SYNERGY
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PAPER

RESEARCH REPORT

CLINICAL TRIALS IN RUSSIA

SUMMER 2018

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FOREWORD

The Orange Paper is a free publication produced by Synergy Research Group for the pharmaceutical industry since 2007. It pulls together data from numerous public sources into a single brief document to aid decision makers planning to conduct clinical trials. It is produced quarterly, with an annual summary at the close of each year.

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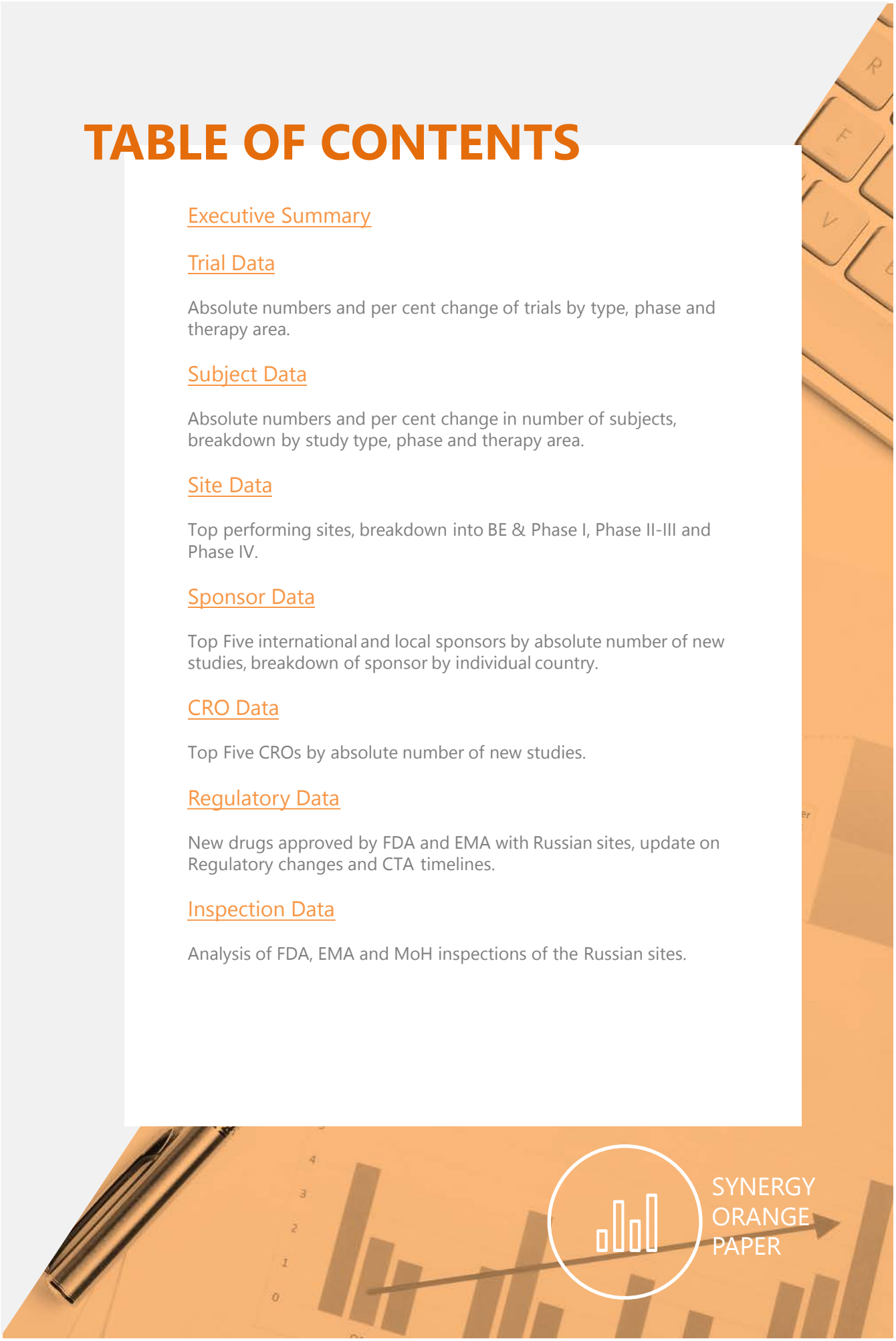

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EXECUTIVE SUMMARY

The Ministry of Health of the Russian Federation approved 153 new clinical trials of all types, including local and bioequivalence studies, during Q2 2018, a 14% decrease from Q2 2017.

The number of new multinational multi-center clinical trials (MMCT) initiated in Q2 2018 is 64, compared to 86 in Q2 2017. The number of bioequivalence studies (BE) decreased from 52 studies in Q2 2017 to 49 in Q2 2018. The number of local clinical trials (LCT) stayed the same at 40 studies.

The number of Phase I clinical trials has increased from 8 studies to 11 new studies in Q2 2018. The number of Phase II trials increased in comparison with Q2 2017 from 17 to 18 new studies. The number of Phase III trials decreased from 94 to 68 studies. The number of Phase IV trials was equal in comparison with Q2 2017, at 7 studies.

Top foreign pharmaceutical manufacturers are *Novartis* (seven new studies), *Roche, AbbVie* and *Bristol-Myers Squibb* (six new trials each).

Top domestic pharmaceutical manufacturers are *Valenta Pharm* and *Atoll* (four trials each).

The top CROs in Russia are: *Parexel, Synergy Research Group, ICON* and *R&D Pharma* (3 studies each).

The top therapeutic areas were: Oncology (19 studies) and Therapy (11 studies).

The Center for Drug Evaluation and Research (CDER) of the FDA approved 11 new drugs, and **four** of them were (or are being) studied in clinical trials conducted in Russia.

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 13 new drug applications (positive opinions on new generic, hybrid and biosimilar medicines as well as extensions of indications are not included). **Sixteen** of the drugs and extensions which received positive opinions were (or are being) tested in clinical trials in Russia.

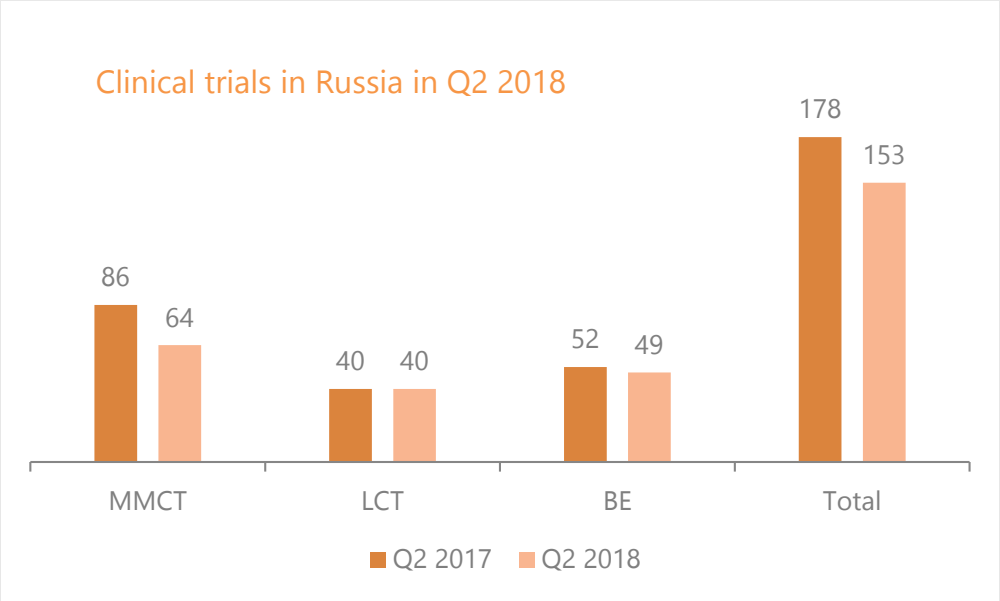
Trial Data

The Russian MoH approved 153 new clinical trials of all types including local and bioequivalence studies during Q2 2018, demonstrating a 14% decrease in comparison with the same point of the last year.

The main contribution into the total number of studies was made by multinational multi-center clinical trials (MMCT); the number of these studies decreased from 86 studies in Q2 2017 to 64 in Q2 2018, a 26% decrease from last year's figure.

The number of bioequivalence studies (BE) decreased from 52 studies in Q2 2017 to 49 in Q2 2018, a 6% decrease from last year's figure.

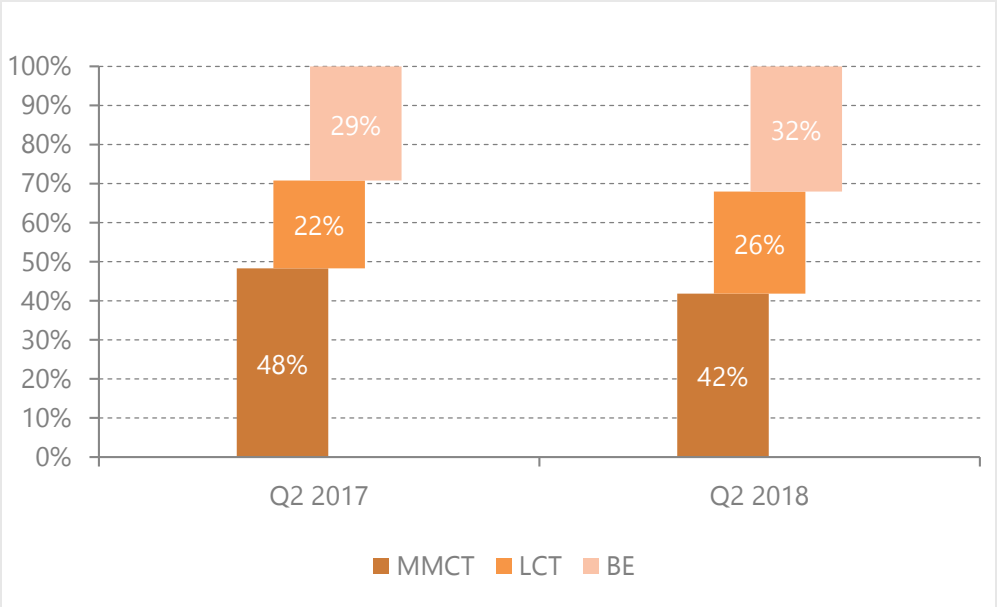
The number of local clinical trials (LCT) stayed equal in comparison with Q2 2017, at 40 studies in Q2 2018.



Breakdown by type

The proportions between different study types (multinational multi-center clinical trials, local clinical trials and bioequivalence studies) conducted in Q2 2018 changed in comparison to Q2 2017.

The share of bioequivalence studies increased from 29% to 32%. The share of the local clinical trials increased from 22% to 26%, and the share of multinational multi-center clinical trials decreased from 48% to 42% of the total number of trials approved during Q2 2018.

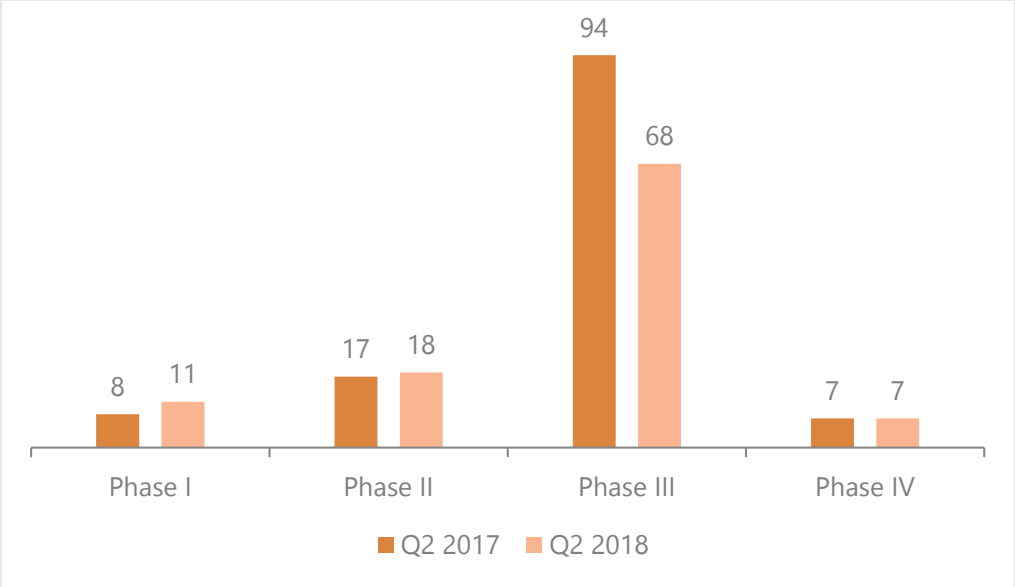


Breakdown by phase

The number of Phase I clinical trials increased from 8 studies in Q2 2017 to 11 new studies in Q2 2018. The number of Phase II trials increased from 17 studies in Q2 2017 to 18 new studies in Q2 2018.

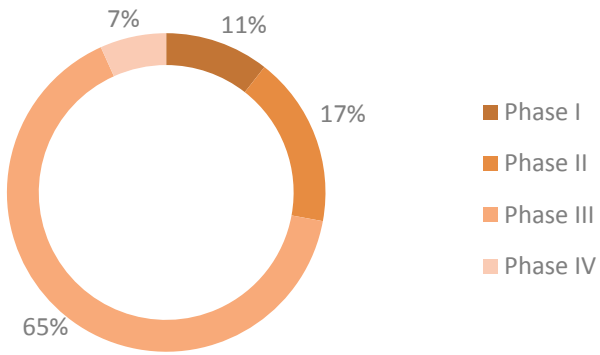
The number of Phase III trials decreased from 94 to 68 studies, 28% less than in Q2 2017. The number of Phase IV trials was equal in comparison with Q2 2017, at seven studies.

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.



The share of Phase III trials in Q2 2018 is 65% of the total number of studies, the share of Phase I trials is 11%, Phase II trials is 17% and the share of Phase IV studies accounted to 7%.

Percentage breakdown of clinical trials by phase



Subject Data

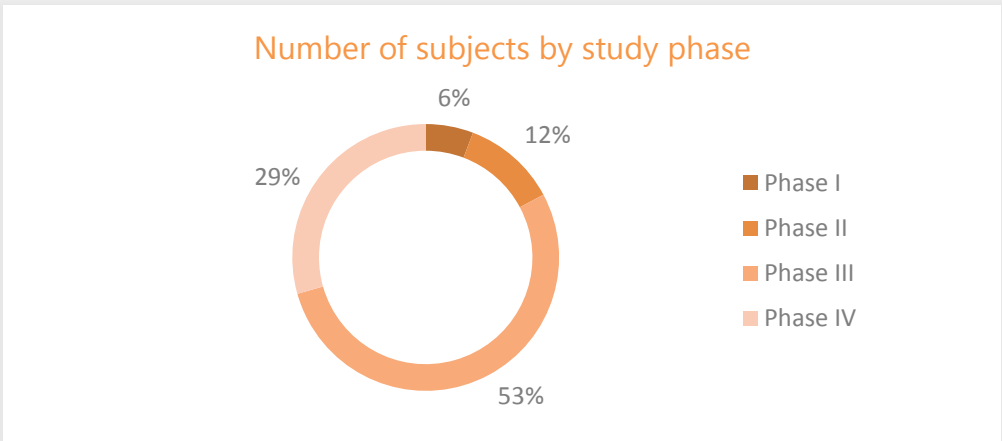
The number of subjects planned to be enrolled in Phase I-IV trials launched in Q2 2018 is 16,336, more than in Q2 2017, when 14,555 subjects were planned to be enrolled.

789 subjects will be recruited in Phase I trials; 1,563 – in Phase II trials; 7,299 – in Phase III studies and 4,018 subjects will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is five, the maximum number is 3500.

Number of study subjects in studies in Q2 2018

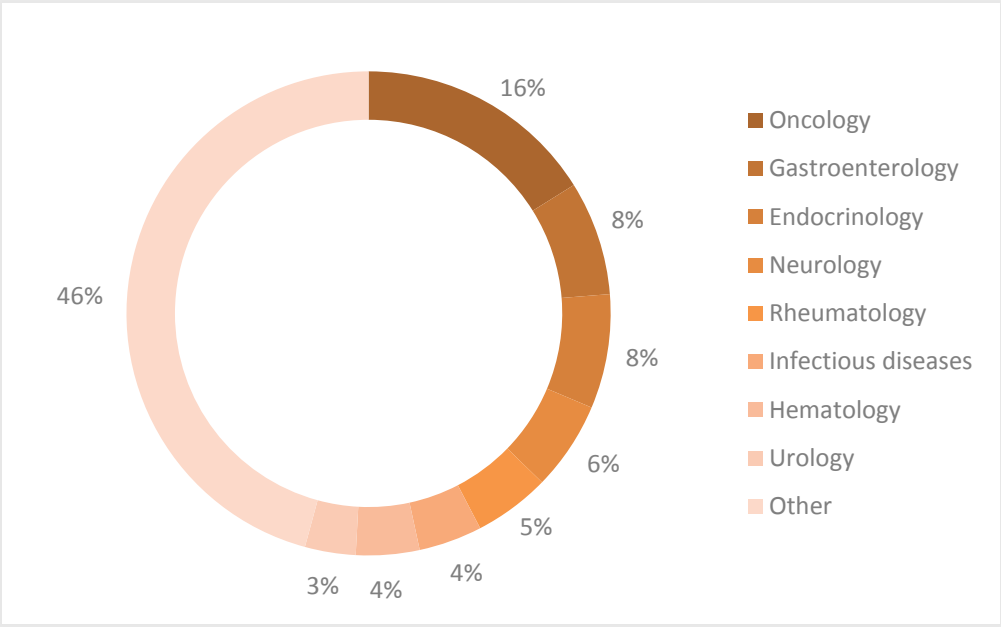
Study Phase	Minimum	Maximum
BE	24	280
I	30	150
II	30	230
III	5	440
IV	22	3500



Therapeutic areas of Russian clinical trials

The largest number of studies were initiated in Oncology (19 studies), Gastroenterology and Endocrinology (9 studies each), Neurology (7 studies), Rheumatology (6 studies), Hematology and Infectious diseases (5 studies each).

More than one therapeutic area could be assigned to a trial. BE studies were not included in any therapeutic area group.



Site Data

Top-5 Russian research sites (BE and Phase I studies)

№	Site Name	City	No. studies
1	Clinical Hospital #2, Yaroslavl region	Yaroslavl	11
2	Road Clinical Hospital at the station Yaroslavl of Russian Railways	Yaroslavl	5
3	Tomsk National Research Medical Center	Tomsk	4
4	Probiotec Medical Center	Moscow Region	4
5	Eco-Bezopasnost Ltd.	Saint-Petersburg	3

Top-5 Russian research sites (Phase II-IV studies)

№	Site Name	City	No. studies
1	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	16
2	Rostov State Medical University	Rostov-on-Don	12
3	North-Western State Medical University named after I.I. Mechnikov	Saint-Petersburg	11
4	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	10
5	City Clinical Oncological Dispensary	Saint-Petersburg	9

Top-5 Russian research sites (all studies)

№	Site Name	City	No. studies
1	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	16
2	Rostov State Medical University	Rostov-on-Don	12
3	Clinical Hospital #2, Yaroslavl region	Yaroslavl	12
4	North-Western State Medical University named after I.I. Mechnikov	Saint-Petersburg	11
5	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	10

Sponsor Data

Top-5 international study sponsors in Q2 2018

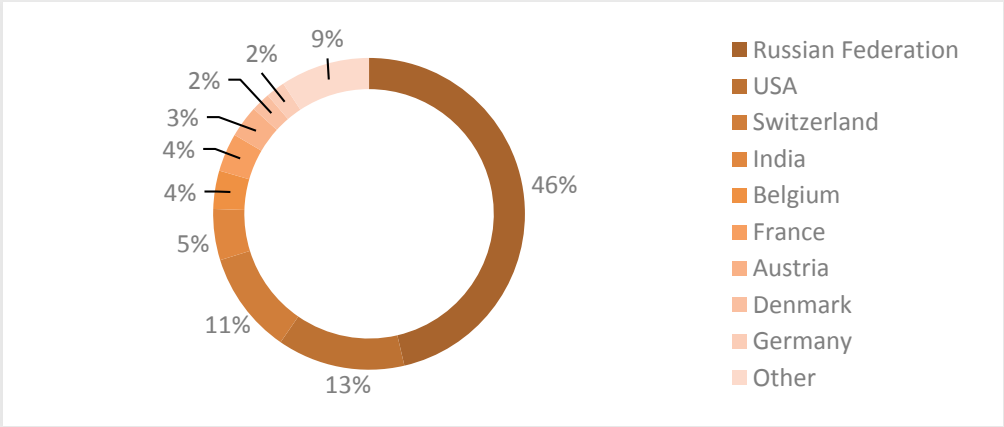
№	Company Name	No. studies (excluding BE studies)	No. patients
1	Novartis	7	392
2	Roche	6	640
3	AbbVie Inc	6	335
4	Bristol-Myers Squibb	6	189
5	Janssen	4	610

Top-5 Russian study sponsors in Q2 2018

№	Company Name	No. studies	No. patients
1	Valenta Pharm	4	282
2	Atoll Ltd.	4	146
3	Generium	3	440
4	Pharmasyntez	3	211
5	Technologia Lekarstv	3	176

The geographic origins of sponsors changed in comparison with last year. 83 of the studies were sponsored by foreign companies, which amounted to 54% of all studies in in Q2 2018 (64% in Q2 2017). 70 studies were initiated by local manufacturers, and their share increased from 36% in Q2 2017 to 46% in Q2 2018.

Clinical trials in Russia in Q2 2018 were sponsored by companies from 22 countries. The maximum number of trials (70) were initiated by Russian sponsors. American sponsors with 20 new studies took the runner-up place; they are followed by Swiss sponsors with 16 trials, then by Indian sponsors with eight new studies, then Belgian and French sponsors (six studies each). The group of leaders is concluded by Austrian sponsors (five studies), and Denmark and Germany, each having three studies. Other sponsors include: Britain, Sweden and Republic of Belarus (two studies each), Bulgaria, Canada, China, Australia, Israel, Netherlands, Poland, Romania, Turkey, Ireland, each of which started one new study in Q2 2018.



CRO Data

Top CROs in Russia in Q2 2018

№	CRO Name	No. studies	No. patients
1	Parexel	3	740
2	Synergy Research Group Ltd.	3	295
3	ICON	3	163
4	R&D Pharma Ltd.	3	104
5	PSI	2	224

Regulatory Data

Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 11 new drugs during Q2 2018; four of them were new molecular entities (NME); other approvals concerned new dosages, combinations or manufacturers. Four of 11 drugs were (or are being) studied in clinical trials involving Russian sites.

The table shows the drugs which were approved by FDA in Q2 2018 that were (or are being) tested in clinical trials in Russia.

Appr.date	Drug (active ingredient)	Company
05/17/2018	Aimovig (erenumab-aooe)	Amgen
05/18/2018	Lokelma (sodium zirconium cyclosilicate)	AstraZeneca
04/19/2018	Akynzeo (fosnetupitant and palonosetron)	Helsinn Healthcare SA
04/17/2018	Tavalisse (fostamatinib)	AstraZeneca
		Source: FDA

During Q2 2018, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 13 new drug applications, four positive recommendation on new generic medicines, four positive recommendations for new biosimilar medicines, and 18 positive opinions on extensions of therapeutic indications. A negative opinion was adopted for one drug. Eighteen of the drugs and extensions which received positive opinions were (or are being) tested in clinical trials in Russia.

The Table represents those of them which were, or are being tested in clinical trials in Russia in Q2 2018. Positive opinions on new generic, hybrid and biosimilar medicines are not included.

Appr. date	Drug (active ingredient)	Manufacturer
04/23/2018	Biktarvy (bictegravir)	Gilead Sciences
04/23/2018	Cimzia (certolizumab pegol)	UCB Pharma
04/23/2018	Perjeta (pertuzumab)	Hoffmann-La Roche
04/23/2018	Prolia (denosumab)	Amgen
04/23/2018	Sprycel (dasatinib)	Bristol-Myers Squibb
04/23/2018	Tagrisso (osimertinib)	AstraZeneca
04/23/2018	Xultophy (insulin degludec / liraglutide)	Novo Nordisk A/S
04/23/2018	Yervoy (ipilimumab)	Bristol-Myers Squibb
05/28/2018	Aimovig (erenumab)	Amgen
05/28/2018	Briviact (brivaracetam)	UCB Pharma S.A.
05/28/2018	Translarna (ataluren)	PTC Therapeutics
05/28/2018	Xeljanz (tofacitinib)	Pfizer Limited
06/25/2018	Nerlynx (neratinib)	Puma Biotechnology, Inc
06/25/2018	Lenvima (lenvatinib)	Eisai Europe Ltd.
06/25/2018	Opdivo (nivolumab)	Bristol-Myers Squibb
06/25/2018	RoActemra (tocilizumab)	Hoffmann-La Roche
		Source: EMA

Inspection Data

FDA inspections

At the moment of the Orange Paper Q2 2018 production no information about FDA inspections conducted in the Russian investigative sites was available.

Roszdravnadzor inspections

At the moment of the Orange Paper Q2 2018 production no information about Roszdravnadzor inspections conducted in the Russian investigative sites was available.