Clinical Trials in Russia
Orange Paper
2nd Quarter 2013

11, 4-Magistralnaya Ul., 123007 Moscow, Russia

www.synrg-pharm.com

Contents

11, 4-Magistralnaya Ul., 123007 Moscow, Russia

www.synrg-pharm.com

Executive Summary

The Ministry of Health of Russian Federation approved 199 new clinical trials of all types including local and bioequivalence studies during the 2nd Quarter of 2013 (23% less than at the same period of the last year).

The main contribution into the total number of studies is made by multinational multi-center clinical trials (MMCT), the number of these studies decreased from 102 to 81 new studies in Q2 2013. The number of bioequivalence studies decreased from 107 studies in Q2 2012 to 76 in Q2 2013. The number of local clinical trials decreased from 48 to 42 clinical trials.

The share of multinational multi-center clinical trials was 41% of the total number of clinical trials in Q2 2013, while the local and bioequivalence studies amounted to 37% and 22%, respectively.

Clinical trials in Russia in Q2 2013 were sponsored by companies from 24 countries. The maximum number of trials (92) was initiated by Russian sponsors. American sponsors with 30 new studies took the runner-up place; they are followed by German and Swiss sponsors with 12 trials, and the group of leaders is concluded by Indian (nine) and French (seven) sponsors.

Nine new clinical trials Phase I were launched in Q2 2013, which is one trial less than in Q2 2012. The number of the Phase II trials decreased from 27 in Q2 2012 to 21 new studies in Q2 2013. The number of Phase III trials decreased from 102 to 88 studies, 14% less than in Q2 2012. Phase IV trials demonstrated the two times decrease from 11 studies in Q2 2012 to 5 studies in Q2 2013.

The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q2 2013 is 14,654 - 15% less than in Q2 2012 figure, when 17,293 patients had been planned to be enrolled.

Novartis sponsoring seven new studies is on the top of the heap in Q2 2013. It is followed by *GlaxoSmithKline* having five new trials. Top five is concluded by *Servier, Merck&Co* and *Bayer* each having four new trials and differentiating in the number of subjects.

The Russian company *OOO Atoll* sponsoring ten new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q2 2013. *Vertex* with nine new trials and *Biocad* with seven new studies took the runner-up place. They are followed by and *Medisorb* with five studies. Top Five of Q2 2013 is concluded by *Sotex* with four new trial.

More than three quarters of new studies in Q2 2013 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (26); 18 new studies were instigated in diseases of the circulatory system, 16 studies – in Musculoskeletal diseases, 12 new studies – in Endocrinology, nine studies – in Pulmonology, seven studies each in Infectious and parasitic diseases and in Neurology.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 20 new drugs during Q2 2013, and four of them were studied in clinical trials conducted in Russia.

During Q2 2013 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) gave positive recommendations on 31 new drug applications[1]. Negative opinion was adopted for one drug. 18 of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

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

Executive Summary – Russian

Во втором квартале 2013 года Министерством здравоохранения Российской Федерации было выдано 199 разрешений на все виды клинических исследований (КИ), что на 23% меньше, чем за аналогичный период 2012 года.

При этом количество международных многоцентровых КИ снизилось и составило 81 новое исследование против 102 за тот же период прошлого года. Количество исследований биоэквивалентности, инициированных во втором квартале 2013 года, снизилось на 29% по сравнению с первым кварталом 2012 года и составило 76 против 107. Количество локальных КИ, проводимых на территории России отечественными и иностранными спонсорами, снизилось с 48 до 42 исследований.

Спонсорами КИ, разрешенных к проведению в России в первом квартале 2013 года, выступили компании из 24 стран. На первое место вышли российские производители с 92 КИ, за ними идут американские спонсоры со 30 новыми исследованиями, Германия и Швейцария с 12 КИ у каждой, а также Индия с девятью КИ. Замыкает группу лидеров Франция с семью новыми исследованиями.

Во втором квартале 2013 года было инициировано девять новых КИ I фазы – на одно исследование меньше, чем за аналогичный период прошлого года. Количество исследований II фазы за этот период несколько снизилось и составило 21 новое исследование против 27. Количество исследований III фазы снизилось со 102 до 88 исследований – на 14% меньше по сравнению с прошлым годом. Количество исследований IV фазы уменьшилось более чем в два раза - с 11 до 5 исследований.

В первом квартале 2013 года первое место среди иностранных производителей по количеству новых исследований заняла фармацевтическая компания *Novartis* с семью новыми исследованиями. *GlaxoSmitnKline* инициировала пять исследований. Замыкают пятерку лидеров *Servier, Merck&Co* и *Bayer* с четырьмя новыми исследованиями у каждой.

Первое место среди отечественных производителей по количеству исследований, начатых в первом квартале 2013 года, занимает *ООО «Атолл»* с десятью новыми КИ. За ним идут *«Вертекс»* с девятью исследованиями и «*Биокад»* с семью исследованиями. В пятёрку лидеров входят также, *«Медисорб»* с пятью исследованиями и *«Сотекс»,* инициировавшая четыре новых исследования.

Во втором квартале 2013 года более трех четвертей всех новых исследований было инициировано в семи терапевтических областях. Наибольшее количество в области онкологии – 26 КИ; 18 новых исследований в области болезней системы кровообращения ; 16 исследований – в области заболеваний опорно-двигательного аппарата, 12 исследований – в области эндокринологии, девять исследований в при заболеваниях органов дыхания, и по семь – в неврологии и инфекционных болезнях.

Центр по оценке и исследованию лекарственных средств (Center for Drug Evaluation and Research, CDER) FDA одобрил во втором квартале 2013 года 20 новых лекарственных препарата, по четырем из которых в России проводились КИ.

В течение второго квартала 2013 года Комитет по лекарственным средствам для применения у человека (Committee for Medicinal Products for Human Use, CHMP) Европейского агентства по лекарственным средствам (European Medicine Agency, EMEA) дал положительные рекомендации по 31 новым заявкам. По 18 лекарствам, входившим в число получивших положительный отзыв, проводились КИ в России.

Clinical Trials by Type and Manufacturing Country

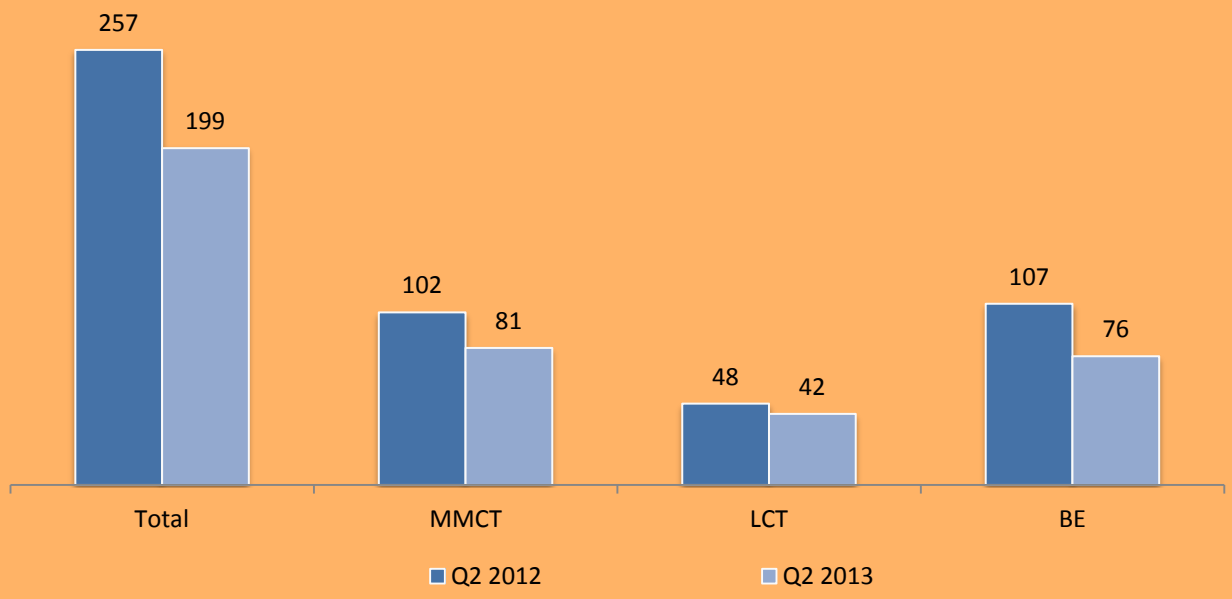
The MoH of Russian Federation approved 199 new clinical trials of all types including local and bioequivalence studies during the 2nd Quarter of 2013, demonstrating 23% decrease in comparison with the same point of the last year.

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 decreased and amounted to 81 new studies in Q2 2013 demonstrating 20% fall of the rate in comparison with the same period of the last year.

The number of bioequivalence studies decreased from 107 studies in Q2 2012 to 76 in Q2 2013.

The number of local clinical trials has slightly decreased from 48 to 42 clinical trials demonstrating the 12,5% fall of the rate in comparison with the same period of the last year.

Figure 1. Clinical trials in Russia in Q2 2013

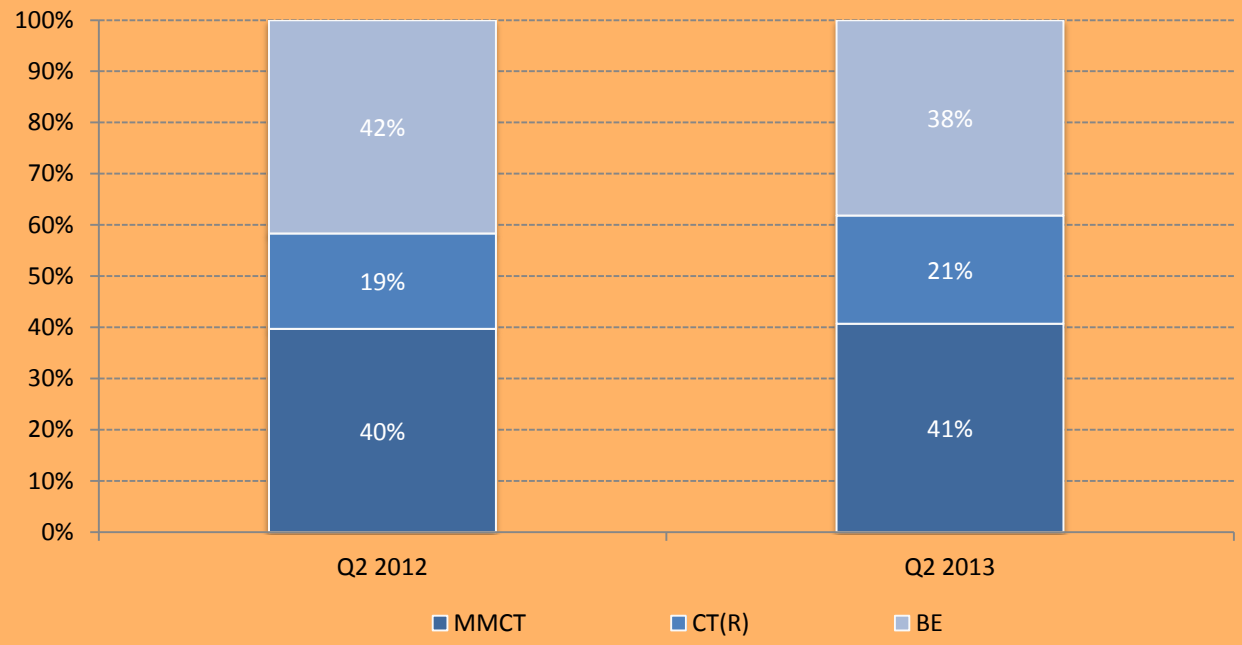


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) slightly changed since last year (see **Figure 2**).

The share of multinational multi-center clinical trials studies stayed almost at the same rate: 41% of the total number of clinical trials approved in Q2 2013.

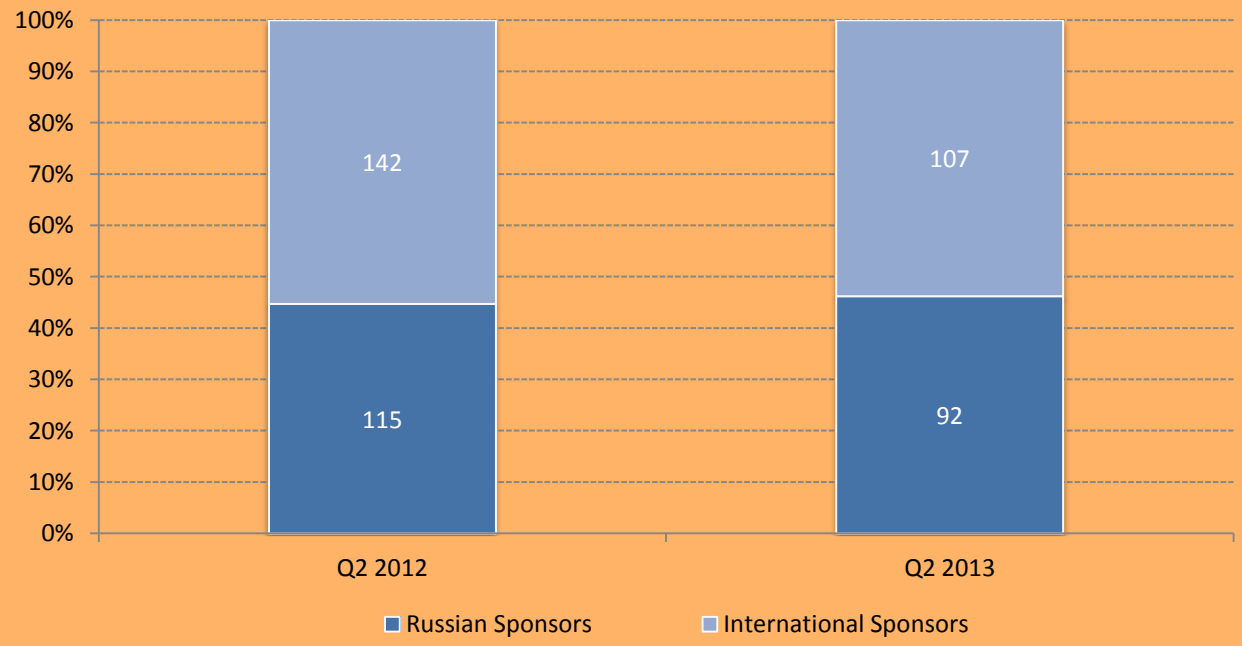
The share of the local trials increased at 21%, and the share of bioequivalence studies decreased from 42% to 38% of the total number of trials approved during Q2 2013.

Figure 2. Clinical trials by type in Q1 2013



The proportions between sponsors did not significantly change in comparison with the same period last year. 54% of the total number of new studies in Q2 2013 is sponsored by foreign companies which is 107 study approvals. The share of studies of local manufacturers insignificantly increased and amounted to 92 studies (**Figure 3**).

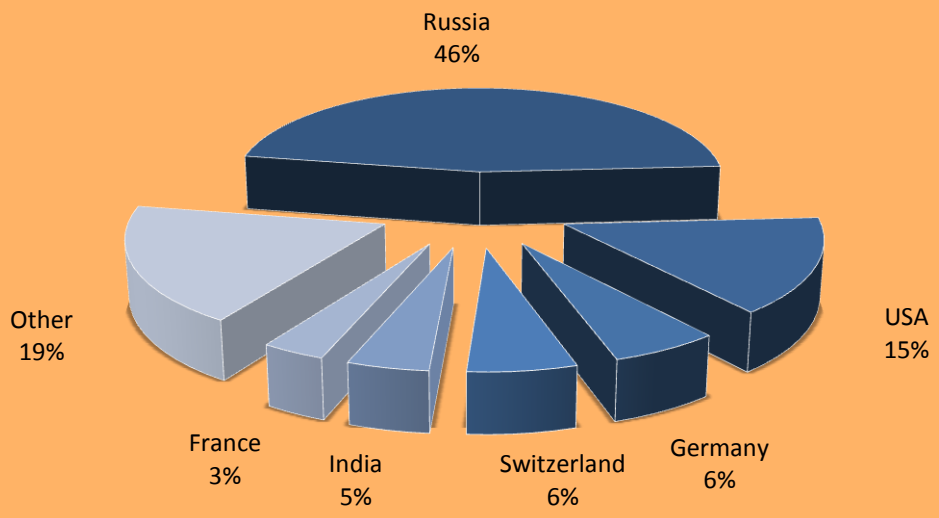
Figure 3. Russian and International sponsors in Q2 2013



Clinical trials in Russia in Q2 2013 were sponsored by companies from 24 countries. **Figure 4** demonstrates the input of the leading countries of sponsors' origin into the total number of clinical

trials. The maximum number of trials (92) was initiated by Russian sponsors. American sponsors with 30 new studies took the runner-up place; they are followed by German and Swiss sponsors with 12 trials, and the group of leaders is concluded by Indian (nine) and French (seven) sponsors.

Figure 4. Countries presented on the Russian clinical trials market in Q2 2013



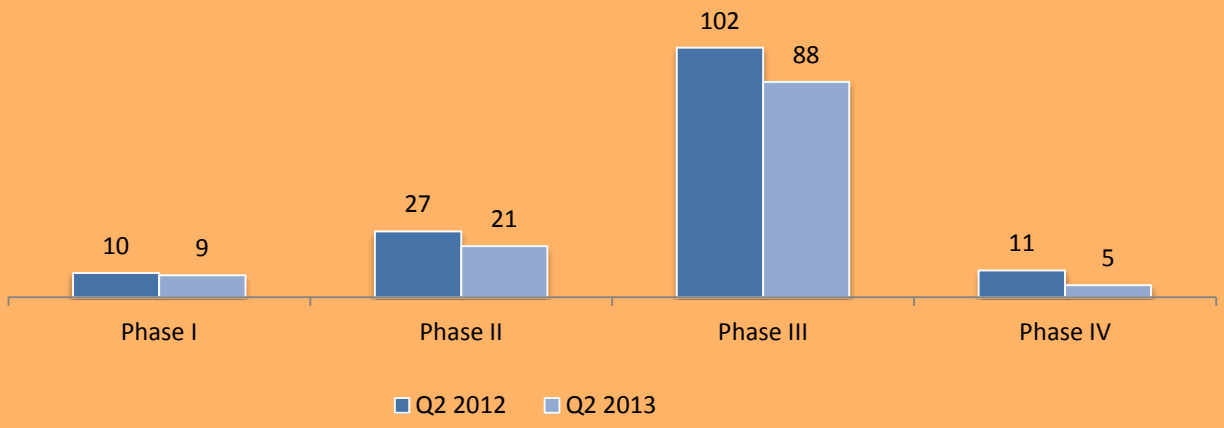
Among others are: UK (six), Belarus, Belgium, Hungary, Denmark, Poland, Czech Republic (three studies each), Italia and Latvia, (two trials each), Austria, Israel, Korea, Luxembourg, Netherlands, Macedonia, Romania, Croatia, Japan each started one new study in Q2 2013.

Clinical trials by Phase

The number of Phase I clinical trials changed insignificantly and stood at nine new studies in Q2 2013. The number of the Phase II trials decreased from 27 in Q2 2012 to 21 new studies in Q2 2013 (**Figure 5**).

The number of Phase III trials decreased from 102 to 88 studies, 14% less than in Q2 2012. Phase IV trials demonstrated the decrease more than two times from 11 studies in Q2 2012 to 5 studies in Q2 2013.

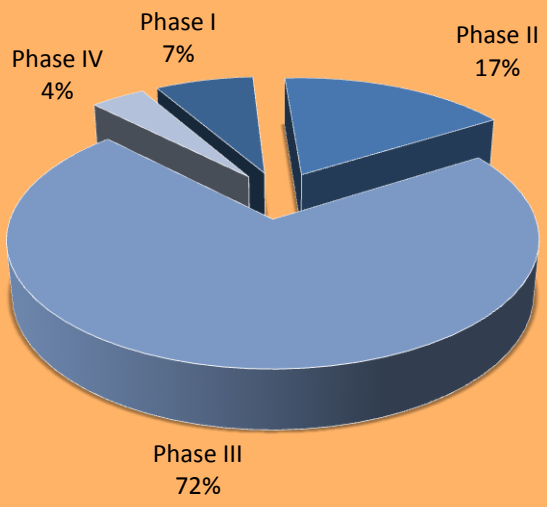
Figure 5. Clinical trials in Russia in Q2 2013 by phase[1]



[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, even in case a specific phase was indicated in the application.

As shown in **Figure 6**, the share of Phase III trials in Q2 2013 is 72% of the total number of studies, the share of Phase II trials accounted at 17%, Phase I trials is 7%, and the share of Phase IV studies amounted to 4%.

Figure 6. The proportions between study phases in Russia in Q2 2013



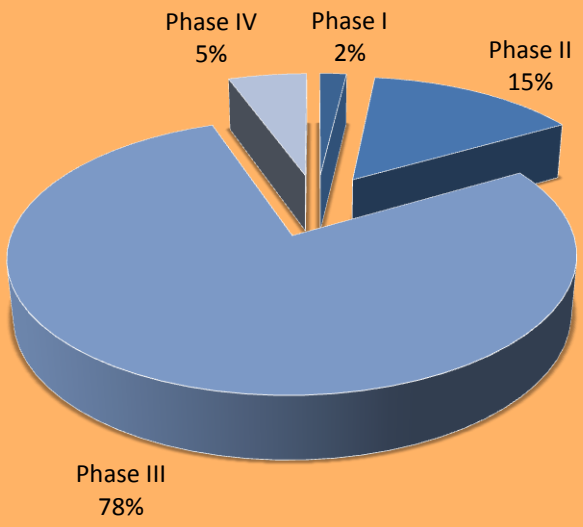
The number of subjects which are planned to be enrolled in Phase I-IV and BE trials launched in Q2 2013 is 14,654, 15% less than in Q2 2012 figure, when 17,293 patients were planned to be enrolled.

236 subjects will be recruited in Phase I trials; 1,873 patients – in Phase II trials; 9,871 subjects – in Phase III studies and 697 patients will be enrolled in Phase IV studies. Other subjects (1977) are healthy volunteers and patients who will enter to bioequivalence studies

The minimal number of subjects in a single study is ten, the maximum number is 800.

The proportion of the number of patients between different Phases is shown on **Figure 7**. Only studies in which phase is specified, were included.

Figure 7. The number of patients in Q2 2013 by study phase



Rating of international sponsors

Novartis sponsoring seven new studies is on the top of the heap in Q2 2013. It is followed by *GlaxoSmithKline* having five new trials. Top five is concluded by *Servier*, *Merck&Co* and *Bayer* each having four new trials and differentiating in the number of subjects.

Top five international sponsors by the number of new studies in Q2 2013 are presented in **Table 1**.

Table 1. Top-5 international study sponsors in Q2 2013

№	*Company Name*	*No. studies*[1]	*No. patients*
1	Novartis	7	698
2	GlaxoSmithKline	5	268
3	Servier	4	605
4	Merck&Co	4	161
5	Bayer	4	54

Rating of Russian sponsors

The Russian company *OOO Atoll* sponsoring ten new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q2 2013. *Vertex* with nine new trials took the runner-up place. It is followed by *Biocad* and *Medisorb* with seven and five studies, respectively. Top Five of Q2 2013 is concluded by *Sotex* with four new trials.

Table 2. Top-5 Russian study sponsors in Q2 2013

№	*Company Name*	*No. studies*[1]	*No. patients*
1	OOO Atoll	10	488
2	Vertex	9	224
3	Biocad	7	671
4	Medisorb	5	90
5	Sotex	4	448

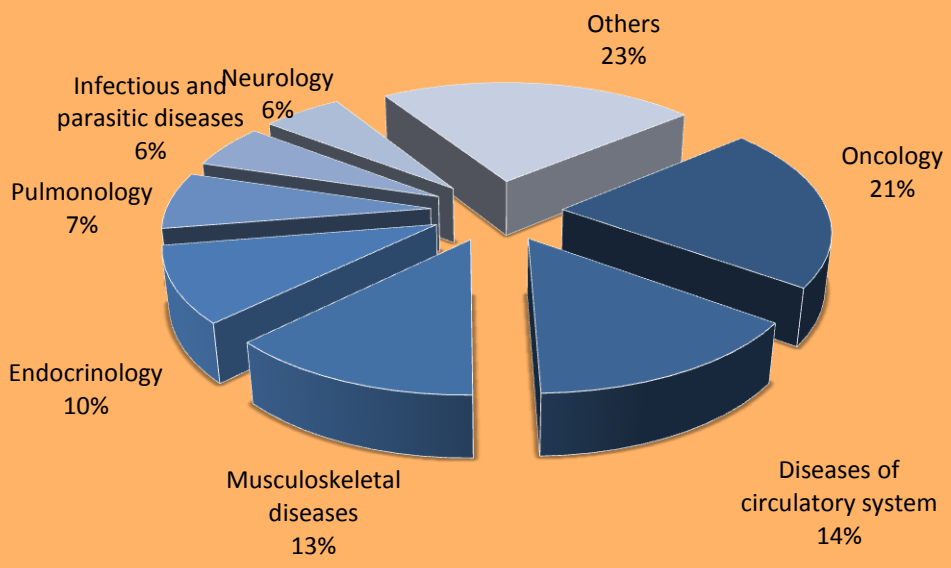
[1] Excluding BE studies

Therapeutic areas of clinical trials in Russia in Q2 2013

More than three quarters of new studies in Q2 2013 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (26); 18 new studies were instigated in diseases of the circulatory system, 16 studies – in Musculoskeletal diseases, 12 new studies – in Endocrinology, nine studies – in Pulmonology, seven studies each in Infectious and parasitic diseases and in Neurology.

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

Figure 8. Clinical trials in Russia in Q2 2013 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 20 new drugs during Q2 2013; four of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. Four drugs were studied in clinical trials involving Russian sites.

The **Table 3** shows the drugs which were approved by FDA in Q2 2013 that were being tested in clinical trials in Russia.

Table 3. New drugs approved by FDA in Q2 2013 and tested in Russian sites

Appr.date	*Drug (active ingredient)*	*Company*
05/03/2013	Liptruzet (Atorvastatin calcium/ ezetimibe)	Merck Sharp Dohme
05/10/2013	Breo Ellipta (Fluticasone furoate/ Vilanterol trifenatate)	Glaxo GRP LTD
05/29/2013	Tafinlar (Dabrafenib mesylate)	GlaxoSmithKline
05/29/2013	Mekinist (Trametinib dimethyl sulfoxide)	GlaxoSmithKline
		Source: FDA

During the second quarter of 2013 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) gave positive recommendations on 31 new drug applications[1]. Negative opinion was adopted for one drug. 18 of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia (See **Table 4**).

Table 4. New Drugs approved by EMEA in Q2 2013 and tested in Russian sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
04/26/2013	Erivedge (Vismodegib)	Roche Registartion Ltd.
04/26/2013	Xtandi (Enzalutamide)	Astellas Pharma Europr B.V.
04/26/2013	Revlimid (Lenalidomide)	Celgene Europe Ltd.
04/26/2013	RoActemra (Tocilizumab)	Roche Registartion Ltd.
05/31/2013	Lonquex (Lipegfilgrastim)	Teva Pharma B.V.
05/31/2013	Pomalidomide Celgene (Pomalidomide)	Celgene Europe Ltd.
05/31/2013	Glivec (Imatinib)	Novartis Europharm Ltd.
05/31/2013	Tysabri (Natalizumab)	Elan Pharma International Ltd.
06/28/2013	Cholib (Fenofibrate / Simvastatin)	Abbot Healthcare Products Ltd.
06/28/2013	Inflectra (Infiximab)	Hospira UK Ltd.
06/28/2013	Lemtrada (Alemtuzumab)	Genzyme Europe B.V.
06/28/2013	Nexium Control (Esomeprazole)	AstraZeneca AB
06/28/2013	Remsima (Infliximab)	Celltrion Healthcare Hungary Kft
06/28/2013	Stivarga (Regorafenib)	Bayer Pharma Ag
06/28/2013	Tafinlar (Dabrafenib)	GlaxoSmithKline Trading Service
06/28/2013	Onglyza (Saxagliptin)	Bristol-Myers Squibb/Astra Zeneca EEIG
06/28/2013	Tyverb (Lapatinib)	Glaxo Group Limited
06/28/2013	Velcade (Bortezomib)	Janssen-Cilag International NV
		Source: EMEA

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