SYNERGY
ORANGE
PAPER

RESEARCH REPORT

CLINICAL TRIALS IN RUSSIA

SPRING 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

The Ministry of Health of the Russian Federation approved 151 new clinical trials of all types, including local and bioequivalence studies, during Q1 2018. This represents a 16% decrease from Q1 2017.

The number of new multinational multi-center clinical trials (MMCT) initiated in Q1 2018 is 70, compared to 64 in Q1 2017. The number of bioequivalence studies (BE) decreased from 64 studies in Q1 2017 to 48 in Q1 2018. The number of local clinical trials (LCT) has decreased from 52 in Q1 2017 to 33 in Q1 2018.

The number of Phase I clinical trials has decreased from 14 studies to 9 new studies in Q1 2018. The number of Phase II trials decreased in comparison with Q1 2017 from 20 to 17 new studies. The number of Phase III trials decreased from 75 to 63 studies. The number of Phase IV trials increased in comparison with Q1 2017 from seven to 14 studies.

Top foreign pharmaceutical manufacturers are *Novartis* (seven new studies), *Pfizer* and *F.Hoffmann-La Roche* (six new trials each).

Top domestic pharmaceutical manufacturers are *Microgen* (nine new trials) and *North Star (Severnaya Zvezda)* (five trials).

The top CROs in Russia are: *PPD Development* and *Parexel* (eight new studies each) and *PSI* (seven studies).

The top therapeutic areas were: Oncology (23 new studies) and Allergology and immunology (16 studies).

The Center for Drug Evaluation and Research (CDER) of the FDA approved 29 new drugs, and **three** 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 11 new drug applications (positive opinions on new generic, hybrid and biosimilar medicines are not included). **Eleven** of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

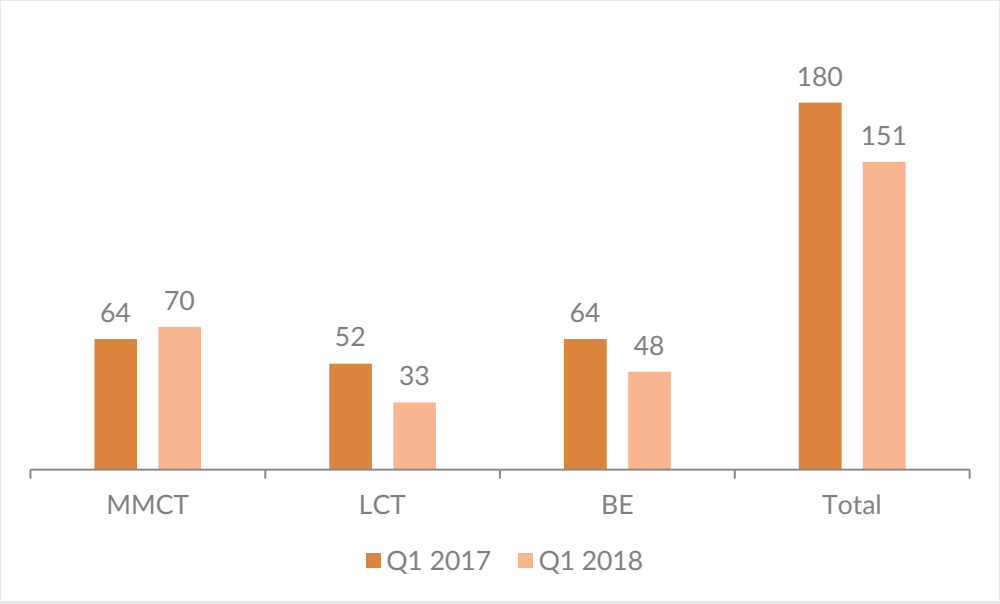
TRIAL DATA

The Russian MoH approved 151 new clinical trials of all types including local and bioequivalence studies during Q1 2018, demonstrating a 16% decrease 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 64 studies in Q1 2017 to 70 in Q1 2018, a 9% increase from last year's figure.

The number of bioequivalence studies (BE) decreased from 64 studies in Q1 2017 to 48 in Q1 2018, a 25% decrease from last year's figure.

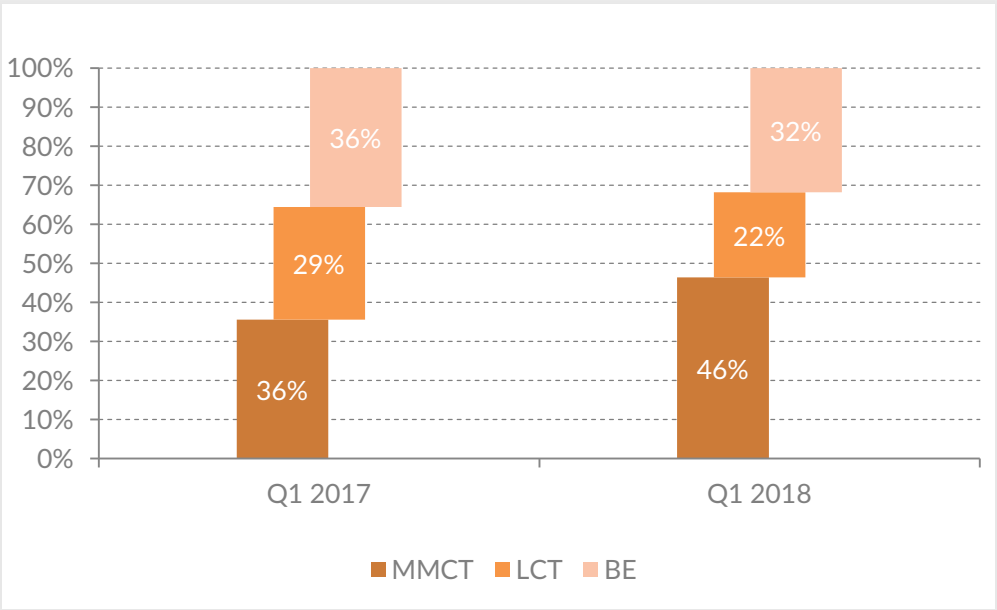
The number of local clinical trials (LCT) has significantly decreased from 52 in Q1 2017 to 33 in Q1 2018, a 37% decrease from last year's figure.



BREAKDOWN BY TYPE

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

The share of bioequivalence studies decreased from 36% to 32% of the total number of clinical trials approved in Q1 2018. The share of the local clinical trials decreased from 29% in Q1 2017 to 22% in Q1 2018, and the share of multinational multi-center clinical trials was 46% of the total number of trials approved during Q1 2018 (36% in Q1 2017).

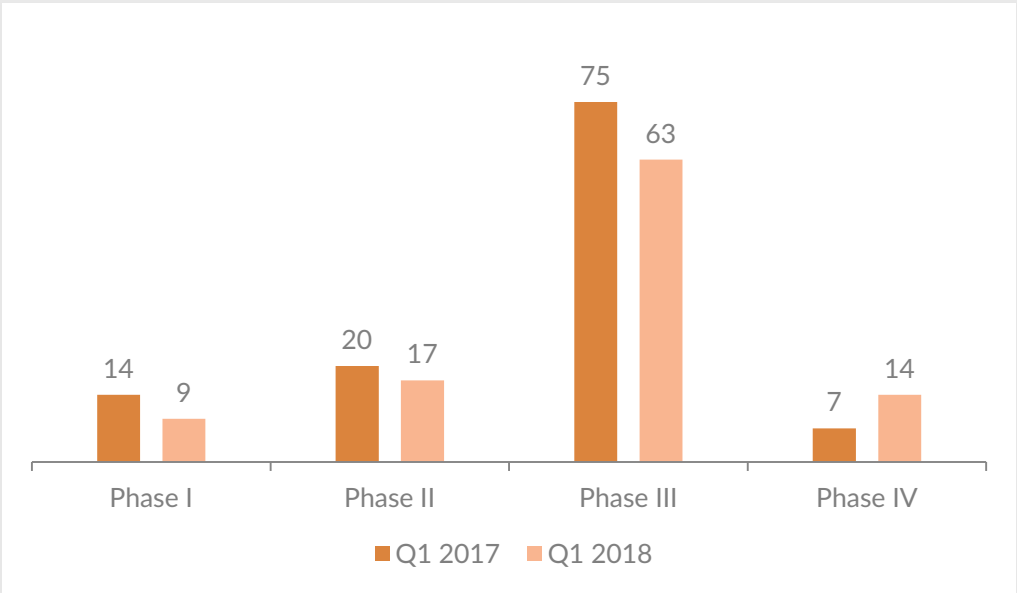


BREAKDOWN BY PHASE

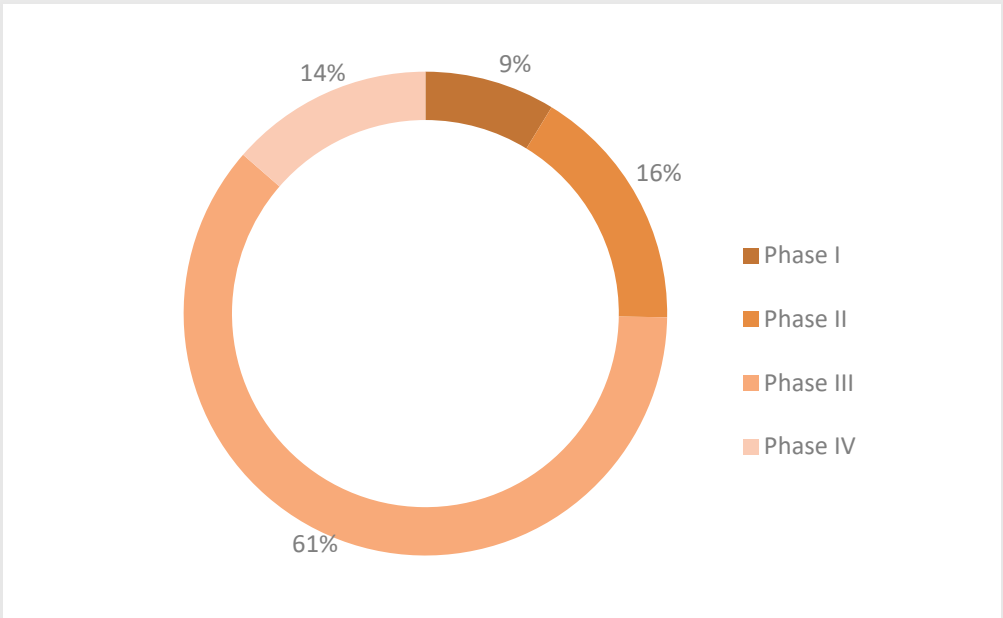
The number of Phase I clinical trials decreased to 36% compared to Q1 2017: from 14 studies to nine new studies in Q1 2018. The number of Phase II trials decreased to 15% compared to Q1 2017 from 20 studies to 17 new studies.

The number of Phase III trials decreased from 75 to 63 studies, 16% less than in Q1 2017. The number of Phase IV trials increased in comparison with Q1 2017 from seven to 14 studies in Q1 2018.

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.



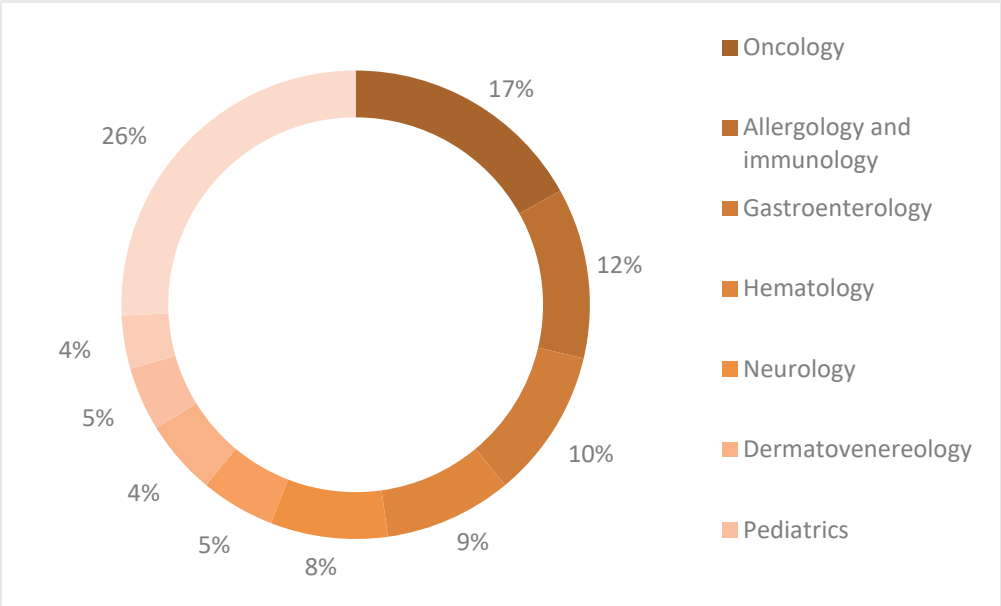
The share of Phase III trials in Q1 2018 is 61% of the total number of studies, the share of Phase I trials is 9%, Phase II trials is 16% and the share of Phase IV studies accounted to 14%.



THERAPEUTIC AREAS OF RUSSIAN CLINICAL TRIALS

The largest number of studies were initiated in Oncology (23 studies), and is followed by Allergology and Immunology (16 studies), Gastroenterology (14 studies), Hematology (12 studies), Neurology (11 studies), Therapy and Dermatovenerology (seven studies each), Pediatrics (six studies), Urology (five studies).

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



SUBJECT DATA

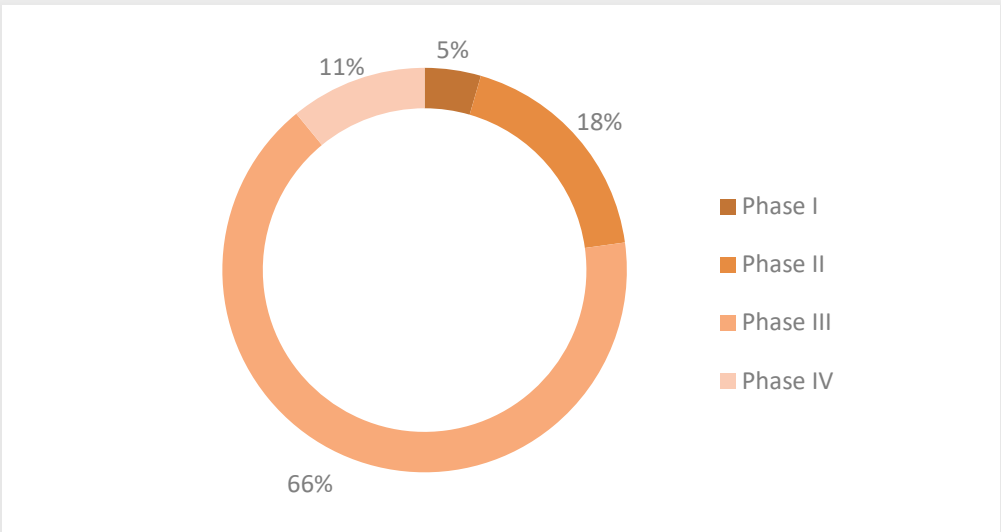
The number of subjects planned to be enrolled in Phase I-IV trials launched in Q1 2018 is 7,726, less than in Q1 2017, when 14,195 subjects were planned to be enrolled.

347 subjects will be recruited in Phase I trials; 1,416 – in Phase II trials; 5,118 – in Phase III studies and 845 subjects will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is seven, the maximum number is 450.

NUMBER OF STUDY SUBJECTS IN STUDIES IN Q1 2018

Study Phase	Minimum	Maximum
BE	20	194
Phase I	16	101
Phase II	14	450
Phase III	7	250
Phase IV	12	240



SITE DATA

TOP-5 RUSSIAN RESEARCH SITES (BE AND PHASE I STUDIES)

№	Site Name	City	No. studies
1	Bioeq Ltd.	Saint-Petersburg	8
2	Clinical Hospital #2, Yaroslavl region	Yaroslavl	6
3	Probiotec Medical Center	Moscow Region	5
4	Road Clinical Hospital at the station Yaroslavl of Russian Railways	Yaroslavl	3
5	Federal Research and Clinical Center of Physical-Chemical Medicine	Moscow	3

TOP-5 RUSSIAN RESEARCH SITES (Phase II-IV STUDIES)

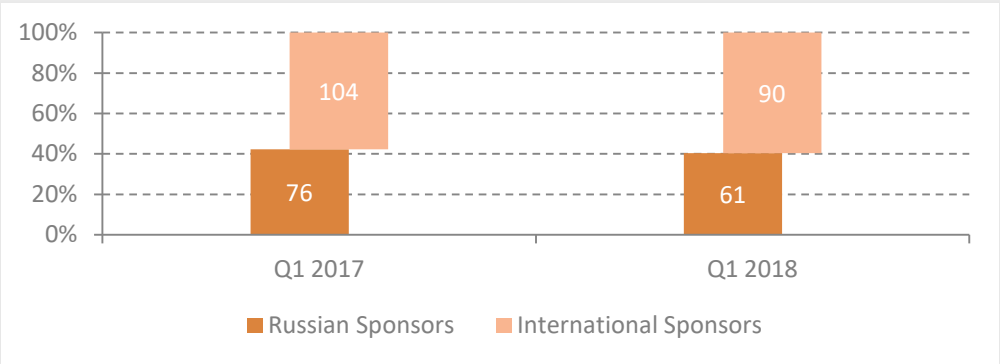
№	Site Name	City	No. studies
1	Rostov State Medical University	Rostov-on-Don	17
2	First Moscow State Medical University named after I.M. Sechenov	Moscow	13
3	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	12
4	Kazan State Medical University	Kazan	12
5	Clinical Oncological Dispensary	Omsk	11

TOP-5 RUSSIAN RESEARCH SITES (ALL STUDIES)

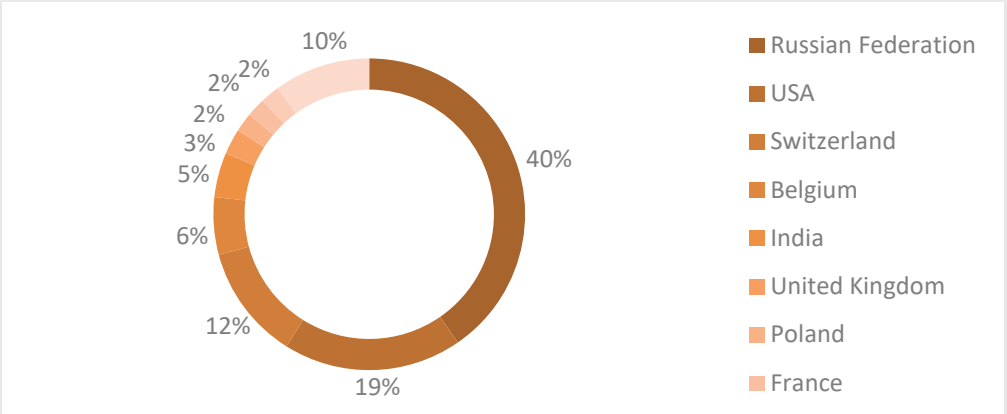
№	Site Name	City	No. studies
1	Rostov State Medical University	Rostov-on-Don	17
2	First St.Petersburg State Medical University named after I.P. Pavlov	Saint-Petersburg	13
3	First Moscow State Medical University named after I.M. Sechenov	Moscow	13
4	Clinical Oncological Dispensary	Omsk	13
5	Bioeq Ltd.	Saint-Petersburg	12

SPONSOR DATA

The geographic origins of sponsors slightly changed in comparison with last year. 60% of the total number of new studies in Q1 2018 were sponsored by foreign companies which received 90 study approvals (58% in Q1 2017). The share of studies of local manufacturers decreased from 42% in Q1 2017 to 40% in Q1 2018, and amounted to 61 studies.



Clinical trials in Russia in Q1 2018 were sponsored by companies from 22 countries. The maximum number of trials (61) were initiated by Russian sponsors. American sponsors with 28 new studies took the runner-up place; they are followed by Swiss sponsors with 18 trials, then by Belgian sponsors with nine new studies, and Indian sponsors (seven studies). The group of leaders is concluded by British sponsors (four studies), and Poland, France and Israel, each having three studies. Other sponsors include: Sweden, China and Denmark (two studies each), Canada, Cyprus, Germany, Netherlands, Republic of Belarus, Singapore, Slovenia, Spain, Lithuania and Luxembourg, each started one new study in Q1 2018.



TOP-5 INTERNATIONAL STUDY SPONSORS IN Q1 2018

№	Company Name	No. studies	No. patients
1	Novartis	7	157
2	Pfizer	6	164
3	F.Hoffmann-La Roche	6	153
4	Janssen	5	425
5	Celgene Corporation	4	292

TOP-5 RUSSIAN STUDY SPONSORS IN Q1 2018

№	Company Name	No. studies	No. patients
1	Microgen	9	510
2	North Star (Severnaya Zvezda)	5	242
3	Petrovax	4	392
4	Pharmasyntez-Tyumen	4	174
5	Biocad	3	276

CRO DATA

TOP-5 CROs IN RUSSIA IN Q1 2018

№	CRO Name	No. studies	No. patients
1	PPD Development	8	372
2	Parexel	8	311
3	PSI	7	613
4	inVentiv Health Clinical	4	181
5	INC Research	2	131

REGULATORY DATA

FDA

The Center for Drug Evaluation and Research (CDER) of the FDA approved 29 new drugs during Q1 2018; four of them are new molecular entities (NME); other approvals concern new dosages, combinations or manufacturers. Three of 29 drugs were (or are being) studied in clinical trials involving Russian sites.

The table shows the drugs which were approved by FDA in Q1 2018 that were (or are being) tested in clinical trials in Russia.

Appr.date	Drug (active ingredient)	Company
02/16/2018	Imbruvica (ibrutinib)	Pharmacyclics Inc
02/22/2018	Lusduna (insulin glargine)	Merck Sharp Dohme
02/26/2018	Verzenio (abemaciclib)	Eli Lilly and Co
		Source: FDA

EMA

During Q1 2018, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) gave positive recommendations on 11 new drug applications, two positive recommendations on new generic medicines and three for new biosimilar medicines. A negative opinion was adopted for five drugs. Eleven of the drugs 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 Q1 2018. Positive opinions on new generic, hybrid and biosimilar medicines are not included.

Appr. date	Drug (active ingredient)	Manufacturer
01/25/2018	Hemlibra (emicizumab)	Roche Registration Limited
01/25/2018	Relvar Ellipta (fluticasone furoate / vilanterol)	Glaxo Group Ltd
01/25/2018	Revinty Ellipta (fluticasone furoate / vilanterol)	Glaxo Group Ltd
02/22/2018	Alpivab (peramivir)	Biocryst UK Limited
02/22/2018	Bosulif (bosutinib)	Pfizer Limited
02/22/2018	Isentress (raltegravir)	Merck Sharp & Dohme Limited
02/22/2018	Lynparza (olaparib)	AstraZeneca AB
02/22/2018	Xgeva (denosumab)	Amgen Europe B.V.
03/22/2018	Juluca (dolutegravir / rilpivirine)	ViiV Healthcare UK Limited
03/22/2018	Rubraca (rucaparib)	Clovis Oncology UK Ltd
03/22/2018	Repatha (evolocumab)	Amgen Europe B.V.
		Source: EMA

INSPECTION DATA

FDA INSPECTIONS

At the moment of the Orange Paper Q1 2018 production no information about FDA inspections conducted in the Russian investigative sites was available.

ROSZDRAVNADZOR INSPECTIONS

According to the Roszdravnadzor quarterly report six inspections were conducted in institutions performing preclinical and clinical trials and located in five Russian cities during Q1 2018. Violations were found in two institutions.

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 scarifying quality. We replace outdated R&D strategies by novel, more efficient approaches to clinical research.