Association of International Pharmaceutical Manufacturers
Ассоциация международных фармацевтических производителей

АОКИ
Ассоциация Организаций по Клиническим Исследованиям

Timeframes' monitoring (2016 year)

The survey was carried out in January-February 2017.

The sample included submissions made from January 1, 2016 till December 31, 2016 as well as submissions made before January 1, 2016 if decisions on granting/refusing approvals were taken in 2016.

35 ACTO members and AIMP members 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 2005-2016. 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 to Conduct Clinical Trials, 2016

Type of Approval	Timeframes according to legislation (business/ calendar days)	Average timeframes (calendar days)	Minimum timeframes (calendar days)	Maximum timeframes (calendar days)	Sampling
To conduct clinical trial*	41/57**	99	39	326	295
To import medicines	8/12	14	3	36	446
To import/export biosamples	13/19	18	4	59	751
To make amendments to the protocol	34/48	44	7	90	416
Other approvals (to prolong clinical trials, to involve new sites, to enroll additional patients etc.)	25/35	29	7	98	633
Total time to obtain approvals to conduct clinical trials and to import/export	54/76	117	~	~	~

* According to all applications regardless of the availability of the expert organizations' requests. The analysis doesn't exclude the time for submitting the answers to the expert organizations' requests, if any.
** In cases the expert organizations made no requests.

Table 2. Changes in average timeframes

	2005	2006	2007	2008	2009	Jan-Aug. 2010	2011	2012	2013	2014	2015	2016
Approvals to conduct clinical trials	66	78	99	78	77	85	130	116	87	95	98	99
Permits to import/export	15	18	24	33	31	27	34	20	20	23	19	18
Total*	81	96	123	111	108	112	164	135	107	118	117	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)

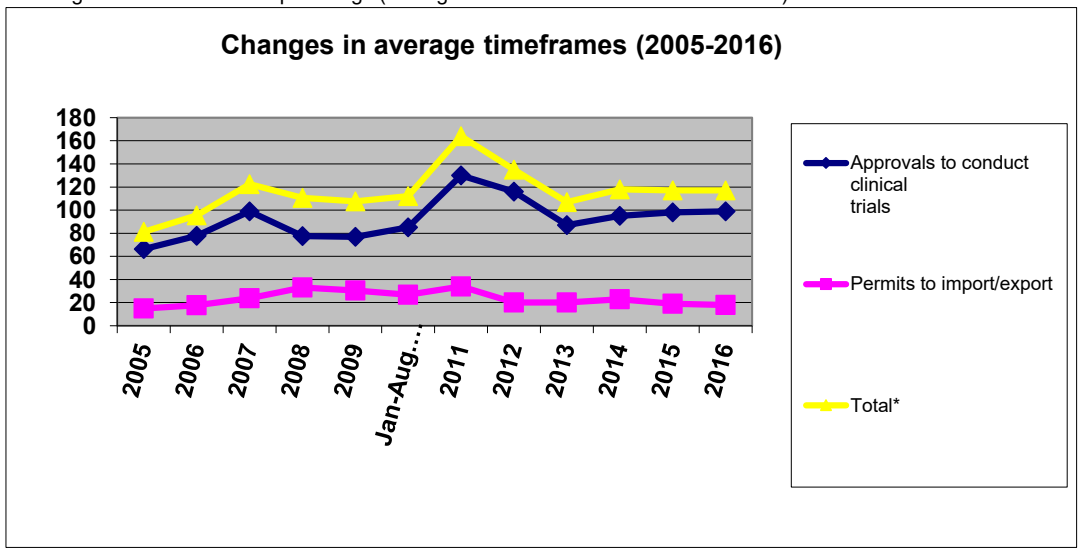

Table 3. Violations of timeframes, 2016

Type of Approval	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
To conduct clinical trials*	19,7%	80,3%	73,2%	4,7%	1,6%	0,8%
To import medicines	42,2%	57,8%	34,1%	20,9%	2,7%	0,2%
To import/export biosamples	65,2%	34,8%	29,2%	5,2%	0,3%	0,1%
To make amendments to the protocol	60,6%	39,4%	34,1%	5,3%	0,0%	0,0%
Other Approvals (to Prolong Clinical Trials, to Include New Sites, to Enroll Additional Patients, etc.)	86,9%	13,1%	11,5%	0,8%	0,8%	0,0%

*Calculation of violations in cases where no expert requests

Table 4. Timeframes for Issuing Approvals to Conduct Clinical Trials, 2016

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) total number of applications is - *309*						Sampling*	Comments
			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	7	259	
Data completeness check and decision on issuance of an assignment to carry out expert examination (from the date of the registration)	5/7	Paragraph 3 of the Article 39 of the Federal Law On Circulation of Medicines	5	0	2	4	6	29	261	
Request for additional documents (in case of an incomplete set of documents)	within 5 business days	Paragraph4 of the Article 39 of the Federal Law On Circulation of Medicines	5	1	3	5	6	15	62	without requests - 246 CTs (79,9%); with one request - 59 CTs (19,2%); with two requests - 3 CTs (1%)
The applicant's reply to the Ministry of Health request for an incomplete set of documents from the date of request directions	90/126	Paragraph 4 of the Article 39 of the Federal Law On Circulation of Medicines	30	3	14	23	38	128	51	
The applicant's respons to the request of the FGBU (if any) from the date of the request by the Ministry of Health	90/126	In the Law, for the case of autorization of CTs the request is not provided. In practice a similar rule applie Paragraph 4.1 of the Article 16 Federal Law On Circulation of Medicines	49	3	26	41	65	132	102	without requests - 208 CTs (68,4%), but 3 of them - the refusals without request; with one request - 86 CTs (28,3%); with two requests - 8 CTs (2,6%); withthree requests - 2 CTs (0,7%)
The applicant's respons to the comments of the Ethics Council (if any) from the date of receipt of comments			21	1	7	15	29	97	56	approved without comments - 217 CTs (73,5%); approved with the comments that are made on a routine basis - 63 CTs (21,4%); not approved (refusal) - 15 CTs (5,1%)
The applicant receives the decision to issue a permit for a clinical trial from the date of the decision to issue a pefrmit	0/0	Paragraph 7 of the Article 39 of the Federal Law On Circulation of Medicines	10	3	7	9	13	36	245	
The time to obtain permissions in case the expert organizations made no requests	41/57	The sum of all stages	66	39	60	64	68	133	127	without requests or comments - 127 CTs (43,1%), but 10 of them (3,4%) - refusals without requests and comments; requests (request 1 or 2) and/or comments - 168 CTs (56,9%)
The time to obtain permissions in case of expert organization(s) request(s)/ The analysis doesn't exclude the time for submitting the answers to the expert organizations' requests.	141/197	The sum of all stages	123	50	91	113	138	326	168	
The time to obtain all permissions. (The analysis excludes the time for submitting the answers to the expert organizations' requests)	It depends on the presence or absence of expert organizations requests	The sum of all stages	73	28	63	70	79	170	295	
The time to obtain all permissions. (The analysis doesn't exclude the time for submitting the answers to the expert organizations' requests)	It depends on the presence or absence of expert organizations requests	The sum of all stages	99	39	66	86	115	326	295	

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

Table 5. Timeframes for Issuing Permits to Import Medicines, 2016

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) total number of applications is *483*						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	6	233
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	28	474
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	8	11	30	446
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	14	3	10	13	17	36	446

Table 6. Timeframes for Issuing Permits to Import/Export Biological Materials, 2016

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) total number of applications is - *780*						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 rder of June 15, 2009 N 477))	0	0	0	0	0	11	459
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)	10	0	7	10	13	50	771
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	25	751
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	18	4	14	17	21	59	751

*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, 2016

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) total number of applications is *458*						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	21	241
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	35	0	20	38	47	89	448
Receipt of the decision (from the date of the decision)	3/5	Paragraph 10 of the MoH Order of August 31, 2010 N 775n	9	0	6	7	11	32	416
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	44	7	33	48	56	90	416

Table 8. Timeframes for Issuing Other Approvals (to Involve New Sites, to Enroll Additional Patients, to Prolong clinical Trials etc.), 2016

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) total number of applications is *663*						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	393
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	20	0	15	21	25	87	653
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	70	633
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	29	7	23	28	34	98	633

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