ACTO
ASSOCIATION OF CLINICAL TRIALS ORGANIZATIONS

Timeframes' monitoring (2015 year)

The survey was carried out in January-February 2016.

The sample included submissions made from January 1, 2015 till December 31, 2015 as well as submissions made before January 1, 2015 if decisions on granting/refusing approvals were taken in 2015.

24 ACTO member companies took part in the survey (pharmaceutical companies and contract research organizations).

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.)

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.

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 2005-2015. It's worth noting that before 2011 year 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 (includes only those applications for which there were no requests from expert organizations).

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	98	50	263	220
To import medicines	8/12	13	3	48	361
To import/export biological materials	13/19	19	6	57	694
To make amendments to the protocol	34/48	52	7	103	342
Other approvals (to prolong clinical trials, to involve new sites, to enroll	25/35	24	5	88	665
Total time to obtain approvals to conduct clinical trials and to import/export	54/76	117	~	~	~

Table 2. Changes in average timeframes

	2005	2006	2007	2008	2009	Jan-Aug 2010	2011	2012	2013	2014	2015
Approvals to conduct clinical trials	66	78	99	78	77	85	130	116	87	95	98
Permits to import/export	15	18	24	33	31	27	34	20	20	23	19
Total*	81	96	123	111	108	112	164	135	107	118	117

* 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)

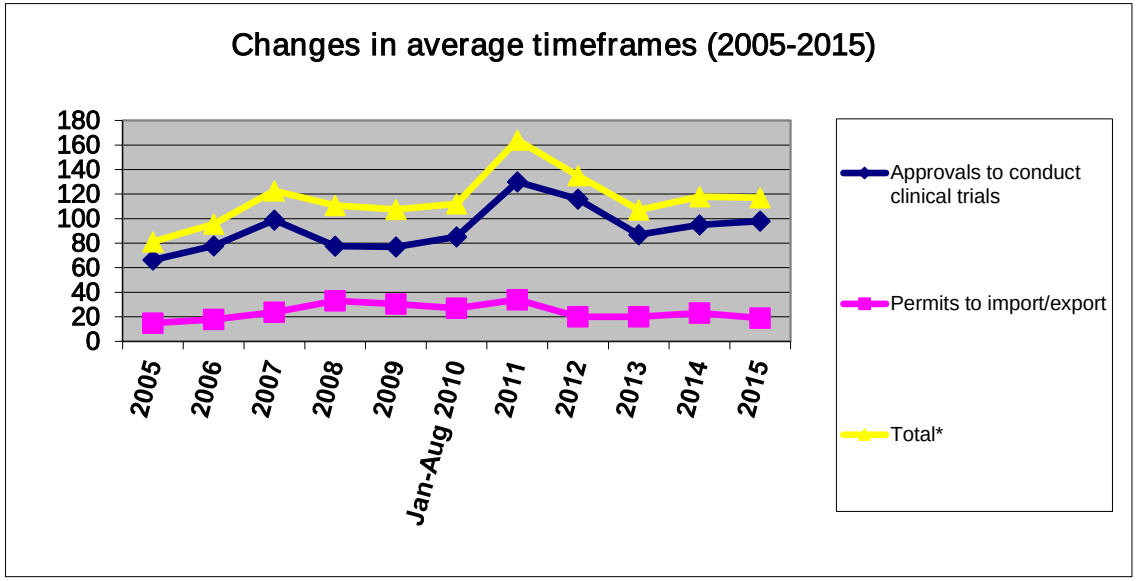

Table 3. Violations of timeframes

	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*	8,2%	91,8%	67,2%	20,9%	3,7%	0,0%	0,0%
to import medicines	59,1%	40,9%	22,4%	14,5%	2,5%	1,2%	0,3%
to import/export biologocal materials	57,2%	42,8%	33,1%	7,6%	1,9%	0,2%	0,0%
to make amendments to the protocol	47,3%	52,7%	42,6%	9,1%	0,9%	0,0%	0,0%
Other Approvals (to Prolong Clinical Trials, to Include New Sites, to Enroll Additional Patients, etc.)	92,1%	7,9%	6,7%	1,0%	0,2%	0,0%	0,0%

*Calculation of violations in cases where no expert requests

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 *264*						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)	0	0	0	0	0	16	172
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	6	0	4	6	6	23	227
Request for additional documents (in case of an incomplete set of documents)	within 5 days	Peragraph4 of the Article 39 of the Federal Law On Circulation of Medicines	6	2	4	6	6	11	30
The applicant's reply to the Ministry of Health request for an incomplete set of documents from the date of request directions	90/126	Peragraph 4 of the Article 39 of the Federal Law On Circulation of Medicines	21	4	8	15	30	62	30
Examinations (from the date of the decision)	30/42	Paragraph 1 of the Article 20 of the Federal Law On Circulation of Medicines	61	23	54	60	68	91	44
The applicant's reply to the request of the expert organization (if any) from the date of the Ministry of Health request	90/126	Request for CT is not provided in the low; in practice, appliesa 'Paragraph 4 of the Article 16 of the Federal Law On Circulation of Medicines	46	4	17	35	62	128	98
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	7	0	0	0	7	53**	37
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	10	0	7	8	12	28	220
Total time to receive a notification that a permit is refused (in case of refusal) from the date of the submission	41/57	the sum of all stages	75	50	64	71	82	121	134 (61% of all permits)
Total time to receive a permit from the date of the submission	141/197	the sum of all stages	132	66	94	128	159	263	86 (39% of all permits)
Total time to receive a permit from the date of the resubmission (if initial submission was refused)	It depends on the presence or absence of expert organizations requests	the sum of all stages	78	40	66	73	83	195	220
Total time to receive a permit after resubmission from the date of the initial submission (if initial submission was refused)	It depends on the presence or absence of expert organizations requests	the sum of all stages	98	50	68	82	113	263	220

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

**The maximum time frame associated with cases of receiving comments from the Ethics Council

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 *353*						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)	0	0	0	0	0	8	167
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)	6	0	3	5	6	35	361
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)	8	1	5	7	9	34	325
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	13	3	9	12	15	48	325

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 *646*						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)	0	0	0	0	0	4	360
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	0	8	11	13	46	694
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)	8	0	6	7	10	46	643
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	19	6	15	18	22	57	643

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

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 *333*						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)	0	0	0	0	0	13	115
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	41	2	34	41	49	98	342
Receipt of the decision (from the date of the decision)	3/5	Paragraph 10 of the MoH Order of August 31, 2010 N 775n	11	0	7	8	13	60	316
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	52	7	42	52	61	103	317

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 *636*						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	1	0	0	0	0	19	243
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	16	1	11	15	21	55	660
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)	8	0	5	7	9	69	611
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	24	5	18	23	28	88	611

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