Clinical Trials in Russia
Orange Paper
3d Quarter 2013

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Contents

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Executive Summary

The Ministry of Health of Russian Federation approved 200 new clinical trials of all types including local and bioequivalence studies during the 3d Quarter of 2013 (5% 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 increased from 93 to 102 new studies in Q3 2013. The number of bioequivalence studies decreased from 64 studies in Q3 2012 to 51 in Q3 2013. The number of local clinical trials decreased from 53 to 47 clinical trials.

The share of multinational multi-center clinical trials was 51% of the total number of clinical trials in Q3 2013, while the local and bioequivalence studies amounted to 23.5% and 25.5%, respectively.

Clinical trials in Russia in Q3 2013 were sponsored by companies from 23 countries. The maximum number of trials (70) was initiated by Russian sponsors. American sponsors with 28 new studies took the runner-up place; then is followed by Swiss sponsors with 19 trials, then is followed by UK sponsors with 12 trails, and the group of leaders is concluded by Indian and Belgium (ten) sponsors.

Thirteen new clinical trials Phase I were launched in Q3 2013, which is three trials more than in Q3 2012. The number of the Phase II trials increased from 29 in Q3 2013 to 32 new studies in Q3 2013. The number of Phase III trials are not changed in comparison to the Q3 2012 and amounted to 94 studies. Phase IV trials demonstrated the two times decrease from 13 studies in Q3 2012 to 5 studies in Q3 2013.

The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q3 2013 is 14.478 – 0.2% more than in Q3 2012 figure, when 15.445 patients had been planned to be enrolled.

Novartis sponsoring 12 new studies is on the top of the heap in Q3 2013. It is followed by *Teva* having seven new trials. Top five is concluded by *Janssen, Roche* and *GlaxoSmithKline* each having six new trials and differentiating in the number of subjects.

The Russian companys *Akrikhin* and *Vertex* sponsoring four new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q3 2013. *Veropharm* and *Biocad* with three new studies took the runner-up place.

About three quarters of new studies in Q3 2013 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (24); 21 studies – in Pulmonology ; 17 new studies were instigated in diseases of the circulatory system, 16 new studies – in Endocrinology; 12 studies – mental and behavioural disorders; 11 studies – in Musculoskeletal diseases; 9 studies – diseases of skin and subcutaneous tissue.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 17 new drugs during Q3 2013, and four of them were studied in clinical trials conducted in Russia.

During Q3 2013 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) gave positive recommendations on 28 new drug applications[1]. 21 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

В третьем квартале 2013 года Министерством здравоохранения Российской Федерации было выдано 200 разрешений на все виды клинических исследований (КИ), что на 5% меньше, чем за аналогичный период 2012 года.

При этом количество международных многоцентровых КИ возросло и составило 102 новых исследование против 93 за тот же период прошлого года. Количество исследований биоэквивалентности, инициированных в третьем квартале 2013 года, снизилось на 25% по сравнению с третьим кварталом 2012 года и составило 51 против 64. Количество локальных КИ, проводимых на территории России отечественными и иностранными спонсорами, снизилось с 53 до 47 исследований.

Спонсорами КИ, разрешенных к проведению в России в третьем квартале 2013 года, выступили компании из 23 стран. На первое место вышли российские производители с 70 КИ, за ними идут американские спонсоры с 28 новыми исследованиями, Швейцария с 19 КИ, а также Соединенное Королевство с 12 КИ. Замыкает группу лидеров Бельгия и Индия с десятью новыми исследованиями.

В третьем квартале 2013 года было инициировано 13 новых КИ I фазы – на три исследования больше, чем за аналогичный период прошлого года. Количество исследований II фазы за этот период возросло и составило 32 новых исследования против 29. Количество исследований III фазы не изменилось по сравнению с прошлым годом и составило 94 исследования. Количество исследований IV фазы уменьшилось более чем в два раза - с 13 до 5 исследований.

В первом квартале 2013 года первое место среди иностранных производителей по количеству новых исследований заняла фармацевтическая компания *Novartis* с 12 новыми исследованиями. *Teva* инициировала семь исследований. Замыкают пятерку лидеров *Janssen, Roche* и *GlaxoSmitnKline* с шестью новыми исследованиями у каждой.

Первое место среди отечественных производителей по количеству исследований, начатых в третьем квартале 2013 года, занимают *«Акрихин»* и *«Вертекс»* с четырьмя новыми КИ у каждой. За ним идут *«Верофарм»* и «*Биокад»* с тремя исследованиями.

В третьем квартале 2013 года около трех четвертей всех новых исследований было инициировано в семи терапевтических областях. Наибольшее количество в области онкологии – 24 КИ; 21 исследований в при заболеваниях органов дыхания, 17 новых исследований в области болезней системы кровообращения ; 16 исследований – в области эндокринологии; 12 исследований – в области психиатрии и поведенческих расстройств; 11 исследований в области заболеваний опорно-двигательного аппарата, и девять – в области заболеваний кожи и подкожных тканей.

Центр по оценке и исследованию лекарственных средств (Center for Drug Evaluation and Research, CDER) FDA одобрил в третьем квартале 2013 года 17 новых лекарственных препаратов, по четырем из которых в России проводились КИ.

В течение третьего 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 28 новым заявкам. По 21 лекарствам, входившим в число получивших положительный отзыв, проводились КИ в России.

Clinical Trials by Type and Manufacturing Country

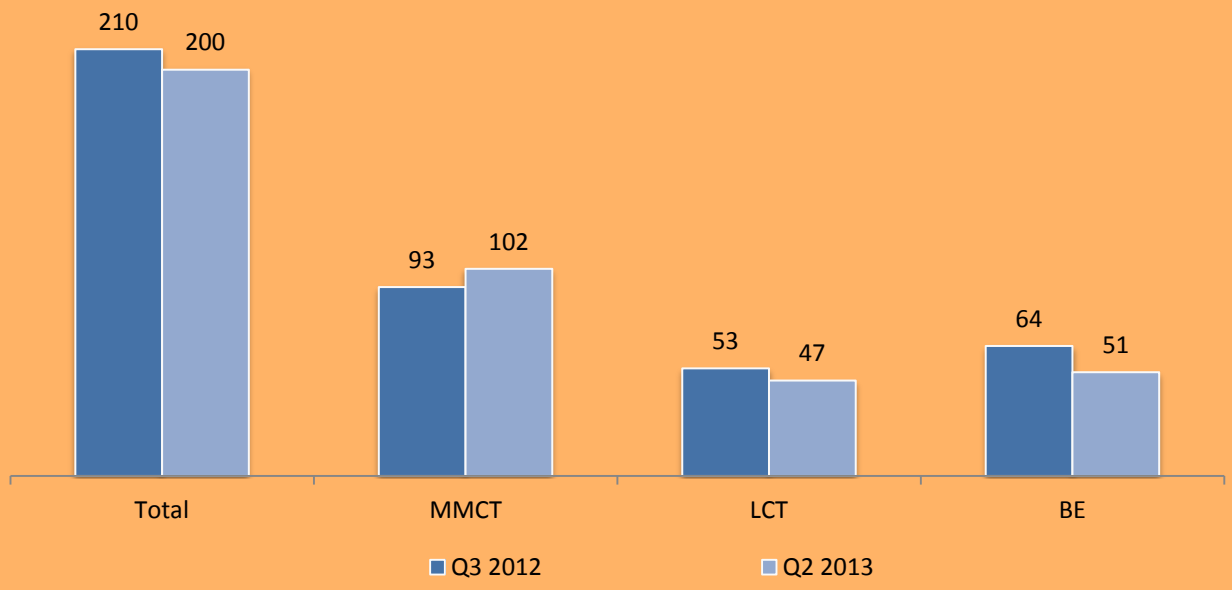
The MoH of Russian Federation approved 200 new clinical trials of all types including local and bioequivalence studies during the 3d Quarter of 2013, demonstrating 5% decrease in comparison with the same point of the last year.

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 increased and amounted to 102 new studies in Q3 2013 demonstrating 17% rise of the rate in comparison with the same period of the last year.

The number of bioequivalence studies decreased from 64 studies in Q3 2012 to 51 in Q3 2013.

The number of local clinical trials has slightly decreased from 53 to 47 clinical trials demonstrating the 11,5% fall of the rate in comparison with the same period of the last year.

Figure 1. Clinical trials in Russia in Q3 2013

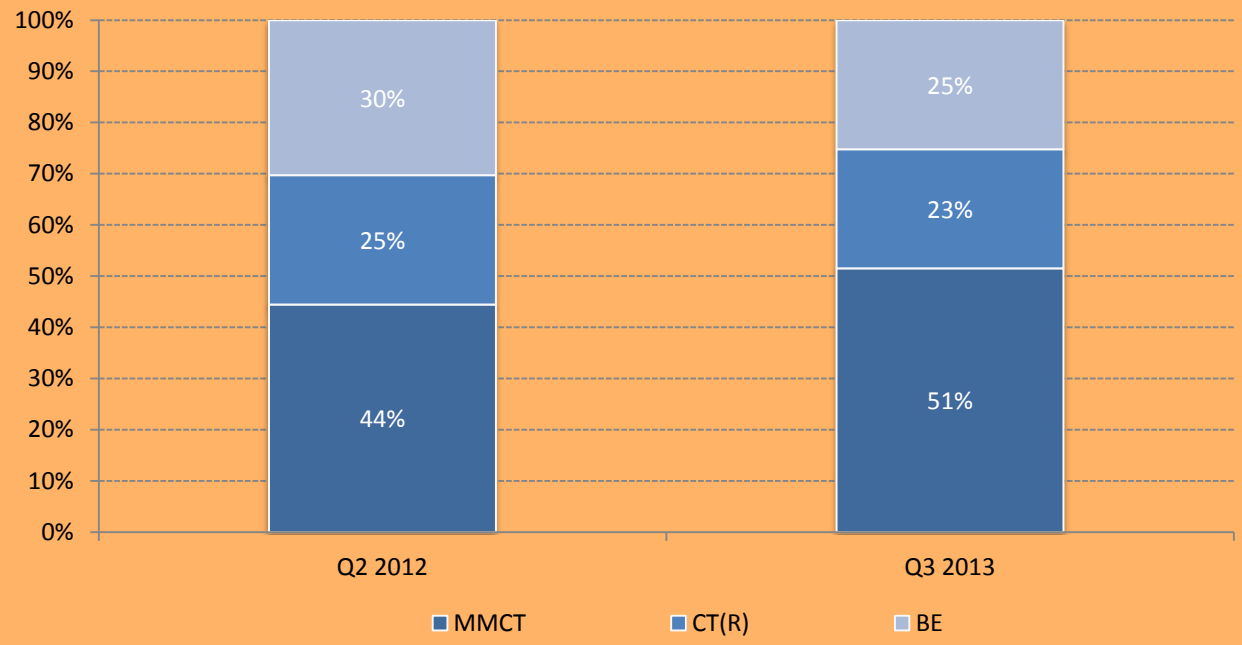


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) slightly changed since last year (see **Figure 2**).

The share of multinational multi-center clinical trials studies stayed almost at the same rate: 51% of the total number of clinical trials approved in Q3 2013.

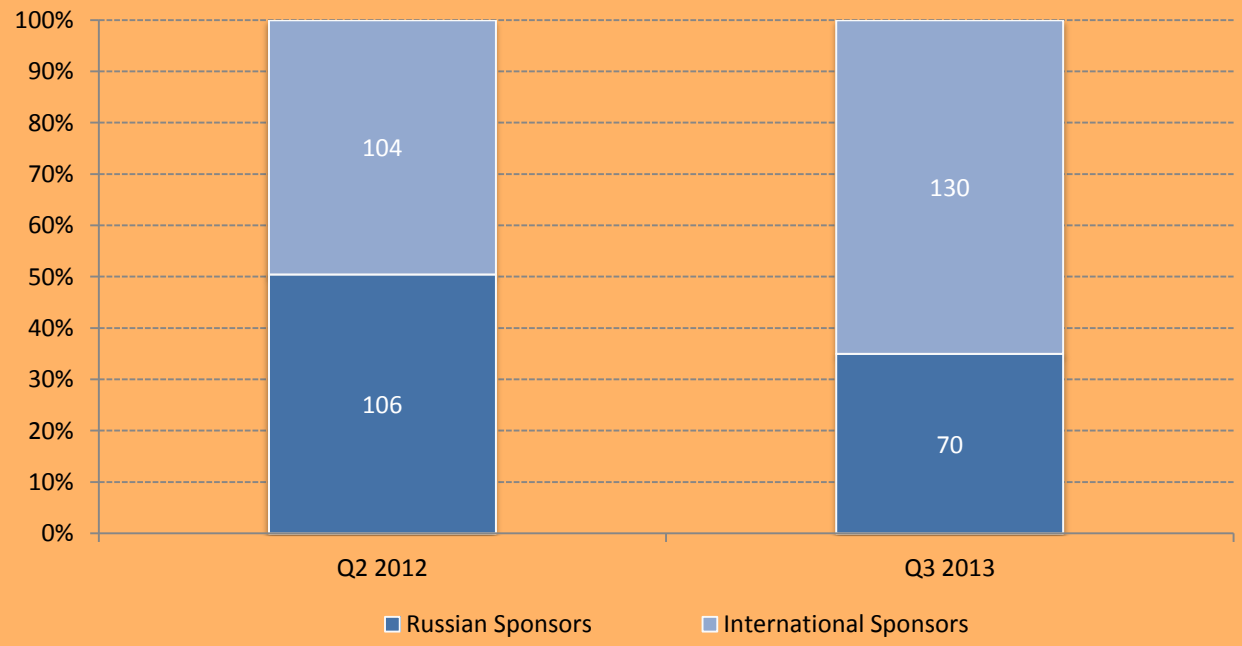
The share of the local trials increased at 23.5%, and the share of bioequivalence studies decreased from 30% to 25.5% of the total number of trials approved during Q3 2013.

Figure 2. Clinical trials by type in Q3 2013



The proportions between sponsors did not significantly change in comparison with the same period last year. 65% of the total number of new studies in Q3 2013 is sponsored by foreign companies which is 130 study approvals. The share of studies of local manufacturers insignificantly decreased and amounted to 70 studies (**Figure 3**).

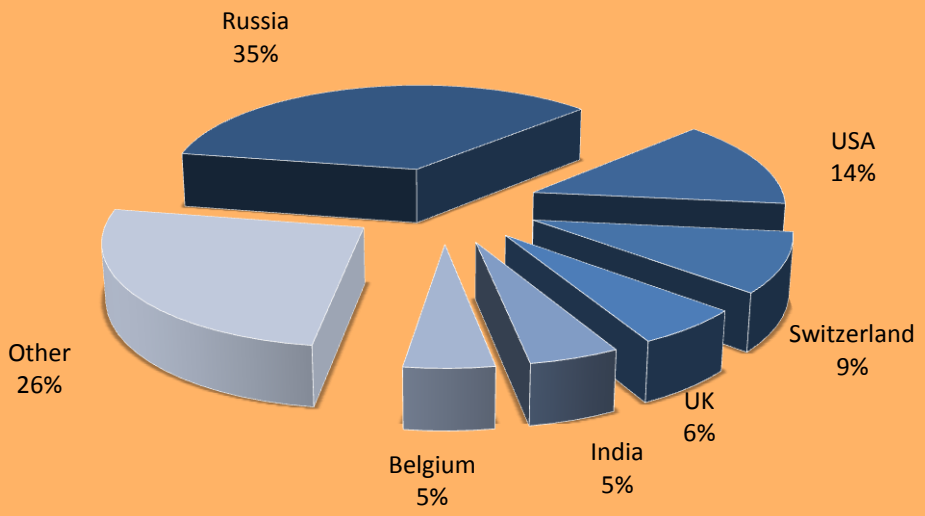
Figure 3. Russian and International sponsors in Q3 2013



Clinical trials in Russia in Q3 2013 were sponsored by companies from 23 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 (70) was initiated by Russian sponsors. American sponsors

with 28 new studies took the runner-up place; they are followed by Swiss sponsors with 19 trials, then is followed by UK sponsors with 12 trails, and the group of leaders is concluded by Indian and Belgium (ten trials each) sponsors.

Figure 4. Countries presented on the Russian clinical trials market in Q3 2013



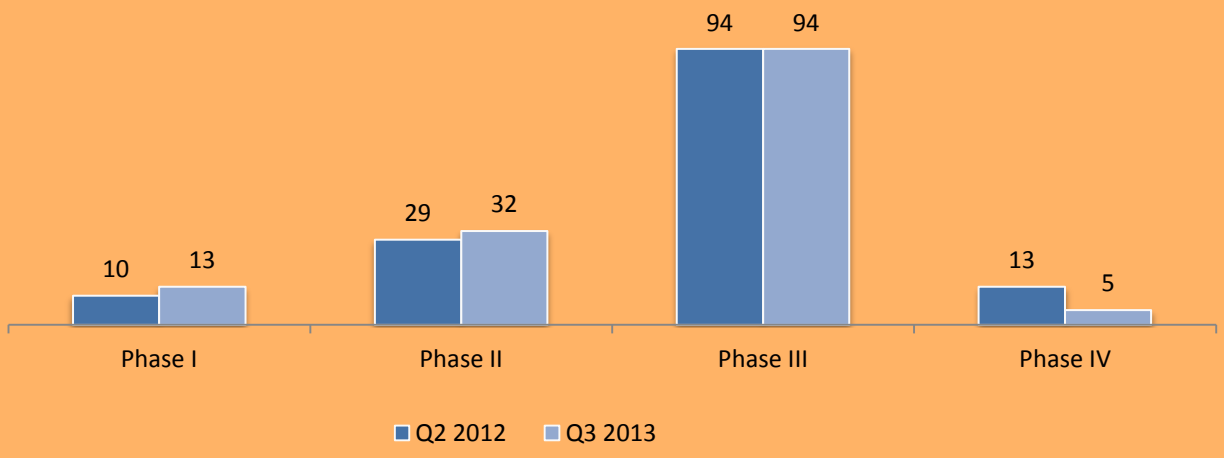
Among others are: French (eight), German and Israel (seven trails each), Denmark (six), Austria and Ukraine (three studies each), Belarus, Hungary, Slovenia, Czech Republic, Japan and Croatia (two trials each), Poland, Italia , Romania, Bulgaria and Sweden each started one new study in Q3 2013.

Clinical trials by Phase

The number of Phase I clinical trials changed insignificantly and stood at 13 new studies in Q3 2013. The number of the Phase II trials increased from 29 in Q3 2012 to 32 new studies in Q3 2013 (**Figure 5**).

The number of Phase III trials are not changed in comparison to the Q3 2012 and amounted to 94 studies. Phase IV trials demonstrated the decrease more than two times from 13 studies in Q3 2012 to 5 studies in Q3 2013.

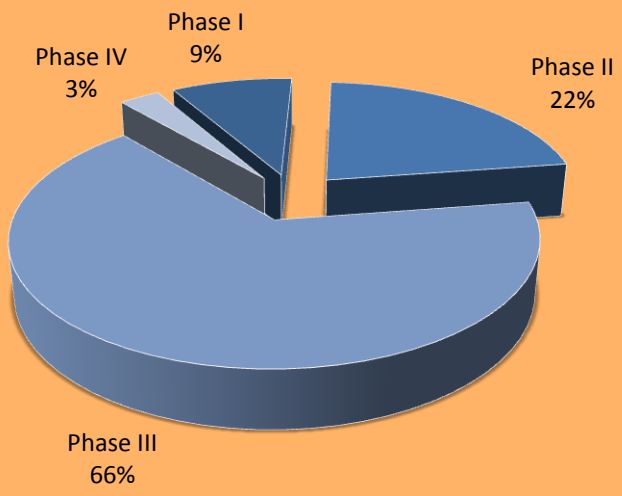
Figure 5. Clinical trials in Russia in Q3 2013 by phase[1]



[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 Q3 2013 is 66% of the total number of studies, the share of Phase II trials accounted at 22%, Phase I trials is 9%, and the share of Phase IV studies amounted to 3%.

Figure 6. The proportions between study phases in Russia in Q3 2013



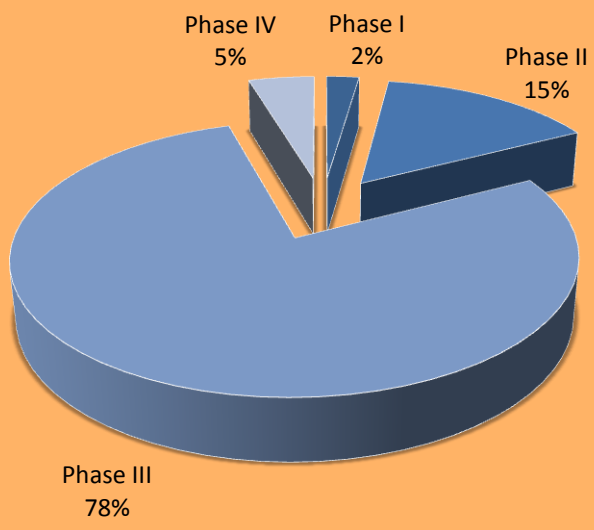
The number of subjects which are planned to be enrolled in Phase I-IV and BE trials launched in Q3 2013 is 15,478, 0.2% more than in Q2 2012, when 15.445 patients were planned to be enrolled.

312 subjects will be recruited in Phase I trials; 2.074 patients – in Phase II trials; 10.692 subjects – in Phase III studies and 631 patients will be enrolled in Phase IV studies. Other subjects (1769) are healthy volunteers and patients who will enter to bioequivalence studies

The minimal number of subjects in a single study is one, the maximum number is 1200.

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 Q3 2013 by study phase



Rating of international sponsors

Novartis sponsoring 12 new studies is on the top of the heap in Q3 2013. It is followed by *Teva* having seven new trials. Top five is concluded by *Janssen*, *Roche* and *GlaxoSmithKline* each having six new trials and differentiating in the number of subjects.

Top five international sponsors by the number of new studies in Q3 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	12	639
2	Teva	7	365
3	Janssen	6	1093
4	Roche	6	421
5	GlaxoSmithKline	6	353

Rating of Russian sponsors

The Russian companys *Akrikhin* and *Vertex* sponsoring four new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q3 2013. *Veropharm* and *Biocad* with three new studies took the third and fourth places. Seven companies (Mir Pharm, Pharma Bio, Atoll, Nativa, F-Syntez, Pranapharm, Pharmsyntez) with 2 new studies each share the fifth place.

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

№	*Company Name*	*No. studies*[1]	*No. patients*
1	Akrikhin	4	314
2	Vertex	4	96
3	Biocad	3	274
4	Veropharm	3	142
5	Mir Pharm, Pharma Bio, Atoll, Nativa, F-Syntez, Pranapharm, Pharmsyntez	2 (each)	902 (total)

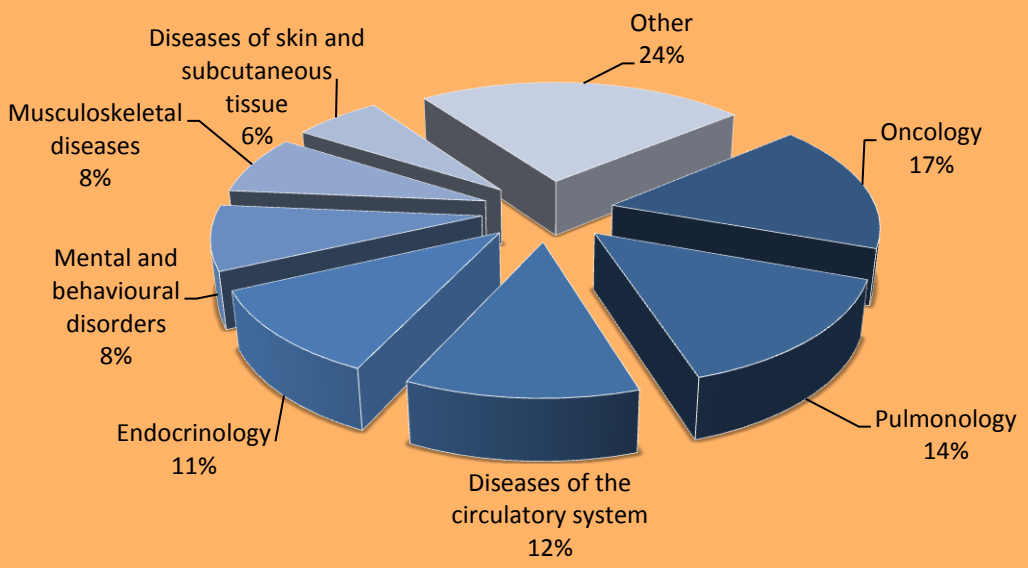
[1] Excluding BE studies

Therapeutic areas of clinical trials in Russia in Q3 2013

About three quarters of new studies in Q3 2013 were initiated in seven leading therapeutic areas: the largest number of studies was initiated in Oncology (24); 21 studies – in Pulmonology ; 17 new studies were instigated in diseases of the circulatory system, 16 new studies – in Endocrinology; 12 studies – mental and behavioural disorders; 11 studies – in Musculoskeletal diseases; 9 studies – diseases of skin and subcutaneous tissue.

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

Figure 8. Clinical trials in Russia in Q3 2013 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 17 new drugs during Q3 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 Q3 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*
18/07/2013	SIMPONI ARIA (GOLIMUMAB)	JANSSEN BIOTECH
19/07/2013	ASTAGRAF XL (TACROLIMUS)	ASTELLAS
07/12/2013	AFATINIB DIMALEATE	BOEHRINGER INGELHEIM
30/09/2013	BRINTELLIX (VORTIOXETINE)	TAKEDA PHARMS USA
		Source: FDA

During the third quarter of 2013 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) gave positive recommendations on 28 new drug

applications[1]. 21 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 Q3 2013 and tested in Russian sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
25/07/2013	Giotrif (afatinib)	Boehringer Ingelheim International GmbH
25/07/2013	Incresync (alogliptin/pioglitazone)	Takeda Pharma A/S
25/07/2013	Tybost (cobicistat)	Gilead Sciences International Ltd
25/07/2013	Ultibro Breezhaler (glycopyrronium bromide / indacaterol)	Novartis Europharm Ltd
25/07/2013	Vipdomet (alogliptin / metformin)	Takeda Pharma A/S
25/07/2013	Vipidia (alogliptin)	Takeda Pharma A/S
25/07/2013	Xoterna Breezhaler (glycopyrronium bromide / indacaterol)	Novartis Europharm Ltd
25/07/2013	Ilaris (canakinumab)	Novartis Europharm Ltd
25/07/2013	Prezista (darunavir)	Janssen-Cilag International N.V.
25/07/2013	Revolade (eltrombopag)	GlaxoSmithKline Trading Services
25/07/2013	Simponi (golimumab)	Janssen Biologics B.V.
25/07/2013	Stelara (ustekinumab)	Janssen-Cilag International N.V.
25/07/2013	Zonegran (zonisamide)	Eisai Ltd
19/09/213	Abilify Maintena (aripiprazole)	Otsuka Pharmaceutical Europe Ltd
19/09/213	Kadcyla (trastuzumab emtansine)	Roche Registration Ltd
19/09/213	Invokana (canagliflozin)	Janssen-Cilag International N.V.
19/09/213	NovoEight (turoctocog alfa)	Novo Nordisk A/S
19/09/213	Relvar Ellipta (fluticasone furoate / vilanterol)	Glaxo Group Ltd
19/09/213	Vitekta (elvitegravir)	Gilead Sciences International Ltd
19/09/213	Cimzia (certolizumab pegol)	UCB Pharma SA
19/09/213	Votubia (everolimus)	Novartis Europharm Ltd
		Source: EMEA

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