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

August 2024

An agency of the European Union

Clinical Trials in the EU/EEA

August 2024

671

-11 %
on previous month

Submissions

600

-10 %
on previous month

Authorised

248 Multinational	
43 Non-Commercial	**205** Commercial
423 Mononational	
299 Non-Commercial	**124** Commercial

244 Multinational	
22 Non-Commercial	**222** Commercial
356 Mononational	
261 Non-Commercial	**95** 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 August 2024, as of 31 August 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 365 submissions per month.

A total of 7,600 clinical trial applications have been submitted since the launch of CTIS.

At the time when the report is generated, more than 3,250 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

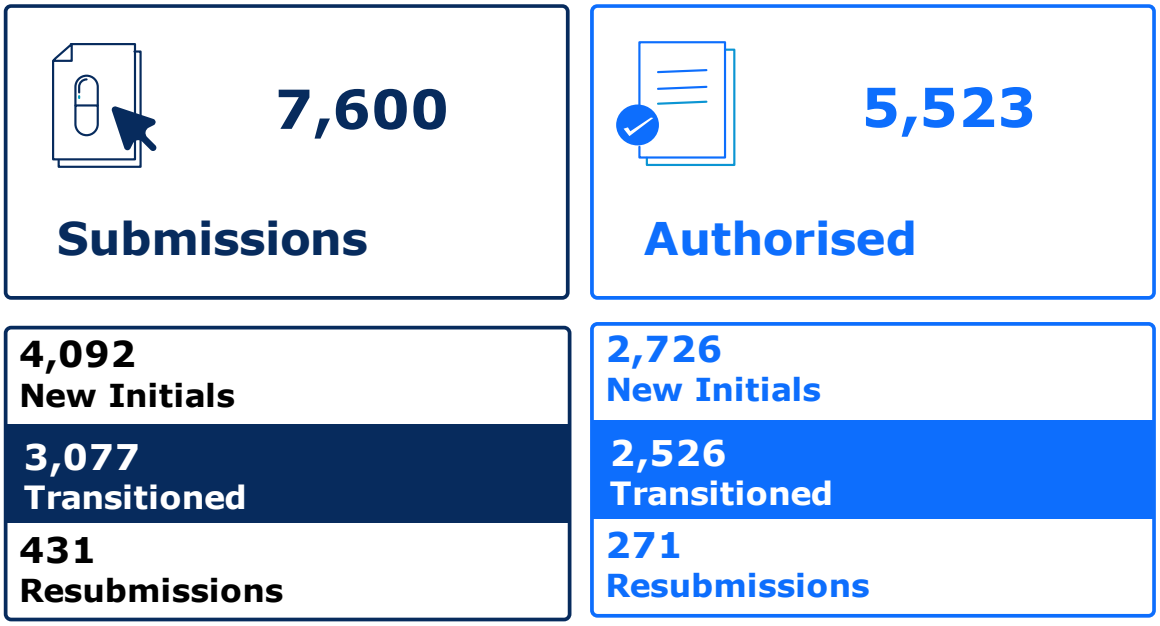
Chapter 1 of this report provides information on **submitted** initial clinical trial applications (CTAs), presented on the applicable statuses.

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

Initial clinical trial applications are those applications:

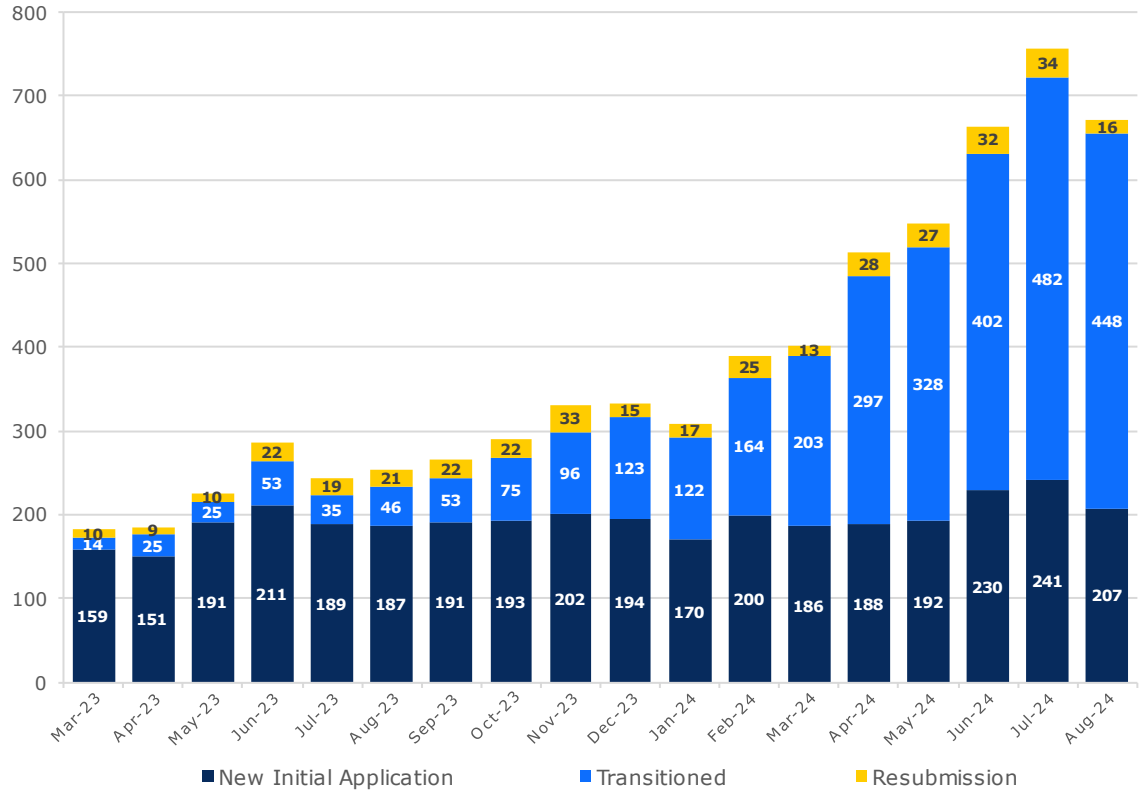
- new initial clinical trial applications submitted in CTIS by the sponsors under the Clinical Trials Regulation (EU) 536/2014 (CTR);
- trials which were already authorised under the regime of Clinical Trials Directive 2001/20/EC (CTD) and that have been transitioned to the regime of CTR;
- resubmitted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



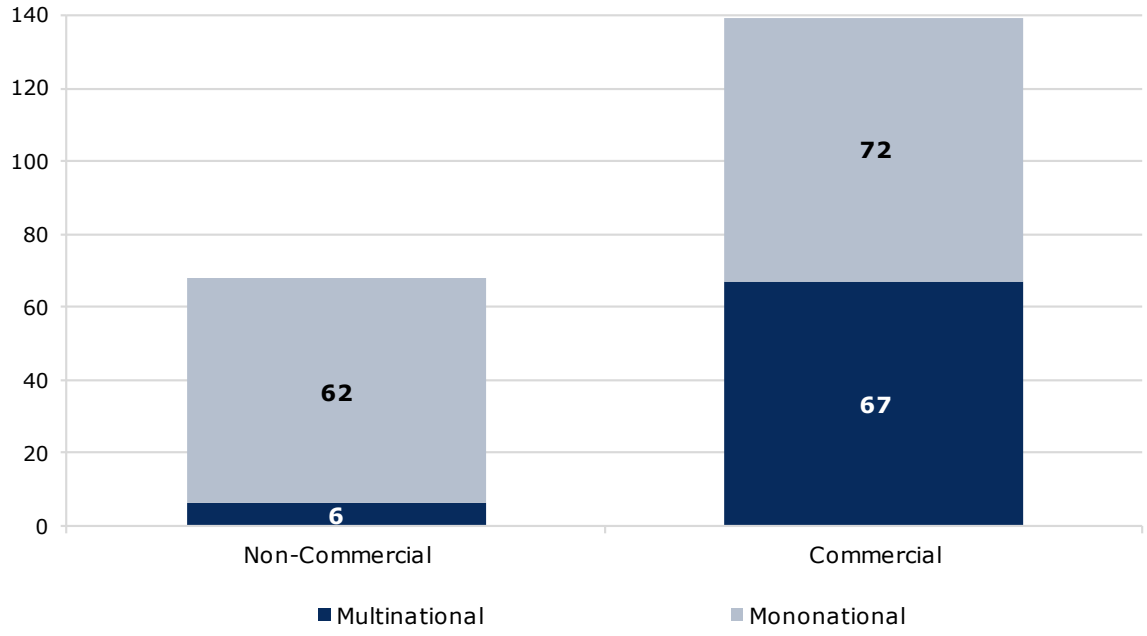
Monthly submissions of initial clinical trial applications

In August 2024, 671 initial clinical trial applications have been submitted, of which 207 new initial CTA, 448 are trials transitioned to CTR, and 16 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

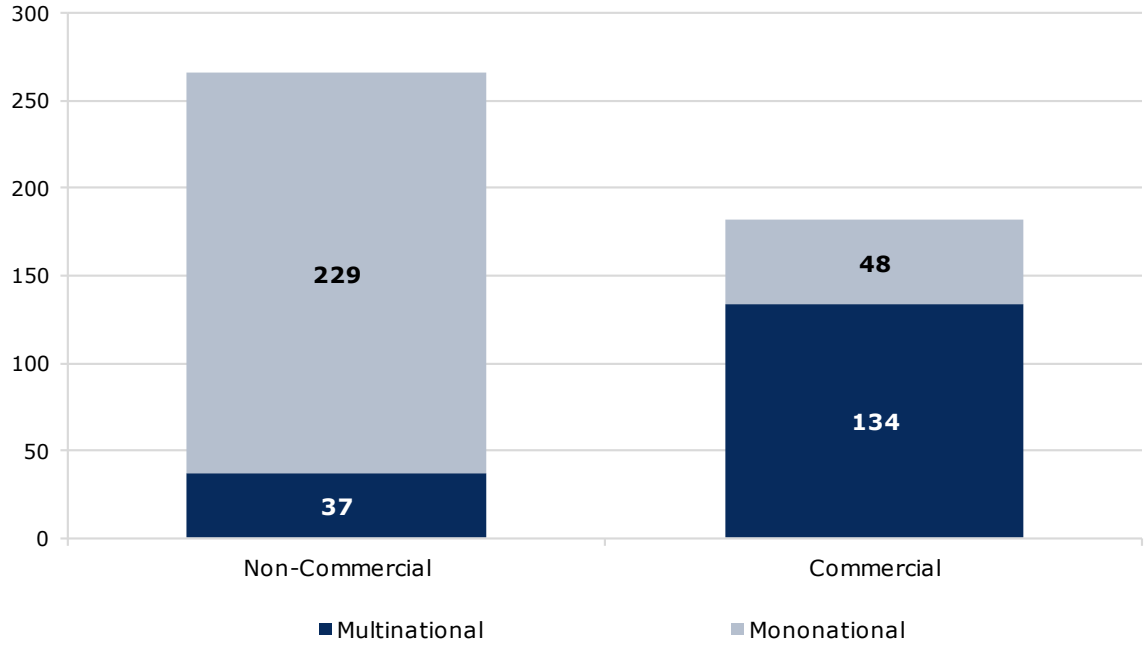
The graph below shows the split of submissions of new initial clinical trial applications in August 2024 into commercial/non-commercial sponsors and mononational versus multinational trials.



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

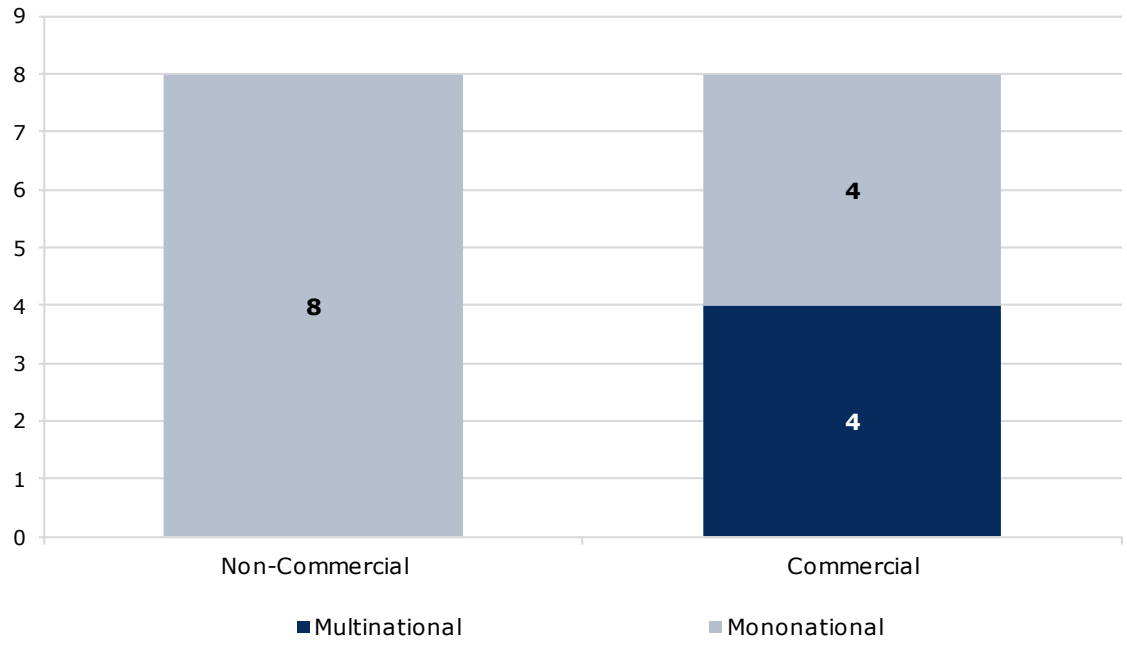


Once notified by the clinical trial sponsors, the National Competent Authorities of the EU/EEA Member States are responsible for keeping, in the EudraCT database, the information on the trial status up to date, including inserting the end of trial date, as applicable.

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



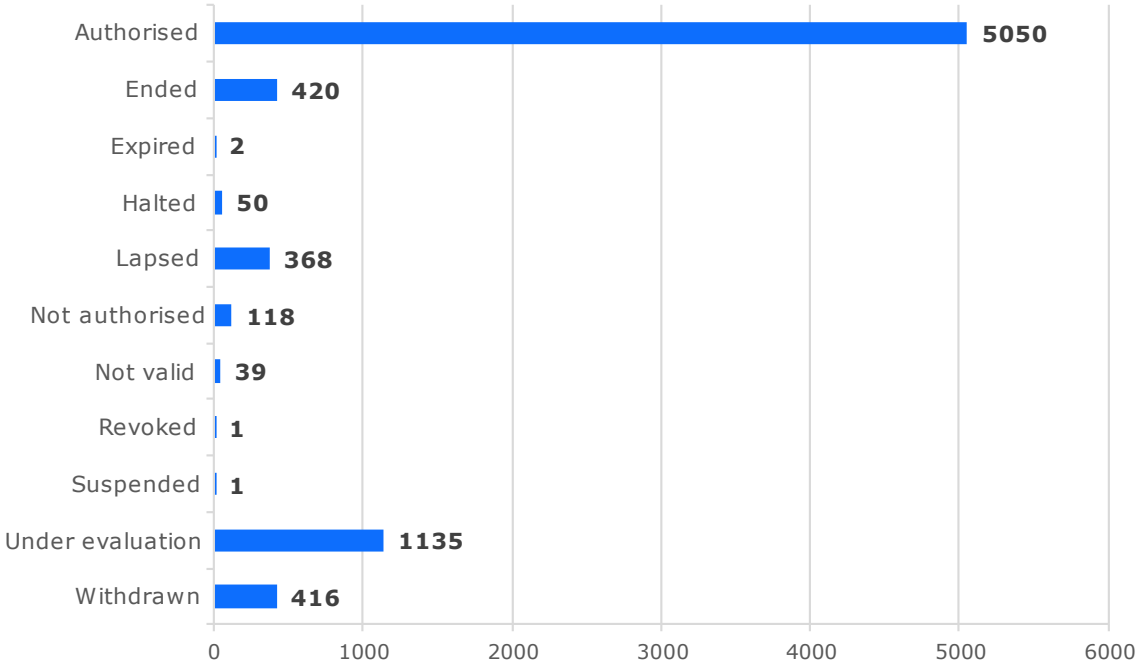
Clinical trials per applicable statuses

Since 31 January 2022, a total of 7,600 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**.

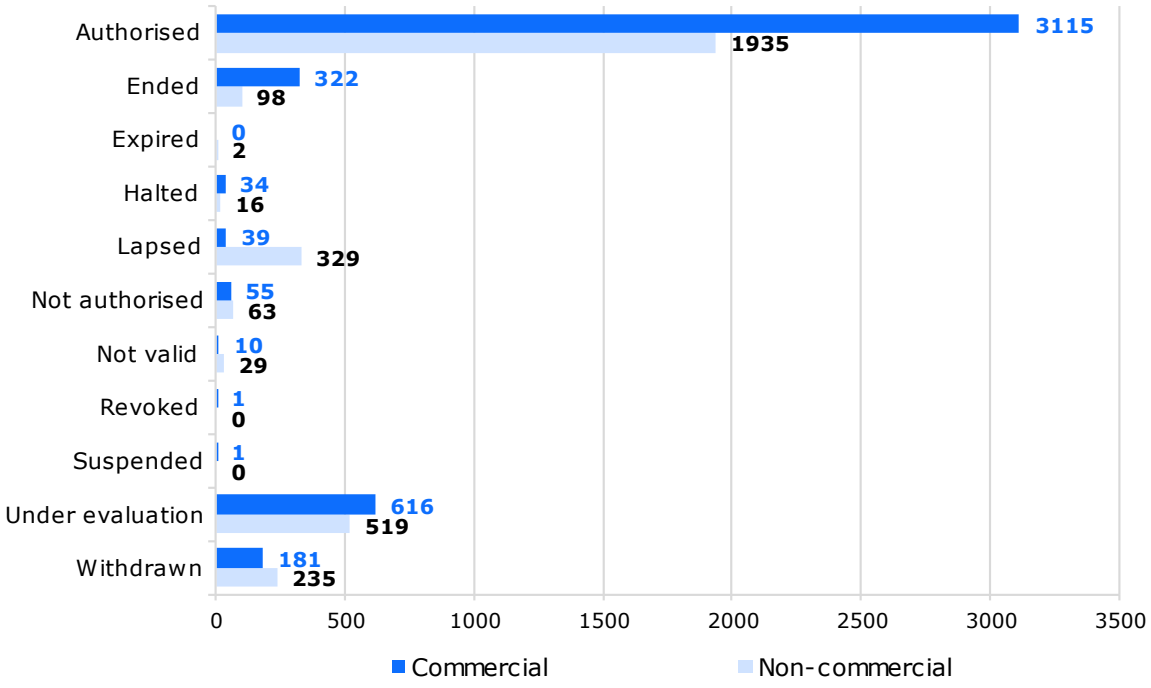
Clinical trials per applicable statuses

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). It is important to contextualise the number reported in the table vis-à-vis the Member States population [Statistics | Eurostat (europa.eu)].

Member State	Multinational Trials		Mononational Trials	Total number of Initial CTAs
	MSC	*Of which as RMS*		
Austria	288	50	37	325
Belgium	572	108	195	767
Bulgaria	290	4	20	310
Croatia	94	0	0	94
Cyprus	4	0	1	5
Czechia	437	83	43	480
Denmark	319	96	212	531
Estonia	53	4	6	59
Finland	126	33	35	161
France	1001	158	404	1405
Germany	1020	320	294	1314
Greece	272	2	14	286
Hungary	405	22	19	424
Iceland	7	0	1	8
Ireland	104	8	14	118
Italy	970	115	132	1102
Latvia	52	5	4	56
Lithuania	69	10	4	73
Luxembourg	2	0	1	3
Netherlands	493	111	318	811
Norway	138	22	43	181
Poland	794	85	68	862
Portugal	214	12	63	277
Romania	232	10	27	259
Slovakia	157	15	2	159
Slovenia	28	2	2	30
Spain	1265	372	309	1574
Sweden	249	59	96	345

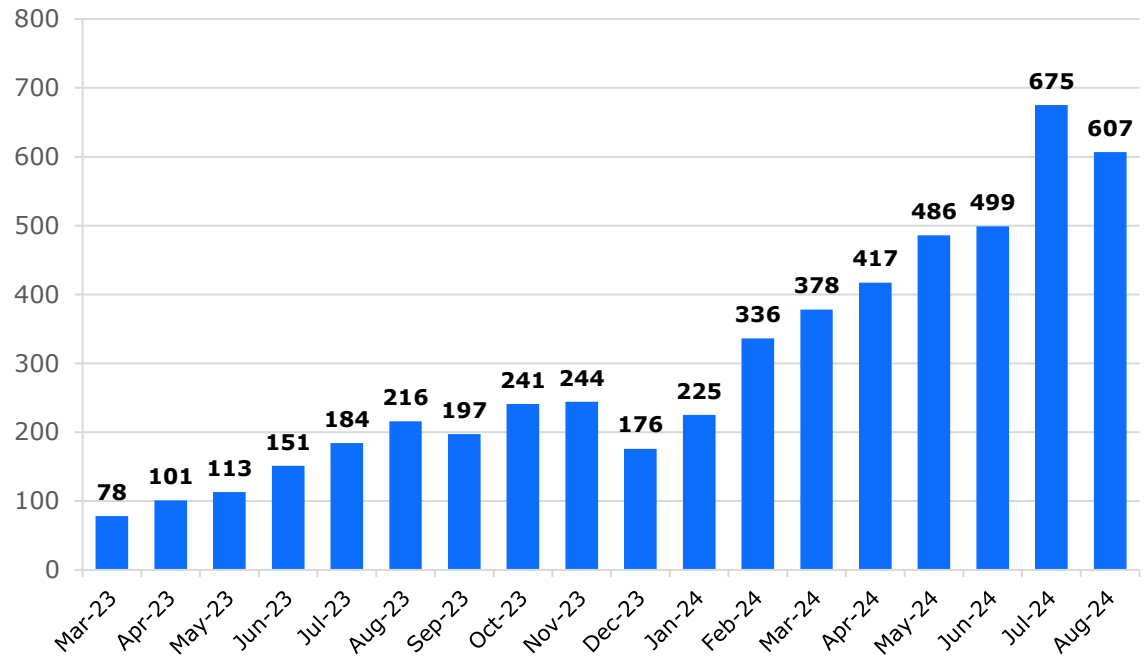
[1] RMS is the Reporting Member State appointed in line with the requirements of Article 5 of the Clinical Trials Regulation (EU) No 536/2014.

Chapter 2

Authorised clinical trials

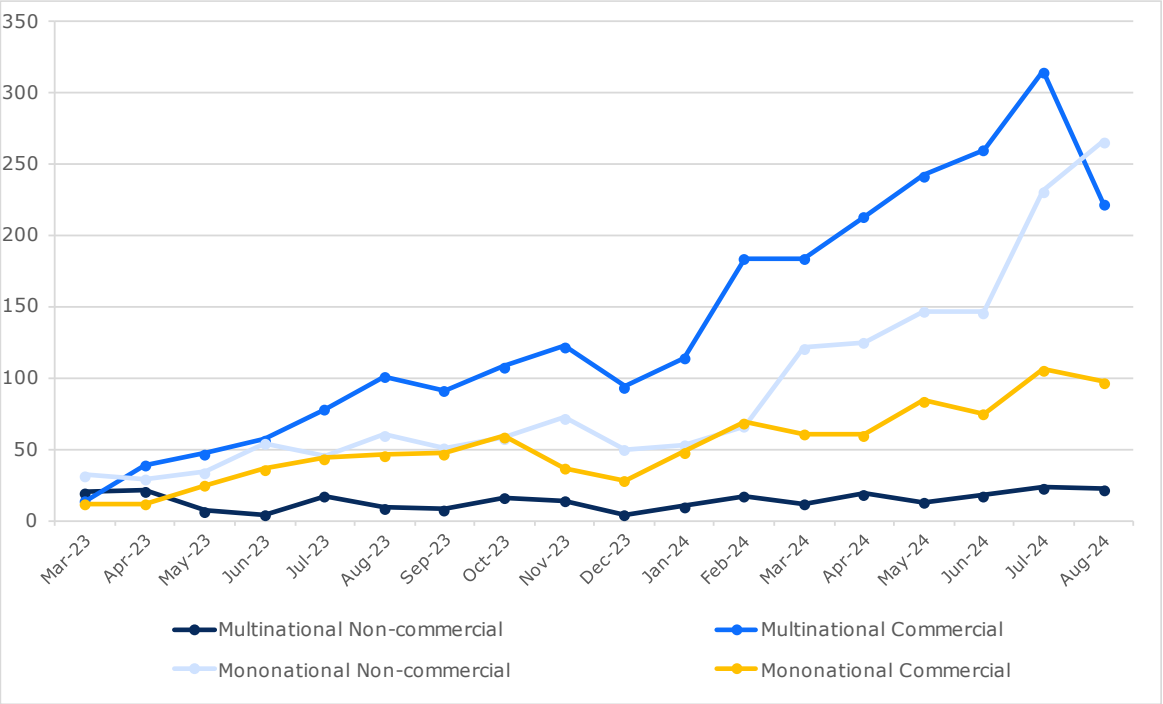
Since 31 January 2022, a total of 5,642 have received a decision in CTIS, of which 5,523 received a positive decision authorising the clinical trial. The graph below includes figures on both authorised and not authorised clinical trials in the last 18 months.

In August 2024, of the 607 initial clinical trial with a decision, 600 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. The graph below includes figures on both authorised and not authorised clinical trials as well as commercial/non-commercial sponsor.

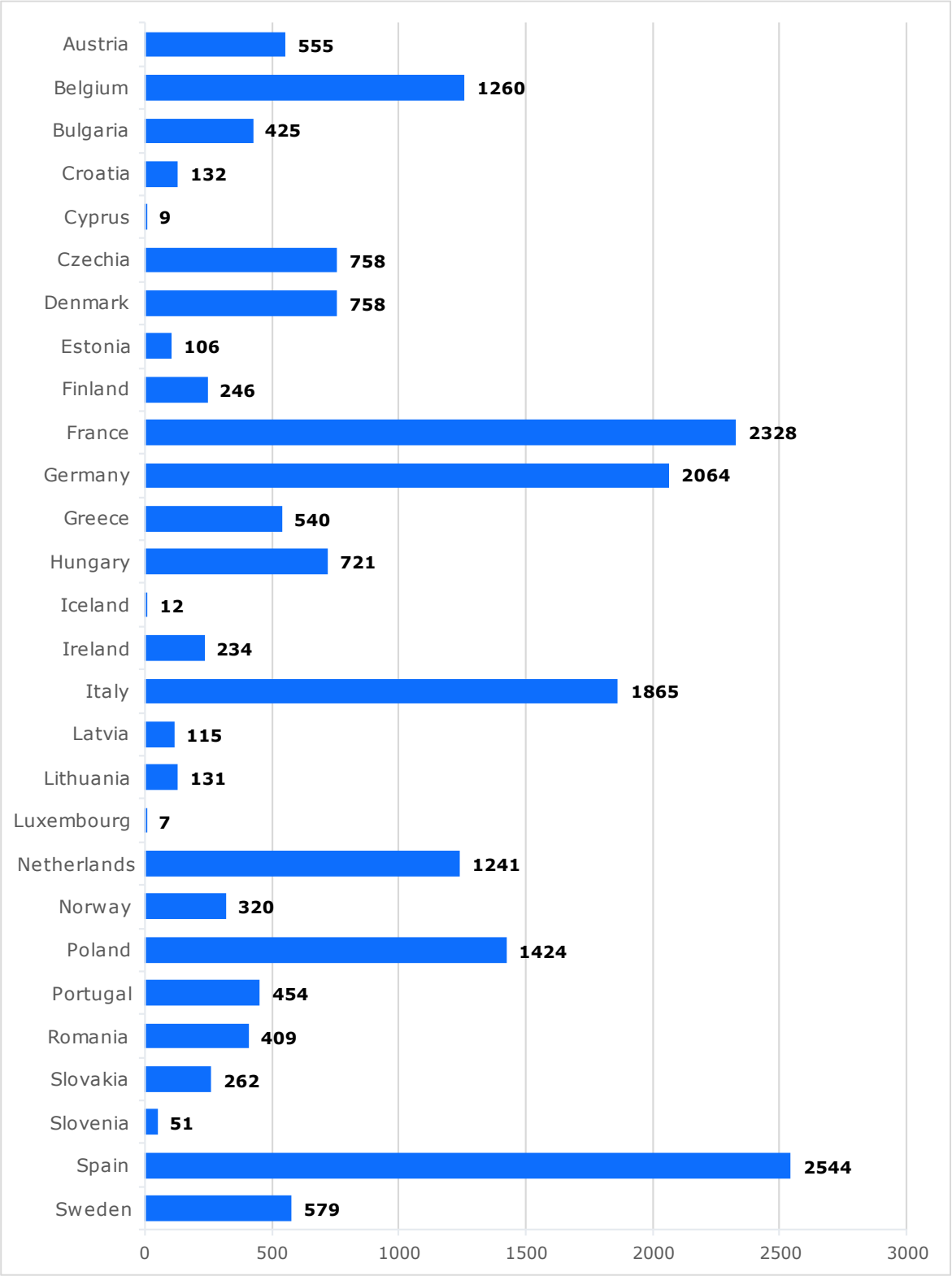


Until August 2024, 2,949 multinational clinical trials have a decision in CTIS with an average of 6 Member States Concerned.

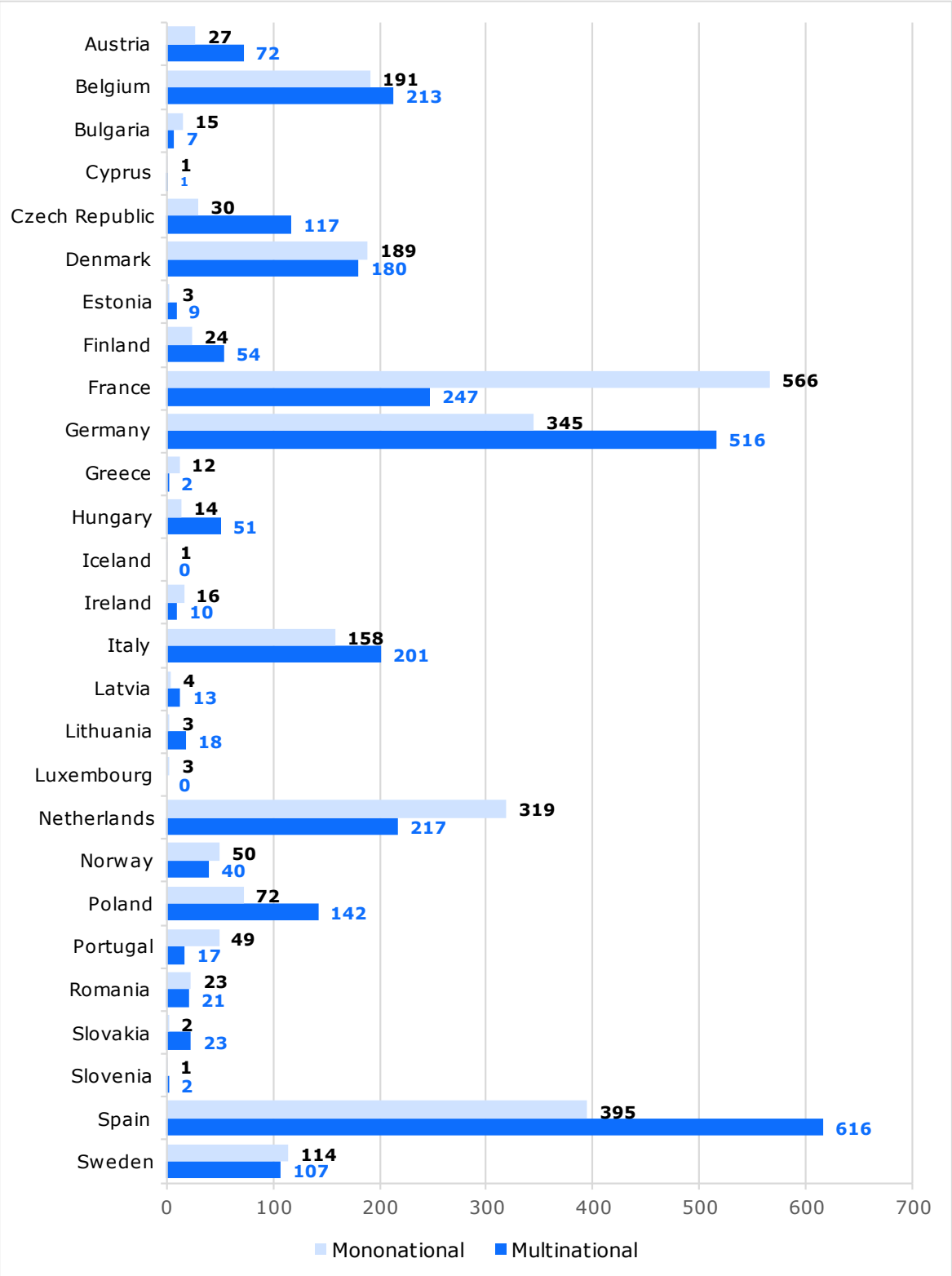
Distribution of **authorised** clinical trials per Member State Concerned and appointment of Reporting Member State

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.



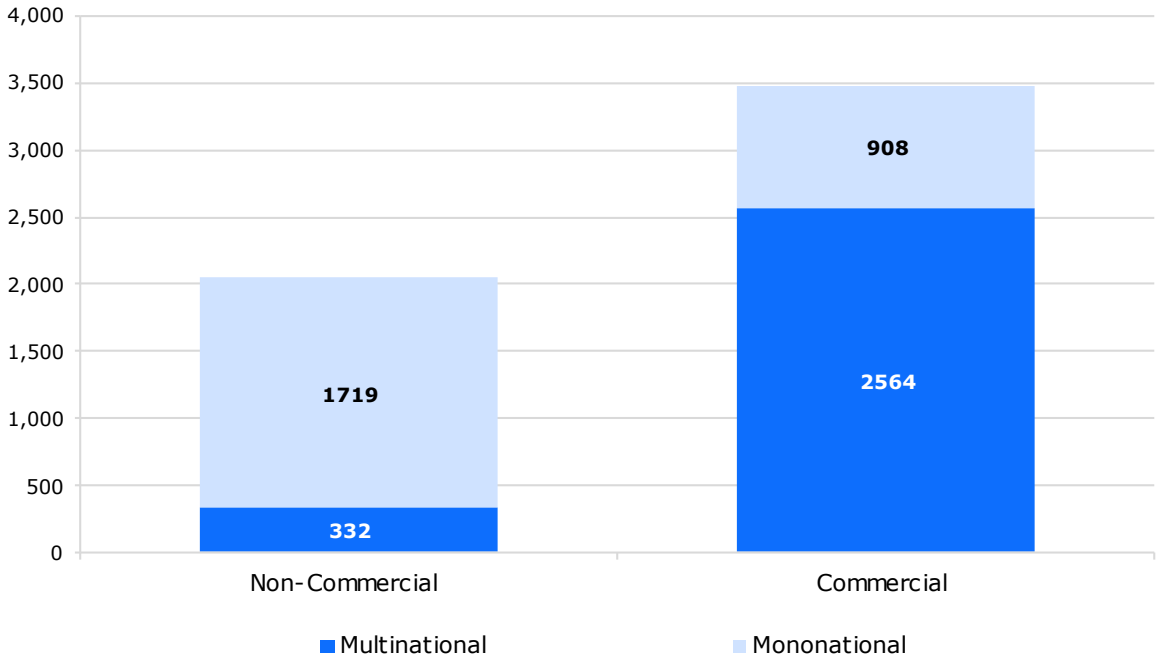
The graph below shows the distribution of appointment of Reporting Member State (RMS), amongst the applicable Member States Concerned, in authorised mono- and multinational trials.


Austria 27 72
Belgium 191 213
Bulgaria 15 7
Cyprus 1 1
Czech Republic 30 117
Denmark 189 180
Estonia 3 9
Finland 24 54
France 566 247
Germany 345 516
Greece 12 2
Hungary 14 51
Iceland 1 0
Ireland 16 10
Italy 158 201
Latvia 4 13
Lithuania 3 18
Luxembourg 3 0
Netherlands 319 217
Norway 50 40
Poland 72 142
Portugal 49 17
Romania 23 21
Slovakia 2 23
Slovenia 1 2
Spain 395 616
Sweden 114 107
0 100 200 300 400 500 600 700
Mononational
Multinational

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

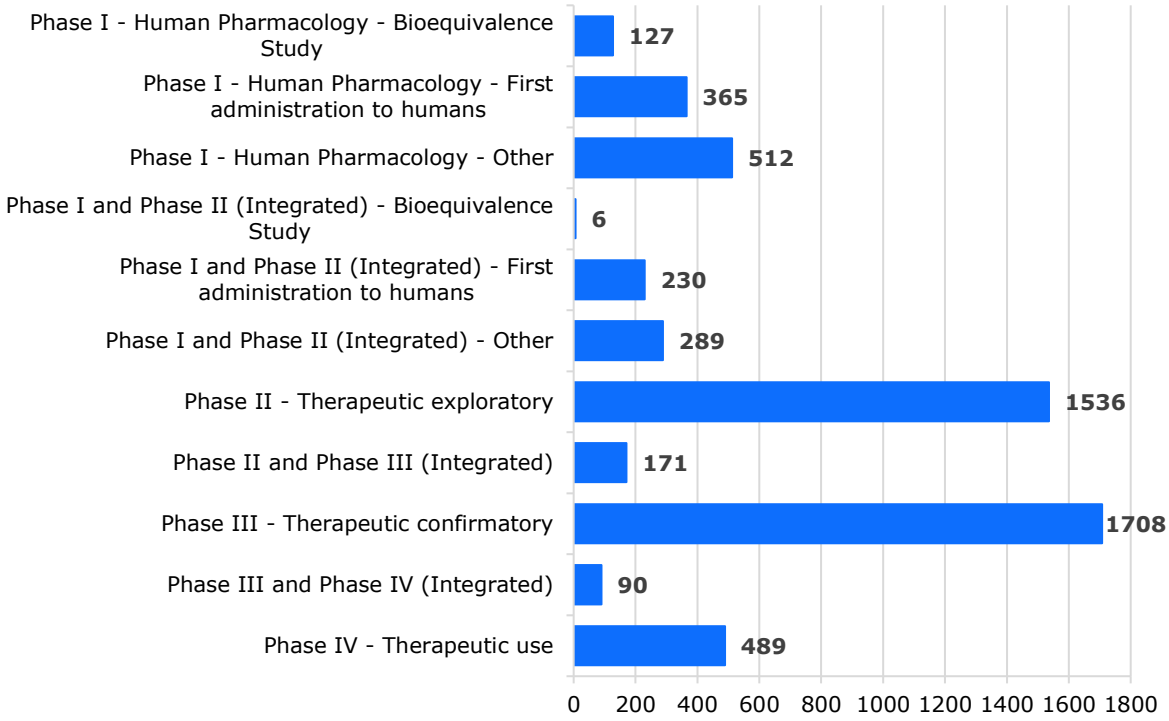
The graph below shows the number of clinical trials authorised since 31 January 2022, split into mono national/ multi-national and per sponsor type.

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.



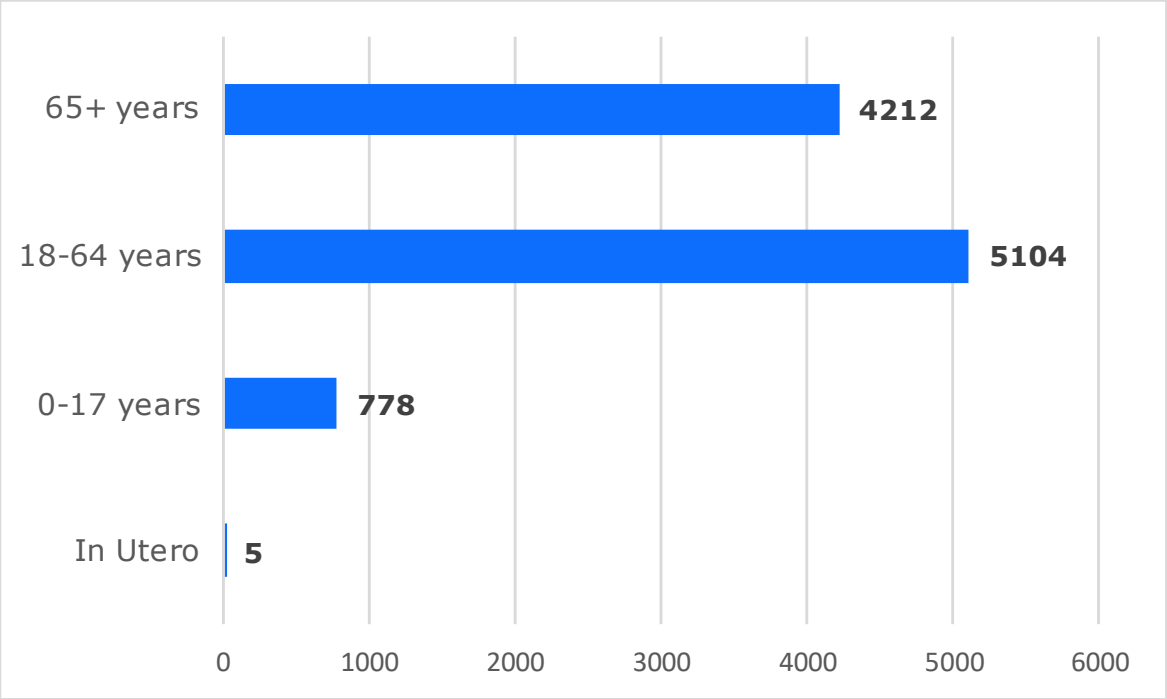
Clinical trials per population type and rare disease

At the end August 2024, 3,352 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.

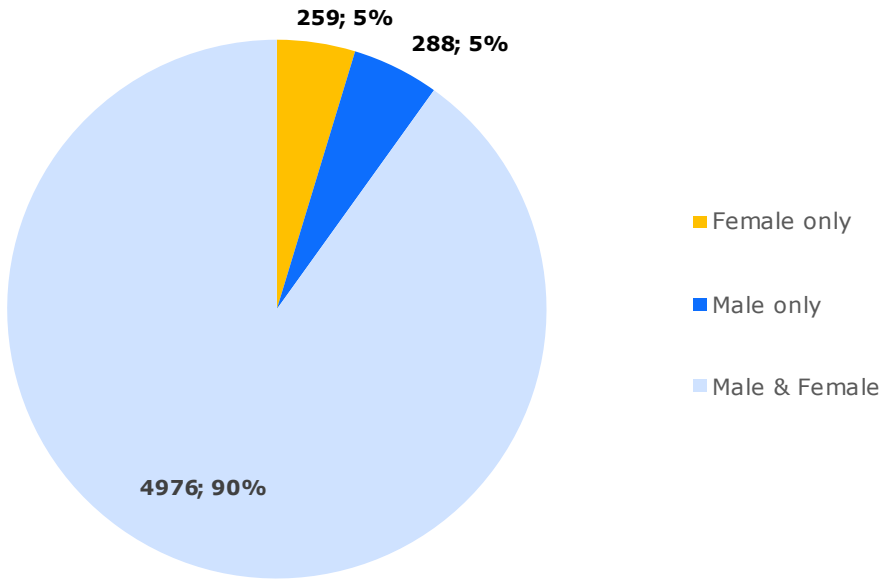
[3] Details on recruitment status are based on the information reported by the trial sponsor in CTIS.

By Age of clinical trials participants

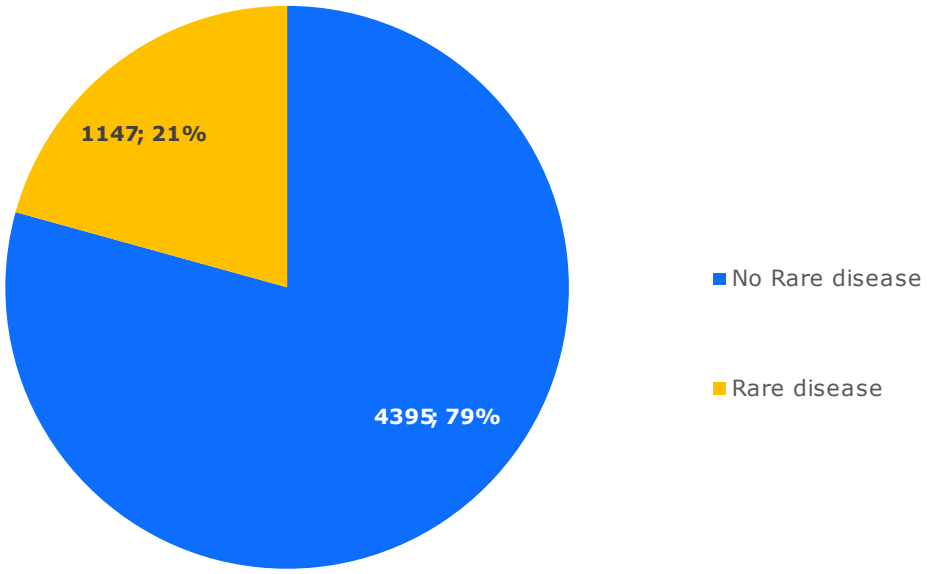


It is important to note that various age categories may be addressed in one clinical trial (e.g. a clinical trial may be for age "+65" as well as for age "18-64" and in this case it would be counted twice). Therefore, the reader should not sum the number of clinical trials for each age category and consider the total as the total of clinical trials.

By Gender of clinical trials participants



Clinical trials with rare disease participants

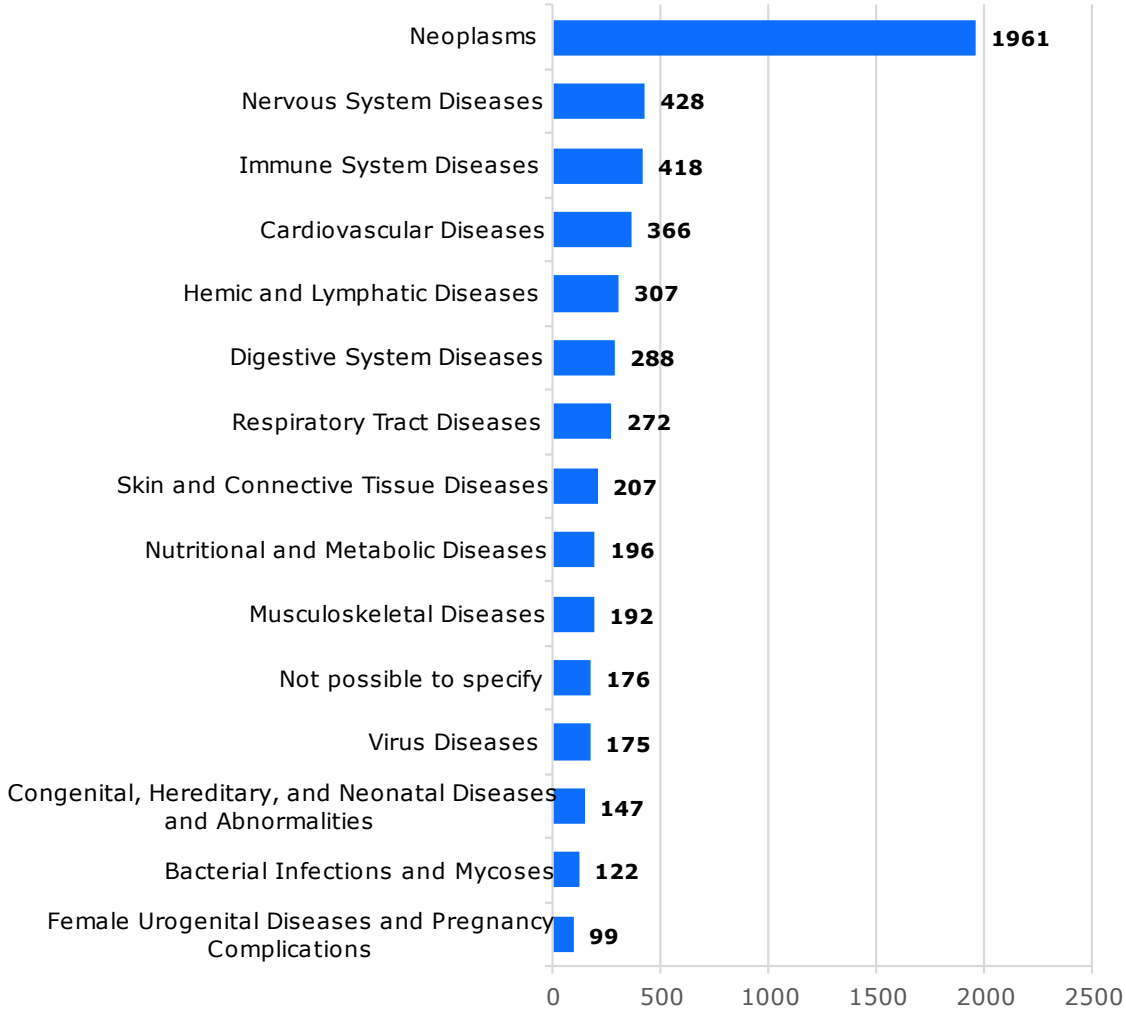


It is important to note that more than one disease could be investigated in one clinical trial (e.g., a clinical trial may be for a rare disease as well as for No rare disease and in this case it would be counted twice). Therefore, the reader should not sum the number of clinical trials for Rare disease/No Rare disease and consider the total as the total of clinical trials.

Authorised clinical trials per therapeutic area

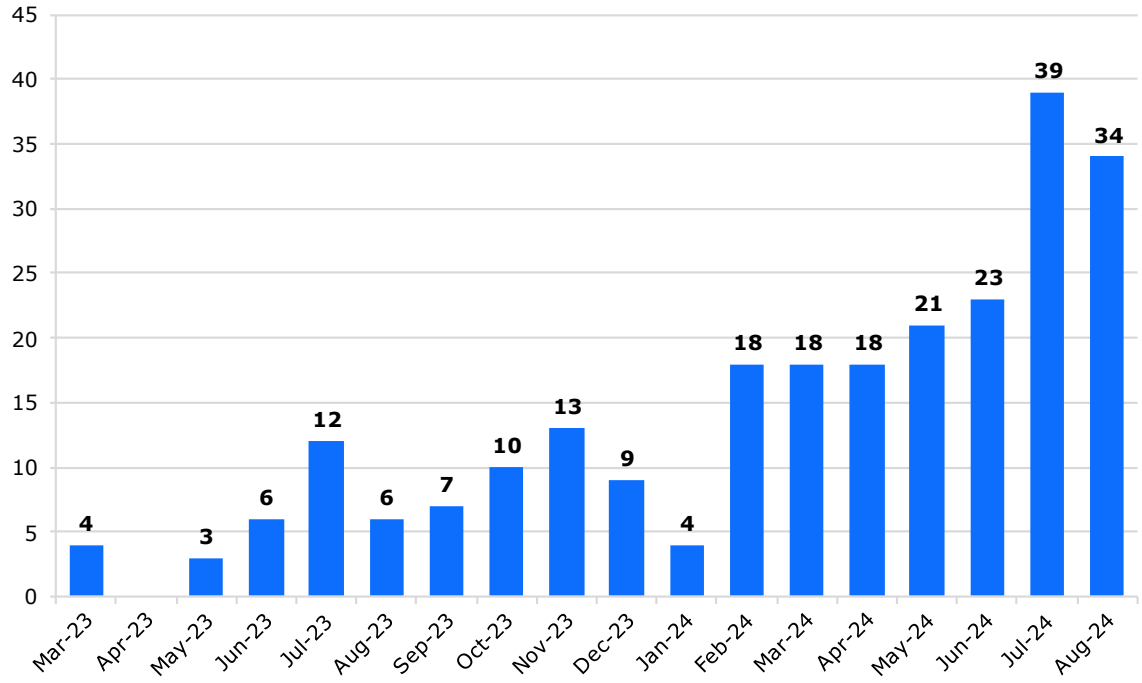
The graph below shows the number of clinical trials authorised since January 2022, broken down per therapeutic area[4], showing the most frequent 15 therapeutic areas.

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



Authorised clinical trials with an ATMP

Thirty-four clinical trials with an Advanced Therapy Medicinal Product (ATMP) have been authorised in August 2024, bringing the total of authorised clinical trials with ATMP to 260, as illustrated in the graph below *(the graph below shows the data for the last 18 months)*.


45
40
35
30
25
20
15
10
5
0
4
3
6
12
6
7
10
13
9
4
18
18
18
21
23
39
34
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
Jun-24
Jul-24
Aug-24

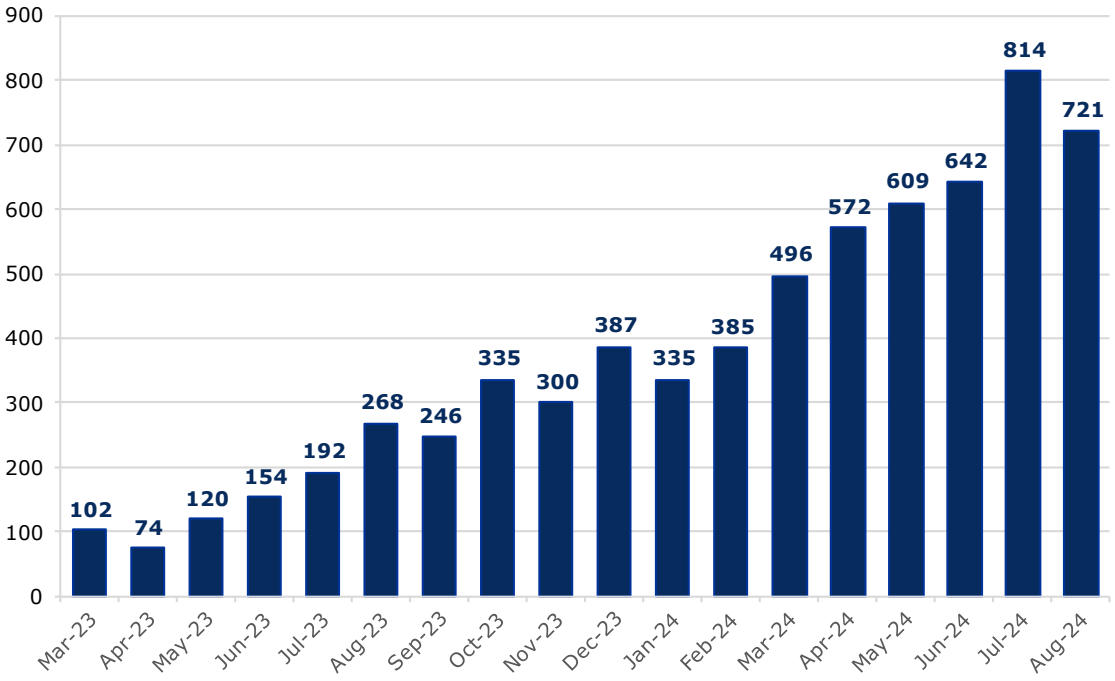
Chapter 3

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

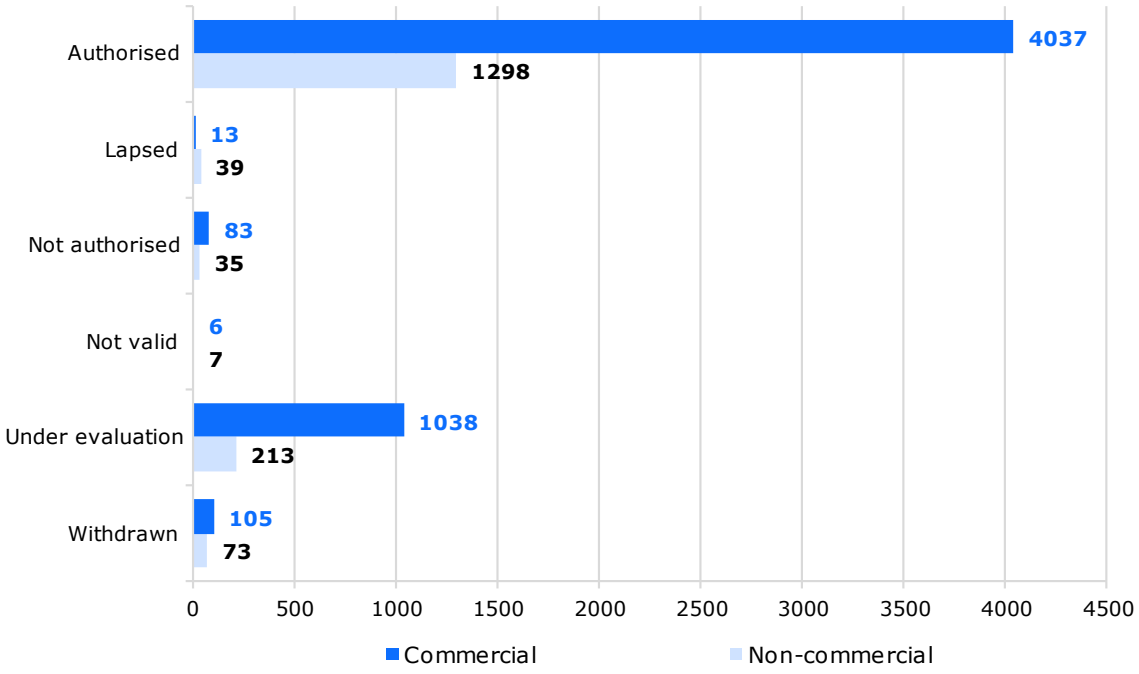
Overall, 6,947 distinct substantial modification applications, affecting 2,854 trials, have been submitted since the launch of the system on 31 January 2022, of which 721 substantial modifications submitted in August 2024, affecting 582 trials *(the graph below shows the data for the last 18 months)*.



Substantial modification applications per applicable statuses and by sponsor type

Since 31 January 2022, 6,947 distinct applications for substantial modifications, were submitted in CTIS, presented below per application status and sponsor type.

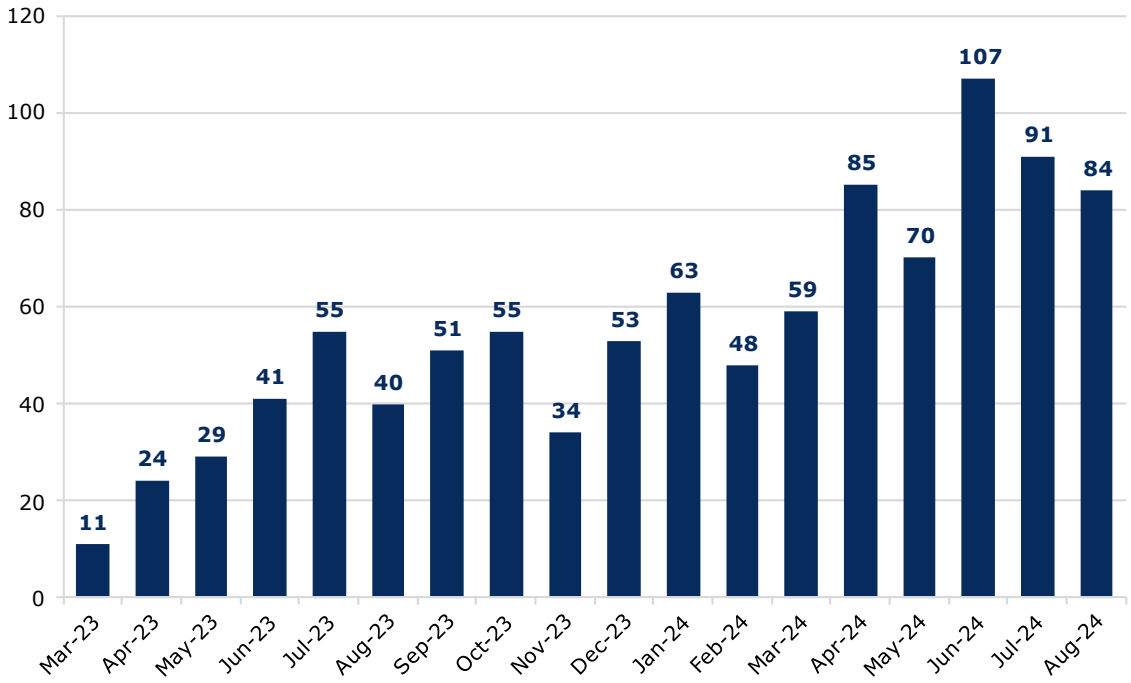
[5] Substantial modifications for part I only, or part II only or part I and part II, are foreseen in chapter II of Regulation (EU) No 536/2014


Authorised
4037
1298
Lapsed
13
39
Not authorised
83
35
Not valid
6
7
Under evaluation
1038
213
Withdrawn
105
73
0
500
1000
1500
2000
2500
3000
3500
4000
4500
Commercial
Non-commercial

Chapter 4
Addition of a Member State Concerned

Submitted addition of Member States Concerned applications

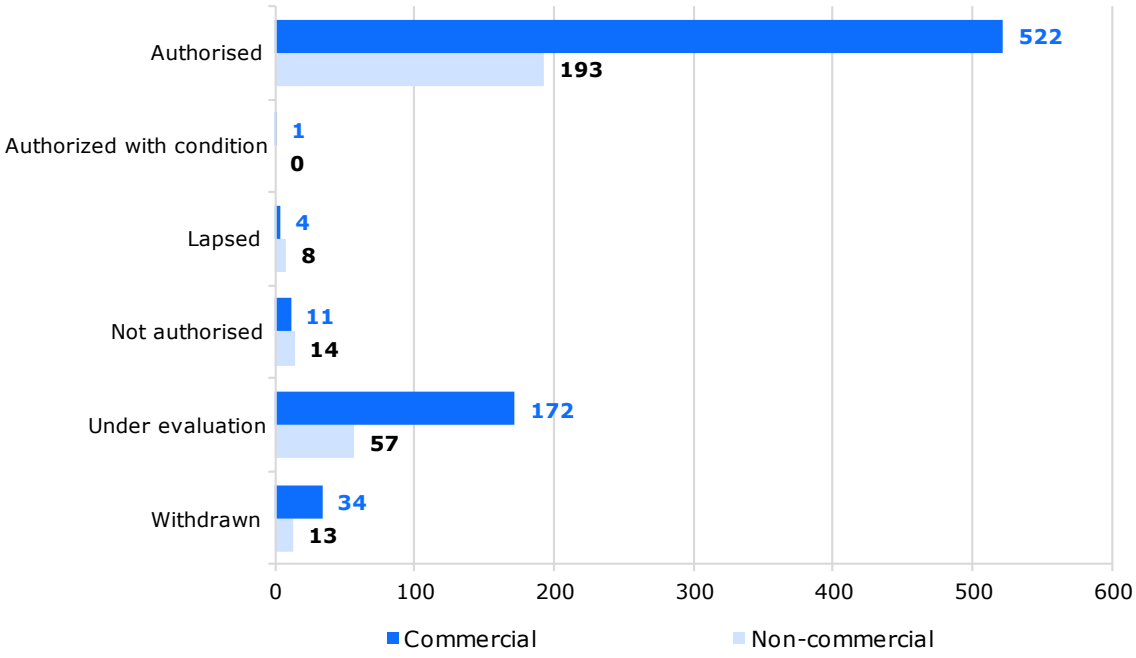
Since 31 January 2022, 1,029 distinct applications for the addition of a new MSC[6], affecting 400 trials, have been submitted in CTIS, of which 84 addition of new MSC submitted in August 2024, affecting 46 trials *(the graph below shows the data for the last 18 months)*.



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

Since 31 January 2022, 1,029 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
522
193
Authorized with condition
1
0
Lapsed
4
8
Not authorised
11
14
Under evaluation
172
57
Withdrawn
34
13
0
100
200
300
400
500
600
Commercial
Non-commercial

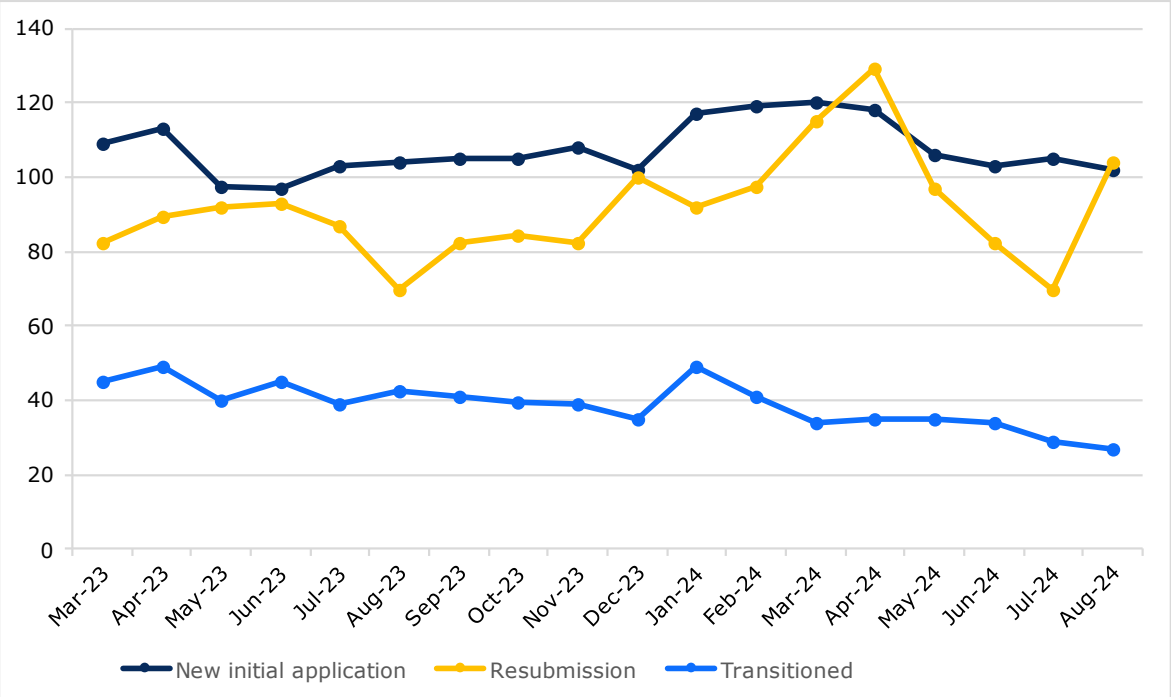
Chapter 5
Timelines

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

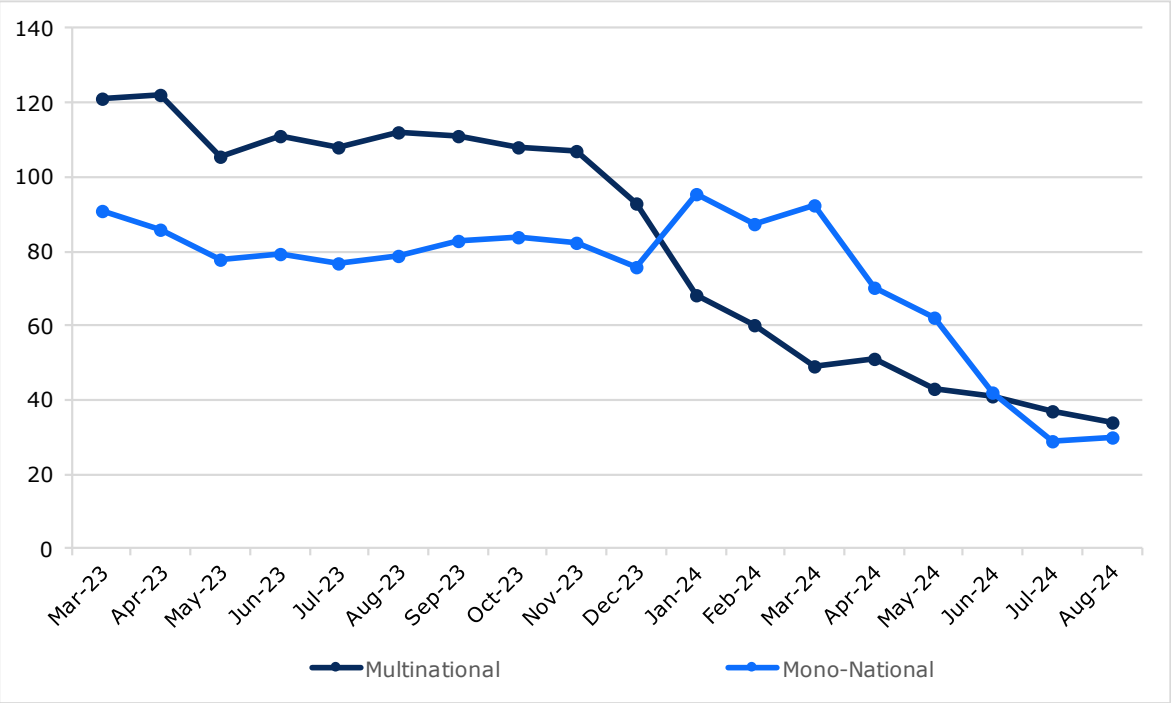
Median time from submission of initial clinical trial applications to decision

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.

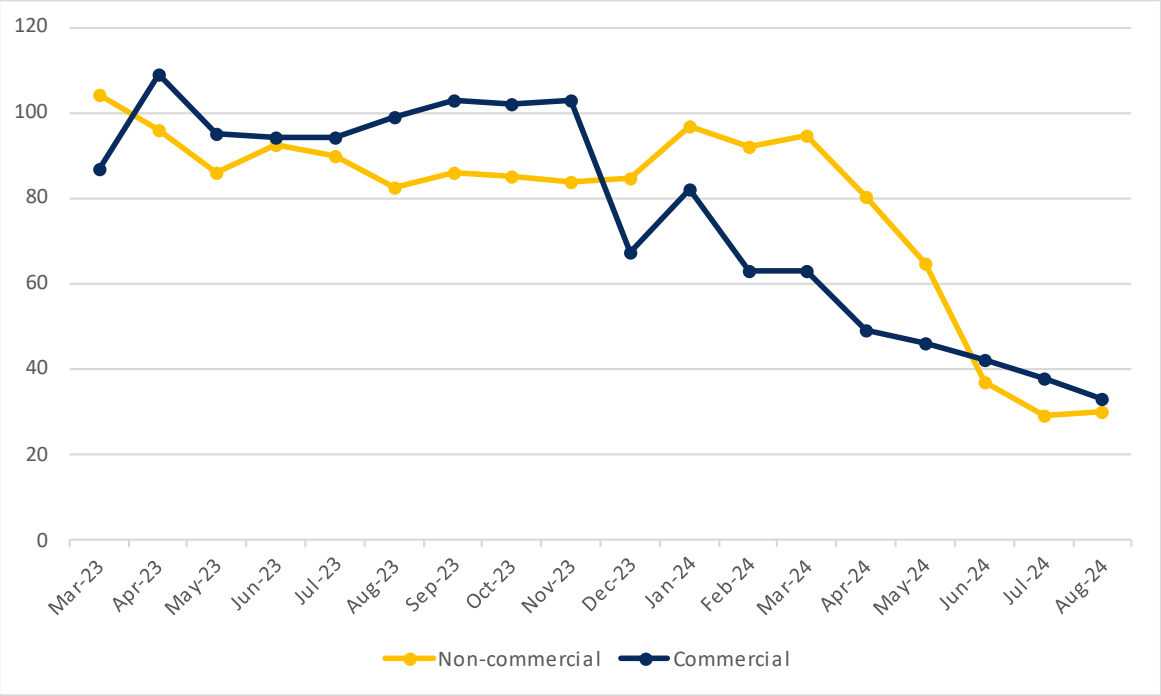
Median time per new initial application/ resubmission and transitional trials from submission of initial clinical trial applications to decision



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

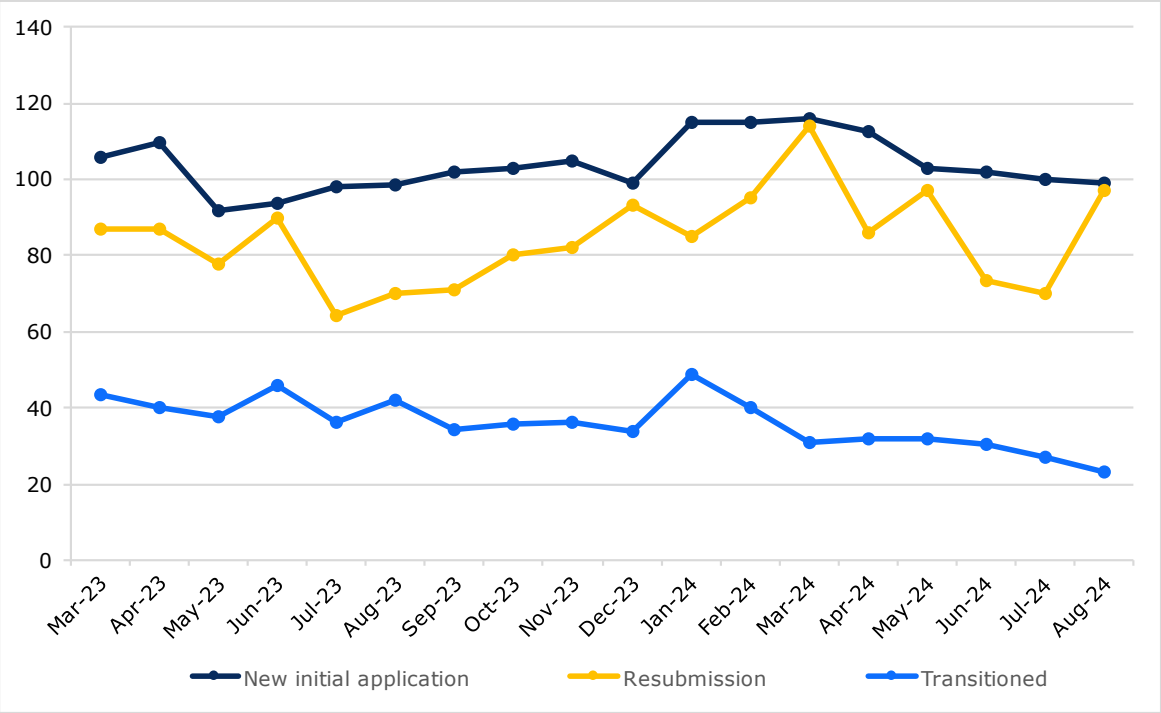


Median time per commercial/ non-commercial sponsors from submission of initial clinical trial applications to decision



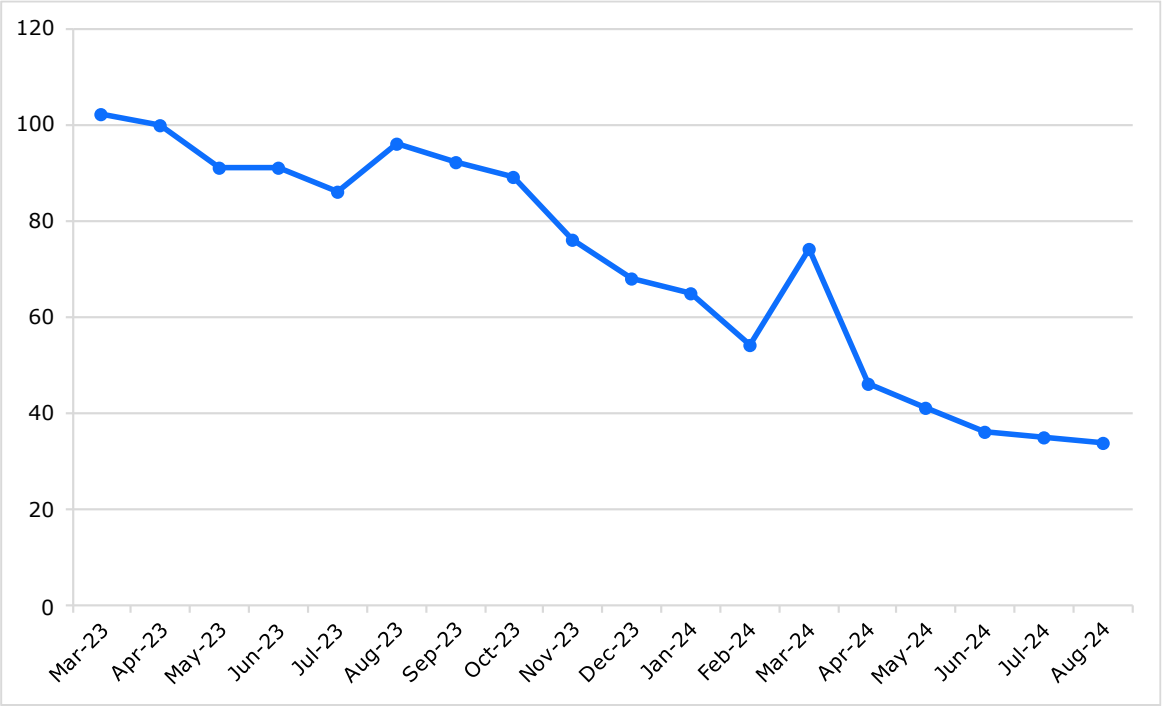
Median time from submission of initial clinical trial applications to Part I conclusion

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
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
Jun-24
Jul-24
Aug-24

Chapter 6
Features of the substances

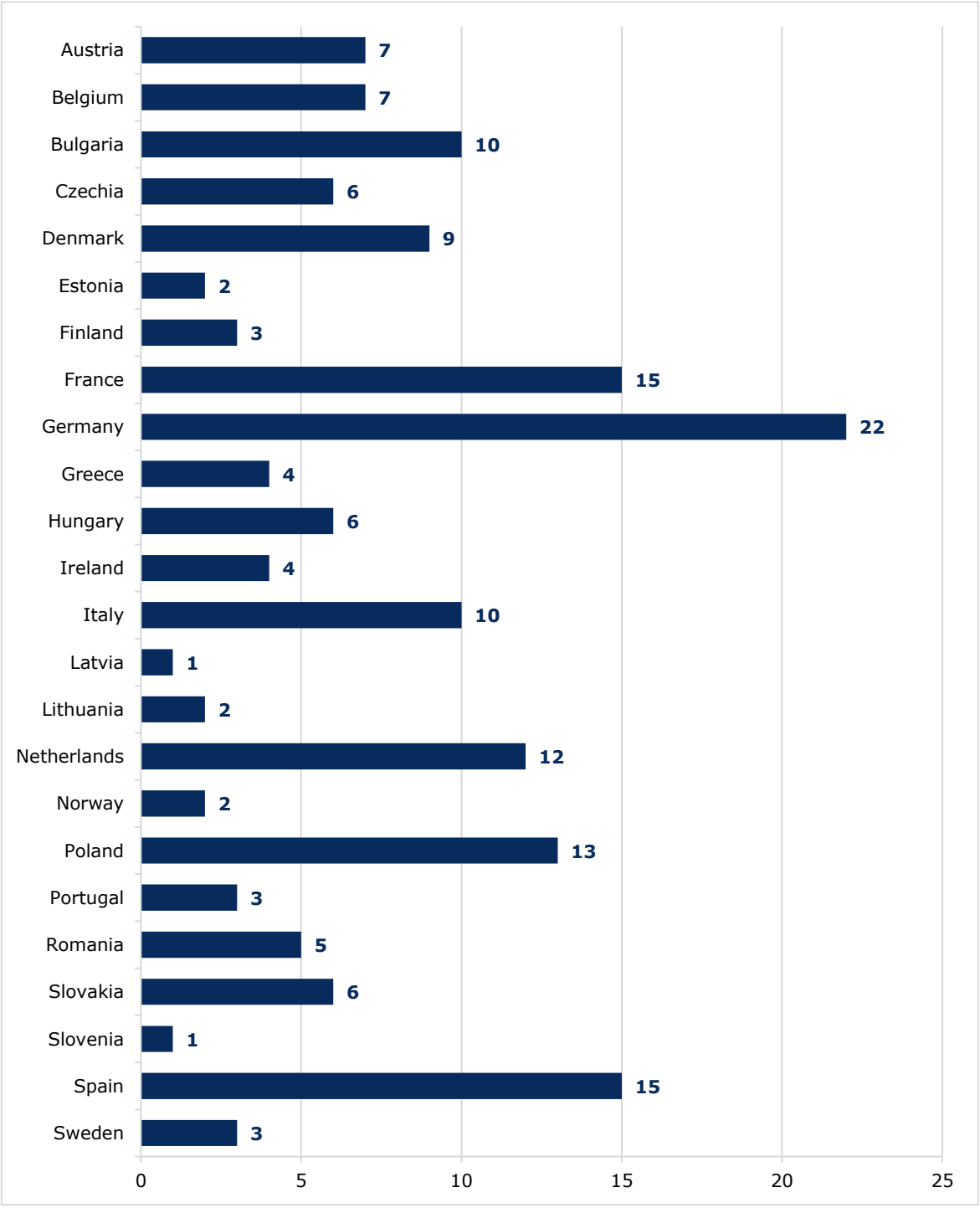
Safety assessing Member States (saMS) appointment

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*.

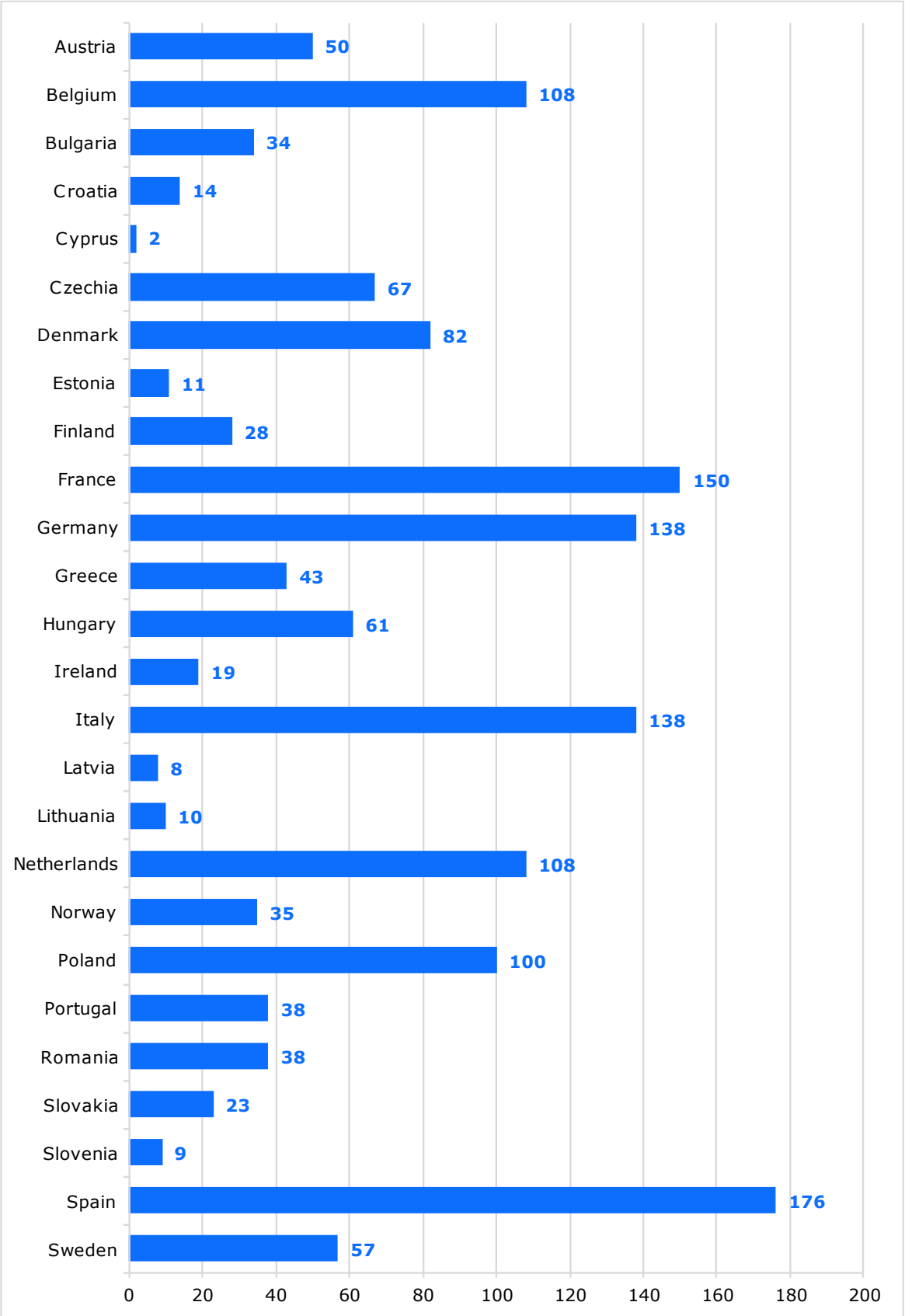
In mono-national clinical trial, the Member State is responsible for the assessment of information related to safety of active substances. Of note, the Implementing Regulation does not apply to mono-national active substances, to active substances in investigational medicinal products used as reference 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 170 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 50
Belgium 108
Bulgaria 34
Croatia 14
Cyprus 2
Czechia 67
Denmark 82
Estonia 11
Finland 28
France 150
Germany 138
Greece 43
Hungary 61
Ireland 19
Italy 138
Latvia 8
Lithuania 10
Netherlands 108
Norway 35
Poland 100
Portugal 38
Romania 38
Slovakia 23
Slovenia 9
Spain 176
Sweden 57
0 20 40 60 80 100 120 140 160 180 200

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 I (cover letter template for sponsors with multinational trials) and Annex II (Fees for transitional trials in MSs). 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;
5. The video recording and presentations of the CTIS event from 25 March 2024, on **Clinical Trials Information System Webinar: Last Year of Transition**, available on the event page.

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 – August 2024
EMA/435400/2024