Clinical Trials in Russia

Orange Paper

3rd Quarter 2010

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 new law “On circulation of medicines” became effective on 1 September 2010. According to this law the right to issue the license for performing Clinical researches was transferred from The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (alias RosZdravNadzor, RZN) to the Ministry of Healthcare and Social Development. Due to this transmission the issue of licenses was temporary suspended in September. In our opinion it caused the decrease of the main indicators of clinical researches’ market comparing to the corresponding period of the last year.

RZN approved 134 new clinical trials of all types including local and bioequivalence studies during the third quarter of 2010 demonstrating a 12% decrease comparing to the last year figure.

The main contribution into the total number of studies is still made by multinational multi-center clinical trials, even though the number of these studies descended by one third over Q3 2009 and stood at 60 new studies in Q3 2010. The number of local clinical trials conducted in Russia by domestic and foreign sponsors demonstrated a 7% increase and stood at 42 trials.

Although most of clinical trials in Russia are still being sponsored by foreign companies (57%), the ratio between foreign and domestic companies changed significantly: in Q3 2009 their shares were 67% and 33% respectively, while in Q3 2010 the share of trials sponsored by domestic companies increased up to 43%.

Clinical trials initiated in Q3 2010 were sponsored by manufacturers from 17 countries. The maximum number of trials was initiated by Russian sponsors, American sponsors took the runner-up place, they are followed by German and Swiss sponsors, and the top six is concluded by French, Belgian and Belarusian sponsors each with four new studies.

Twelve new Phase I clinical trials were launched in the third quarter of 2010; three trials more than in the corresponding quarter of last year. The number of the Phase II trials decreased significantly from 47 trials in the third quarter of 2009 to 18 in the third quarter of 2010. The number of Phase III trials also demonstrated a decrease over last year number, down from 86 to 61 studies, while the number of Phase IV studies remained almost unchanged – 10 new trials.

The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the third quarter of 2010 stood at 11,758 – a bit less than the last year number. The number of Phase III subjects increased by 24% from last year’s figure.

The Swiss giant *Novartis* sponsoring 7 new studies is on the top of the heap in the third quarter of 2010. The German *Boehringer Ingelheim* with five new trials in Q3 2010 took the runner-up place. It is followed by British *Pantheon* and *GlaxoSmithKline* each sponsoring five new studies. The top five is concluded by French s*anofi-aventis* having four new studies in Q3 2010.

The Russian pharmaceutical company ZAO *Rafarma* sponsoring five new clinical trials ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the third quarter 2010. They are followed by *NIOPIK* and ZAO *Pharm-sintez* with three new trials each and ZAO *Firn M* with two new trials. ZAO *Vector-Medica* and OOO *Niarmedik* with one new study each and the same number of patients and sites conclude top six.

62% per cent of the new studies in Q3 2010 were conducted in the five leading therapeutic areas. The maximum number of trials (20) was initiated in Oncology; 13 clinical trials in Neurology; 10 new studies in Infectious Diseases; nine – in Respiratory diseases and eight new Endocrinology studies were initiated in Q3 2010.

According to the FDA data as of November 12 2010, there were two FDA inspections conducted at the Russian investigative sites during Q3 2010. Both were performed at investigative sites in Saint-Petersburg with *NAI – No Actions Indicated* in conclusion.

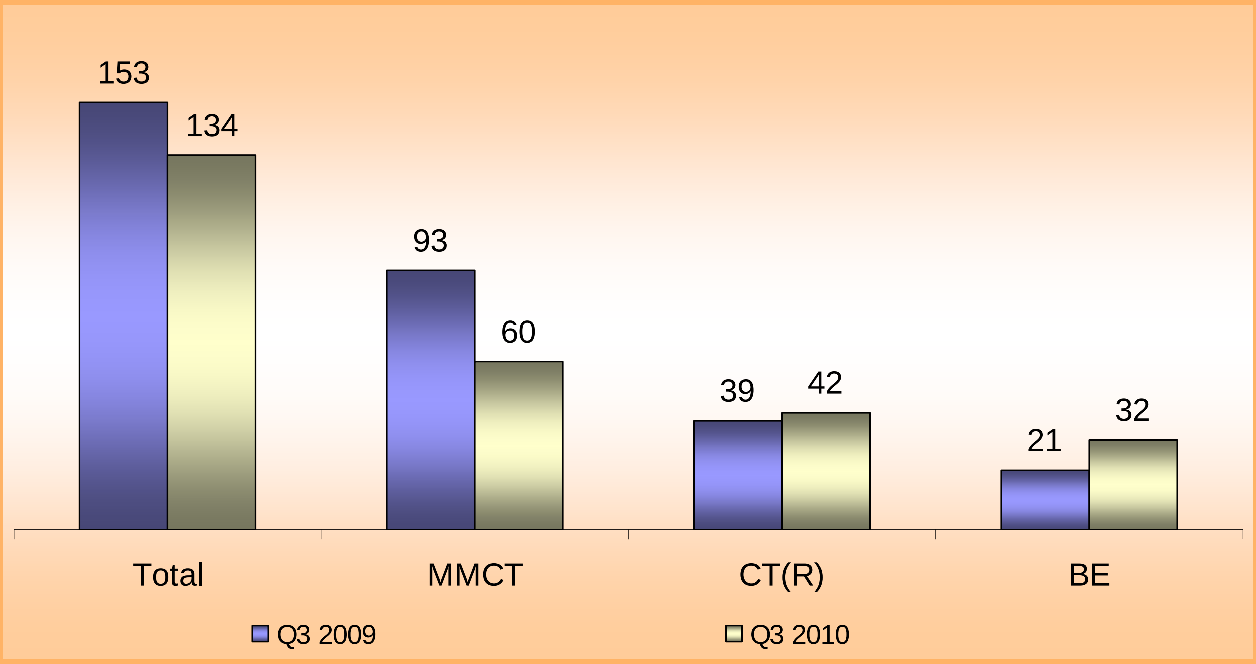
Clinical Trials by Type and Manufacturing Country

The RZN approved 134 new clinical trials of all types including local and bioequivalence studies during the third quarter of 2010 demonstrating a 12% decrease comparing to the corresponding period of last year. As shown in the Figure 1, the main contribution into the total number of studies is still made by multinational multi-center clinical trials (presented as MMCT in Figure 1), even though the number of these studies descended by one third over Q3 2009 and stood at 60 new studies in Q3 2010.

The number of the local clinical trials conducted in Russia by domestic and foreign sponsors (the CT(R) bar in the Figure 1) insignificantly increased from 39 to 42 clinical trials demonstrating a 7% increase over the same point in 2009.

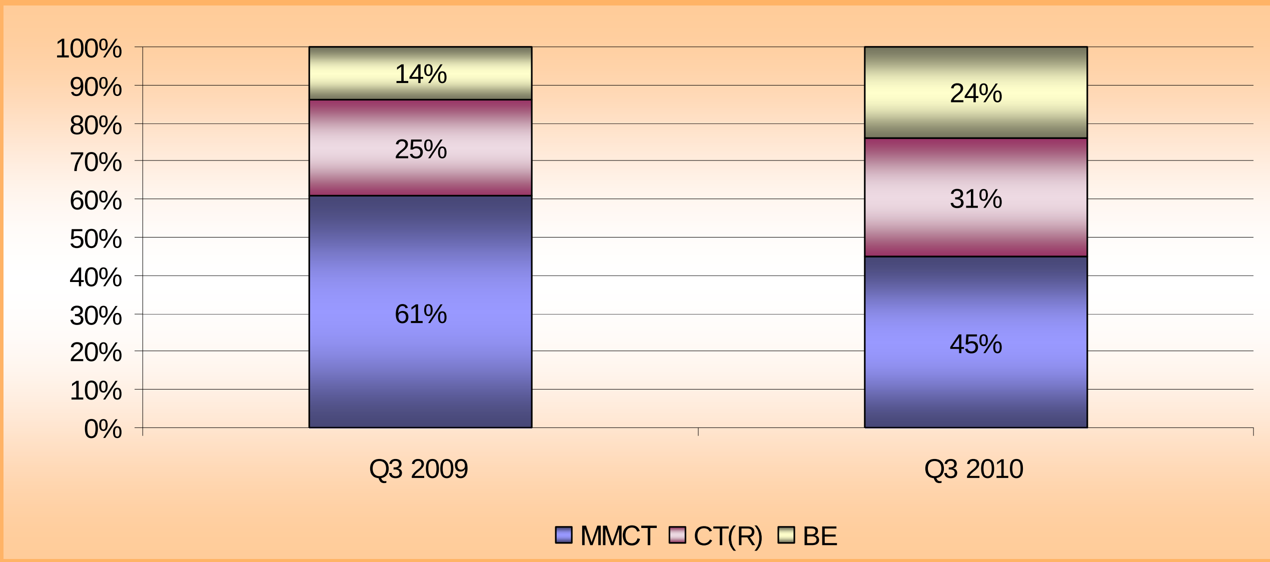
The number of bioequivalence studies (BE in Figure 1) initiated in the third quarter of 2010 stood at 32 new trials, eleven studies up over last year's figure.

Figure 1. Clinical trials approved by RZN in Q3 2010



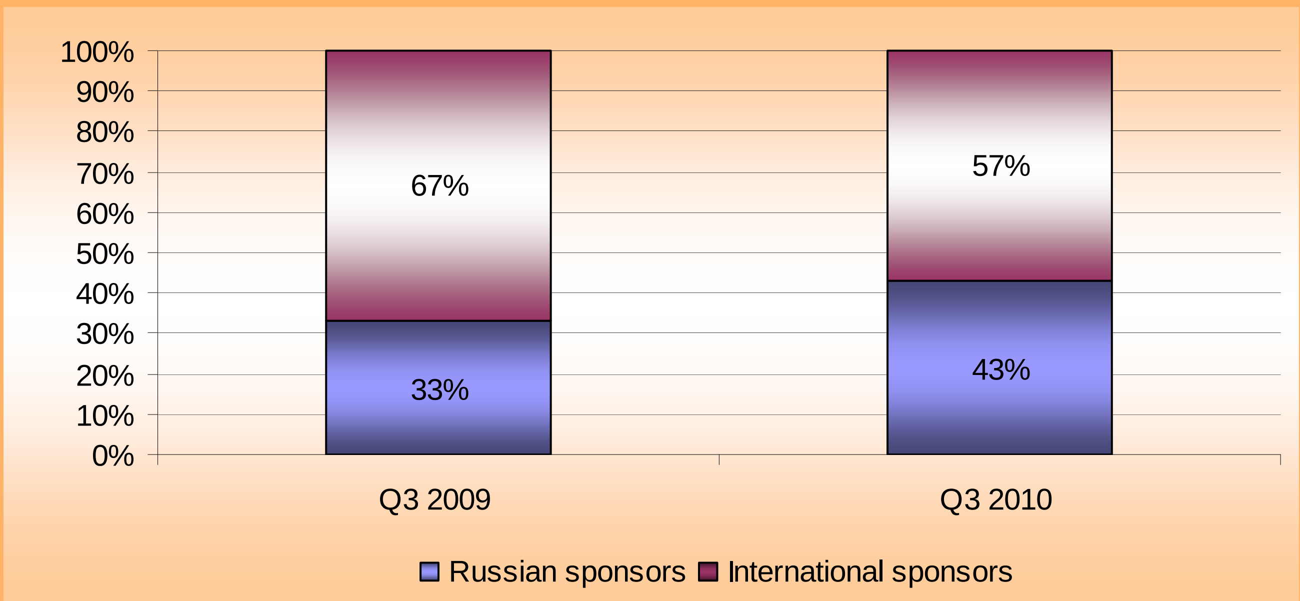
The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) changed significantly over the same point in 2009. Along with the decrease in the number of studies, the share of multinational multi-center clinical trials significantly descended from last year's figure and stood at 45% of the total number of clinical trials approved by RZN in the third quarter of 2010. The shares of the local trials and bioequivalence studies in Q3 2010 stood at 31% and 24% of the total number of studies, respectively, while they accounted to 25% and 14% in Q3 2009.

Figure 2. Clinical trials by type in Q3 2010



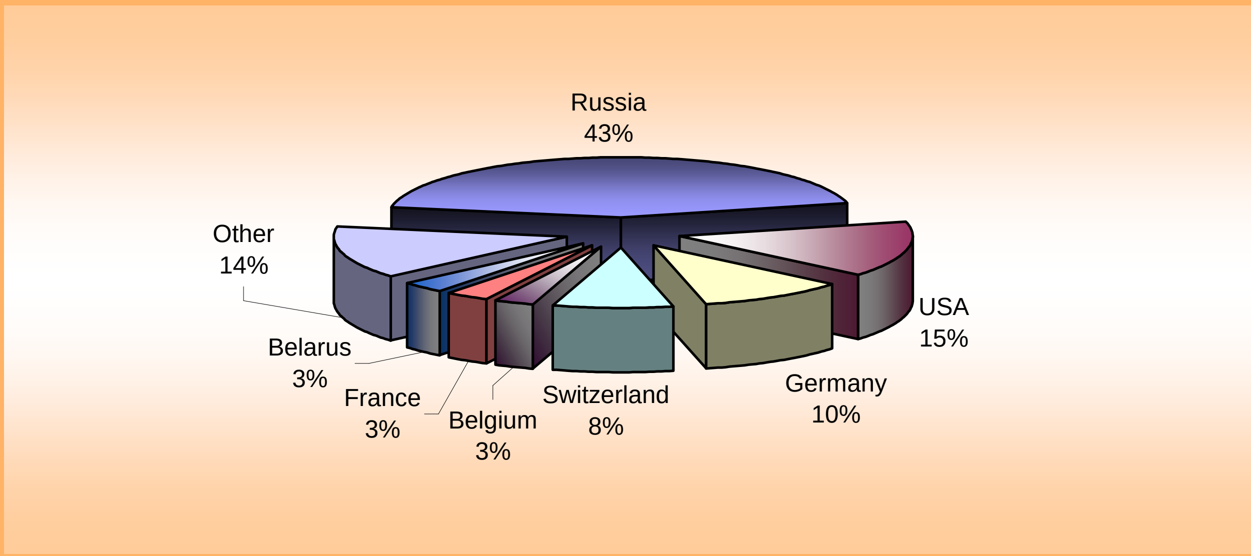
Although most of clinical trials in Russia are still being sponsored by foreign companies (57%), the ratio between foreign and domestic companies changed significantly comparing to the same period of the last year. Thus, shares of trials sponsored by foreign and domestics companies were 67% and 33% respectively in Q3 2009, while in the Q3 2010 share of trials sponsored by domestic companies increased up to 43%.

Figure 3. Russian and International sponsors in Q3 2010



Clinical trials in Russia in Q3 2010 were sponsored by companies from 17 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 (58) was initiated by Russian sponsors, American sponsors with 20 studies took the runner-up place, they are followed by German sponsors with 14 trials. 11 new trials were instigated by Swiss manufacturers, and the top six is concluded by French, Belgian and Belarusian sponsors each with four new studies in Q3 2010.

Figure 4. Countries presented on the Russian clinical trials market in Q3 2010

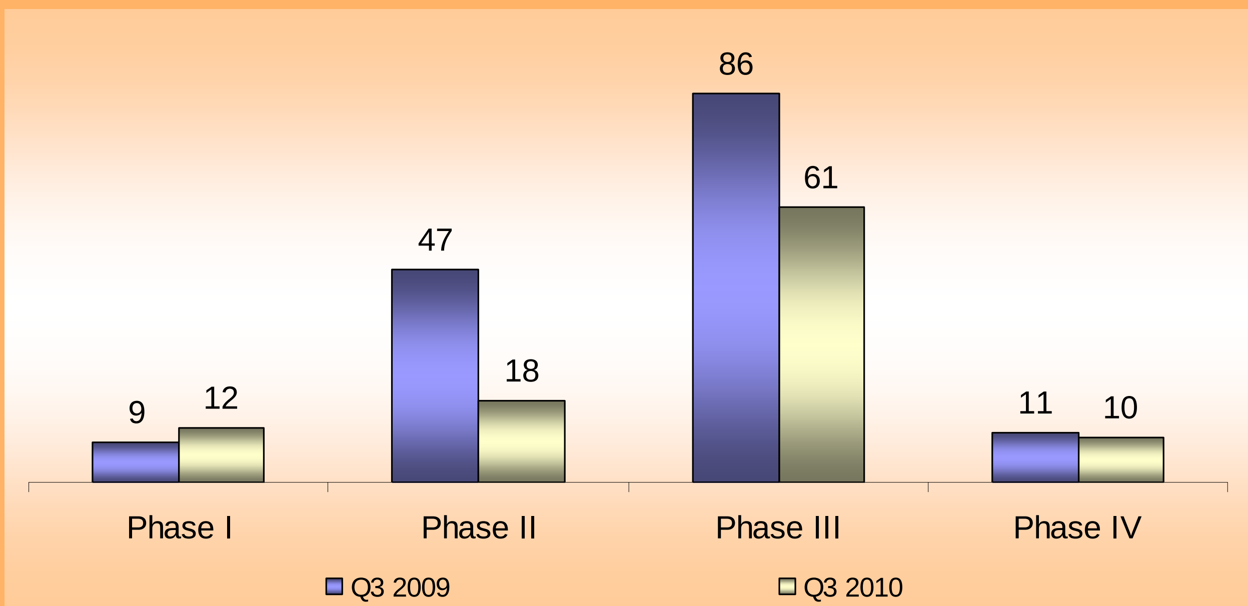


Canada, the United Kingdom, Israel, Sweden, Japan, Austria, Dania, Poland, Portugal and Croatia are represented among others.

Clinical trials by Phase

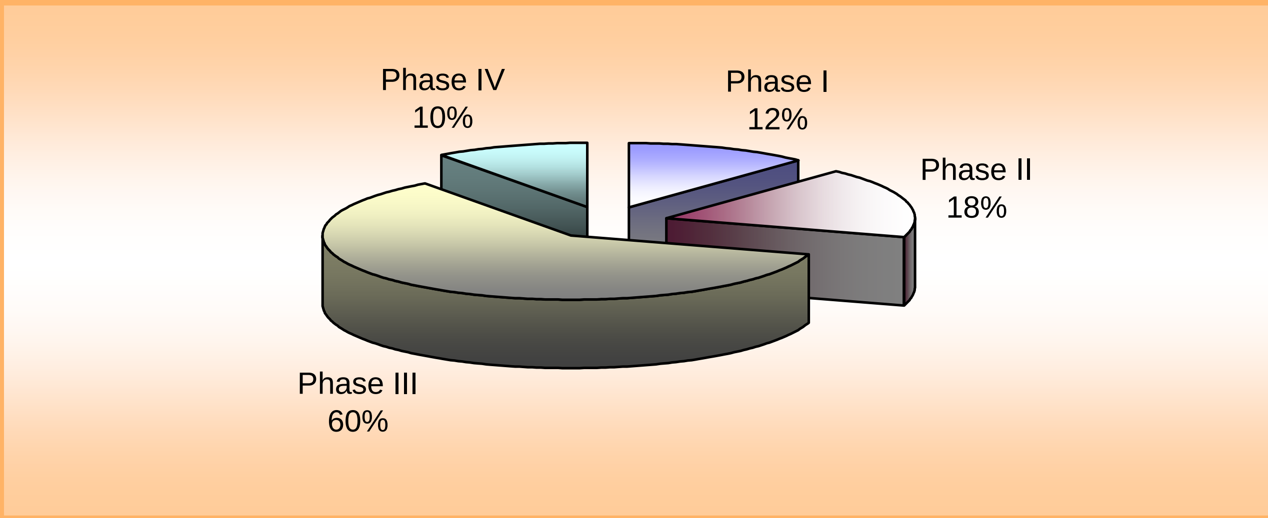
Twelve new Phase I clinical trials were launched in the third quarter of 2010; three trials more than in the corresponding quarter of last year. The number of the Phase II trials decreased from 47 trials in the third quarter of 2009 to 18 in the third quarter of 2010. The number of Phase III trials also demonstrated a decrease over last year number, down from 86 to 61 studies. The number of Phase IV trials remained almost unchanged – 10 trials in this period.

Figure 5. Clinical trials in Russia in Q3 2010 by phase



As shown in Figure 6, the share of Phase III trials in Q3 2010 stood at almost 60% of the total number of studies, the share of Phase II trials accounted at 18%, Phase IV trials stood at ten per cent, and the share of Phase I studies amounted to twelve per cent.

Figure 6. The proportions between study phases in Russia in Q3 2010



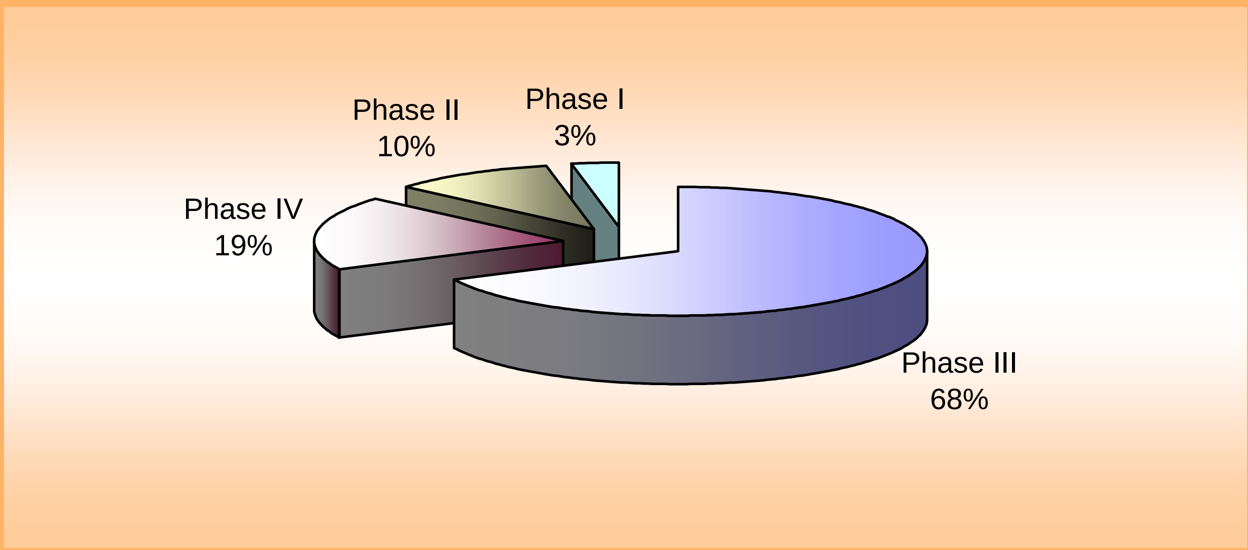
The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the third quarter of 2010 stood at 11,758 patients, a bit less than the last year number (11,956). The number of Phase III subjects increased by 24% from last year's figure.

Three hundred and sixty five subjects will be recruited in Phase I trials; 1,220 patients – in Phase II trials; 7,973 subjects – in Phase III studies and 2,200 patients will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is twenty four, the maximum number is 1,050.

The proportion of the number of patients between different Phases is shown on the Figure 7.

Figure 7. The number of patients in Q3 2010 by study phase



The duration of the shortest trial is three months, the longest one will last almost nine and a half years.

Rating of international sponsors

The Swiss *Novartis* sponsoring 7 new studies again is on the top of the heap in the third quarter of

2010. The German *Boehringer Ingelheim* with five new trials in Q3 2010 took the runner-up place. It is followed by British *Pantheon* and *GlaxoSmithKline* each sponsoring five new studies. The top five is concluded by French *sanofi-aventis* having four new studies in Q3 2010.

Top five international sponsors by the number of new studies in Q3 2010 are presented in Table 1.

Table 1. Top-5 international study sponsors in Q3 2010

№	Sponsor	No. of trials	No. of patients	No. of sites
1	Novartis	7	1051	70
2	Boehringer Ingelheim	5	1192	78
3	Pantheon	5	462	49
4	GlaxoSmithKline	5	310	24
5	sanofi-aventis	4	1098	62

Rating of Russian sponsors

The Russian pharmaceutical company ZAO *Rafarma* sponsoring five new clinical trials enrolling 260 patients in five sites, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the third quarter 2010.

NIOPIK with three new trials and 170 subjects in eight sites, took the runner-up place. It is followed by ZAO *Pharm-sintez* with three new trials but less patients number, and ZAO *Firn M* with two new studies. The top six is concluded by ZAO *Vector-Medica* and OOO *Niarmedik* with one new study each and the same number of patients and sites.

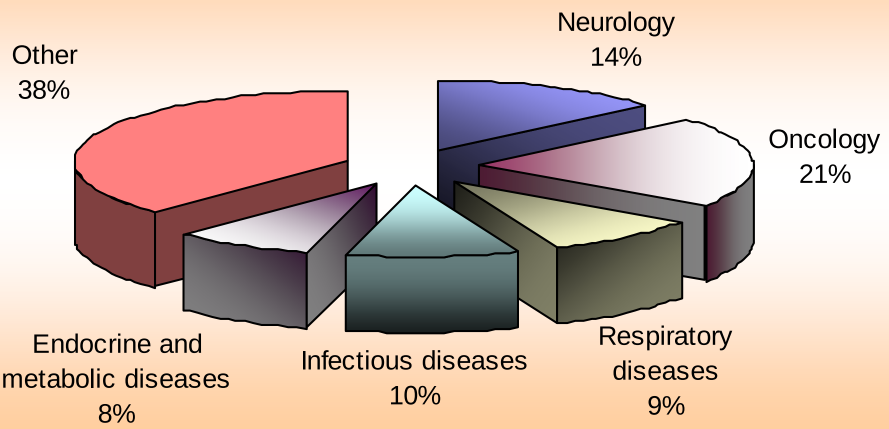
Table 2. Top-5 Russian study sponsors in Q3 2010

№	Sponsor	No. of trials	No. of patients	No. of sites
1	Rafarma	5	260	5
2	NIOPIK	3	170	8
3	Pharm-sintez	3	148	6
4	Firn M	2	160	3
5	Vector-Medica	1	200	2
6	Niarmedik	1	200	2

Therapeutic areas of clinical trials in Russia in Q3 2010

Sixty two per cent of the new studies in Q3 2010 were conducted in the five leading therapeutic areas. The maximum number of trials (20) was initiated in Oncology; 13 clinical trials in Neurology; 10 new studies in Infectious Diseases Endocrinology; nine – in Respiratory diseases and eight new Endocrinology studies were initiated in Q3 2010. The proportions between different therapeutic areas are shown in Figure 8.

Figure 8. Clinical trials in Russia in Q3 2010 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 22[1] new drugs during Q3 2010; only three of them are new molecular entities (NME); others are the new dosages, manufacturers or indications of the already marketed drugs. The Table 3 represents the three which were tested in clinical trials in Russia.

Table 3. New Drugs approved by FDA in Q3 2009 and tested in Russian sites

Approval date	Drug	Manufacturer
07/23/2010	Aricept (Donepezil Hydrochloride)	Eisai Inc
08/13/2010	Ella (Ulipristal Acetate)	Lab HRA Pharma
08/19/2010	Atazanavir Sulfate	Emcure Pharms
		Source: CDER FDA http://www.fda.gov/cder

No negative opinion was adopted for any of the drugs which had been approved earlier. Seven of the drugs which received positive opinions from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) were (or are being) tested in clinical trials in Russia (see Table 4).

Table 4. New Drugs approved by EMEA in Q3 2010 and tested in Russian sites

Approval date	Drug	Manufacturer
29/07/10	Twynsta(telmisartran/amlodipine)	Boehringer Ingelheim International GmbH
29/07/10	Arixtra (fondaparinux sodium)	Glaxo Group Ltd
29/07/10	M-M-RVAXPRO (measles, mumps and rubella vaccine live)	Sanofi Pasteur MSD
29/07/10	Viread (tenofovir disoproxil)	Gilead Sciences International Ltd
01/10/10	Mabthera (rituximab),	Roche Registration Ltd
01/10/10	Tasigna (nilotinib)	Novartis Europharm Ltd

[1] CDER FDA http://www.fda.gov/cder

01/10/10	Invega (paliperidone)	Janssen-Cilag International N.V.
Source: CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm		

FDA inspections

According to the FDA data as of November 12 2010, there were two FDA inspections conducted at the Russian investigative sites during Q3 2010. Both were performed at investigative sites in Saint-Petersburg with NAI – no actions indicated in conclusion.