

**Clinical Trials in Russia**  
**Orange Paper**  
**Year 2010**



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## Executive Summary

The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (Roszdravnadzor) and the Ministry of Health and Social Development of the Russian Federation (MoH) approved 492 new clinical trials of all types including local and bioequivalence studies during 2010, demonstrating a 15% decrease from the last year figure.

The number of the local clinical trials conducted in Russia by domestic and foreign sponsors increased from 144 to 161 clinical trials demonstrating a 12% increase over last year number. The number of multinational multi-center clinical trials decreased by 29% over 2009 and stood at 247 new studies in 2010.

The share of the local trials increased from 25% in 2009 to 33% of the total number of studies in 2010, and the share of bioequivalence studies also slightly increased from 15% to 17% of the total number of trials approved during Year 2010. The share of multinational multi-center clinical trials decreased from 60% to 50% of the total number of clinical trials approved in 2010.

Clinical trials in Russia in 2010 were sponsored by the companies from 31 countries. The maximum number of trials (210) was initiated by the Russian sponsors. American sponsors with 79 new studies took the runner-up place, they are followed by German sponsors with 41 trials, 33 new trials were instigated by Swiss companies, 23 trials were instigated by the UK sponsors and the group of leaders is concluded by French sponsors with 17 new studies in 2010.

The share of Phase III trials in 2010 stood at 58% of the total number of studies, the share of Phase II trials accounted at 22%, Phase IV trials stood at 9%, and the share of Phase I studies amounted to 11%.

The number of patients which are planned to be enrolled in the Phase II-IV trials launched in 2010 stood at 45,072, a 7% decrease from 2009 figure, when 48,521 patients were planned to be enrolled.

The Swiss pharmaceutical giant *Novartis* sponsoring 27 new studies is on the top of the heap in 2010. *GlaxoSmithKline* with 19 new trials in 2010 took the runner-up place; it is followed by *Patheon*, *Boehringer Ingelheim* and *Merck & Co.* each having nine new trials and differentiating only in the number of patients and sites.

The Russian company *ZAO "Rapharma"* sponsoring 10 new clinical trials, ranked number one among Russian sponsors by the number of new studies in 2010. It is followed by *OAO "STI-MED-SORB"*, *ZAO "Biocad"* and *FGUP "NIOPIK"* each having five new trials and number of patients and sites. The top five is concluded by *OOO "NPF Materia Medica"* having four new trials in 2010.

In 2010, 63% of new studies were initiated in nine therapeutic areas: the largest number of studies has been initiated in Oncology (81); Endocrine and metabolic diseases and Respiratory System (37); Circulatory System (29); Infectious and parasitic diseases (28); Nervous System (27); Mental and behavioural disorders (25); Diseases of the musculoskeletal system (24) and 22 new clinical trials were dedicated to the Diseases of the genitourinary system.

Pavlov State Medical University of St. Petersburg with 79 new studies ranked the number one in the number of trials in 2010; it is followed by the Russian Oncology Scientific Center n/a N.N.Blokhin (47 studies); I.M. Sechenov First Moscow State Medical University (46 studies); the Russian State Medical University (39 studies) and the top five is concluded by the Kirov Military Medical Academy with 37 new trials in 2010.

Twenty three inspections were conducted by Roszdravnadzor in Russia during 2010, 15 violations of the clinical practice were found, seven of them were qualified as critical. Six FDA inspections were conducted in the Russian investigative sites during 2010, all ended with NAI result – no actions indicated.



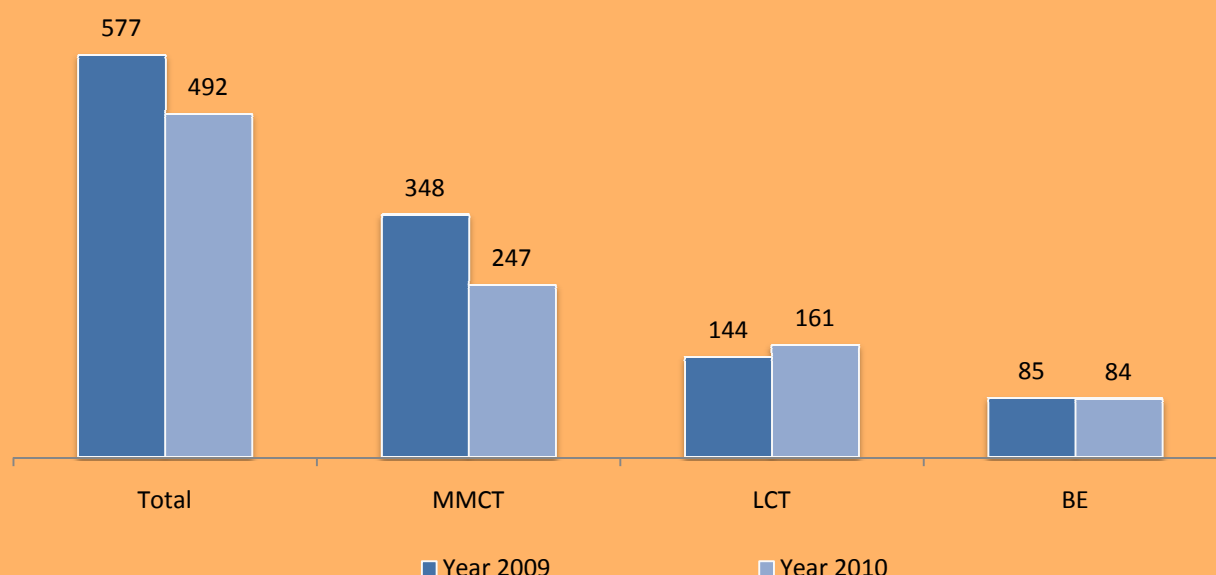
## Clinical Trials by Type and Manufacturing Country

The Roszdravnadzor (before 1 September 2010) and MoH (after 1 September 2010) approved 492 new clinical trials of all types including local and bioequivalence studies during 2010, demonstrating a 15% decrease from the last year figure. As shown in the Figure 1, the main contribution into the total number of studies is still made by multinational multi-center clinical trials (MMCT), even though the number of these studies decreased by 29% over 2009 and stood at 247 new studies in 2010.

The number of the local clinical trials (LCT) conducted in Russia by domestic and foreign sponsors increased from 144 to 161 clinical trials demonstrating a 12% increase over last year number.

The number of bioequivalence studies (BE) in 2010 stood at 84 new trials, one study less than in 2009.

**Figure 1. Clinical trials in Russia in 2010**

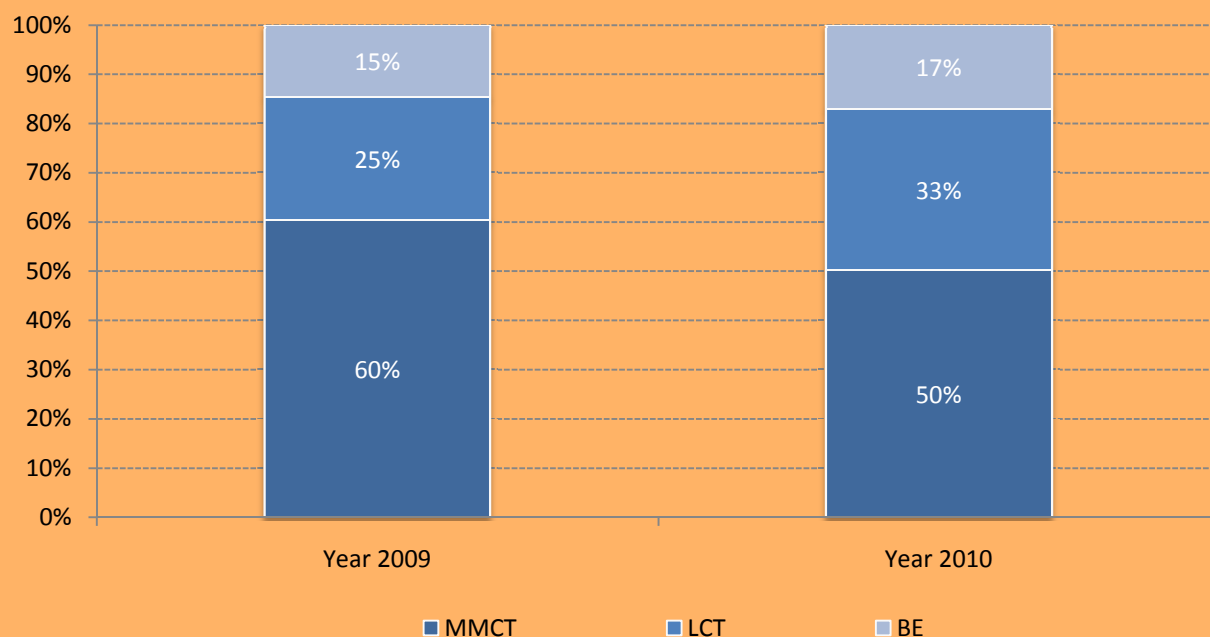


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) changed since 2009.

The share of multinational multi-center clinical trials decreased from 60% to 50% of the total number of clinical trials approved in 2010.

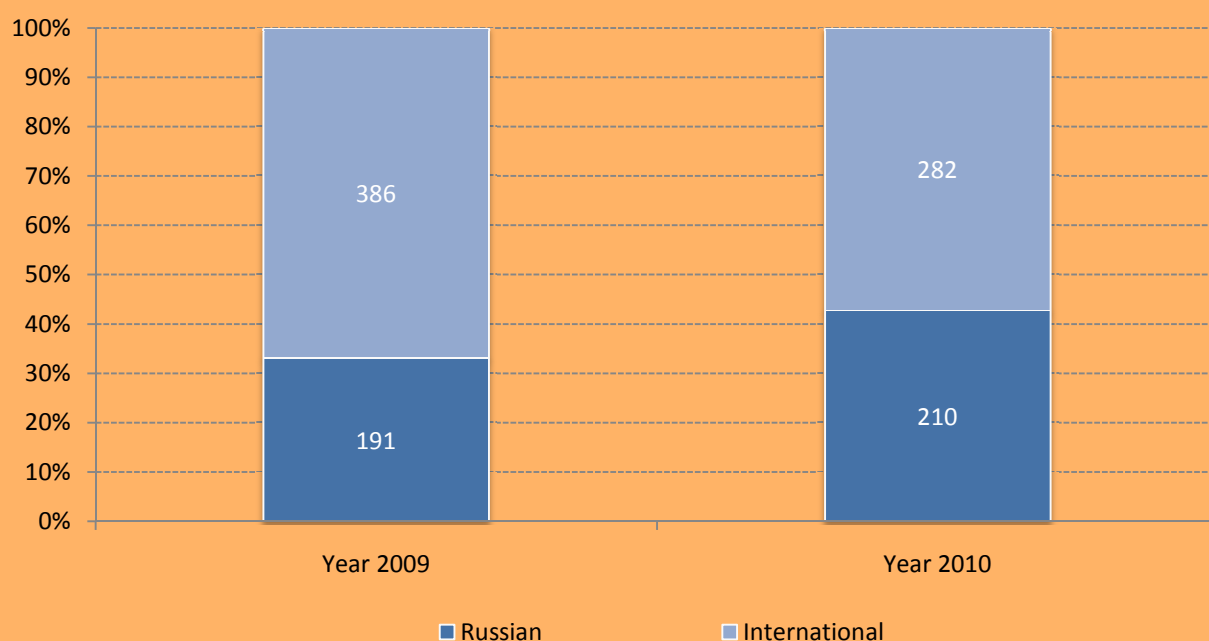
The share of the local trials increased from 25% in 2009 to 33% of the total number of studies in 2010, and the share of bioequivalence studies also slightly increased from 15% to 17% of the total number of trials approved during Year 2010.

**Figure 2. Clinical trials by type in 2010**



The major share of clinical trials in Russia is sponsored by foreign companies, in 2010 they received 282 study approvals, or 57% of the total number of new studies in 2010. The share of studies of local manufacturers increased from 33% in 2009 to 43% in 2010, from 191 to 210 studies, respectively.

**Figure 3. Russian and International sponsors in 2010**

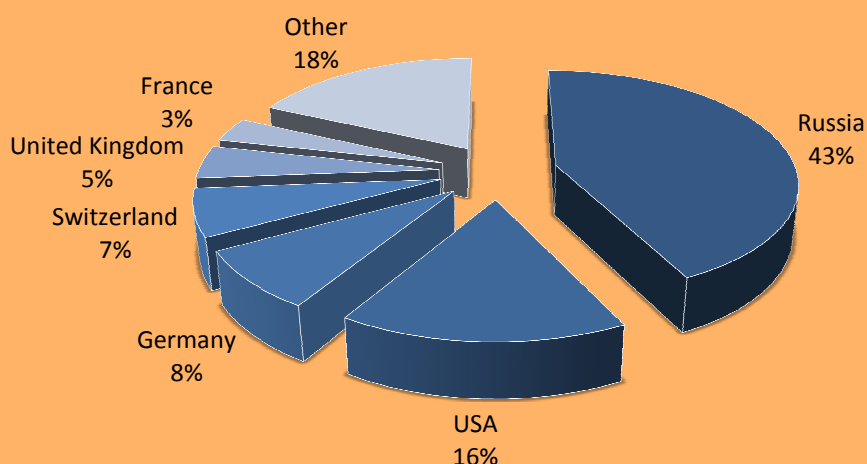


Clinical trials in Russia in 2010 were sponsored by the companies from 31 countries. Figure 4 demonstrates the input of the leading countries of sponsor's origin into the total number of clinical



trials. The maximum number of trials (210) was initiated by the Russian sponsors. American sponsors with 79 new studies took the runner-up place, they are followed by German sponsors with 41 trials, 33 new trials were instigated by Swiss companies, 23 trials were instigated by the UK sponsors and the group of leaders is concluded by French sponsors with 17 new studies in 2010.

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



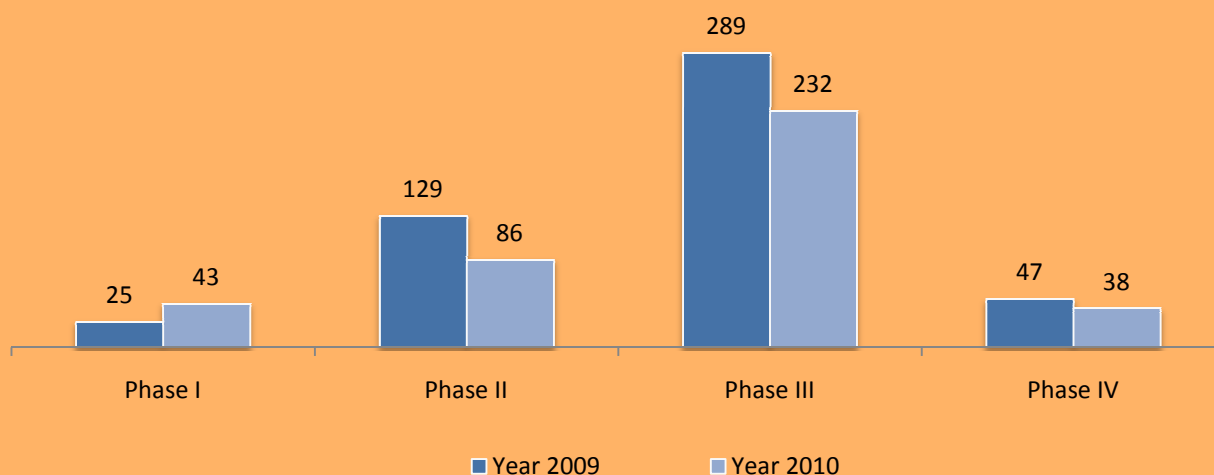
Among others are: Denmark (12); Austria (9); Japan (8); Belgium and Canada (7 each); Israel and Sweden (6 studies each); Italy and the Netherlands (4 each); Belarus, India, Spain, Hungary, Ireland, Kazakhstan, Korea and Portugal have 2 new studies each; and Bulgaria, Vietnam, China, Norway Poland, Ukraine, Finland and Croatia each started one new study in 2010.

### Clinical trials by Phase

Forty three new Phase I clinical trials were launched in 2010, which is 18 trials more than during the year 2009. The number of the Phase II trials fell by one-third and stood at 86 new studies in 2010.

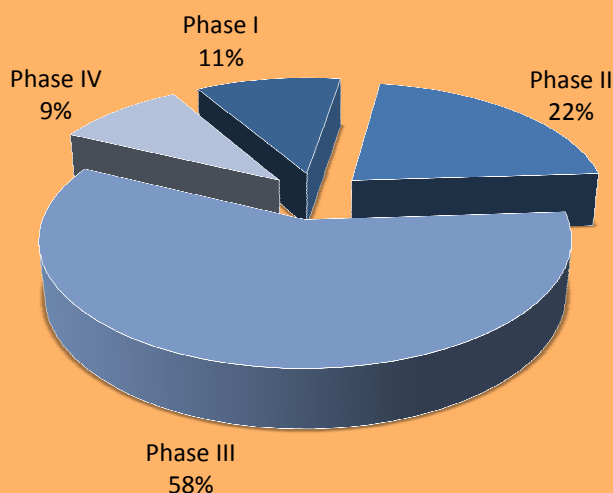
The number of Phase III trials also decreased from 289 to 232 studies, almost 20% less than in 2009. Phase IV trials also demonstrated a 20% decrease (from 47 in 2009 to 38 studies in 2010).

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



As shown in Figure 6, the share of Phase III trials in 2010 stood at 58% of the total number of studies, the share of Phase II trials accounted at 22%, Phase IV trials stood at 9%, and the share of Phase I studies amounted to 11%.

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

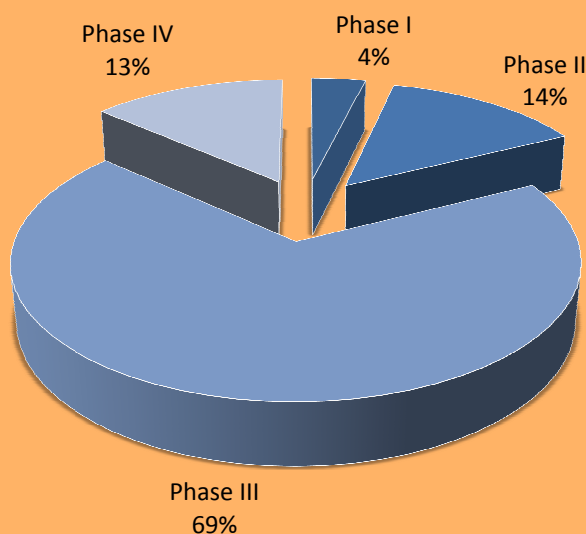


The number of patients which are planned to be enrolled in the Phase II-IV trials launched in 2010 stood at 45,072, a 7% decrease from 2009 figure, when 48,521 patients were planned to be enrolled.

One thousand six hundred and seventy nine subjects will be recruited in Phase I trials; 6,261 patients – in Phase II trials; 31,062 subjects – in Phase III studies and 6,070 patients will be enrolled in Phase IV studies.

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

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



## Rating of international sponsors

The Swiss pharmaceutical giant *Novartis* sponsoring 27 new studies is on the top of the heap in 2010. *GlaxoSmithKline* with 19 new trials in 2010 took the runner-up place; it is followed by *Patheon*, *Boehringer Ingelheim* and *Merck & Co.* each having nine new trials and differentiating in the number of patients and sites.

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

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

<i>No</i>	<i>Company Name</i>	<i>No. studies</i>	<i>No. patients</i>	<i>No. sites</i>
1	Novartis	27	3 804	259
2	GlaxoSmithKline	19	4 360	187
3	Patheon	9	1 602	109
4	Boehringer Ingelheim	9	1 410	98
5	Merck & Co.	9	726	46

## Rating of Russian sponsors

The Russian company *ZAO "Rapharma"* sponsoring 10 new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in 2010. *OAO "STI-MED-SORB"* with five new trials took the runner-up place.

It is followed by *ZAO "Biocad"* and *FGUP "NIOPIK"* also having five new trials, but fewer number of patients and sites. The top five is concluded by *OOO "NPF Materia Medica"* having four new trials in 2010.

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

<i>No</i>	<i>Company Name</i>	<i>No. studies<sup>1</sup></i>	<i>No. patients</i>	<i>No. sites</i>
1	Rapharma	10	760	10
2	STI-MED-SORB	5	470	7
3	Biocad	5	427	20
4	NIOPIK	5	208	13
5	Materia Medica	4	714	24

<sup>1</sup> Excluding BE studies

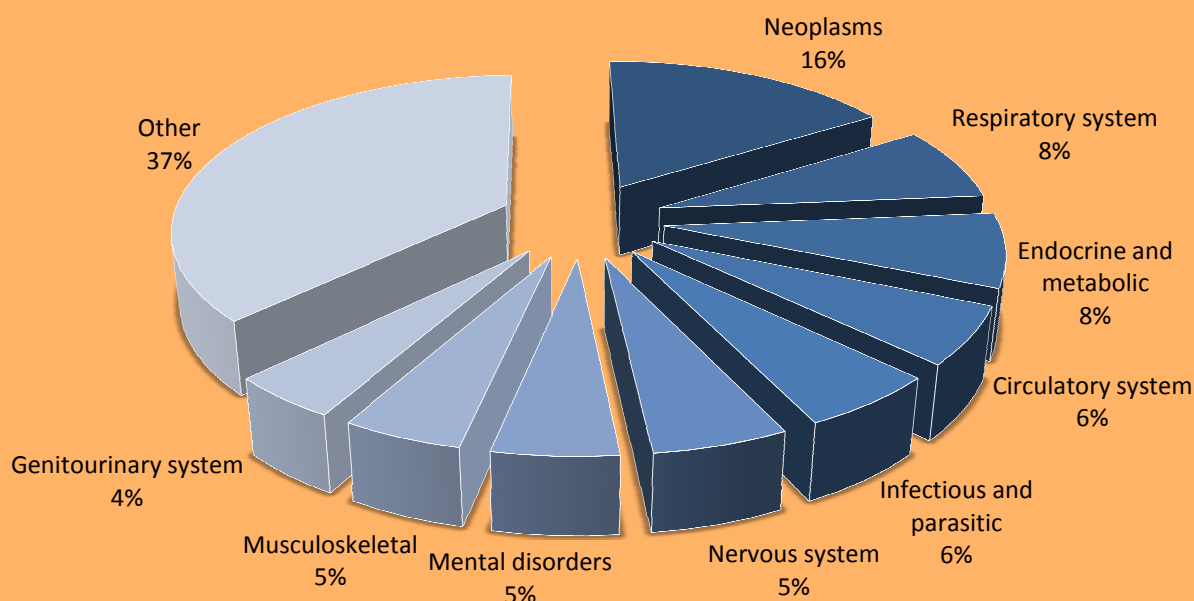


## Therapeutic areas of clinical trials in Russia in 2010

In 2010, 63% of new studies were initiated in nine therapeutic areas: the largest number of studies has been initiated in Oncology (81); 37 new studies were instigated in Endocrine and metabolic diseases and Respiratory System; 29 studies - in Circulatory System; 28 studies – in Infectious and parasitic diseases; 27 studies in the diseases of the Nervous System; 25 – in Mental and behavioural disorders; 24 – in the Diseases of the musculoskeletal system and connective tissue and 22 new clinical trials were dedicated to the Diseases of the genitourinary system.

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

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



## Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 101 new drugs during Year 2010; 21 of them are really new molecular entities; others are new dosages, manufacturers or indications of the already marketed drugs. Twenty of 101 drugs were studied in clinical trials conducted in Russia.

The Table 3 represents drugs which were approved by FDA and were being tested in clinical trials in Russia in Q4 2010 (Q1 – Q3 data is presented in the previous issues of SynRG Orange Paper).

**Table 3. New drugs approved by FDA in Q4 2010 and tested in Russian sites**

<i>Appr.date</i>	<i>Drug (active ingredient)</i>	<i>Manufacturer</i>
19\10\2010	Pradaxa (Dabigatran Etexilate Mesylate)	Boehringer Ingelheim
28\10\2010	Latuda (Lurasidone Hydrochloride)	Sunovion
29\10\2010	Teflaro (Ceftaroline Fosamil)	Cerexa
04\11\2010	Cymbalta (Duloxetine Hydrochloride)	Lilly
05\11\2010	Kombiglyze Xr (Metformin Hydrochloride; Saxagliptin)	Bristol-Myers Squibb

15\11\2010	Halaven (Eribulin Mesylate)	Eisai
23\11\2010	AXIRON (Testosterone)	Lilly
<i>Source: FDA</i>		

During the year 2010 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) approved 51 applications to market drugs in the EU. Negative opinion was adopted for two drugs. Twenty two of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

The Table 4 represents those of them which were, or are being tested in clinical trials in Russia in Q4 2010 (Q1 – Q3 data is presented in the previous issues of SynRG Orange Paper).

**Table 4. New Drugs approved by EMA in Q4 2010 and tested in Russian sites**

<i>Apr. date</i>	<i>Drug (active ingredient)</i>	<i>Manufacturer</i>
18\10\2010	Sprycel (dasatinib)	Bristol-Myers Squibb
18\10\2010	Sutent (sunitinib)	Pfizer
15\11\2010	Plavix (clopidogrel)	Sanofi
13\12\2010	Xeplion (paliperidone)	Janssen-Cilag
<i>Source: EMA</i>		

## Investigative sites

Forty five new sites were approved by Roszdravnadzor during 2010, and the total number of sites in Russia by the end of the year accounted to 1,076 sites.

As shown in Table 5, “the capitals”, i.e. Moscow and St. Petersburg are still the leaders in the numbers of sites.

**Table 5. Top ten Russian regions in the number of sites**

<i>No</i>	<i>Region</i>	<i>No. Sites</i>
1	Moscow	227
2	St. Petersburg	156
3	Novosibirsk region	41
4	Moscow region	37
5	Sverdlovsk region	30
6	Nizhegorod region	28
7	Tatarstan region	26
8	Yaroslavl region	25
9	Krasnodar region	21
10	Rostov region	20



Pavlov State Medical University of St. Petersburg with 79 new studies ranked the number one in the number of trials in 2010; it is followed by the Russian Oncology Scientific Center n/a N.N.Blokhin (47 studies); I.M. Sechenov First Moscow State Medical University (46 studies); the Russian State Medical University (39 studies) and the top five is concluded by the Kirov Military Medical Academy with 37 new trials in 2010.

**Table 6. Top five Russian sites in 2010**

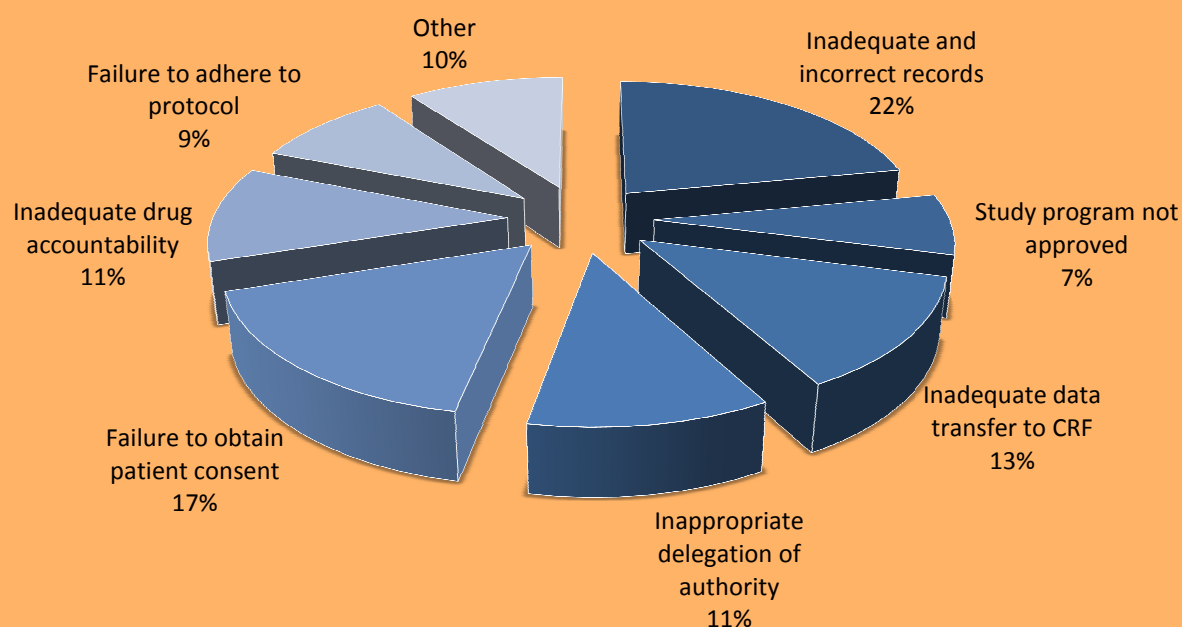
1	Pavlov State Medical University of St. Petersburg	79
2	Russian Oncology Scientific Center n/a N.N.Blokhin	47
3	I.M. Sechenov First Moscow State Medical University	46
4	Russian State Medical University	39
5	Kirov Military Medical Academy	37

### Roszdraznadzor inspections

According to the annual Roszdraznadzor report<sup>1</sup>, 23 inspections were conducted in nine Russian cities during 2010: Arkhangelsk, Izhevsk, Kemerovo, Moscow, Nizhny Novgorod, Novosibirsk, Rostov-on-Don, St. Petersburg and Ufa. Fifteen violations of the clinical practice were found, seven of them were qualified as critical.

The analysis of findings is shown in the Figure below.

**Figure 9. Findings during Roszdraznadzor inspections in 2010**



### FDA inspections

According to the FDA data, six FDA inspections were conducted in the Russian investigative sites during 2010, five in St. Petersburg and one in Leningrad region. All inspections ended with NAI result – no actions indicated.

<sup>1</sup> <http://www.roszdraznadzor.ru/i/upload/files/1299135828.15741-25515.doc>