# Clinical Trials in Russia

# Orange Paper

# 3rd Quarter 2009



11, 4-Magistralnaya Ul., 123007 Moscow, Russia

www.synrg-pharm.com

## Contents





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## Executive Summary

The Federal Service on Surveillance in Healthcare and Social Development of the Russian Federation (alias RosZdravNadzor, RZN) approved 153 new clinical trials of all types including local and bioequivalence studies during the third quarter of 2009; demonstrating a 10% 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 such studies decreased by 5% from Q3 2008 figure and stood at 93 new studies in Q3 2009.

The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) did not change significantly over the same point in 2008 and will doubtfully change in the near future. Despite the decrease in the number of studies, the share of multinational multi-center clinical trials slightly increased from last year's figure and stood at 61% of the total number of clinical trials approved by RZN in the third quarter of 2009.

More than the two thirds of clinical trials in Russia is being sponsored by foreign companies - 67% of the total number of new studies in Q3 2009, almost the same as the last year figure (66%).

The maximum number of trials (51) were initiated by Russian sponsors, American sponsors with 30 studies took the runner-up place, they are followed by German sponsors with 14 trials, 12 new trials was instigated by Swiss manufacturers, the UK sponsors with seven new studies, and the top six is concluded by Japan and Danish sponsors each with six new studies in Q3 2009.

Nine new Phase I clinical trials were launched in the third quarter of 2009; one trial less than in the corresponding quarter of last year. The number of the Phase II trials increased by 20%, from 39 trials in the third quarter of 2008 to 47 in the third quarter of 2009. The number of Phase III trials demonstrated a slight decrease from last year number, down from 94 to 86 studies.

The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the third quarter of 2009 stood at 11,956.

The Swiss giant *Novartis* sponsoring 10 new studies is on the top of the heap in the third quarter of 2009. The Danish top five "debutant" *Novo Nordisk* with six new trials in Q3 2009 took the runner-up place. It is followed by *GlaxoSmithKline* sponsoring five new studies, and *Merck & Co.* with four. The top five is concluded by *Eli Lilly* having four new studies and fewer patients in Q3 2009.

The Russian pharmaceutical company OAO *Ozon* sponsoring five new clinical trials ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the third quarter 2009. OAO *Canonpharma Production* with four new trials took the runner-up place. It is followed by NPO *Microgen* with three new trials and OAO *Sintez* with the same number of studies but less patient number. The top five is concluded by OAO *Valenta* with two new studies.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 38[1] new drugs during Q3 2009, three of which were tested in clinical trials in Russia.

During the period from July 1 to September 30 2009 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) reviewed 49[2] applications to market drugs in the EU. Two of the drugs which received positive opinions were (or are being) tested in clinical trials in Russia.

According to the FDA data as of November 16 2009, there were no FDA inspections conducted in the Russian investigative sites during Q3 2009.

[1] CDER FDA http://www.fda.gov/cder
[2] CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm

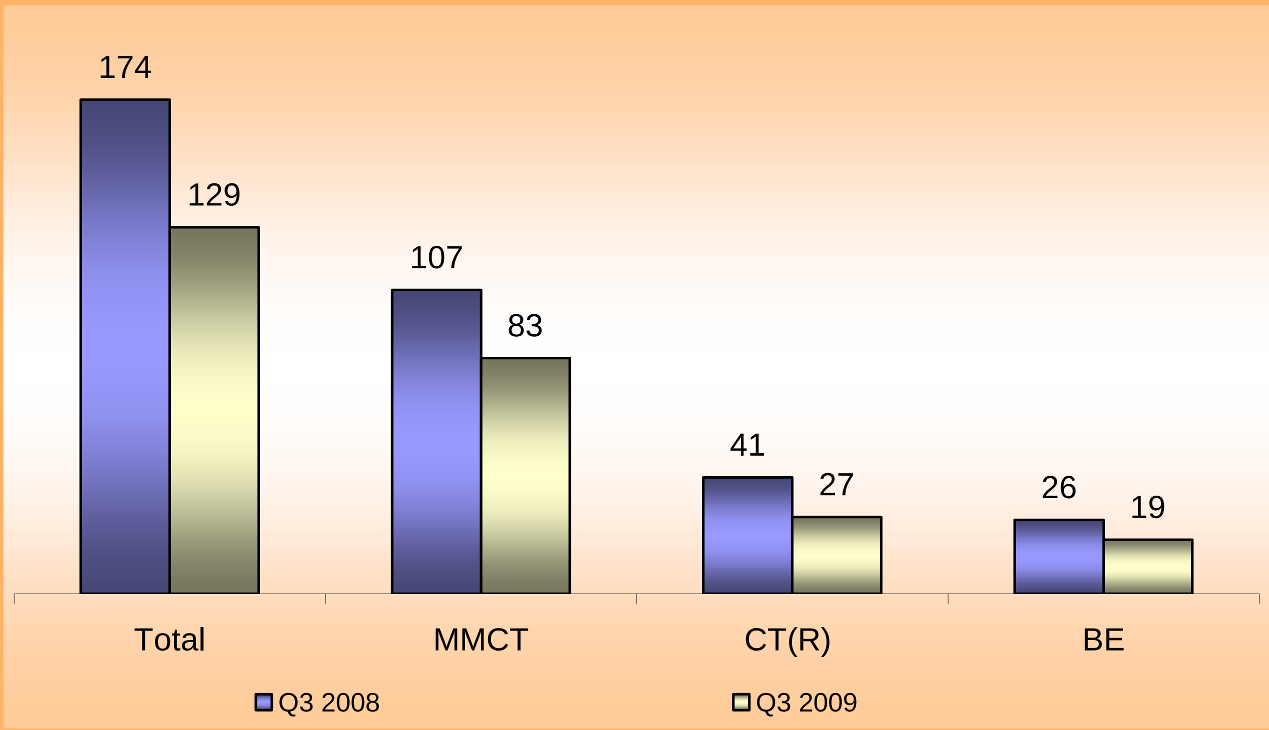
## Clinical Trials by Type and Manufacturing Country

The RZN approved 153 new clinical trials of all types including local and bioequivalence studies during the third quarter of 2009; demonstrating a 10% 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 decreased by 5% over Q3 2008 and stood at 93 new studies in Q3 2009.

The number of the local clinical trials conducted in Russia by domestic and foreign sponsors (the CT(R) bar in the Figure 1) is also down from 57 to 39 clinical trials demonstrating a notable 32% fall over the same point in 2008.

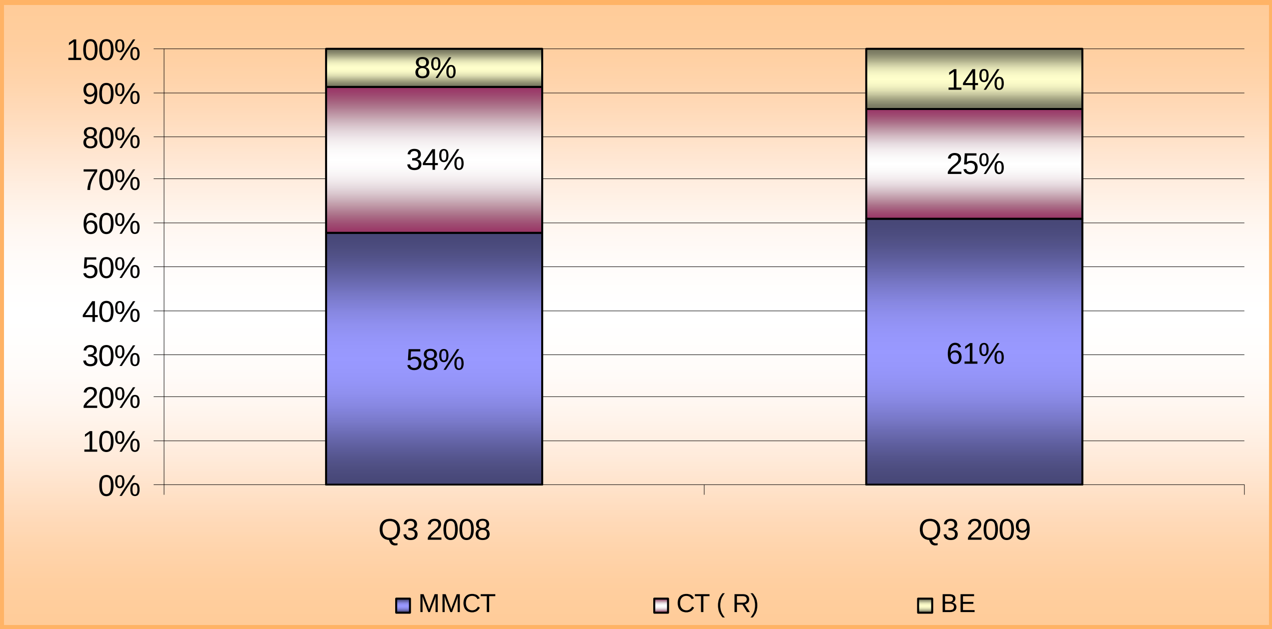
The number of bioequivalence studies (BE in Figure 1) in the third quarter of 2009 stood at 21 new trials, six studies up over last year's figure.

**Figure 1. Clinical trials approved by RZN in Q3 2009**



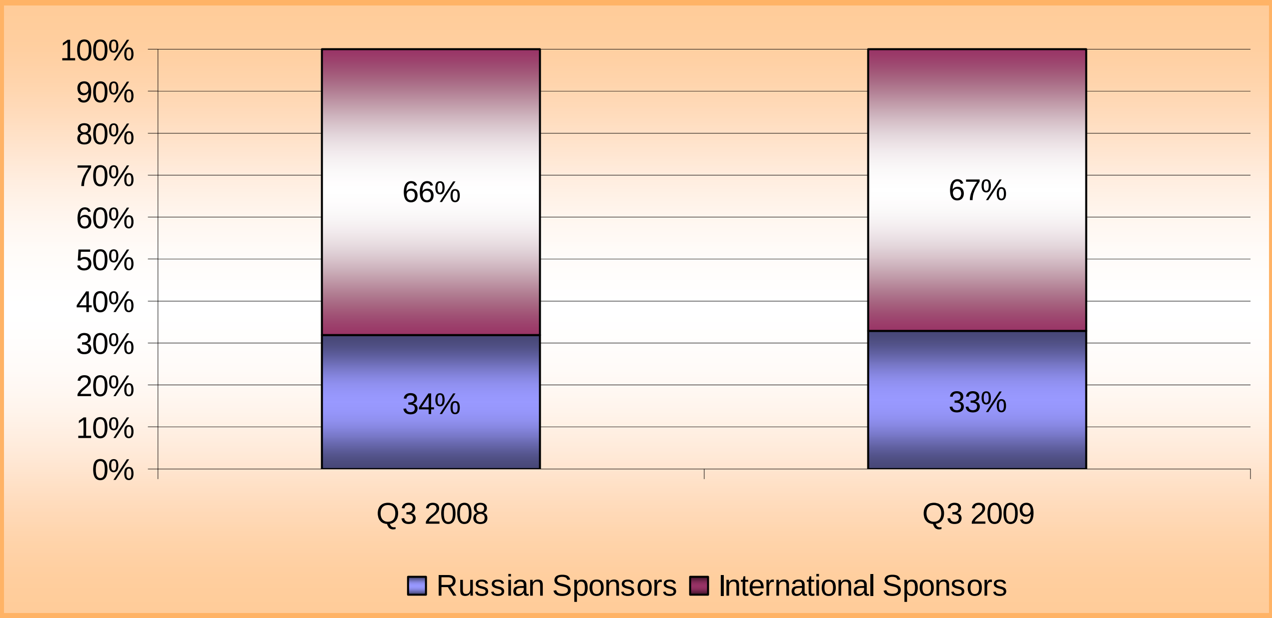

The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) did not change significantly over the same point in 2008 and will doubtfully change in the near future. Despite the decrease in the number of studies, the share of multinational multi-center clinical trials slightly increased from last year's figure and stood at 61% of the total number of clinical trials approved by RZN in the third quarter of 2009. The shares of the local trials and bioequivalence studies in Q3 2009 stood at 25% and 14% of the total number of studies, respectively, while they accounted to 34% and 8% in Q3 2008.

**Figure 2. Clinical trials by type in Q3 2009**



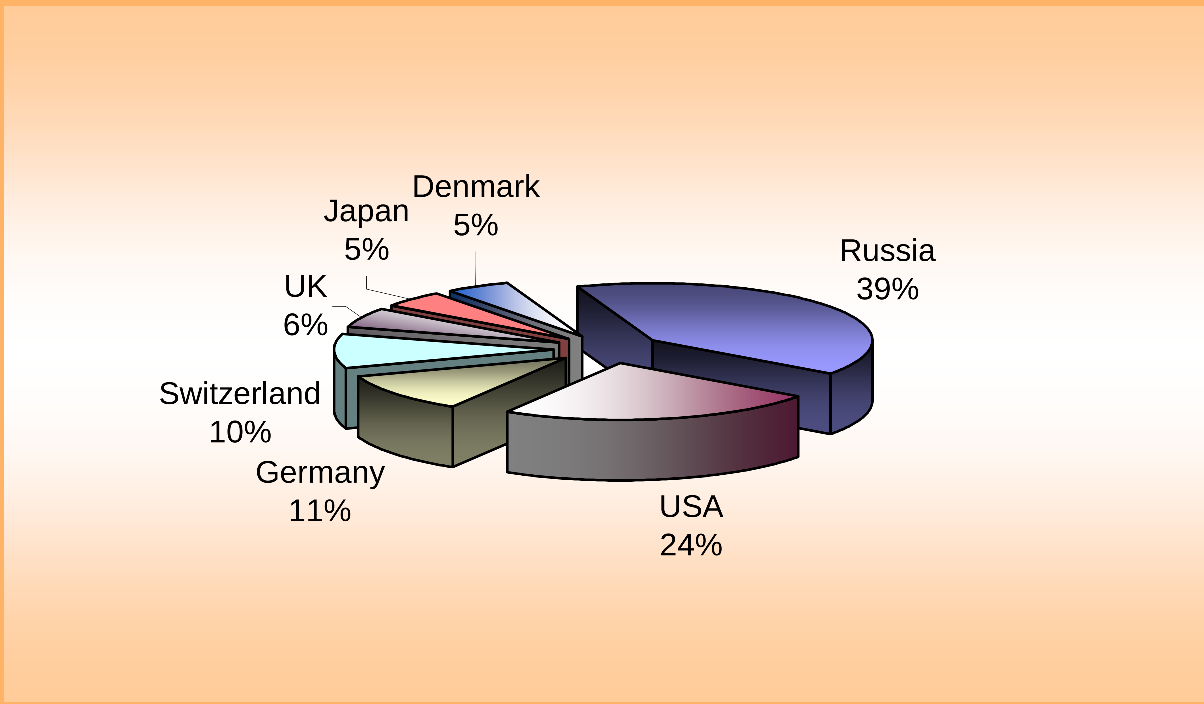

The lion's share of clinical trials in Russia is being sponsored by foreign companies - 67% of the total number of new studies in Q3 2009, almost the same as the last year figure (66%).

**Figure 3. Russian and International sponsors in Q3 2009**




Clinical trials in Russia in Q3 2009 were sponsored by companies from 19 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 (51) were initiated by Russian sponsors, American sponsors with 30 studies took the runner-up place, they are followed by German sponsors with 14 trials, 12 new trials was instigated by Swiss manufacturers, the UK sponsors with seven new studies, and the top six is concluded by Japan and Danish sponsors each with six new studies in Q3 2009.

**Figure 4. Countries presented on the Russian clinical trials market in Q3 2009**




Belgium, India, Ireland, Canada, the Netherlands, Poland, Portugal and Sweden are represented among others.

## Clinical trials by Phase

Nine new Phase I clinical trials were launched in the third quarter of 2009; one trial less than in the corresponding quarter of last year. The number of the Phase II trials increased by 20%, from 39 trials in the third quarter of 2008 to 47 in the third quarter of 2009. The number of Phase III trials demonstrated a slight decrease over last year number, down from 94 to 86 studies. The number of Phase IV trials also decreased from 13 in Q3 2008 to 11 in Q3 2009.

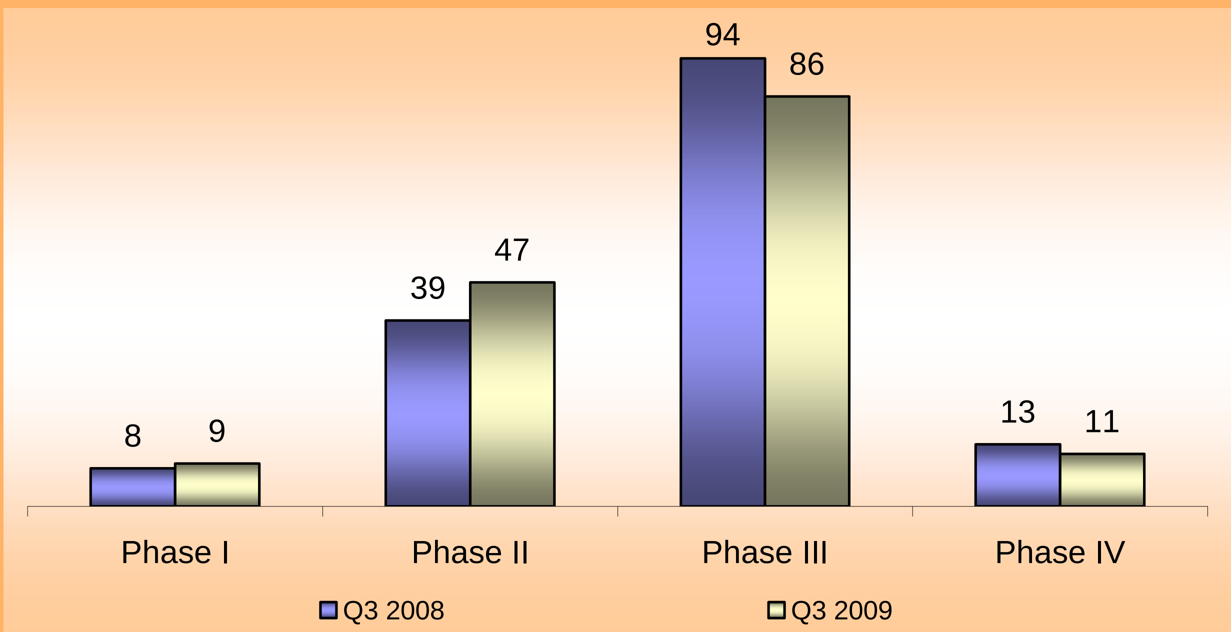
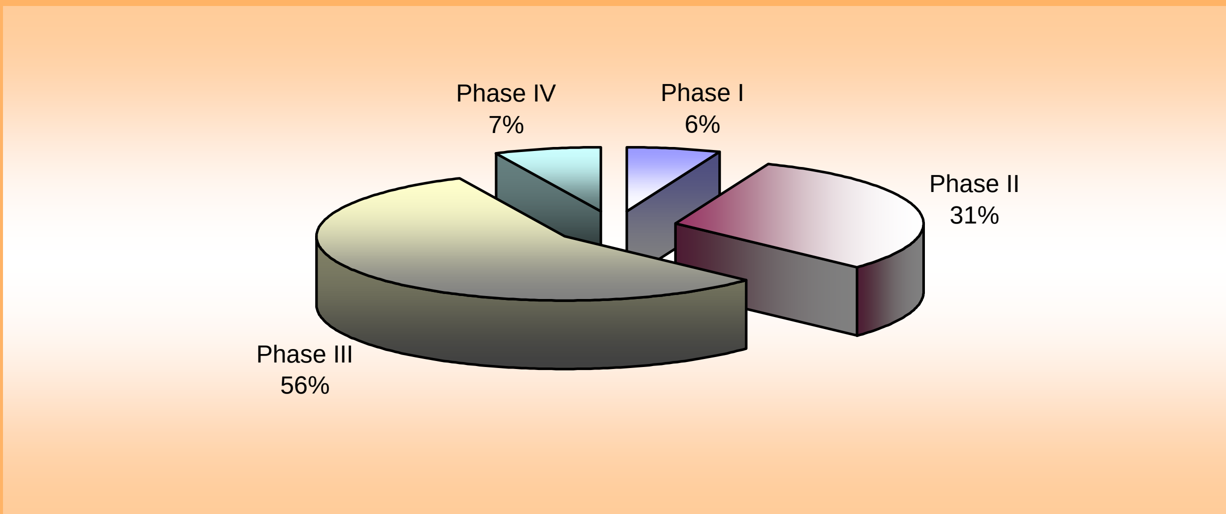


**Figure 5. Clinical trials in Russia in Q3 2009 by phase**

As shown in Figure 6, the share of Phase III trials in Q3 2009 stood at almost 56% of the total number of studies, the share of Phase II trials accounted at 31%, Phase IV trials stood at seven per cent, and the share of Phase I studies amounted to six per cent.

**Figure 6. The proportions between study phases in Russia in Q3 2009**



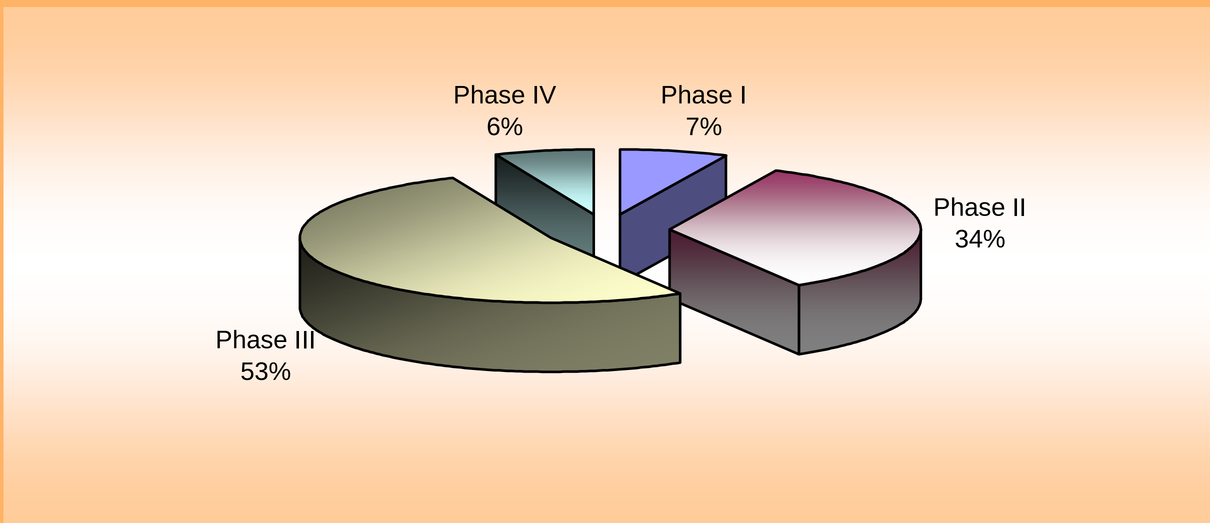

The number of patients which are planned to be enrolled in the Phase II-IV trials launched in the third quarter of 2009 stood at 11,956 patients, almost twice less than the last year number (23,540). The number of Phase III subjects decreased by 35% from last year's figure.

Seven hundred and ninety two subjects will be recruited in Phase I trials; 3,947 patients – in Phase II trials; 6,025 subjects – in Phase III studies and 720 patients will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is five, the maximum number is 2,300.

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

**Figure 7. The number of patients in Q3 2009 by study phase**




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

## Rating of international sponsors

The Swiss *Novartis* sponsoring 10 new studies is on the top of the heap in the third quarter of 2009. The Danish *Novo Nordisk* with six new trials in Q3 2009 took the runner-up place. It is followed by *GlaxoSmithKline* sponsoring five new studies, and *Merck & Co.* with four. The top five is concluded by *Eli Lilly* having four new studies and fewer patients in Q3 2009.

It is worth mentioning that *Roche* and *Boehringer Ingelheim* also initiated four new studies each, but with less number of patients/sites.

Top five international sponsors by the number of new studies in Q3 2009 are presented in Table 1.

**Table 1. Top-5 international study sponsors in Q2 2009**

| № | Sponsor | No. of trials | No. of patients | No. of sites |
|---|---|---|---|---|
| 1 | Novartis | 10 | 340 | 49 |
| 2 | Novo Nordisk | 6 | 385 | 46 |
| 3 | GlaxoSmithKline | 5 | 240 | 19 |
| 4 | Merck & Co. | 4 | 991 | 36 |
| 5 | Eli Lilly | 4 | 423 | 14 |

## Rating of Russian sponsors

The Russian pharmaceutical company OAO *Ozon* sponsoring five new clinical trials enrolling 112 patients in six sites, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in the third quarter 2009.

OAO *Canonpharma Production* with four new trials and 276 subjects in three sites, took the runner-up place. It is followed by NPO *Microgen* with three new trials and OAO *Sintez* with the same number of studies but less patient number. The top five is concluded by OAO *Valenta* with two new studies.

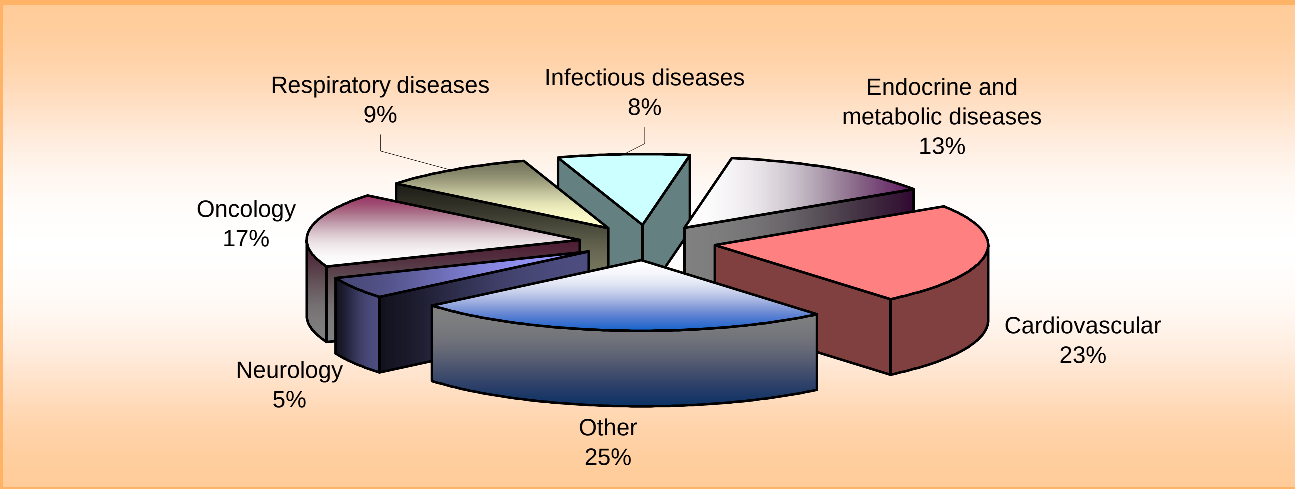
**Table 2. Top-5 Russian study sponsors in Q3 2009**

| № | Sponsor | No. of trials | No. of patients | No. of sites |
|---|---|---|---|---|
| 1 | Ozon | 5 | 112 | 6 |
| 2 | Canonpharma | 4 | 276 | 6 |
| 3 | Microgen | 3 | 500 | 6 |
| 4 | Sintez | 3 | 200 | 6 |
| 5 | Valenta | 2 | 458 | 4 |

## Therapeutic areas of clinical trials in Russia in Q3 2009

Seventy five per cent of the new studies in Q2 2009 were conducted in the six leading therapeutic areas. The maximum number of trials (29) were initiated in Cardiovascular diseases; 22 clinical trials in Oncology; 17 new studies in Endocrinology; 12 – in Respiratory diseases; 10 new studies in Infectious Diseases and six new Neurology studies were initiated in Q2 2009. The proportions between different therapeutic areas are shown in Figure 8.

**Figure 8. Clinical trials in Russia in Q2 2009 by therapeutic area**




## Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 38[1] new drugs during Q3 2009; eight 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 was 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 |
|---|---|---|
| 07/01/2009 | Multaq (Dronedarone Hydrochloride) | sanofi-aventis |
| 07/10/2009 | Effient (Prasugrel Hydrochloride) | Eli Lilly |
| 08/03/2009 | Livalo (Pitavastatin Calcium) | Kowa |
| Source: CDER FDA http://www.fda.gov/cder | | |

During the period from July 1 to September 30 2009 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) reviewed 49[2] applications to market drugs in the EU. No negative opinion was adopted for any of the drugs which had been approved earlier. Two 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 2009 and tested in Russian sites**

| Approval date | Drug | Manufacturer |
|---|---|---|
| 23/07/09 | Ilaris (canakinumab) | Novartis Europharm Ltd |
| 24/09/09 | Multaq (dronedarone) | sanofi-aventis |
| Source: CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm | | |

## FDA inspections

According to the FDA data as of November 16 2009, there were no FDA inspections conducted in the Russian investigative sites during Q3 2009.

[1] CDER FDA http://www.fda.gov/cder
[2] CHMP EMEA http://www.emea.europa.eu/index/indexh1.htm