European Commission

EMA
EUROPEAN MEDICINES AGENCY

HMA
Heads of Medicines Agencies

Monitoring the European clinical trials environment

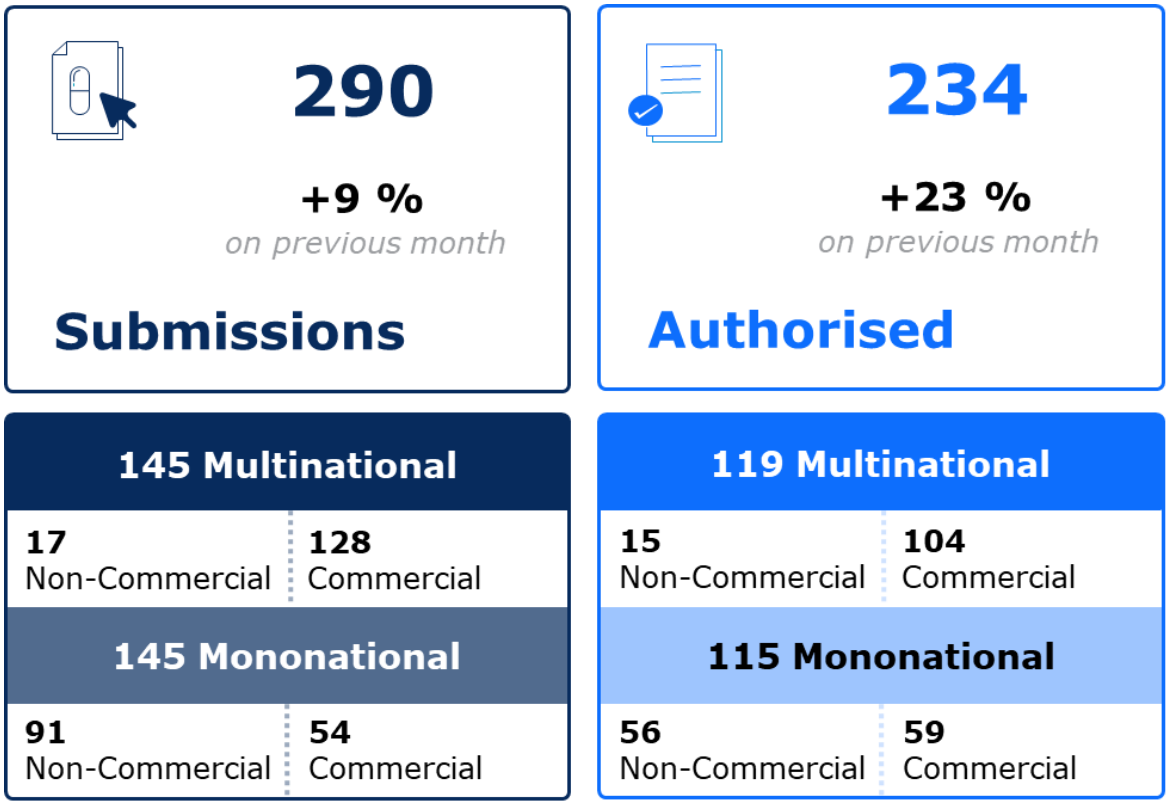
A deliverable of the ACT EU Priority Action 2

October 2023

An agency of the European Union

Clinical Trials in the EU/EEA

October 2023



The metrics in this report provide information on the trend of the clinical research environment in the European Union (EU) and European Economic Area (EEA). The numbers used are based on data retrieved from the Clinical Trials Information System (CTIS) for clinical trials regulated under the regime of the Clinical Trials Regulation (EU) No 536/2014 (CTR).

The data set for this report shows data for the month of October 2023, as of 31 October 2023, as well as cumulative numbers since the launch of CTIS on 31 January 2022.

Since the mandatory use of CTIS for initial clinical trial applications, 31 January 2023, the average submission of clinical trials applications, of any type, has seen a significant increase, averaging 228 submissions per month.

A total of 2,685 clinical trial applications have been submitted since the launch of CTIS.

At the time when the report is generated, more than 740 initial clinical trials are ongoing in EU/EEA under the CTR.

The therapeutic areas mostly investigated is Neoplasms (Tumour).

If you have any questions about this document, please contact us at
www.ema.europa.eu/contact

Contents

Chapter 1

Submitted initial clinical trial applications

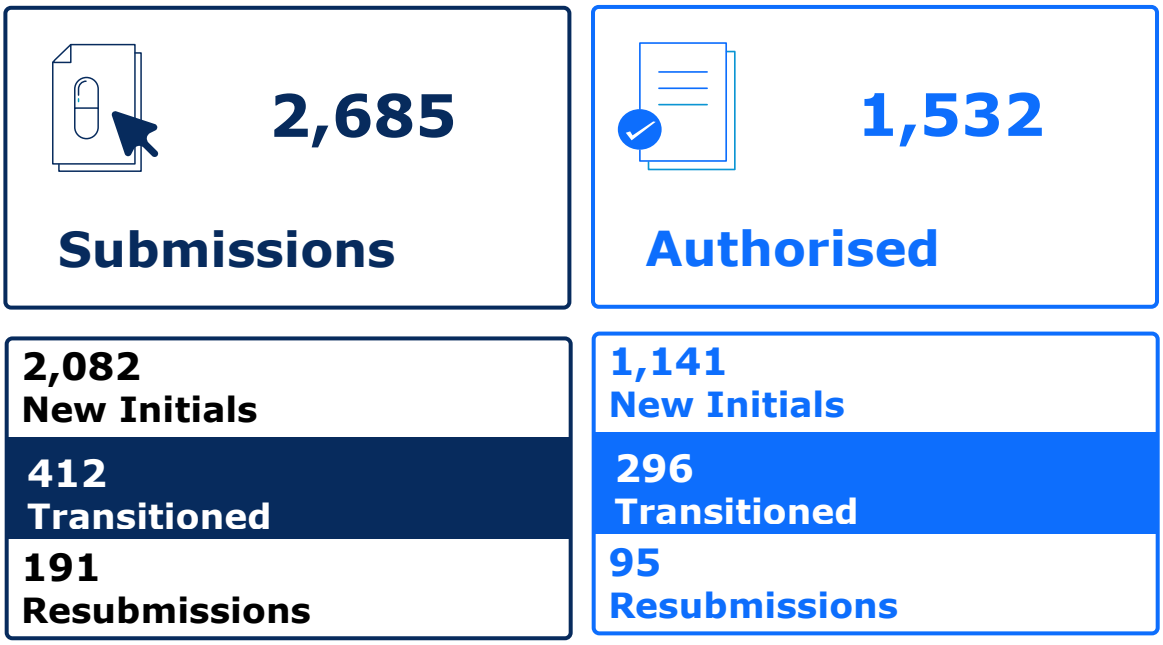
Chapter 1 of this report provides information on **submitted** initial clinical trial applications (CTAs), presented on the applicable statuses.

For detailed information on **authorised** clinical trials please refer to chapter 2 of this report.

Initial clinical trial applications are those applications:

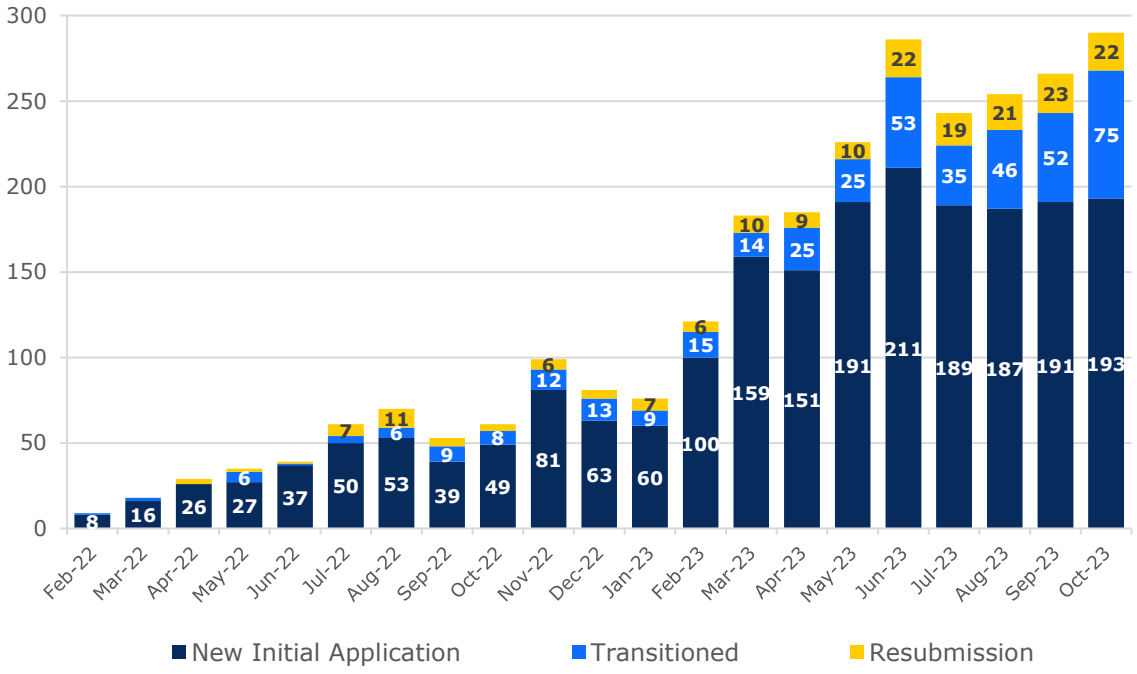
- new initial clinical trial applications submitted in CTIS by the sponsors under the Clinical Trials Regulation (EU) 536/2014 (CTR);
- trials which were already authorised under the regime of Clinical Trials Directive 2001/20/EC (CTD) and that have been transitioned to the regime of CTR;
- resubmitted initial clinical trial applications, which were previously either withdrawn, lapsed, or not authorised.

The overview below presents the **cumulative numbers** for initial clinical trial applications submitted since 31 January 2022:



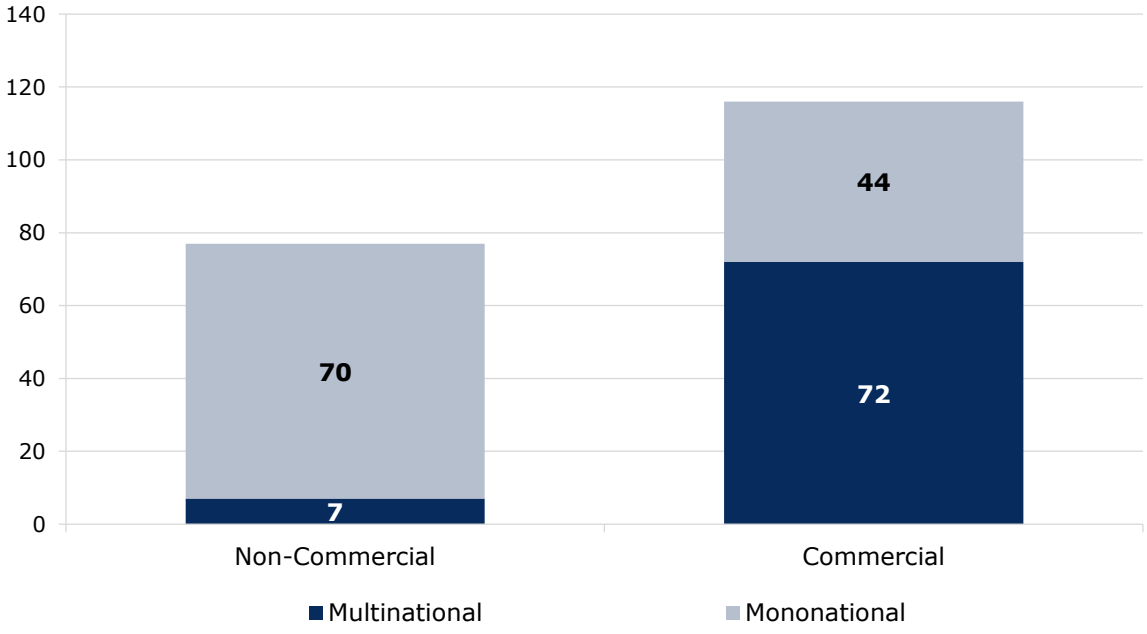
Monthly submissions of initial clinical trial applications

In **October 2023**, 290 initial clinical trial applications have been submitted, of which 193 new initial CTA, 75 are trials transitioned to CTR, and 22 are resubmissions of previously submitted initial applications.



New initial clinical trial applications per sponsor type and mono- vs multinational trials

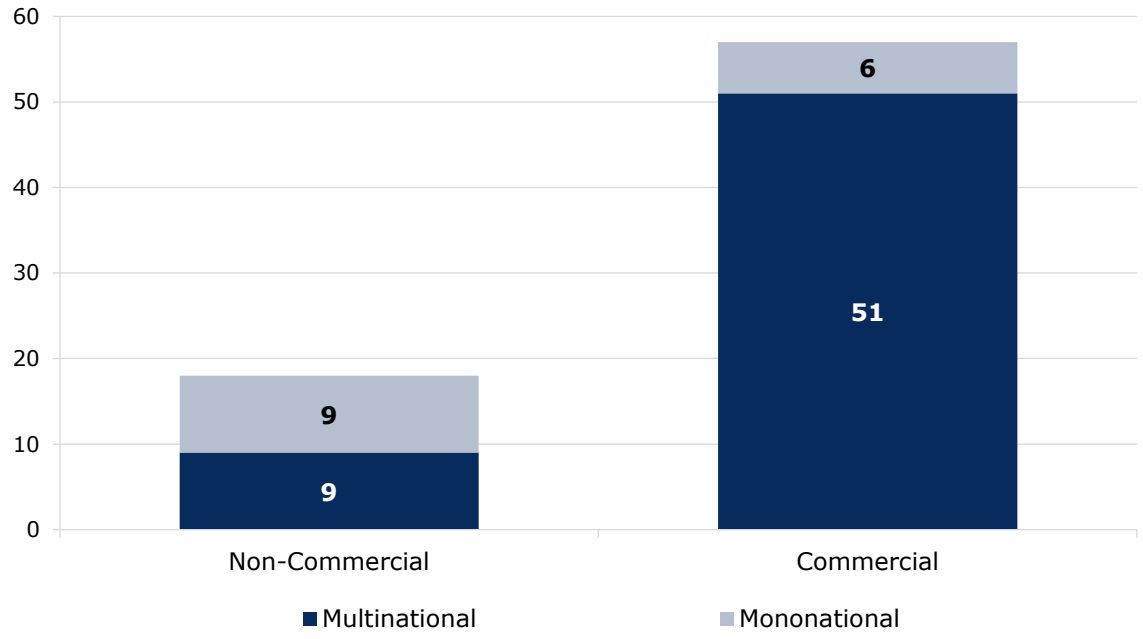
The graph below shows the split of submissions of new initial clinical trial applications in October 2023 into commercial/non-commercial sponsors and mononational versus multinational trials.



Clinical trials transitioned from CTD to CTR per sponsor type and mono- vs multinational trials

Since 31 January 2022 the CTR repealed the Clinical Trial Directive 2001/20/EC (CTD) and a 3-year transition period is foreseen from the implementation of the CTR. During this period, sponsors have to transition those clinical trials that are planned to continue after the end of the transition period. From 31 January 2025 onwards, all clinical trials have to follow the regime of the CTR.

The graph below shows the split of submissions of transitioned clinical trials in October 2023 into commercial/non-commercial sponsors and mononational versus multinational trials.



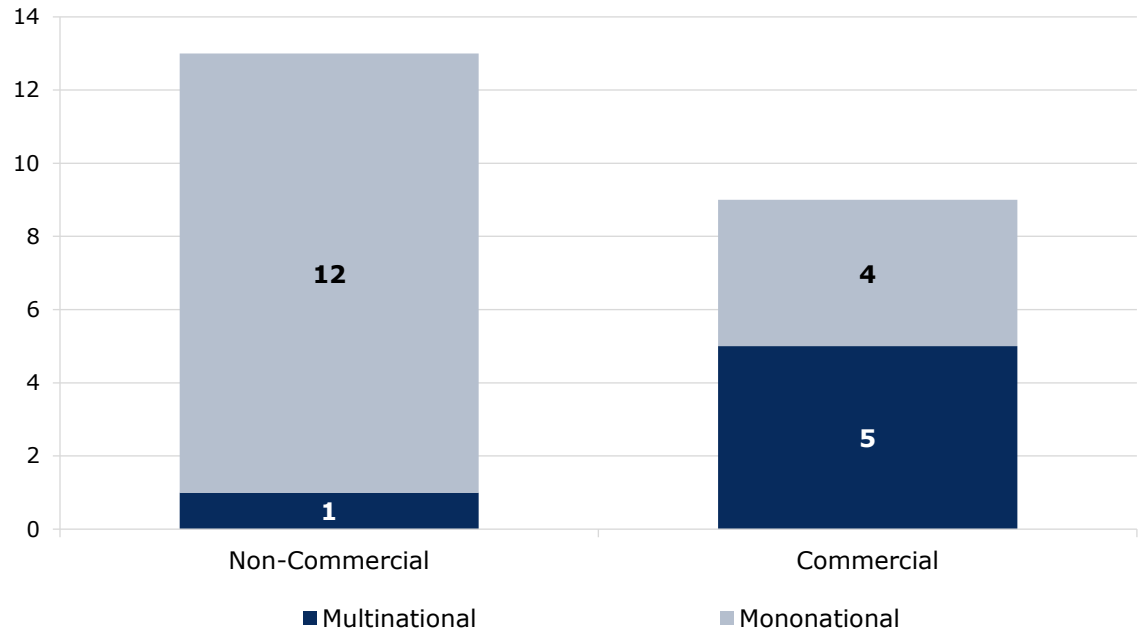
Once notified by the clinical trial sponsors, the National Competent Authorities of the EU/EEA Member States are responsible for keeping, in the EudraCT database, the information on the trial status up to date, including inserting the end of trial date, as applicable.

Further information can be found under the following links:

- Guidance for the transition of clinical trials from the Clinical trials Directive to the Clinical Trials Regulation
- CTCG Best Practice Guide for sponsors of multinational clinical trials under CTD transitioned to CTR
- CTCG Annex cover letter template - CTCG Best Practice Guide for sponsors of multinational clinical trials under CTD transitioned to CTR

Resubmitted initial clinical trial applications per sponsor type and mono- vs multinational trials

The graph below shows the split of resubmitted initial clinical trial applications in October 2023 into commercial/non-commercial sponsors and mononational versus multinational trials.



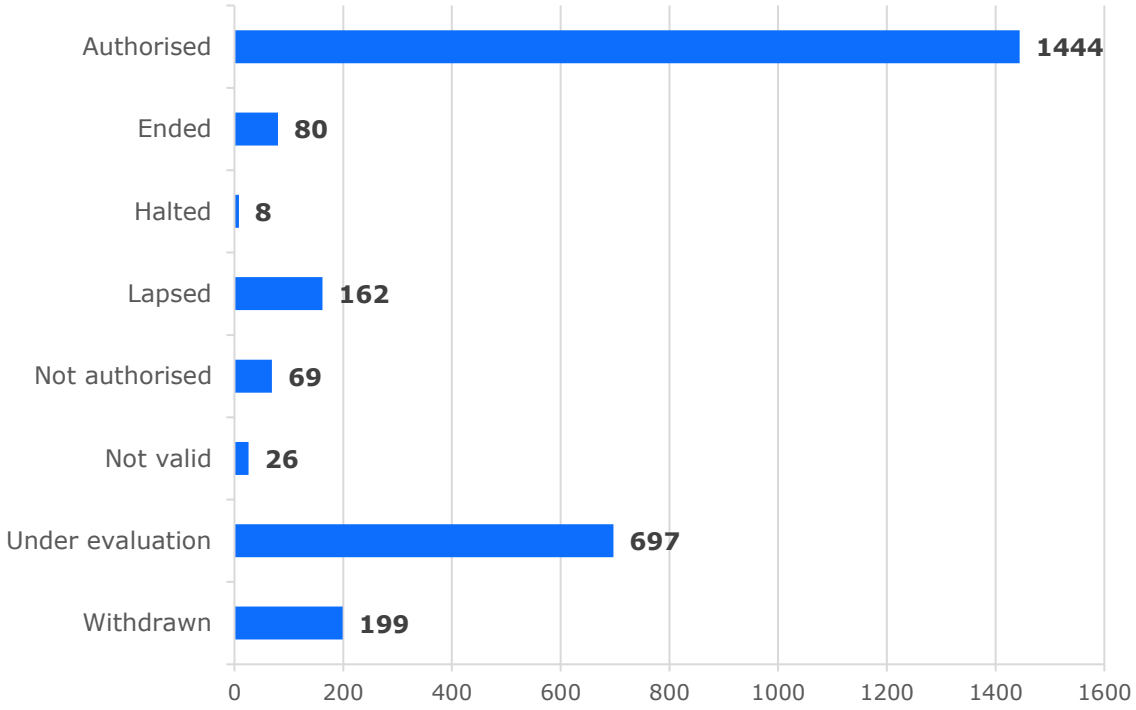
Clinical trials per applicable statuses

Since 31 January 2022, a total of 2,685 initial clinical trial applications have been submitted in CTIS.

The graph below shows the number of trials submitted since 31 January 2022 per applicable overall status at EU level. It should be noted that the status 'authorised with conditions' does not appear in the graph below as it is a status applicable **at the level of the Member States Concerned**.

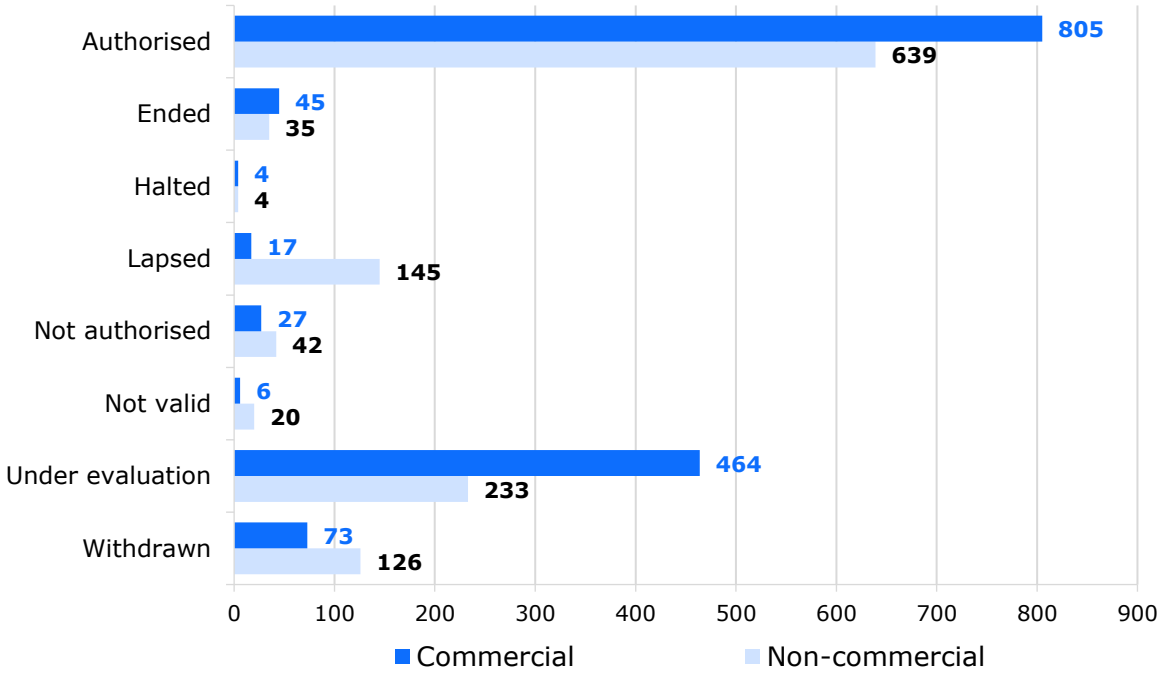
Clinical trials per applicable statuses

The graph below shows the status of each clinical trial as recorded in CTIS at the time when the report is generated.



Clinical trials classified per statuses and per sponsor type

The graph below shows the cumulative figure per status of each clinical trial as recorded in CTIS at the time when the report is generated, in combination with information on sponsor type.



Distribution of submitted **new** initial clinical trial applications per Member State Concerned

The overview below provides information on new initial clinical trial applications submitted since 31 January 2022 by looking at Member States involvement in mono/multi-national trials, as Reporting Member State (RMS)[1] and Member State Concerned (MSC).

Member State	Multinational Trials		Mono-national Trials	Total number of Initial CTAs
	MSC	*Of which as RMS*		
Austria	147	28	14	161
Belgium	295	54	113	408
Bulgaria	131	0	6	137
Croatia	43	0	0	43
Cyprus	3	0	0	3
Czechia	227	41	21	248
Denmark	150	47	128	278
Estonia	33	3	4	37
Finland	67	16	16	83
France	527	82	191	718
Germany	532	173	140	672
Greece	136	2	4	140
Hungary	222	12	9	231
Iceland	4	0	1	5
Ireland	45	4	8	53
Italy	495	65	55	550
Latvia	32	2	2	34
Lithuania	40	7	2	42
Luxembourg	2	0	0	2
Netherlands	253	57	155	408
Norway	63	11	29	92
Poland	411	47	26	437
Portugal	111	4	30	141
Romania	108	4	13	121
Slovakia	80	10	0	80
Slovenia	12	1	1	13
Spain	664	189	156	820
Sweden	125	30	47	172

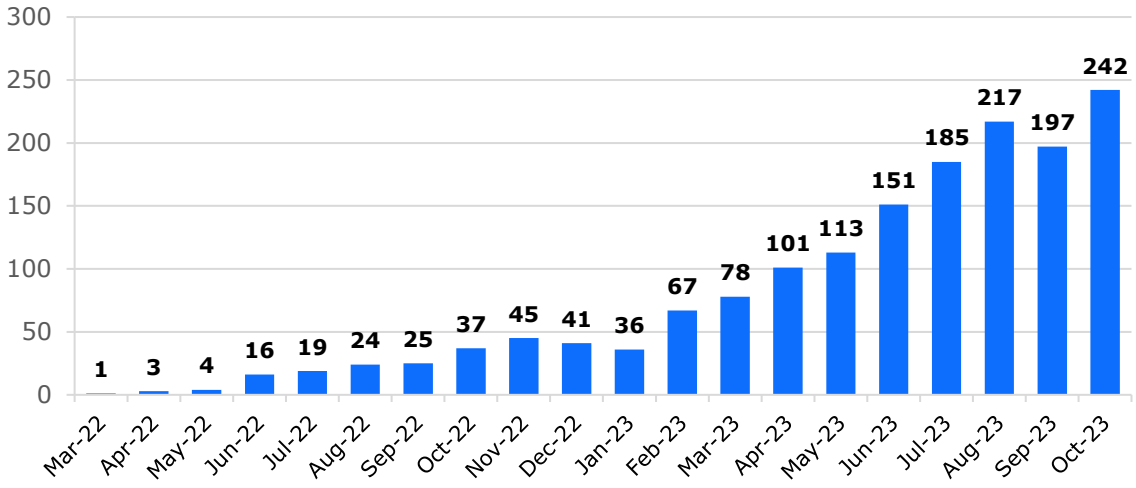
[1] RMS is the Reporting Member State appointed in line with the requirements of Article 5 of the Clinical Trials Regulation (EU) No 536/2014.

Chapter 2

Authorised clinical trials

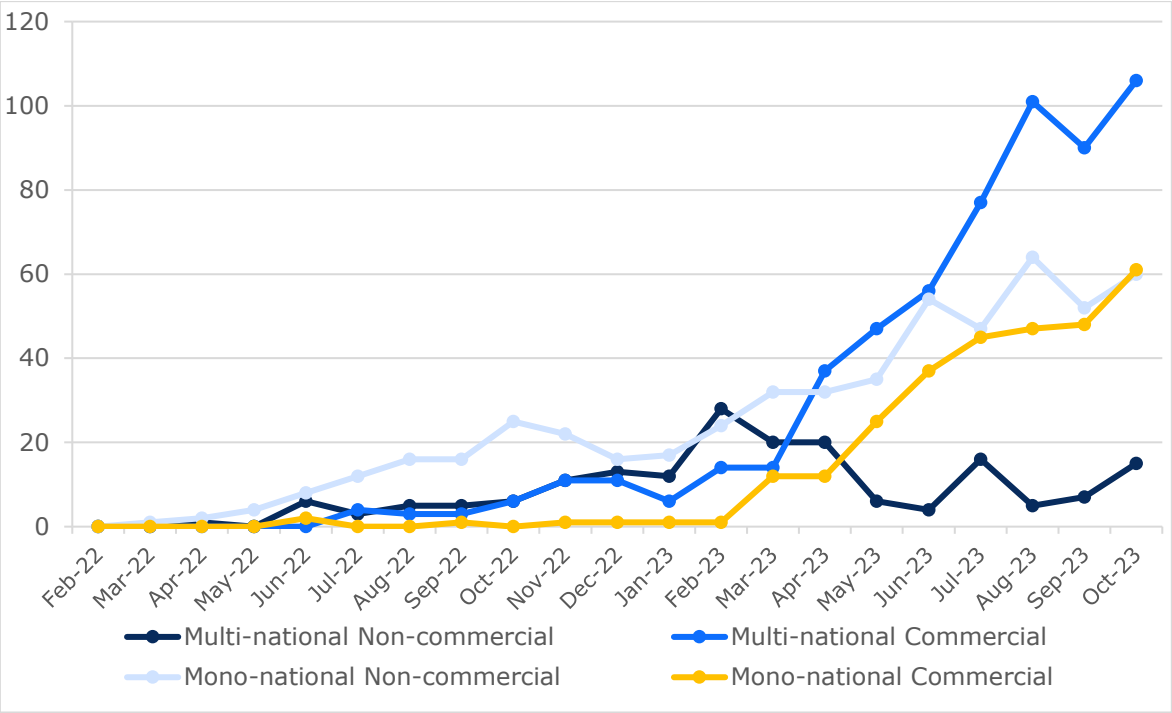
Since 31 January 2022, a total of 1,602 have received a decision in CTIS, of which 1,532 received a positive decision authorising the clinical trial. The graph below includes figures on both authorised and not authorised clinical trials.

In October 2023, of the 242 initial clinical trial with a decision, 234 have been authorised.



Mono- vs multinational trial, for which a decision has been issued, and in relation to the sponsor type

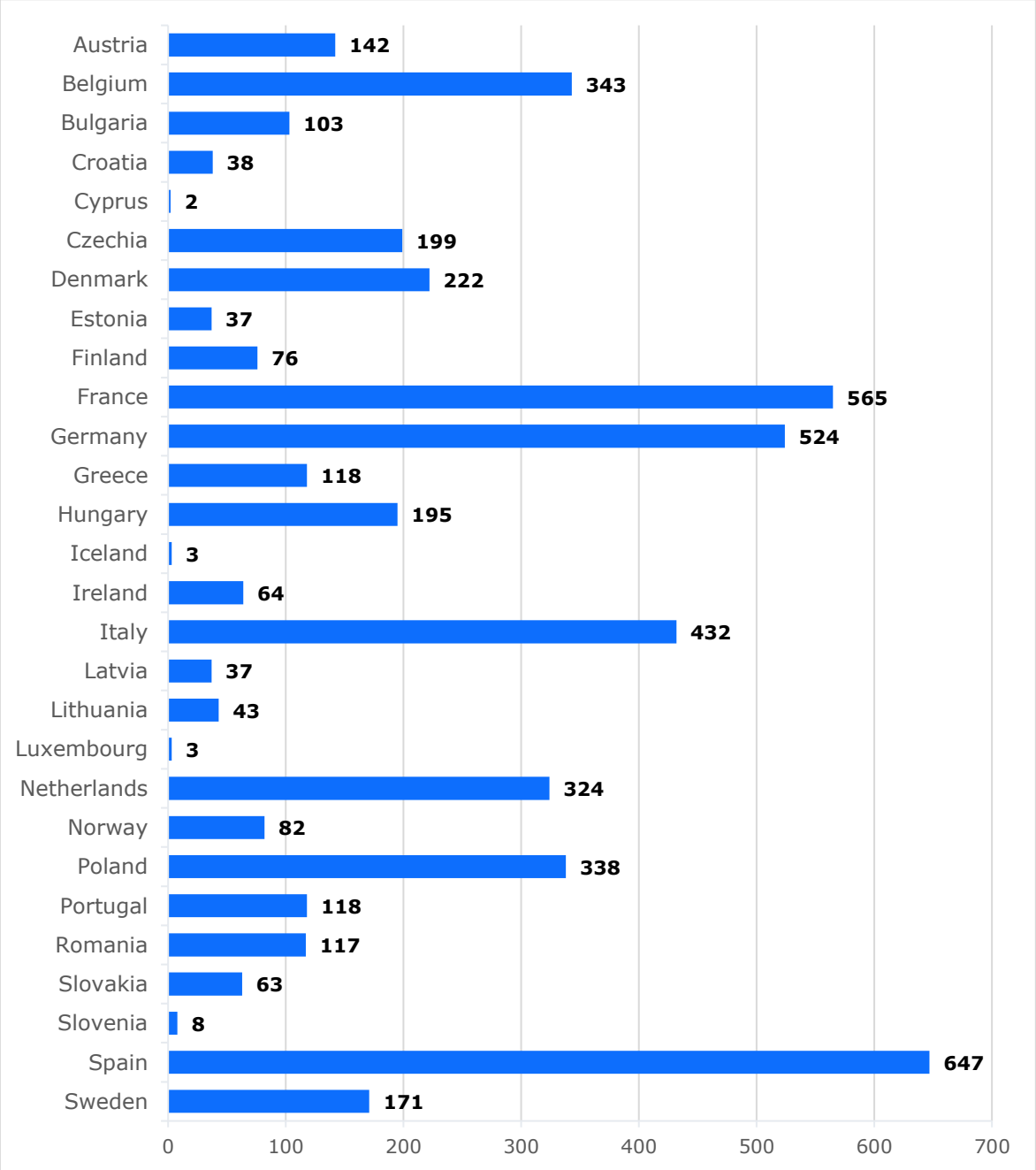
The graph below shows the number of trials for which a decision has been issued in CTIS, per month, since 31 January 2022. The graph below includes figures on both authorised and not authorised clinical trials as well as commercial/non-commercial sponsor.



Until October 2023, 775 multinational clinical trials have a decision in CTIS with an average of 6 Member States Concerned.

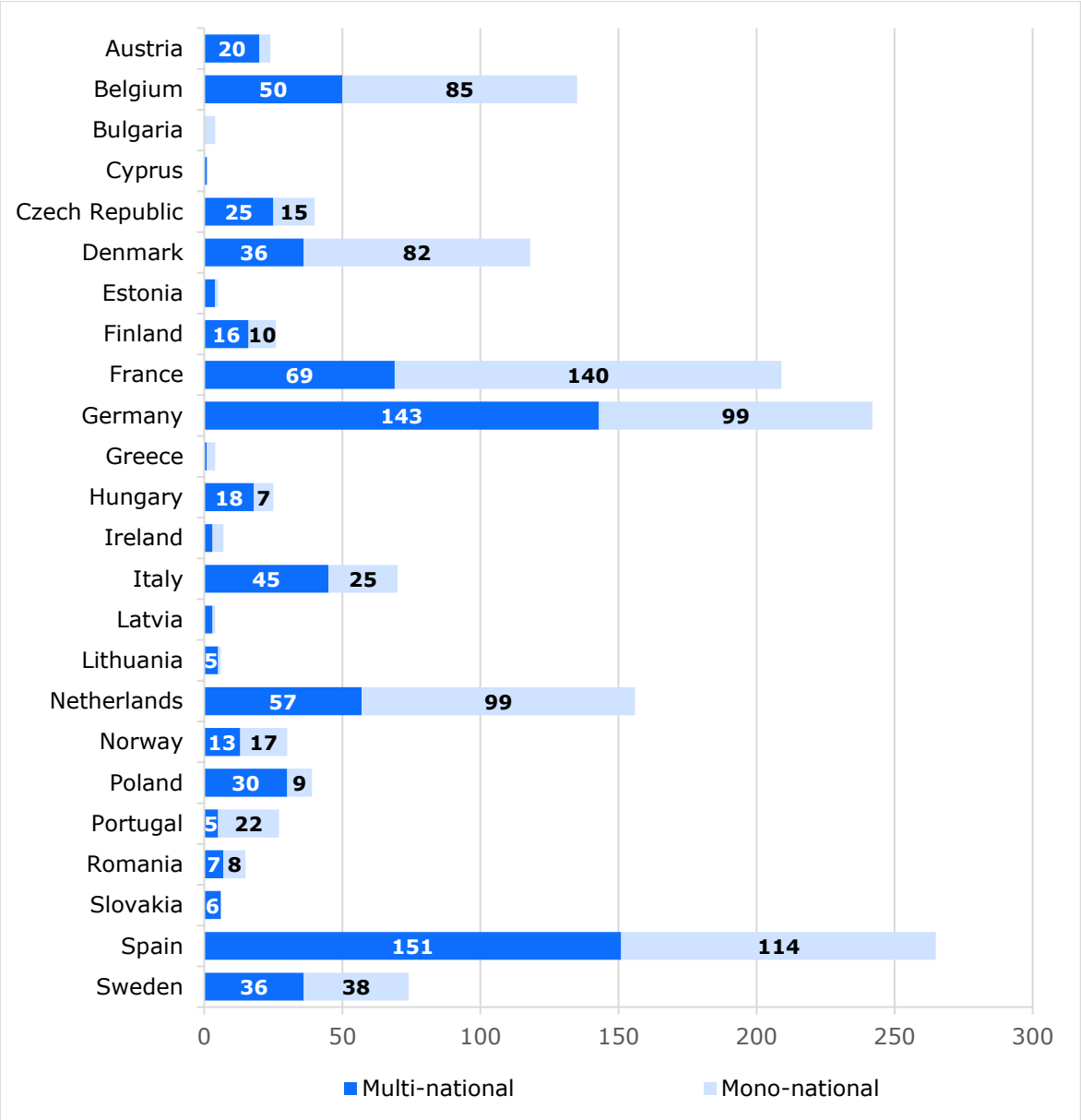
Distribution of **authorised** clinical trials per Member State Concerned and appointment of Reporting Member State

The graph below shows the number of clinical trials authorised since 31 January 2022, at the level of the Member States Concerned[2].



The graph below shows the distribution of appointment of Reporting Member State (RMS), amongst the applicable Member States Concerned, in authorised mono- and multinational trials.

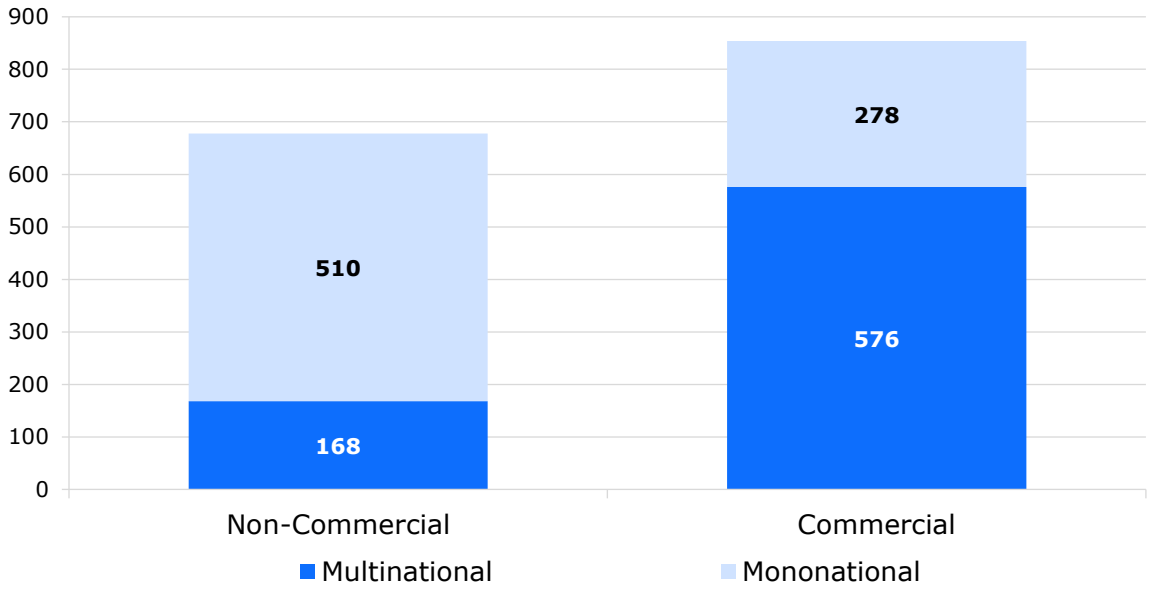
[2] In multinational clinical trials the same initial clinical trial application has been submitted to multiple Member State Concerned, and it is counted in the graph in each applicable MSC.



Authorised clinical trials, with information whether the trial is a mono- vs multinational and in relation to sponsor type

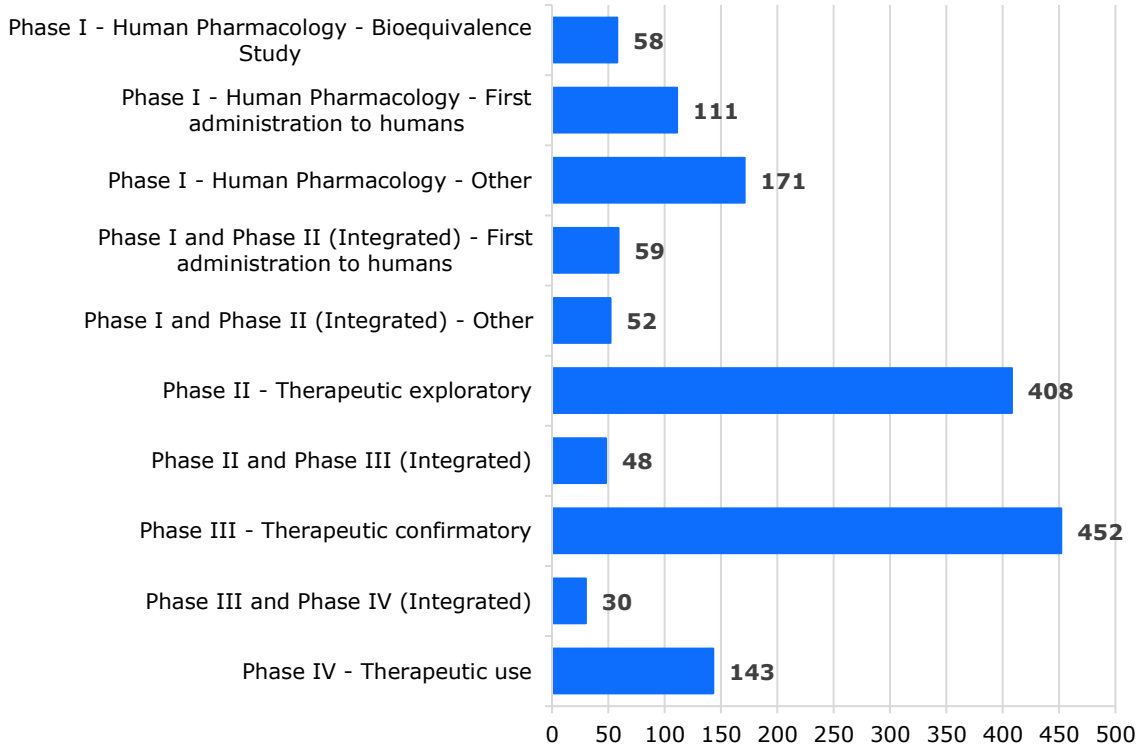
The graph below shows the number of clinical trials authorised since 31 January 2022, split into mono national/ multi-national and per sponsor type.

The graph shows a majority of mono-national CTs authorised conducted by non-commercial sponsors. On the contrary the majority of CTs authorised, conducted by commercial sponsors, are multinational.



Authorised clinical trials per phase (i.e. I, II, III, IV, as well as first in human clinical trials or combined phases early (I and II))

The graph below shows the number of clinical trials authorised since 31 January 2022, broken down per trial phase.

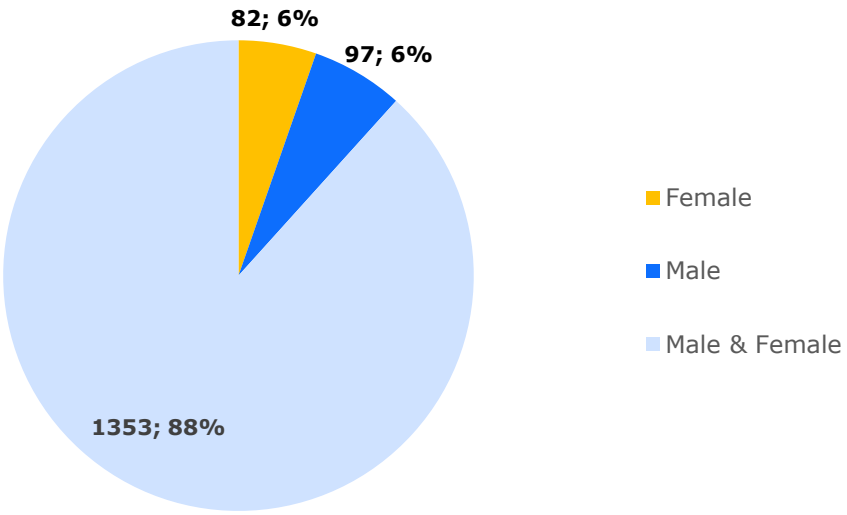


Clinical trials per population type and rare disease

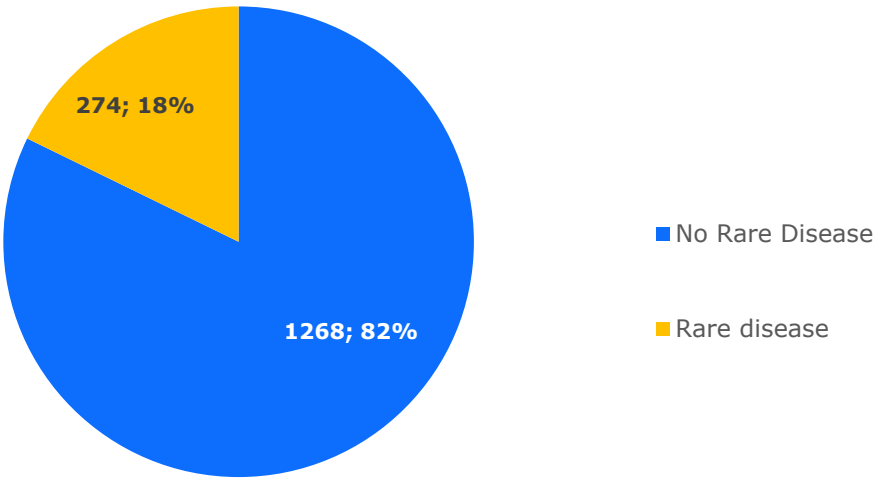
At the end October 2023, 748 clinical trials were reported as ongoing in CTIS. The term 'ongoing' refers to clinical trials that have been authorised in at least one Member State Concerned where the recruitment of patients has started at the clinical investigator sites[3].

The graph below illustrates some features of the groups and subgroups of the clinical trial participants taking part in clinical trials that have been authorised in the EU/EEA.

By Gender of clinical trials participants



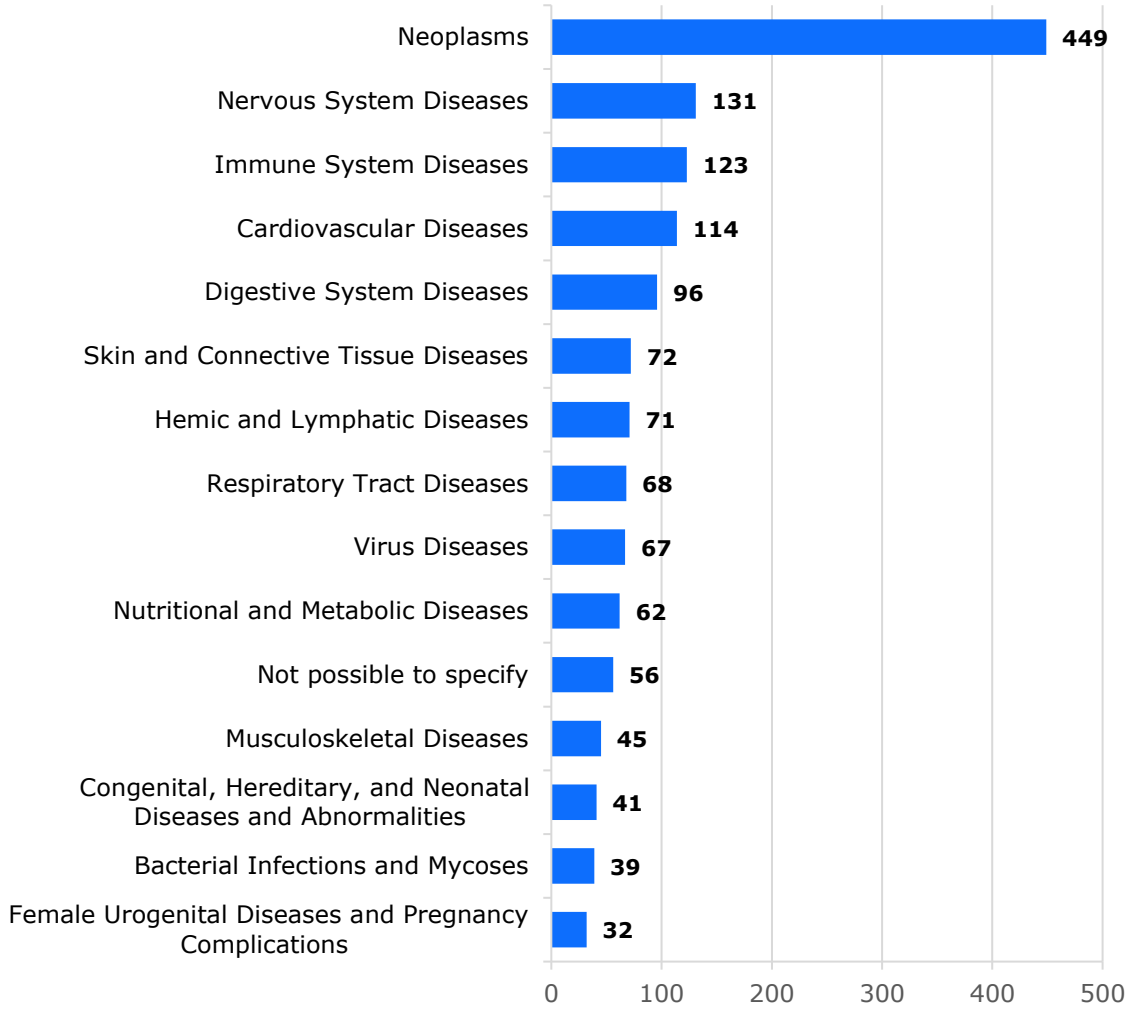
Clinical trials participants with rare disease



[3] Details on recruitment status are based on the information reported by the trial sponsor in CTIS.

Authorised clinical trials per therapeutic area

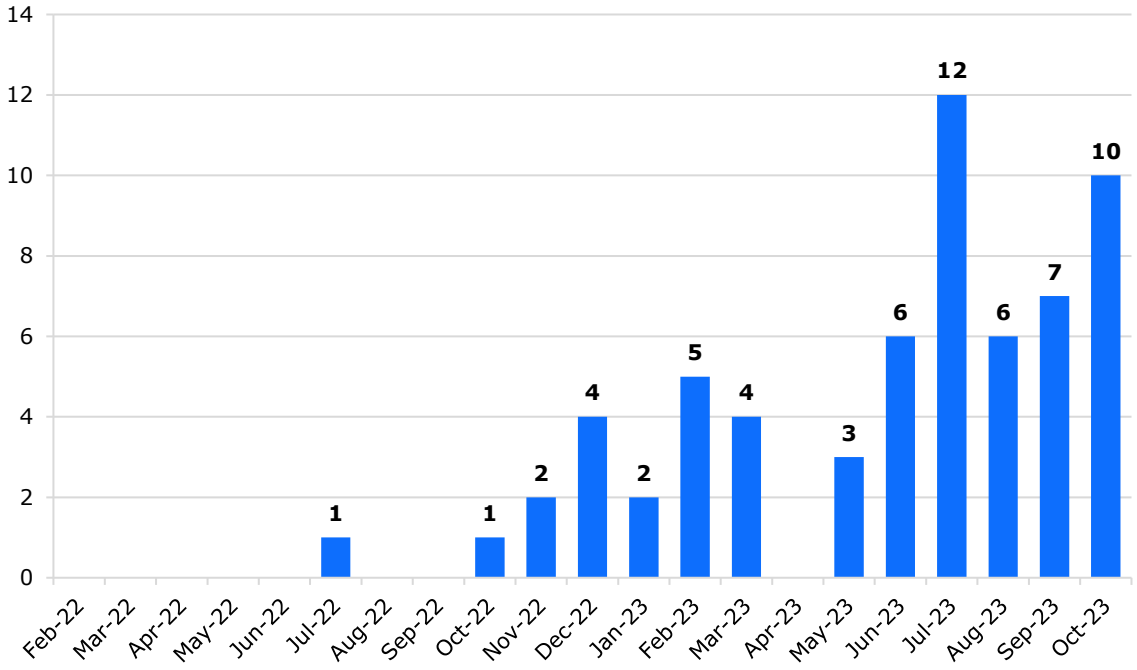
The graph below shows the number of clinical trials authorised since January 2022, broken down per therapeutic area[4], showing the most frequent 15 therapeutic areas.



Authorised clinical trials with an ATMP

Ten clinical trials with an Advanced Therapy Medicinal Product (ATMP) have been authorised in October 2023, bringing the total of authorised clinical trials with ATMP to 63, as illustrated in the graph below.

[4] In case a clinical trial investigates several therapeutic areas, it is counted in each of such identified therapeutic areas.


14
12
10
8
6
4
2
0
1
1
2
4
2
5
4
3
6
12
6
7
10
Feb-22
Mar-22
Apr-22
May-22
Jun-22
Jul-22
Aug-22
Sep-22
Oct-22
Nov-22
Dec-22
Jan-23
Feb-23
Mar-23
Apr-23
May-23
Jun-23
Jul-23
Aug-23
Sep-23
Oct-23

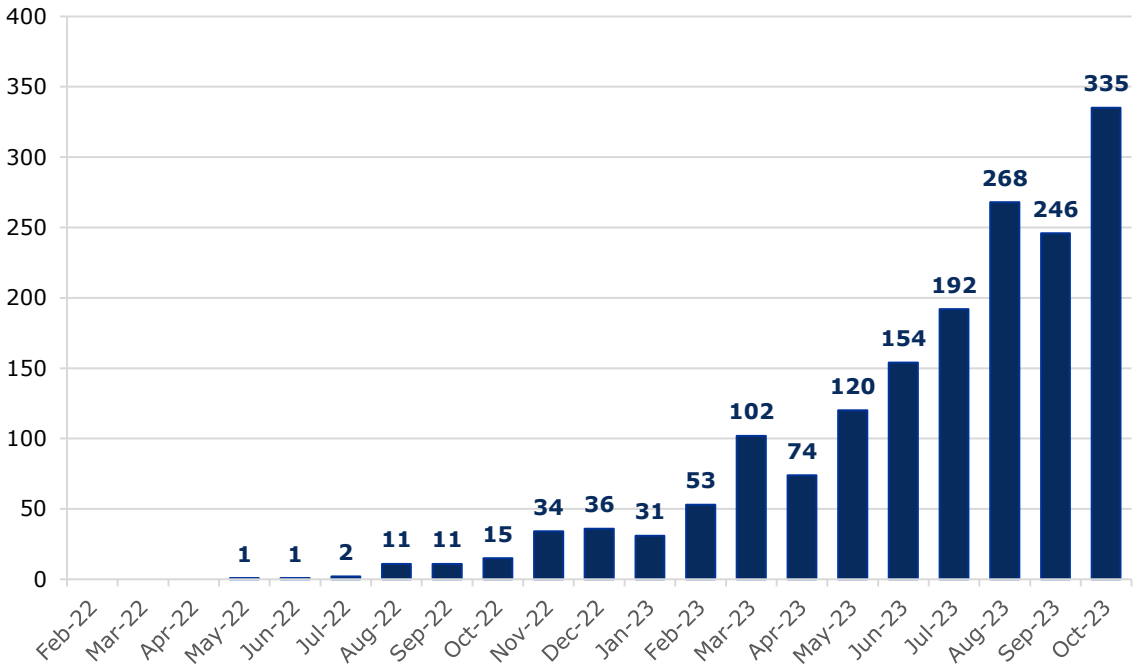
Chapter 3

Substantial modification applications

Substantial modifications[5] are those modifications that have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial.

Submitted substantial modification applications

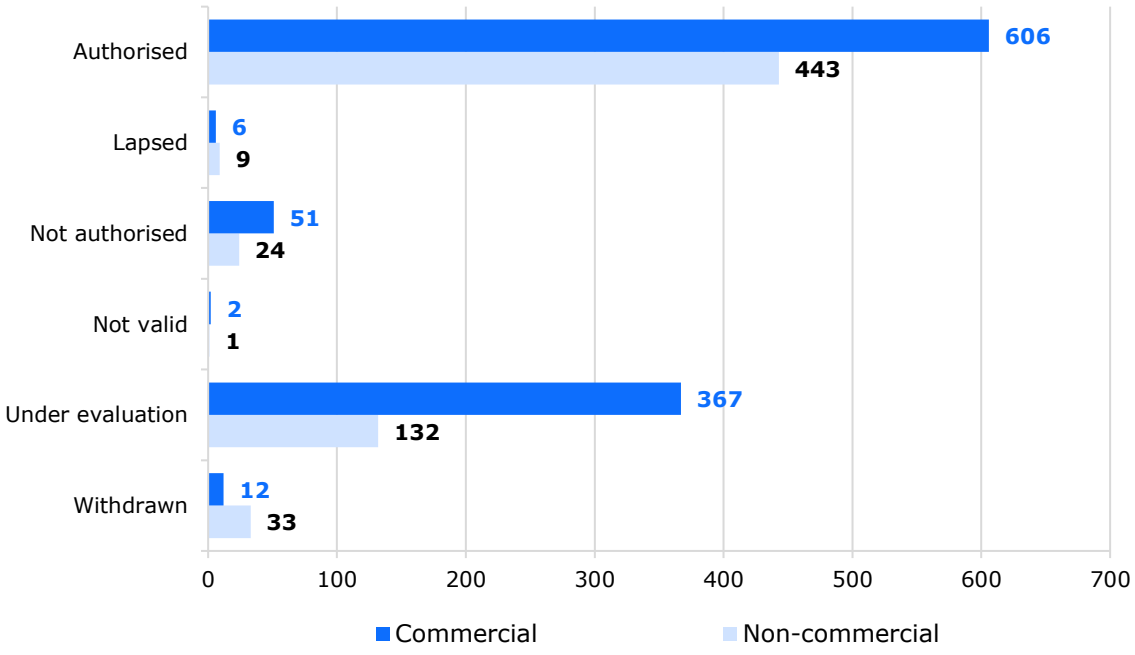
Overall, 1,686 distinct substantial modification applications, affecting 757 trials, have been submitted since the launch of the system on 31 January 2022, of which 335 substantial modifications submitted in October 2023, affecting 239 trials.



[5] Substantial modifications for part I only, or part II only or part I and part II, are foreseen in chapter II of Regulation (EU) No 536/2014

Substantial modification applications per applicable statuses and by sponsor type

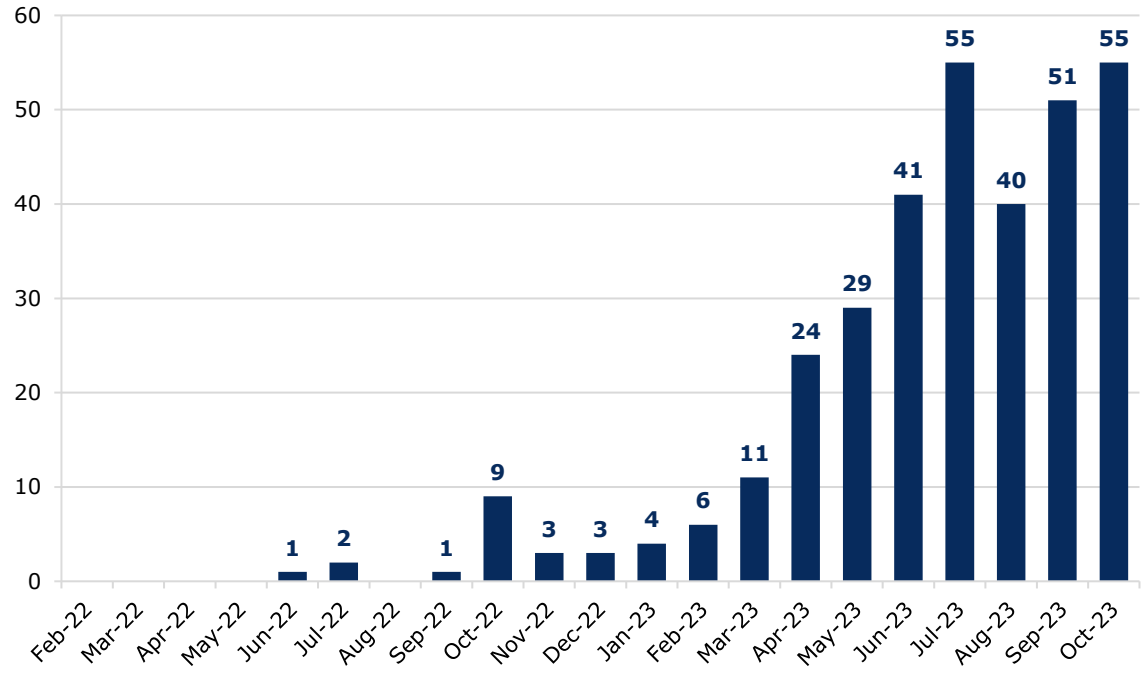
Since 31 January 2022, 1,686 distinct applications for substantial modifications, were submitted in CTIS, presented below per application status and sponsor type.



Chapter 4
Addition of a Member State Concerned

Submitted addition of Member States Concerned applications

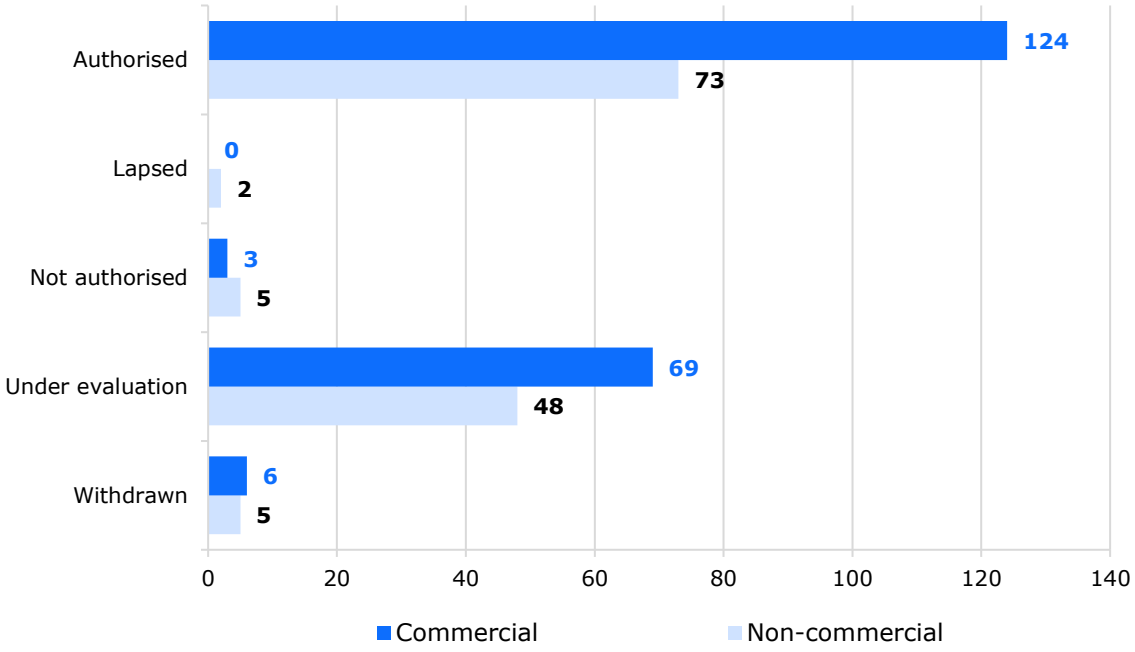
Since 31 January 2022, 335 distinct applications for the addition of a new MSC[6], affecting 128 trials, have been submitted in CTIS, of which 55 addition of new MSC submitted in October 2023, affecting 25 trials.



Addition of Member States Concerned applications per applicable statuses by sponsor type

Since 31 January 2022, 335 distinct applications for the addition of a new MSC have been submitted in CTIS, presented below per application status and sponsor type.

[6] Applications to add a new Member States Concerned are submitted in accordance with the requirements of Article 14 of Regulation (EU) No 536/2014


Authorised
124
73
Lapsed
0
2
Not authorised
3
5
Under evaluation
69
48
Withdrawn
6
5
0
20
40
60
80
100
120
140
Commercial
Non-commercial

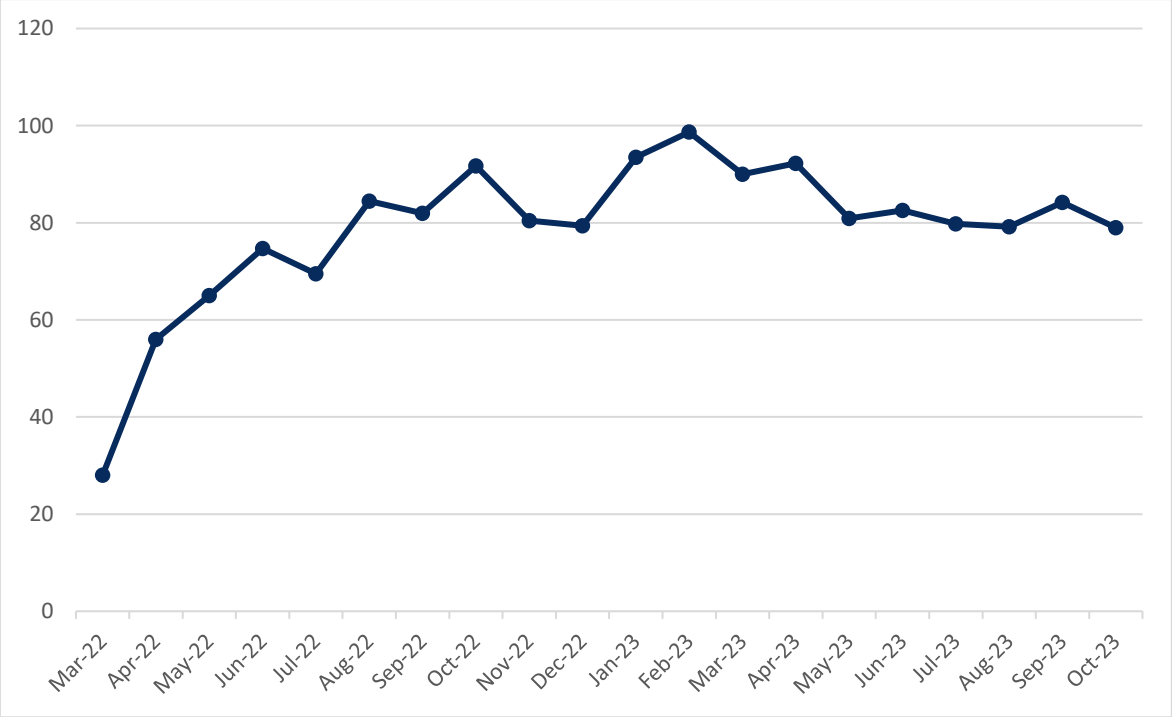
Chapter 5

Timelines

The graphs below show average timelines from submission of initial clinical trials applications to different points in time.

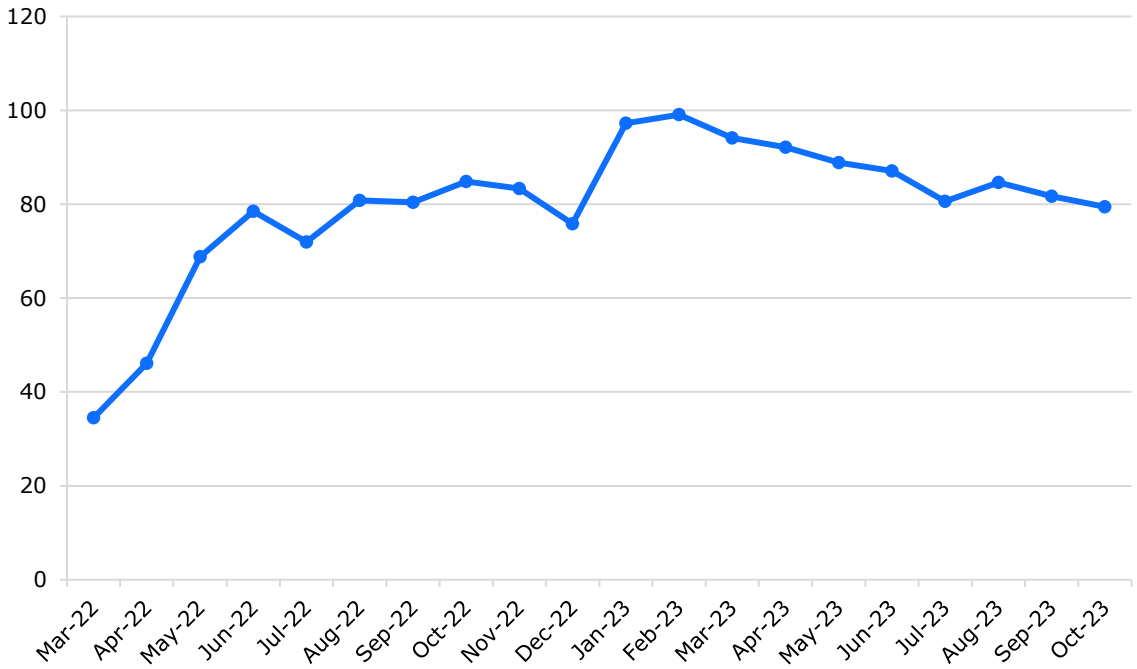
Average time from submission of initial clinical trial applications to Part I conclusion

This graph takes into consideration the average number of days between the part I conclusion and the submission date for the trials for which the part I conclusion has been issued in that particular month.



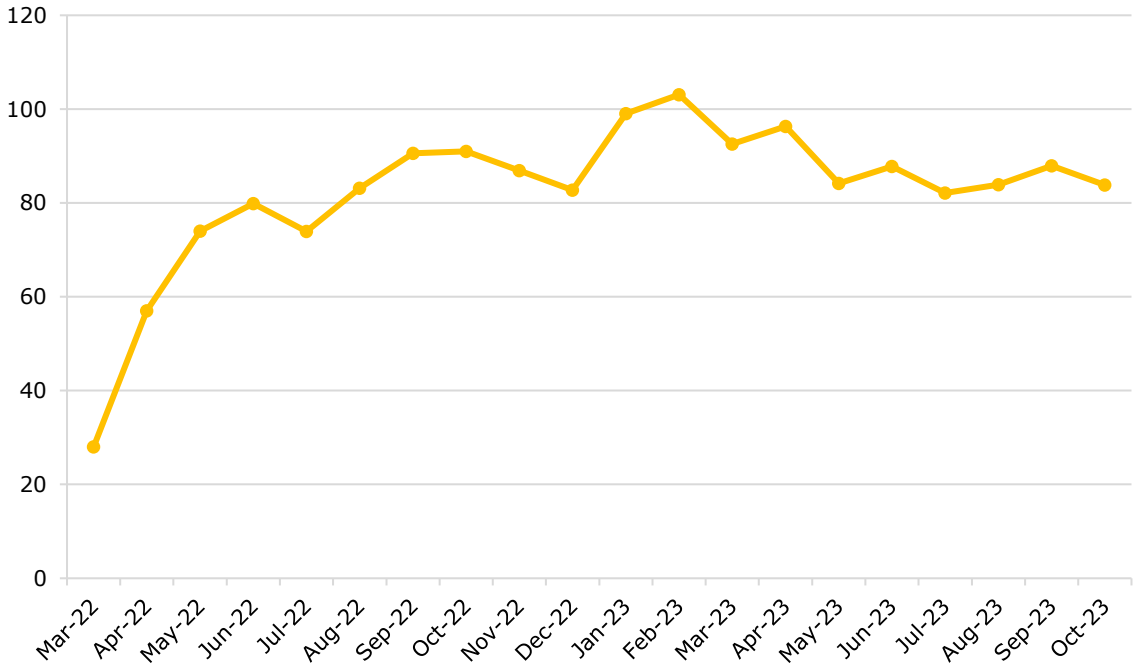
Average time from submission of initial clinical trial applications to part II conclusions

This graph takes into consideration the average number of days between the part II conclusion, for each MSC, and the submission dates for the trials for which the part II conclusion has been issued in that particular month.

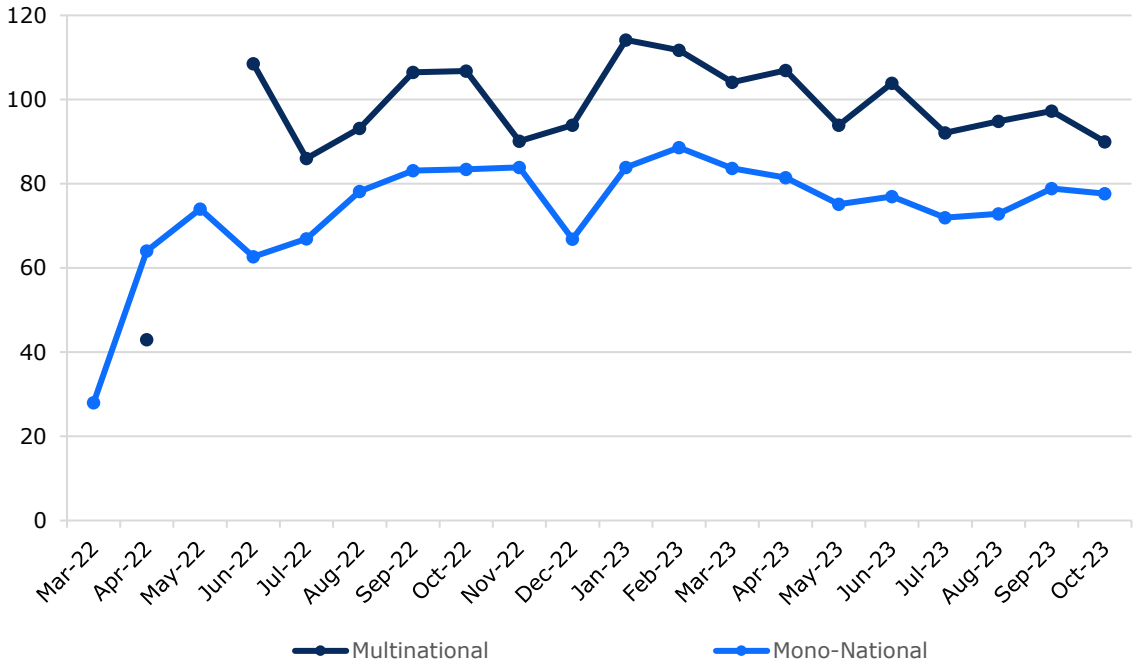


Average time from submission of initial clinical trial applications to decision

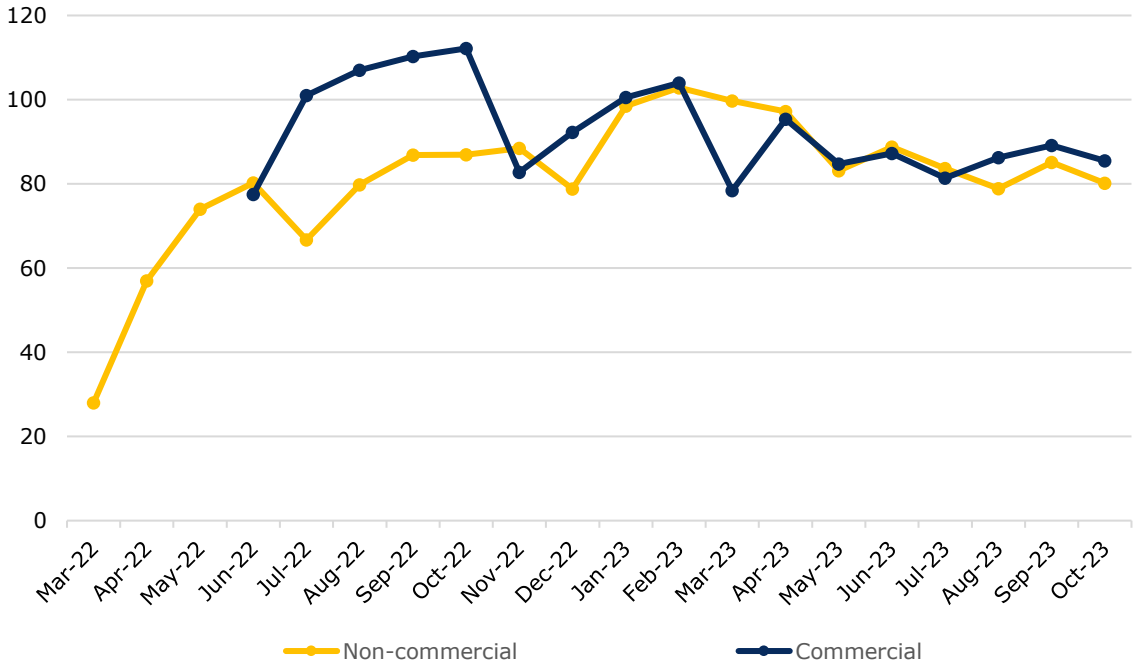
This graph takes into consideration the average number of days between the decision date, and the submission date for the trials for which the decision has been issued in that particular month.



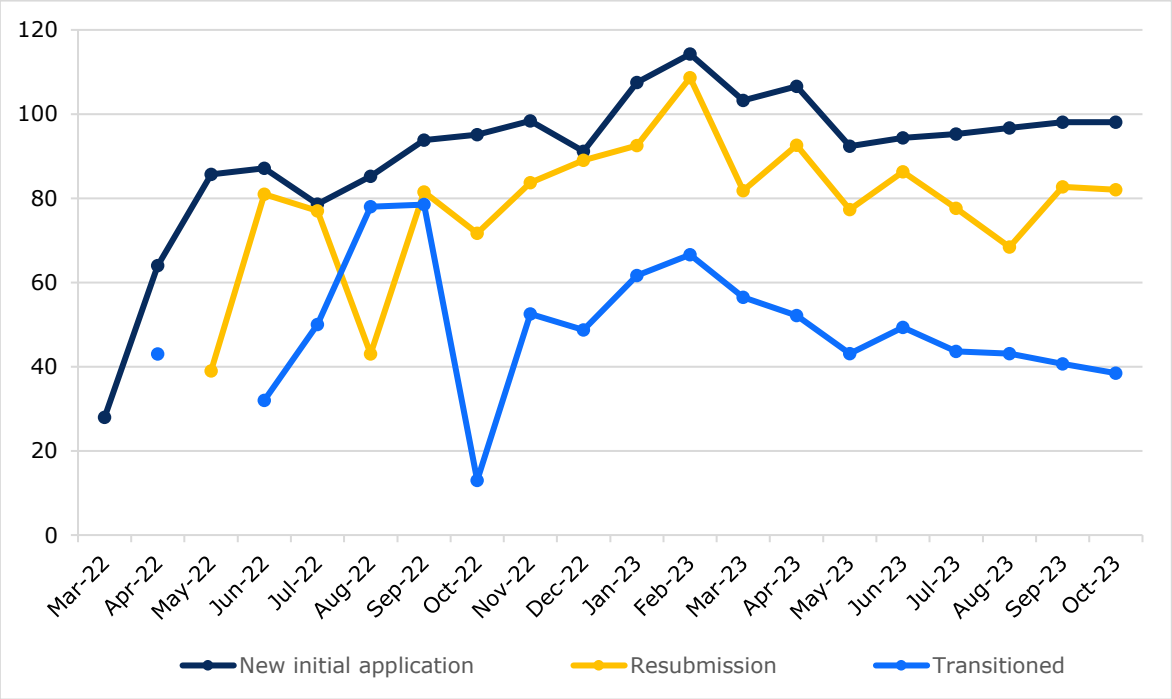
Average time per mono- vs multinational clinical trials from submission of initial clinical trial applications to decision



Average time per commercial/ non-commercial sponsors from submission of initial clinical trial applications to decision



Average time per new initial application/ resubmission and transitional trials



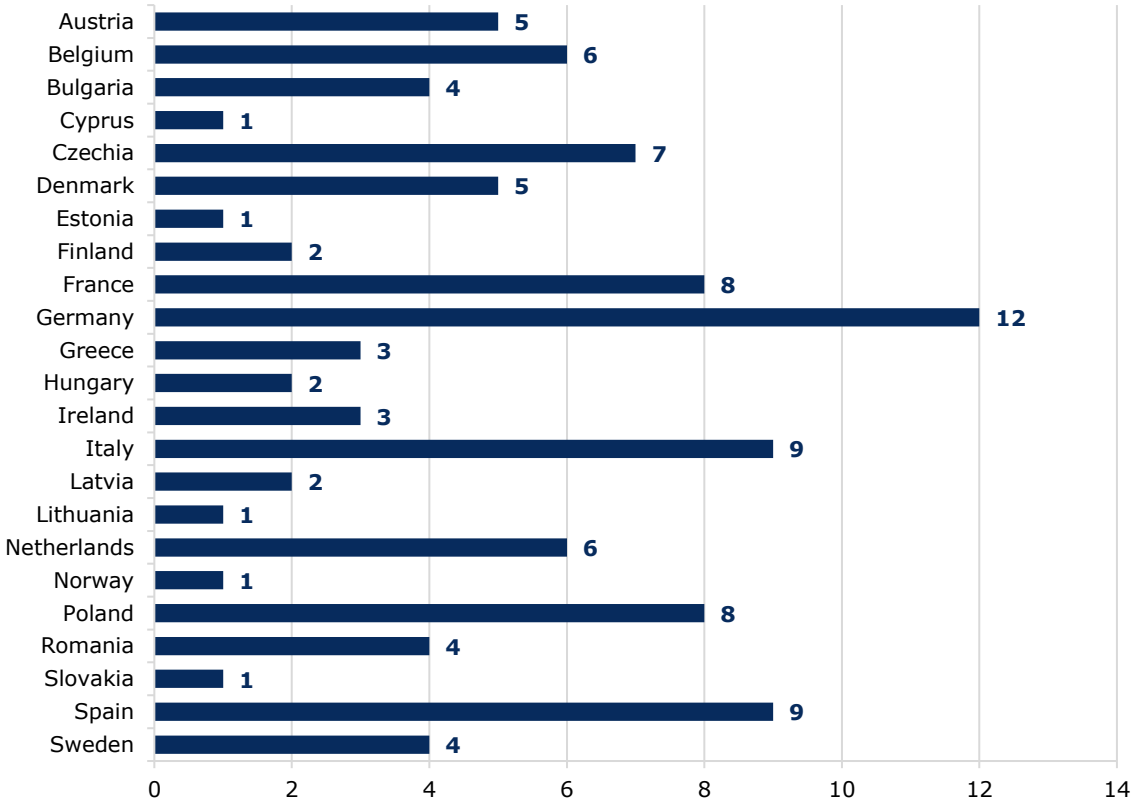
Chapter 6
Features of the substances

Safety assessing Member States (saMS) appointment

The saMSs for active substances that are used in mononational clinical trials is the RMS.

The saMSs for active substances that are used in multinational clinical trials is appointed.

During the reporting period, 23 Safety Assessing Member State (saMS) were appointed for 104 active substances as presented below.



European Medicines Agency

Domenico Scarlattilaan 6
1083 HS Amsterdam
The Netherlands

Telephone +31 (0)88 781 6000
Send a question www.ema.europa.eu/contact

www.ema.europa.eu

Monitoring the European clinical trials environment
A deliverable of the ACT EU Priority Action 2 – October 2023
EMA/513695/2023