Clinical Trials in Russia
Orange Paper
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Executive Summary – English

The Ministry of Health of the Russian Federation approved 226 new clinical trials of all types, including local and bioequivalence studies, during Q2 2016. This represents a 16% increase over Q2 2015.

The main contribution into the total number of studies in Q2 2016 was made by multinational multi-center clinical trials (MMCT), the number of these studies is 97 and it is 24% more than in Q2 2015. The number of bioequivalence studies (BE) increased from 62 studies in Q2 2015 to 76 in Q2 2016, a 23% increase from last year's figure. The number of local clinical trials (LCT) slightly decreased from 54 in Q2 2015 to 53 in Q2 2016.

Clinical trials in Russia in Q2 2016 were sponsored by companies from 28 countries. The maximum number of trials (94) were initiated by Russian sponsors. American sponsors with 38 new studies took the runner-up place; they are followed by Indian sponsors with 22 trials, then by UK and Swiss sponsors, each having eight new studies.

The number of Phase I clinical trials has increased from 12 studies to 23 new studies in Q2 2016 (92% increase). The number of Phase II trials decreased by 17% from 23 in Q2 2015 to 19 new studies in Q2 2016. The number of Phase III trials increased from 88 to 103 studies, 17% more than in Q2 2015. The number of Phase IV trials decreased in comparison with Q2 2015 from nine to five studies.

The number of subjects planned to be enrolled in Phase I-IV trials launched in Q2 2016 is 16,001, 36% more than Q2 2015 figure, when 11,725 patients were planned to be enrolled.

Pfizer is on the top of the heap in Q2 2016 by sponsoring six new studies. It is followed by *Merck & Co.,* having five new trials. Top five is concluded by *Novartis, Astra Zeneca* and *Roche*, each with four new studies in Q2 2016, differentiating in number of patients.

Top five domestic pharmaceutical manufacturers by the number of new studies in Q2 2016 is headed by *Biocad* and *Pharmasyntez,* each having five new trials. It is followed by *R-Pharm* with three new studies. Top five is concluded by companies *Petrovax* and *Polisan*, each having two new studies and differentiating in the number of patients.

The top five Russian study sites are: *Russian Oncological Scientific Center named after N.N. Blokhin* (33 new studies), *First Moscow State Medical University named after I.M. Sechenov* (28 studies), *First St.Petersburg State Medical University named after I.P. Pavlov* (26 studies), *Clinical Emergency Care Hospital of the Yaroslav Region named after N.V. Soloviev* (20 studies), *Siberian State Medical University* (19 studies).

The top five Russian CROs are: *Quintiles* (eight new studies), *OCT RUS* and *INC Research UK Limited* (four studies each), *Parexel* and *PSI* (three studies each).

The top five therapeutic areas were: Oncology (37 studies); Musculoskeletal diseases (20 new studies), Pulmonology (19 studies), Gastroenterology (11 studies), Neurology (10 studies).

The Center for Drug Evaluation and Research (CDER) of the FDA approved 34 new drugs during Q2 2016, and **eight** of them were (or are being) studied in clinical trials conducted in Russia.

During Q2 2016, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 34 new drug applications[1]. **Twenty four** of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

[1] Positive opinions on new generic and hybrid medicines are not included.

Executive Summary – Russian

Во втором квартале 2016 года Министерством здравоохранения Российской Федерации было выдано 226 разрешений на все виды клинических исследований (КИ), что на 16% больше, чем за аналогичный период 2015 года.

При этом количество новых международных многоцентровых КИ, инициированных во втором квартале 2016 года, составило 97 исследований, что на 24% больше по сравнению с аналогичным периодом прошлого года. Количество исследований биоэквивалентности увеличилось на 23% по сравнению с 2015 годом и составило 76 против 62. Количество локальных КИ, проводимых на территории России, незначительно уменьшилось по сравнению со вторым кварталом 2015 года и составило 53 исследования против 54.

Спонсорами КИ, разрешенных к проведению в России во втором квартале 2016 года, выступили компании из 28 стран. На первое место вышли российские производители с 94 КИ, за ними идут американские спонсоры с 38 новыми исследованиями, Индия с 22 исследованиями, затем Великобритания и Швейцария с восемью новыми исследованиями каждая.

Во втором квартале 2016 года было инициировано 23 новых КИ I фазы, что на 92% больше, чем за тот же период 2015 года (12 КИ). Количество исследований II фазы уменьшилось по сравнению со вторым кварталом 2015 года на 17% и составило 19 новых исследований против 23. Количество КИ III фазы увеличилось с 88 до 103 исследований, что на 17% больше по сравнению с аналогичным периодом прошлого года. Количество исследований IV фазы уменьшилось по сравнению со вторым кварталом 2015 года с девяти до пяти исследований.

Во втором квартале 2016 года лидирующие позиции среди иностранных производителей по количеству новых исследований заняла компания *Pfizer* с шестью новыми исследованиями. Далее следует компания *Merck & Co.* с пятью новыми КИ. Пятерку лидеров замыкают компании *Novartis, Astra Zeneca* и *Roche*, каждая с четырьмя новыми КИ, но с разным количеством пациентов.

Список пяти лидирующих отечественных производителей по количеству новых исследований во втором квартале 2016 года возглавили компании *Биокад* и *Фармасинтез* с пятью исследованиями каждая. Далее следует компания *Р-Фарм* (три новых КИ). Пятерку лидеров замыкают компании *Петровакс* и *Полисан* (два новых исследования каждая, но с разным количеством пациентов).

В пятерку передовиков второго квартала 2016 года вошли следующие исследовательские центры: *Российский онкологический научный центр имени Н.Н. Блохина* (33 новых исследования), *Первый Московский государственный медицинский университет имени И.М. Сеченова* (28 исследований), *Первый Санкт-Петербургский государственный медицинский университет имени академика И.П. Павлова* (26 исследований), *Клиническая больница скорой медицинской помощи имени Н.В. Соловьева Ярославской области* (20 исследований), *Сибирский государственный медицинский университет* (19 исследований).

Пятерка лидеров среди российских КИО: *Quintiles* (восемь новых исследований), *OCT RUS* и *INC Research UK Limited* (по четыре исследования), *Parexel* и *PSI* (по три исследования)

Наибольшее количество исследований проведено в следующих областях: онкология – 37, заболевания опорно-двигательного аппарата – 20, пульмонология – 19; гастроэнтерология – 11; неврология – 10 новых КИ.

FDA одобрено во втором квартале 2016 года 34 новых лекарственных препарата, по **8** из которых в России проводились (или проводятся) КИ. EMA одобрено во втором квартале 2016 года 34 новых лекарственных препарата, по **24** из которых в России проводились (или проводятся) КИ.

Clinical Trials by Type and Manufacturing Country

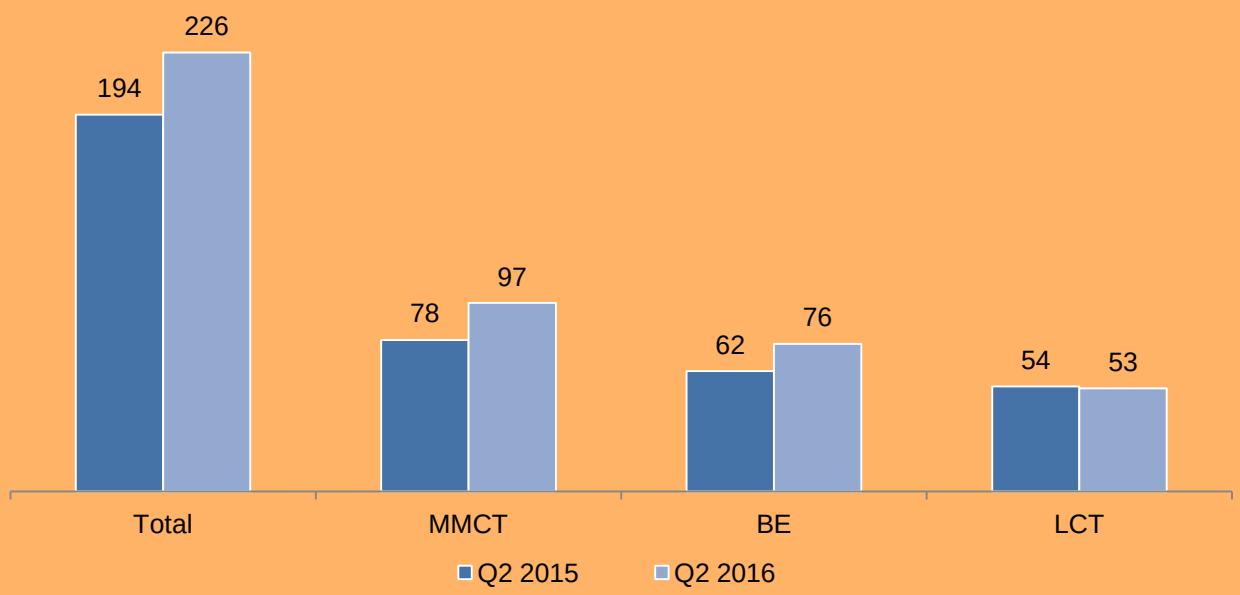
The Russian MoH approved 226 new clinical trials of all types including local and bioequivalence studies during Q2 2016, demonstrating a 16% increase in comparison with the same point of the last year.

As shown in **Figure 1**, the main contribution into the total number of studies was made by multinational multi-center clinical trials (MMCT); the number of these studies has increased from 78 studies in Q2 2015 to 97 in Q2 2016, 24% increase from last year's figure.

The number of bioequivalence studies (BE) increased from 62 studies in Q2 2015 to 76 in Q2 2016, 23% increase from last year's figure.

The number of local clinical trials (LCT) has slightly decreased from 54 in Q2 2015 to 53 in Q2 2016.

Figure 1. Clinical Trials in Russia in Q2 2016

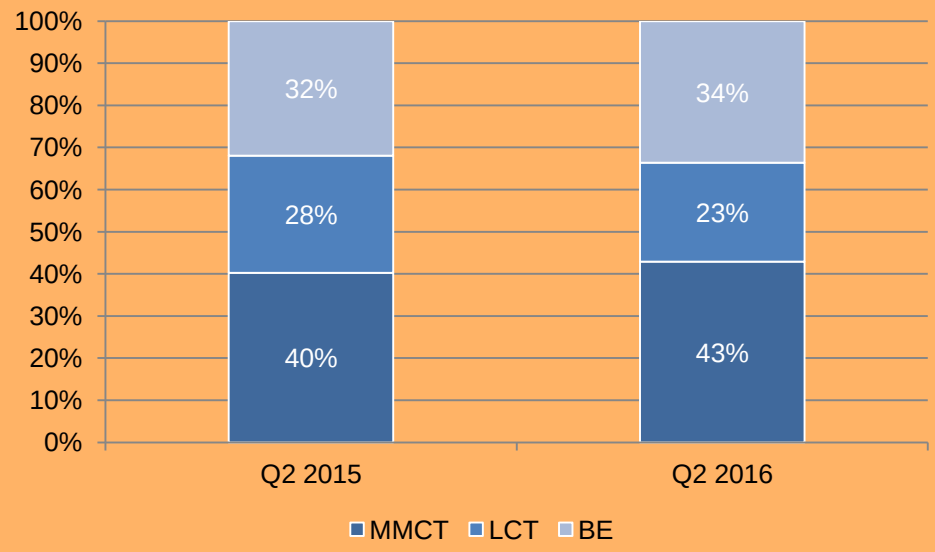


The proportions between different study types (multinational multi-center clinical trials, local clinical trials and bioequivalence studies) changed slightly since last year (see **Figure 2**).

The share of bioequivalence studies increased from 32% to 34% of the total number of clinical trials approved in Q2 2016.

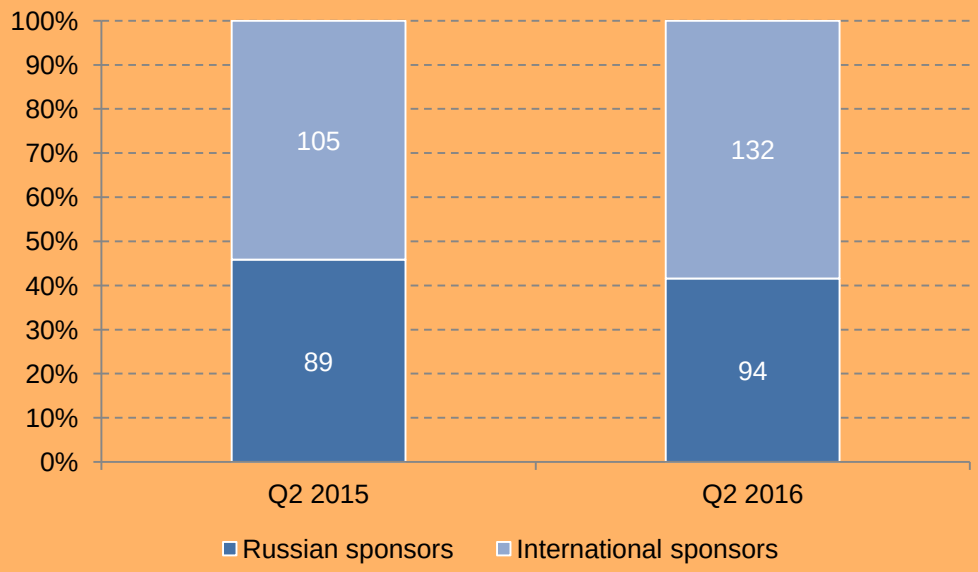
The share of the local clinical trials decreased from 28% in Q2 2015 to 23% in Q2 2016, and the share of multinational multi-center clinical trials was 43% of the total number of trials approved during Q2 2016 (40% in Q2 2015).

Figure 2. Clinical Trials by Type in Q2 2016



The geographic origins of sponsors changed slightly in comparison with last year. 58% of the total number of new studies in Q2 2016 was sponsored by foreign companies which received 132 study approvals (54% in Q2 2015). The share of studies of local manufacturers decreased from 46% in Q2 2015 to 42% in Q2 2016, and amounted to 94 studies (**Figure 3**).

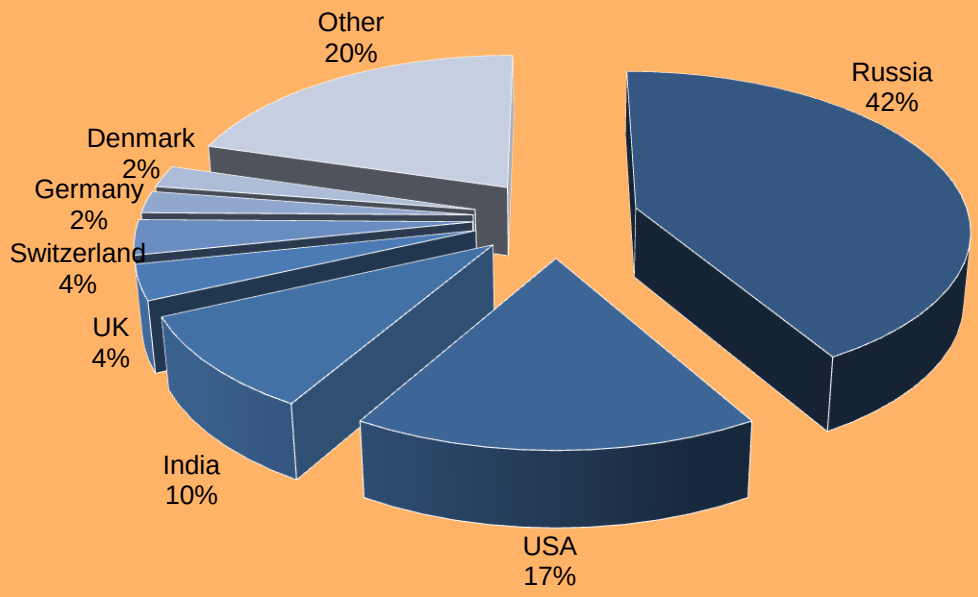
Figure 3. Russian vs International Sponsors in Q2 2016



Clinical trials in Russia in Q2 2016 were sponsored by companies from 28 countries. **Figure 4** indicates the geographic breakdown in sponsors' country of origin.

The maximum number of trials (94) was initiated by Russian sponsors. American sponsors with 38 new studies took the runner-up place; they are followed by Indian sponsors with 22 trials, then by UK and Swiss sponsors, each having eight new studies. The group of leaders is concluded by German and Danish Sponsors, each having five studies.

Figure 4. Sponsors' Country of Origin for Q2 2016 Clinical Trials in Russia



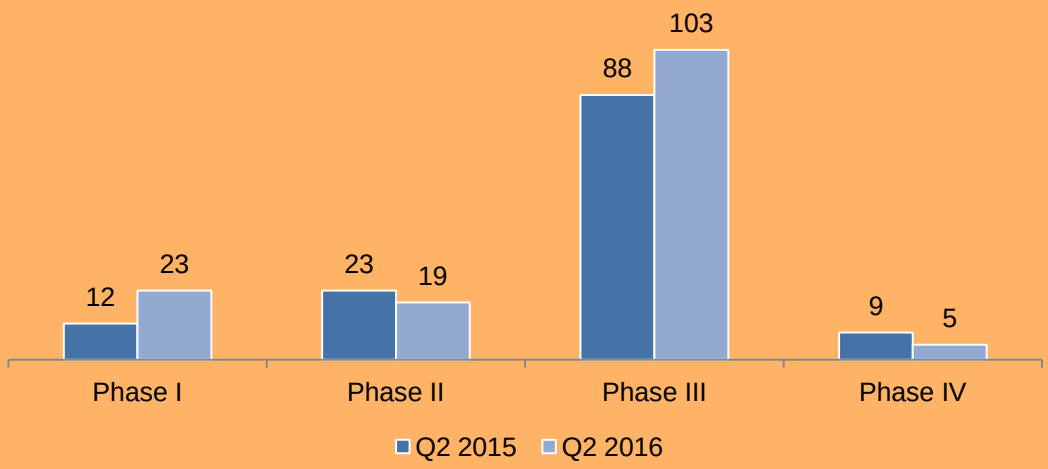
Other sponsors include: Poland, France and Sweden (four studies each), Bulgaria, Hungary, Israel, Italy and Turkey (three studies each), Austria, Belgium, Spain, Republic of Korea, Netherlands and Slovenia (two studies each) and Belarus, New Zealand, UAE, Republic of Macedonia, Romania, Czech Republic and Japan, each started one new study in Q2 2016.

Clinical trials by Phase

The number of Phase I clinical trials increased to 92% compared to Q2 2015: from 12 studies to 23 new studies in Q2 2016. The number of Phase II trials decreased from 23 in Q2 2015 to 19 new studies in Q2 2016, 17% less than in Q2 2015 (**Figure 5**).

The number of Phase III trials increased from 88 to 103 studies, 17% more than in Q2 2015. The number of Phase IV trials decreased in comparison with Q2 2015 from nine to five studies.

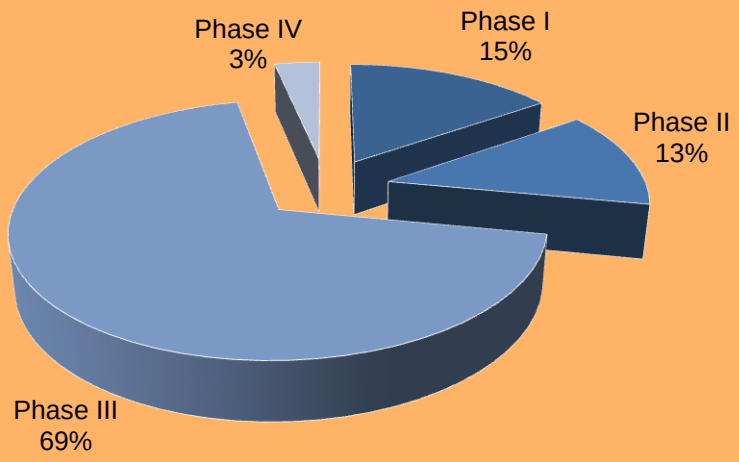
Figure 5. Clinical Trials in Russia in Q2 2016 by Phase[1]



As shown in **Figure 6**, the share of Phase III trials in Q2 2016 is 69% of the total number of studies, the share of Phase I trials is 15%, Phase II trials is 13% and the share of Phase IV studies accounted to 3%.

[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 6. Percentage Breakdown of Russian Clinical Trials by Phase



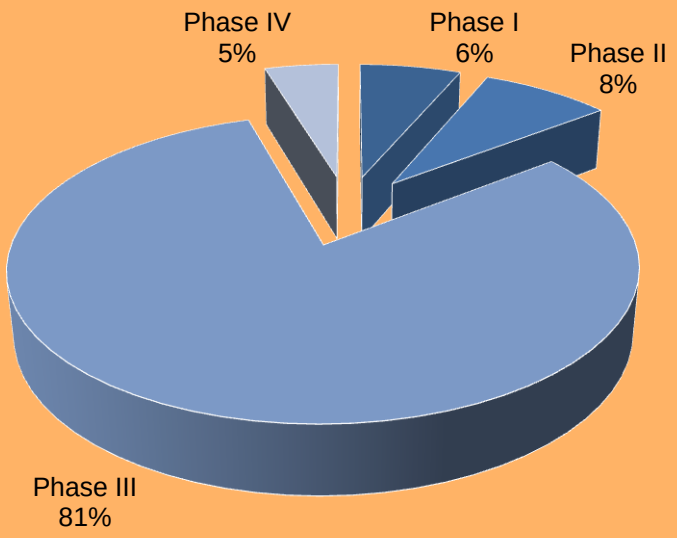
The number of subjects planned to be enrolled in Phase I-IV trials launched in Q2 2016 is 16,001, 36% more than in Q2 2015, when 11,725 patients were planned to be enrolled.

1,024 subjects will be recruited in Phase I trials; 1,309 – in Phase II trials; 12,922 – in Phase III studies and 746 subjects will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is six, the maximum number is 750.

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 Q2 2016 by Study Phase



The Top Five: Sponsors, Sites and CROs

Table 1. Top-5 International Study Sponsors in Q2 2016

№	Company Name	No. studies[1]	No. patients
1	Pfizer	6	603
2	Merck & Co.	5	510
3	Novartis	4	800
4	AstraZeneca	4	590
5	Roche	4	253

Table 2. Top-5 Russian Study Sponsors in Q2 2016

№	Company Name	No. studies	No. patients
1	Biocad	5	370
2	Pharmasyntez	5	364
3	R-Pharm	3	913
4	Petrovax	2	474
5	Polisan	2	254

Table 3. Top-5 Russian Research Sites in Q2 2016

№	Site Name	City	No. studies
1	N.N. Blokhin Russian Oncological Scientific Center	Moscow	33
2	I.M. Sechenov First Moscow State Medical University	Moscow	28
3	I.P. Pavlov First St.Petersburg State Medical University	Saint-Petersburg	26
4	N.V. Soloviev Clinical Emergency Care Hospital of the Yaroslav Region	Yaroslavl	20
5	Siberian State Medical University	Tomsk	19

[1] Excluding BE studies.

Table 4. Top-5 Russian CROs in Q2 2016

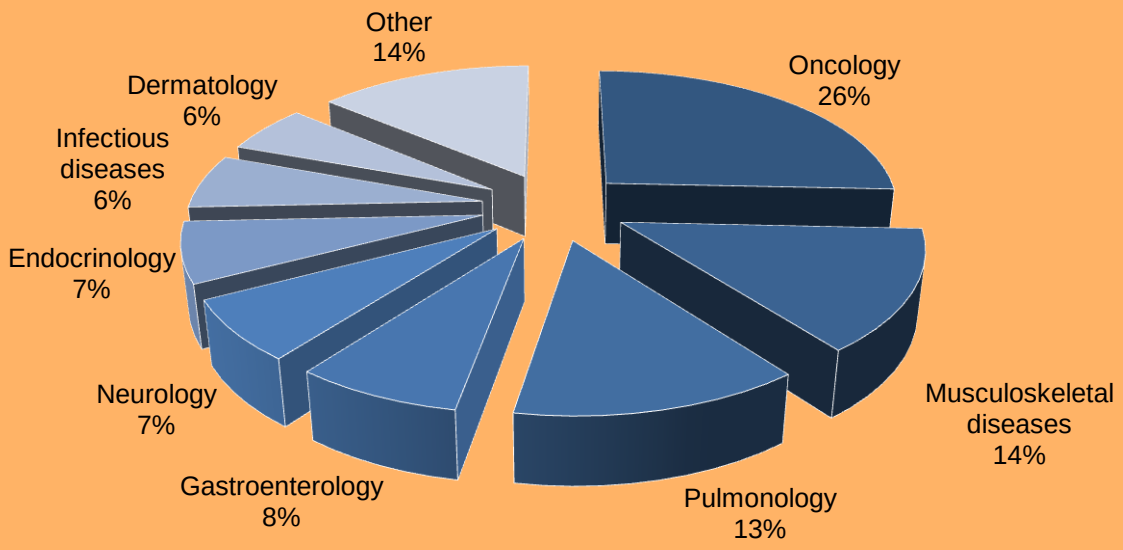
№	*CRO Name*	*No. studies*	*No. patients*
1	Quintiles	8	484
2	OCT RUS	4	785
3	INC Research UK Limited	4	222
4	Parexel	3	245
5	PSI	3	180

Therapeutic Areas of Russian Clinical Trials in Q2 2016

Eighty seven percent of new studies in Q2 2016 were initiated in eight leading therapeutic areas: the largest number of studies was initiated in Oncology (37 studies); it is followed by Musculoskeletal diseases (20 new studies), Pulmonology (19 studies), Gastroenterology (11 studies), Neurology and Endocrinology (10 studies each), Infectious diseases (nine studies) and Dermatology (eight studies).

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

Figure 8. Clinical Trials in Russia in Q2 2016 by Therapeutic Area



Clinical Trials Results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 34 new drugs during Q2 2016; six of them are new molecular entities (NME); other approvals concern new active ingredients, dosages, combinations, manufacturers or indications of already marketed drugs. Eight of 34 drugs were (or are being) studied in clinical trials involving Russian sites.

The **Table 3** shows the drugs which were approved by FDA in Q2 2016 that were (or are being) tested in clinical trials in Russia.

Table 3. New Drugs Approved by FDA in Q2 2016 and Tested in Russian Sites

Appr.date	*Drug (active ingredient)*	*Company*
04/04/2016	Descovy (emtricitabine, tenofovir alafenamide fumarate)	Gilead Sciences Inc
04/25/2016	Cabometyx (cabozantinib s-malate)	Exelixis Inc
04/29/2016	Nuplazid (pimavanserin tartrate)	Acadia Pharms Inc
04/29/2016	Fycompa (perampanel)	Eisai Inc
05/18/2016	Tecentriq (atezolizumab)	Genentech Inc
05/27/2016	Jentadueto XR (linagliptin, metformin hydrochloride)	Boehringer Ingelheim
05/27/2016	Zinbryta (daclizumab)	Biogen
06/28/2016	Epclusa (sofosbuvir, velpatasvir)	Gilead Sciences Inc
		Source: FDA

During Q2 2016, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 34 new drug applications[1], four positive recommendations on new generic medicines and three for new hybrid medicines. Negative opinion was adopted for three drugs. 24 of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

The **Table 4** represents those of them which were, or are being tested in clinical trials in Russia in Q2 2016.

Table 4. New Drugs Approved by EMA in Q2 2016 and Tested in Russian Sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
04/28/2016	Odefsey (emtricitabine / rilpivirine / tenofovir alafenamide)	Gilead Sciences International Ltd
04/28/2016	Ongentys (opicapone)	Bial - Portela & Cª, S.A.
04/28/2016	Zavicefta (ceftazidime / avibactam)	AstraZeneca AB
04/28/2016	Zinbryta (daclizumab)	Biogen Idec Ltd
04/28/2016	Afinitor (everolimus)	Novartis Europharm Ltd
04/28/2016	Avastin (bevacizumab)	Roche Registration Limited
04/28/2016	Gazyvaro (obinutuzumab)	Roche Registration Limited
04/28/2016	HyQvia (human normal immunoglobulin)	Baxalta Innovations GmbH
04/28/2016	Imbruvica (ibrutinib)	Janssen-Cilag International NV
04/28/2016	Reyataz (atazanavir / atazanavir sulfate)	Bristol-Myers Squibb Pharma EEIG
04/28/2016	Victoza (liraglutide)	Novo Nordisk A/S

[1] Positive opinions on new generic and hybrid medicines are not included.

04/28/2016	Zinforo (ceftaroline fosamil)	AstraZeneca AB
05/26/2016	Epclusa (sofosbuvir / velpatasvir)	Gilead Sciences International Ltd
05/26/2016	Qtern (saxagliptin / dapagliflozin)	AstraZeneca AB
05/26/2016	Humira (adalimumab)	AbbVie Ltd
05/26/2016	Kyprolis (carfilzomib)	Amgen Europe B.V.
05/26/2016	Simponi (golimumab)	Janssen Biologics B.V.
05/26/2016	Tysabri (natalizumab)	Biogen Idec Ltd
06/23/2016	Cinqaero (reslizumab)	Teva Pharmaceuticals Limited
06/23/2016	Cervarix (human papillomavirus vaccine)	GlaxoSmithKline Biologicals
06/23/2016	Ilaris (canakinumab)	Novartis Europharm Ltd
06/23/2016	Keytruda (pembrolizumab)	Merck Sharp & Dohme Limited
06/23/2016	RoActemra (tocilizumab)	Roche Registration Limited
06/23/2016	Ryzodeg (insulin degludec / insulin aspart)	Novo Nordisk A/S
		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.