



Monitoring the European clinical trials environment

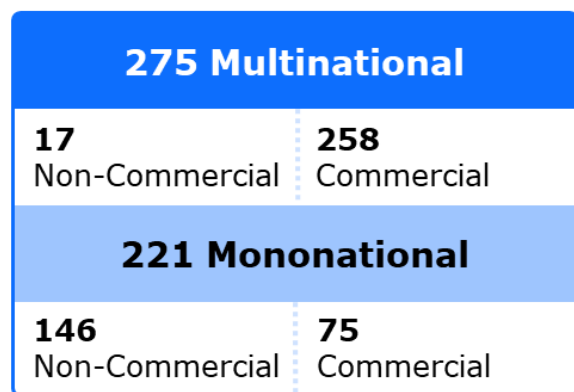
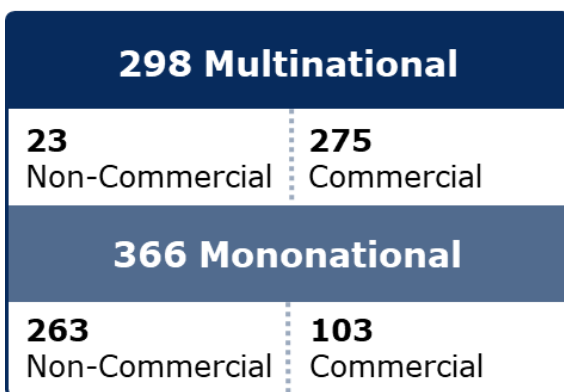
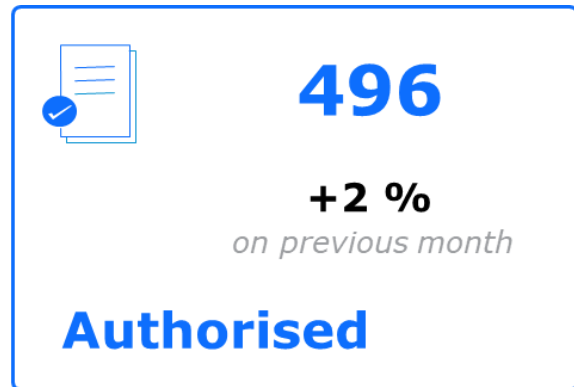
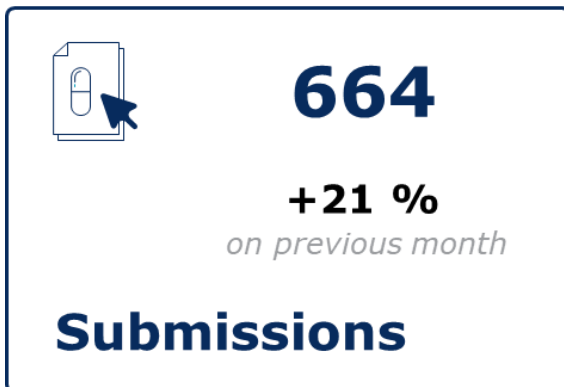
A deliverable of the ACT EU
Priority Action 2

June 2024



Clinical Trials in the EU/EEA

June 2024



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 June 2024, as of 30 June 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 325 submissions per month.

A total of 6,172 clinical trial applications have been submitted since the launch of CTIS.

At the time when the report is generated, more than 2,430 initial clinical trials are ongoing in EU/EEA under the CTR.

The therapeutic area mostly investigated is Neoplasms (Tumour).

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Chapter 1

Submitted initial clinical trial applications

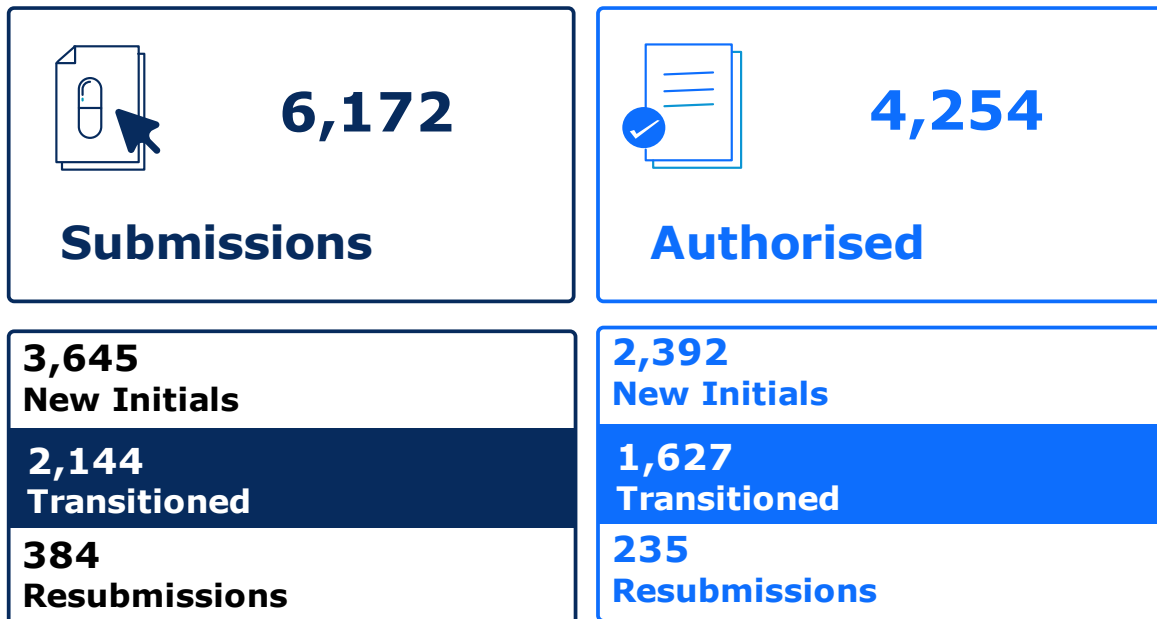
Chapter 1 of this report provides information on **submitted** initial clinical trial applications (CTAs), presented on the applicable statuses.

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

Initial clinical trial applications are those applications:

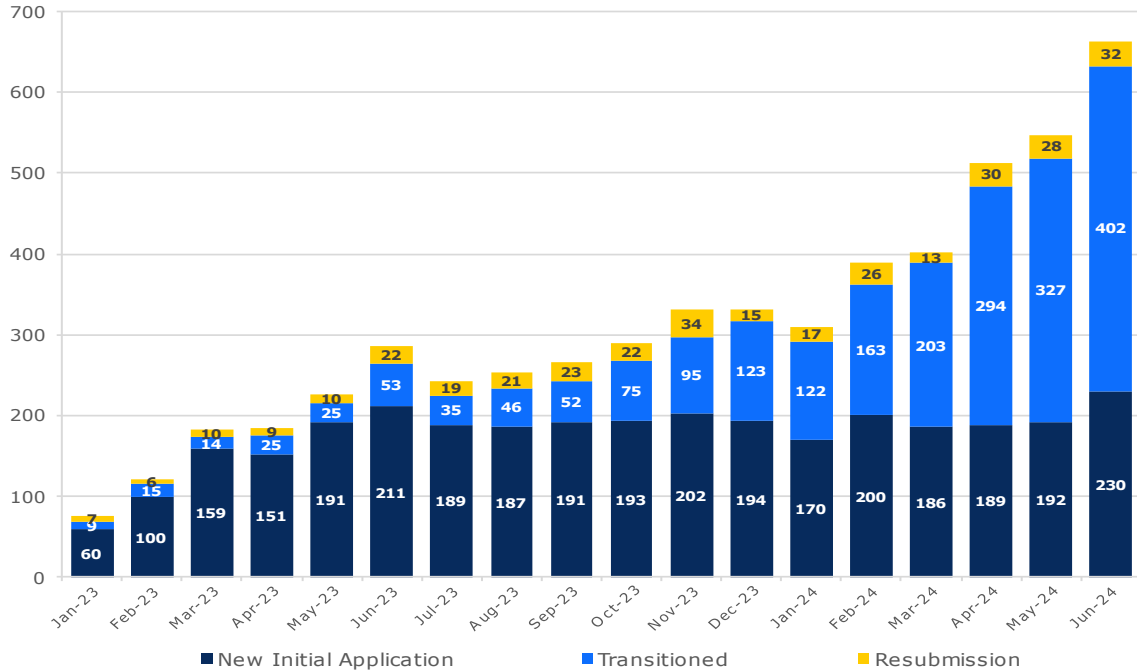
- new initial clinical trial applications submitted in CTIS by the sponsors under the Clinical Trials Regulation (EU) 536/2014 (CTR);
- trials which were already authorised under the regime of Clinical Trials Directive 2001/20/EC (CTD) and that have been transitioned to the regime of CTR;
- resubmitted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



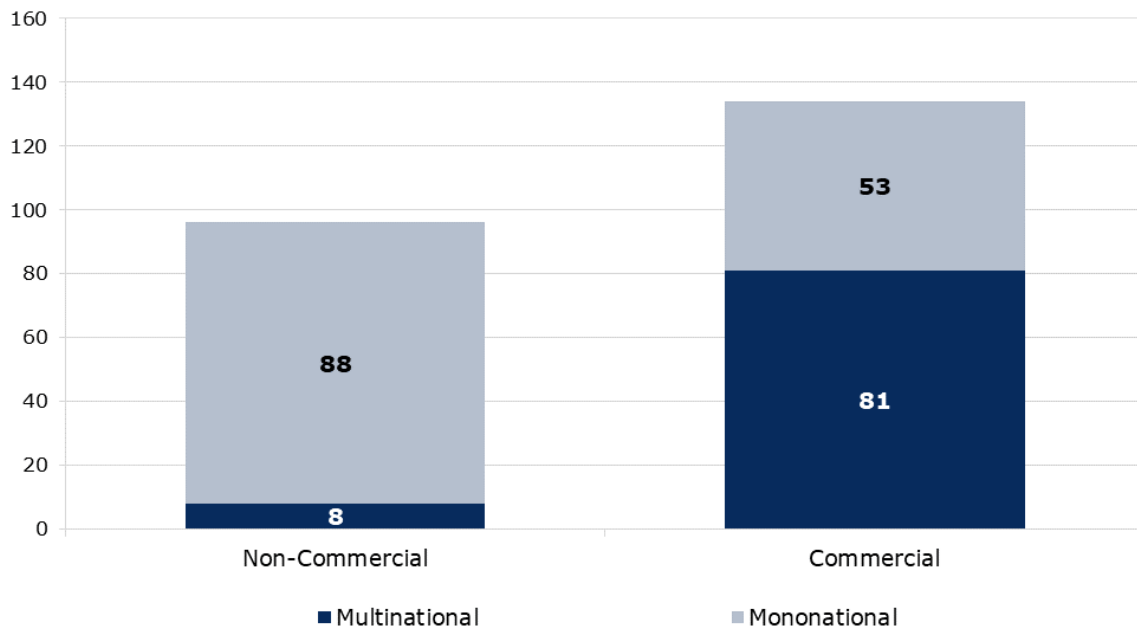
Monthly submissions of initial clinical trial applications

In June 2024, 664 initial clinical trial applications have been submitted, of which 230 new initial CTA, 402 are trials transitioned to CTR, and 32 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

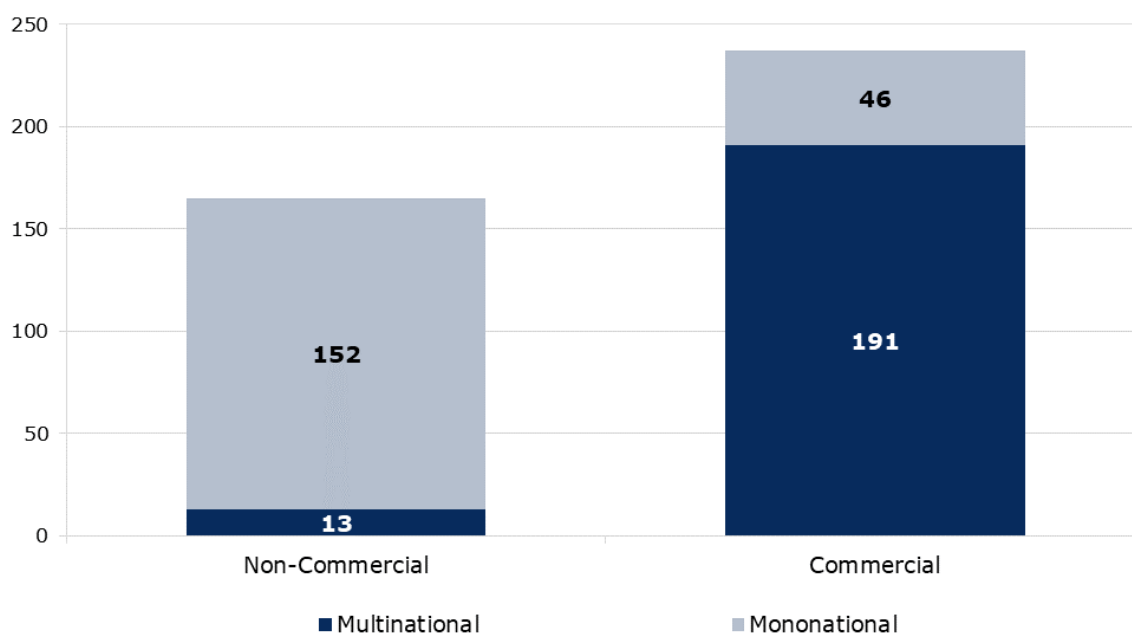
The graph below shows the split of submissions of new initial clinical trial applications in June 2024 into commercial/non-commercial sponsors and mononational versus multinational trials.



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

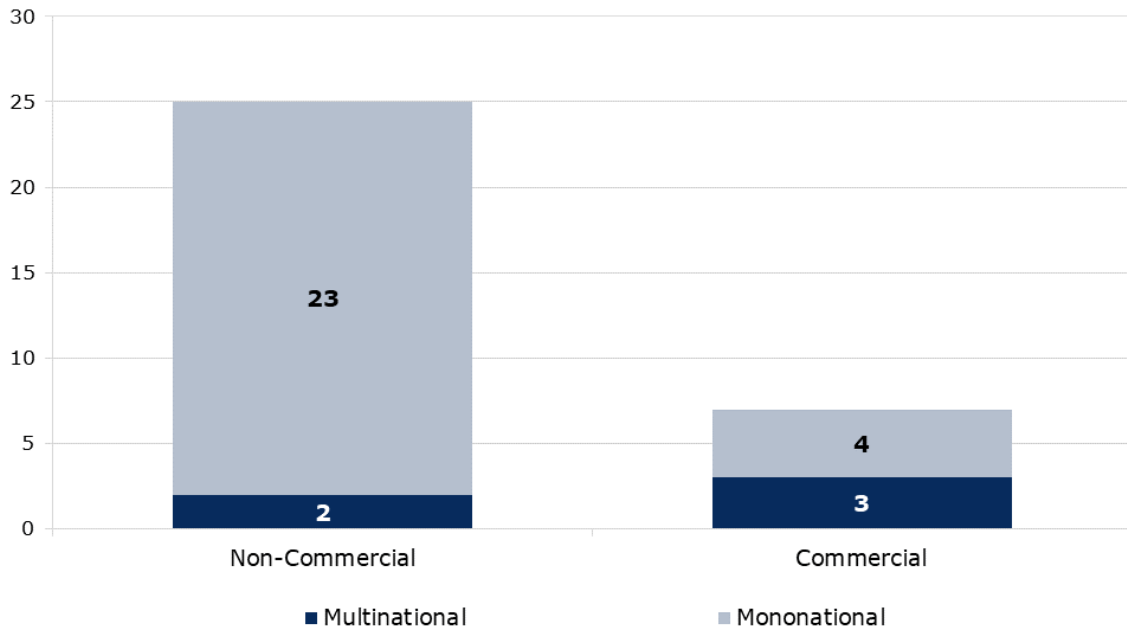


Once notified by the clinical trial sponsors, the National Competent Authorities of the EU/EEA Member States are responsible for keeping, in the EudraCT database, the information on the trial status up to date, including inserting the end of trial date, as applicable.

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



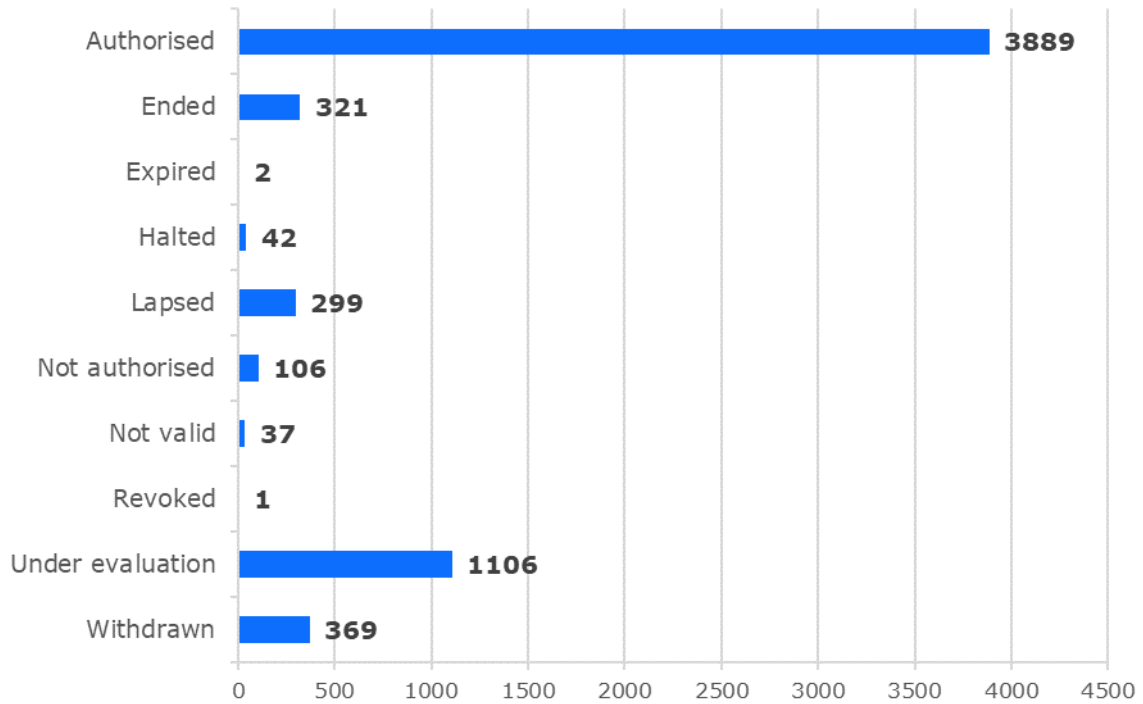
Clinical trials per applicable statuses

Since 31 January 2022, a total of 6,172 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**.

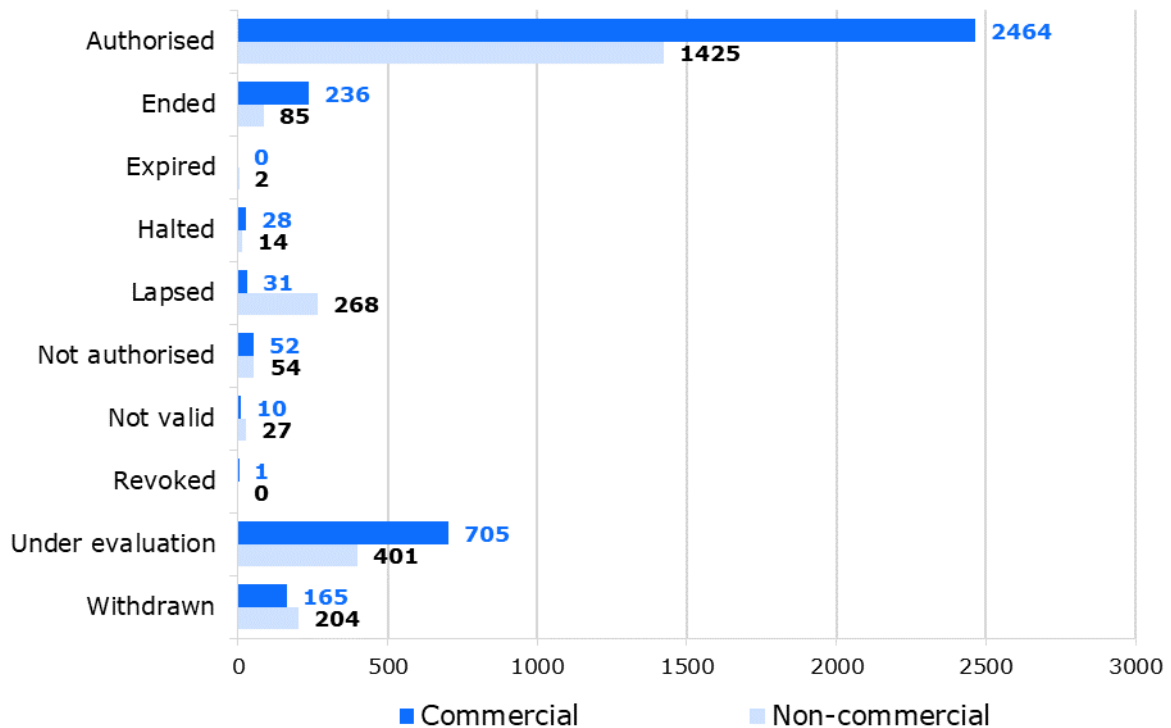
Clinical trials per applicable statuses

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		Mono-national Trials	Total number of Initial CTAs
	MSC	<i>Of which as RMS</i>		
Austria	258	44	28	286
Belgium	516	94	175	691
Bulgaria	259	2	15	274
Croatia	79	0	0	79
Cyprus	4	0	1	5
Czech Republic	392	80	33	425
Denmark	287	85	197	484
Estonia	48	4	5	53
Finland	114	32	28	142
France	910	148	359	1269
Germany	918	286	262	1180
Greece	248	2	12	260
Hungary	376	22	17	393
Iceland	7	0	1	8
Ireland	94	7	13	107
Italy	879	102	110	989
Latvia	48	5	4	52
Lithuania	61	9	3	64
Luxembourg	2	0	1	3
Netherlands	445	97	280	725
Norway	125	20	40	165
Poland	719	75	63	782
Portugal	194	12	53	247
Romania	210	9	23	233
Slovakia	140	15	2	142
Slovenia	26	2	2	28
Spain	1148	330	269	1417

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.

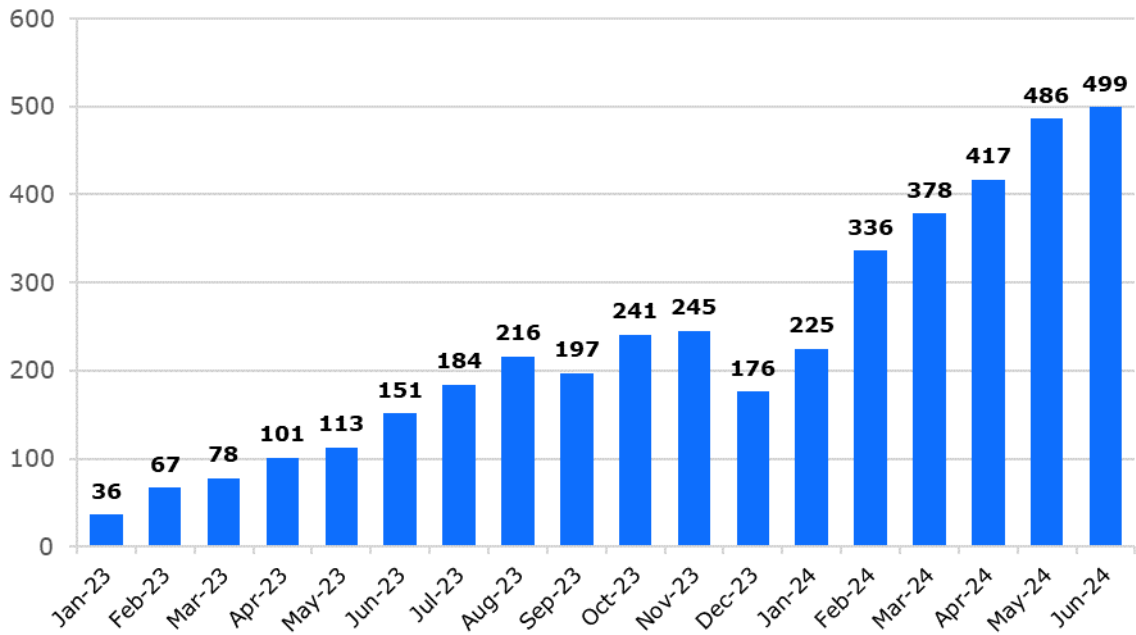
Sweden	229	51	88	317
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Chapter 2

Authorised clinical trials

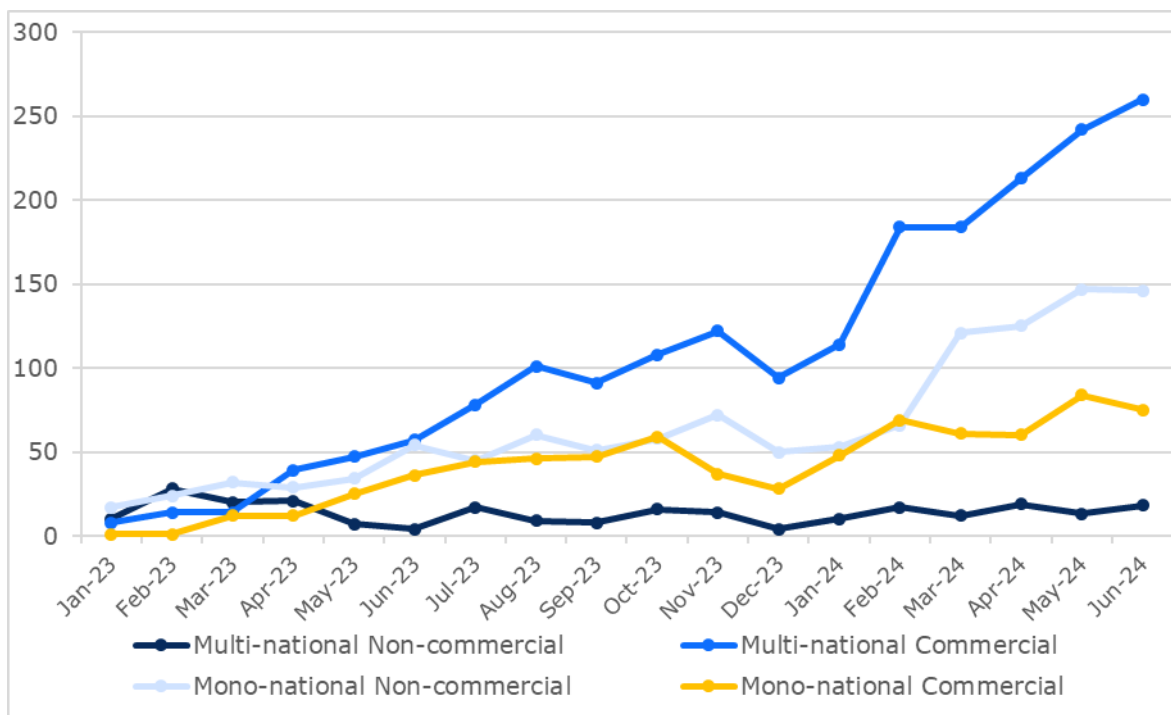
Since 31 January 2022, a total of 4,361 have received a decision in CTIS, of which 4,254 received a positive decision authorising the clinical trial. The graph below includes figures on both authorised and not authorised clinical trials in the last 18 months.

In June 2024, of the 499 initial clinical trial with a decision, 496 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.

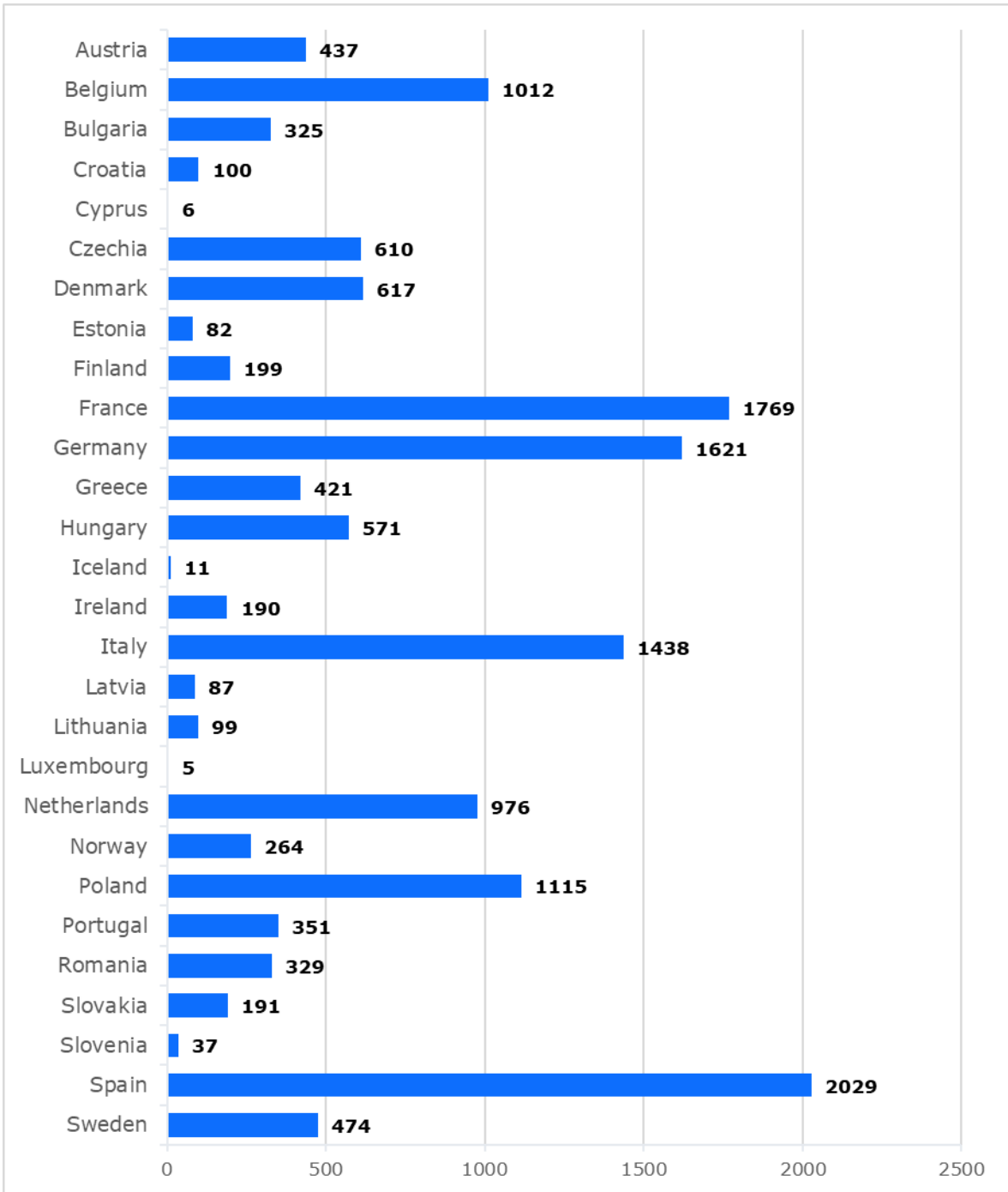


Until June 2024, 2,350 multinational clinical trials have a decision in CTIS with an average of 6 Member States Concerned.

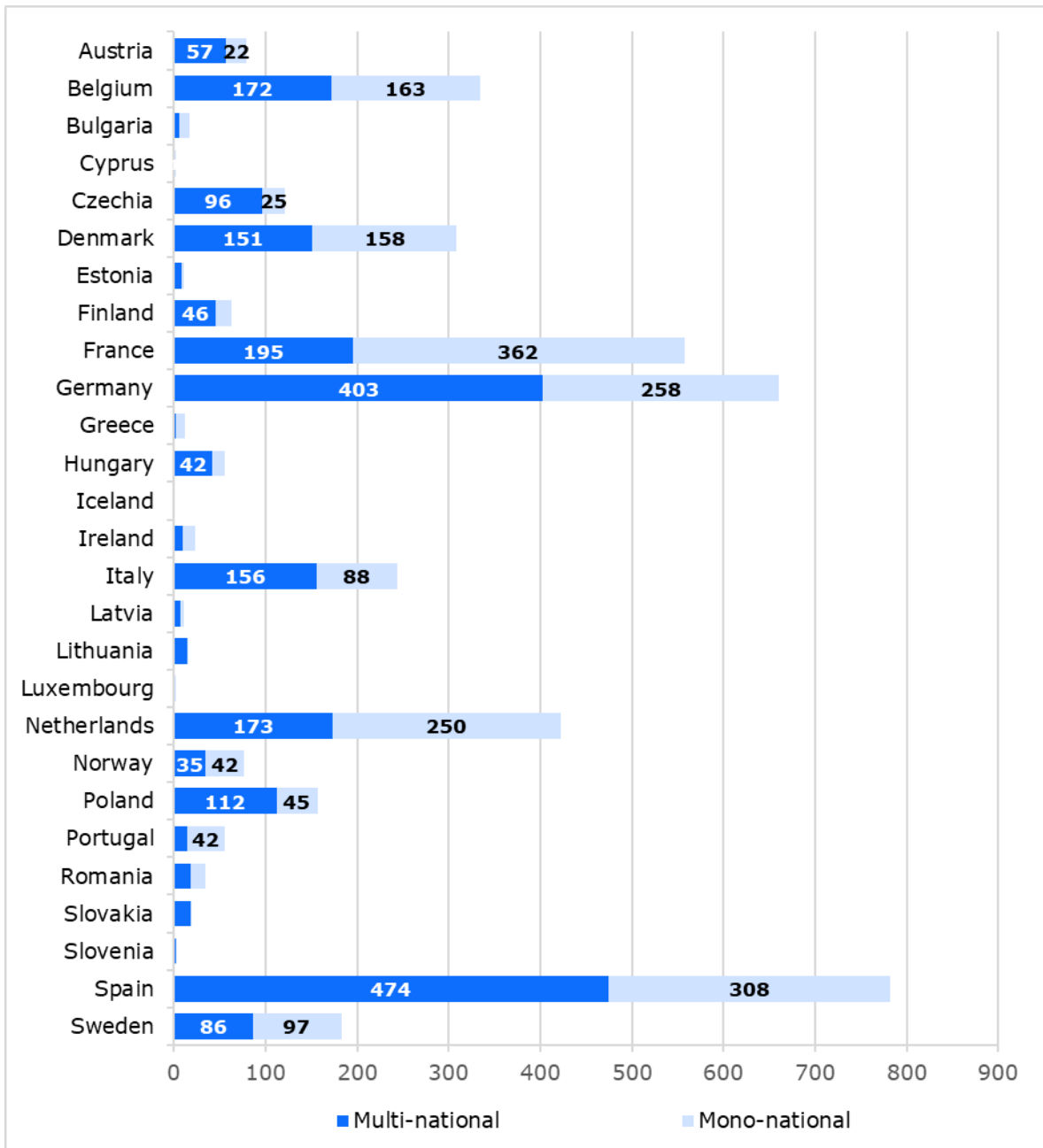
Distribution of **authorised** clinical trials per Member State Concerned and appointment of Reporting Member State

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 Concerned² 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.



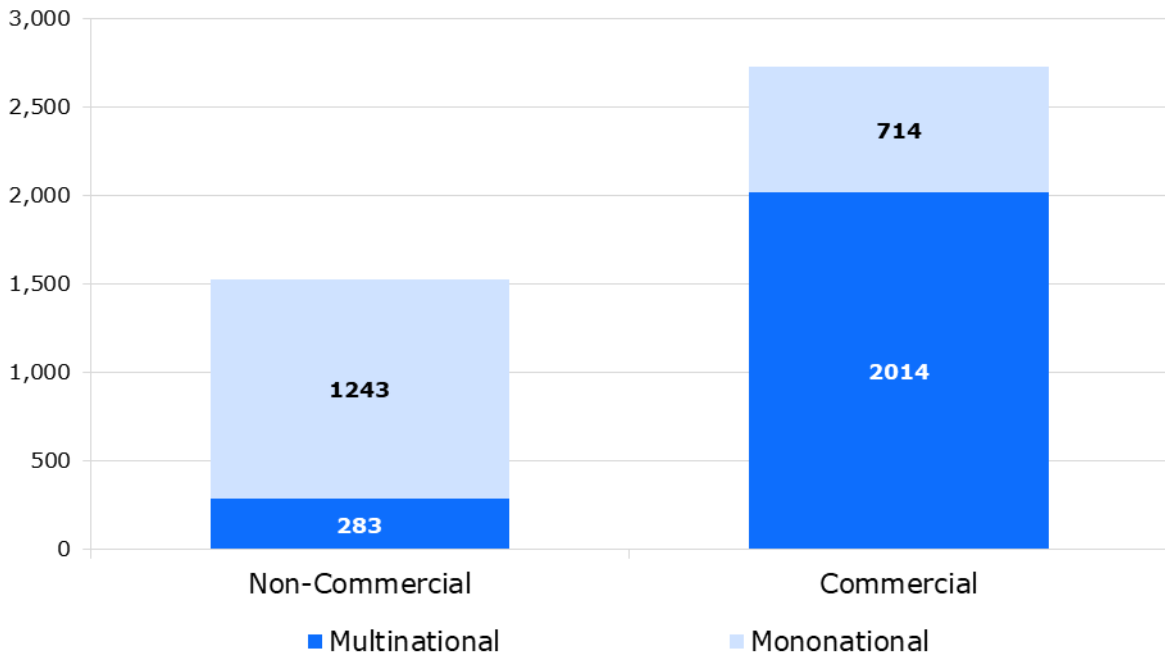
The graph below shows the distribution of appointment of Reporting Member State (RMS), amongst the applicable Member States Concerned, in authorised mono- and multinational trials (figures less than 20 are not shown).



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

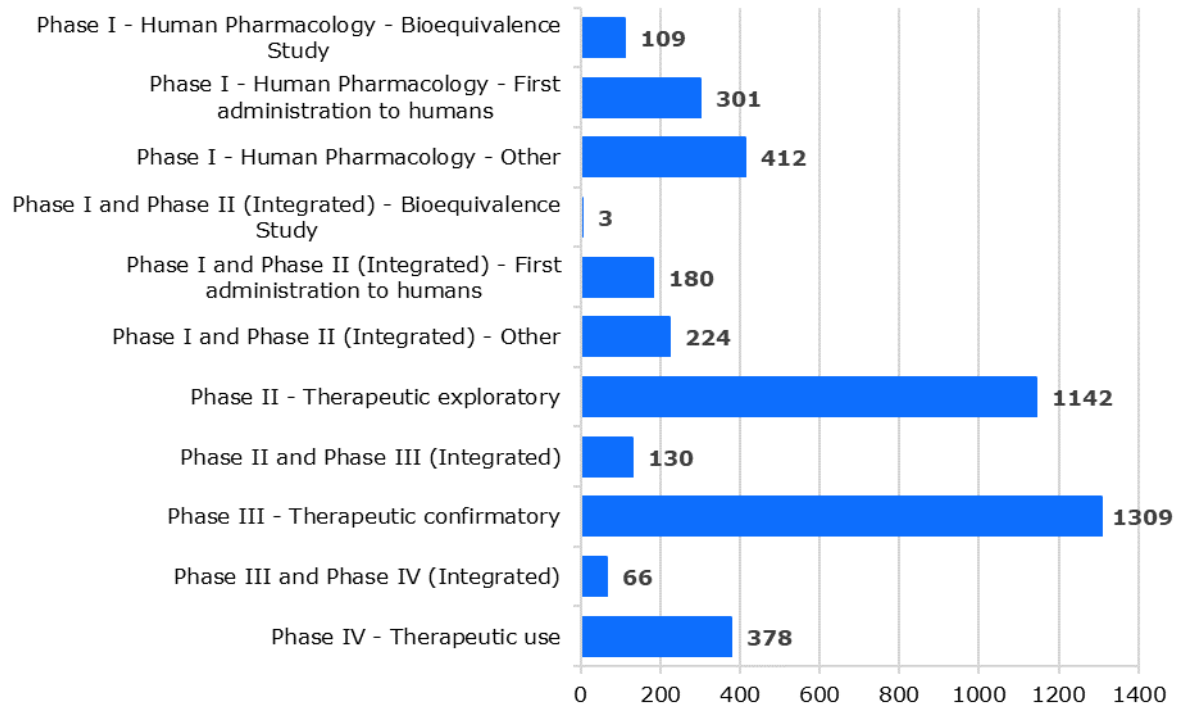
The graph below shows the number of clinical trials authorised since 31 January 2022, split into mono national/ multi-national and per sponsor type.

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.

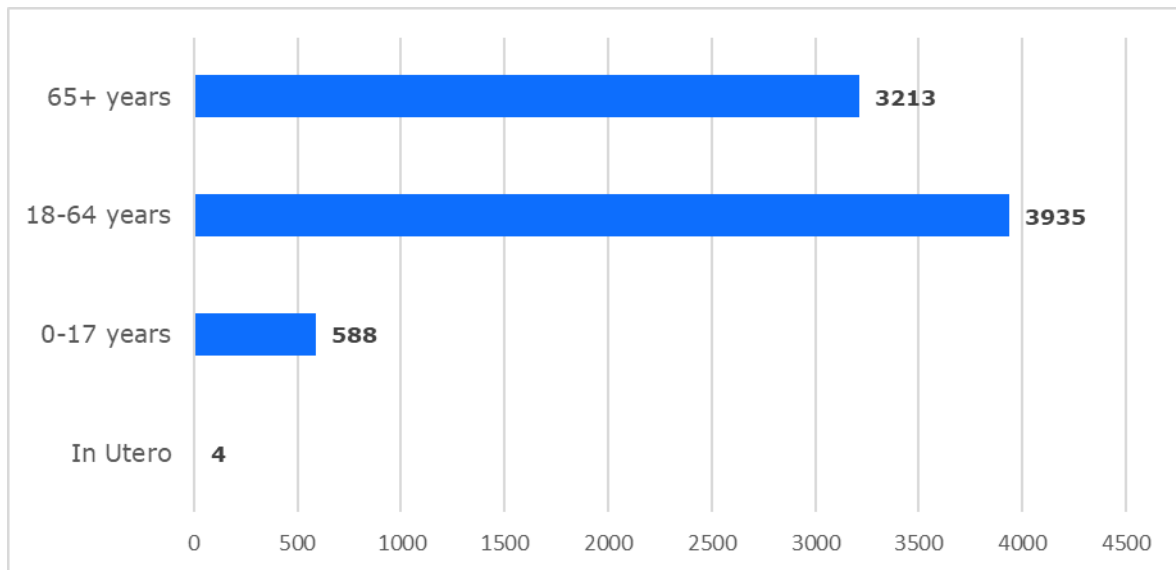


Clinical trials per population type and rare disease

At the end June 2024, 2,432 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 sites³.

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.

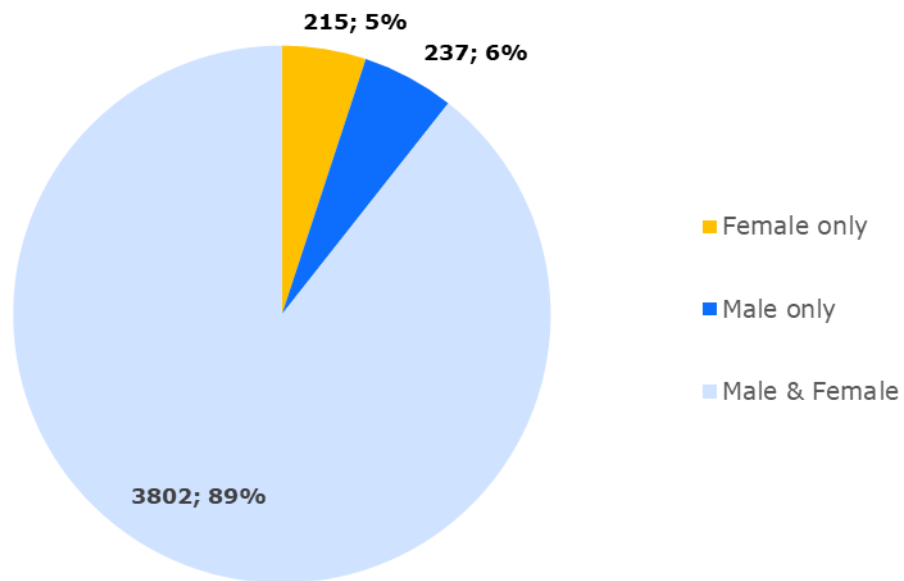
By Age of clinical trials participants



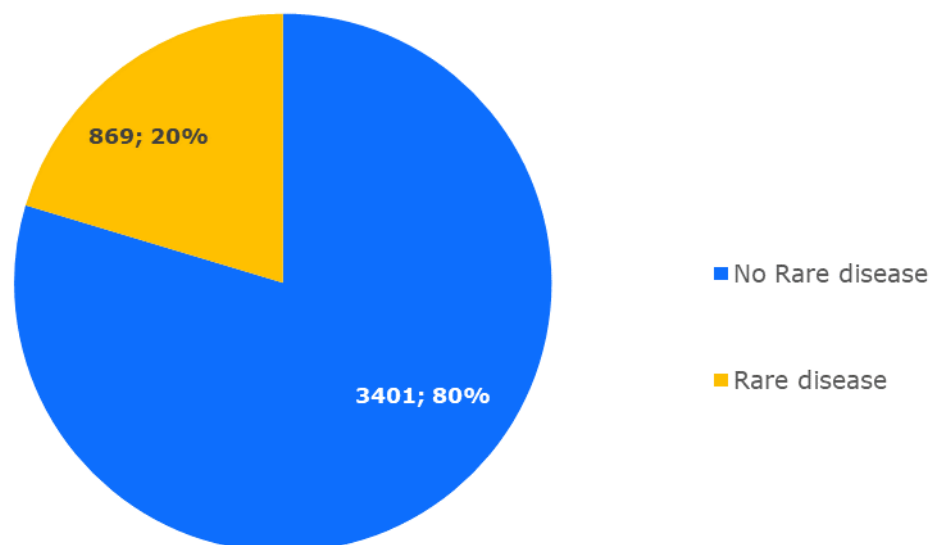
It is important to note that various age categories may be addressed in one clinical trial (e.g. a clinical trial may be for age "+65" as well as for age "18-64" and in this case it would be counted twice). Therefore, the reader should not sum the number of clinical trials for each age category and consider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

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

By Gender of clinical trials participants



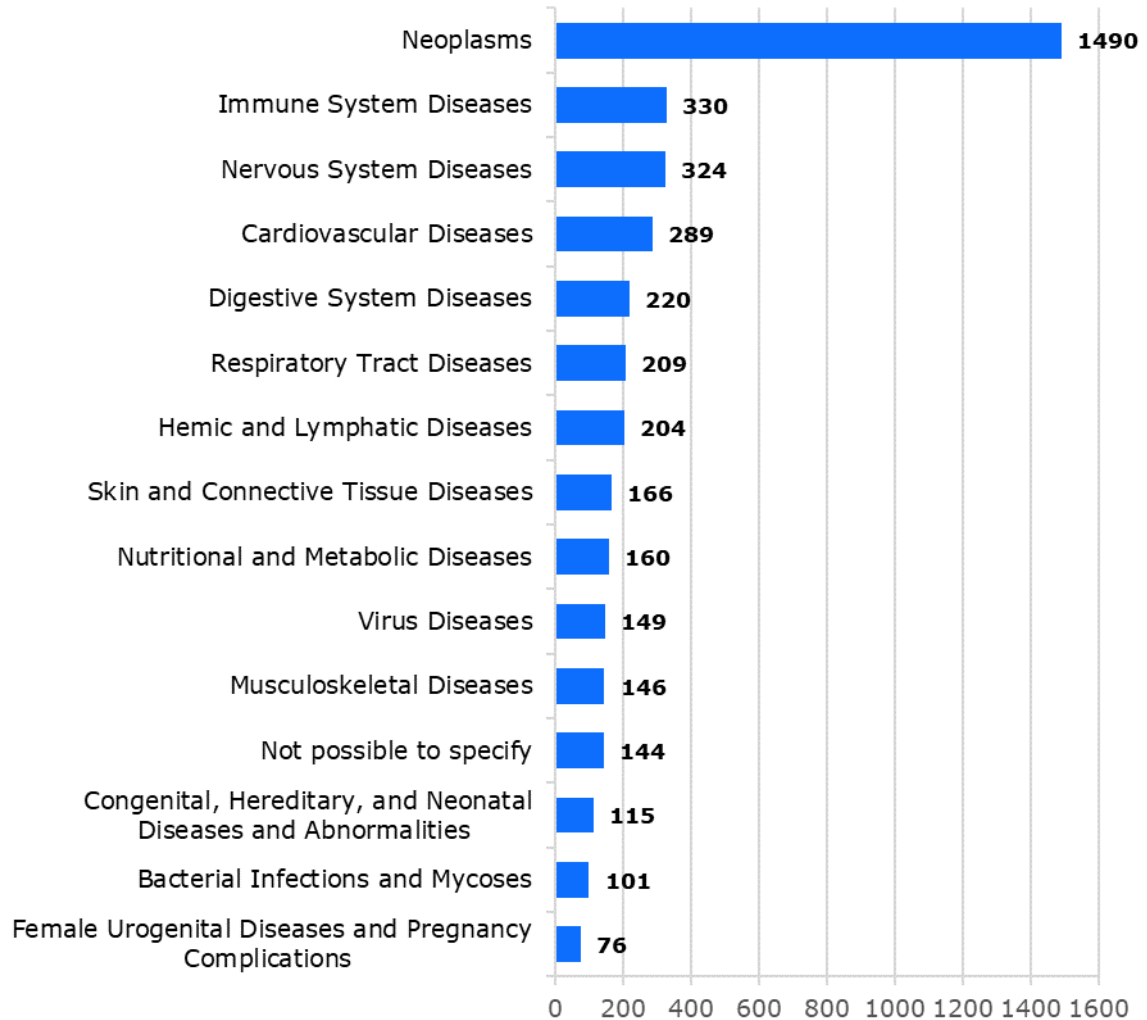
Clinical trials with rare disease participants



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

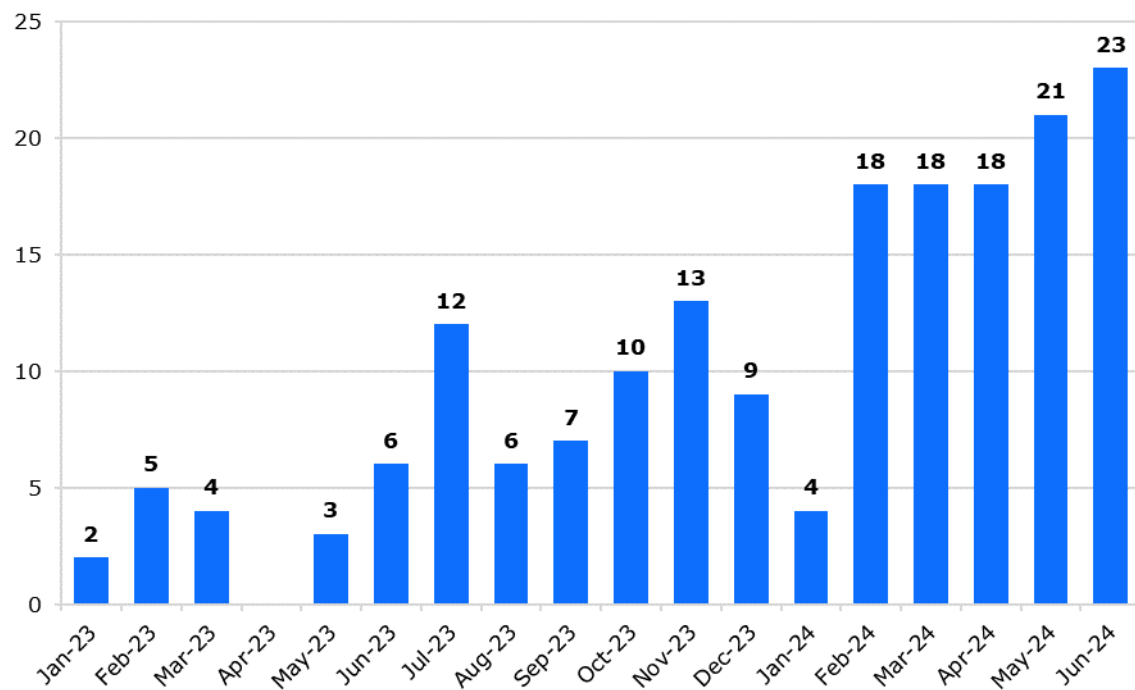
The graph below shows the number of clinical trials authorised since January 2022, broken down per therapeutic area⁴, showing the most frequent 15 therapeutic areas.



Authorised clinical trials with an ATMP

Twenty-three clinical trials with an Advanced Therapy Medicinal Product (ATMP) have been authorised in June 2024, bringing the total of authorised clinical trials with ATMP to 187, 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.



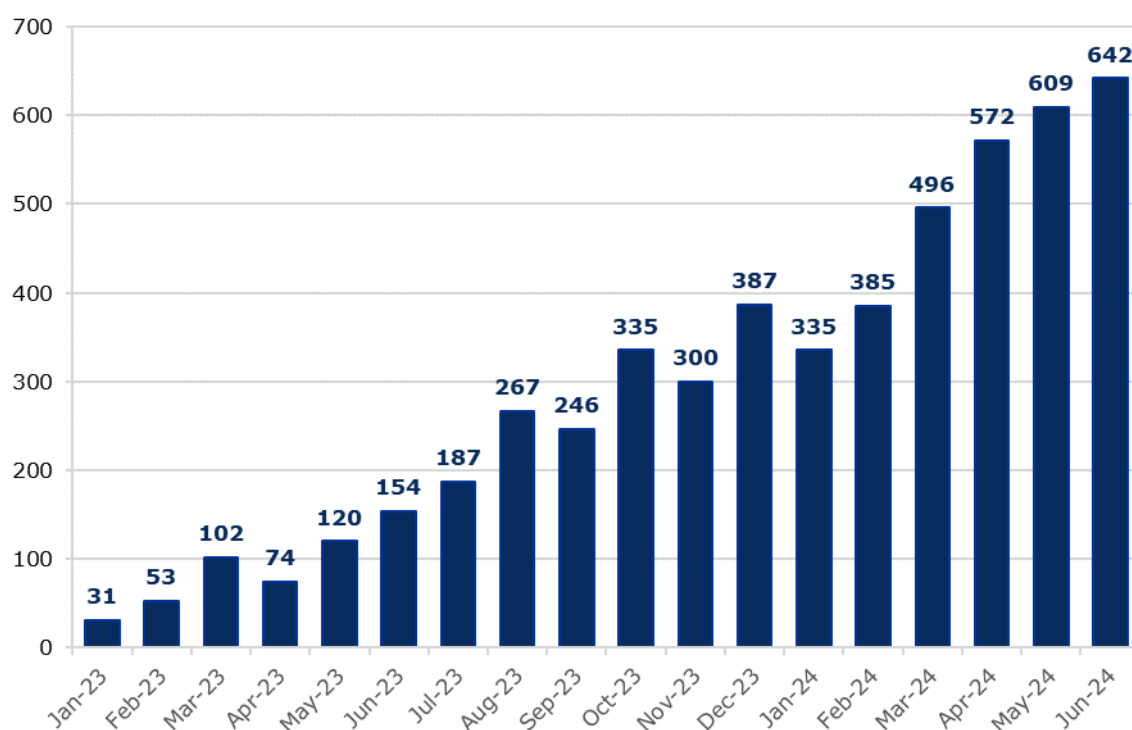
Chapter 3

Substantial modification applications

Substantial modifications⁵ 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

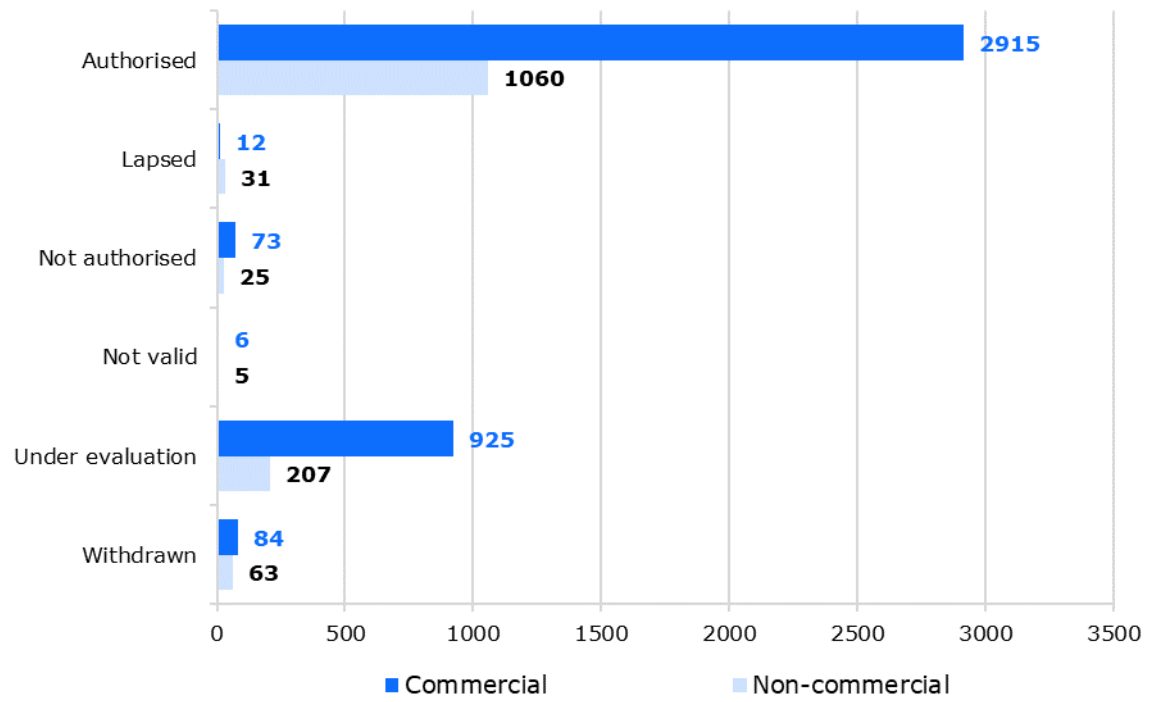
Overall, 5,406 distinct substantial modification applications, affecting 2,259 trials, have been submitted since the launch of the system on 31 January 2022, of which 642 substantial modifications submitted in June 2024, affecting 518 trials (*the graph below shows the data for the last 18 months*).



Substantial modification applications per applicable statuses and by sponsor type

Since 31 January 2022, 5,406 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

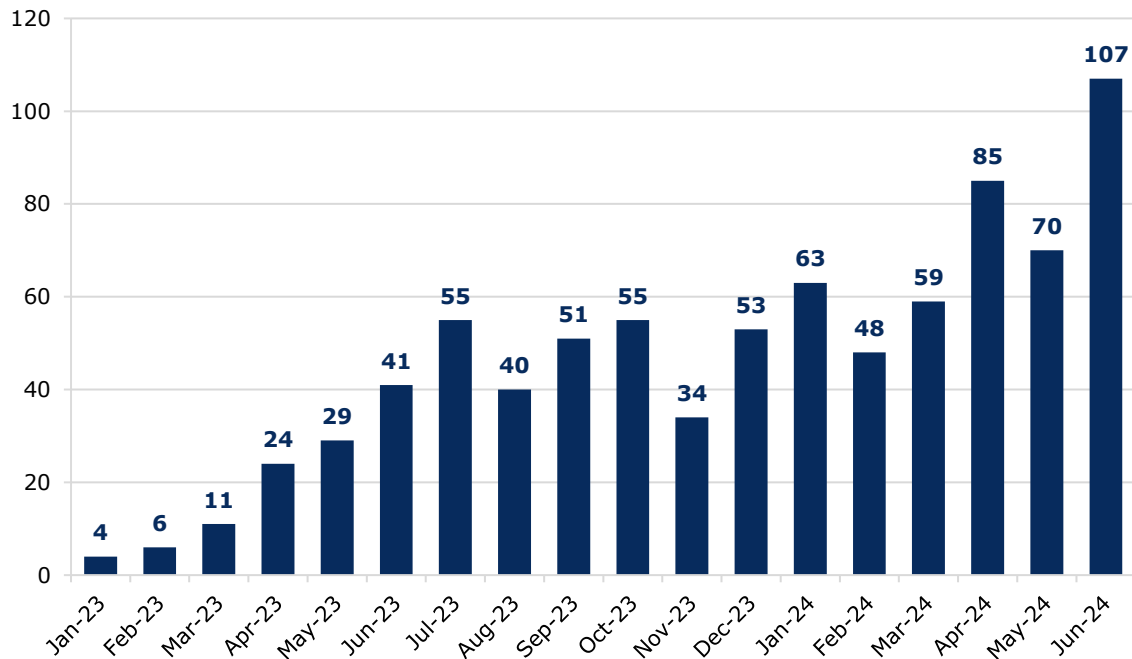


Chapter 4

Addition of a Member State Concerned

Submitted addition of Member States Concerned applications

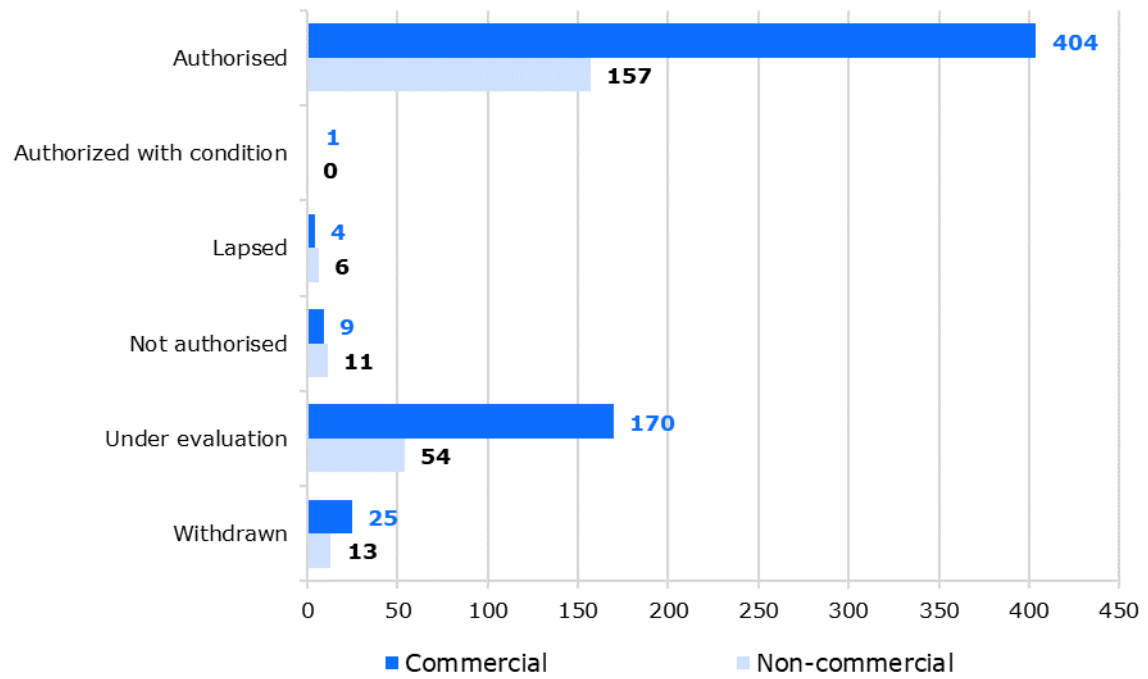
Since 31 January 2022, 854 distinct applications for the addition of a new MSC⁶, affecting 325 trials, have been submitted in CTIS, of which 107 addition of new MSC submitted in June 2024, affecting 47 trials (*the graph below shows the data for the last 18 months*).



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

Since 31 January 2022, 854 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



Chapter 5

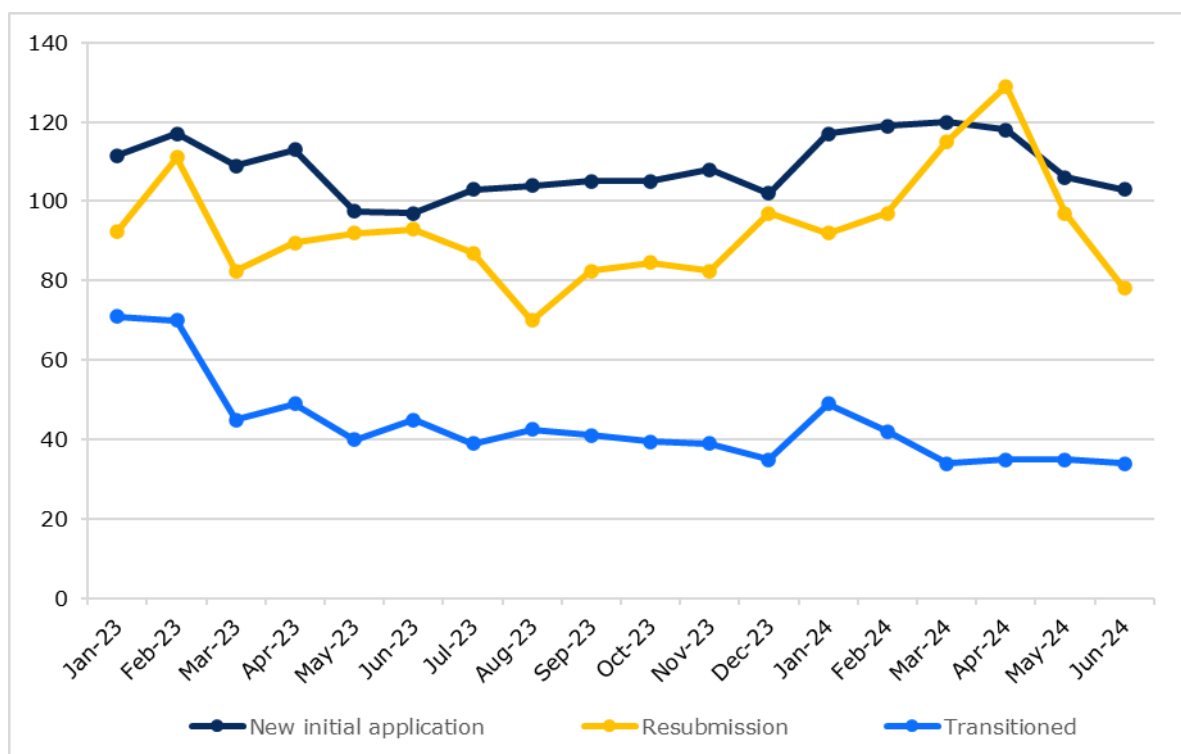
Timelines

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

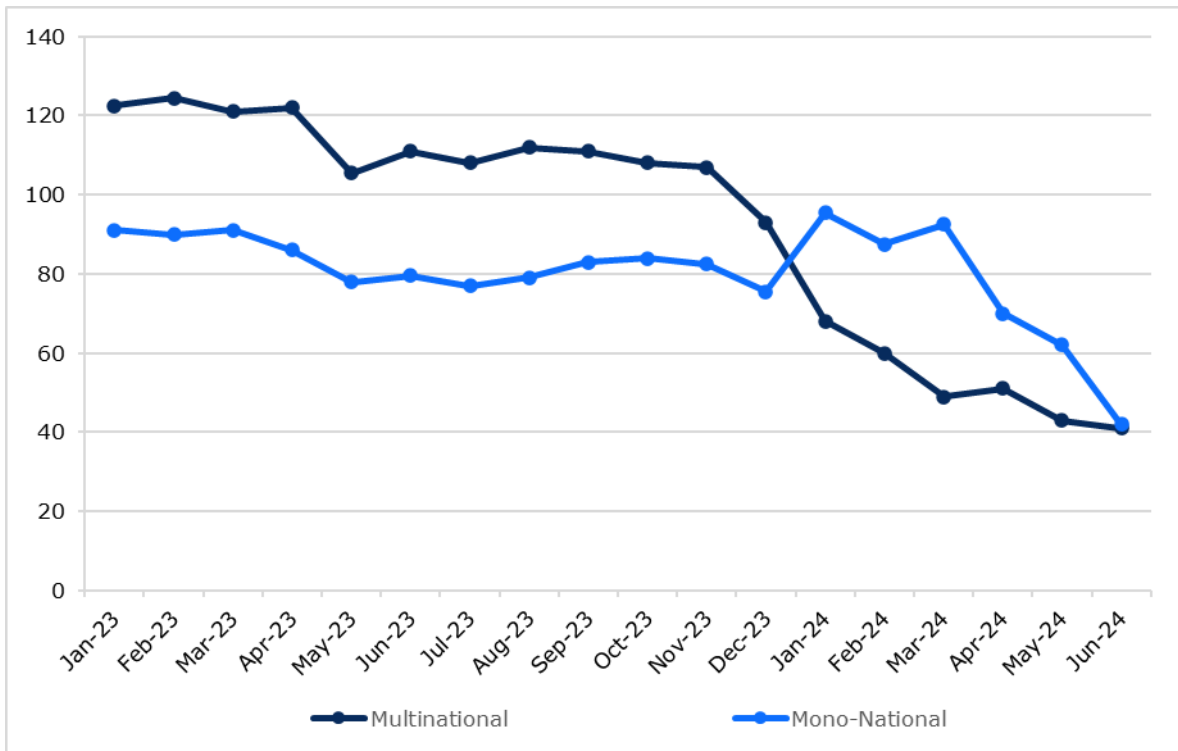
Median time from submission of initial clinical trial applications to decision

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.

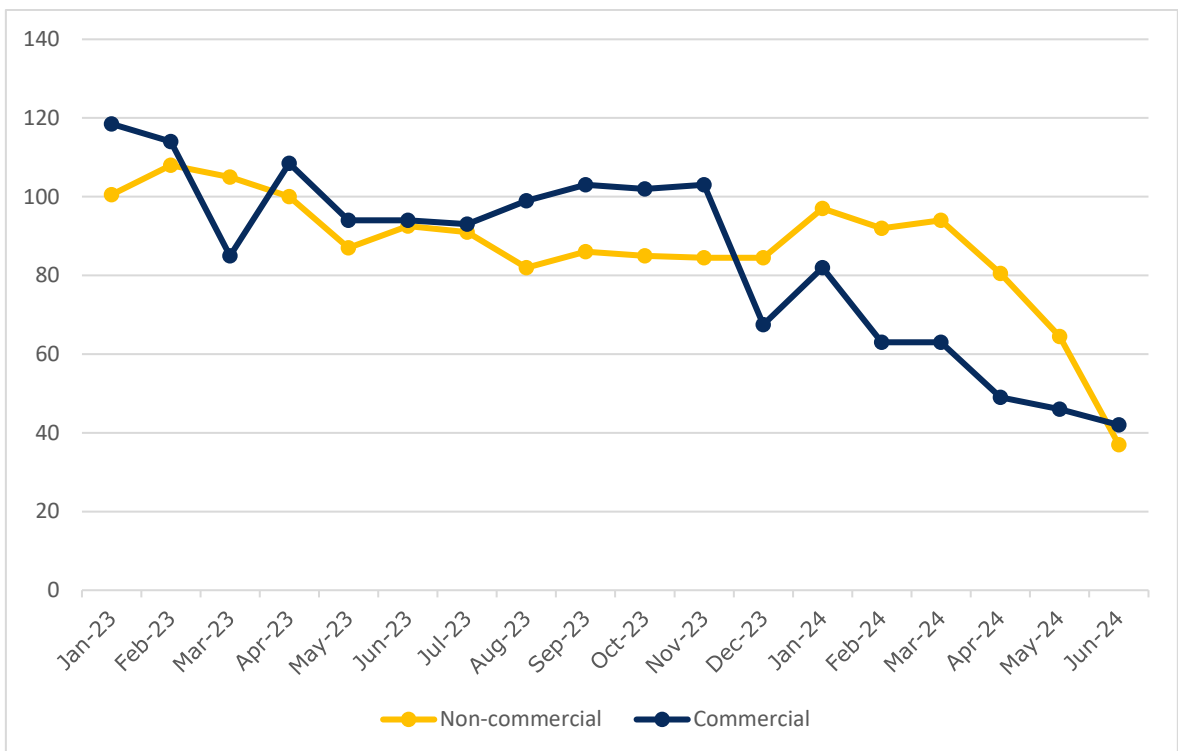
Median time per new initial application/ resubmission and transitional trials from submission of initial clinical trial applications to decision



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

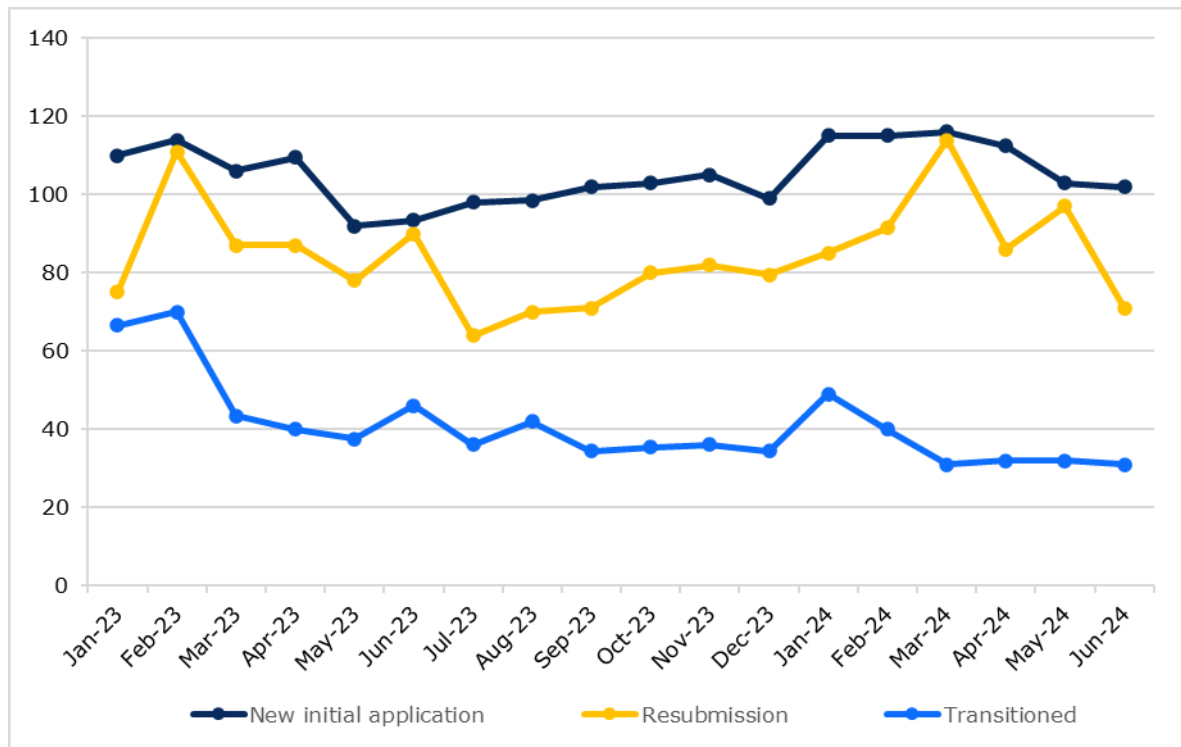


Median time per commercial/ non-commercial sponsors from submission of initial clinical trial applications to decision



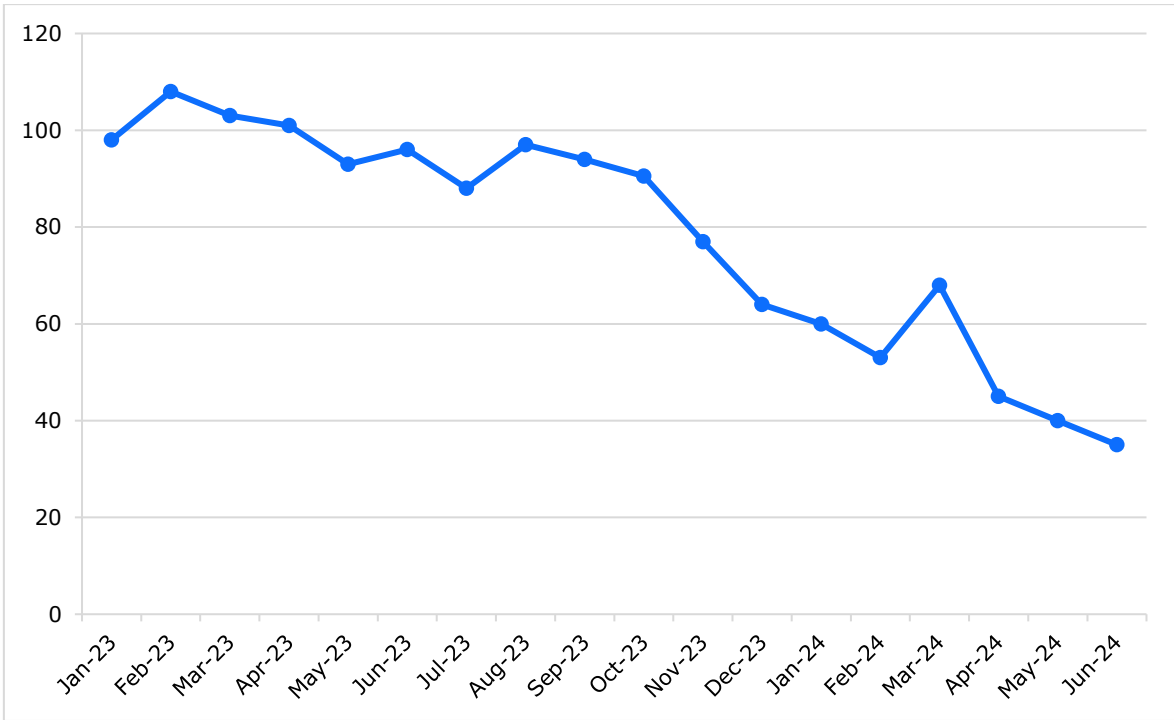
Median time from submission of initial clinical trial applications to Part I conclusion

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).



Chapter 6

Features of the substances

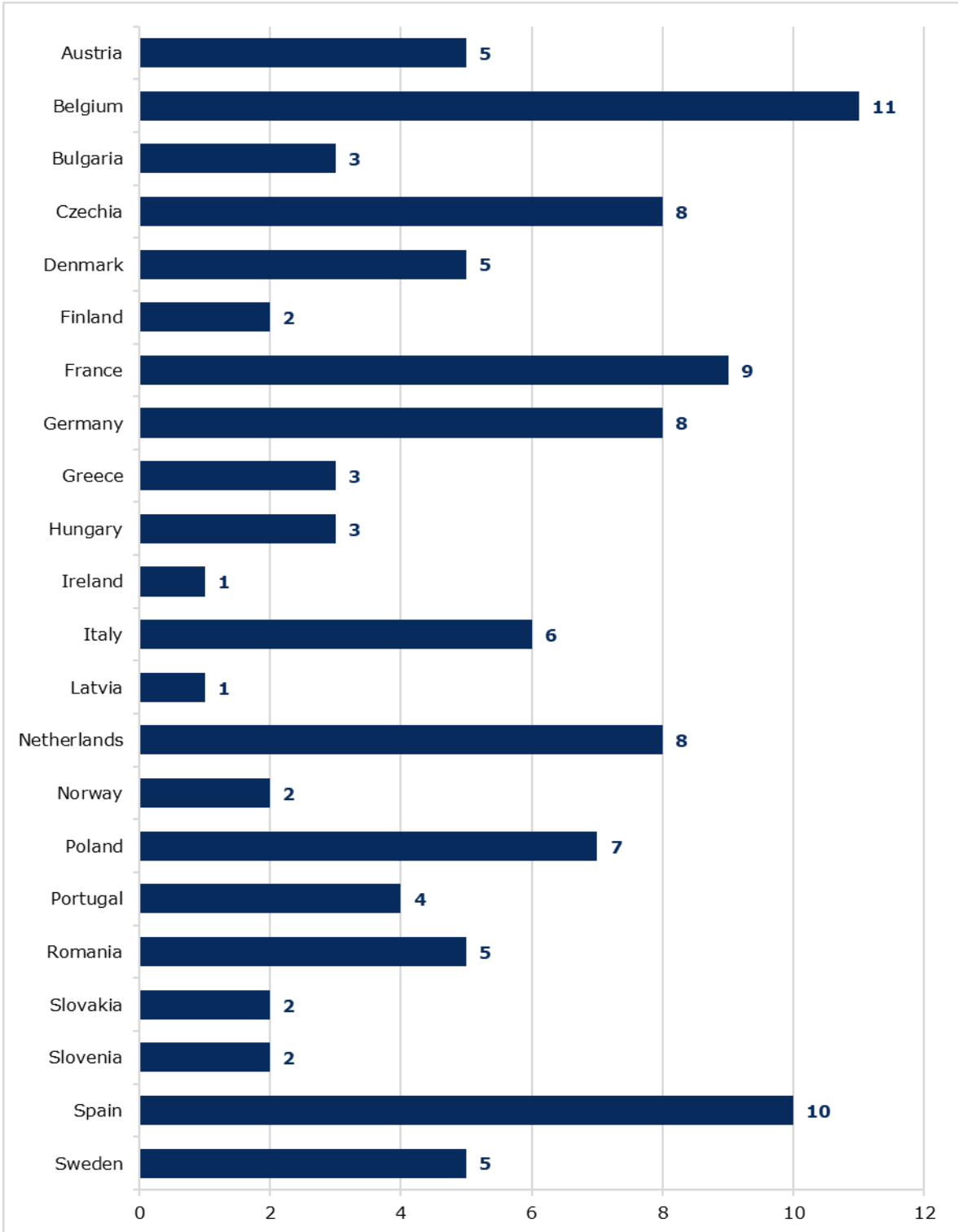
Safety assessing Member States (saMS) appointment

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.

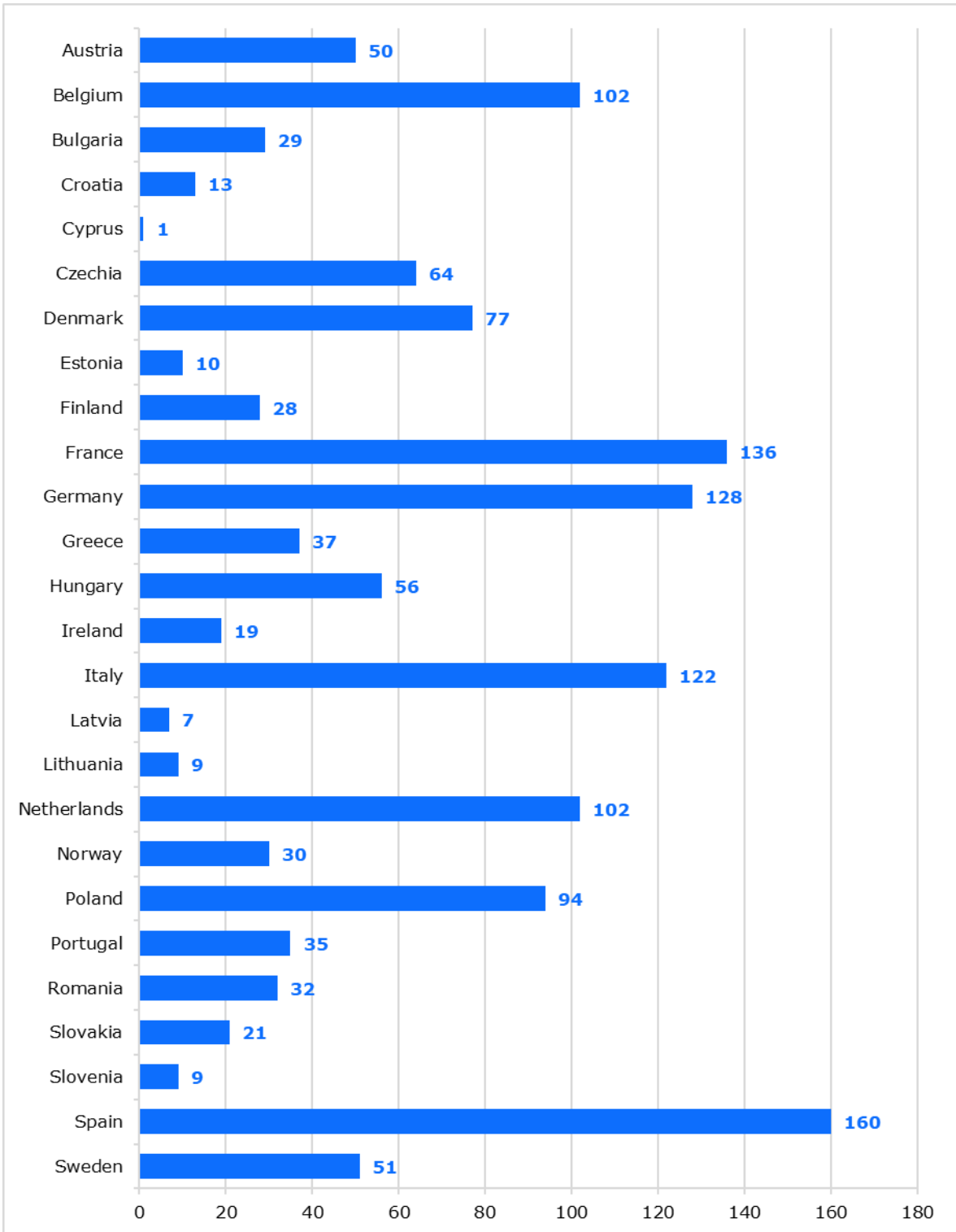
In mono-national clinical trial, the Member State is responsible for the assessment of information related to safety of active substances. Of note, the Implementing Regulation does not apply to mono-national active substances, to active substances in investigational medicinal products used as reference 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 166 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.



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 CTICG [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](#).

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