Association of International Pharmaceutical Manufacturers
Ассоциация международных фармацевтических производителей

ACTO
Association of Clinical Trials Organizations

Timeframes' monitoring (2021 year)

The survey was carried out in February 2022.

The sample included submissions made from January 1, 2021 till December 31, 2021 as well as submissions made before January 1, 2021 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 (in total, according to all data for the year, incl. submissions made both before and after the introduction of the electronic system), 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 (regardless of whether there were requests from expert organizations in the process of reviewing applications or not) and permits to import/export as well as total time to begin a trial in 2005-2021. Data on the timing of obtaining approvals for clinical trials on Covid-19 in 2021 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). Since the implementation of electronic document flow system was carried out in 2021 for two types of permits (import of medicines and import/export of biological samples), data are presented separately before and after the implementation. Data on the timing of obtaining approvals for clinical trials on Covid-19 in 2021 was not taken into account.

Tables 4, 7 and 8 as well as 4C, 7C and 8C 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".

Tables 5 and 6, as well as 5e and 6e, provide statistics on the timing of obtaining an approval for the import of medicines and the import /export of biological samples. The calculation did not take into account whether the study was related to Covid-19 or not. Tables 5 and 6 present data on approvals obtained before the implementation of electronic document flow system. Tables 5e and 6e contain data on approvals received after the implementation of electronic document flow system.

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, 2021 (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**	111	52	82	100	132	345	291
To import medicines***	8/12	15	1	10	14	15	51	450
To import/export biosamples***	13/19	17	1	13	15	21	61	1 059
To make amendments to the protocol	34/48	77	34	69	76	83	132	519
Other approvals (to prolong clinical trials, to involve new sites, to enroll additional patients etc.)	25/35	44	10	38	44	50	104	865
Total time to obtain approvals to conduct clinical trials and to import/export	54/76	128	~	~	~	~	~	~

* 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.
*** All data, including those obtained before the introduction of the electronic system and after.

Table 2. Changes in average timeframes

	2005	2006	2007	2008	2009	Jan-Aug 2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Approvals to conduct clinical trials	66	78	99	78	77	85	130	116	87	95	98	99	95	92	87	103	111
Permits to import/export	15	18	24	33	31	27	34	20	20	23	19	18	20	21	20	22	17
Total*	81	96	123	111	108	112	164	135	107	118	117	117	115	113	107	125	128

* 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)

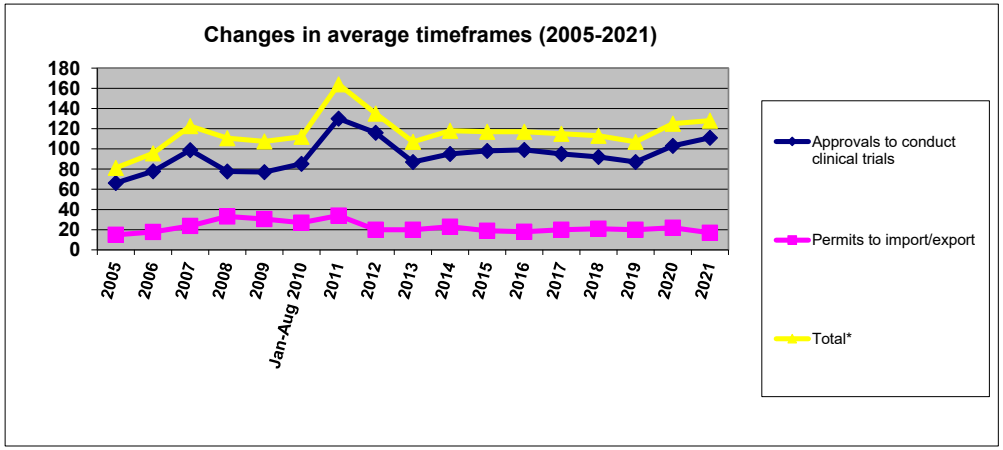

Table 3. Violations of timeframes, 2021 (excluding CTs on Covid-19)

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*	0,7%	99,3%	50,7%	47,2%	1,4%	~	~
To import medicines (before switching to the electronic system from September 1, 2021)	12,7%	87,3%	47,2%	26,6%	11,7%	1,5%	0,3%
To import medicines (after switching to the electronic system from September 1, 2021)	85,7%	14,3%	7,9%	6,4%	~	~	~
To import/export biosamples (before switching to the electronic system from July 1, 2021)	42,6%	57,4%	44,4%	11,7%	1,3%	~	~
To import/export biosamples (after switching to the electronic system from July 1, 2021)	88,5%	11,5%	8,8%	2,5%	~	0,2%	~
To make amendments to the protocol	0,4%	99,6%	26,6%	62,8%	10,2%	~	~
Other approvals (to prolong clinical trials, to include new sites, to enroll additional patients, etc.)	19,6%	80,4%	56,8%	20,8%	2,7%	0,1%	~

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

Table 4. Timeframes for issuing approvals to conduct clinical trials, 2021 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *311*						Sampling*	Comments
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes		
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	11	274	
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	6	0	6	6	7	34	301	
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	0	5	6	7	9	34	without requests - 277 CTs (89,1%); with one request - 30 CTs (9,6%); with two requests - 4 CTs (1,3%)
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	25	2	13	23	32	69	38	
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	43	3	25	36	52	131	61	without requests - 250 CTs (80,4%); with one request - 56 CTs (18,0%); with two requests - 1 CT (0,3%) refusal - 4 CTs (1,3%)
The applicant's respons to the comments of the Ethics Council (if any) from the date of receipt of comments			19	1	9	15	26	99	104	approved without comments - 204 CTs (65,5%); approved with a single comment - 101 CTs (32,5%); approved with two comments - 3 CTs (1%) refusal - 3 CTs (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	12	0	8	11	15	36	279	
The time to obtain permissions in case the expert organizations/MoH made no requests	41/57	The sum of all stages	83	52	77	82	91	119	140	without requests or comments - 140 CTs (46,7%);
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	137	71	114	128	152	345	150	requests (request 1 or 2) and/or comments or refusal - 160 CTs (53,3%)
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	95	52	81	92	101	191	291	
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	111	52	82	100	132	345	291	

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

Table 4C. Timeframes for issuing approvals to conduct clinical trials, 2021 (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 - *12*						Sampling*	Comments
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes		
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	1	10	
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	6	4	4	7	7	14	12	
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	12	4	10	15	16	17	3	without requests - 9 CTs (75%); with one request - 2 CTs (16,7%); with two requests - 1 CT (8,3%)
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	9	11	13	32	86	4	
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	39	10	29	35	49	77	7	without requests - 6 CTs (50%); with one request - 5 CTs (41,7%); with two requests - 1 CT (8,3%)
The applicant's respons to the comments of the Ethics Council (if any) from the date of receipt of comments			18	13	14	14	20	26	3	approved without comments - 9 CTs (75%); approved with a single comment - 3 CTs (25%);
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	8	4	7	8	10	13	11	
The time to obtain permissions in case the expert organizations/MoH made no requests	41/57	The sum of all stages	62	37	44	72	72	85	5	without requests or comments - 5 CTs (41,7%);
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	77	114	134	163	182	6	requests (request 1 or 2) and/or comments or refusal - 7 CTs (58,3%)
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	76	37	69	72	94	106	11	
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	101	37	72	85	134	182	11	

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

Table 5. Timeframes for issuing permits to import medicines, 2021
(before the implementation of electronic document flow system from September 1, 2021)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 336						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	1	171
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	Item 9 of the Rules for the import of medicinal products for medical use into the territory of the Russian Federation (Decree No. 853 of 01.06.2010)	6	0	4	6	6	36	336
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	12	0	8	11	15	36	324
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	18	7	14	16	21	51	324

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

Table 5e. Timeframes for issuing permits to import medicines, 2021
(after the implementation of electronic document flow system from September 1, 2021)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 164						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	0	99
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	Item 9 of the Rules for the import of medicinal products for medical use into the territory of the Russian Federation (Decree No. 853 of 01.06.2010)	5	0	4	6	6	13	164
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	3	0	1	2	4	17	126
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	8	1	6	7	9	22	126

*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, 2021 (before the implementation of electronic document flow system from July 1, 2021)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *578*						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	7	346
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	29	578
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	11	0	7	10	14	49	547
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	15	21	24	56	547

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

Table 6e. Timeframes for issuing permits to import/export biological materials, 2021 (after the implementation of electronic document flow system from July 1, 2021)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - *559*						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	0	361
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	Item 9 of the Rules for the import of medicinal products for medical use into the territory of the Russian Federation (Decree No. 853 of 01.06.2010)	10	0	8	11	13	59	558
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	3	0	1	2	4	26	513
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	13	1	10	13	15	61	512

*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, 2021 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 563						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	10	530
Appointment by the MoH of expertise from the date of receipt of materials	5/7	The law does not establish, it is applied by analogy with Part 3 of Article 39 of the Federal Law On Circulation of Medicines	8	0	4	6	11	35	502
Receipt of documents to the Ethics Council from the date of appointment of the examination			8	1	4	7	9	49	486
Consideration by the Ethics Council from the date of receipt of materials	30/42	The law does not establish, it is applied by analogy with Part 6 of Article 39 of the Federal Law On Circulation of Medicines	38	9	26	40	48	62	486
Decision on whether to grant an approval or to notify that an approval is refused (from the date of the consideration by the Ethics Council)	5/7	The law does not establish, it is applied by analogy with Part 7 of Article 39 of the Federal Law On Circulation of Medicines	10	6	8	9	13	72	548
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	65	19	57	64	71	121	552
Receipt of the decision (from the date of the decision)	3/5	Paragraph 10 of the MoH Order of August 31, 2010 N 775n	12	1	8	11	14	41	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	77	34	69	76	83	132	519

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

Table 7C. Timeframes for issuing approvals to make amendments to the protocol, 2021 (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 - 14						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	0	12
Appointment by the MoH of expertise from the date of receipt of materials	5/7	The law does not establish, it is applied by analogy with Part 3 of Article 39 of the Federal Law On Circulation of Medicines	3	0	1	2	4	14	13
Receipt of documents to the Ethics Council from the date of appointment of the examination			3	1	1	2	5	7	13
Consideration by the Ethics Council from the date of receipt of materials	30/42	The law does not establish, it is applied by analogy with Part 6 of Article 39 of the Federal Law On Circulation of Medicines	13	1	11	12	13	43	13
Decision on whether to grant an approval or to notify that an approval is refused (from the date of the consideration by the Ethics Council)	5/7	The law does not establish, it is applied by analogy with Part 7 of Article 39 of the Federal Law On Circulation of Medicines	8	0	3	7	9	25	14
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	26	9	21	23	31	57	14
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	2	6	8	11	16	14
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	35	25	29	34	36	63	14

*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.), 2021 (excluding CTs on Covid-19)

Stages of review	Timeframes according to legislation (business/calendar days)	Legislation (references)	Practice (calendar days) Total number of applications - 922						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	19	772
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	32	0	28	33	37	80	992
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	12	0	8	11	14	65	865
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	44	10	38	44	50	104	865

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

Table 8C. Timeframes for issuing other approvals (to involve new sites, to enroll additional patients, to prolong clinical trials etc.), 2021 (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 - 39						Sampling*
			Average timeframes	Minimum timeframes	1st quartile	Median	3rd quartile	Maximum timeframes	
Application registration (from the date of the submission)	1/1	Item 3.22 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	0	0	0	0	0	0	28
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	23	0	12	27	35	42	39
Receipt of the decision (from the date of the decision)	2/4	Item 3.35 of the Rules of record keeping in state bodies, local self-government bodies (Order of the Federal Archive of 22.05.2019 N 71)	9	3	7	8	12	23	39
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	32	8	19	38	42	57	39

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