

**Clinical Trials in Russia**  
**Orange Paper**  
**Year 2008**





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## Executive Summary

The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (alias RosZdravNadzor, RZN) approved 615 new clinical trials during 2008, a 9% increase over last year's figure. The main contribution (59%) is made by multinational multi-center clinical trials, though their number decreased by 1.2% over 2007 and stood at 364 new studies in 2008.

Clinical trials in Russia in 2008 were sponsored by the pharmaceutical manufacturers from 36 countries. The maximum number of trials (201) was initiated by Russian sponsors. American sponsors (145 trials) took the runner-up place, they are followed by the German (60) and the UK (43) companies, and the top five is concluded by the Swiss sponsors with 34 new trials.

Thirty eight new Phase I clinical trials were launched in 2008; which is six trials increase over last year. The number of the Phase II trials slightly decreased from 158 trials in 2007 to 152 in 2008. The number of Phase III trials demonstrated the biggest increase, 21% up over last year, from 232 to 282 studies. The number of Phase IV trials slightly increased from 60 in 2007 to 62 in 2008.

More than sixty thousand patients are planned to be enrolled in the Phase I-IV trials instigated in 2008.

The Swiss pharmaceutical giant *Novartis* sponsoring 22 new studies was on the top of the pile by the number of new trials started in 2008. The French sanofi-aventis instigating 21 new trials in 2008 took the runner-up place, it is followed by the UK *GlaxoSmithKline* with the maximum number of patients – more than eight thousand.

The Russian *Valenta*, sponsoring 14 new clinical trials ranked number one among domestic pharmaceutical manufacturers by the number of new studies in 2008. ZAO *Biocad* with 11 new trials took the runner-up place. It is followed by OAO *Sintez* which instigated 9 new studies in 2008.

St. Petersburg State Medical University n/a Pavlov ranked number one among the Russian investigative centers by the number of new studies (104) in 2008. Russian Scientific Oncology Center n/a Blokhin with 84 new studies took the runner-up place. It is followed by the St. Petersburg Military Medical Academy n/a Kirov accommodating 78 new trials in 2008.

Almost three-fourth of the new studies in 2008, or 73%, were instigated in the following seven therapeutic areas: Oncology (91); Circulatory System (87); Respiratory System (60); Endocrine and metabolic diseases (57); Musculoskeletal System (54); Infectious diseases (51) and diseases of the Nervous System (50).

As of 12 November 2008, there were 946 hospitals entitled to conduct clinical trials in Russia. Ninety two new sites were designated by the RZN during 2008.

Thirteen FDA inspections were conducted in the Russian investigative sites during 2008: during seven of them no objectionable conditions or practices were found, and six inspections resulted in VAI (Voluntary Action Indicated).

## Clinical Trials by Type and Manufacturing Country

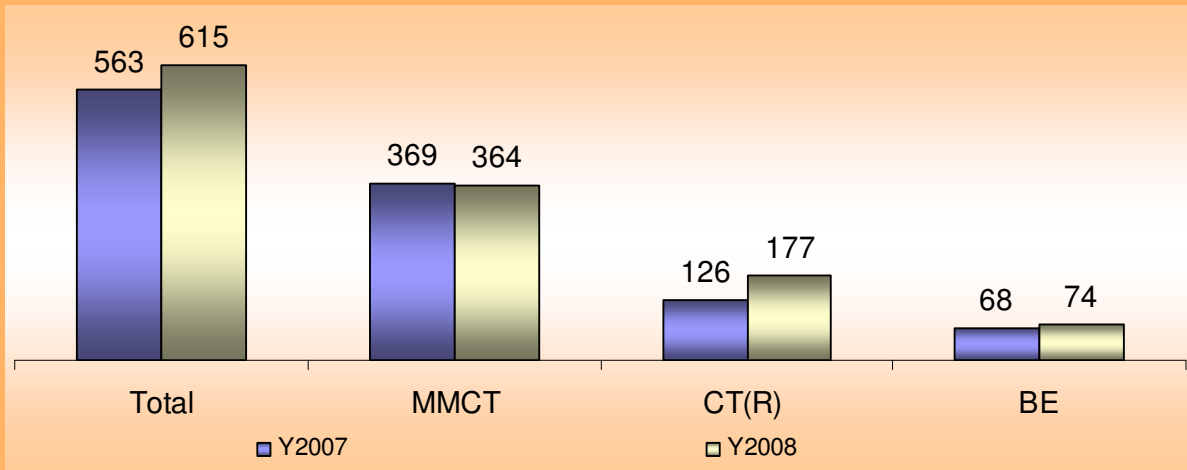
The RZN approved 615 new clinical trials of all types including local and bioequivalence studies during 2008; demonstrating a 9% increase over last year. As shown in the Figure 1, the main contribution into the total number of studies is still made by multinational multi-center clinical trials (presented as MMCT in Figure 1), even though the number of these studies slightly decreased by 1.2% over 2007 and stood at 364 new studies in 2008.

The number of the local clinical trials conducted in Russia by domestic and foreign sponsors (the CT(R) bar in the Figure 1) is up from 126 to 177 clinical trials demonstrating a notable 40% increment over 2007.



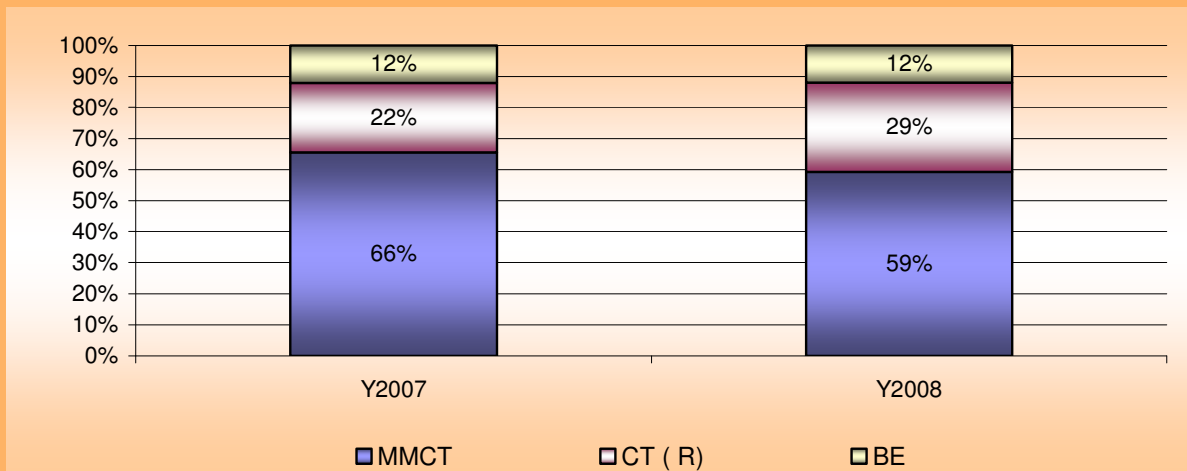
The number of bioequivalence studies (BE in Figure 1) in 2008 stood at 74 new trials, a 9% increase from last year's figure.

**Figure 1. Clinical trials approved by RZN in 2008**



The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) did not change significantly over 2007 figures. The share of multinational multi-center clinical trials slightly decreased from last year's figure and stood at 59% of the total number of clinical trials approved by RZN in 2008. The share of the local trials in 2008 stood at 29% of the total number of studies, respectively, while it accounted to 22% in 2007. The share of bioequivalence studies remained the same – 12% of the total number of trials approved during Y2008.

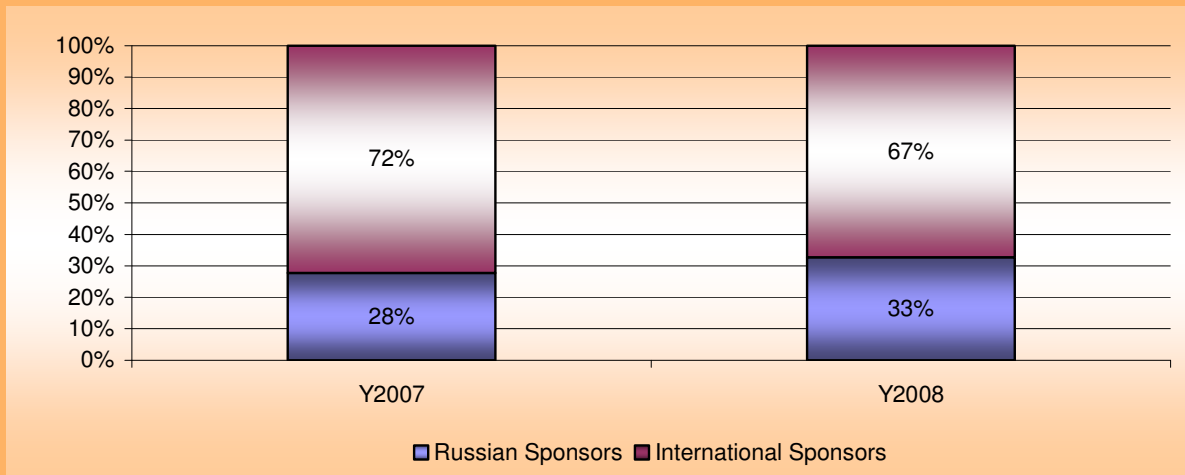
**Figure 2. Clinical trials by type in 2008**



The lion's share of clinical trials in Russia is still being sponsored by foreign companies. Whilst their share slightly decreased from 72% to 67%, their number is up from 407 in 2007 to 414 new studies in 2008, since the number of local studies grew faster during the period. The number of clinical trials initiated by the Russian sponsors, including bioequivalence studies, rose from 156 to 201, their share also increased from 28% to 33%.

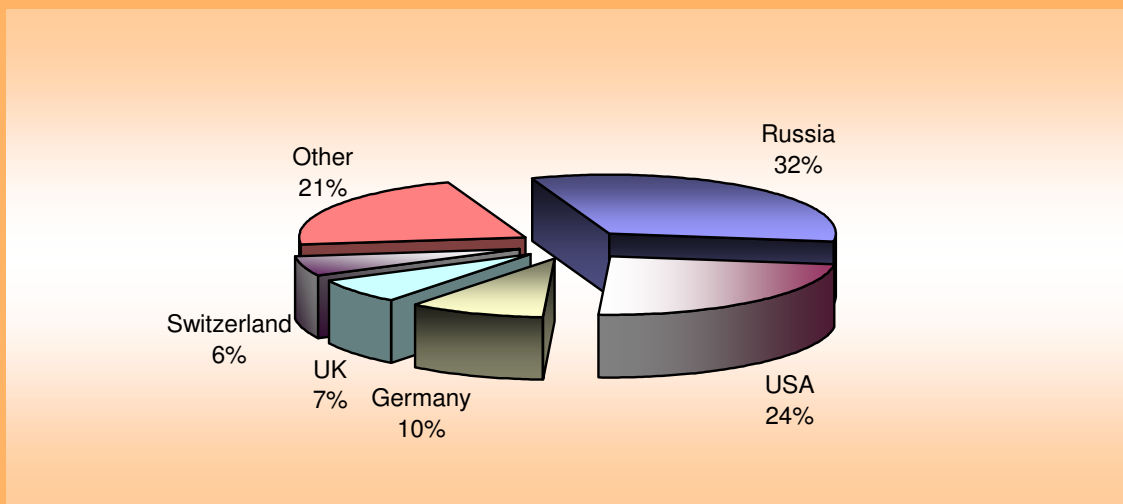


**Figure 3. Russian and International sponsors in 2008**



Clinical trials in Russia in 2008 were sponsored by the companies from 36 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 (201) was initiated by the Russian sponsors, American sponsors with 145 studies took the runner-up place, they are followed by the German sponsors with 60 trials, 43 new trials were instigated by the UK companies, and the top five is concluded by the Swiss sponsors with 34 new studies in 2008.

**Figure 4. Countries presented on the Russian clinical trials market in 2008**

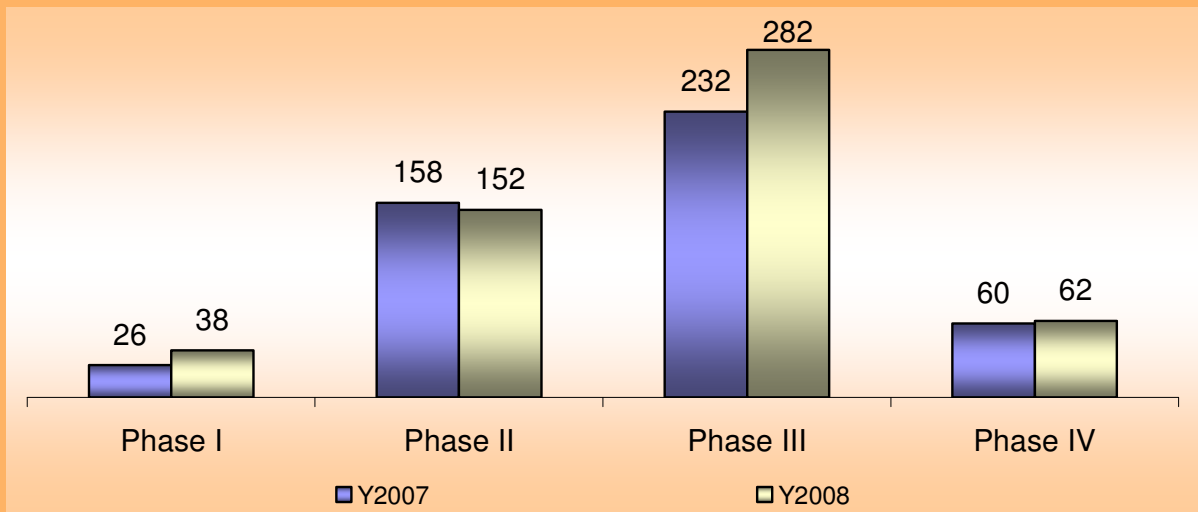


Austria, Belgium, Israel, Spain, Italy, Canada, the Netherlands, Norway, Pakistan, Portugal, Serbia, Sweden, Japan, Ukraine, as well as Vietnam and Puerto-Rico are represented among others.

### Clinical trials by Phase

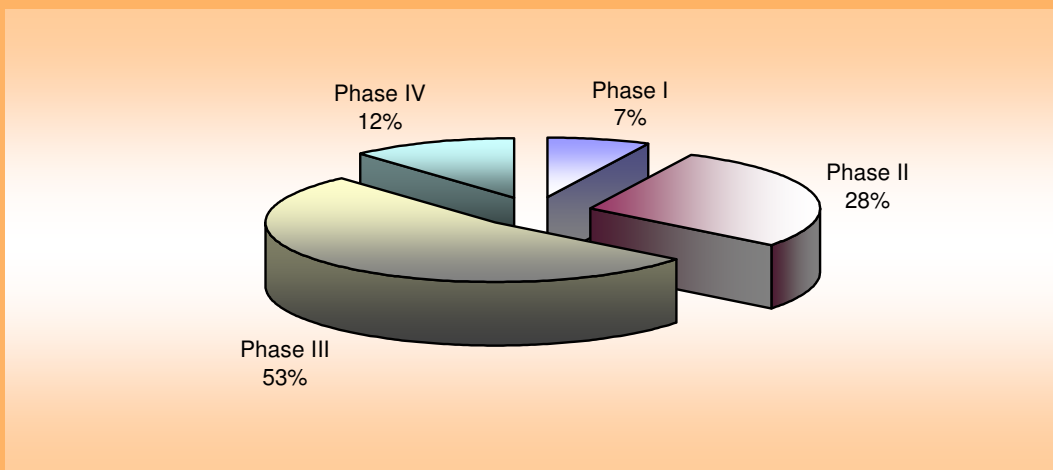
Thirty eight new Phase I clinical trials were launched in 2008, which is 6 trials more than during the year 2007. The number of the Phase II trials slightly decreased from 158 trials in 2007 to 152 in 2008. The number of Phase III trials demonstrated the substantial 21% increase over last year number, up from 232 to 282 studies. The number of Phase IV trials slightly increased from 60 in 2007 to 62 in 2008.

**Figure 5. Clinical trials in Russia in 2008 by phase**



As shown in Figure 6, the share of Phase III trials in 2008 stood at 53% of the total number of studies, the share of Phase II trials accounted at 28%, Phase IV trials stood at 12%, and the share of Phase I studies amounted to seven per cent.

**Figure 6. The proportions between study phases in Russia in 2008**



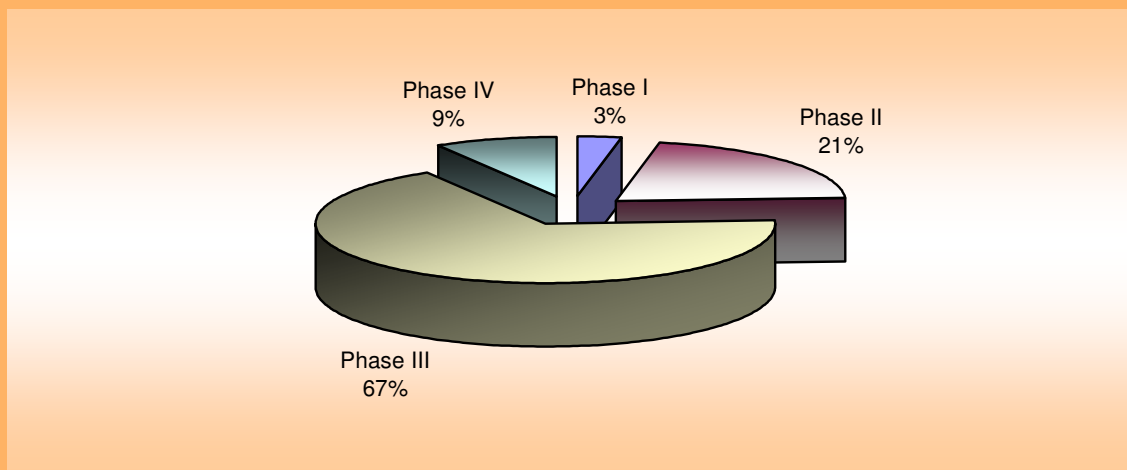
The number of patients which are planned to be enrolled in the Phase II-IV trials launched in 2008 stood at 60,643 patients.

1,770 subjects will be recruited in Phase I trials; 12,850 patients – in Phase II trials; 40,767 subjects – in Phase III studies and 5,256 patients will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is three, the maximum number is 5,500.

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

**Figure 7. The number of patients in 2008 by study phase**



The duration of the shortest trial is three month; of the longest one – seven years.

### Rating of international sponsors

The Swiss pharmaceutical giant *Novartis* sponsoring 22 new studies is on the top of the heap in 2008. The French *sanofi-aventis* with 21 new trials in 2008 took the runner-up place, it is followed by the UK *GlaxoSmithKline* and two American pharmaceutical manufacturers – *Pfizer* and *Merck & Co.* with 18 trials each, and different number of patients.

Top five international sponsors by the number of new studies in 2008 are presented in Table 1.

**Table 1. Top-5 international study sponsors in 2008**

No	Sponsor	No. of trials	No. of patients	No. of sites
1	Novartis	22	1,551	148
2	sanofi-aventis	21	3,409	221
3	GlaxoSmithKline	20	8,029	153
4	Pfizer	18	1,305	79
5	Merck & Co.	18	1,196	74

### Rating of Russian sponsors

The Russian company *ZAO Valenta Pharmaceutica* sponsoring 14 new clinical trials enrolling more than thousand patients in 24 sites, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in 2008.

*ZAO Biocad* with 11 new trials and 630 subjects in 64 sites, took the runner-up place. It is followed by *OAO Sintez*, *OAO Nizhpharm* and *FGUP NIOPIK*.

**Table 2. Top-5 Russian study sponsors in 2008**

No	Sponsor	No. of trials	No. of patients	No. of sites
1	Valenta	14	1,060	24
2	Biocad	11	630	64
3	Sintez	9	526	12



4	Nizhpharm	9	456	10
5	NIOPIK	8	295	24

### Rating of Russian investigative sites

St. Petersburg State Medical University n/a Pavlov ranked number one among the Russian investigative centers by the number of new studies (104) in 2008. Russian Scientific Oncology Center n/a Blokhin with 84 new studies took the runner-up place. It is followed by the St. Petersburg Military Medical Academy n/a Kirov accommodating 78 new trials in 2008.

The leading ten Russian sites by the number of new trials in 2008 are presented in Table 3.

**Table 3. The leading Russian sites by the number of trials in 2008**

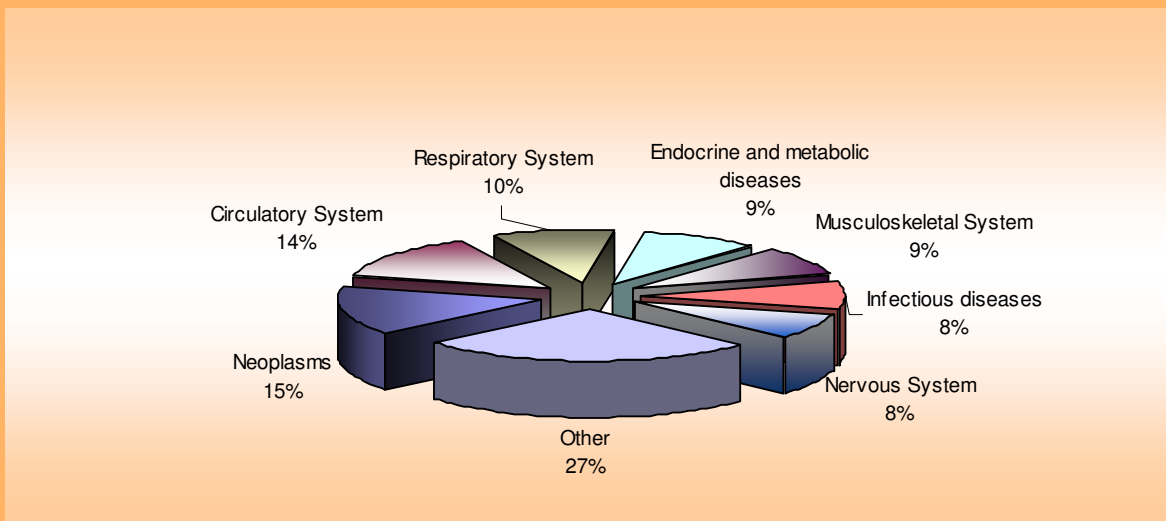
№	Name	КМ
1	St. Petersburg State Medical University n/a Pavlov	104
2	Russian Scientific Oncology Center n/a Blokhin	82
3	St. Petersburg Military Medical Academy n/a Kirov	78
4	Clinical Hospital #6 FMBA of Russia	73
5	Moscow Medical Academy n/a Sechenov	67
6	Russian State Medical University	65
7	Moscow State Medical Dental University	56
8	St. Petersburg State Medical Academy n/a Mechnikov	54
9	Moscow City Clinical Hospital #4	50
10	Russian Cardiology Scientific Complex of Rosmedtechnology	47

### Therapeutic areas of clinical trials in Russia in 2008

During 2008 about three-fourth of the new studies in 2008, or 73%, was conducted in seven therapeutic areas. The maximum number of trials (91) were initiated in Oncology; 87 clinical trials in Circulatory System diseases; 60 studies were targeted at Respiratory System diseases; 57 – in Endocrine and metabolic diseases; 54 studies in Musculoskeletal System diseases; 51 studies were initiated in Infectious diseases, and 50 new studies were instigated in the diseases of the Nervous System. The proportions between different therapeutic areas are shown in Figure 8.



**Figure 8. Clinical trials in Russia in 2008 by therapeutic area**



### Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 81<sup>1</sup> new drugs during Year 2008; 22 of them are new molecular entities; others had new dosages, manufacturers or indications of the already marketed drugs. Thirty four drugs were studied in Russia.

The Table 4 represents those of them which were, or are being tested in clinical trials in Russia in Q4 2008 (Q1 – Q3 data is presented in the previous issues of SynRG Orange Paper).

**Table 4. New Drugs approved by FDA in Q4 2008 and tested in Russian sites**

Approval date	Drug	Manufacturer
28-10-08	Vimpat (Lacosamide)	Schwarz Biosciences
31-10-08	Toviaz (Fesoterodine Fumarate)	Pfizer
31-10-08	Apriso (Mesalamine)	Salix
20-11-08	Promacta (Eltrombopag Olamine)	GlaxoSmithKline
20-11-08	Tapentadol	Janssen
05-12-08	Arimidex (Anastrozole)	Astrazeneca
12-12-08	Efavirenz	Aurobindo Pharma
15-12-08	Trilipix (Fenofibric Acid)	Abbott
19-12-08	Abacavir Sulfate; Lamivudine	Aurobindo Pharma
19-12-08	Casodex (Bicalutamide)	AstraZeneca
24-12-08	Degarelix	Ferring
24-12-08	Nexterone (Amiodarone Hydrochloride)	Prism Pharma

Source: CDER FDA <http://www.fda.gov/cder>

During the year 2008 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) reviewed 98<sup>2</sup> applications to market drugs in the EU. Negative opinion was adopted for thirteen drugs. Thirty five of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

<sup>1</sup> CDER FDA <http://www.fda.gov/cder>

<sup>2</sup> CHMP EMA <http://www.emea.europa.eu/index/indexh1.htm>



The Table 5 represents those of them which were, or are being tested in clinical trials in Russia in Q4 2008 (Q1 – Q3 data is presented in the previous issues of SynRG Orange Paper).

**Table 5. New Drugs approved by EMEA in Q4 2008 and tested in Russian sites**

Approval date	Drug	Manufacturer
23/10/08	Pegasys (Peginterferon)	Roche
23/10/08	Pramipexole	Teva
23/10/08	Lunivia (Eszopiclone)	Sepracor
23/10/08	Vidaza (Azacitidine)	Celgene
20/11/08	Rasilez Hct (Aliskiren hemifumarate/hydrochlorothiazide)	Novartis
20/11/08	Zevtera (Ceftobiprole medocartil)	Janssen-Cilag
20/11/08	Roactemra (Tocilizumab)	Roche
18/12/08	Firmagon (Degarelix)	Ferring
18/12/08	Fablyn (Lasofloxifene)	Pfizer
18/12/08	Efient (Prasugrel)	Eli Lilly

Source: CHMP EMEA <http://www.emea.europa.eu/index/indexh1.htm>

### New investigative sites

According to the RZN data, as of the 12 November 2008 there were 946 hospitals entitled to conduct clinical trials in Russia. Ninety two new sites were designated by the RZN during 2008.

More than one third (35%) of all Russian investigative sites are located in Moscow and St. Petersburg.

The Top 10 Russian regions by the number of new sites are shown in Table 6.

**Table 6. Top 10 Russian regions by the number of investigative sites**

No	City	No. of new sites
1	Moscow	201
2	St. Petersburg	134
3	Novosibirsk region	38
4	Moscow region	29
5	Sverdlovsk region	26
6	Nizhegorod region	25
7	Tatar republic	25
8	Yaroslavl region	22
9	Perm region	19
10	Rostov region	18

Source: RZN

### FDA inspections

According to the FDA data, as of 7 January 2009, 13 FDA inspections were conducted in the Russian investigative sites during 2008, - the maximum annual number since 1995 when the first FDA inspection was conducted in Russia.

No objectionable conditions or practices were found during seven inspections (NAI - No Action Indicated), six inspections resulted in VAI (Voluntary Action Indicated), i.e. objectionable



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conditions were found but the problems did not justify further regulatory action, and any corrective action was left to the investigator to take voluntarily.

Three inspections were conducted in Moscow, six – in St. Petersburg, two – in Saratov, one – in Novosibirsk, and one in Yaroslavl.