



SYNERGY
ORANGE
PAPER

RESEARCH REPORT

CLINICAL TRIALS IN RUSSIA

ANNUAL 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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EXECUTIVE SUMMARY

During the year 2018 the Ministry of Health of the Russian Federation approved the start of 653 new clinical trials of all types, with an overall year on year decline of 6,7% by total number of studies.

The dominant type of clinical trials conducted in Russian sites during 2018 were MMCT (Multinational Multi-center Clinical Trials) with 44% market share. The most prevalent Phase of clinical trials conducted in Russian sites by total number of studies was Phase III.

There is a significant level of oligopoly within the Russian Clinical trials market – with the top-10 International Sponsors accounting for 24% of the total number of studies conducted, and for 25% of all patients enrolled during the year 2018. The top-10 Russian sponsors take up approximately 9% of the market by total number of trials conducted, and have 15% of all patients enrolled in these trials. The twenty largest pharmaceutical companies combined account for 33% of all clinical trials and for 40% of all patients enrolled.

During Y 2018 the Center for Drug Evaluation and Research (CDER) of the U.S. FDA approved 162 new drugs, including new molecular entities (NME), new dosages, combinations or manufacturers. Fourteen of these drugs were tested (or being studied) in clinical trials involving Russian sites.

In Y 2018 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) evaluated 78 new drugs, including 16 generics and 6 biosimilar drugs. 70 of these drugs received positive opinions and were approved for marketing. 43 of the approved drugs were tested (or being studied) in clinical trials involving Russian sites.

The top-5 domestic pharmaceutical manufacturers in Russia during 2018 were *Microgen, Biocad, Valenta Pharmaceuticals, Materia Medica Holding* and *Petrovax Pharma*.

The top-5 International Sponsors in Russia during 2018 were *Novartis, Roche, Janssen, Pfizer* and *AstraZeneca*.

According to the U.S. FDA data, there were no FDA inspections conducted at Russian investigative sites during 2018; 300 FDA inspections were conducted at U.S. investigative sites, and 38 FDA inspections were conducted at investigative sites located in the 18 leading European countries. European countries receiving the most inspections were Poland (9 inspections), Germany (6 inspections) and France (5 inspections).



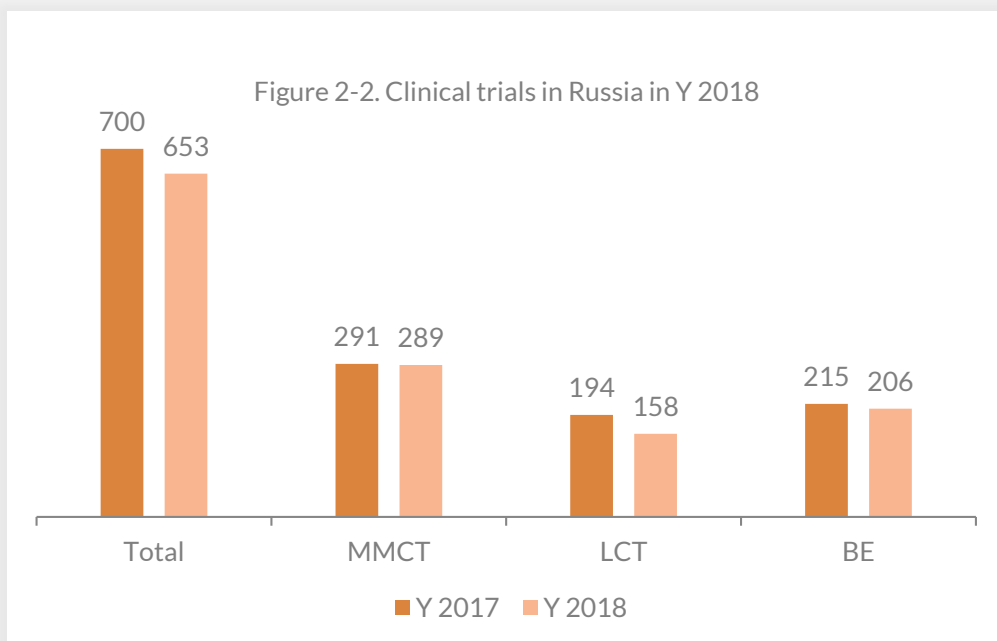


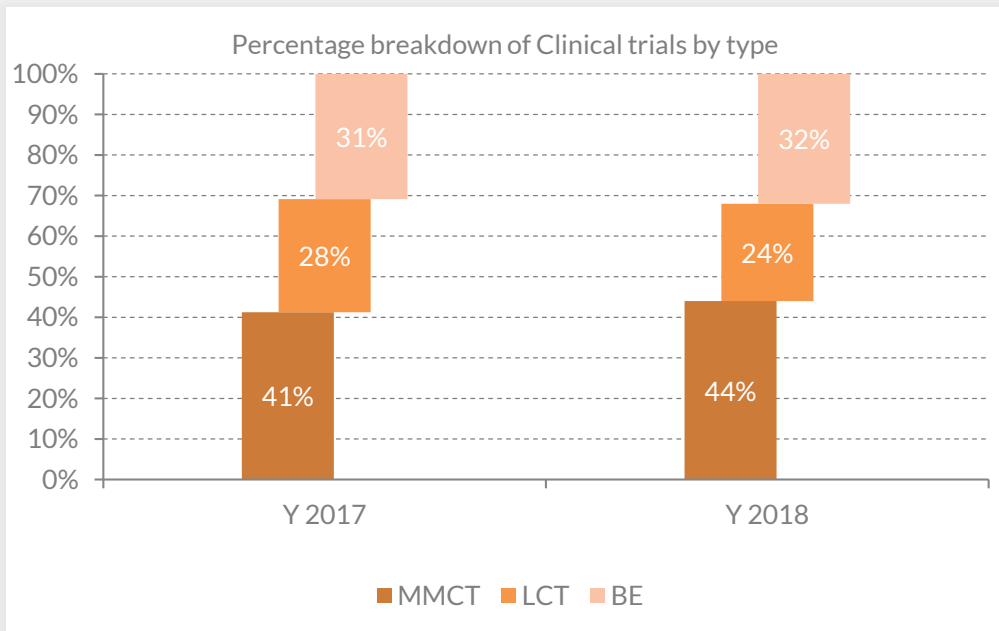
CLINICAL TRIALS IN RUSSIA

Trial Data

During the year 2018 the Ministry of Health of the Russian Federation approved the start of 653 new clinical trials of all types, including local and bioequivalence studies. This represents a 6,7% year on year decline by the total number of studies.

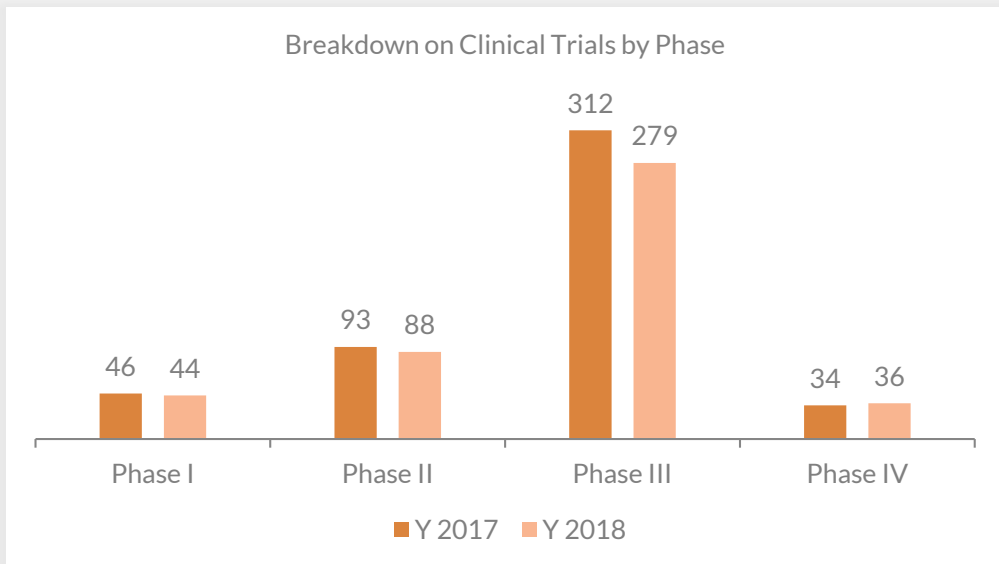
The dominant type of clinical trials conducted across Russian sites in 2018 were MMCT (Multinational Multi-center Clinical Trials). The market share of MMCT climbed by 3% and is now at 44% of the total number of trials. The market share of LCT dipped by 4% down to 24%, and BE's share increased slightly from 31% to 32%.





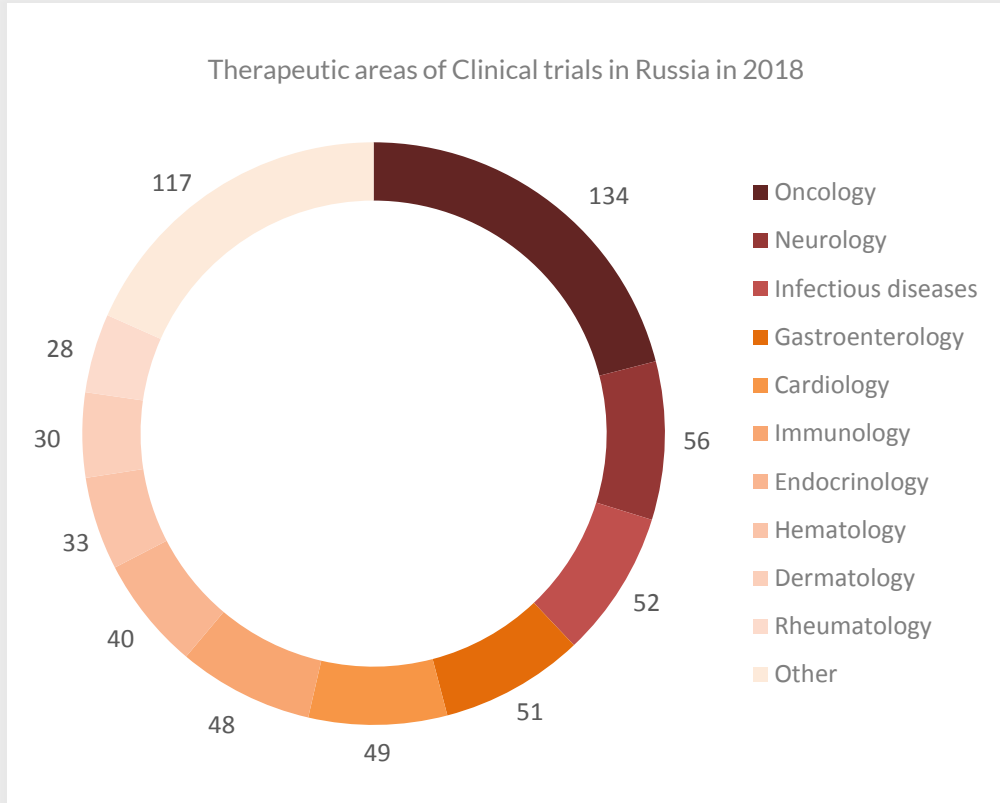
The most prevalent Phase of clinical trials conducted in Russian sites by total number of studies was Phase III.

The total number of Phase III trials went down by 12% - from 312 trials in 2017 to 279 trials in 2018.



The largest number of clinical trials initiated in Russia during 2018 were related to Oncology, Neurology, and Infectious Diseases. Other popular areas include Gastroenterology, Cardiology, and Immunology.

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



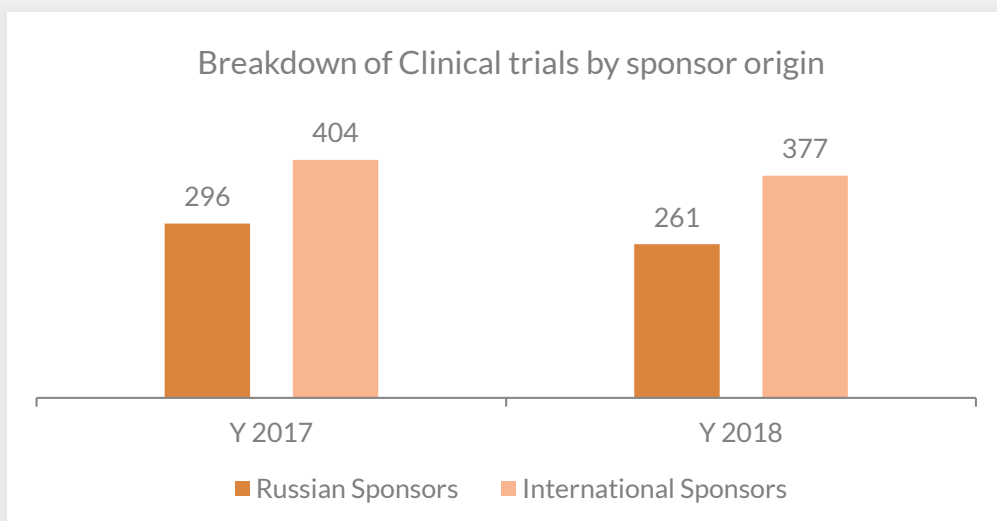


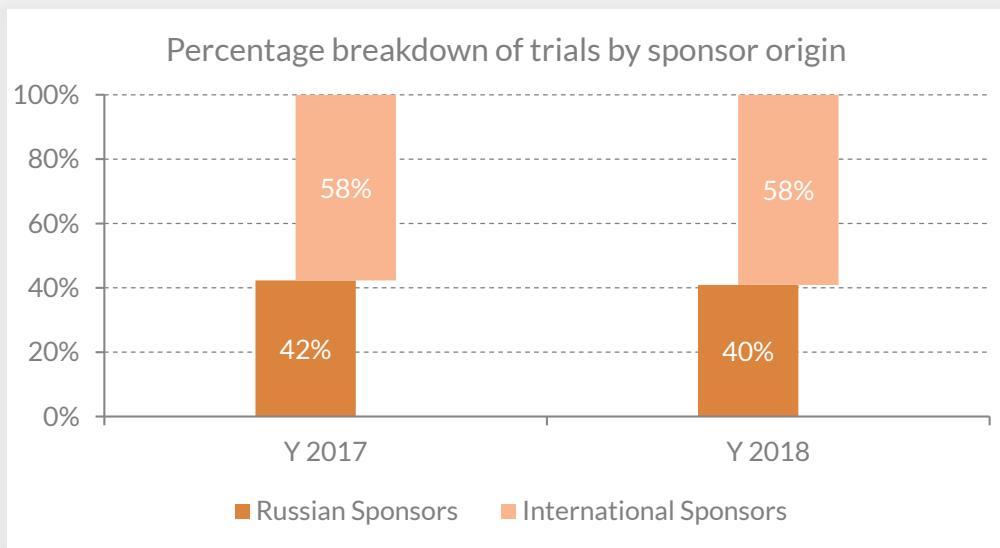
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Sponsor Data

Clinical trials initiated in Russia in during 2018 were sponsored by pharmaceutical companies from 36 countries.

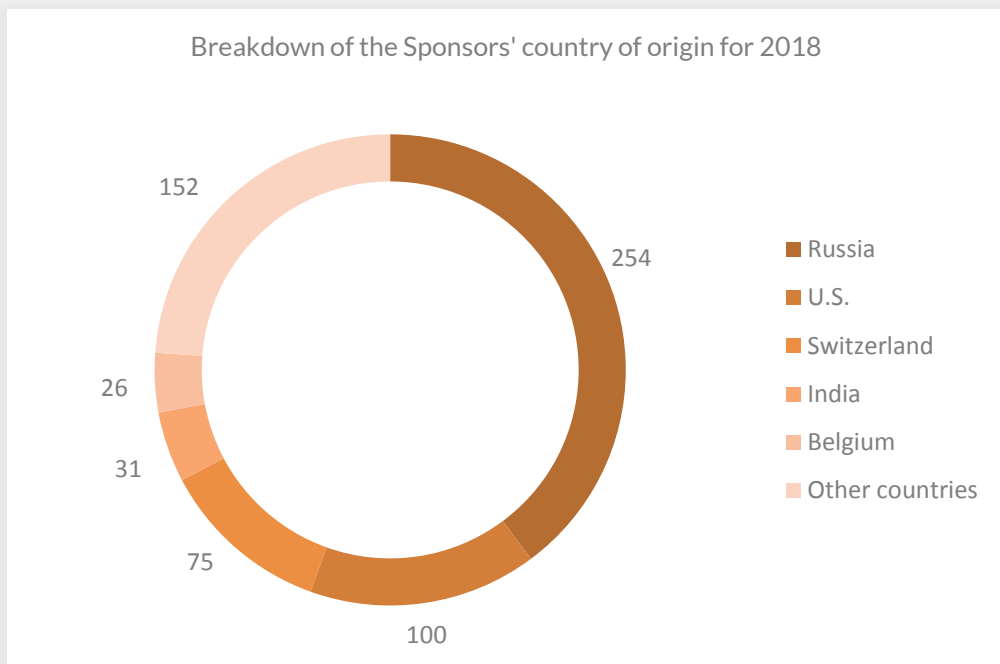
The combined market share of international pharmaceutical companies involved in the Russian Clinical trials market remained fairly static with a year on year growth rate of just 1% (from 58% in 2017 to 59% in 2018).





The most prevalent Sponsor's countries of origin in Y 2018 were Russia (265 studies), U.S. (107 studies) and Switzerland (76 studies). Other countries include India (31 studies), Belgium (26 studies).

The list of leaders is concluded by The United Kingdom and France (19 studies each), Sweden (13 studies), Germany and Poland (12 studies each).



Top-10 International Trial Sponsors in Russia in 2018

No	Company Name	No. studies	No. patients
1	Novartis	35	2 050
2	Hoffman-La Roche	21	1 397
3	Janssen	15	1 714
4	Pfizer	15	662
5	AstraZeneca	13	2 391
6	Merck	13	2 040
7	AbbVie	13	725
8	Bristol-Myers	12	464
9	Sanofi	9	1 276
10	Allergan	8	850
Combined market share of these companies		24%	25%

Observational Clinical trials and Clinical trials without FDA-defined phases (from I to IV) were not counted in this ranking

Top-10 Russian Trial Sponsors in Russia in 2018

No	Company Name	No. studies	No. patients
1	Microgen	12	863
2	Biocad	8	989
3	Valenta Pharmaceuticals	7	815
4	Materia Medica Holding	5	1 462
5	Petrovax Pharma	5	602
6	Gamaleya Research Institute of Epidemiology and Microbiology	5	1 232
7	Medsintez	4	827
8	Generium	4	478
9	Vertex	3	466
10	Organica	3	318
Combined market share of these companies		9%	15%

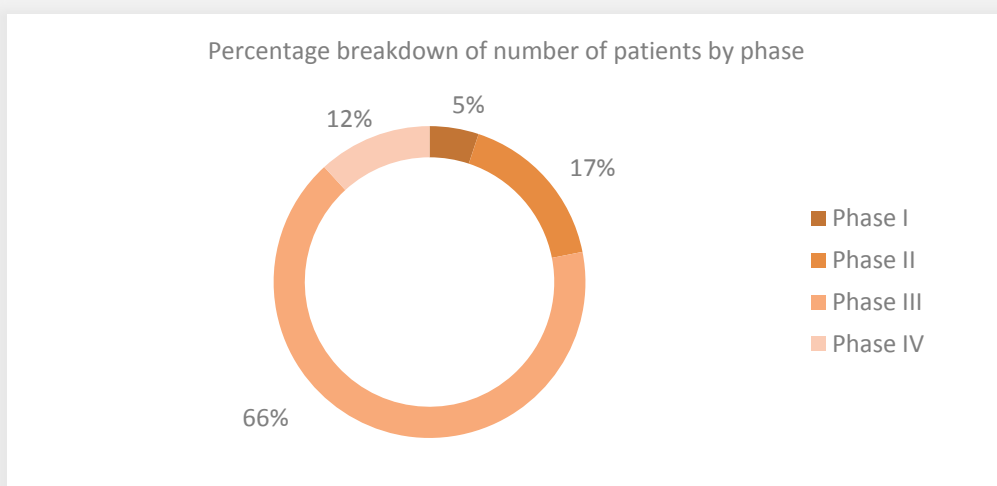
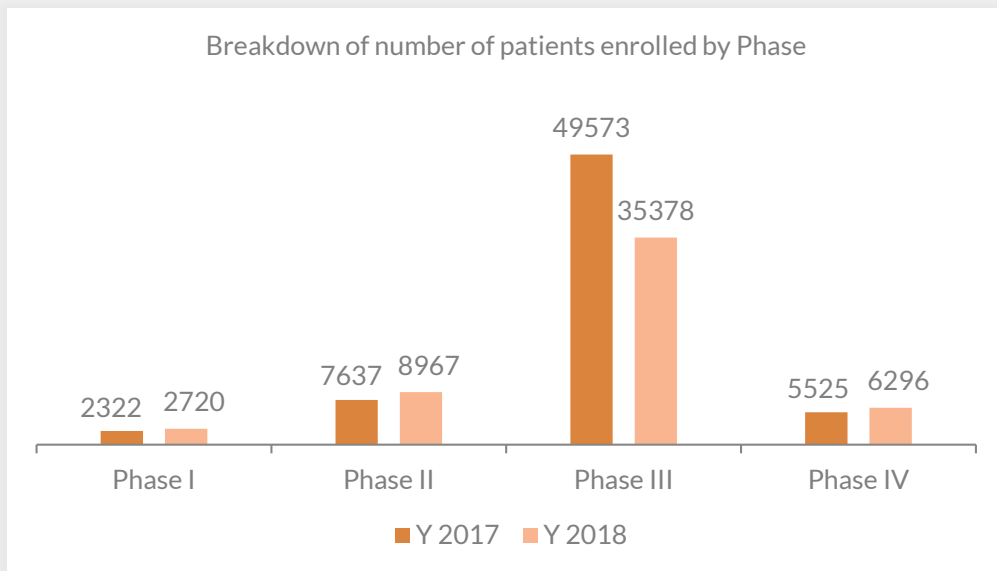
Bio-Equivalence (BE) studies were not included in this ranking table.



CLINICAL TRIALS IN RUSSIA

Patient Data

The overall number of patients involved in clinical trials initiated in Russia in 2018 reached a total of 53,361 individuals – a 22% drop in comparison with 2017, when 65,057 patients were involved. The most prevalent Phase of clinical trials by the number of participating patients was Phase III, with 66% of all patients involved.





CLINICAL TRIALS IN RUSSIA

Site Data

Top-5 Russian research sites (BE and Phase I studies) in 2018

No	Site Name	City	No. studies
1	Clinical Hospital #2, Yaroslavl region	Yaroslavl	32
2	Road Clinical Hospital at the station Yaroslavl of Russian Railways	Yaroslavl	19
3	Ecosafety Ltd.	Saint-Petersburg	18
4	Clinical Hospital named after V.P. Demikhov	Moscow	18
5	Probiotec Medical Center	Moscow Region	16
Combined market share of these research sites			16%

Top-5 Russian research sites (Phase II-IV studies) in 2018

No	Site Name	City	No. studies
1	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	58
2	Rostov State Medical University	Rostov-on-Don	50
3	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	49
4	Russian North-West State Medical University named after I.I. Mechnikov	Saint-Petersburg	44
5	Kazan State Medical University	Kazan	42
Combined market share of these research sites			37%



Top-10 Russian research sites (all studies) in 2018

No	Site Name	City	No. studies
1	Russian Oncological Scientific Center named after N.N. Blokhin	Moscow	59
2	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	52
3	Rostov State Medical University	Rostov-on-Don	50
4	Ecosafety Ltd.	Saint-Petersburg	49
5	First Moscow State Medical University named after I.M. Sechenov	Moscow	46
6	Clinical Oncological Dispensary	Omsk	45
7	Russian North-West State Medical University named after I.I. Mechnikov	Saint-Petersburg	44
8	Clinical Hospital #2, Yaroslavl region	Yaroslavl	42
9	Russian National Oncology Medical Research Center named after N.N. Petrov	Saint-Petersburg	39
10	Clinical Oncological Dispensary	Archangelsk	30
Combined market share of these research sites			70%

CRO Data

No	CRO Name	No. studies	No. patients
1	Parexel	22	1 760
2	PPD	17	1 026
3	PSI	13	1 399
4	ICON	10	1 077
5	INC Research (Syneos Health)	10	870
6	IQVIA	10	620
7	iPharma	9	804
8	Synergy Research Group	7	710
9	inVentiv Health (Syneos Health)	7	322
10	Pharmaceutical Research Associates, Inc.	6	469
Combined market share of these companies		17%	17%

Observational Clinical trials and Clinical trials without FDA-defined phases (from I to IV) were not included in this ranking



Regulatory & Inspection Data

During Q4 2018 the Center for Drug Evaluation and Research (CDER) of the U.S. FDA approved 13 new drugs as new molecular entities (NME); other approvals concerned new dosages, combinations or manufacturers. Three of these 13 drugs were being studied in clinical trials involving Russian sites.

Overall, during the Year 2018 the FDA approved 158 new drugs (37 of these being NME). Fourteen of these drugs were being studied in clinical trials involving Russian sites.

Appr.date	Drug (active ingredient)	Company
10/02/2018	Nuzyranda (Omadacycline Tosylate)	Paratek Pharms
10/16/2018	Talzennanda (Talazoparib Tosylate)	Pfizer
11/21/2018	Daurismonda (Glasdegib)	Pfizer

Source: FDA

In Q4 2018 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) evaluated 8 new drugs. No drugs received negative opinion and as such 8 drugs received positive opinions and were approved for marketing. Two of the eight drugs being studied in clinical trials involved Russian sites.

Overall, during the Year 2018 the CHMP of the EMA evaluated 78 new drugs, including 16 generics and 6 biosimilar drugs. Eight drugs were disapproved / received negative opinion, whilst 70 drugs received positive opinions and were approved for marketing. Forty-three of these drugs were tested (or being studied) in clinical trials involving Russian sites.

Appr.date	Drug (active ingredient)	Company
17/10/2018	Alecensa (Alectinib)	Roche
01/10/2018	Jardiance (Empagliflozin)	Boehringer Ingelheim

Source: EMA

The data for the FDA and EMA approvals during Q1-Q3 2018 can be found in previous issues of SynRG Orange Paper.



Inspection Data

FDA Inspections

According to the available U.S. FDA data, there were no FDA inspections conducted at Russian investigative sites during Q4 2018, and the year 2018 in general.

Roszdravnadzor Inspections

According to the Roszdravnadzor quarterly report, during Q4 2018 there were 15 Regulatory inspections conducted at Russian sites performing preclinical and clinical trials, with 10 violations found.

Overall, during the Year 2018 Roszdravnadzor conducted 51 inspections at Russian sites. Violations were found at 29 sites.

About Synergy

With its unique **prevolutionary** mind-set, Synergy is now the World's First Agile Risk Based CRO.

Prevolution is the implementation of thoughtful premeditated change resulting from the anticipation and analysis of future trends before they happen – in other words, being 'one step ahead of evolution'.

The high recruitment rates of the emerging markets combined with innovative technology allows our clients conduct faster, cost-effective studies without sacrificing quality. We replace outdated R&D strategies by novel, more efficient approaches to clinical research.