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ASSOCIATION OF CLINICAL TRIALS ORGANIZATIONS

Timeframes' monitoring (1st half of 2012)

The survey was carried out in July 2012.

The sample included submissions made from January 1, 2012 till June 30, 2012 as well as submissions made before January 1, 2012 if decisions on granting/refusing approvals were taken in 2012.

25 ACTO member companies took part in the survey.

Table 1 (Timeframes for Issuing Approvals) provides information on average, minimum and maximum timeframes for issuing approvals to conduct clinical trials, permits to import medicines for clinical trials, permits to import/export biological materials, approvals to make amendments to the protocols and other approvals (to prolong clinical trials, to involve new sites, to enroll additional patients, etc.) It's worth noting that time spent to reply to Ethical Council's and FGBU requests wasn't taken into account.

The total time to begin a trial is the sum of average timeframes for issuing approvals to conduct clinical trials and average timeframes for issuing permits to import/export biological materials.

Actual timeframes are given in calendar days. Timeframes according to legislation are given in calendar as well as in business days.

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Table 2 (Changes in average timeframes for issuing approvals to conduct clinical trials and permits to import/export) provides information on average timeframes for issuing approvals to conduct clinical trials and permits to import/export as well as total time to begin a trial in 2005-2012. It's worth noting that before ACTO didn't differentiate timeframes for issuing permits to import/export biological materials and medicines.

Before September 2010 examinations carried out by FGU and Ethics Committee weren't part of the approval process. That's why average timeframes for issuing approvals to conduct clinical trials in 2004-2010 were calculated as the sum of average timeframes for carrying out examinations by Ethics Committee and FGU (the highest number was taken into account) and timeframes for issuing approvals by Roszdravnadzor.

Table 3 provides information on violations of timeframes.

Tables 4-8 provide detailed information on timeframes for issuing all sorts of approvals. Actual timeframes are given in calendar days. Timeframes according to legislation are given in business and calendar days. The column «Legislation» provides information on relevant sources of the numbers in the column «Timeframes according to legislation».

The column «Sampling» provides information on the number of submitted applications. The samples are different at different stages because companies apply various approaches to timeframes monitoring.

Table 1. Timeframes for Issuing Approvals

	Timeframes according to legislation (business/calendar days)	Average timeframes (calendar days)	Minimum timeframes (calendar days)	Maximum timeframes (calendar days)	Sampling
to conduct clinical trials*	41/57	118	16	410	101
to import medicines	8/12	21	8	54	143
to import/export biological materials	13/19	21	7	47	337
to make amendments to the protocol	34/48	71	15	246	176
other approvals (to prolong clinical trials, to involve new sites, to enroll additional patients, etc.)	25/35	48	9	148	301
Total time to obtain approvals to conduct clinical trials and to import/export**	54/76	139	~	~	~

*Time spent to reply to Ethical Council's and FGBU requests wasn't taken into account

** It's the sum of average timeframes for issuing approvals to conduct clinical trials and average timeframes for issuing permits to import/export biological materials or to import drugs (the highest number was taken into account)

Table 2. Changes in average timeframes, 2005- 1st half of 2012

	2005	2006	2007	2008	2009	Jan-Aug 2010	2011	Jan-June 2012
Approvals to conduct clinical trials	66,3	77,8	98,9	77,6	77,0	85,2	130,0	118,0
Permits to import/export	14,9	17,8	23,7	33,1	30,5	26,9	34,0	21,0
Total	81,2	95,6	122,6	110,7	107,5	112,1	164,0	139,0

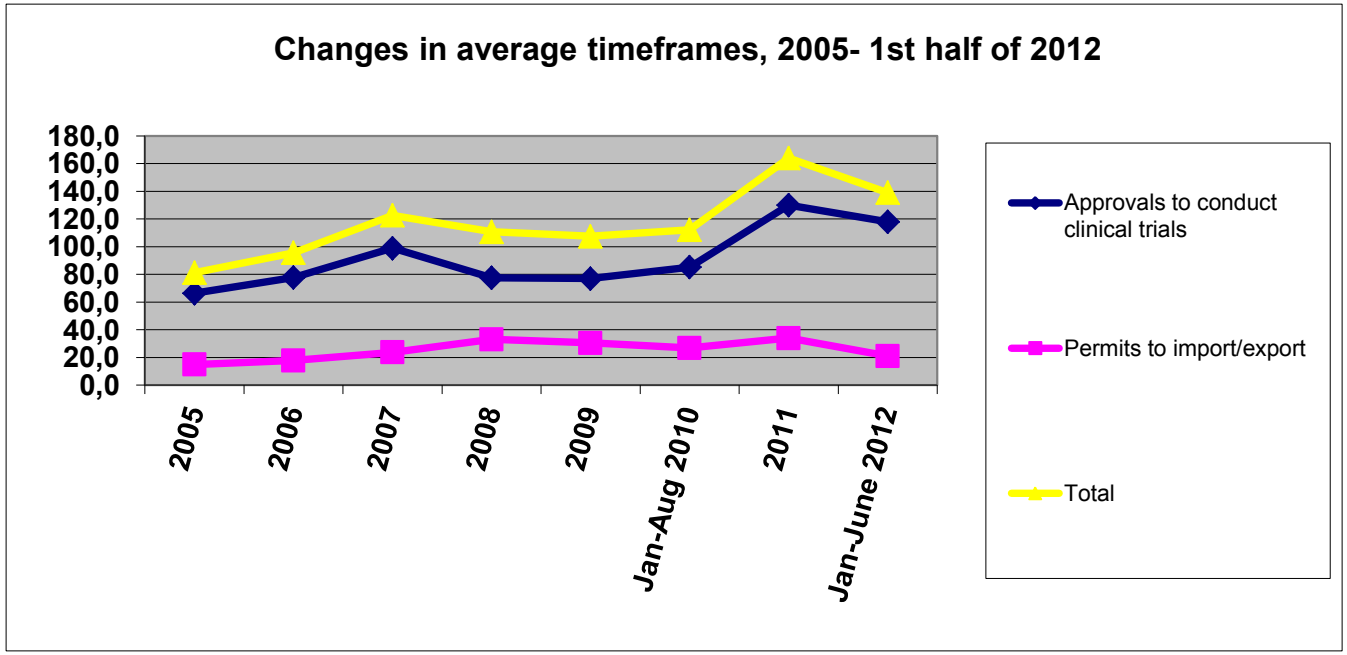

Table 3. Violations of timeframes

	Approvals issued on time	Approvals issued in violation of timeframes					
		Total	less than in 1,5 times	in 1,5-1,9 times	in 2-2,9 times	in 3-3,9 times	in 4 times and more
to conduct clinical trials*	2,0%	98,0%	12,9%	46,5%	23,7%	11,9%	3,0%
to import medicines	13,3%	86,7%	29,4%	32,8%	18,2%	4,9%	1,4%
to import/export biologocal materials	43,6%	56,4%	40,9%	13,1%	2,4%	0,0%	0,0%
to make amendments to the protocol	21,0%	79,0%	36,9%	19,9%	19,9%	1,7%	0,6%
clinical trials, to involve new sites, to enroll	28,9%	71,1%	33,2%	24,3%	10,3%	3,0%	0,3%

*Time spent to reply to Ethical Council's and FGBU requests wasn't taken into account

Table 4. Timeframes for Issuing Approvals to Conduct Clinical Trials

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) *total number of applications is 166*						Sampling*
			average timeframes	minimum timeframes	1st quartile	median	3rd quartile	maximum timeframes	
Application registration (from the date of the submission)	1/1	Paragraph 16 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	3	1	2	2	4	29	139
Data completeness check and decision on issuance of an assignment to carry out expert examination (from the date of the registration)	5/7	Peragraph 3 of the Article 39 of the Federal Law On Circulation of Medicines	20	1	11	20	27	62	106
Receipt of the decision on carrying out/not carriyng out examinations (from the date of the decision)	6/8	1+2	33	10	22	30	38	118	80
Examinations (from the date of the decision)**	30/42	Paragraph 1 of the Article 20 of the Federal Law On Circulation of Medicines	83	15	53	65	95	365	58
Second application submission (from the date of the first application submission)	~	There is no such requirement in the legislation	109	56	78	87	114	431	91
Second application registration (from the date of the submission)	~	There is no such requirement in the legislation	3	1	2	2	4	24	59
Decision on issuance of an approval to conduct a clinical trial	5/7	Paragraph 2 of the Article 22 of the Federal Law On Circulation of Medicines	11	1	7	8	11	41	56
Receipt of the decision on issuance of an approval to conduct a clinical trial (from the date of the decision on issuance of an approval)	0/0	Paragraph 2 of the Article 22 of the Federal Law On Circulation of Medicines	11	1	8	10	13	24	101
Total time to begin a trial**	41/57	the sum of all stages	118	16	88	102	127	410	101

*The samples are different as different companies apply different approaches to timeframes' monitoring

** Time spent to reply to Ethical Council's and FGU requests wasn't taken into account

Table 5. Timeframes for Issuing Permits to Import Medicines

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) *total number of applications is 167*						Sampling*
			average timeframes	minimum timeframes	1st quartile	median	3rd quartile	maximum timeframes	
Application registration (from the date of the submission)	1/1	Paragraph 16 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	3	1	2	2	4	14	111
Data completeness check and decision on whether to grant a permit or to notify that a permit is refused (from the date of the registration)	5/7	Paragraph 12 of the Rules of Import of Medicines for Medical Use into the Russian Federation (Government Order of September 29, 2010 № 771)	9	1	4	8	12	37	108
Receipt of the decision (from the date of the decision)*	2/4	Paragraph 22 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	10	2	6	9	13	45	143
Total time to receive a permit or a notification that a permit is refused (from the date of the submission)	8/12	the sum of all stages	21	8	15	19	23	54	143

Table 6. Timeframes for Issuing Permits to Import/Export Biological Materials

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) *total number of applications is 372*						Sapmling*
			Average timeframes	minimum timeframes	1st quartile	median	3rd quartile	maximum timeframes	
Application registration (from the date of the submission)	1/1	Paragraph 16 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	3	1	2	2	4	14	298
Data completeness check and decision on whether to grant a permit or to notify that a permit is refused (from the date of the registration)	10/14	Paragraph 5 of the Rules for Import and Export of Biological Materials into and outside of the Russian Federation (Government Order of September 3, 2010 №673)	11	1	6	9	15	29	276
Receipt of the decision (from the date of the decision)*	2/4	Paragraph 22 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	10	1	5	9	14	34	336
Total time to receive a permit or a notification that a permit is refused (from the date of the submission)	13/19	the sum of all stages	21	7	17	21	25	47	337

*величина выборки варьируется из-за различий в отслеживании отдельных этапов процесса в различных компаниях

Table 7. Timeframes for Issuing Approvals to Make Amendments to the Protocol

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) *total number of applications is 220*						Sampling*
			average timeframes	minimum timeframes	1st quartile	median	3rd quartile	maximum timeframes	
Application registration (from the date of the submission)	1/1	'''Paragraph 16 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	3	1	2	3	4	22	160
Decision on whether to grant an approval or to notify that an approval is refused (from the date of the registration)	30/42	Paragraph 5 of the Article 40 of the Federal Law On Circulation of Medicines, Paragraph 7 of the MoH Order of August 31, 2010 N 775n	58	5	35	53	73	236	138
Receipt of the decision (from the date of the decision)*	3/5	Paragraph 10 of the MoH Order of August 31, 2010 N 775n	13	1	6	10	16	41	186
Total time to receive an approval or a notification that an approval is refused (from the date of the submission)*	34/48	the sum of all stages	71	15	54	66	85	246	176

Table 8. Timeframes for Issuing Other Approvals (to Involve New Sites, To Enroll Additional Patients, to Prolong Clinical Trials etc.)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) *total number of applications is 346*						Sampling*
			average timeframes	minimum timeframes	1st quartile	median	3rd quartile	maximum timeframes	
Application registration (from the date of the submission)	1/1	Paragraph 16 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477	3	1	2	2	4	12	268
Decision on whether to grant an approval or to notify that an approval is refused (from the date of the registration)	22/30	Article 12 of the Federal Law On Russian citizens' requests consideration of May 2, 2006 № 59	34	2	20	32	44	128	248
Receipt of the decision (from the date of the decision)*	2/4	Paragraph 22 of the Rules of proceedings in the federal executive bodies (Government Order of June 15, 2009 N 477)	12	1	5	10	15	92	301
Total time to receive an approval or a notification that an approval is refused (from the date of the submission)*	25/35	the sum of all stages	48	9	36	43	58	148	301

*The samples are different as different companies use different approaches to timeframes' monitoring