Clinical Trials in Russia
Orange Paper
1st Quarter 2012

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Contents

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Executive Summary

The Ministry of Health and Social Development of the Russian Federation (MoH) approved 220 new clinical trials of all types including local and bioequivalence studies during the first quarter of 2012, demonstrating 132% increase comparing to the same point of the last year.

The main contribution into the total number of studies is made by multinational multi-center clinical trials, the number of them increased by 20% from Q1 2011 and stood at 89 new studies in Q1 2012. The number of bioequivalence studies increased dramatically from 3 to 77 new studies, and the number of local clinical trials also increased significantly from 18 to 54 clinical trials.

The share of multinational multi-center clinical trials stood at 40% of the total number of clinical trials in Q1 2012, while the local and bioequivalence studies amounted to 25% and 35%, respectively.

Clinical trials in Russia in Q1 2012 were sponsored by companies from 22 countries. The maximum number of trials (105) was initiated by Russian sponsors. American sponsors with 31 new studies took the runner-up place, they are followed by Israeli sponsors with 18 trials. The group of leaders is concluded by Swiss and British sponsors each with 13 new studies in Q1 2012.

Seven new Phase I clinical trials were launched in Q1 2012, three trials more than in Q1 2011. The number of the Phase II trials almost did not change and stood at 23 new studies in Q1 2012. The number of Phase III trials increased significantly from 57 to 94 studies. Phase IV trials also demonstrated the significant increase from 9 studies in Q1 2011 to 18 studies in Q1 2012.

The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q1 2012 stood at 17,270, 55% more than in Q1 2011, when 11,123 patients were planned to be enrolled.

GlaxoSmithKline sponsoring ten new studies is on the top of the heap in Q1 2012. It is followed by *Roche* having seven new trials, *Boehringer Ingelheim* with six, and *Teva* with five new trials. Top five is concluded by *Merck & Co.* with four new studies in Q1 2012.

The Russian company *Microgen* sponsoring eight new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q1 2012. *Veropharm* with four new trials took the runner-up place. It is followed by *Vertex* with three new trials, and *Materia Medica* and *Virpharm* each having two new trials and differentiating in the number of patients.

More than two thirds of new studies in Q1 2012 were initiated in seven leading therapeutic areas: the largest number of studies has been initiated in Oncology (27); 15 new studies were instigated in Musculoskeletal diseases and 14 new studies in Pulmonology; 13 studies – in Infectious diseases; 11 – in Endocrinology, ten new clinical trials were instigated each in Gastroenterology and Psychiatry.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 33 new drugs during Q1 2012; seven of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. Five drugs were studied in clinical trials involving Russian sites.

During the first quarter of 2012 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 23 new drug applications, seven of which were tested in clinical trials in Russia.

No FDA inspections were conducted in Russia during Q1 2012.

Clinical Trials by Type and Manufacturing Country

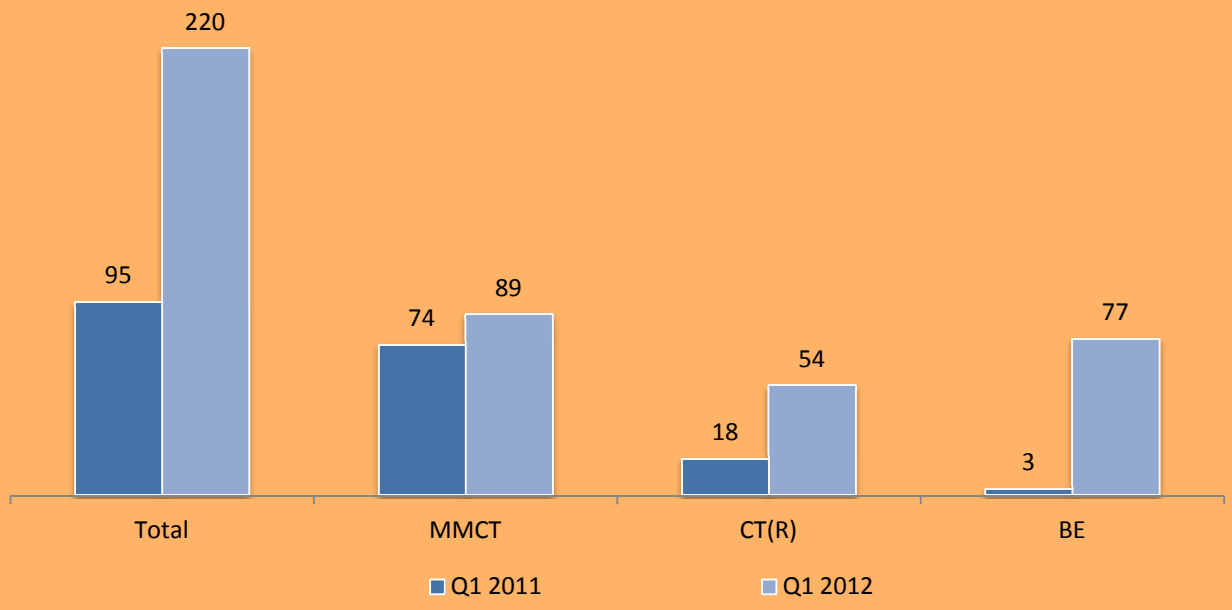
The Russian MoH approved 220 new clinical trials of all types including local and bioequivalence studies during the first quarter of 2012, demonstrating a 132% increase in comparison with the same point last year.

As shown in Figure 1, the main contribution into the total number of studies is made by multinational multi-center clinical trials (MMCT), the number of these studies stood at 89 new trials in Q1 2012 demonstrating 20% increase comparing with Q1 2011.

The number of bioequivalence studies (BE) increased dramatically: >25 times more than in Q1 2011, and stood at 77 new studies in Q1 2012.

The number of the local clinical trials (CT(R)) conducted in Russia by domestic and foreign sponsors also increased significantly from 18 to 54 clinical trials, 300% increase from last year's figure.

Figure 1. Clinical trials in Russia in Q1 2012

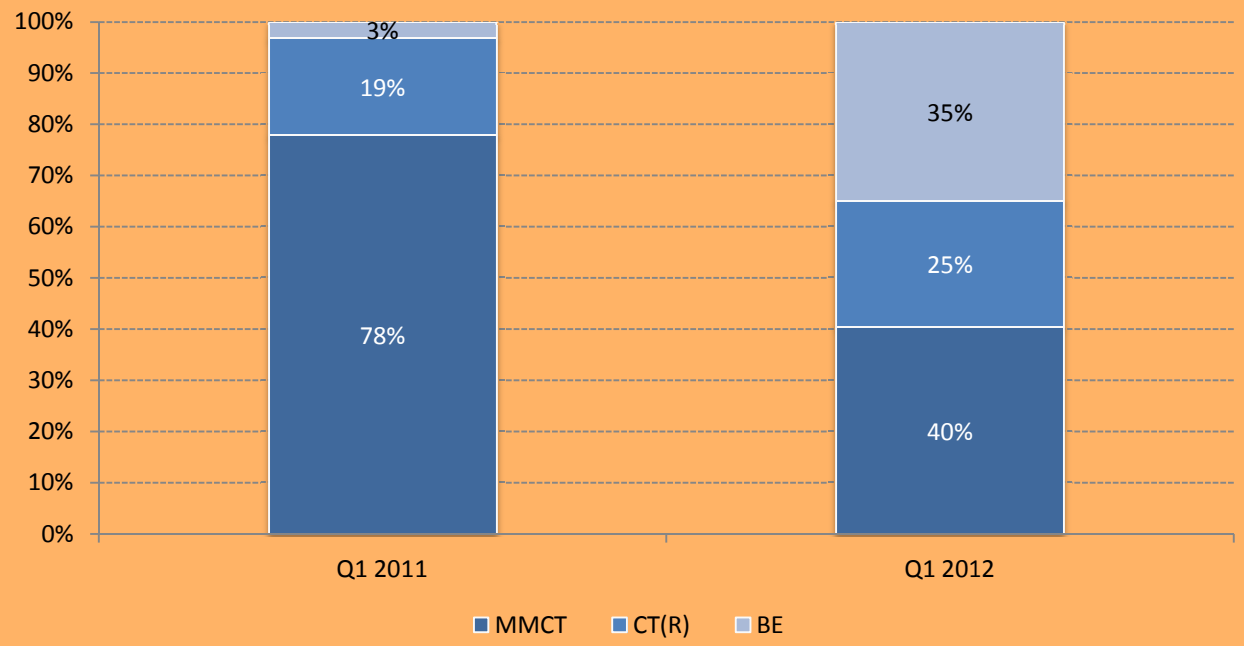


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) changed significantly since last year (see Figure 2).

The share of bioequivalence trials increased dramatically from 3% in Q1 2012 to 35% of the total number of clinical trials approved in Q1 2012.

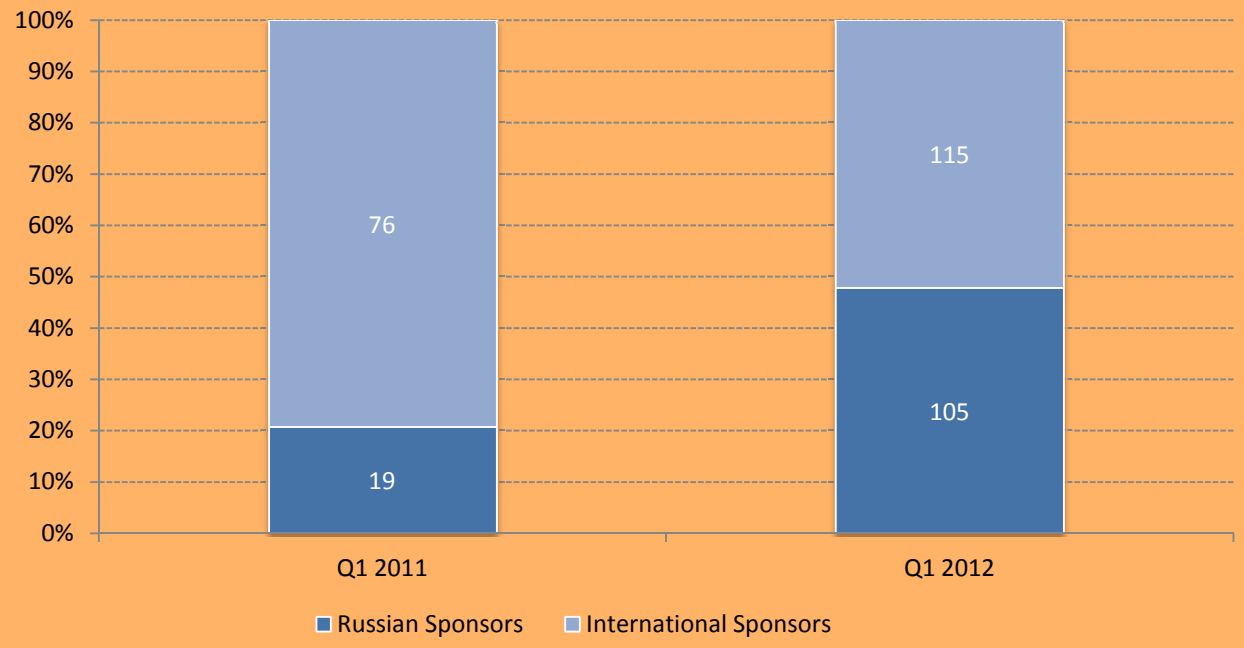
The share of the local trials increased from 19% in Q1 2011 to 25% of the total number of studies in Q1 2012, and the share of multinational multi-center clinical studies decreased from 78% to 40% of the total number of trials approved during the first quarter of 2012.

Figure 2. Clinical trials by type in Q1 2012



The larger share of clinical trials in Russia is sponsored by foreign companies which received 115 study approvals, or 52% of the total number of new studies in Q1 2012. The share of studies of local manufacturers increased from 20% in Q1 2011 to 48% in Q1 2012, from 19 to 105 studies, respectively.

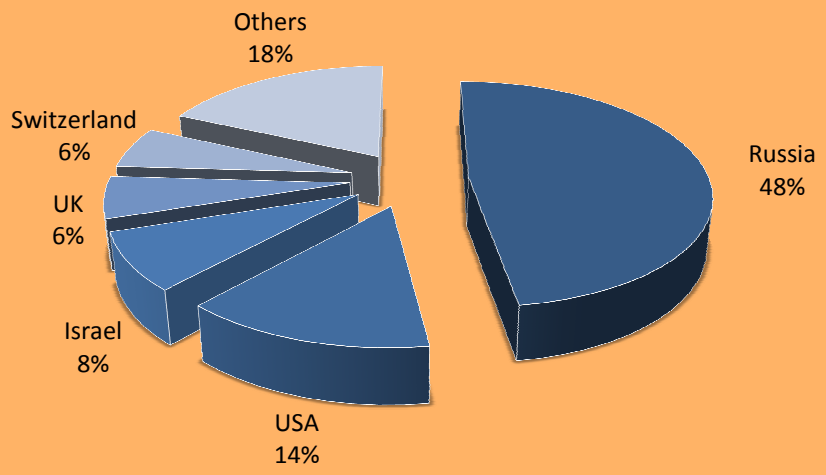
Figure 3. Russian and International sponsors in Q1 2012



Clinical trials in Russia in Q1 2012 were sponsored by companies from 22 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 (105) was initiated by Russian sponsors. American sponsors

with 31 new studies took the runner-up place, they are followed by Israeli sponsors with 18 trials. The group of leaders is concluded by Swiss and British sponsors each with 13 studies in Q1 2012.

Figure 4. Countries presented on the Russian clinical trials market in Q1 2012



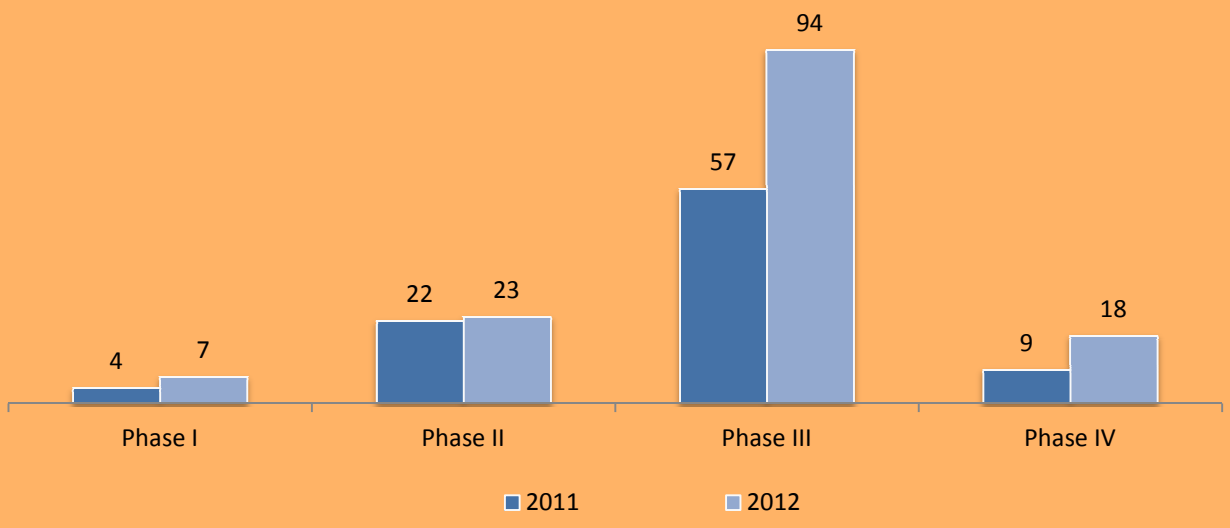
Among others are: Austria and France (7 studies each); Belgium and Germany (5 each); Denmark, Slovenia and Sweden have 2 new studies each; Argentina, Belarus, Hungary, Ireland, Italy, Cuba, Netherlands, Republic of Macedonia, Tunisia and Japan each started one new study in Q1 2012.

Clinical trials by Phase

Seven new Phase I clinical trials were launched in Q1 2012, which is three trials more than in Q1 2011. The number of the Phase II trials almost did not change and stood at 23 new studies in Q1 2012.

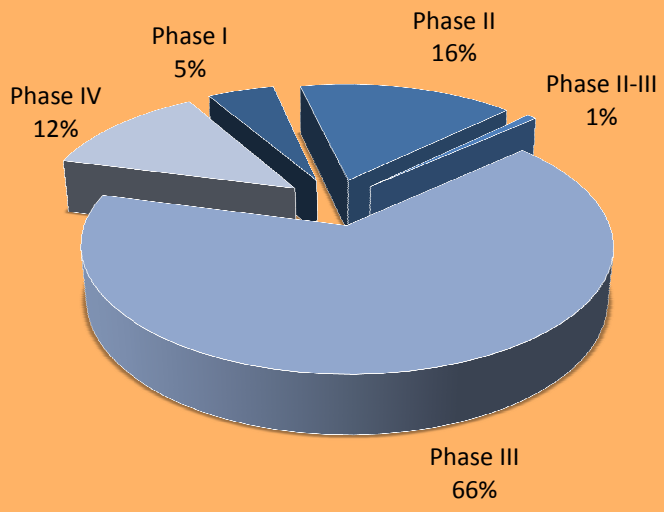
The number of Phase III trials increased significantly from 57 to 94 studies, 65% more than in Q1 2011. Phase IV trials demonstrated the increase from 9 studies in Q1 2011 to 18 studies in Q1 2012. One Phase II-III study was launched in Q1 2012.

Figure 5. Clinical trials in Russia in Q1 2012 by phase



As shown in Figure 6, the share of Phase III trials in Q1 2012 stood at 66% of the total number of studies, the share of Phase II trials accounted at 16%, Phase IV trials stood at 12%, the share of Phase I studies amounted to 5%, and one Phase II-III study stood at 1%.

Figure 6. The proportions between study phases in Russia in Q1 2012



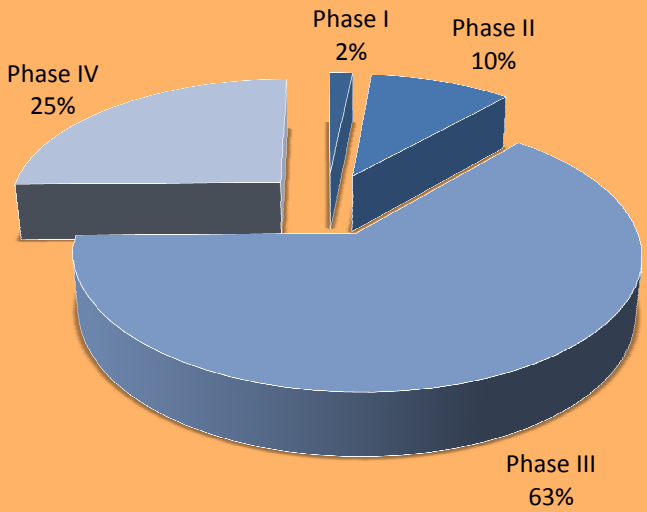
The number of subjects which are planned to be enrolled in Phase I-IV trials launched in Q1 2012 stood at 17,270, 55% more than in Q1 2011 figure, when 11,123 subjects were planned to be enrolled.

266 subjects will be recruited in Phase I trials; 1,701 subjects – in Phase II trials; 10,918 subjects – in Phase III studies; 4,343 subjects – in Phase IV studies, and 42 subjects will be enrolled in Phase II-III study.

The minimal number of subjects in a single study is two, the maximum number is 2,200.

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 Q1 2012 by study phase



Rating of international sponsors

GlaxoSmithKline sponsoring ten new studies is on the top of the heap in Q1 2012. It is followed by *Roche* having seven new trials, *Boehringer Ingelheim* with six, and *Teva* with five new studies. Top five is concluded by *Merck & Co.* with four new studies in Q1 2012.

Top five international sponsors by the number of new studies in Q1 2012 are presented in Table 1.

Table 1. Top-5 international study sponsors in Q1 2012

№	*Company Name*	*No. studies*[1]	*No. patients*
1	GlaxoSmithKline	10	713
2	Roche	7	2,593
3	Boehringer Ingelheim	6	605
4	Teva	5	726
5	Merck & Co.	4	588

Rating of Russian sponsors

The Russian company *Microgen* sponsoring eight new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in Q1 2012. *Veropharm* with four new trials took the runner-up place.

It is followed by *Vertex* with three new trials, and *Materia Medica* and *Virpharm* each having two new trials and differentiating in the number of patients.

Table 2. Top-5 Russian study sponsors in Q1 2012

№	*Company Name*	*No. studies*[2]	*No. patients*
1	Microgen	8	1,815
2	Veropharm	4	304
3	Vertex	3	180
4	Materia Medica	2	402
5	Virpharm	2	240

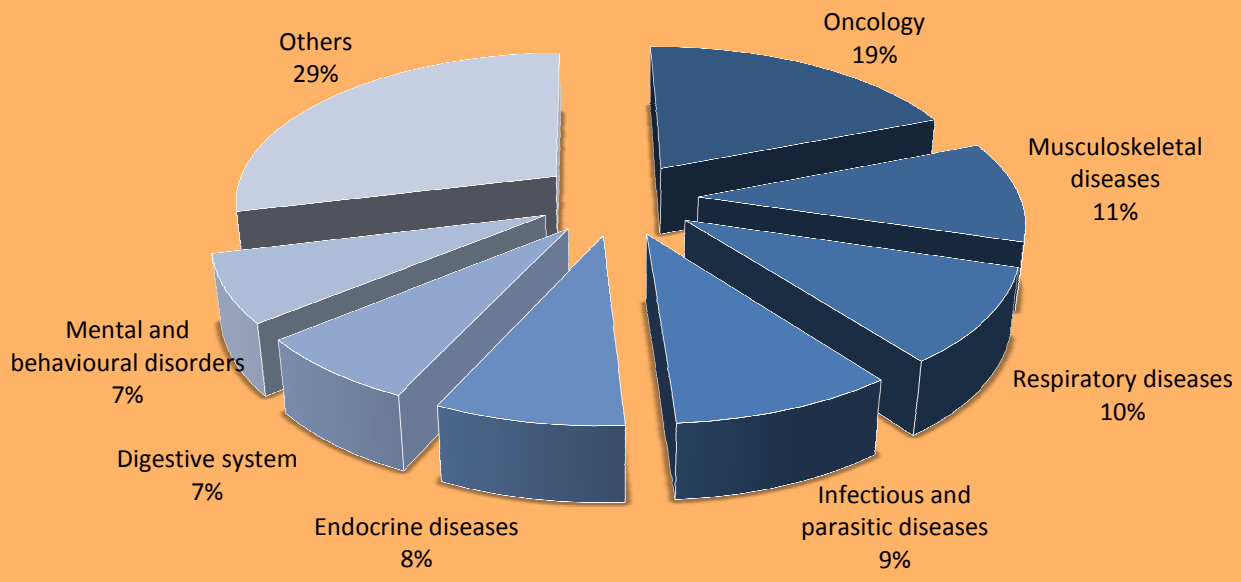
[1, 2] Excluding BE studies

Therapeutic areas of clinical trials in Russia in 2012

More than two thirds of new studies in Q1 2012 were initiated in seven leading therapeutic areas: the largest number of studies has been initiated in Oncology (27); 15 new studies were instigated in Musculoskeletal diseases and 14 new studies in Pulmonology; 13 studies – in Infectious diseases; 11 – in Endocrinology, and ten studies were instigated each in Gastroenterology and Psychiatry.

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

Figure 8. Clinical trials in Russia in Q1 2012 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 33 new drugs during Q1 2012; seven of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. Five drugs were studied in clinical trials involving Russian sites.

The Table 3 represents drugs which were approved by FDA and were being tested in clinical trials in Russia in Q1 2012.

Table 3. New drugs approved by FDA in Q1 2012 and tested in Russian sites

Appr.date	*Drug (active ingredient)*	*Company*
20/01/2012	Zetonna (Ciclesonide)	Nycomed
27/01/2012	Bydureon (Exenatide synthetic)	Amylin
27/01/2012	Inlyta (Axitinib)	Pfizer
30/01/2012	Jentadueto (Linagliptin; Metformin hydrochloride)	Boehringer Ingelheim
27/03/2012	Omontys (Peginesatide)	Affymax Inc
		Source: FDA

During the first quarter of 2012 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 23 new drug applications. Negative opinion

was adopted for one drug. Seven 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 Q1 2012 and tested in Russian sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
19/01/2012	Signifor (Pasireotide)	Novartis Europharm Ltd
16/02/2012	Pixuvri (Pixantrone dimaleate)	CTI Life Sciences Ltd
16/02/2012	Byetta (Exenatide)	Eli Lilly Nederland B.V
16/02/2012	Humira (Adalimumab)	Abbott Laboratories Ltd
16/02/2012	PegIntron (Peginterferon alfa-2b)	Schering-Plough Europa
16/02/2012	Rebetol (Ribavirin)	Schering-Plough Europa
16/02/2012	ViraferonPeg (Peginterferon alfa-2b)	Schering-Plough Europa
		Source: EMEA

FDA inspections

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