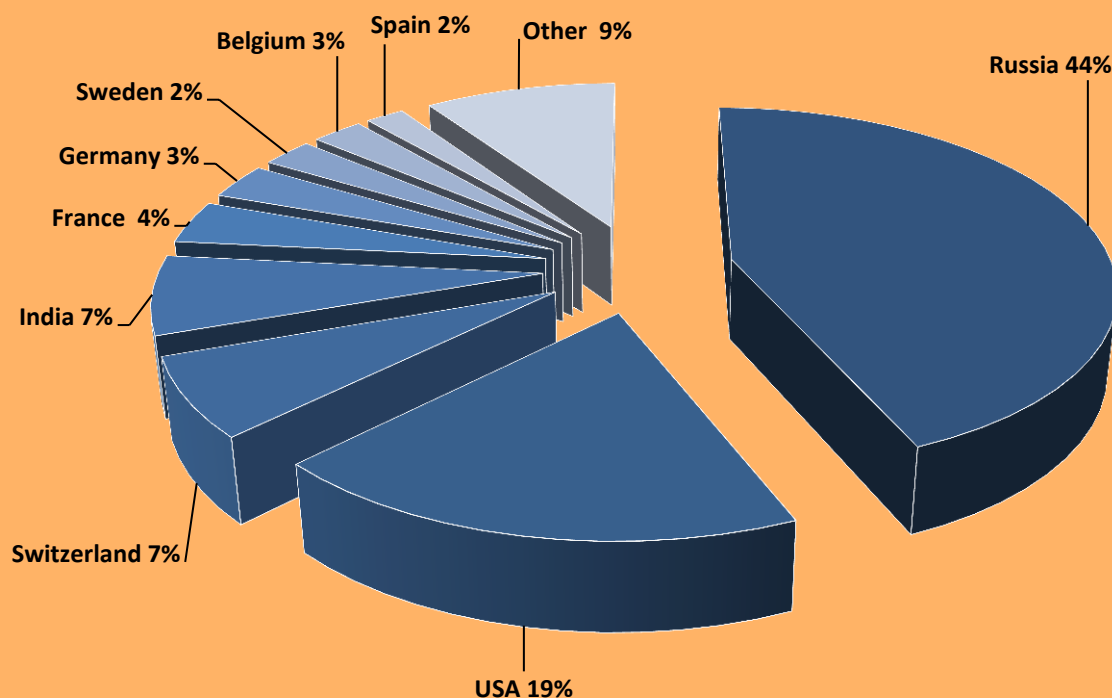
Figure 3. Russian vs International Sponsors in Q3 2017



Clinical trials in Russia in Q3 2017 were sponsored by companies from 22 countries. **Figure 4** indicates the geographic breakdown by sponsors' country of origin.

The largest number of trials (69) were initiated by Russian sponsors. American sponsors with 30 new studies secured the runners-up place; they were followed by Indian and Swiss sponsors with 11 studies each, then by French sponsors with six new studies. The group of leaders is concluded by German sponsors (five studies), Sweden and Belgium (each having four studies), and Spain (three studies).

Figure 4. Sponsors' Country of Origin for Q3 2017 Clinical Trials in Russia



Other sponsors included: Macedonia and Portugal (two studies each), and Bosnia-Herzegovina, Croatia, Denmark, Japan, Jordan, Republic of Korea, New Zealand, Slovenia, Turkey, Ukraine and United Kingdom, each started one new study in Q3 2017.

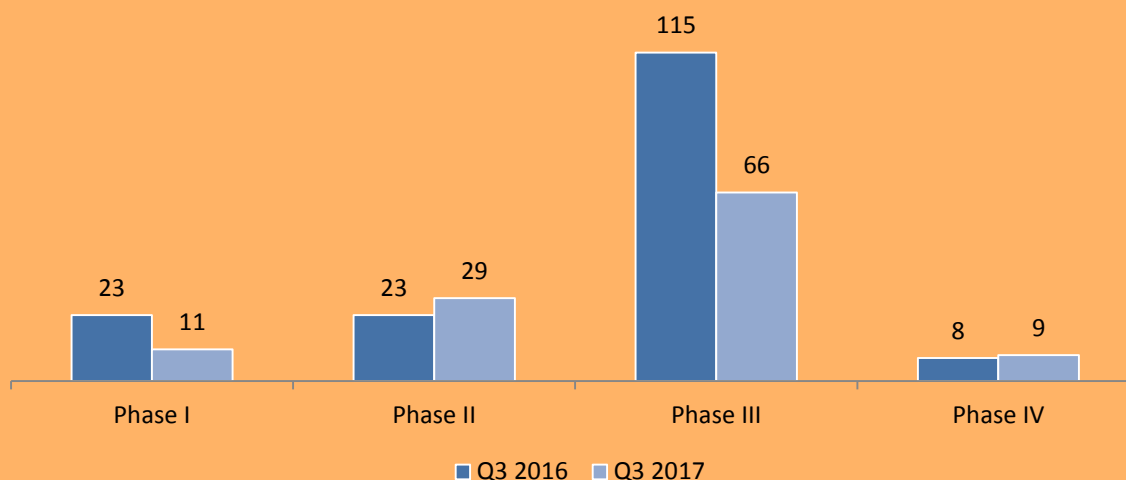
All Clinical Trials by Phase

The number of Phase I clinical trials decreased by 52% compared to Q3 2016: from 23 studies to 11 new studies in Q3 2017. The number of Phase II trials increased by 26% compared to Q3 2016 from 23 studies to 29 new studies (**Figure 5**).

The number of Phase III trials decreased from 115 to 66 studies, 43% less than in Q3 2016. The number of Phase IV trials increased slightly in comparison with Q3 2016 from eight to nine studies in Q3 2017.

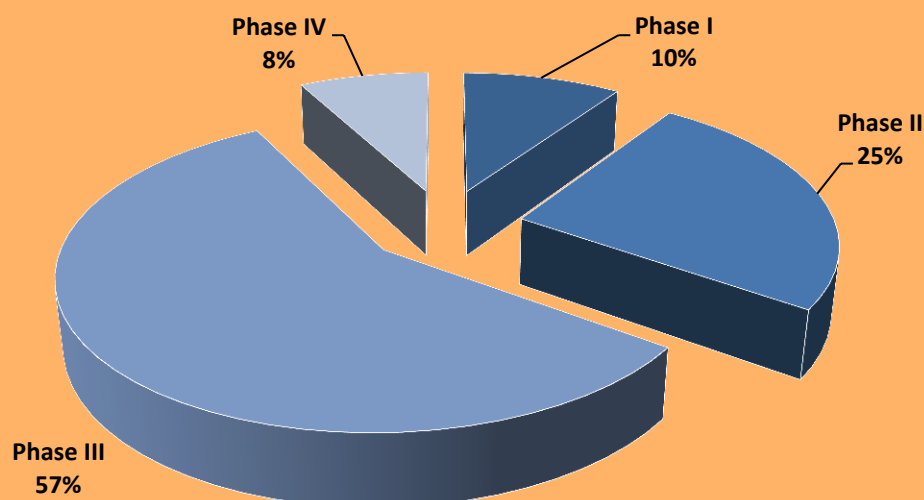


Figure 5. All Clinical Trials in Russia in Q3 2017 by Phase¹



If we look specifically at Russian Clinical Trials by Phase, then as shown in **Figure 6**, the share of Phase III trials in Q3 2017 is 57% of the total number of studies, the share of Phase II trials is 25% of Phase I trials is 10%, and the share of Phase IV studies accounted for 8%.

Figure 6. Percentage Breakdown of Russian Clinical Trials by Phase



The number of subjects planned to be enrolled in Phase I-IV trials launched in Q3 2017 is 11,652, less than in Q3 2016, when 22,226 subjects were planned to be enrolled.

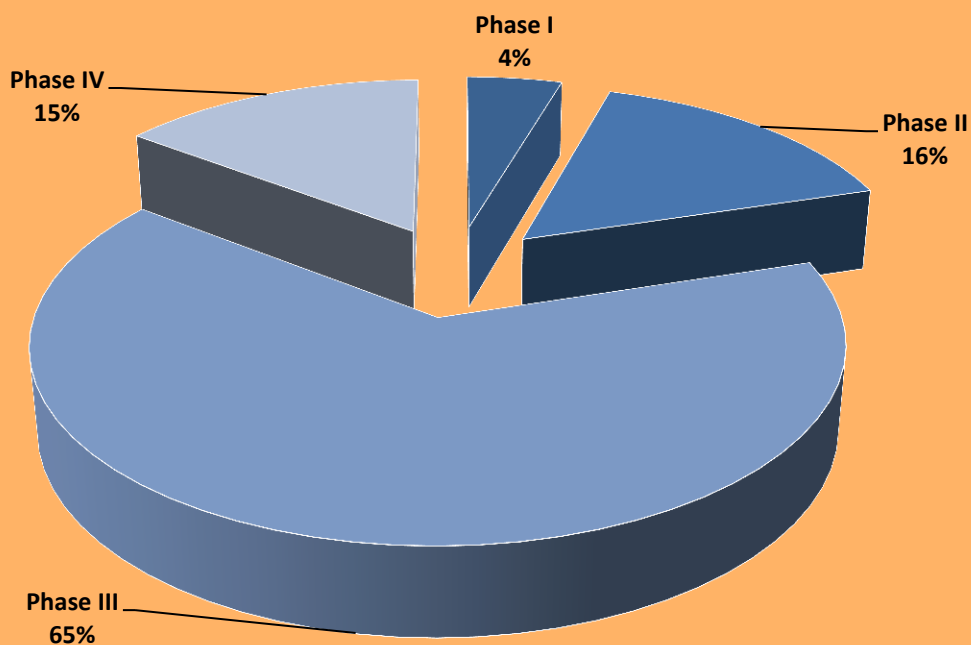
531 subjects are planned to be enrolled in Phase I trials; 1,832 – in Phase II trials; 7,572 – in Phase III studies and 1,717 subjects are planned to be enrolled in Phase IV studies.

The minimal number of subjects in a single study is seven, the maximum number is 448.

¹ Studies indicated by sponsors as Phase I-II in the applications submitted to MoH, are shown in Phase II studies group; Phase II-III – in Phase III group; Phase III-IV – in Phase IV group. BE studies were not included in any phase group.

Figure 7 indicates the distribution of subjects by study phase (only studies in which phase is specified were included), with Phase III clearly enrolling the majority of patients, as is to be expected.

Figure 7. Number of Study Subjects in Q3 2017 by Study Phase





The Top Five: Sponsors, Sites and CROs

Table 1. Top-5 International Study Sponsors in Q3 2017

<i>No</i>	<i>Company Name</i>	<i>No. studies¹</i>	<i>No. patients</i>
1	AbbVie Inc	7	264
2	Eli Lilly and Company	5	382
3	Novartis	5	286
4	Merck & Co.	4	280
5	AstraZeneca	4	373

Table 2. Top-5 Russian Study Sponsors in Q3 2017

<i>No</i>	<i>Company Name</i>	<i>No. studies</i>	<i>No. patients</i>
1	Biocad	6	789
2	North Star	6	300
3	Sotex	4	804
4	Pharmasyntez	4	561
5	Obnovlenie Pharmaceutical Company	3	105

Table 3. Top-5 Russian Research Sites (BE and Phase I studies) in Q3 2017

<i>No</i>	<i>Site Name</i>	<i>City</i>	<i>No. studies</i>
1	Medical Center Probiotec	Serpukhov, Moscow region	7
2	Clinical Hospital N2, Yaroslavl	Yaroslavl	6
3	Ecosafety Ltd.	Saint-Petersburg	6
4	Bioeq Ltd.	Saint-Petersburg	5
5	Road Clinical Hospital at the station Yaroslavl of Russian Railways	Yaroslavl	3
6	Regional Clinical Cardiology Center, Ivanovo	Ivanovo	3
7	Federal North-West Medical Research Centre named after V.A. Almazov	Saint-Petersburg	3
8	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	3

¹ Excluding BE studies.



Table 4. Top-5 Russian Research Sites (Phase II-IV studies) in Q3 2017

<i>No</i>	<i>Site Name</i>	<i>City</i>	<i>No. studies</i>
1	First Moscow State Medical University named after I.M. Sechenov	Moscow	13
2	First St. Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	11
3	Research Institute of Oncology named after N.N. Petrov	Saint-Petersburg	11
4	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	10
5	Moscow State University of Medicine and Dentistry	Moscow	9
6	Clinical emergency hospital named after N.V. Solovyov, Yaroslavl	Yaroslavl	9
7	Volgograd Regional Clinical Oncology Center	Volgograd	9

Table 5. Top-5 Russian Research Sites (all studies) in Q3 2017

<i>No</i>	<i>Site Name</i>	<i>City</i>	<i>No. studies</i>
1	First Moscow State Medical University named after I.M. Sechenov	Moscow	13
2	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	13
3	Research Institute of Oncology named after N.N. Petrov	Saint-Petersburg	12
4	Bioeq Ltd.	Saint-Petersburg	11
5	First St. Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	11

Table 6. Top-CROs in Russia in Q3 2017

<i>No</i>	<i>CRO Name</i>	<i>No. studies</i>	<i>No. patients</i>
1	OST RUS	3	378
2	Quintiles	3	293
3	PSI	3	275
4	Synergy Research Group	3	164
5	iPharma	2	440

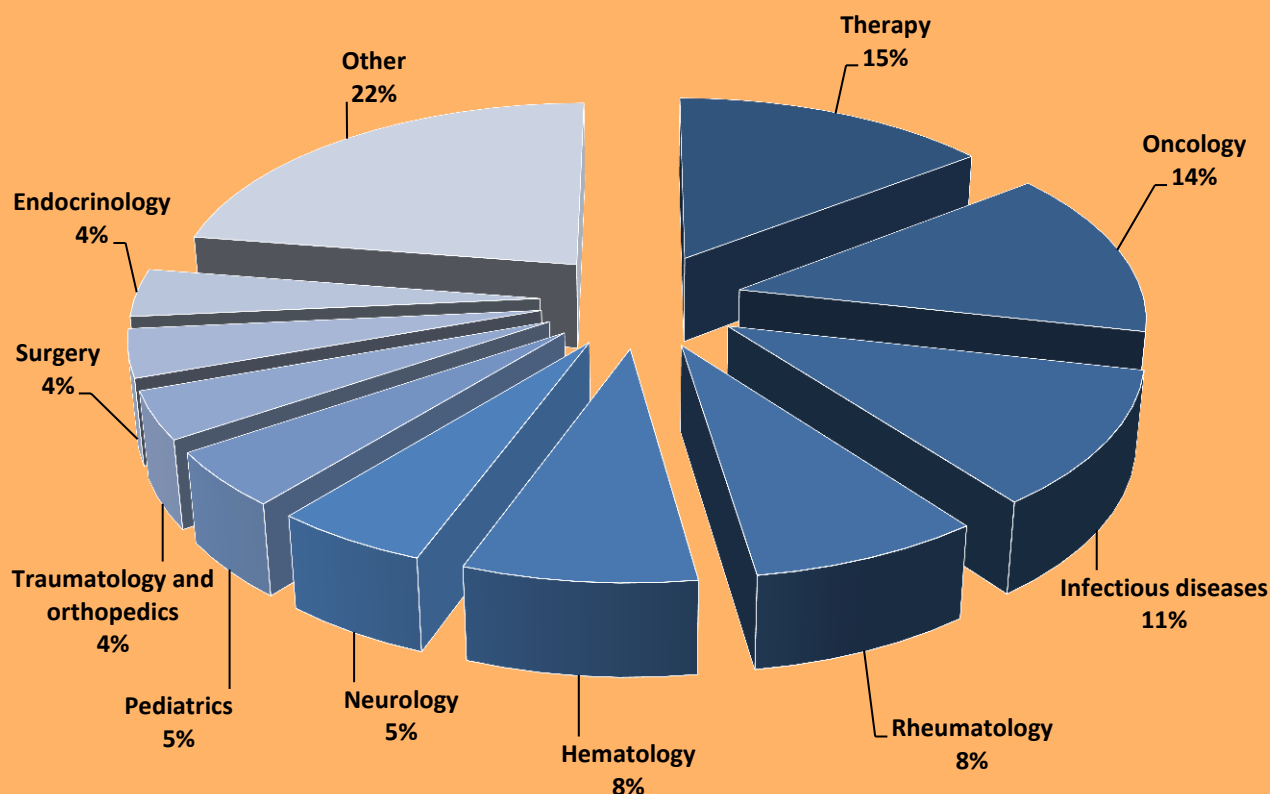


Therapeutic Areas of Russian Clinical Trials in Q3 2017

The largest number of studies were initiated in Therapy (22 new studies); and is followed by Oncology (21 new studies), Infectious diseases (17 new studies), Rheumatology (12 new studies), Hematology (12 new studies), Neurology (eight studies), Pediatrics (seven studies), Traumatology and orthopedics, Surgery and Endocrinology (six studies each).

The breakdown of therapeutic areas is shown in **Figure 8**.

Figure 8. Clinical Trials in Russia in Q3 2017 by Therapeutic Area



Clinical Trials Results

The U.S. Center for Drug Evaluation and Research (CDER) of the FDA approved 41 new drugs during Q3 2017; nine of them are new molecular entities (NME); other approvals concern new dosages, combinations or manufacturers. Nine of 41 drugs were (or are being) studied in clinical trials involving Russian sites.

Table 7 shows the drugs which were approved by FDA in Q3 2017 that were (or are being) studied in clinical trials in Russia.



Table 7. New Drugs Approved by FDA in Q3 2017 and Tested in Russian Sites

<i>Appr. date</i>	<i>Drug (active ingredient)</i>	<i>Company</i>
07/13/2017	Tremfya (guselkumab)	Janssen Biotech
07/20/2017	Benlysta (belimumab)	GlaxoSmithKline LLC
08/03/2017	Mavyret (glecaprevir/pibrentasvir)	Abbvie Inc
08/17/2017	Lynparza (olaparib)	Astrazeneca Pharms
09/05/2017	Tracleer (bosentan)	Actelion Pharmaceuticals Ltd
09/14/2017	Aliqopa (copanlisib)	Bayer Healthcare Pharms
09/18/2017	Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol)	GlaxoSmithKline
09/28/2017	Verzenio (abemaciclib)	Eli Lilly and Co
09/29/2017	Fiasp (insulin aspart)	Novo Nordisk Inc
<i>Source: FDA</i>		

During Q3 2017, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 28 new drug applications¹, six positive recommendations on new generic medicines and two for new biosimilar medicines. A negative opinion was adopted for six drugs. 20 of the drugs which received positive opinions were (or are being) studied in clinical trials in Russia.

Table 8 represents those drugs which were, or are being studied in clinical trials in Russia in Q3 2017.

Table 8. New Drugs Approved by EMA in Q3 2017 and Tested in Russian Sites

<i>Appr. date</i>	<i>Drug (active ingredient)</i>	<i>Manufacturer</i>
07/20/2017	Bavencio (avelumab)	Merck Serono Europe Ltd
07/20/2017	Dupixent (dupilumab)	Sanofi-Aventis groupe
07/20/2017	Symtuza (darunavir / cobicistat / emtricitabine / tenofovir alafenamide)	Janssen-Cilag International N.V.
07/20/2017	Tecentriq (atezolizumab)	Roche Registration Ltd
07/20/2017	Lacosamide Accord (lacosamide)	Accord Healthcare Ltd
07/20/2017	Bydureon (exenatide)	AstraZeneca AB
07/20/2017	Gazyvaro (obinutuzumab)	Roche Registration Ltd
07/20/2017	Humira (adalimumab)	AbbVie Ltd
07/20/2017	Keytruda (pembrolizumab)	Merck Sharp & Dohme Ltd
07/20/2017	RoActemra (tocilizumab)	Roche Registration Ltd

¹ Positive opinions on new generic, hybrid and biosimilar medicines are not included.



07/20/2017	Signifor (pasireotide)	Novartis Europharm Ltd
07/20/2017	Sovaldi (sofosbuvir)	Gilead Sciences International Ltd
07/20/2017	Vimpat (lacosamide)	UCB Pharma S.A.
09/14/2017	Elebrato Ellipta (fluticasone furoate / umeclidinium / vilanterol)	GlaxoSmithKline Trading Services
09/14/2017	Tremfya (guselkumab)	Janssen-Cilag International N.V.
09/14/2017	Trelegy Ellipta (fluticasone furoate / umeclidinium / vilanterol)	GlaxoSmithKline Trading Services
09/14/2017	Cyltezo (adalimumab)	Boehringer Ingelheim International GmbH
09/14/2017	Benlysta (belimumab)	Glaxo Group Ltd
09/14/2017	Tasigna (nilotinib)	Novartis Europharm Ltd
09/14/2017	Firazyr (icatibant)	Shire Orphan Therapies GmbH

Source: EMA

About Synergy Research Group

Synergy Research Group is a Russian contract research organization successfully operating in Russia since 2002. Synergy provides a full range of CRO services to help Russian and foreign pharmaceutical and biotechnological companies conduct cost-effective clinical trials. Today, Synergy is represented in Moscow, Saint-Petersburg, Novosibirsk, Yekaterinburg, Perm, Krasnodar, and also in Almaty and Astana (Kazakhstan) and Kyiv (Ukraine). The company's headquarters are in Moscow.