Clinical Trials in Russia
Orange Paper
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Contents

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Executive Summary - English

The Ministry of Health and Social Development of the Russian Federation (MoH) approved 257 new clinical trials of all types including local and bioequivalence studies during the second quarter of 2012, demonstrating a 44% increase compared to the same point of the last year.

The main contribution into the total number of studies is made by the bioequivalence studies, the number of them increased by 224% from Q2 2011 and stood at 107 new studies in Q2 2012. The number of multinational multi-center clinical trials increased from 77 to 102 new studies, and the number of local clinical trials decreased from 68 to 48 clinical trials.

The share of bioequivalence clinical trials stood at 42% of the total number of clinical trials in Q2 2012, while the local and multinational multi-center studies amounted to 19% and 40%, respectively.

Clinical trials in Russia in Q2 2012 were sponsored by companies from 29 countries. The maximum number of trials (115) was initiated by the Russian sponsors. American sponsors with 47 new studies took the runner-up place, they are followed by Israeli sponsors with 16, and Swiss sponsors with 15 trials. The group of leaders is concluded by British and Swedish sponsors each with 7 new studies in Q2 2012.

Ten new Phase I clinical trials were launched in Q2 2012, seven trials more than in Q2 2011. The number of the Phase II trials changed insignificantly and stood at 27 new studies in Q2 2012. The number of Phase III trials increased significantly from 64 to 102 studies. Phase IV trials demonstrated the decrease from 14 studies in Q2 2011 to 11 studies in Q2 2012.

The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q2 2012 stood at 17,293, 54% more than in Q2 2011 figure, when 11,203 subjects were planned to be enrolled.

Roche sponsoring seven new studies is on the top of the heap in Q2 2012. It is followed by *Pfizer* having the same number of new trials but with a smaller number of subjects to be enrolled, and *AstraZeneca* and *GlaxoSmithKline* with six new trials each. Top five is concluded by *Teva* with five new studies in Q2 2012.

The Russian company *OOO FK Slavyanskaya Apteka* sponsoring four new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q2 2012. It is followed by *Biocad* and *OAO Sintez* each having three new trials and differentiating in the number of subjects. Top five is concluded by *OOO Feron* and *Akrikhin* each with two new trials.

More than two thirds of the new studies in Q2 2012 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (29); 18 new studies were instigated in Pulmonology; 17 – in Endocrinology; 13 studies were instigated each in Cardiology and Musculoskeletal diseases; ten – in Neurology and nine – in Gastroenterology.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 15 new drugs during Q2 2012; five of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. One drug was studied in clinical trials involving Russian sites.

During the second quarter of 2012 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 22 new drug applications, 13 of which were tested in clinical trials in Russia.

No FDA inspections were conducted in Russia during Q2 2012.

Executive Summary - Russian

Во II квартале 2012 года Минздравсоцразвития России было выдано 257 разрешений на все виды клинических исследований, что на 44% больше, чем в соответствующем квартале прошлого года.

При этом количество международных многоцентровых клинических исследований возросло на 32% и составило 102 новых исследований. Количество исследований биоэквивалентности, инициированных во II квартале 2012 года, значительно возросло с 33 до 107 исследований по сравнению с II кварталом 2011 года. Количество локальных клинических исследований, проводимых на территории России отечественными и иностранными спонсорами, уменьшилось с 68 до 48 исследований.

Это повлекло за собой изменение соотношения между видами клинических исследований по сравнению с II кварталом 2011 года: доля исследований биоэквивалентности увеличилась с 19% до 42% от общего количества исследований; при этом доля локальных клинических исследований и ММКИ уменьшилась с 38% до 19% и с 43% до 40%, соответственно.

Спонсорами клинических исследований, разрешенных к проведению в России во II квартале 2012 года, выступили компании из 29 стран. На первое место вышли российские производители со 115 КИ, за ними идут американские спонсоры с 47 новыми исследованиями, Израиль с 16 и Швейцария с 15 КИ. Замыкают группу лидеров Великобритания и Швеция, каждая с семью новыми исследованиями.

Во II квартале 2012 года было инициировано десять новых клинических исследований первой фазы, что на семь КИ больше, чем во II квартале прошлого года. Количество исследований II фазы за этот период незначительно увеличилось и составило 27 новых исследований. Количество исследований III фазы заметно возросло с 64 до 102 исследований – на 59% по сравнению с прошлым годом. Количество исследований IV фазы незначительно уменьшилось и составило 11 новых исследований.

Всего в клинических исследованиях I-IV фаз, начатых во II квартале 2012 года, примет участие 17293 субъектов, что на 54% больше, чем в соответствующем квартале прошлого года, когда в исследования планировалось включить 11203 субъектов.

Во II квартале 2012 года первое место среди иностранных производителей по количеству новых исследований заняла фармацевтическая компания Roche с семью новыми исследованиями. Далее идет Pfizer с тем же количеством исследований, но меньшим количеством субъектов, AstraZeneca и GlaxoSmithKline с шестью новыми исследованиями. Замыкает пятёрку Teva с пятью новыми исследованиями.

Первое место среди отечественных производителей по количеству исследований, начатых во II квартале 2012 года, занимает ООО ФК «Славянская аптека» с четырьмя новыми клиническими исследованиями. За ним идут «Биокад» и ОАО «Синтез» с тремя новыми исследованиями, но с разным количеством субъектов. Завершают пятёрку лидеров ООО «Ферон» и «Акрихин», каждый из которых инициировал два новых исследования.

Во II квартале 2012 года более двух третей всех новых исследований было инициировано в семи терапевтических областях: наибольшее количество в области онкологии – 29 КИ; 18 новых исследований в пульмонологии; 17 исследований – в эндокринологии; по 13 – в кардиологии и в области заболеваний опорно-двигательного аппарата; десять исследований – в неврологии и девять – в гастроэнтерологии.

За II квартал 2012 года Центром по оценке и исследованию лекарственных средств (Center for Drug Evaluation and Research, CDER) FDA было одобрено 15 новых препаратов, один из них проходил клинические исследования в России.

За II квартал 2012 года Комитетом по лекарственным средствам для применения у человека (Committee for Medicinal Products for Human Use, CHMP) Европейского агентства по лекарственным средствам (European Medicine Agency, EMEA) было принято 22 положительных решения на маркетинг лекарственных средств на территории Евросоюза, 13 препаратов из одобренных проходили клинические исследования в России.

Инспекции FDA за отчётный период в России не проводились.

Clinical Trials by Type and Manufacturing Country

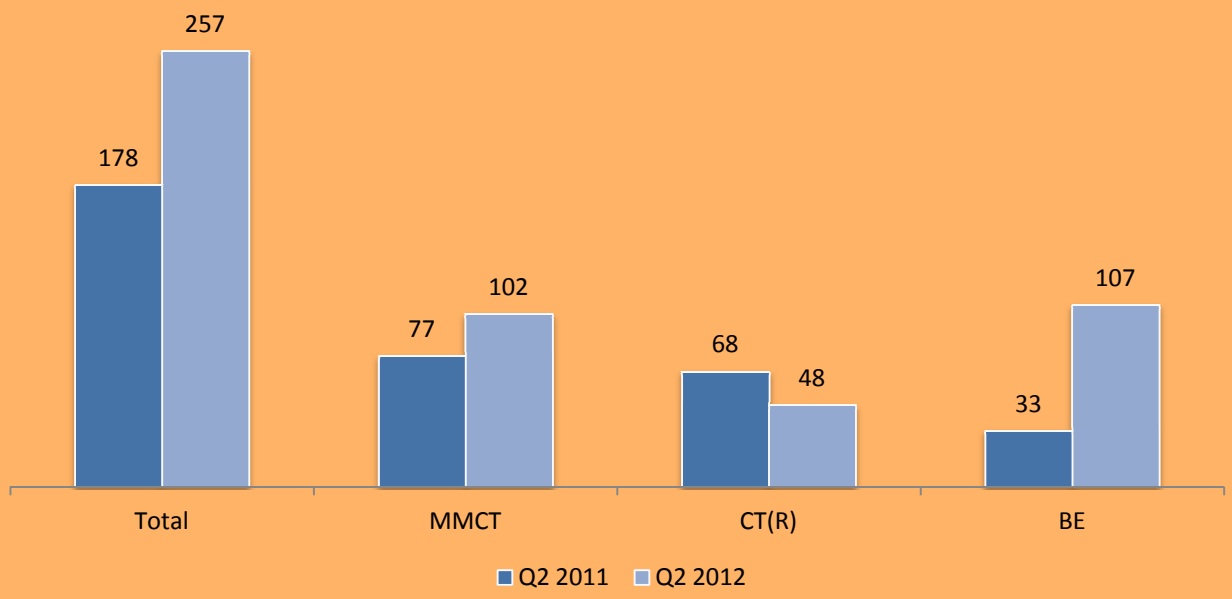
The Russian MoH approved 257 new clinical trials of all types including local and bioequivalence studies during the second quarter of 2012, demonstrating a 44% increase in comparison with the same point last year.

As shown in **Figure 1**, the main contribution into the total number of studies is made by bioequivalence studies (BE), the number of these studies stood at 107 new trials in Q2 2012 demonstrating 224% increase comparing with Q2 2011.

The number of multinational multi-center clinical trials (MMCT) increased as well: 32% more than in Q2 2011, and stood at 102 new studies in Q2 2012.

The number of the local clinical trials (CT(R)) conducted in Russia by domestic and foreign sponsors decreased from 68 to 48 clinical trials, 29% drop from last year's figure.

Figure 1. Clinical trials in Russia in Q2 2012

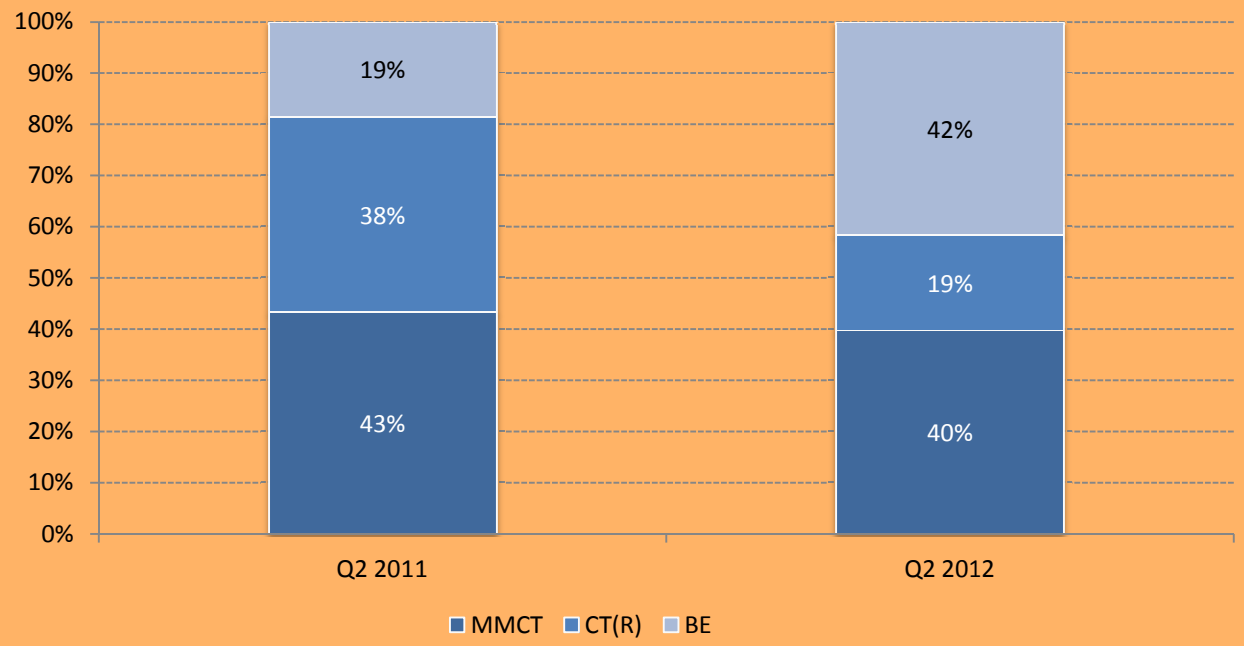


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) changed significantly since last year (see Figure 2).

The share of bioequivalence trials increased dramatically from 19% in Q2 2011 to 42% of the total number of clinical trials approved in Q2 2012.

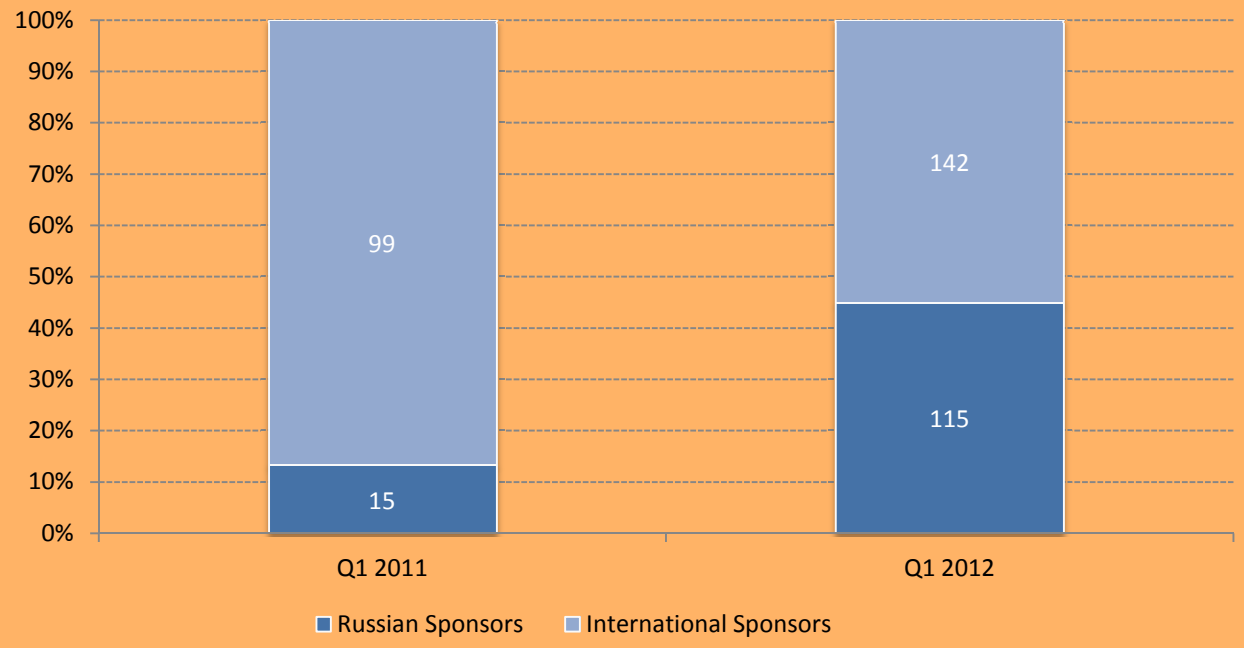
The share of the local trials decreased from 38% in Q2 2011 to 19% of the total number of studies in Q2 2012, and the share of multinational multi-center clinical studies decreased from 43% to 40% of the total number of trials approved during the second quarter of 2012.

Figure 2. Clinical trials by type in Q2 2012



The major share of clinical trials in Russia is sponsored by foreign companies which received 142 study approvals, or 55% of the total number of new studies in Q2 2012. The share of studies of local manufacturers increased from 13% in Q2 2011 to 45% in Q2 2012, and amounted to 115 studies (**Figure 3**).

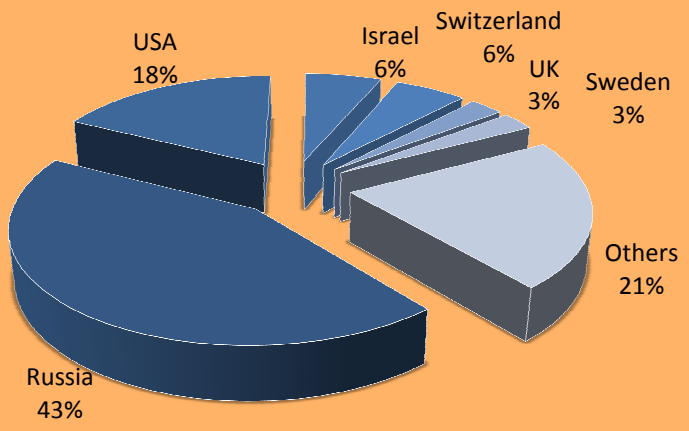
Figure 3. Russian and International sponsors in Q2 2012



Clinical trials in Russia in Q2 2012 were sponsored by companies from 29 countries. **Figure 4** demonstrates the input of the leading countries of sponsor's origin into the total number of clinical trials. The maximum number of trials (115) was initiated by Russian sponsors. American sponsors with 47 new studies took the runner-up place, they are followed by Israeli sponsors with 16, and

Swiss sponsors with 15 trials. The group of leaders is concluded by British and Swedish sponsors each with 7 studies in Q2 2012.

Figure 4. Countries presented on the Russian clinical trials market in Q2 2012



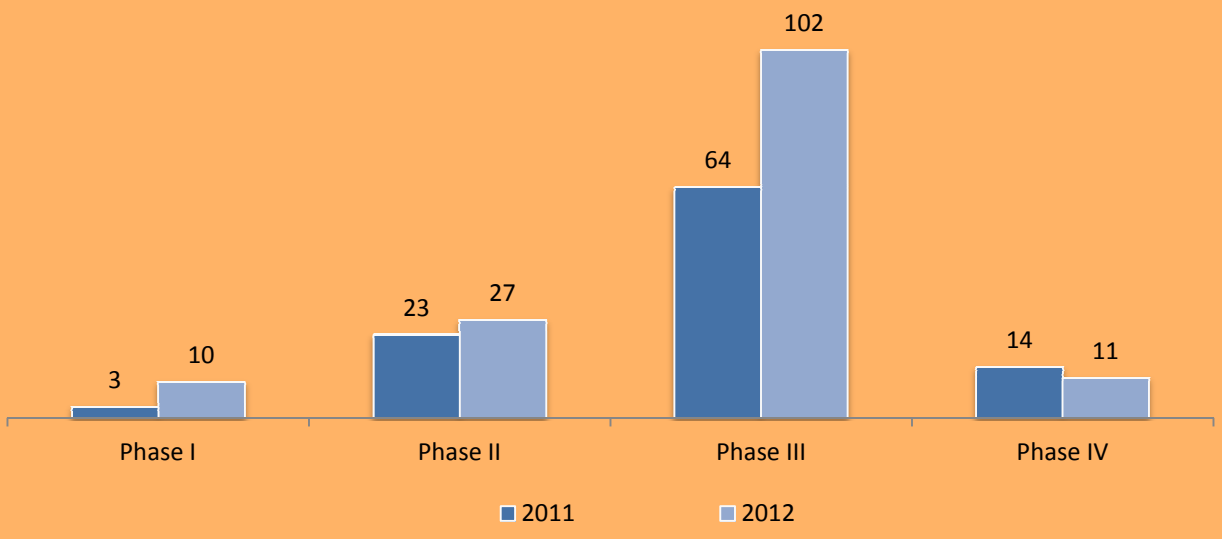
Among others are: France (6 studies); Germany (5); Belarus, India and Netherlands have four new studies each; Denmark, Italy, Poland, Hungary, Tunisia and Ukraine started two new studies each; Austria, Argentina, Belgium, Brazil, Ireland, Spain, Republic of Korea, Latvia, Portugal, Republic of Macedonia, Romania and Slovenia each started one new study in Q2 2012.

Clinical trials by Phase

Ten new Phase I clinical trials were launched in Q2 2012, which is seven trials more than in Q2 2011. The number of the Phase II studies changed insignificantly and stood at 27 new studies in Q2 2012 (**Figure 5**).

The number of Phase III trials increased significantly from 64 to 102 studies, 59% more than in Q2 2011. Phase IV trials demonstrated the decrease from 14 studies in Q2 2011 to 11 studies in Q2 2012.

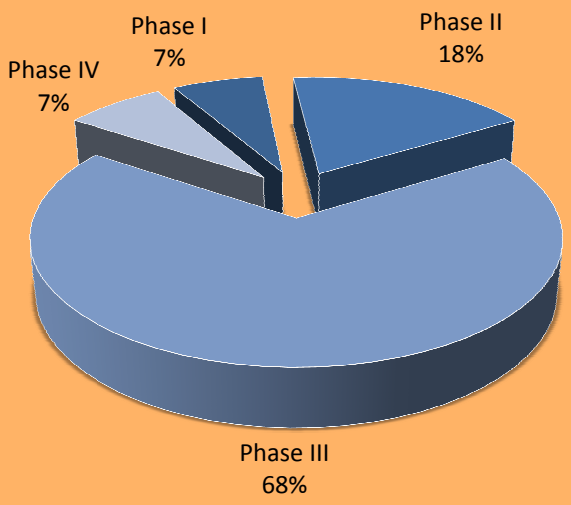
Figure 5. Clinical trials in Russia in Q2 2012 by phase[1]



[1] Studies indicated by sponsors as phase I-II in the applications submitted to MoH, are included 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, even in case a specific phase was indicated in the application.

As shown in **Figure 6**, the share of Phase III trials in Q2 2012 stood at 68% of the total number of studies, the share of Phase II trials accounted at 18%, the shares of Phase I and IV trials stood at 7% each.

Figure 6. The proportions between study phases in Russia in Q2 2012



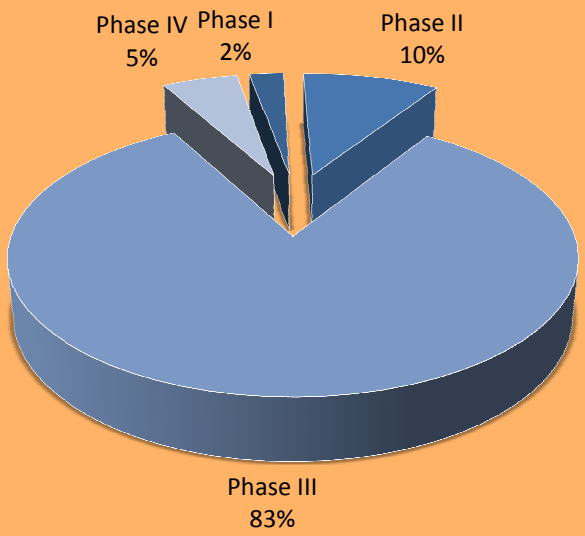
The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q2 2012 stood at 17,293, 54% more than in Q2 2011 figure, when 11,203 subjects were planned to be enrolled.

405 subjects will be recruited in Phase I trials; 1,635 subjects – in Phase II trials; 14,351 subjects – in Phase III trials; 902 subjects – in Phase IV trials.

The minimal number of subjects in a single study is eight, the maximum number is 2,373.

The proportion of the number of subjects between different Phases is shown on Figure 7. Bioequivalence studies were not included.

Figure 7. The number of subjects in Q2 2012 by study phase



Rating of international sponsors

Roche sponsoring seven new studies is on the top of the heap in Q2 2012. It is followed by *Pfizer* having the same number of new trials but a smaller number of subjects, and *AstraZeneca* and *GlaxoSmithKline* with six new studies each. Top five is concluded by *Teva* with five new studies in Q2 2012.

Top five international sponsors by the number of new studies in Q2 2012 are presented in **Table 1**.

Table 1. Top-5 international study sponsors in Q2 2012

№	*Company Name*	*No. studies*[1]	*No. subjects*
1	Roche	7	712
2	Pfizer	7	288
3	AstraZeneca	6	1,161
4	GlaxoSmithKline	6	1,080
5	Teva	5	675

Rating of Russian sponsors

The Russian company *OOO FK Slavyanskaya Apteka* sponsoring four new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q2 2012. It is followed by *Biocad* and *OAO Sintez* each having three new trials and differentiating in the number of subjects. Top five is concluded by *OOO Feron* and *Akrikhin* each with two new trials (**Table 2**).

Table 2. Top-5 Russian study sponsors in Q2 2012

№	*Company Name*	*No. studies*[2]	*No. subjects*
1	OOO FK Slavyanskaya Apteka	4	240
2	Biocad	3	264
3	OAO Sintez	3	150
4	OOO Feron	2	360
5	Akrikhin	2	140

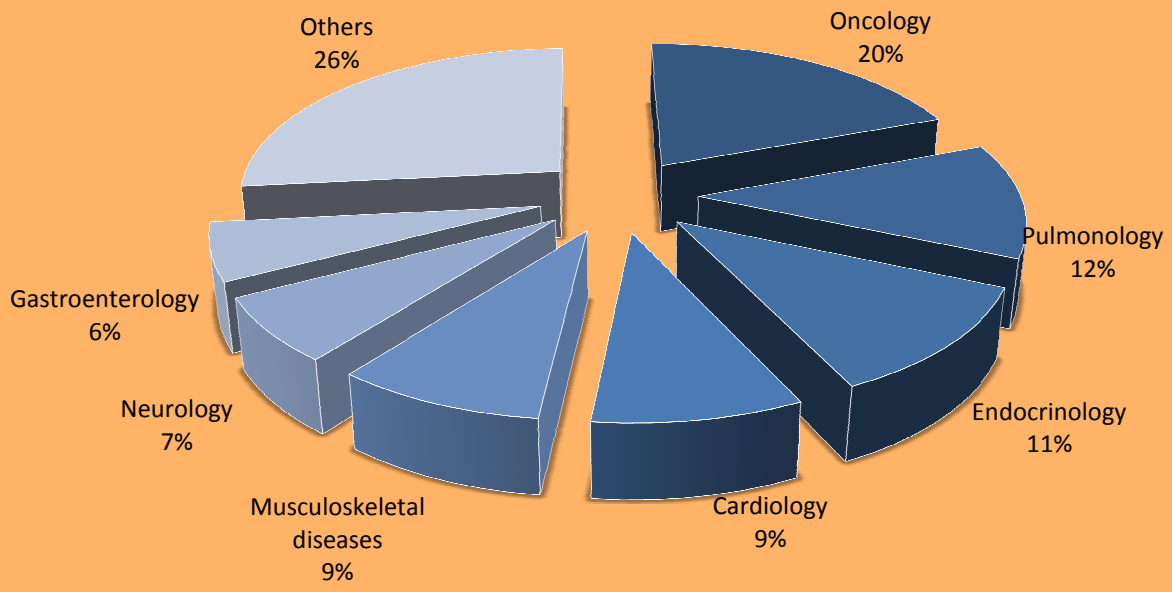
[1, 2] Excluding BE studies

Therapeutic areas of clinical trials in Russia in 2012

More than two thirds of the new studies in Q2 2012 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (29); 18 new studies were instigated in Pulmonology and 17 new studies in Endocrinology; 13 studies were instigated each in Cardiology and Musculoskeletal diseases; ten – in Neurology, and nine studies – in Gastroenterology.

The proportions between different therapeutic areas are shown in **Figure 8**.

Figure 8. Clinical trials in Russia in Q2 2012 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 15 new drugs during Q2 2012; five of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. One drug was studied in clinical trials involving Russian sites.

The **Table 3** shows a drug which was approved by FDA and was being tested in clinical trials in Russia in Q2 2012.

Table 3. New drugs approved by FDA in Q2 2012 and tested in Russian sites

Appr.date	*Drug (active ingredient)*	*Company*
06/08/2012	Perjeta (Pertuzumab)	Genentech
		Source: FDA

During the second quarter of 2012 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 22 new drug applications[1]. Negative opinion was adopted for one drug. 13 of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia (See **Table 4**).

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

Table 4. New Drugs approved by EMEA in Q2 2012 and tested in Russian sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
19/04/2012	Forxiga (dapagliflozin)	Bristol-Myers Squibb / AstraZeneca EEIG
19/04/2012	Optisulin / Lantus (insulin glargine)	Sanofi-aventis Deutschland GmbH
24/05/2012	Bretaris Genuair / Eklira Genuair (aclidinium bromide)	Almirall, S.A.
24/05/2012	Fycompa (perampanel)	Eisai Europe Ltd
24/05/2012	Inlyta (axitinib)	Pfizer Ltd
24/05/2012	Jentadueto (linagliptin / metformin)	Boehringer Ingelheim International GmbH
24/05/2012	Votrient (pazopanib)	Glaxo Group Ltd
24/05/2012	Zonegran (zonisamide)	Eisai Ltd
21/06/2012	Enurev Breezhaler / Seebri Breezhaler / Tovanor Breezhaler (glycopyrronium bromide)	Novartis Europharm Ltd
21/06/2012	Zinforo (ceftaroline fosamil)	AstraZeneca AB
21/06/2012	Afinitor (everolimus)	Novartis Europharm Ltd
21/06/2012	Enbrel (etanercept)	Pfizer Ltd
21/06/2012	Humira (adalimumab)	Abbott Laboratories Ltd
		Source: EMEA

FDA inspections

According to the FDA data, no FDA inspections were conducted in the Russian investigative sites during the second quarter of 2012.