Clinical Trials in Russia
Orange Paper
Year 2011

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Contents

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Executive Summary

The Ministry of Health and Social Development of the Russian Federation (MoH) approved 571 new clinical trials of all types including local and bioequivalence studies during 2011, demonstrating a 16% increase from the last year figure.

The number of multinational multi-center clinical trials increased by 49% and stood at 369 new studies in 2011. The number of the local clinical trials conducted in Russia by domestic and foreign sponsors decreased from 161 to 117 clinical trials, demonstrating a 27% decrease over last year figure. The number of bioequivalence studies in 2011 stood at 85 new trials, one study more than in 2010.

The share of multinational multi-center clinical trials increased from 50% to 65% of the total number of clinical trials approved in 2011. The share of the local trials decreased and stood at 20% of the total number of studies, and the share of bioequivalence studies decreased from 17% to 15% of the total number of trials approved during Year 2011.

Clinical trials in Russia in 2011 were sponsored by companies from 31 countries. The maximum number of trials (169) was initiated by Russian sponsors. American sponsors with 146 new studies took the runner-up place, they are followed by Swiss sponsors with 74 trials and UK sponsors with 37 new studies, the group of leaders is concluded by French sponsors with 22 new studies in 2011.

64 new Phase I clinical trials were launched in 2011, which is 21 trials more than in 2010. The number of the Phase II trials stood at 87 new studies in 2011, one study more than in 2010. The number of Phase III trials increased from 232 to 327 studies, almost 41% more than in 2010. Phase IV trials also demonstrated the significant increase from 38 studies in 2010 to 75 studies in 2011.

The number of patients which are planned to be enrolled in Phase I-IV trials launched in 2011 stood at 53,958, a 20% more than in 2010 figure, when 45,072 patients were planned to be enrolled.

Novartis sponsoring 26 new studies is on the top of the heap in 2011. It is followed by *GlaxoSmithKline*, *Roche* and *Eli Lilli* each having 21, 18 and 16 new trials respectively. Top five is concluded by *Pfizer* with 14 new studies in 2011.

The Russian pharmaceutical company *Biocad* sponsoring 13 new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in 2011. *Materia Medica* with 10 new trials took the runner-up place. It is followed by *Valenta, Petrovax* and *State Research Center of Virology and Biotechnology Vector* with six, four and three new trials in 2011, respectively.

More than three quarters of new studies in 2011 were initiated in seven leading therapeutic areas: the largest number of studies has been initiated in Oncology (121); 58 new studies were instigated in Pulmonology, 42 new studies – in Musculoskeletal diseases; 39 studies – in Endocrine diseases; 35 – in Infectious diseases, 34 studies each in Cardiology and Neurology.

The Center for Drug Evaluation and Research (CDER) of the FDA approved 102 new drugs during Year 2011 and 34 of them were studied in clinical trials conducted in Russia.

During the year 2011 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 67 new drug applications, 32 of which were in clinical trials in Russia.

Roszdravnadzor conducted 85 inspections during 2011. Violations of the clinical practice were found in 16 institutions. Two FDA inspections were conducted in the Russian investigative sites during 2011. One inspection ended with NAI result – no action indicated, and one inspection ended with VAI result – voluntary action indicated.

Clinical Trials by Type and Manufacturing Country

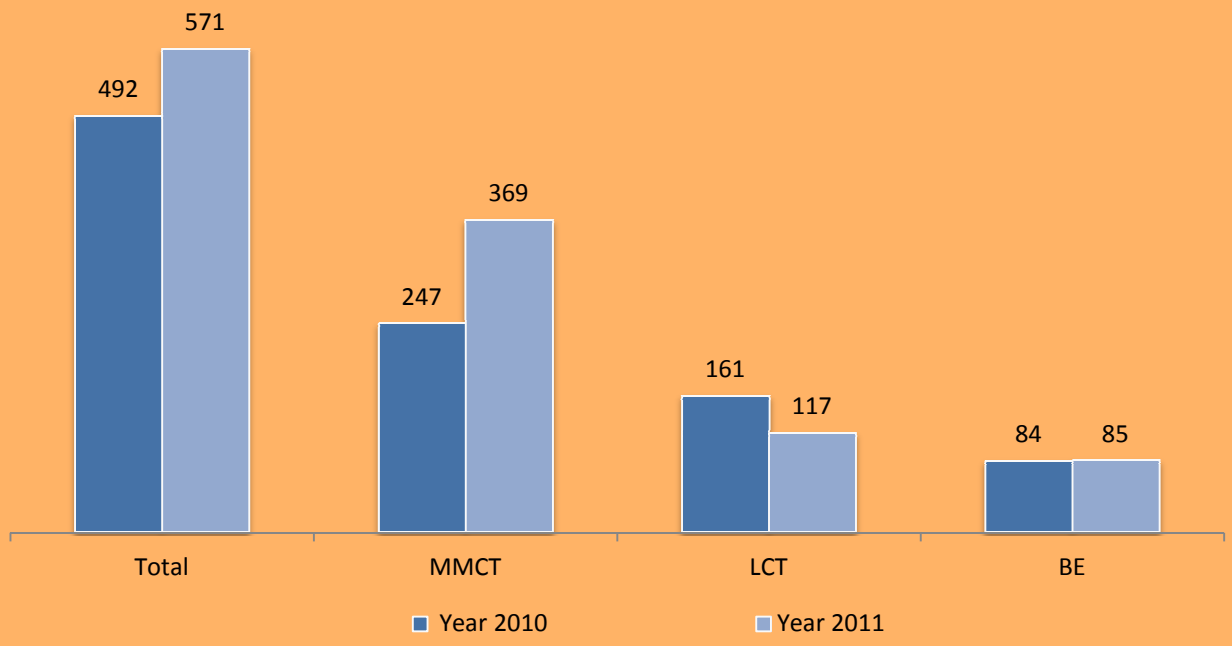
The Russian MoH approved 571 new clinical trials of all types including local and bioequivalence studies during 2011, demonstrating a 16% increase from the last year figure.

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 increased by 49% and stood at 369 new studies in 2011.

The number of the local clinical trials (LCT) conducted in Russia by domestic and foreign sponsors decreased from 161 to 117 clinical trials, demonstrating a 27% decrease over last year figure.

The number of bioequivalence studies (BE) in 2011 stood at 85 new trials, one study more than in 2010.

Figure 1. Clinical trials in Russia in 2011

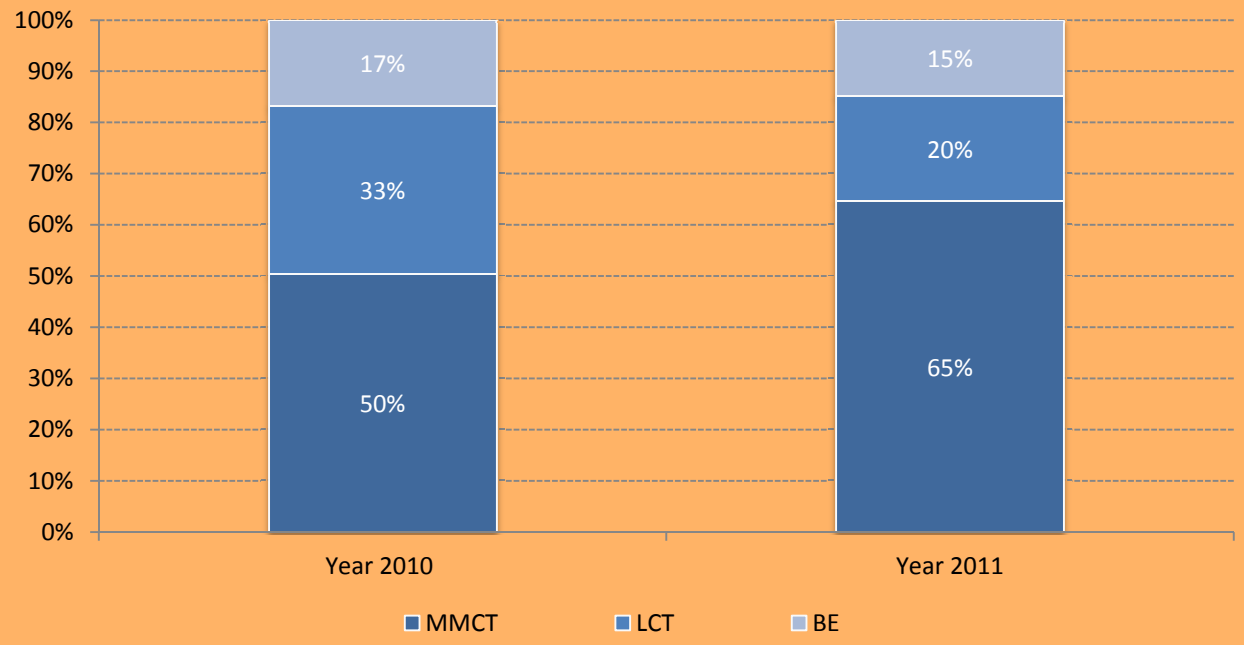


The proportions between different study types (multinational multi-center clinical trials, local studies and bioequivalence trials) changed since last year (see Figure 2).

The share of multinational multi-center clinical trials increased from 50% to 65% of the total number of clinical trials approved in 2011.

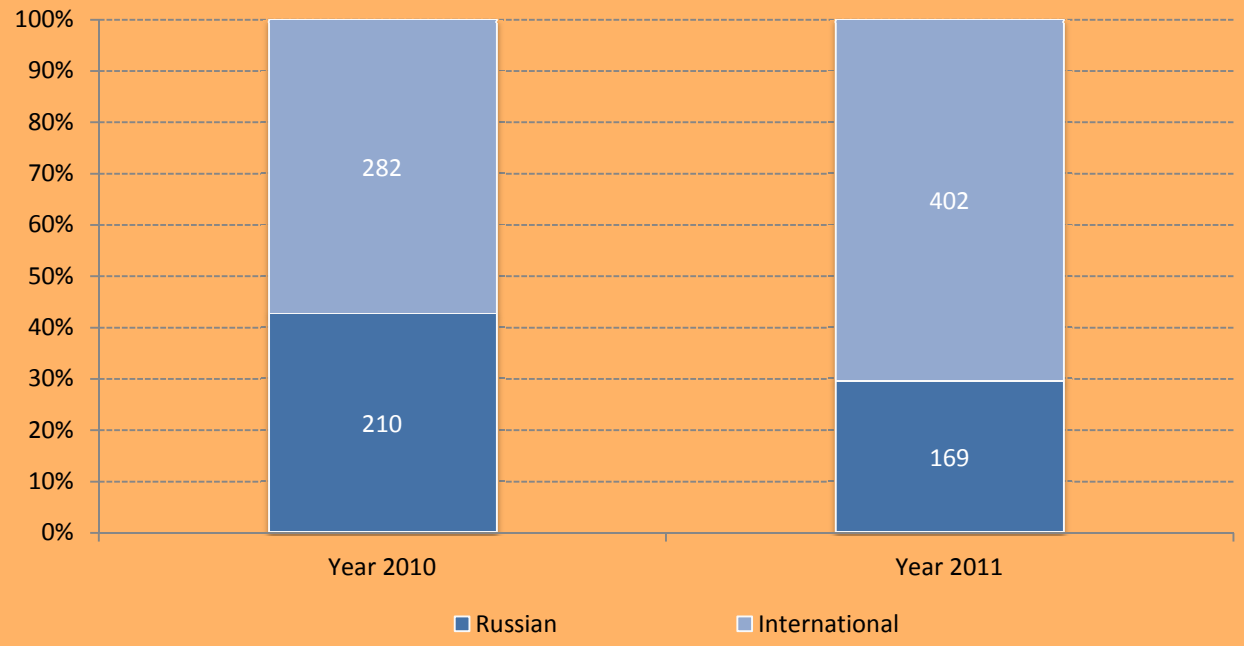
The share of the local trials decreased and stood at 20% of the total number of studies, and the share of bioequivalence studies decreased from 17% to 15% of the total number of trials approved during Year 2011.

Figure 2. Clinical trials by type in 2011



The major share of clinical trials in Russia is sponsored by foreign companies which received 402 study approvals or 70% of the total number of new studies in 2011. The share of studies of local manufacturers decreased from 43% in 2010 to 30% in 2011, from 210 to 169 studies, respectively.

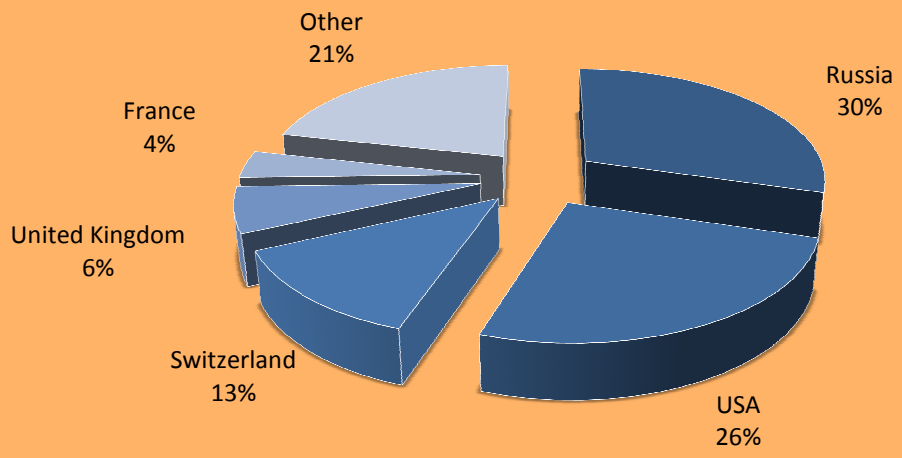
Figure 3. Russian and International sponsors in 2011



Clinical trials in Russia in 2011 were sponsored by 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 (169) was initiated by Russian sponsors. American sponsors with 146 new studies took the runner-up place, they are followed by Swiss sponsors with 74 trials

and UK sponsors with 37 new studies, the group of leaders is concluded by French sponsors with 22 new studies in 2011.

Figure 4. Countries presented on the Russian clinical trials market in 2011



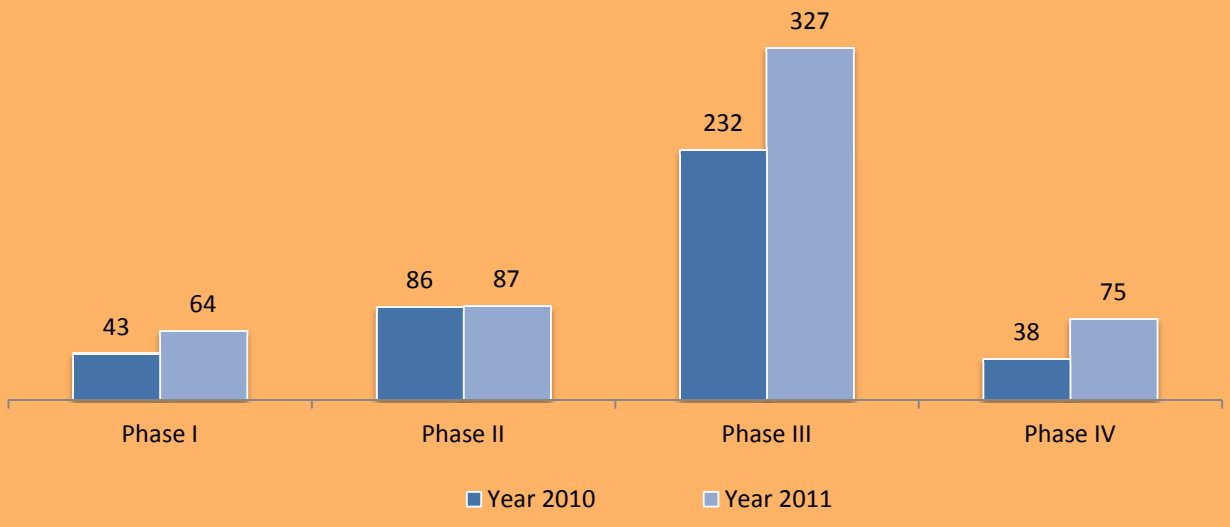
Among others are: Germany (19); Austria (18); Sweden (14); Denmark (13); Belgium (10); Italy (6); Belarus, Ireland and Slovenia (5 each); India (4); the Netherlands and Portugal (3 each); Argentina, Israel, Kazakhstan and Canada have 2 new studies each; Australia, Hungary, Spain, Cyprus, Korea, Latvia, Romania, Ukraine, Finland and Japan each started one new study in 2011.

Clinical trials by Phase

64 new Phase I clinical trials were launched in 2011, which is 21 trials more than in 2010. The number of the Phase II trials stood at 87 new studies in 2011, one study more than in 2010.

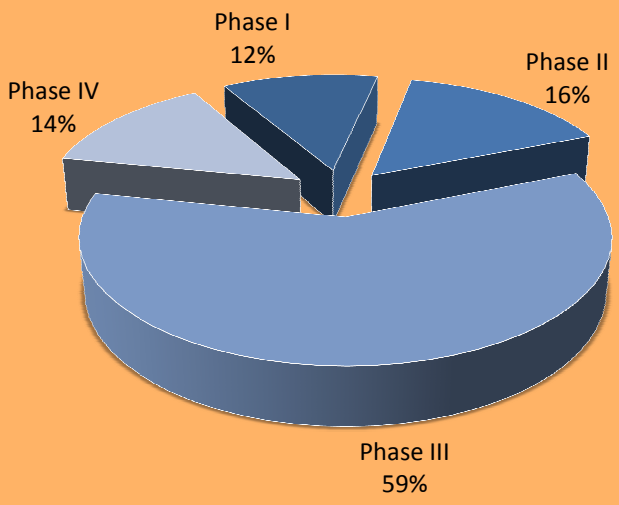
The number of Phase III trials increased from 232 to 327 studies, almost 41% more than in 2010. Phase IV trials also demonstrated the significant increase from 38 studies in 2010 to 75 studies in 2011.

Figure 5. Clinical trials in Russia in 2011 by phase



As shown in Figure 6, the share of Phase III trials in 2011 stood at 59% of the total number of studies, the share of Phase II trials accounted at 16%, Phase IV trials stood at 14%, and the share of Phase I studies amounted to 12%.

Figure 6. The proportions between study phases in Russia in 2011



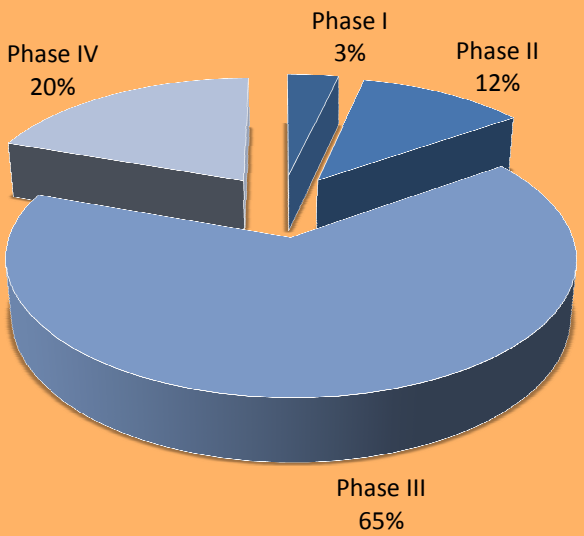
The number of patients which are planned to be enrolled in Phase I-IV trials launched in 2011 stood at 53,958, a 20% more than in 2010 figure, when 45,072 patients were planned to be enrolled.

1,920 subjects will be recruited in Phase I trials; 6,241 patients – in Phase II trials; 34,990 subjects – in Phase III studies and 10,507 patients will be enrolled in Phase IV studies.

The minimal number of subjects in a single study is two, the maximum number is 2,375.

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

Figure 7. The number of patients in 2011 by study phase



Rating of international sponsors

Novartis sponsoring 26 new studies is on the top of the heap in 2011. It is followed by *GlaxoSmithKline*, *Roche* and *Eli Lilli* each having 21, 18 and 16 new trials respectively. Top five is concluded by *Pfizer* with 14 new studies in 2011.

Top five international sponsors by the number of new studies in 2011 are presented in Table 1.

Table 1. Top-5 international study sponsors in 2011

№	*Company Name*	*No. studies*	*No. patients*
1	Novartis	26	2 542
2	GlaxoSmithKline	21	4 223
3	Roche	18	2 630
4	Eli Lilli	16	1 884
5	Pfizer	14	2 470

Rating of Russian sponsors

The Russian company *Biocad* sponsoring 13 new clinical trials, ranked number one among domestic pharmaceutical manufacturers by the number of new studies in 2011. *Materia Medica* with ten new trials took the runner-up place. It is followed by *Valenta, Petrovax* and *State Research Center of Virology and Biotechnology Vector* with six, four and three new trials, respectively (see Table 2 for details).

Table 2. Top-5 Russian study sponsors in 2011

№	*Company Name*	*No. studies*[1]	*No. patients*
1	Biocad	13	1 360
2	Materia Medica	10	2 350
3	Valenta	6	1 240
4	Pertovax	4	359
5	State Research Center of Virology and Biotechnology Vector	3	325

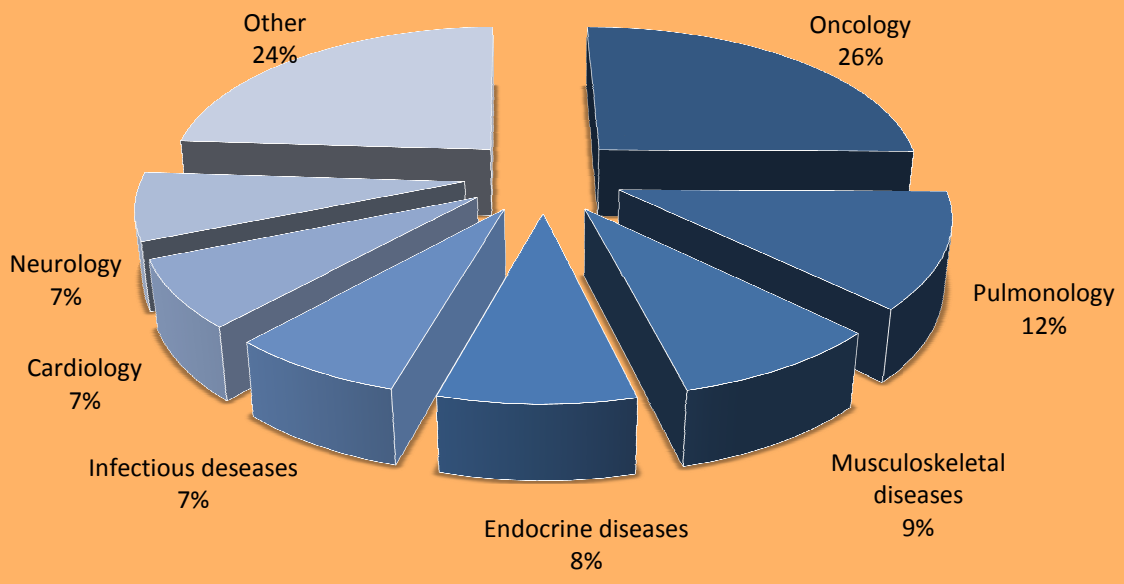
[1] Excluding BE studies

Therapeutic areas of clinical trials in Russia in 2011

More than three quarters of new studies in 2011 were initiated in seven leading therapeutic areas: the largest number of studies has been initiated in Oncology (121); 58 new studies were instigated in Pulmonology, 42 new studies – in Musculoskeletal diseases; 39 studies – in Endocrine diseases; 35 – in Infectious diseases, 34 studies each in Cardiology and Neurology.

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

Figure 8. Clinical trials in Russia in 2011 by therapeutic area



Clinical trials results

The Center for Drug Evaluation and Research (CDER) of the FDA approved 102 new drugs during Year 2011; 24 of them are new molecular entities (NME); others are new dosages, manufacturers or indications of the already marketed drugs. 34 of 102 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 2011 (Q1-Q3 data is presented in the previous issues of SynRG Orange Paper).

Table 3. New drugs approved by FDA in Q4 2011 and tested in Russian sites

Appr.date	*Drug (active ingredient)*	*Company*
06/10/2011	Fluoxetine hydrochloride (Fluoxetine hydrochloride)	Edgemont Pharms LLC
07/10/2011	Combivent respimat (Albuterol sulfate; Ipratropium bromide)	Boehringer Ingelheim
04/11/2011	Xarelto (Rivaroxaban)	Janssen Pharms
09/11/2011	Levetiracetam in sodium chloride (Levetiracetam)	HQ Speciality Pharma
10/11/2011	Forfivo XL (Bupropion hydrochloride)	Intelgenx Corp
14/11/2011	Morphine sulfate (Morphine sulfate)	Hospira Inc
16/11/2011	Jakafi (Ruxolitinib phosphate)	Incyte Corp

18/11/2011	Atazanavir sulfate and Ritonavir (Atazanavir sulfate; Ritonavir)	Matrix Labs Ltd
18/11/2011	Eylea (Aflibercept)	Regeneron Pharmaceuticals
16/12/2011	Prezista (Darunavir ethanolate)	Tibotec
20/12/2011	Edarbyclor (Azilsartan kamedoxomil; chlorthalidone)	Takeda Pharms
21/12/2011	Isentress (Raltegravir potassium)	Merck Sharp Dohme
		Source: FDA

During the year 2011 the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMEA) approved 67 new drug applications. Negative opinion was adopted for eight drugs. 32 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 2011 (Q1-Q3 data is presented in the previous issues of SynRG Orange Paper)

Table 4. New Drugs approved by EMEA in Q4 2011 and tested in Russian sites

Appr. date	*Drug (active ingredient)*	*Manufacturer*
20/10/2011	Cervarix (human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed))	GlaxoSmithKline Biologicals S.A.
20/10/2011	Onglyza (saxagliptin)	Bristol-Myers Squibb / AstraZeneca EEIG
17/11/2011	Caprelsa (vandetanib)	AstraZeneca AB
17/11/2011	Erbitux (cetuximab)	Merck
17/11/2011	Herceptin (trastuzumab)	Roche
17/11/2011	Rebif (interferon beta-1a)	Merck
15/12/2011	Esmya (ulipristal)	PregLem France SAS
15/12/2011	Galvus (vildagliptin)	Novartis
		Source: EMEA

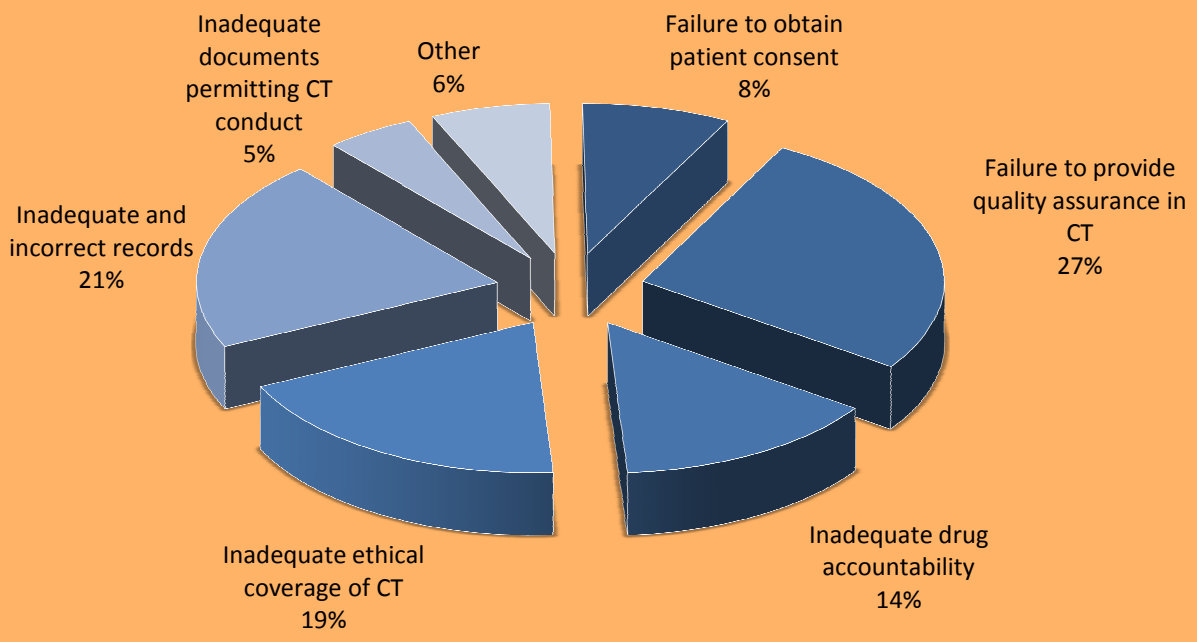
Roszdravnadzor inspections

According to the annual Roszdravnadzor report[1], 85 inspections were conducted in 75 institutions performing preclinical and clinical trials and located in 31 Russian cities during 2011. Violations of the clinical practice were found in 16 institutions.

The analysis of findings is shown in the Figure below.

[1] http://www.roszdravnadzor.ru/i/upload/files/1325236362.66925-17293.pdf

Figure 9. Findings during Roszdravnadzor inspections in 2011



FDA inspections

According to the FDA data, two FDA inspections were conducted in the Russian investigative sites during 2011, one in Kazan (28th February, 2011) and one in Moscow (on 11th April, 2011). One inspection ended with NAI result – no action indicated, and one inspection ended with VAI result – voluntary action indicated.