Clinical Trials in Russia
Orange Paper
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Executive Summary

According to the Roszdravnadzor (The Federal Agency for Health Care and Social Development), a considerable growth in the number of conducted clinical trials could be seen in the 1st Quarter of 2007 as compared to the respective quarter of the previous year (by 38%).

A growth in the absolute number of international multi-center clinical trials with the participation of Russian centers, bioequivalence studies and number of clinical trials conducted in Russia only (mainly due to the growth in the participation of Russian sponsors) has been seen for the reporting period. The share of local clinical trials in the total number of clinical trials conducted in 1st Quarter of 2007 has increased thereby surpassing the number of international multi-center clinical trials and bioequivalence studies.

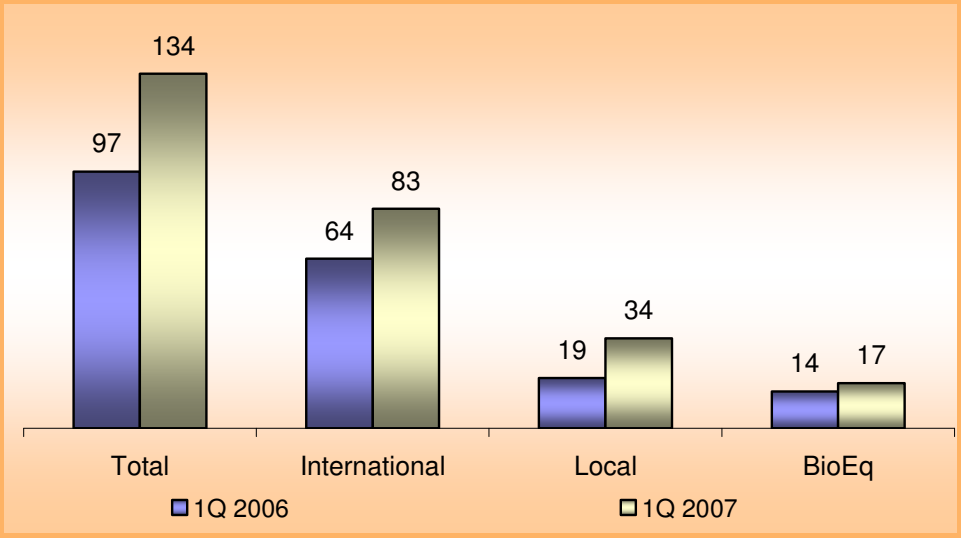
The share of Phase IV studies has substantially increased by the number of trials, centers and patients involved. However, Phase III studies keep dominating in the structure of clinical trials.

GlaxoSmithKline is the leader among foreign study sponsors; Microgen (Russian Public Health Ministry) is the leader among Russian sponsors. As for the studies sponsored by Russian manufacturers, one can see a shift from the equal shares of clinical trials and bioequivalence studies towards properly clinical studies of investigational new drugs.

Structure of the clinical trials approved by the Federal Agency for Health Care and Social Development (Roszdravnadzor) in the 1st quarter of 2007

The Federal Agency for Health Care and Social Development (Roszdravnadzor) issued 134 permits in the 1st quarter of 2007, which is 38% as much as in the 1st quarter of 2006. As compared to the respective quarter of the previous year, a growth in the number of all types of clinical trials is observed (Fig. 1).

Figure 1. Trials approved by the Roszdravnadzor in the 1st Quarter of 2007.

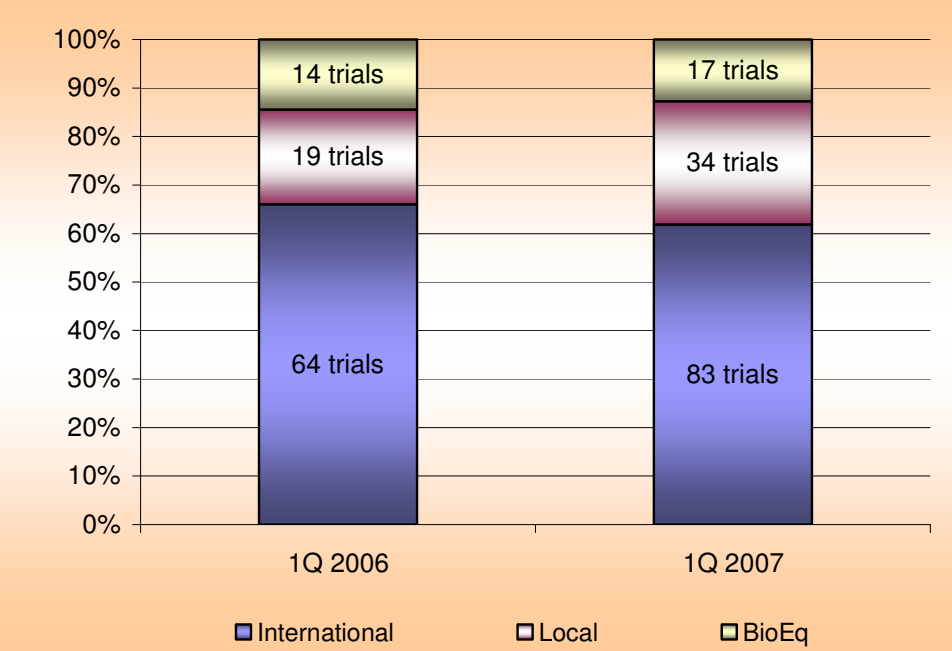


'International' means international multicenter clinical trials with investigative sites located in different countries including Russia. 'Local' as used in the diagrams means clinical trials conducted exclusively in the territory of Russia. 'BioEq' means drug bioequivalence studies.

The balance between international, local and bioequivalence trials has slightly changed in this quarter. A moderate growth in the specific share of clinical studies conducted in the territory of Russia in the total number of clinical studies can be observed both at the expense of international

and bioequivalence studies. While in the 1st quarter of 2006 international, local and bioequivalence trials made up to 66%, 20% and 14%, respectively, they amounted to 62%, 25% and 13% in the 1st Quarter of 2007

Figure 2. Balance between different types of trials in the 1st Quarter of 2007.



The current change in the share of different types of clinical studies can be apparently explained by the more active participation of study sponsors in favor of Russian manufacturers (from 26.8% to 30.6%).

In the 1st quarter of 2007, a trend towards the growth in the share of Russian sponsors in the total number of initiated trials remained in effect. In spite of the fact that drug bioequivalence studies cannot be considered as full-fledged clinical studies, the ratio between Russian and foreign sponsors made up 30.6% vs. 69.4% (see Fig. 3), which is 3.8% as much as in the 1st quarter of 2006 (26.8% and 73.2%, respectively).

Figure 3. Balance between study initiators in the 1st Quarter of 2007.

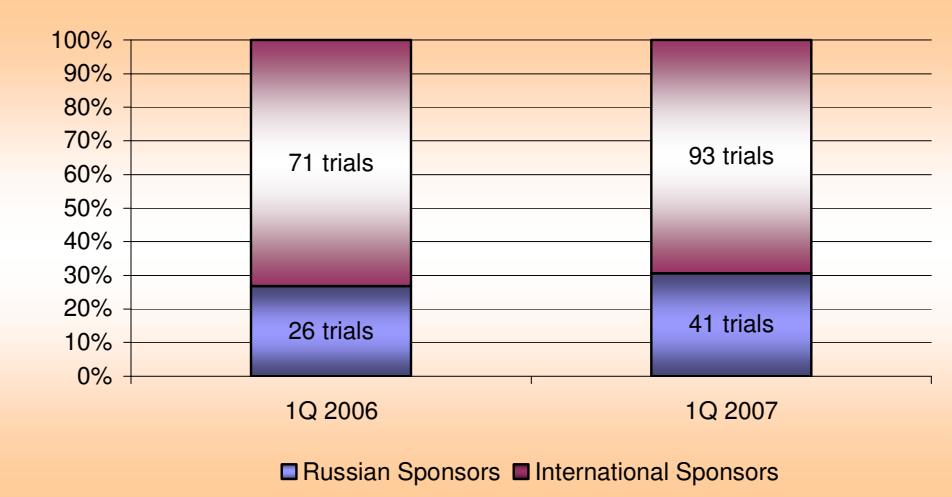


Figure 4. Sponsors of clinical trials in the 1st Quarter of 2007.

In general, clinical trials sponsored by foreign drug manufacturers still dominate on the Russian market (Fig. 4): their share is twice as much as that of the studies sponsored by Russian manufacturers – 69% vs. 31%.

Distribution of clinical trials by Phase

In the 1st Quarter of 2007, more balanced distribution of clinical studies approved by the Roszdravnadzor can be observed. While Phase III clinical studies dominated in the 1st quarter of 2006 (62% of studies, 69.3% of centers, and 81.5% of patients), Phase II trials lagged behind considerably (30.4% of studies, 25.5% of centers and 15.7% of patients) and Phase I and IV studies made up minor shares, the situation changed substantially a year later. At present Phase IV trials involve a considerable number of centers (11.0% in 2007 vs. 1.8% in 2006) and, in particular, patients (18.0% vs. 1.9%, respectively).

These estimates are quite approximate due to a number of reasons. First, the study phase is declared only for international multicenter clinical studies (IMCSs) and clinical studies conducted in Russia. No phase is indicated for bioequivalence studies. Second, five of the studies approved by the Federal Agency for Health Care and Social Development (Roszdravnadzor) in the 1st Quarter of 2007 have no study phase indicated. Third, a number of clinical studies are referred to in the application form submitted to the Roszdravnadzor as Phase II for one drug and Phase III for another drug at the same time (as a rule, they are control groups). As a result, we can just make an assumption about the final number of centers and patients for the different clinical trials.

Figure 5. Growth in the number of trials in the 1st Quarter of 2007 by Phase.

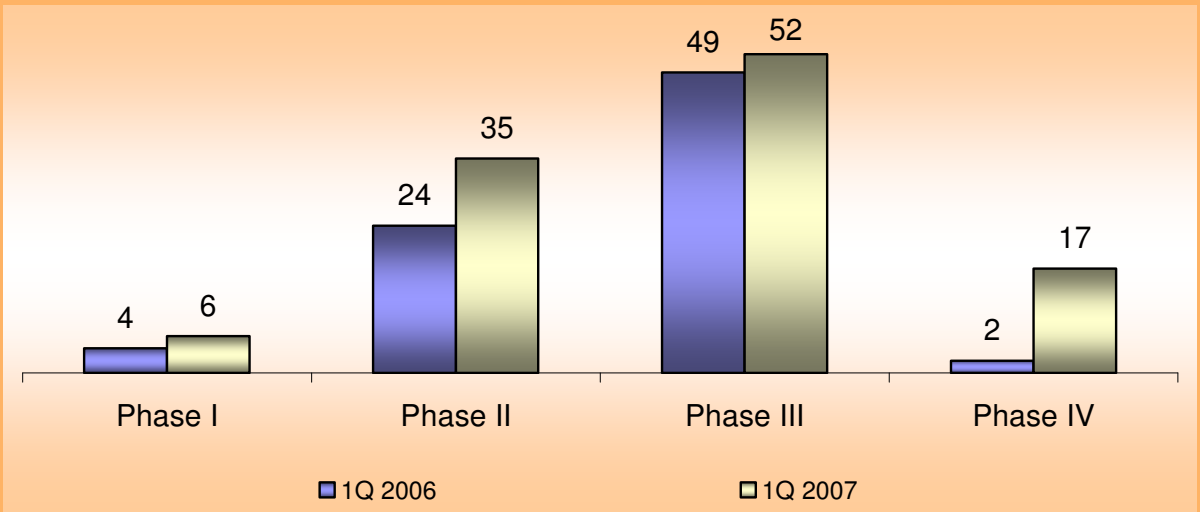


Figure 6. Growth in the number of investigative sites in the 1st Quarter of 2007.

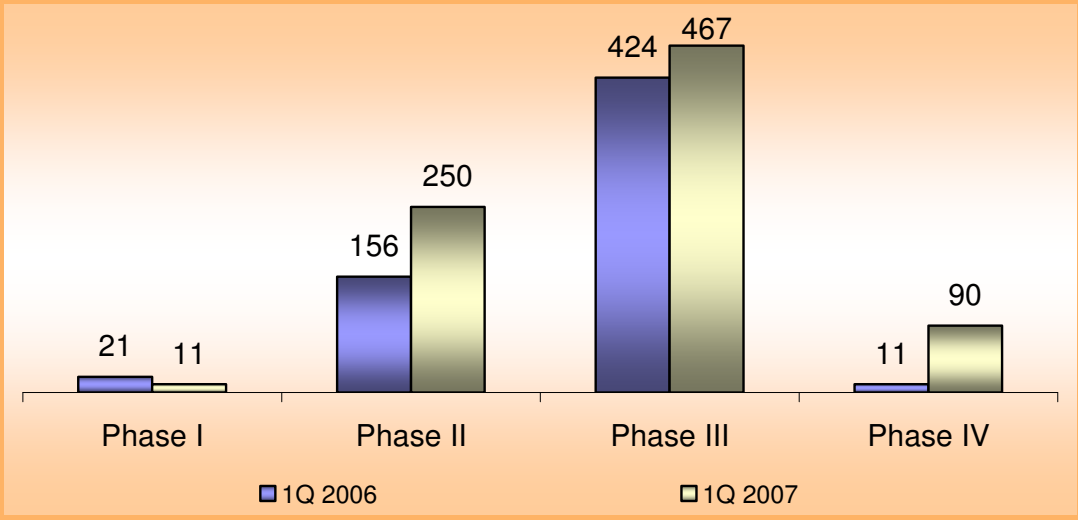
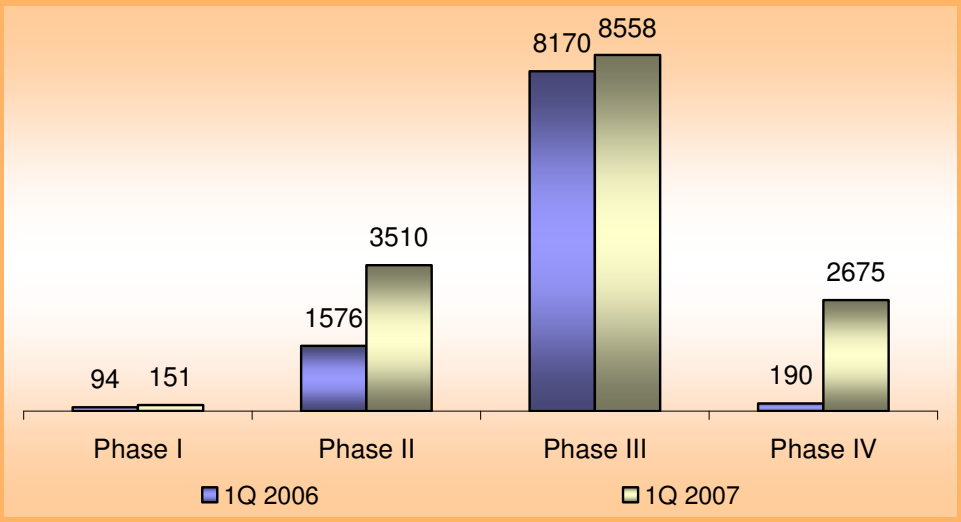


Figure 7. Growth in the number of patients in the 1st Quarter of 2007 by Phase.



Rating of International Study Sponsors

GlaxoSmithKline remains the leader by such indices as the number of studies, total number of patients scheduled for randomization and total number of CS centers in the 1st quarter of 2007 (over 60 studies being currently conducted in Russia involving over 300 centers). Sanofi-Aventis ranks approximately the same by the number of applications for studies (both of the sponsors have eight new CSs) but lags behind considerably by the number of centers (50 vs. 87) and patients (735 vs. 1,848).

AstraZeneca ranks second by the number of patients (1,604 patients); its studies involve 78 centers taking part in 4 studies. No data about the approval of Bristol-Myers Squibb's CSs in the 1st quarter of 2007 are available. In general, the data on the approved CSs are more prognostic in nature and rather indicate the sponsors' plans rather than their actual activities at present. First of all, this is explained by the fact that a lot of the studies approved of in the 3rd and 4th quarters of 2006 are also being conducted now on an active basis (with the average duration of the studies approved by the Roszdravnadzor in the 4th quarter of 2006 being 20.4 months).

Table 1. Top 10 International Study Sponsors in the 1st Quarter of 2007.

№	Company Name	No of Trials in 1Q 2007	No of Patients	No of Sites
1	GlaxoSmithKline	8	1848	87
2	Sanofi-Aventis	8	735	50
3	3M Health Care Limited	5	740	46
4	Pfizer Inc.	5	420	31
5	AstraZeneca	4	1604	78
8	Takeda Chemical Industries Ltd.	3	650	27

(Table 1. Continued)

7	Bayer Corp.	3	515	29
9	Novartis	3	360	25
6	Astellas Pharma Inc.	3	335	35
10	Eli Lilly and Company	3	230	11

Leader's Portfolio Analysis – GlaxoSmithKline

Table 2. Therapeutic areas of studies conducted by GlaxoSmithKline with the participation of Russian sites (according to www.clinicaltrials.org).

Disease group	Number of clinical trials	Total number of patients	Number of centers in Russia
Oncology	15	21,447	85
Immune system diseases	11	4,171	61
Viral infections	9	15,837	16
Nervous system diseases	9	3,046	58
Gastrointestinal disorders	4	3,225	23
Bacterial and fungal infections	4	1,885	14
Endocrine diseases	2	5,052	8
Blood and lymph composition disorders	2	454	11
Cardiovascular system diseases	1	2,500	30
Behavioral and thinking disorders	1	338	9

According to www.clinicaltrials.org (Table 2), the major part of developments and implementations for GlaxoSmithKline in Russia falls on the drugs used to treat cancer (15 studies and 85 centers in Russia; 21,400 patients took part in the studies on the whole).

Such GlaxoSmithKline's activities in Russia as viral infections rank second by their volume (9 studies, over 15,800 patients and 16 centers). Immune system (11 studies, 61 centers), nervous system (9 studies, 58 centers) and cardiovascular system (30 centers) studies are less considerable by the number of patients but involve a greater number of Russian centers.

Rating of Russian Study Sponsors

Table 3. Top 10 Russian Sponsors in the 1st Quarter of 2007.

No.	Sponsor	Number of trials in 1Q 2007	Total number of patients	Total number of centers
1	Doctor N	4	240	4
2	Nizhpharm	4	198	5
3	Veropharm	4	192	5
4	Microgen, Russian Public Health Ministry	3	720	5
5	Polysan	2	700	12
6	Biosintez	2	36	4
7	KRKA-RUS	1	300	10
8	Abidopharma	1	120	2
9	Nearmedic Plus	1	120	2
10	Canonpharma Production	1	100	2

As many as 28 studies (68%) out of the 41 studies approved of in the 1st quarter of 2007 belong to drug efficacy clinical trials, and much fewer studies are bioequivalence studies – 13 studies (32%). Both the growth in the total number of conducted studies and share of clinical trials is observed (50% in the 1st quarter of 2006).

The leaders by the number of patients are as follows: Microgen, Russian Public Health Ministry (720 patients), Polysan (700 patients) and KRKA-RUS (300 patients).

Clinical Trials Results

In the 1st quarter of 2007 FDA (Food and Drug Administration) approved 13 new drugs including new indications and combinations. Four of them were partially involved in clinical studies in Russian research centers (according to www.fda.gov, www.drugs.com и www.clinicaltrials.gov).

Table 4. New drugs approved by the FDA in the 1st Quarter of 2007 and studied in Russia.

Date	Drug	Manufacturer	Indication
16.01.2007	LIALDA™ (Mesalamine)	Shire plc	Ulcerous colitis
26.02.2007	Cymbalta	Eli Lilly and Company	Major depressive disorder
06.03.2007	Tekturna® (aliskiren)	Novartis	Arterial hypertension
13.03.2007	TYKERB® (lapatinib) + Xeloda® (capecitabine)	GlaxoSmithKline	Breast cancer