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

May 2024

An agency of the European Union

Clinical Trials in the EU/EEA

May 2024

547

+7 %
on previous month

Submissions

485

+19 %
on previous month

Authorised

281 Multinational	
26 Non-Commercial	**255** Commercial
266 Mononational	
183 Non-Commercial	**83** Commercial

225 Multinational	
13 Non-Commercial	**242** Commercial
230 Mononational	
146 Non-Commercial	**84** Commercial

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 May 2024, as of 31 May 2024, 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 more than 300 submissions per month.

A total of 5,508 clinical trial applications have been submitted since the launch of CTIS.

At the time when the report is generated, more than 2,185 initial clinical trials are ongoing in EU/EEA under the CTR.

The therapeutic area mostly investigated is Neoplasms (Tumour).

Contents

Chapter 1

Submitted initial clinical trial applications

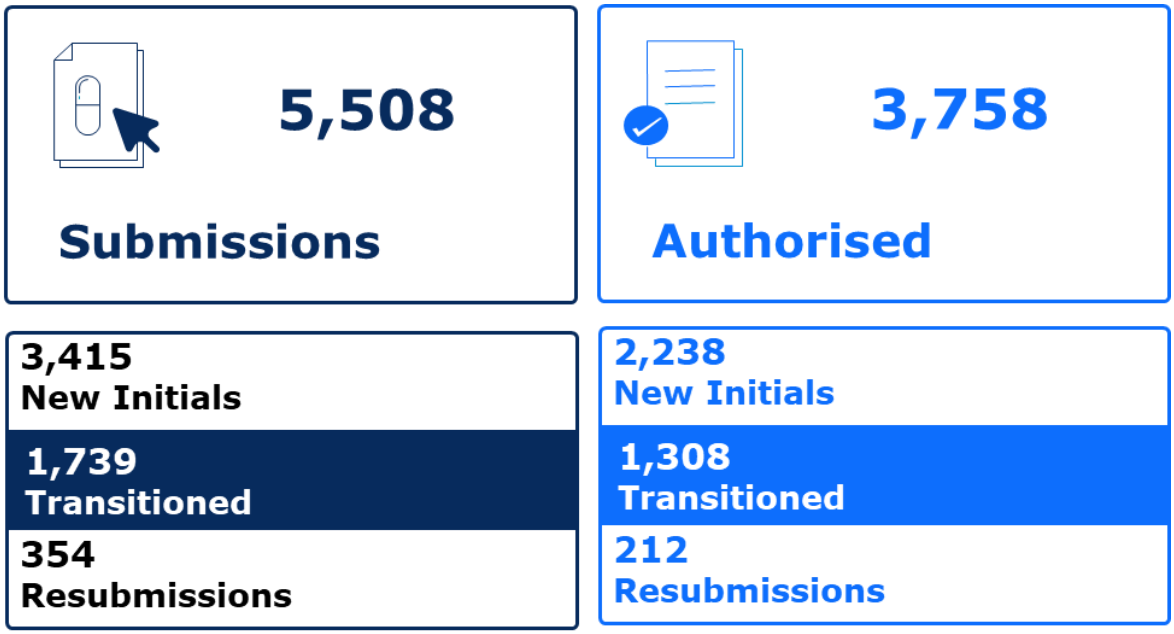
Chapter 1 of this report provides information on **submitted** initial clinical trial applications (CTAs), presented on the applicable statuses.

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

Initial clinical trial applications are those applications:

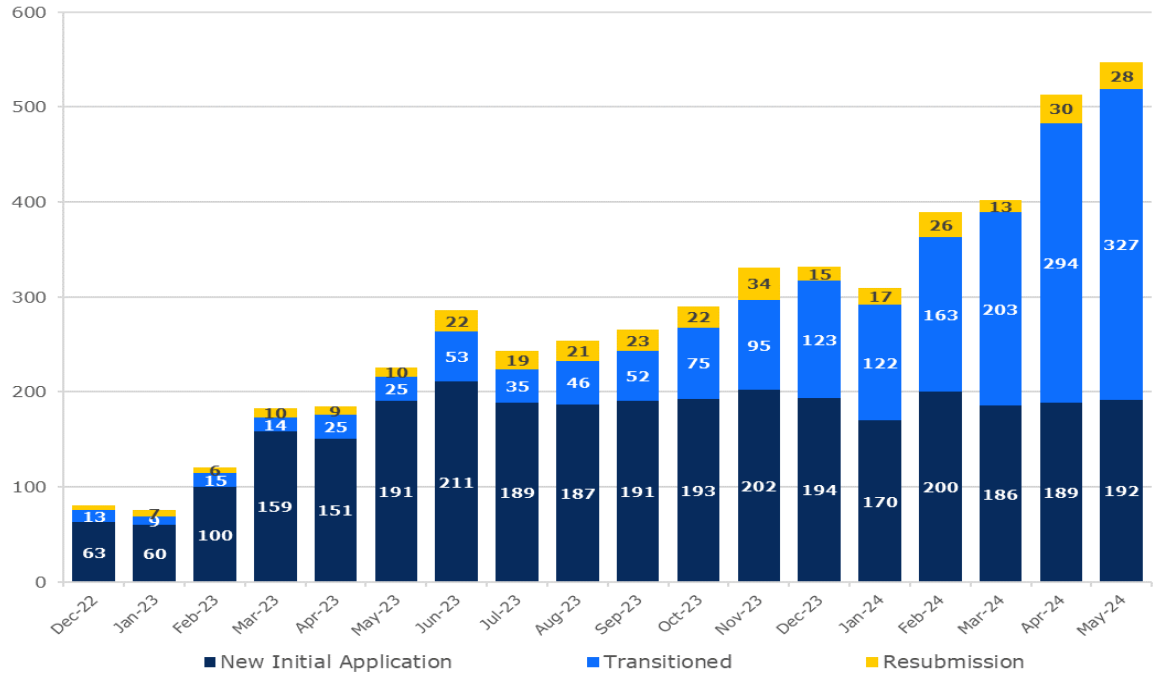
- new initial clinical trial applications submitted in CTIS by the sponsors under the Clinical Trials Regulation (EU) 536/2014 (CTR);
- trials which were already authorised under the regime of Clinical Trials Directive 2001/20/EC (CTD) and that have been transitioned to the regime of CTR;
- resubmitted 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:



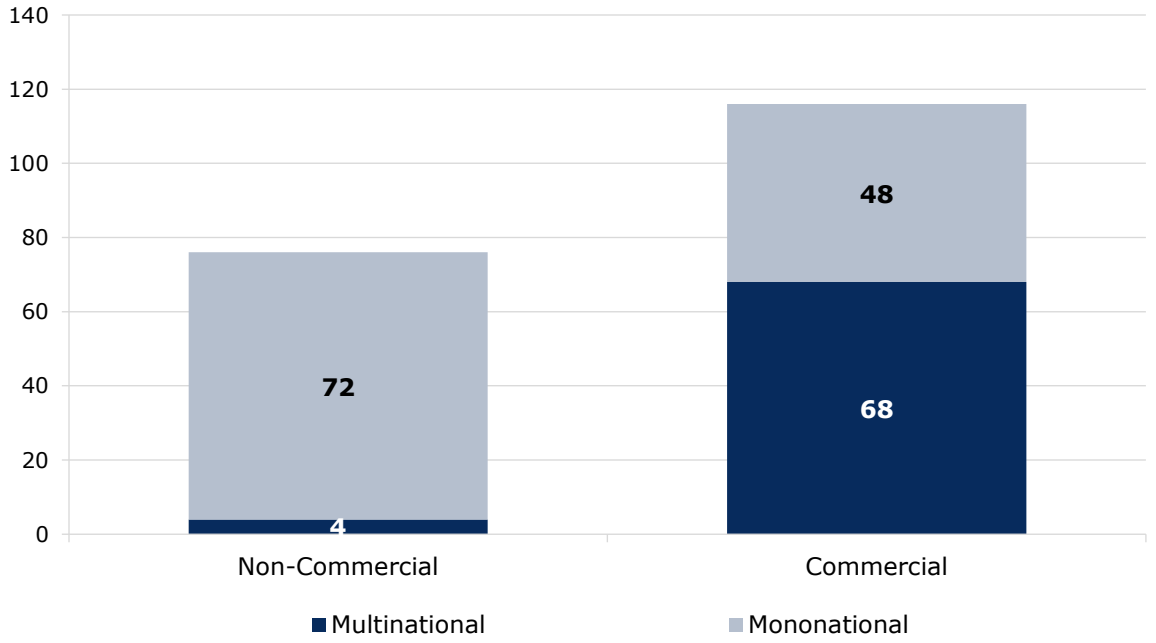
Monthly submissions of initial clinical trial applications

In May 2024, 547 initial clinical trial applications have been submitted, of which 192 new initial CTA, 327 are trials transitioned to CTR, and 28 are resubmissions of previously submitted initial applications *(the graph below shows the data for the last 18 months)*.



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

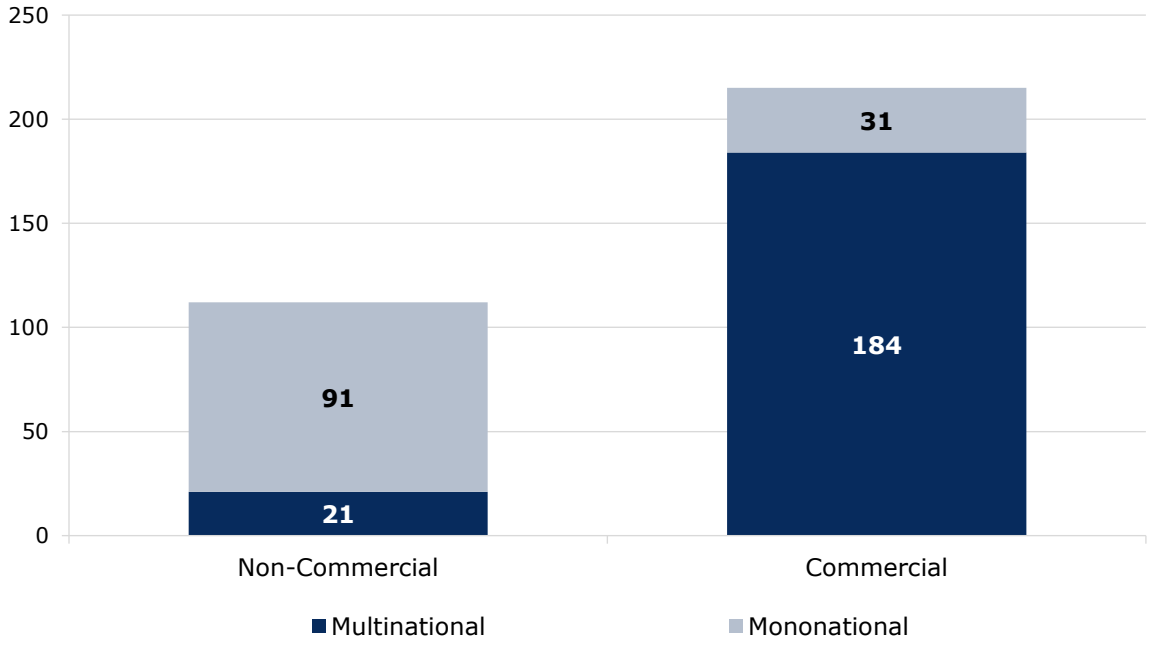
The graph below shows the split of submissions of new initial clinical trial applications in May 2024 into commercial/non-commercial sponsors and mononational versus multinational trials.



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 May 2024 into commercial/non-commercial sponsors and mononational versus multinational trials.

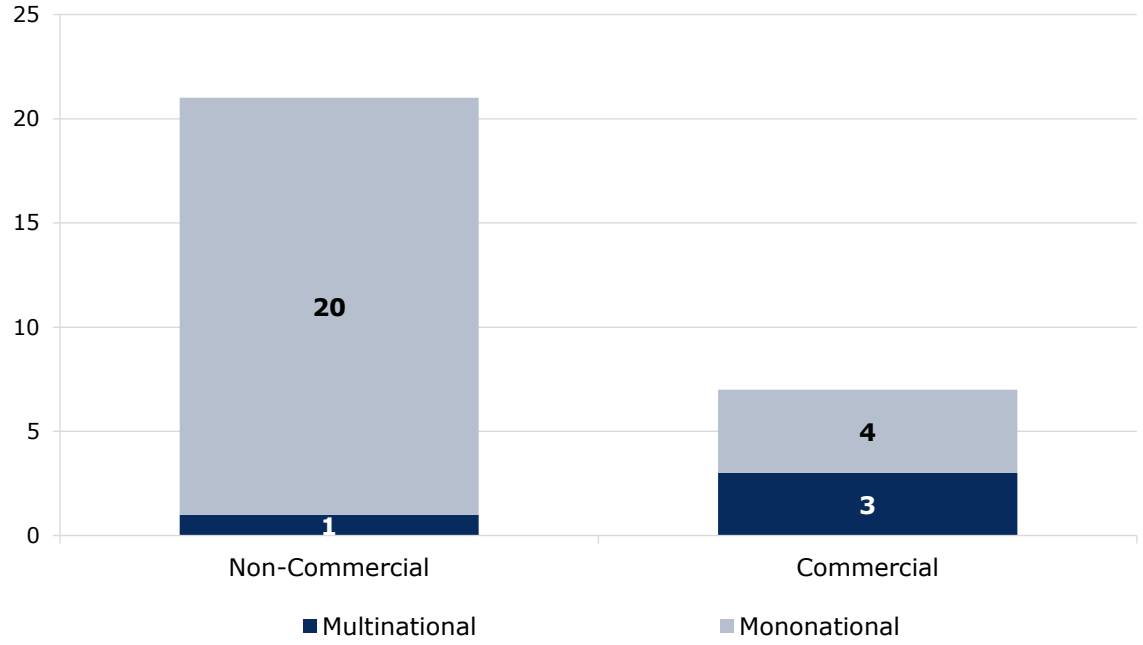


Once notified by the clinical trial sponsors, the National Competent Authorities of the EU/EEA Member States are responsible for keeping, in the EudraCT database, the information on the trial status up to date, including inserting the end of trial date, as applicable.

*Further information can be found under **Annex I**.*

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 May 2024 into commercial/non-commercial sponsors and mononational versus multinational trials.



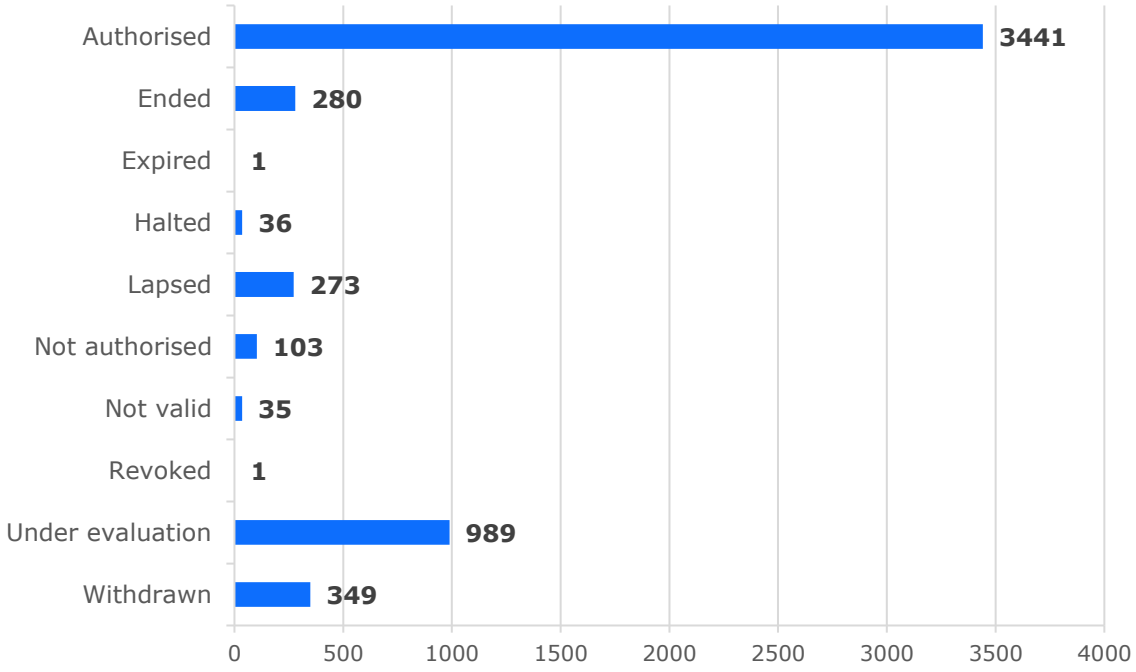
Clinical trials per applicable statuses

Since 31 January 2022, a total of 5,508 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**.

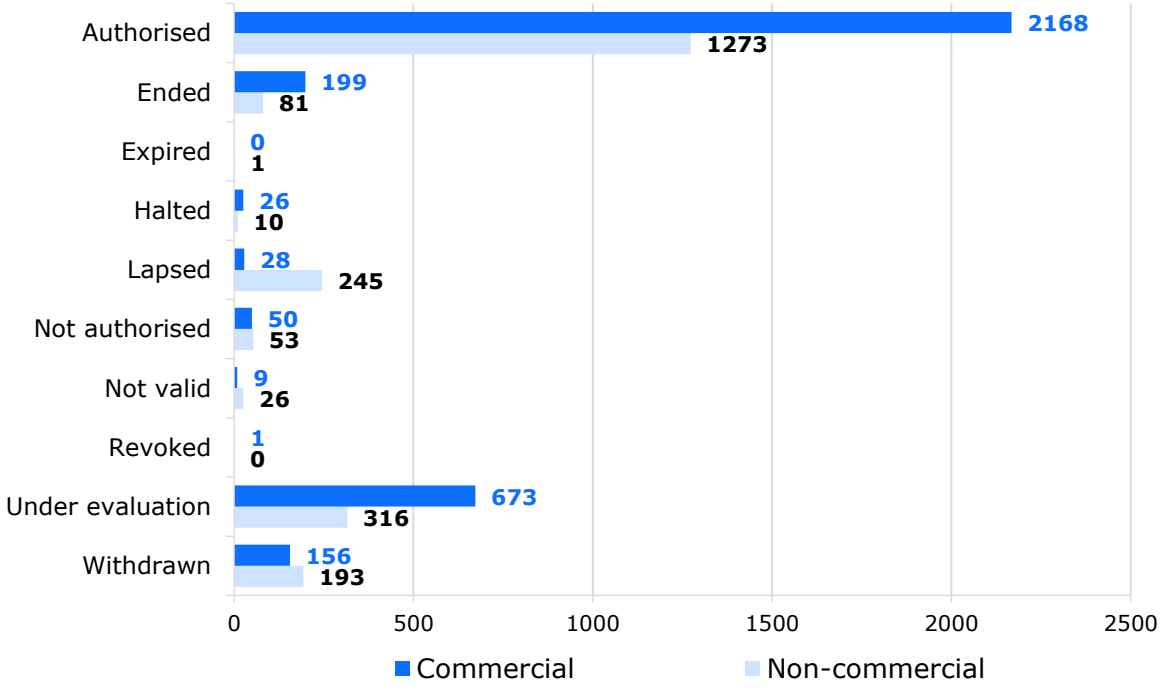
Clinical trials per applicable statuses

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 – full applications (part I and part II) or part I only – 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	238	40	28	266
Belgium	478	88	164	642
Bulgaria	246	2	15	261
Croatia	72	0	0	72
Cyprus	3	0	1	4
Czechia	368	75	30	398
Denmark	266	78	189	455
Estonia	48	4	5	53
Finland	105	30	27	132
France	859	142	335	1194
Germany	861	268	247	1108
Greece	233	2	11	244
Hungary	353	18	17	370
Iceland	6	0	1	7
Ireland	87	6	13	100
Italy	828	97	98	926
Latvia	45	5	4	49
Lithuania	60	9	3	63
Luxembourg	2	0	1	3
Netherlands	417	93	263	680
Norway	120	20	39	159
Poland	679	73	58	737
Portugal	178	9	48	226
Romania	199	9	22	221
Slovakia	131	14	2	133
Slovenia	23	2	2	25
Spain	1081	311	249	1330
Sweden	211	47	77	288

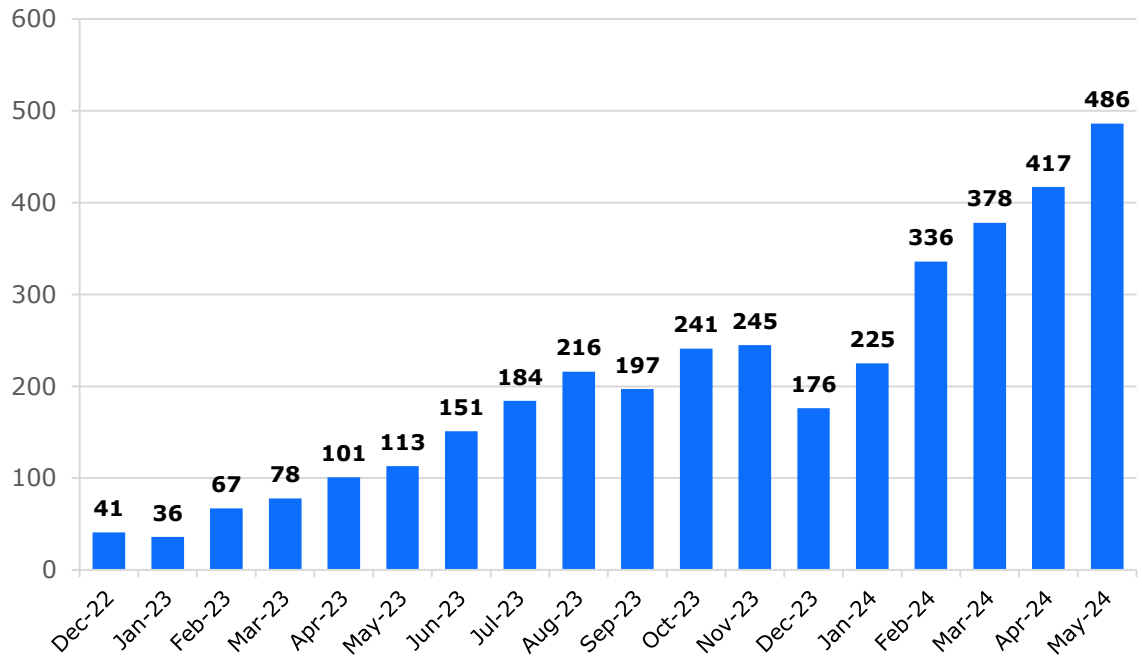
[1] RMS is the Reporting Member State appointed in line with the requirements of Article 5 of the Clinical Trials Regulation (EU) No 536/2014.

Chapter 2

Authorised clinical trials

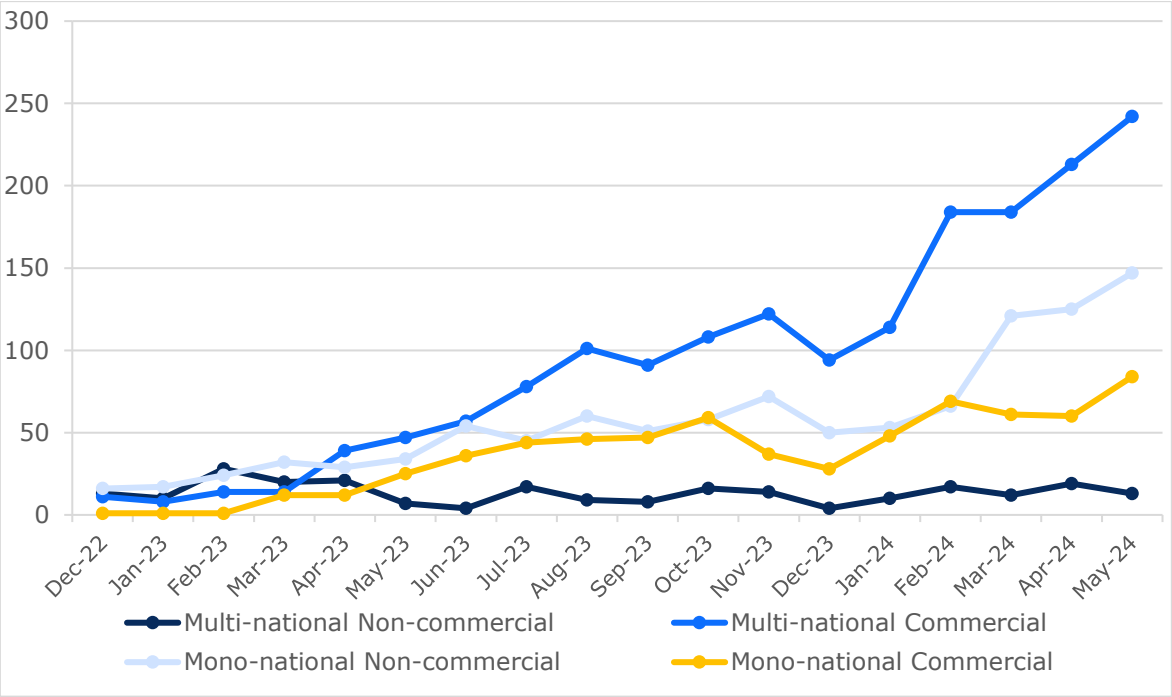
Since 31 January 2022, a total of 3,862 have received a decision in CTIS, of which 3,758 received a positive decision authorising the clinical trial. The graph below includes figures on both authorised and not authorised clinical trials in the last 18 months.

In May 2024, of the 486 initial clinical trial with a decision, 485 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, in the last 18 months, 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.

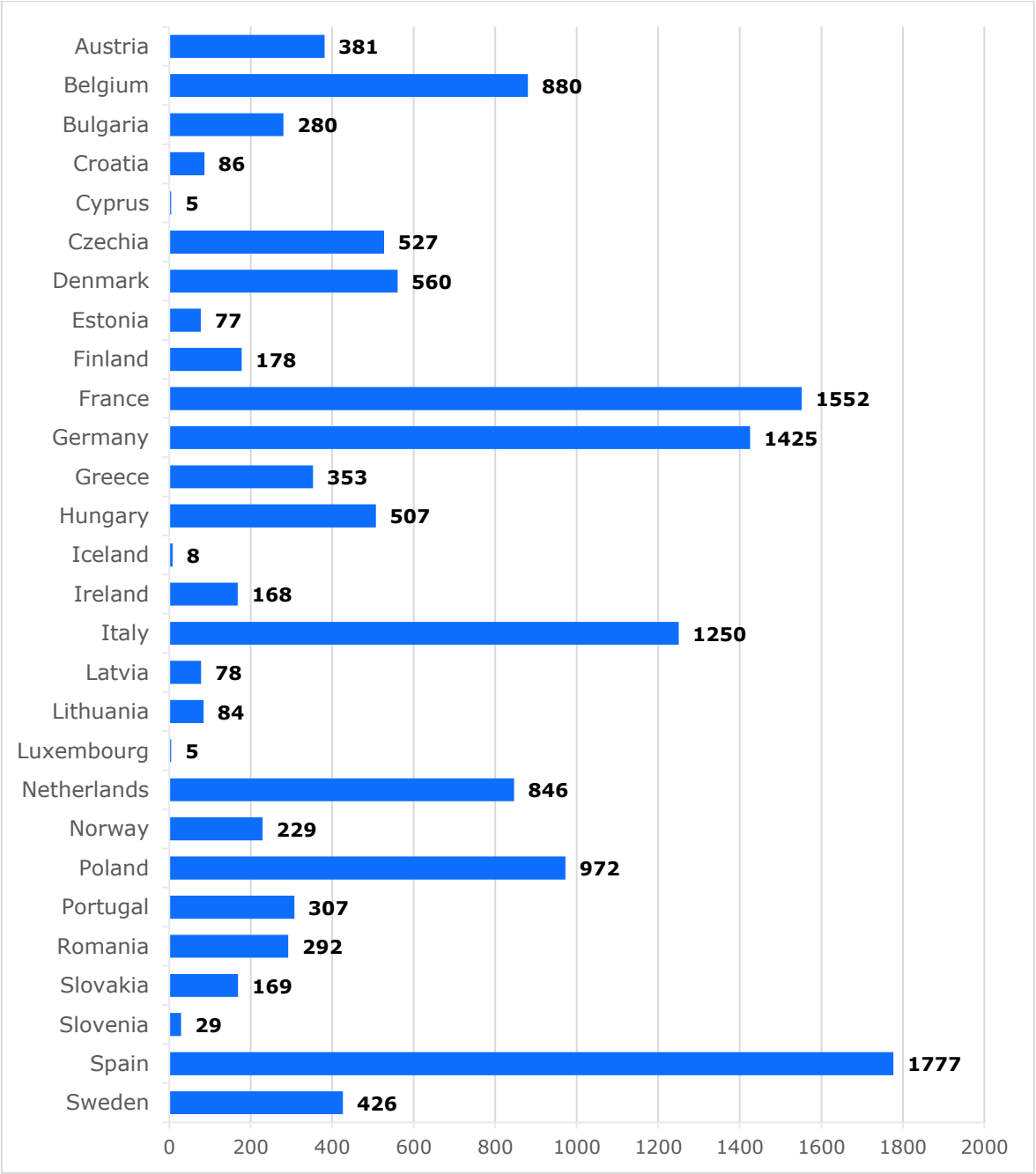


Until May 2024, 2,063 multinational clinical trials have a decision in CTIS with an average of 6 Member States Concerned.

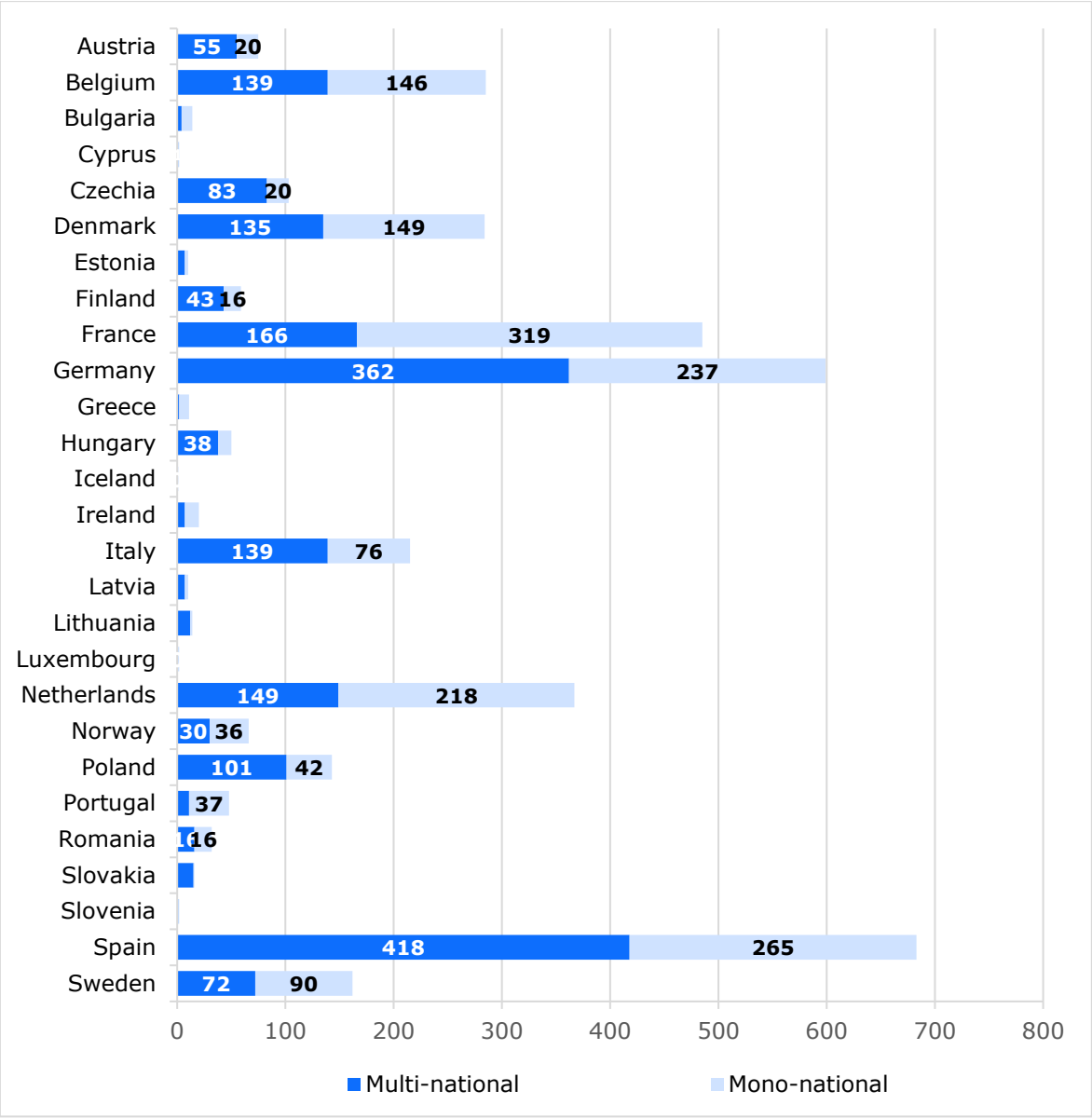
Distribution of **authorised** clinical trials per Member State Concerned and appointment of Reporting Member State

The graph below shows the number of clinical trials authorised since 31 January 2022. The figures indicate how many times a Member State has been involved as Member States Concerned[2] in an initial clinical trial application even if it has not authorised yet the trial in its country.

[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.



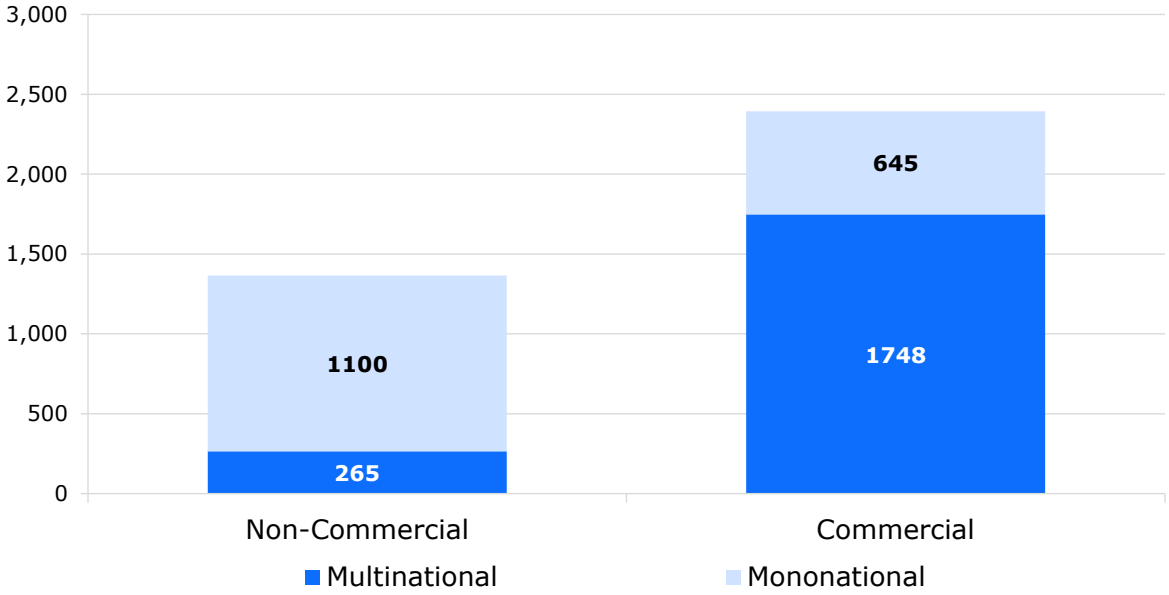
The graph below shows the distribution of appointment of Reporting Member State (RMS), amongst the applicable Member States Concerned, in authorised mono- and multinational trials (figures less than 15 are not shown).



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

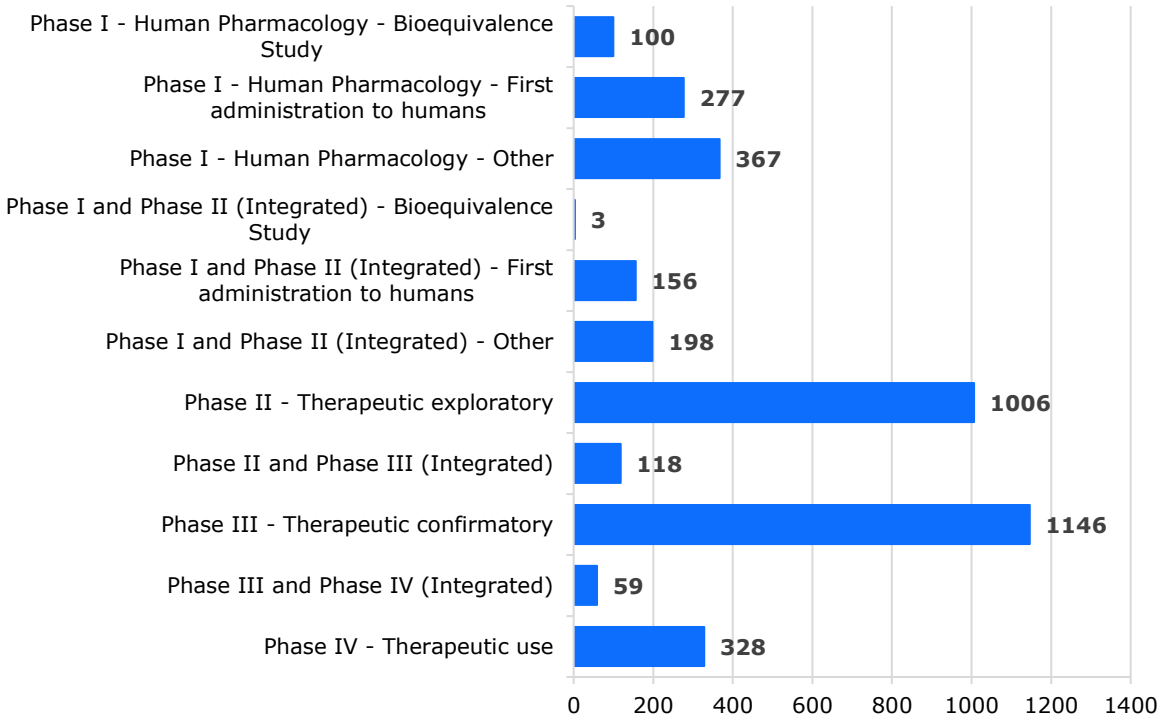
The graph below shows the number of clinical trials authorised since 31 January 2022, split into mono national/ multi-national and per sponsor type.

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.

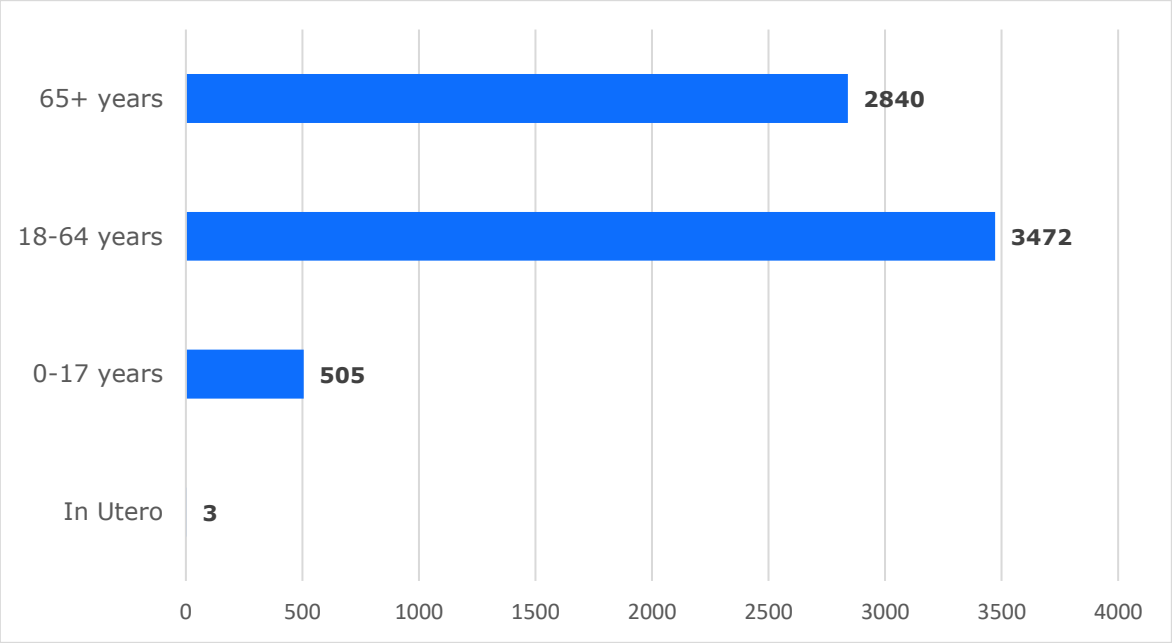


Clinical trials per population type and rare disease

At the end May 2024, 2,188 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].

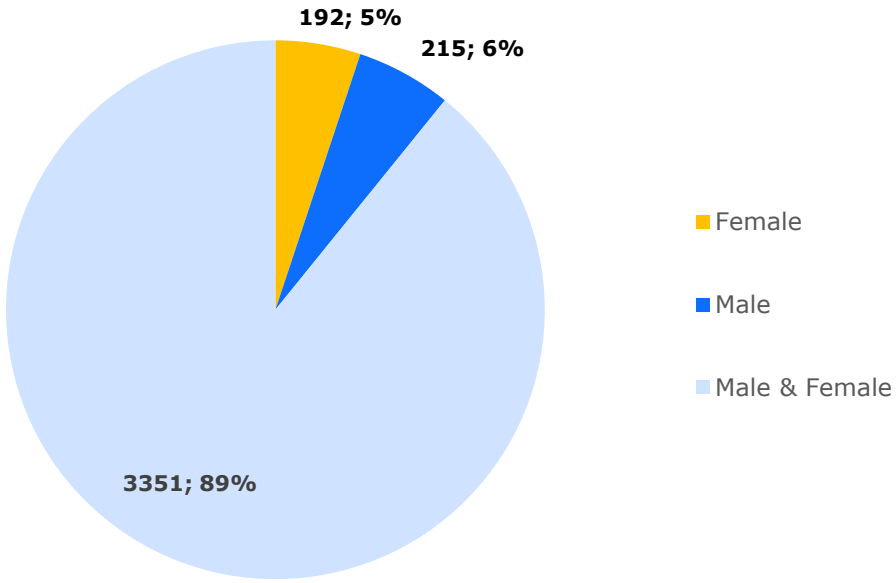
The graph below illustrates some features of the groups and subgroups of the clinical trial participants taking part in clinical trials that have been authorised in the EU/EEA.

By Age of clinical trials participants

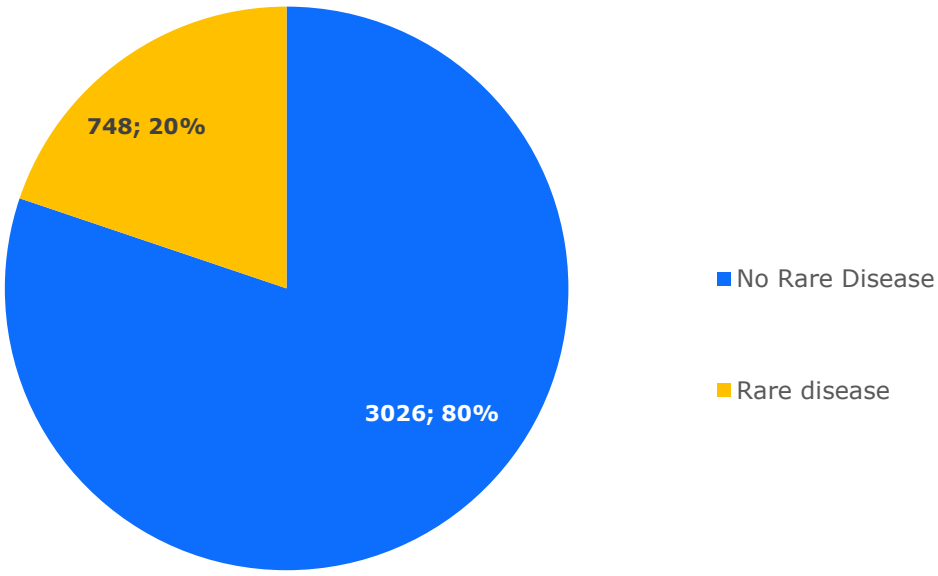


[3] Details on recruitment status are based on the information reported by the trial sponsor in CTIS.

By Gender of clinical trials participants

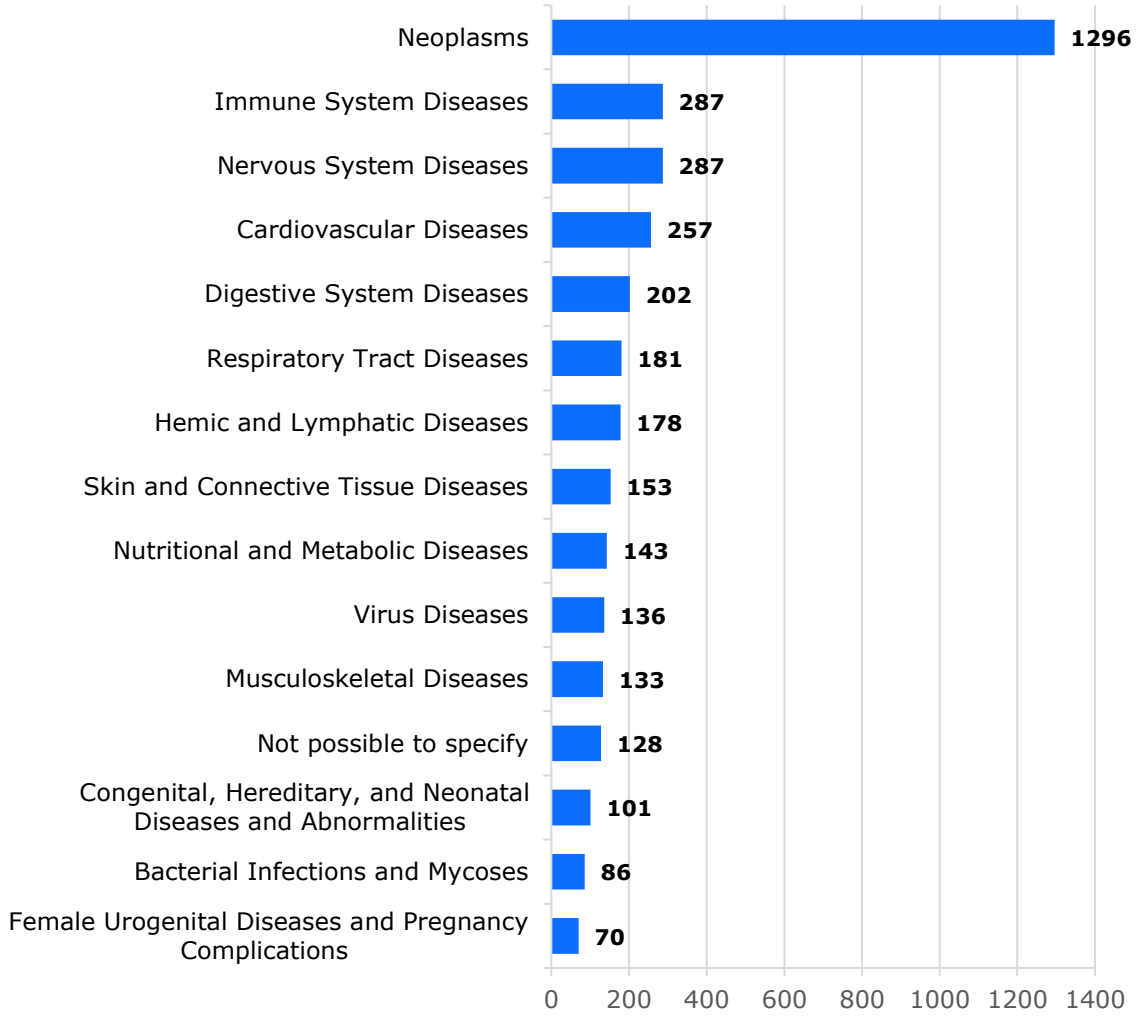


Clinical trials participants with rare disease



Authorised clinical trials per therapeutic area

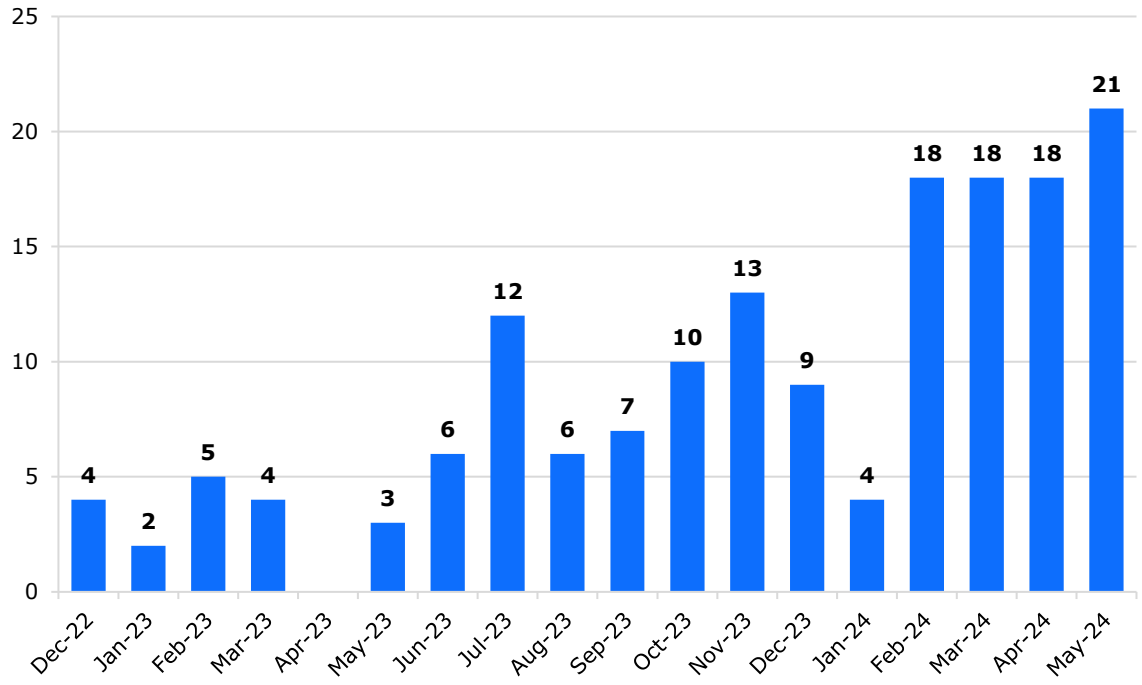
The graph below shows the number of clinical trials authorised since January 2022, broken down per therapeutic area[4], showing the most frequent 15 therapeutic areas.



Authorised clinical trials with an ATMP

Twenty-one clinical trials with an Advanced Therapy Medicinal Product (ATMP) have been authorised in May 2024, bringing the total of authorised clinical trials with ATMP to 164, as illustrated in the graph below *(the graph below shows the data for the last 18 months)*.

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


25
20
15
10
5
0
4
2
5
4
3
6
12
6
7
10
13
9
4
18
18
18
21
Dec-22
Jan-23
Feb-23
Mar-23
Apr-23
May-23
Jun-23
Jul-23
Aug-23
Sep-23
Oct-23
Nov-23
Dec-23
Jan-24
Feb-24
Mar-24
Apr-24
May-24

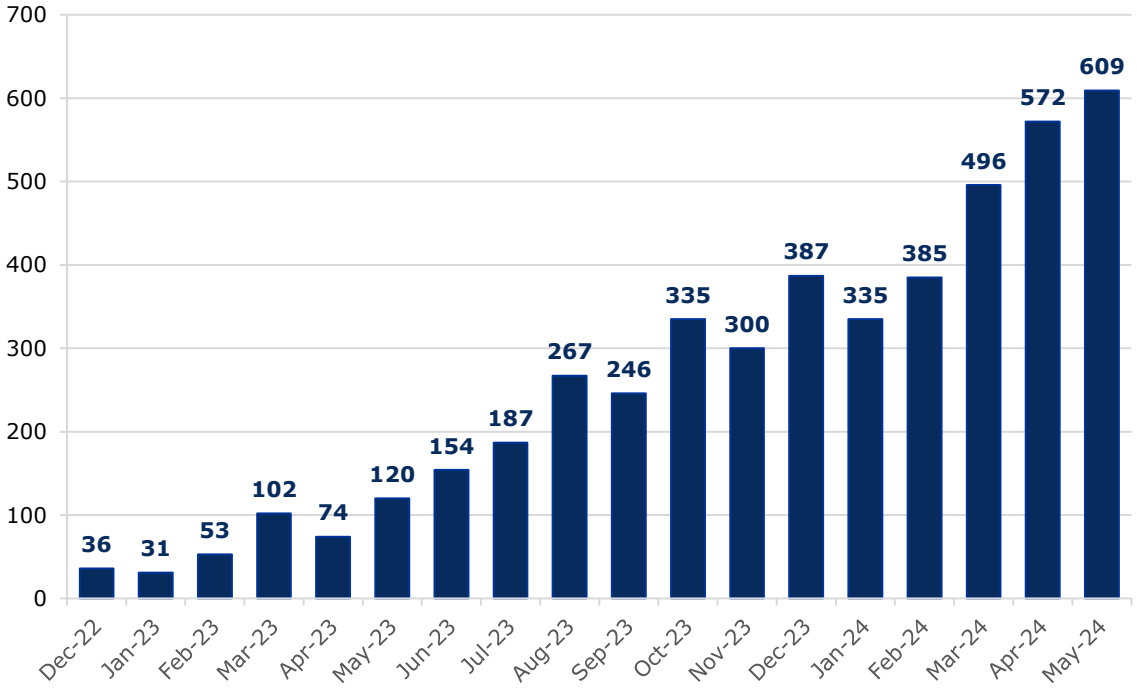
Chapter 3

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

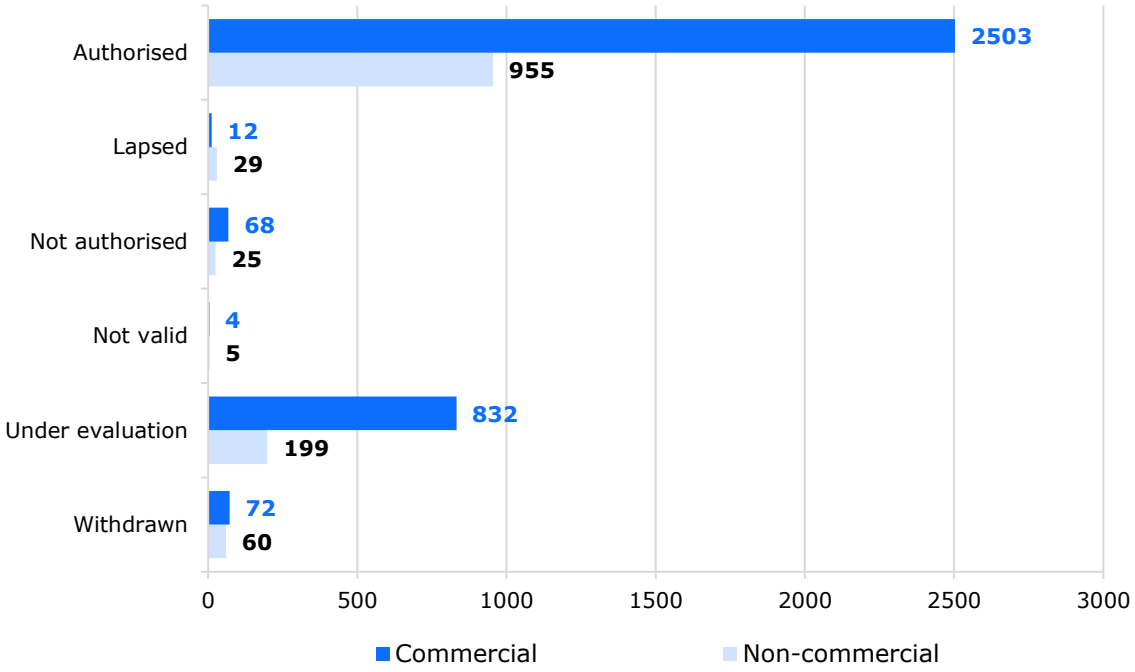
Overall, 4,764 distinct substantial modification applications, affecting 1,998 trials, have been submitted since the launch of the system on 31 January 2022, of which 609 substantial modifications submitted in May 2024, affecting 469 trials *(the graph below shows the data for the last 18 months)*.



Substantial modification applications per applicable statuses and by sponsor type

Since 31 January 2022, 4,764 distinct applications for substantial modifications, were submitted in CTIS, presented below per application status and sponsor type.

[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

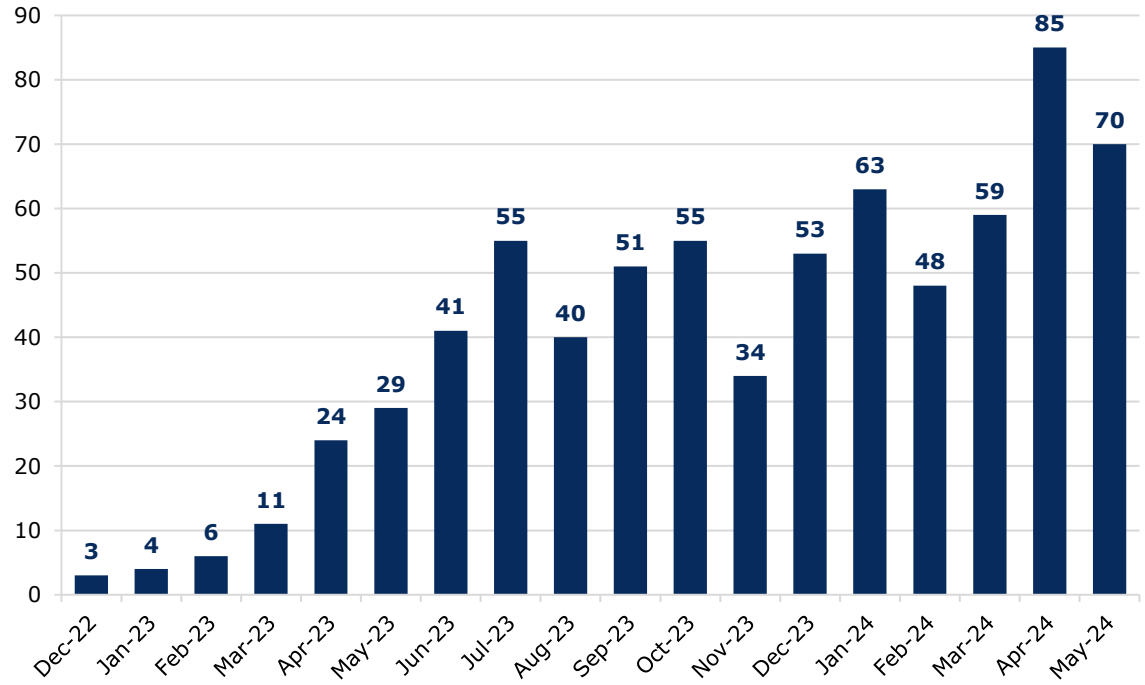

Authorised
2503
955
Lapsed
12
29
Not authorised
68
25
Not valid
4
5
Under evaluation
832
199
Withdrawn
72
60
0
500
1000
1500
2000
2500
3000
Commercial
Non-commercial

Chapter 4

Addition of a Member State Concerned

Submitted addition of Member States Concerned applications

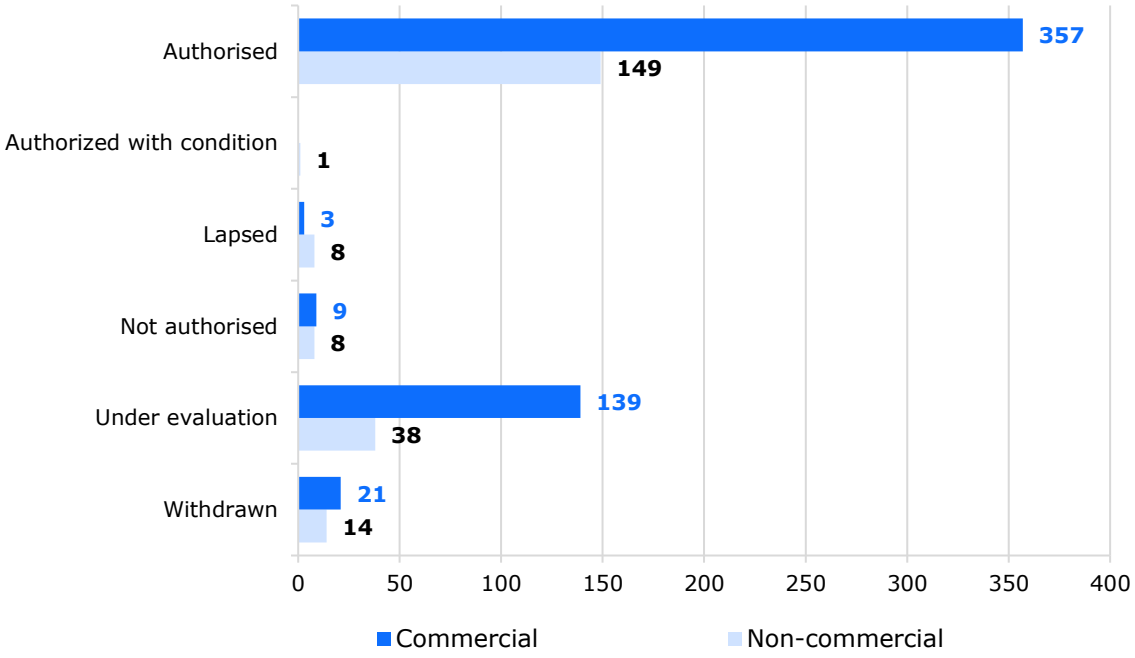
Since 31 January 2022, 747 distinct applications for the addition of a new MSC[6], affecting 291 trials, have been submitted in CTIS, of which 70 addition of new MSC submitted in May 2024, affecting 37 trials *(the graph below shows the data for the last 18 months)*.



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

Since 31 January 2022, 747 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
Authorized with condition
Lapsed
Not authorised
Under evaluation
Withdrawn
357
149
1
3
8
9
8
139
38
21
14
0
50
100
150
200
250
300
350
400
Commercial
Non-commercial

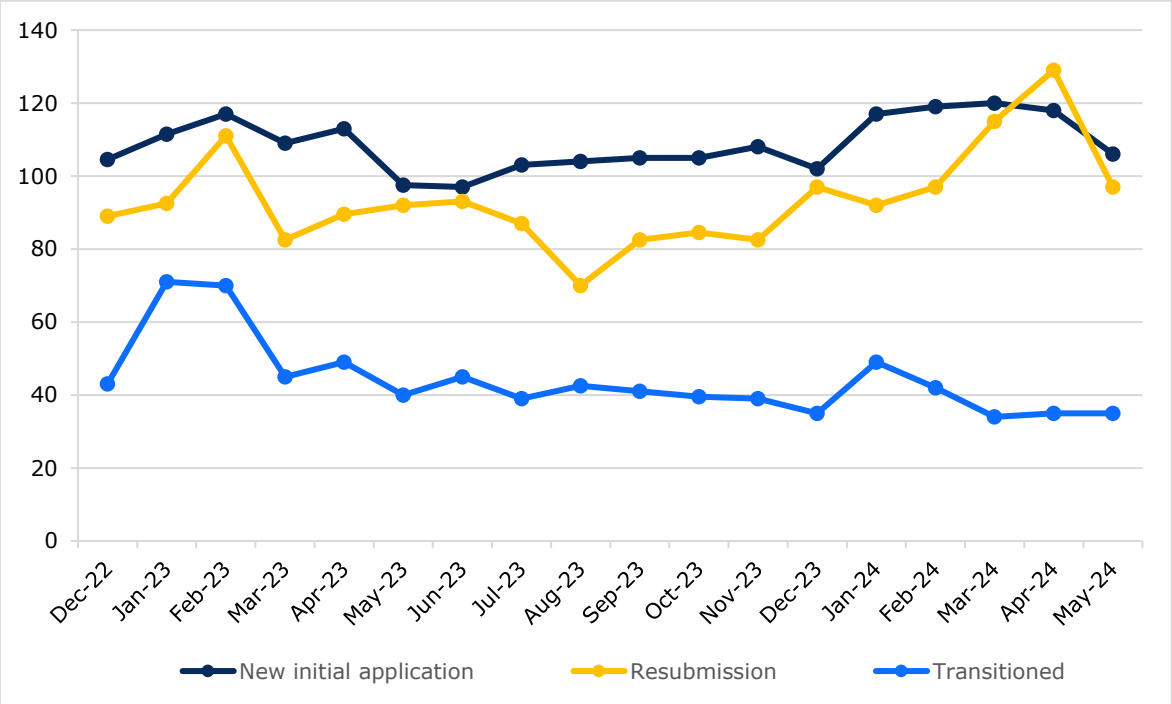
Chapter 5
Timelines

The graphs below show median timelines, for the last 18 months, from the submission of initial clinical trial applications to different points in time.

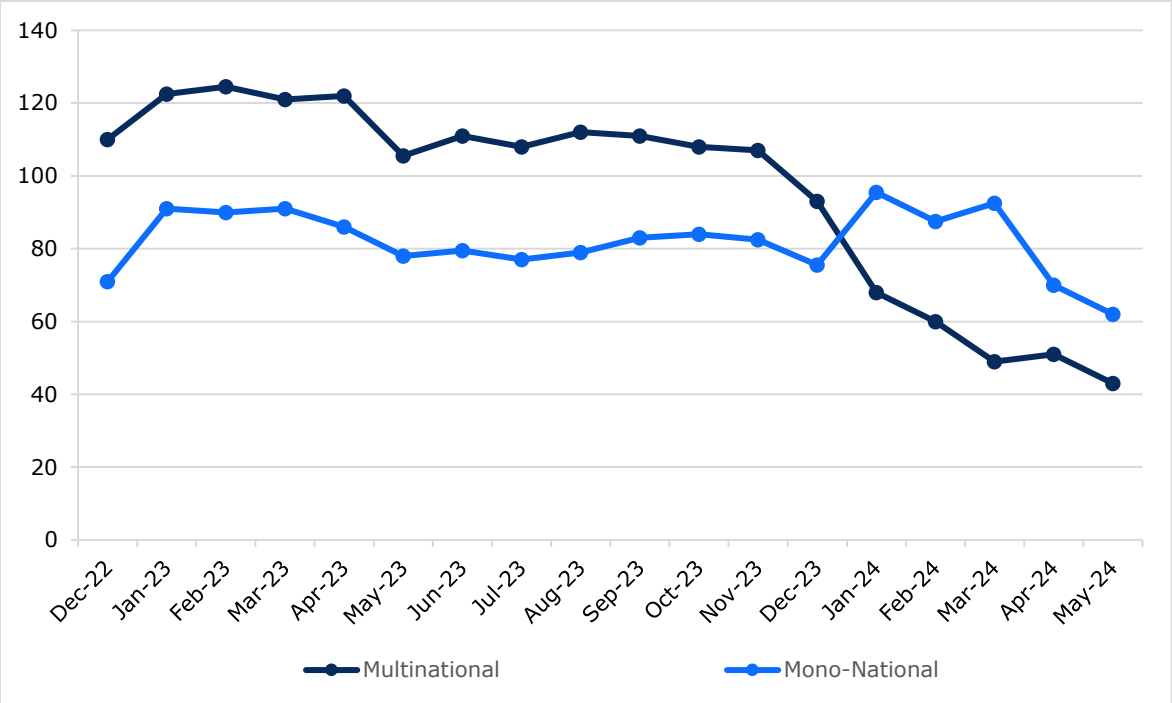
Median time from submission of initial clinical trial applications to decision

This graph takes into consideration the median 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. The time requested to issue a decision is related to the date when sponsors decide to submit Part II documents in case of partial initial application.

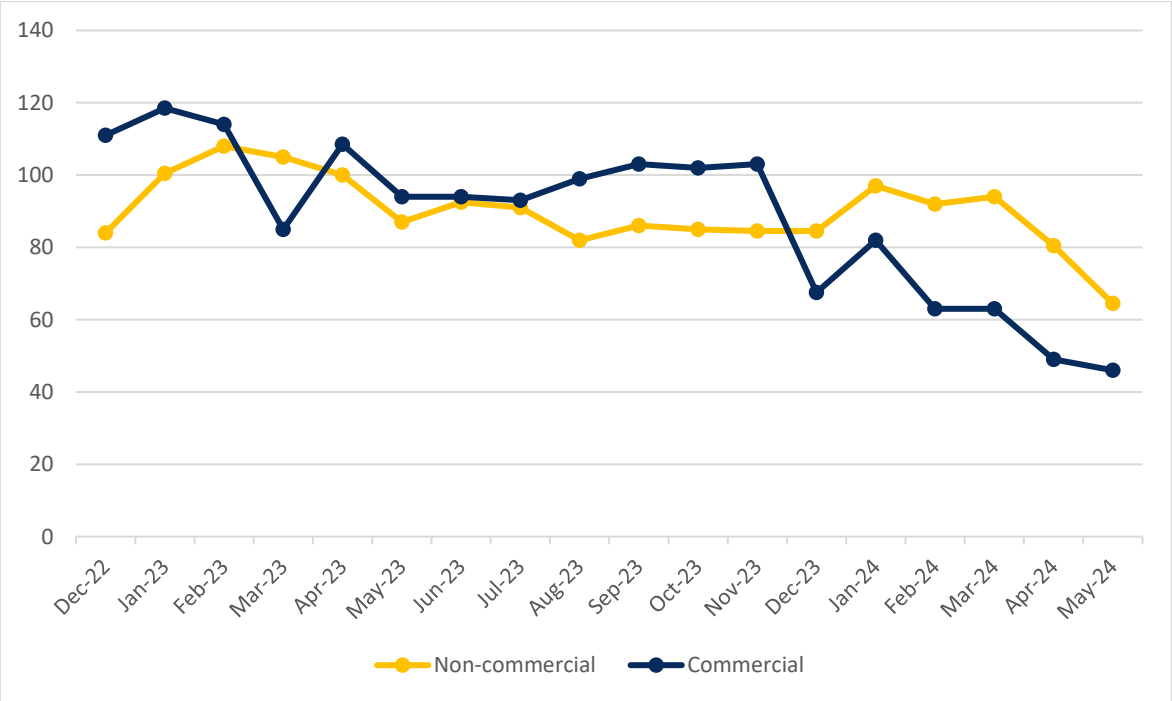
Median time per new initial application/ resubmission and transitional trials from submission of initial clinical trial applications to decision



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

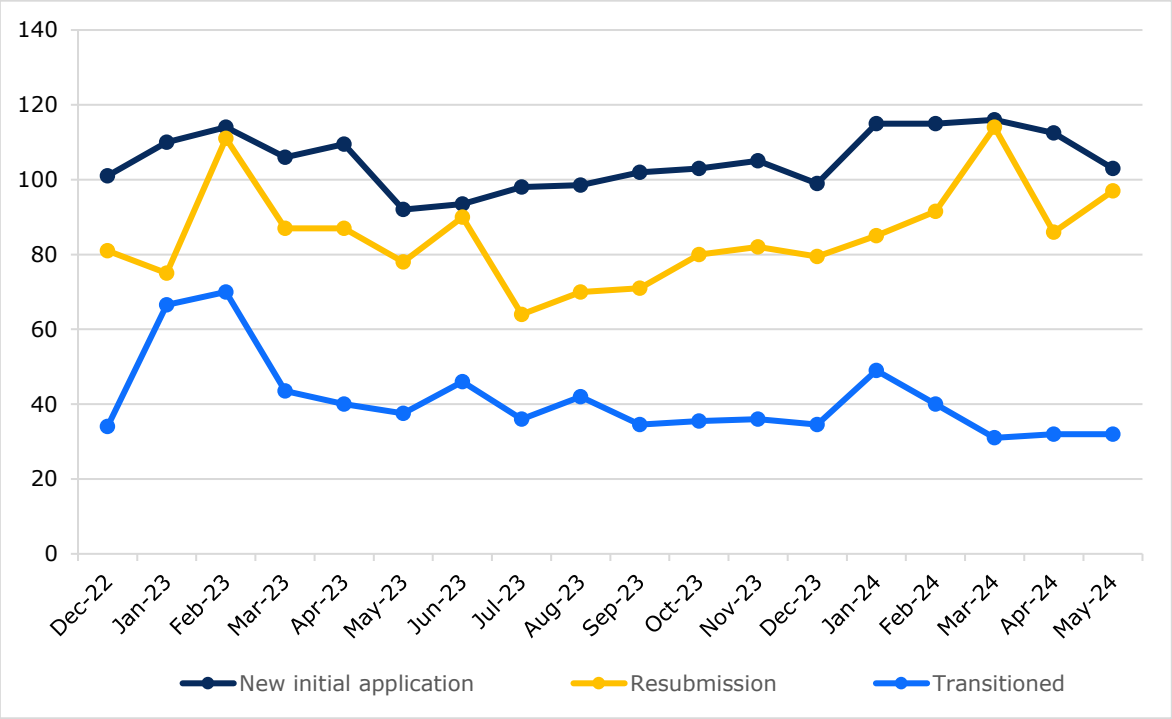


Median time per commercial/ non-commercial sponsors from submission of initial clinical trial applications to decision



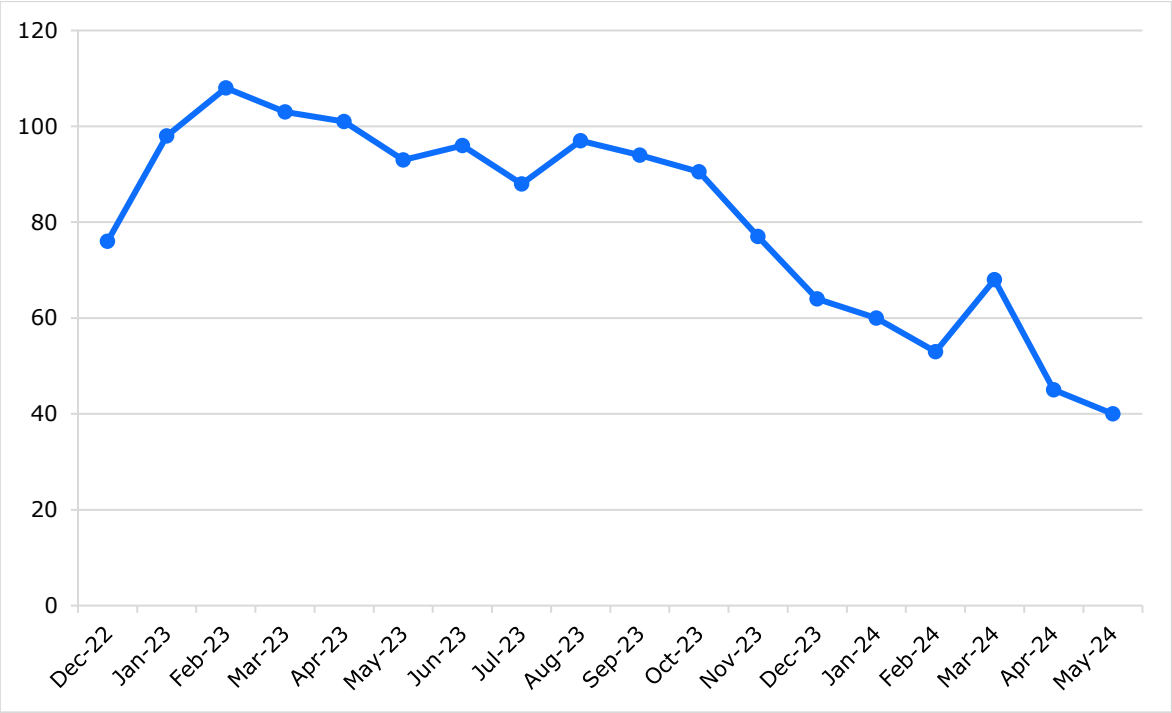
Median time from submission of initial clinical trial applications to Part I conclusion

This graph takes into consideration the median 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.



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

This graph takes into consideration the median number of days between the part II conclusion, for each MSC, and the submission dates for the part I (regardless of whether the application was a full application or a partial application) for the trials for which the part II conclusion has been issued in that particular month. The time requested to reach part II conclusions depends on: (i) when conclusion on part I is issued, (ii) when sponsors submit part II documents and (iii) the time to assess part II documents and issue a part II conclusion. Sponsors are allowed to submit part II documents later than part I (still within 2 years after the notification of the conclusion on the aspects covered by Part I of the assessment report or the trial lapses – art. 11).


120
100
80
60
40
20
0
Dec-22
Jan-23
Feb-23
Mar-23
Apr-23
May-23
Jun-23
Jul-23
Aug-23
Sep-23
Oct-23
Nov-23
Dec-23
Jan-24
Feb-24
Mar-24
Apr-24
May-24

Chapter 6
Features of the substances

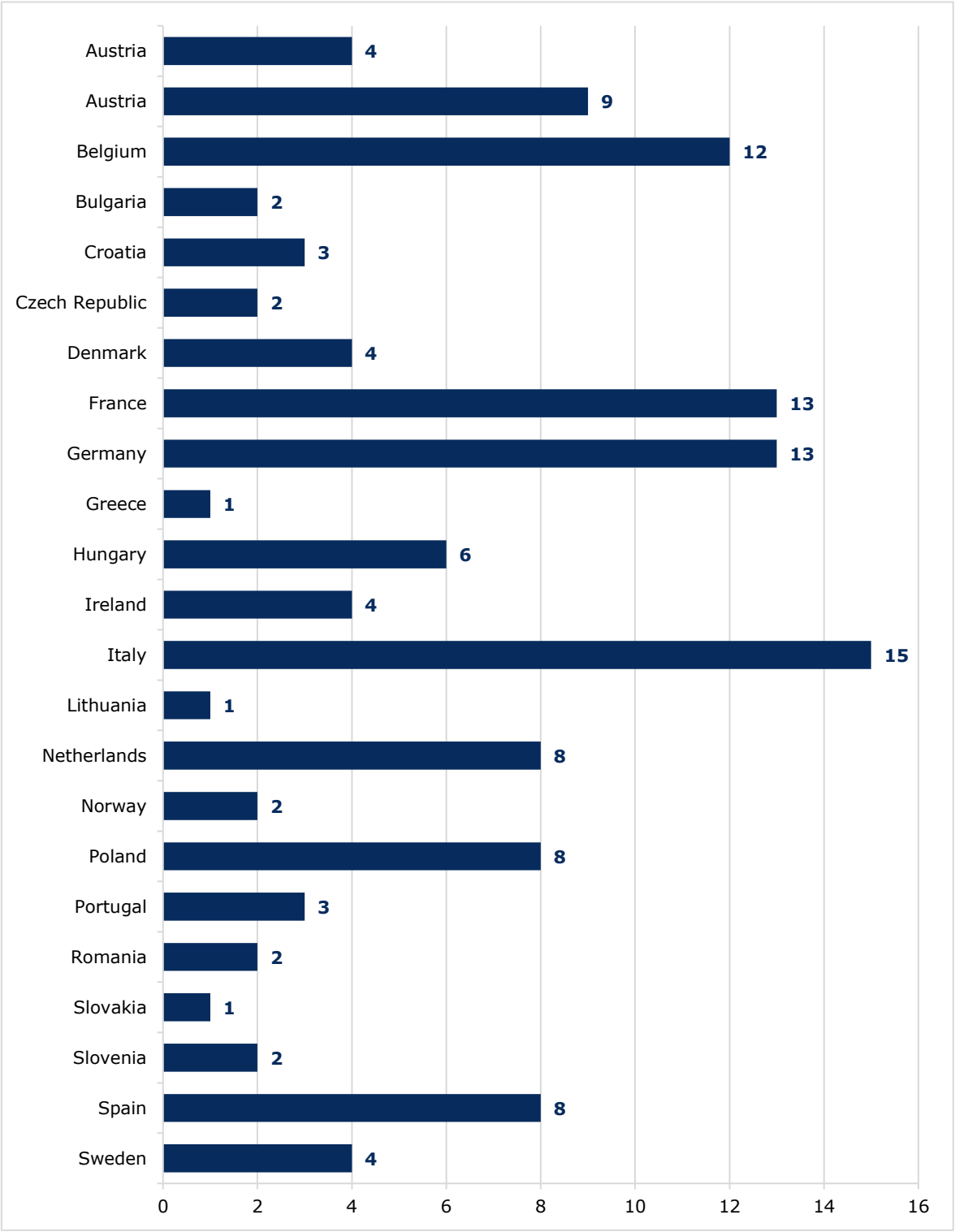
Safety assessing Member States (saMS) appointment

In multi-national clinical trials, the safety assessing Member State (saMS) is selected and responsible for the assessment of the safety report and relevant safety information of the active substances used, as described in Article(3) of **Implementing Regulation (EU) 2022/20** *of 7 January 2022 laying down rules for the application of Regulation (EU) No 536/2014 of the European Parliament and of the Council as regards setting up the rules and procedures for the cooperation of the Member States in safety assessment of clinical trials*.

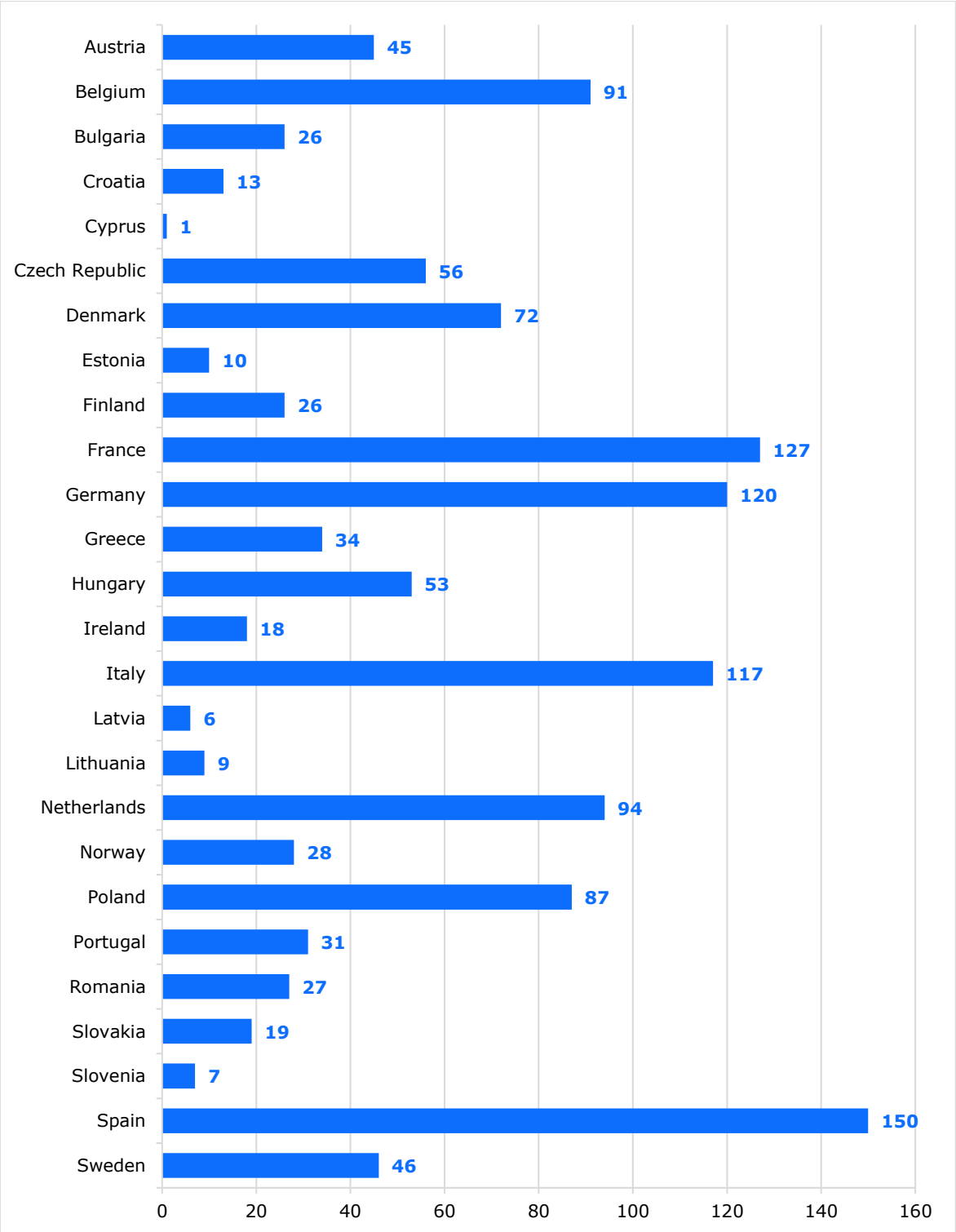
In mono-national clinical trial, the Member State is responsible for the assessment of information related to safety of active substances. Of note, the Implementing Regulation does not apply to mono-national active substances, to active substances in investigational medicinal products used as reference products, including as a placebo, or to active substances used in auxiliary medicinal products. Numbers are not displayed.

During the reporting period, Member States authorised application dossiers with 202 new active substances.

The graph below illustrates how many times each Member State has been appointed as safety assessing Member State for an active substance used in multi-national clinical trials during the reporting period.



The graph below illustrates the cumulative figures on how many times each Member State has been appointed as safety assessing Member State for an active substance used in multi-national clinical trials since February 2022.


Austria 45
Belgium 91
Bulgaria 26
Croatia 13
Cyprus 1
Czech Republic 56
Denmark 72
Estonia 10
Finland 26
France 127
Germany 120
Greece 34
Hungary 53
Ireland 18
Italy 117
Latvia 6
Lithuania 9
Netherlands 94
Norway 28
Poland 87
Portugal 31
Romania 27
Slovakia 19
Slovenia 7
Spain 150
Sweden 46
0 20 40 60 80 100 120 140 160

Annex

Annex I - Information on Transitional Trials

Guidance and documents:

1. The European Commission Guidance for the transition of clinical trials as well as the Quick Guide on CTR.
2. CTIS: how to get started and how to transition a trial - collection of training and reference documents for new CTIS users.
3. The CTCG best practice guide and accompanying annex cover letter template for sponsors with multinational trials. The guide aims to support sponsors transitioning multinational trials with protocols, IMPD or Investigator's Brochure that are not harmonised across Member States. The annex provides a template with information that should be provided in the cover letter of applications for transitioning a clinical trial authorised under the CTD to the CTR.
4. Chapter 5 of the CTIS Sponsor Handbook - it includes an overview of the transition period, general considerations for transitioning trials, the assessment timelines, and information on creating and managing trials transitioned to CTIS.
5. Module 23 of the CTIS online training programme - it includes instructions on how to submit a transitional trial, including submitting notifications and clinical trial results. An overview of the content is also available in the Quick Guide for Sponsors.

Past events:

1. The video recording and presentation of the CTIS Bitesize talk from 21 June 2023 on **how to submit a transitional trial in CTIS**, available on the event page;
2. The video recording of the CTIS webinar on 4 July 2023 on the **second year of transition**, available on the event page;
3. The video recording and presentations of the **Training** from 9 February 2024 **for non-commercial sponsors** on transitioning trials to the CTR and CTIS, available on the event page. This is of particular importance as it was organised specifically to support non-commercial sponsors and it also contains information on OMS and xEVMPD;
4. The video recording of the CTIS Bitesize talk from 29 February 2024, on **how to submit a transitional trial in CTIS**, available on the event page.

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