AIPM Association of International Pharmaceutical Manufacturers Ассоциация международных фармацевтических производителей

ACTO Association of Clinical Trials Organizations

Timeframes' monitoring (2020 year)

The survey was carried out in February 2021.

The sample included submissions made from January 1, 2020 till December 31, 2020 as well as submissions made before January 1, 2020 if decisions on granting/refusing approvals were taken in 2021.

28 pharmaceutical companies and contract research organizations (ACTO and AIMP members) 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.). The calculation did not include clinical trials on Covid-19.

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 2005-2020. Data on the timing of obtaining approvals for clinical trials on COVID-19 in 2020 was not taken into account. It's worth noting that before 2011 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). Data on the timing of obtaining approvals for clinical trials on COVID-19 in 2020 was not taken into account.

Tables 4-8 provide detailed information on timeframes for issuing all sorts of approvals. The corresponding tables without the letter "C" contain data for all clinical trials excluding trials on Covid-19. Tables with data on the timing of obtaining approvals for clinical trials related to Covid-19 are indicated with the letter "C".

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, 2020 (excluding CTs on Covid-19)

Type of approval	Timeframes according to legislation (business/ calendar days)	Average timeframes (calendar days)	Minimum timeframes (calendar days)	1st quartile	Median	3rd quartile	Maximum timeframes (calendar days)	Sampling
To conduct clinical trial*	41/57**	103	58	74	90	120	286	197
To import medicines	8/12	17	6	14	16	21	49	434
To import/export biosamples	13/19	22	6	18	21	26	80	772
To make amendments to the protocol	34/48	65	10	58	65	74	120	517
Other approvals (to prolong clinical trials, to involve new sites, to enroll additional patients etc.)	25/35	39	7	29	37	44	126	836
Total time to obtain approvals to conduct clinical trials and to import/export	54/76	125	~	~	~	~	~	~

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

Table 2. Changes in average timeframes

	2005	2006	2007	2008	2009	Jan-Aug 2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Approvals to conduct clinical trials	66	78	99	78	77	85	130	116	87	95	98	99	95	92	87	103
Permits to import/export	15	18	24	33	31	27	34	20	20	23	19	18	20	21	20	22
Total*	81	96	123	111	108	112	164	135	107	118	117	117	115	113	107	125

* 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)

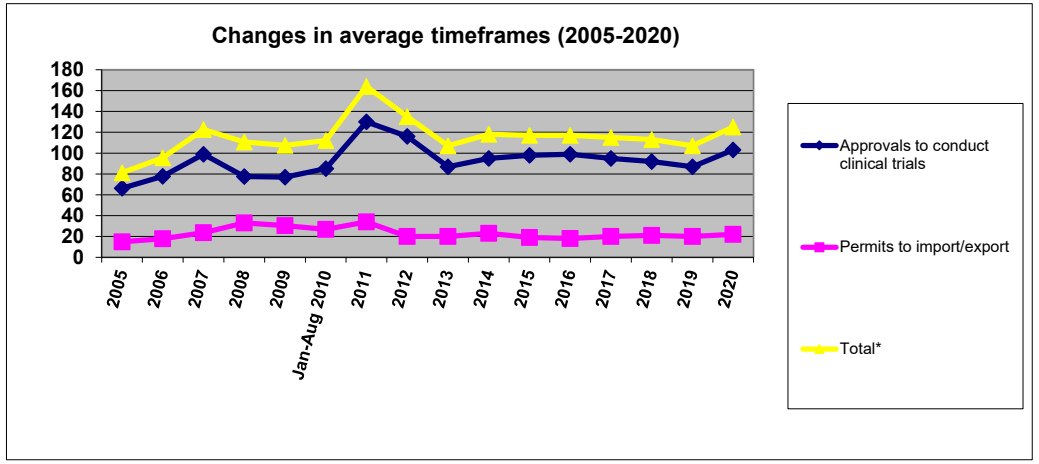

Table 3. Violations of timeframes, 2020 (excluding CTs on Covid-19)

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	In 4 times and more
To conduct clinical trials*	2,8%	97,3%	71,6%	20,2%	5,5%	0,0%	0,0%
To import medicines	15,9%	84,1%	42,2%	28,6%	12,4%	0,7%	0,2%
To import/export biosamples	35,0%	65,0%	44,8%	16,1%	3,5%	0,5%	0,1%
To make amendments to the protocol	12,4%	87,6%	48,5%	36,6%	2,5%	0,0%	0,0%
Other approvals (to prolong clinical trials, to include new sites, to enroll additional patients, etc.)	47,1%	52,9%	43,7%	7,1%	1,9%	0,2%	0,0%

*Calculation of violations in cases where were no expert/MoH requests

Table 4. Timeframes for issuing approvals to conduct clinical trials, 2020 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *232*						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	6	198	
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	4	6	6	17	205	
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	6	1	6	6	7	14	23	without requests - 209 CTs (90,1%); with one request - 22 CTs (9,5%); with two requests - 1 CT (0,4%)
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	24	5	15	23	30	57	24	
The applicant's respons to the request of the FSBI (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	45	4	25	41	57	116	58	without requests - 168 CTs (73%) with one request - 58 CTs (25,2%); refusal - 4 CTs (1,7%)
The applicant's respons to the comments of the Ethics Council (if any) from the date of receipt of comments			16	1	5	11	22	79	39	approved without comments - 189 CTs (81,5%); comments - 41 CTs (17,7%); refusal - 2 CTs (0,9%)
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	13	2	8	11	15	58	202	
The time to obtain permissions in case the expert organizations/MoH made no requests	41/57	The sum of all stages	78	58	70	74	83	127	109	without requests or comments - 109 CTs (54%); requests (request 1 or 2) and/or comments or refusal - 93 CTs (46%)
The time to obtain permissions in case the expert organizations/MoH made requests (The analysis doesn't exclude the time for submitting the answers to the requests)	141/197	The sum of all stages	134	72	105	124	158	286	87	
The time to obtain all permissions. (The analysis is excluded the time for submitting the answers to the expert organizations/MoH requests)	It depends on the presence or absence of expert organizations/MoH requests	The sum of all stages	86	58	71	81	94	165	197	
The time to obtain all permissions. (The total analysis doesn't exclude the time for submitting the answers to the expert organizations/MoH requests)	It depends on the presence or absence of expert organizations/MoH requests	The sum of all stages	103	58	74	90	120	286	197	

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

Table 4C. Timeframes for issuing approvals to conduct clinical trials, 2020 (only for CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *22*						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)	1	0	0	0	1	6	19	
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	3	0	1	3	5	6	19	
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	1						1	without requests - 21 CTs (95,5%); with one request - 1 CT (4,5%)
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	12						1	
The applicant's respons to the request of the FSBI (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	28	18	24	29	32	35	4	without requests - 18 CTs (81,8%) with one request - 4 CTs (18,2%)
The applicant's respons to the comments of the Ethics Council (if any) from the date of receipt of comments			22	4	4	14	33	54	5	approved without comments - 16 CTs (72,7%); comments - 5 CTs (22,7%); refusal - 1 CT (4,6%)
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	6	2	3	6	7	18	18	
The time to obtain permissions in case the expert organizations/MoH made no requests	41/57	The sum of all stages	21	11	17	20	25	32	11	without requests or comments - 11 CTs (61,1%);
The time to obtain permissions in case the expert organizations/MoH made requests (The analysis doesn't exclude the time for submitting the answers to the requests)	141/197	The sum of all stages	27	10	16	23	28	63	6	requests (request 1 or 2) and/or comments or refusal - 7 CTs (38,9%)
The time to obtain all permissions. (The analysis is excluded the time for submitting the answers to the expert organizations/MoH requests)	It depends on the presence or absence of expert organizations/MoH requests	The sum of all stages	19	5	12	18	23	37	16	
The time to obtain all permissions. (The total analysis doesn't exclude the time for submitting the answers to the expert organizations/MoH requests)	It depends on the presence or absence of expert organizations/MoH requests	The sum of all stages	25	10	16	20	28	65	17	

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

Table 5. Timeframes for issuing permits to import medicines, 2020 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *462*						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	3	246
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)	5	0	3	5	6	27	445
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	2	8	11	15	47	434
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	17	6	14	16	21	49	434

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

Table 5C. Timeframes for issuing permits to import medicines, 2020 (only for CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 17						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	1	8	17
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)	4	1	1	3	6	7	17
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)	6	2	4	7	7	9	14
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	10	5	9	10	13	15	14

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

Table 6. Timeframes for issuing permits to import/export biological materials, 2020 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *820*						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	12	448
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	8	11	13	56	804
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)	11	0	8	11	14	49	772
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	22	6	18	21	26	80	772

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

Table 6C. Timeframes for issuing permits to import/export biological materials, 2020 (only for CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 21						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	1	8
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)	5	0	1	2	8	14	21
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	4	7	8	13	20	17
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	15	8	10	13	15	33	17

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

Table 7. Timeframes for issuing approvals to make amendments to the protocol, 2020 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 575						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	9	415
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	52	0	44	53	62	109**	563
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	0	8	12	15	74	517
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	65	10	58	65	74	120**	517

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

**Not a mistake

Table 7C. Timeframes for issuing approvals to make amendments to the protocol, 2020 (only for CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 22						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	1	16
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	13	1	7	12	17	30	22
Receipt of the decision (from the date of the decision)	3/5	Paragraph 10 of the MoH Order of August 31, 2010 N 775n	7	2	5	7	7	15	16
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	22	10	15	20	28	37	16

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

Table 8. Timeframes for issuing other approvals (to involve new sites, to enroll additional patients, to prolong clinical trials etc.), 2020 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 868						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	27	603
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	27	1	19	26	31	95	854
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	0	7	10	14	94**	836
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	39	7	29	37	44	126**	836

*The samples are different as different companies apply different approaches to timeframe's monitoring
**Not a mistake

Table 8C. Timeframes for issuing other approvals (to involve new sites, to enroll additional patients, to prolong clinical trials etc.), 2020 (only for CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 22						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	2	17
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	6	0	1	3	12	33	22
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	8	32	22
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	15	2	8	12	19	48	22

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