19 July 2023
EMA/316137/2023

# Key performance indicators (KPIs) to monitor the European clinical trials environment

## Metrics on the Clinical Trials Regulation and Clinical Trials Directive

## 1 - 30 June 2023, edition 15

On the 31 January 2022 the Clinical Trials Regulation (EU) No 536/2014, hereinafter 'CTR', repealing the Clinical Trials Directive 2001/20/EC, hereinafter 'CTD', became applicable and the Clinical Trial Information System (CTIS) was launched. In line with the provisions outlined in Article 97 of the Clinical Trials Regulation, the European Commission shall assess the impact of the Regulation on scientific and technological progress.

This report provides an overview of Key Performance Indicators (KPIs) related to the implementation of the CTR. The Clinical Trials Regulation Metrics report has been published on a monthly basis since May 2022. The latest and previous reports can be found at this link.

This report is published as part of the business change programme Accelerating Clinical Trials EU (ACT EU), involving the European Commission, the Heads of Medicines Agencies (HMA), Clinical Trial Coordination Group (CTCG) and the Agency.

One of the priority actions of ACT EU focusses on monitoring the implementation of the CTR.

The metrics presented in the report reflect the status of applications in CTIS and EudraCT[1] as of 30 June 2023 for Clinical Trial applications (CTA) submitted between 1-30 June 2023[2] as well as cumulative figures.

[1] EudraCT is the (European Union Drug Regulating Authorities Clinical Trials Database) European database for all interventional clinical trials on medicinal products authorised in the European Union (EEA) under the Clinical Trial Directive and outside the EU/EEA if they are part of a Paediatric Investigation Plan (PIP)
[2] The two 'smoke test' trials, submitted to CTIS for testing purposes just before the CTIS launch, are not counted)

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# Clinical Trial Information System (CTIS) and EudraCT metrics

This report shows the key performance indicators (KPIs) generated from EudraCT and CTIS containing information on clinical trials in the EU/EEA.

### *1.1. Clinical trial applications submitted under the Clinical Trials Regulation in CTIS*

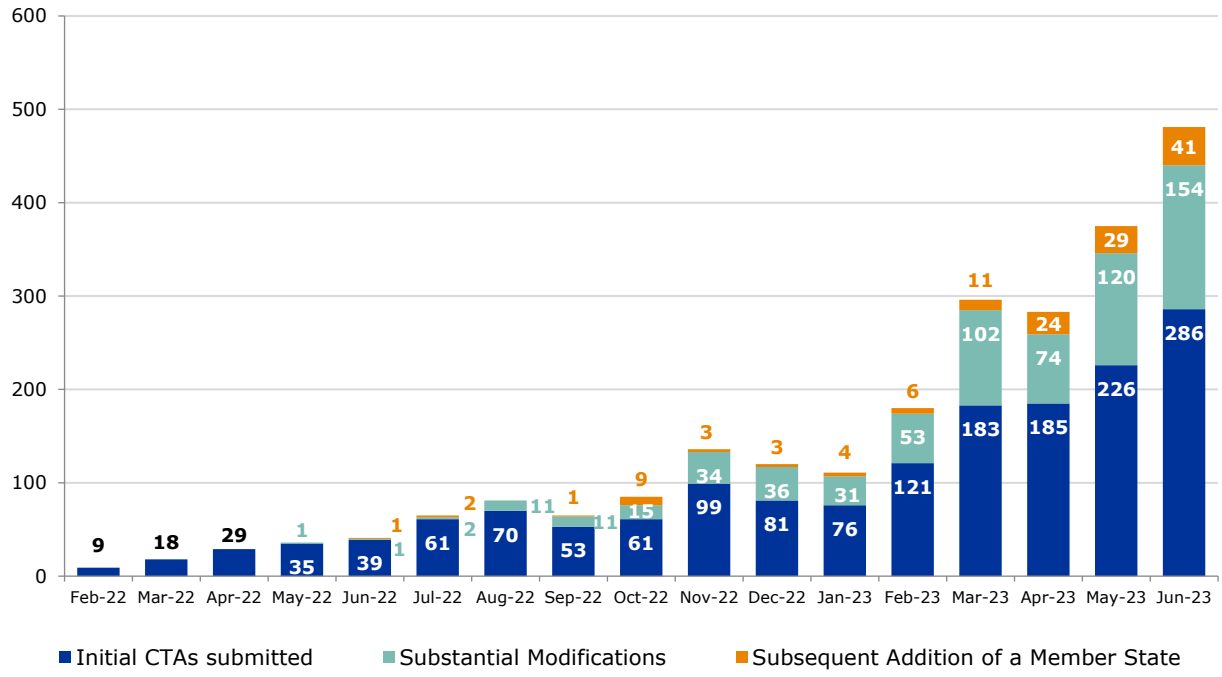
Following the mandatory use of CTIS since 31 January 2023, the submission of initial clinical trials applications has seen an increase from month to month.

Overall, 2,411 clinical trial applications (CTAs) have been submitted in CTIS since the launch of the system on 31 January 2022, of which 1,632 are initial clinical trial applications, 645 are substantial modification applications and 134 are applications for the addition of a Member State Concerned.

Of the submitted applications during June 2023, 22 are re-submissions of applications that previously lapsed (12), were withdrawn (9) and not-authorised (1).

Specifically, the applications submitted in May 2023 include initial clinical trial applications[3], substantial modifications[4] and addition of a new Member State Concerned[5] applications in the selected period.[6]

**CTAs submitted in CTIS per month**




[3] Initial clinical trials applications are those submitted in accordance with the requirements of Article 5 and Article 11, as applicable, of the Clinical Trials Regulation (EU) No 536/2014

[4] Substantial modifications are those submitted in accordance with the requirements of chapter III of the Clinical Trials Regulation (EU) No 536/2014

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

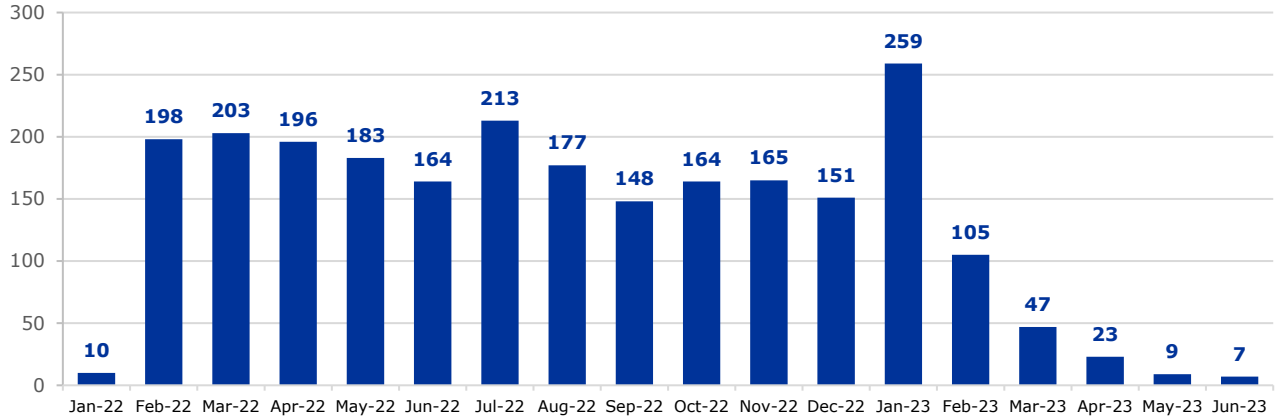
[6] Corrigendum: the graph shows the corrected figures for initial clinical trial applications submitted in July which are 60 and not 58 as displayed in the report edition 4. The incorrect calculation was due to an error in the reporting system.

### *1.2. CTAs under Clinical Trial Directive (CTD) uploaded by Member States (MSs) in EudraCT, counted as individual clinical trial protocol*

The graph below shows the number of CTAs uploaded by the Member States in EudraCT as individual clinical trial protocol, per month during the selected period[7].

Overall 2,422 CTAs have been uploaded in EudraCT, since 31 January 2022, including those ones submitted to the Member States prior to the mandatory use of CTIS for new initial applications applicable since 31 January 2023 and uploaded in EudraCT after this date. In June 2023 7 CTAs were uploaded in EudraCT.

**CTs in EudraCT per month**




### *1.3. Ongoing clinical trials (CTs)*

**CTs under the CTR with at least one positive decision in the EU**

The term 'ongoing' refers to clinical trials, authorised in at least one Member State Concerned, where the sponsor has notified in CTIS the start date of the recruitment of patients at the clinical investigator sites[8].

Since 31 January 2022, 284 clinical trials were reported as ongoing in CTIS.

**CTs under the CTD**

In EudraCT there are no fields available to capture recruitment status at the level of the Member States.

### *1.4. Trial with a decision under the CTR with/without deferral[9] for the protocol*

Due to a CTIS known issue, a mitigation measure has been put in place to prevent publication of clinical trials with deferrals. As a consequence, clinical trials with any type of deferrals with a decision issued mid-August onwards are not available in the public domain. This is a temporary measure until the functionality of the deferral mechanism is restored. Sponsors and EU/EEA Members have the possibility to apply deferrals to clinical trials data, which will be published in due course once the issue is resolved.

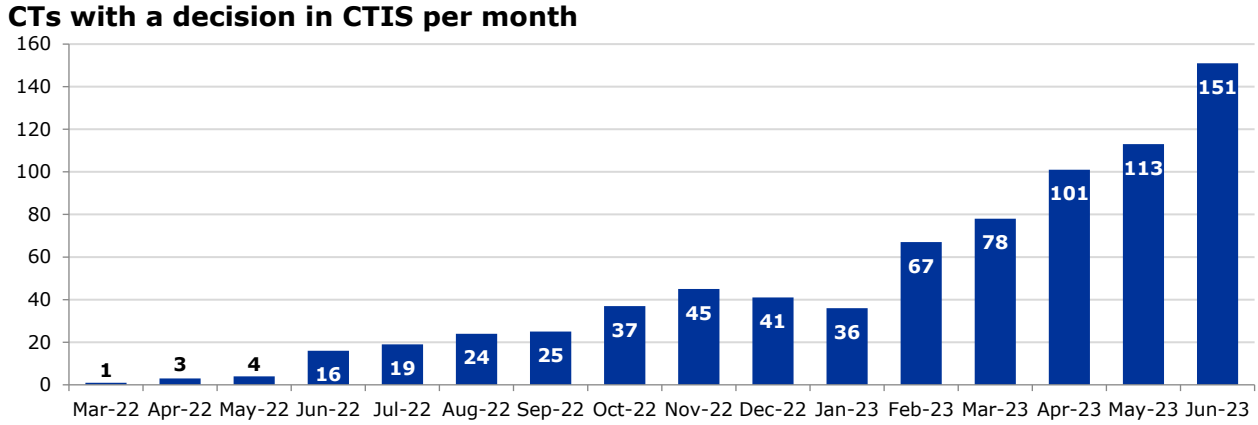
[7] The data for January 2022 in the graph refers to CTA uploaded by the Member State on the 31 January 2022 only.
[8] Details on recruitment status are based on the information reported by the trial sponsor in CTIS
[9] The option to defer the protocol is only available in CTIS.

Therefore, information on number of deferrals applied for the protocol will be reinstate once the functionality of the deferral mechanism is restored.

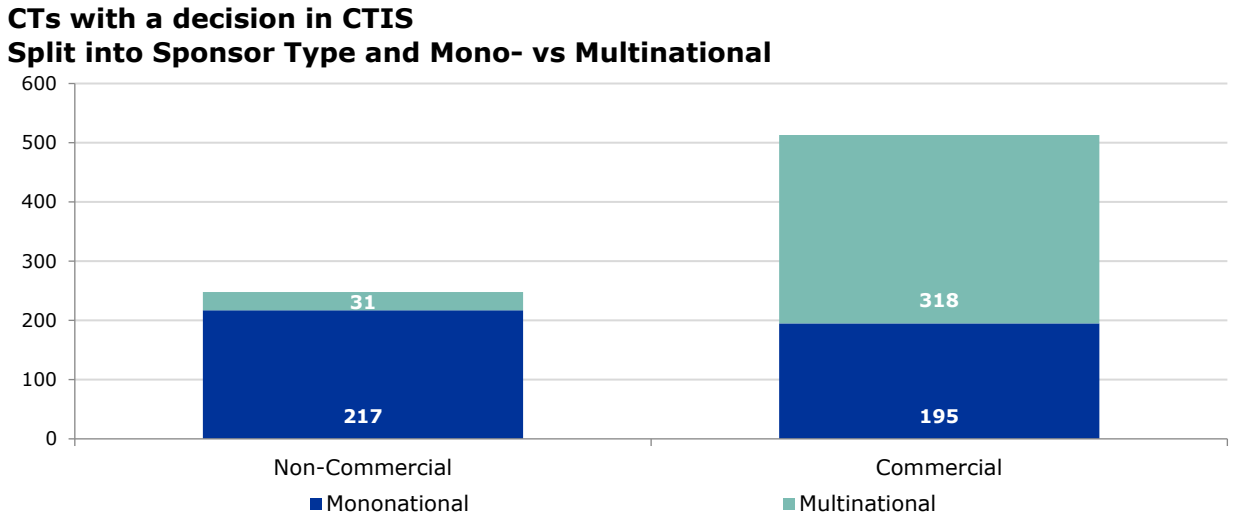
### *1.5. Mononational-multinational trials with a decision has been issued by the Member States Concerned (MSC) under the Clinical Trials Regulation, broken down per sponsor type (commercial vs. non-commercial) and average number of MSCs[10]*

The graph below shows the number of trials for which at least one decision has been issued in CTIS by a Member State Concerned, per month, since 31 January 2022; meaning a trial has been authorised, not authorised or trials previously authorised that have now ended. In March 2022 the first positive decision for a trial was issued.

As visible in the graph below, the number of trials with a decision are steadily increasing from month to month leading to the cumulative total of clinical trials with a decision rising by 25%, from 610 to a total of 761 clinical trials, of which 20 were reported as ended and 1 trial as halted.




The graph below shows the number of clinical trials for which a decision has been issued by the first MSC, with information whether the trial is a mono- or multinational and in relation to sponsor type.



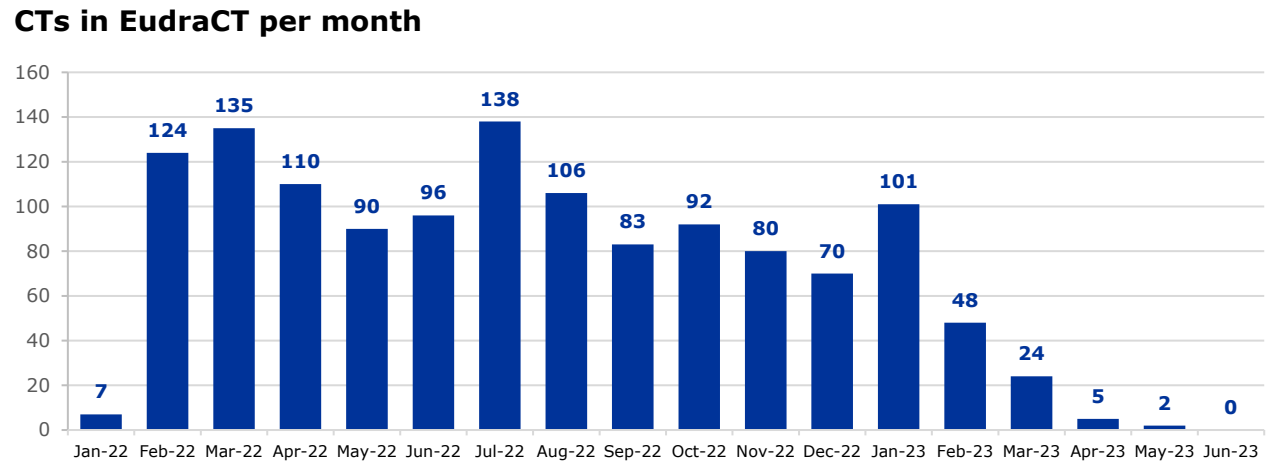

Multinational clinical trials with a decision rose by 22% to a total of 349 from 287 with an average of 7 Member States Concerned in CTIS.

[10] Details on trial sponsor type, commercial *vs* non-commercial are derived based on information reported at the time of registration of an organisation in OMS: Organisation Management Service database, and are not recorded as such in the clinical trial application form. Commercial classification includes for example industry, pharmaceutical company, while non-commercial classification includes values such as academia, health care facility, micro, small and medium enterprises.

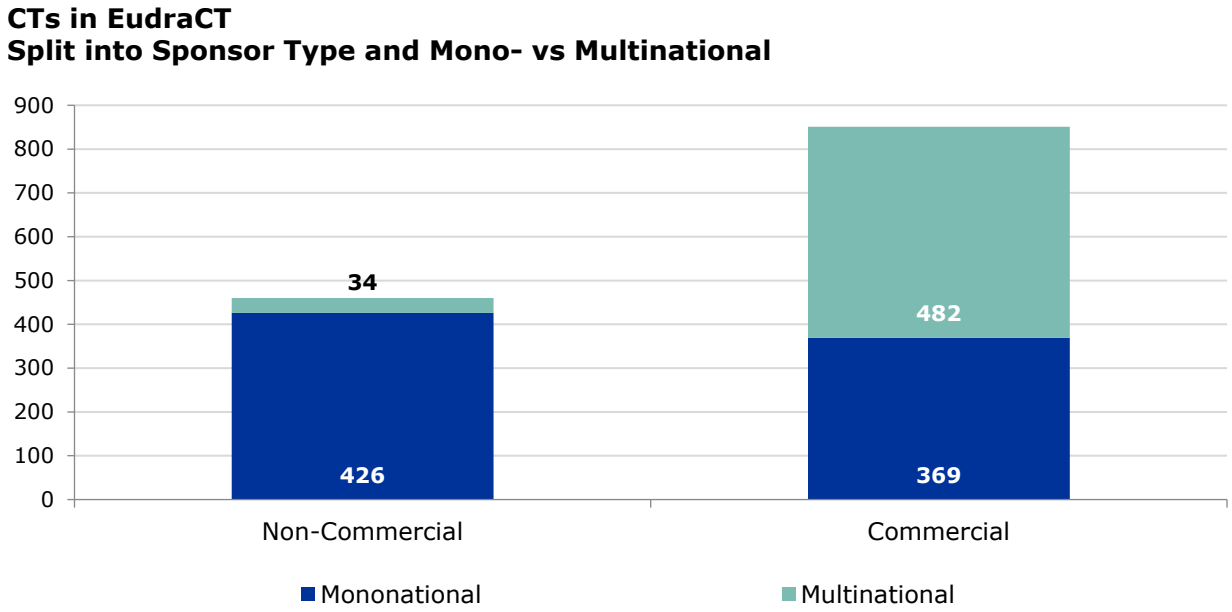
### *1.6. Mononational-multinational trials with a NCA decision and an Ethics Committee opinion have been issued by the Member States under the Clinical Trials Directive, broken down per sponsor type (commercial vs. non-commercial) and average number of MSs*

The graph below shows the number of clinical trials, as individual clinical trials protocols, that received a National Competent Authority decision and an Ethics Committee opinion from the first Member State uploading the CTA in EudraCT, per month, since 31 January 2022[11] displayed by upload date in EudraCT.

The numbers of applications with a NCA decision and Ethics Committee opinion may increase overtime, as soon as additional information is provided in EudraCT by the Member States.




The graph below shows the number of clinical trials with a decision and opinion issued by the Member states, with information whether the trial is a mono- or multinational and in relation to sponsor type.

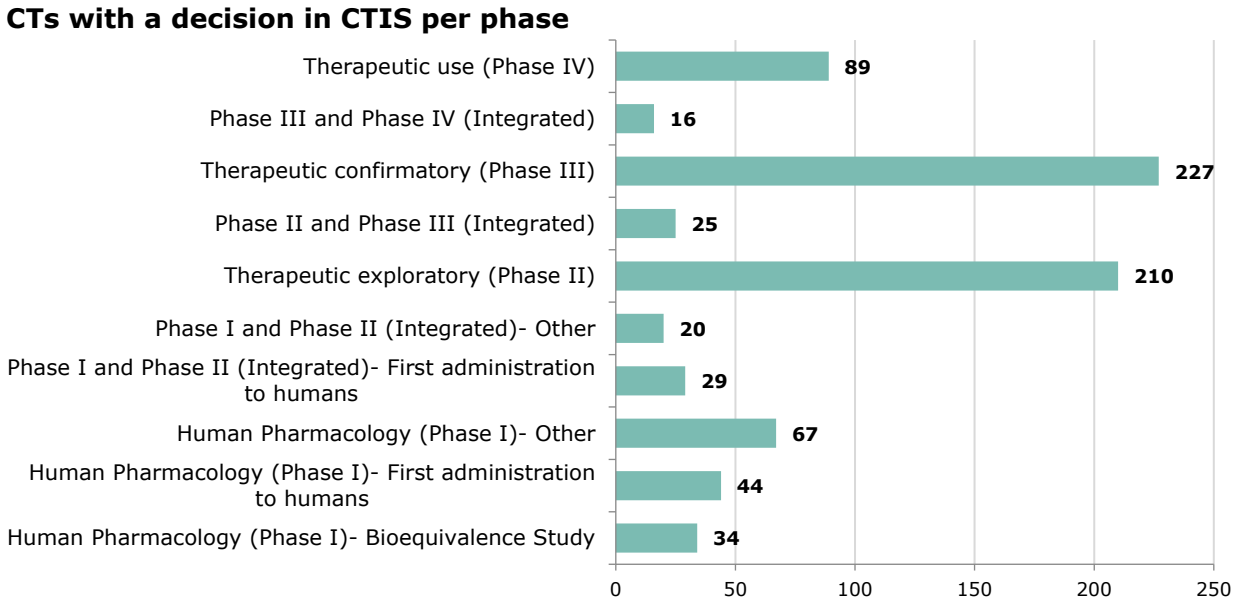



Considering clinical trials with an issued decision and opinion, on average 4 Member States are involved in multinational trials.

[11] The data shown in the graph for January 2022 refers to CTA loaded in EudraCT on 31 January 2022 only having a subsequent decision by the national Competent Authority and Ethic Committee opinion loaded in EudraCT.

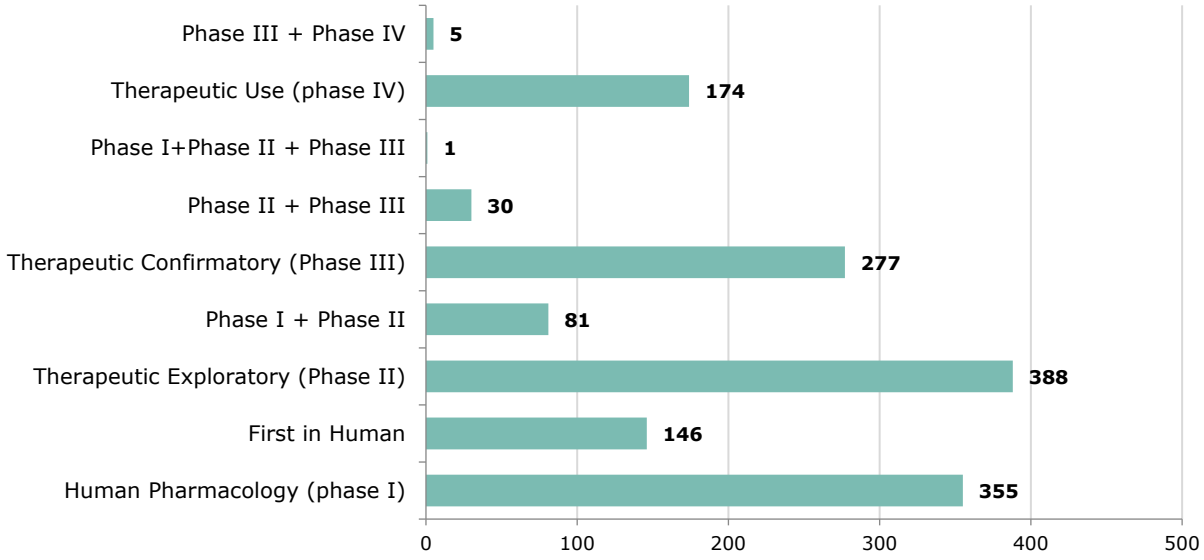
### *1.7. Clinical trials with a decision per phase (i.e. I, II, III, IV, as well as CT first in human or combined phases early (I and II)) under CTR[12]*

The graph below shows the number of clinical trials with a decision, broken down per trial phase.




### *1.8. Clinical trials for which a NCA decision and an Ethics Committee opinion have been issued per phase (i.e. I, II, III, IV, as well as CT first in human or combined phases early (I and II)) under CTD*

The graph below shows the number of clinical trials, as individual clinical trial protocol, uploaded in EudraCT since 31 January 2022, with a decision by the National Competent Authority and an opinion by the Ethics Committee inserted by the first Member State uploading the CTA in EudraCT, broken down per trial phase.

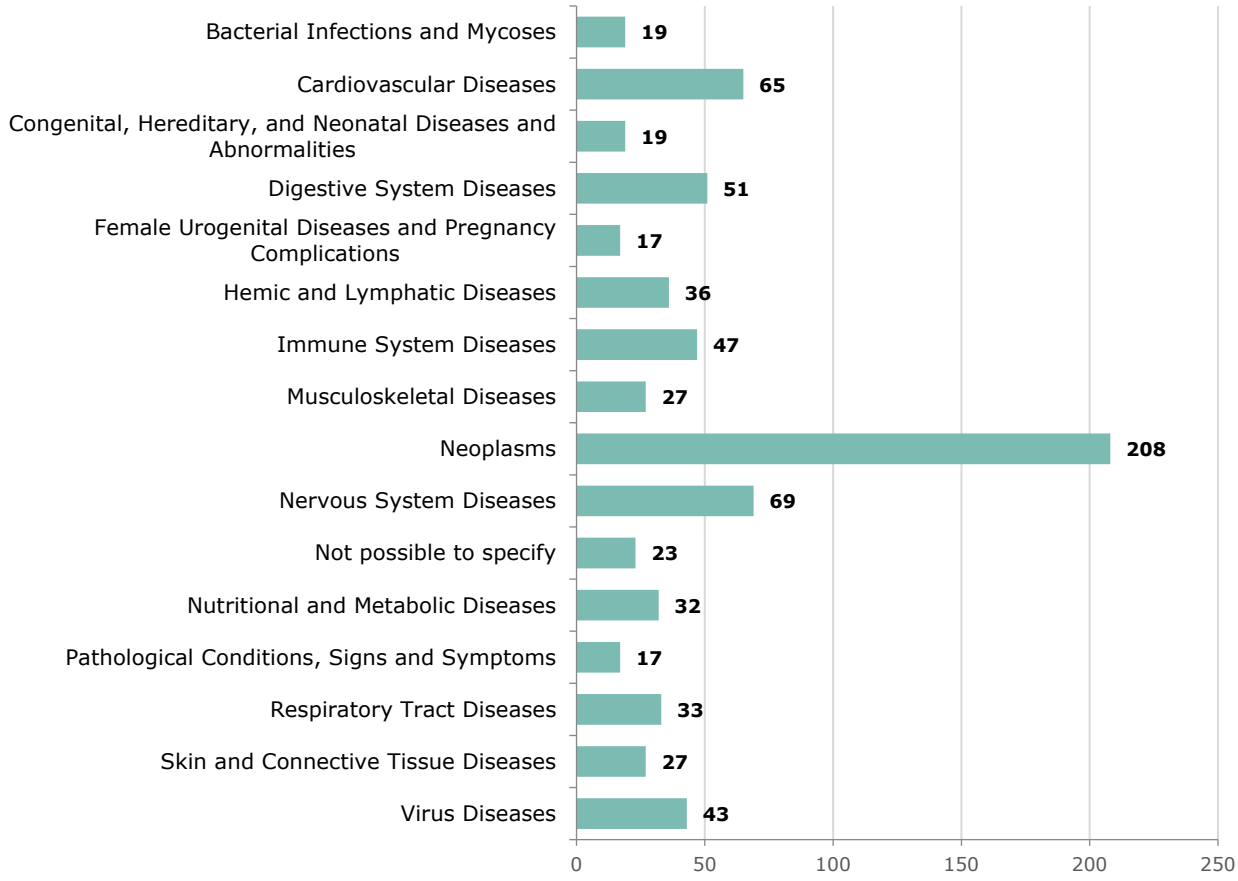



[12] More than one trial phase can be selected for a single trial and it is counted in each trial. The graph shows the applicable trial phases in the selected period.

### *1.9. Clinical trials with a decision under CTR, per therapeutic area*[13]

The graph below shows the number of clinical trials with a decision in CTIS showing the 15 most frequent therapeutic areas.

**CTs with a decision in CTIS per therapeutic area**

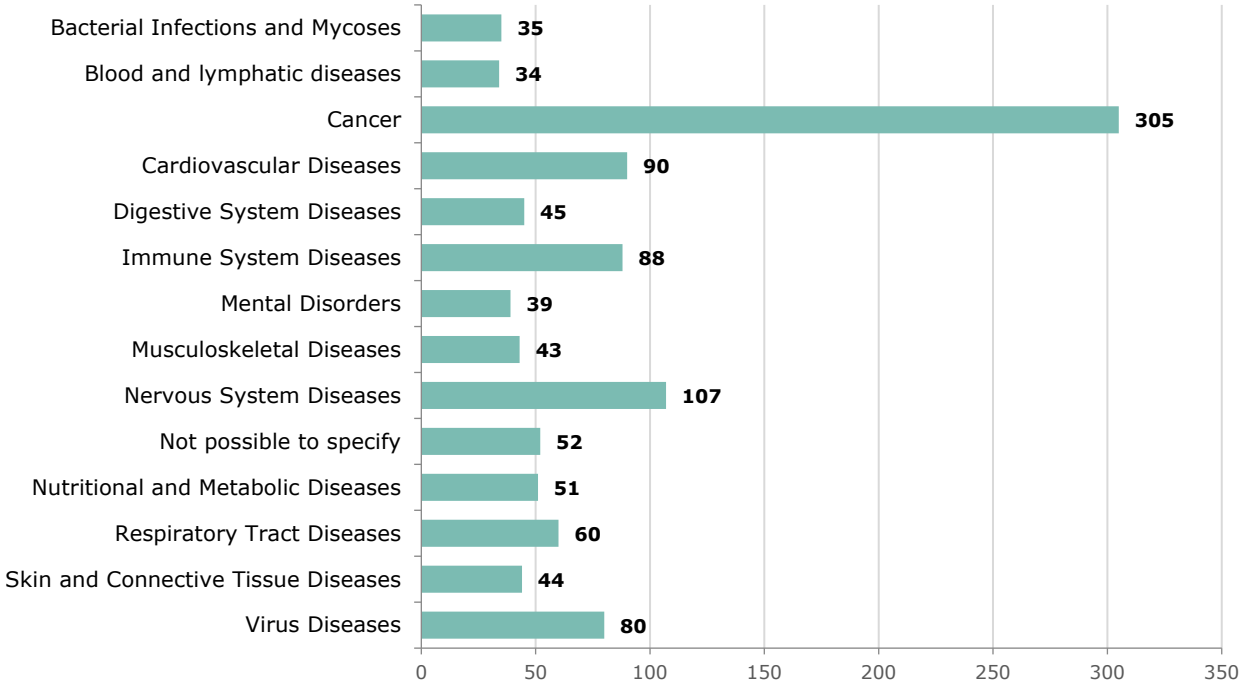



[13] In case a clinical trial investigates several therapeutic areas, it is counted in each of such identified therapeutic areas.

### *1.10. Clinical trials with a NCA decision and an Ethics Committee opinion under CTD, per therapeutic area[14]*

The graph below shows the number of clinical trials, as individual clinical trial protocol, for which a decision by the National Competent Authority and an opinion by the Ethics Committee have been inserted by the first Member State uploading the CTA in EudraCT, showing the most frequent 15 therapeutic areas.[15]

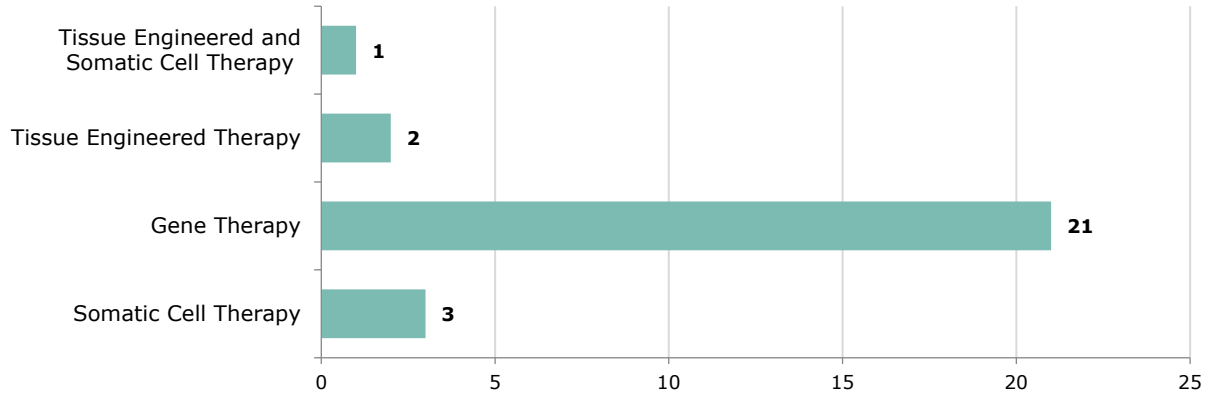
**CTs in EudraCT per therapeutic area**




### *1.11. Clinical trials with a decision with an ATMP and per type under CTR*

Twenty-seven clinical trials with a decision included an ATMP, with the following therapeutic types.

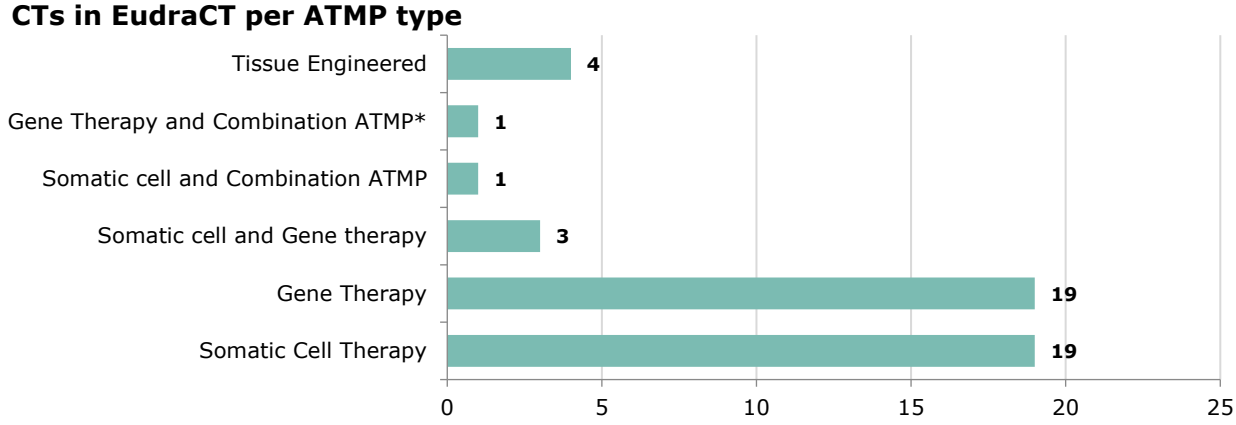
**CTs in CTIS per ATMP type**




[14] In case a clinical trial investigates several therapeutic areas, it is counted in each of such identified therapeutic areas.
[15] The value 'not possible to specify' in the graph above reflects the fact that section E.1.1.2 of the CTA was not filled in

### *1.12. Clinical trials with a NCA decision and an Ethics Committee opinion, with an ATMP and per type under CTD*

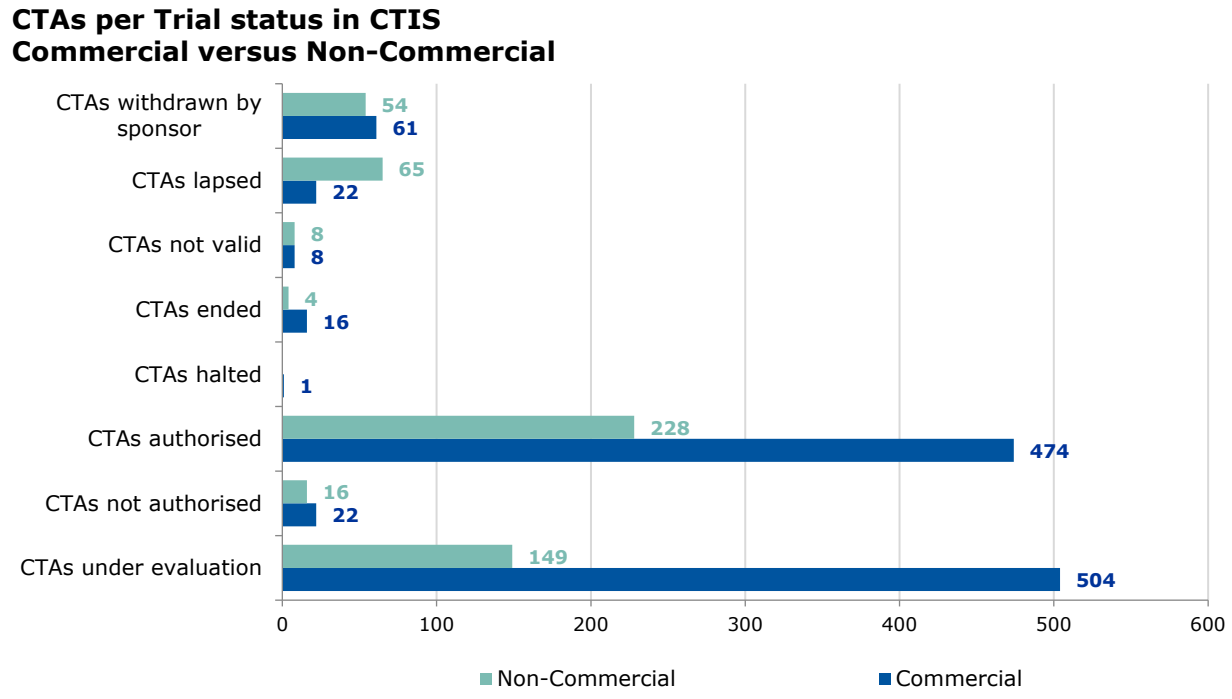
There were 47 clinical trials in EudraCT since 31 January 2022, with a decision and an opinion issued by 30 June 2023 by the first Member State uploading the CTA in EudraCT, including an advanced therapy medicinal products. The graph below shows the number of clinical trials per ATMP type as reported in EudraCT.




* Combination ATMP with a medical device.

### *1.13. Clinical trial applications under the CTR per applicable trial status during the selected period, broken down per sponsor type: non- commercial/commercial*

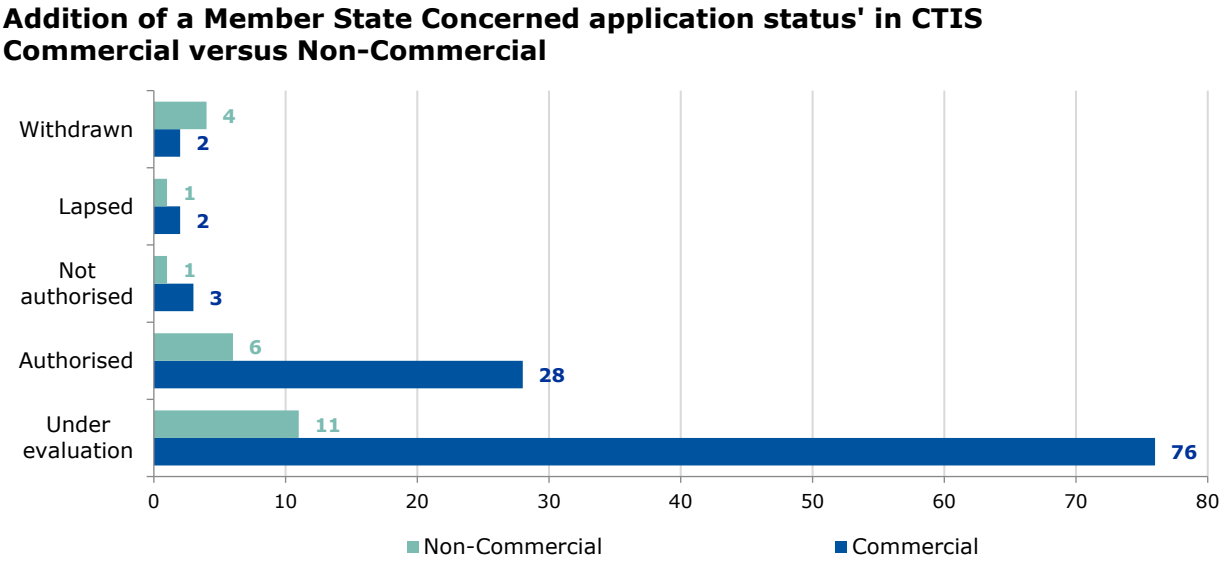
The graph below shows the number of initial clinical trial applications, per applicable overall trial status[16] and information of sponsor type submitted in CTIS since 31 January 2022.




[16] Overall trial status is the status per application and not per individual Member State Concerned. The Overall trial status it is derived based on defined business rules, for example in an initial trial application is under evaluation in two MSC and authorised in a third MSC, the overall trial status for the application will be: authorised.

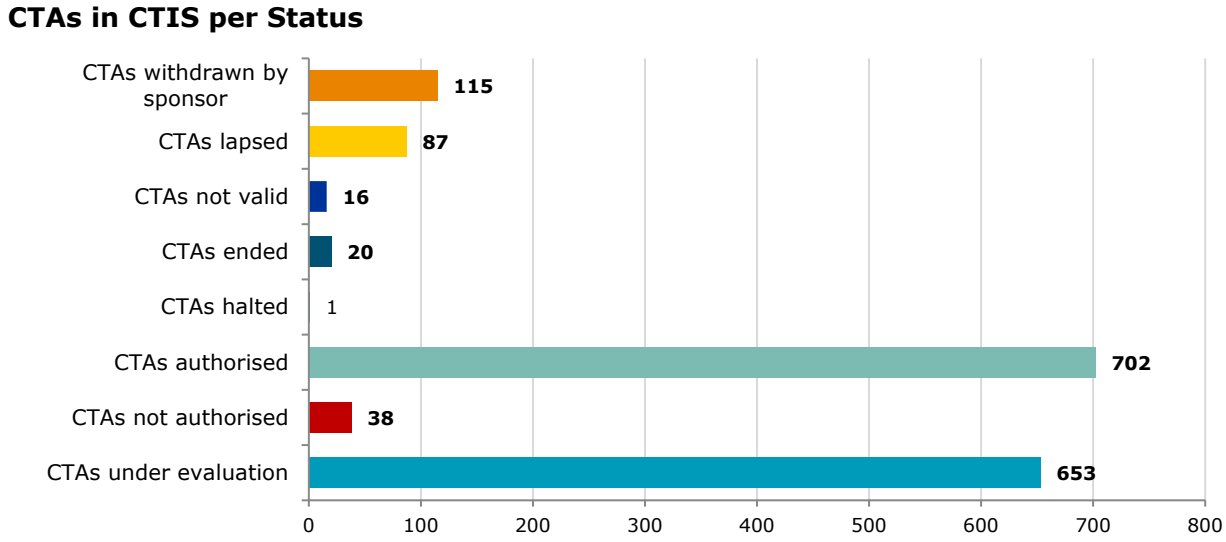
### *1.14. Art 14 applications to add a new Member State Concerned: (re-)submission, authorisation, rejection, lapsed and withdrawn dossiers*

Since 31 January 2022, 134 clinical trial applications for the addition of a new MSC, foreseen under Article 14 of Regulation (EU) No 536/2014, have been submitted in CTIS for 39 clinical trials. The below graph provides overview status per application submitted until 30 June 2023.[17]




### *1.15. CTAs under Article 5 of CTR [full dossier initial applications] per applicable trial status, at EU, at MS level and with Reporting Member State (RMS) details*

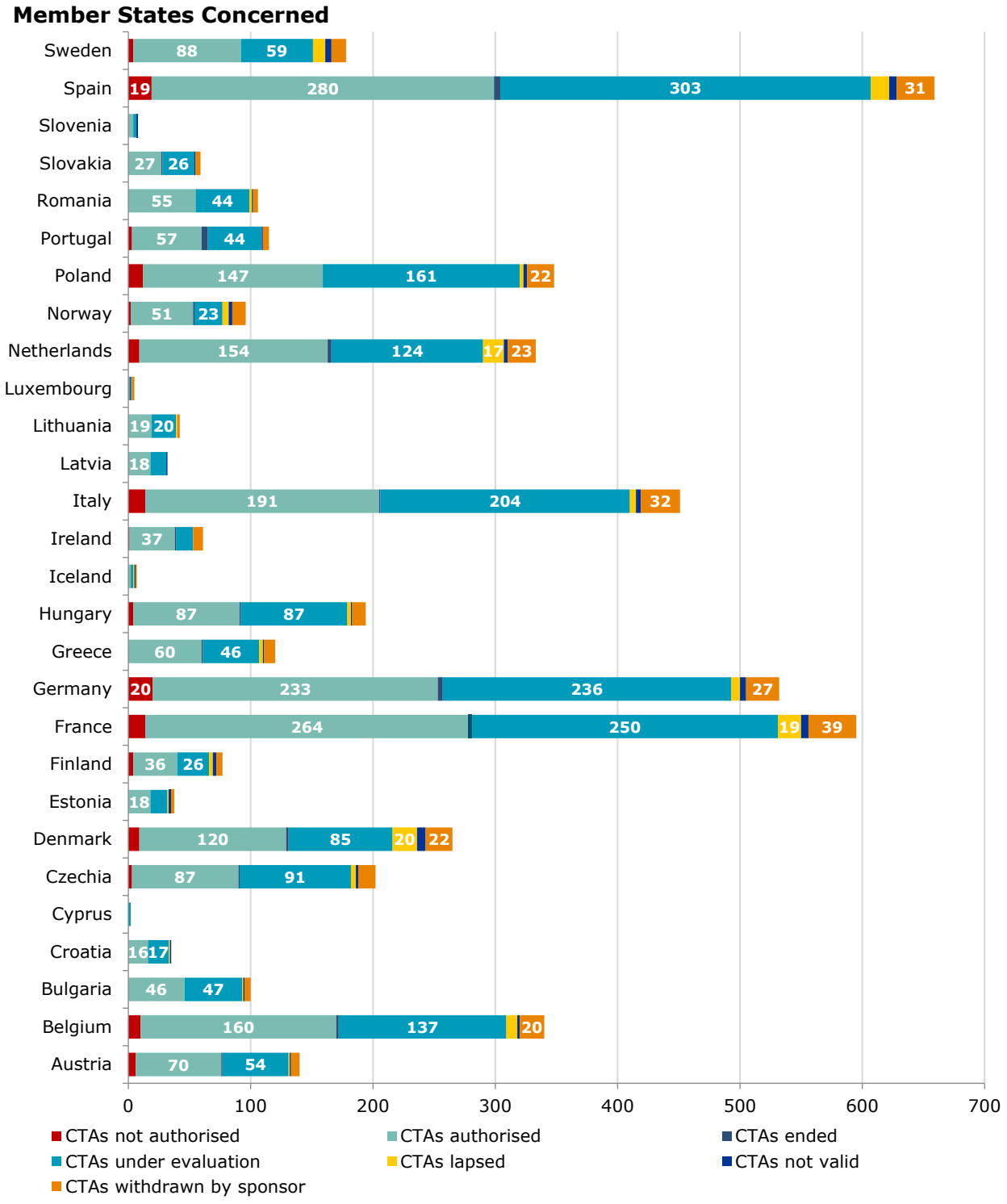
The graph below shows the number of initial clinical trial applications with full dossier, submitted in accordance with Article 5 of CTR since 31 January 2022, per applicable overall status at EU level.




Clinical trial applications under evaluation have increased by 17%, and by 25% for clinical trial applications authorised compared to the previous reporting period.

17 The status of a previously lapsed application to add a new Member State Concerned has changed since the last published report to withdrawn.

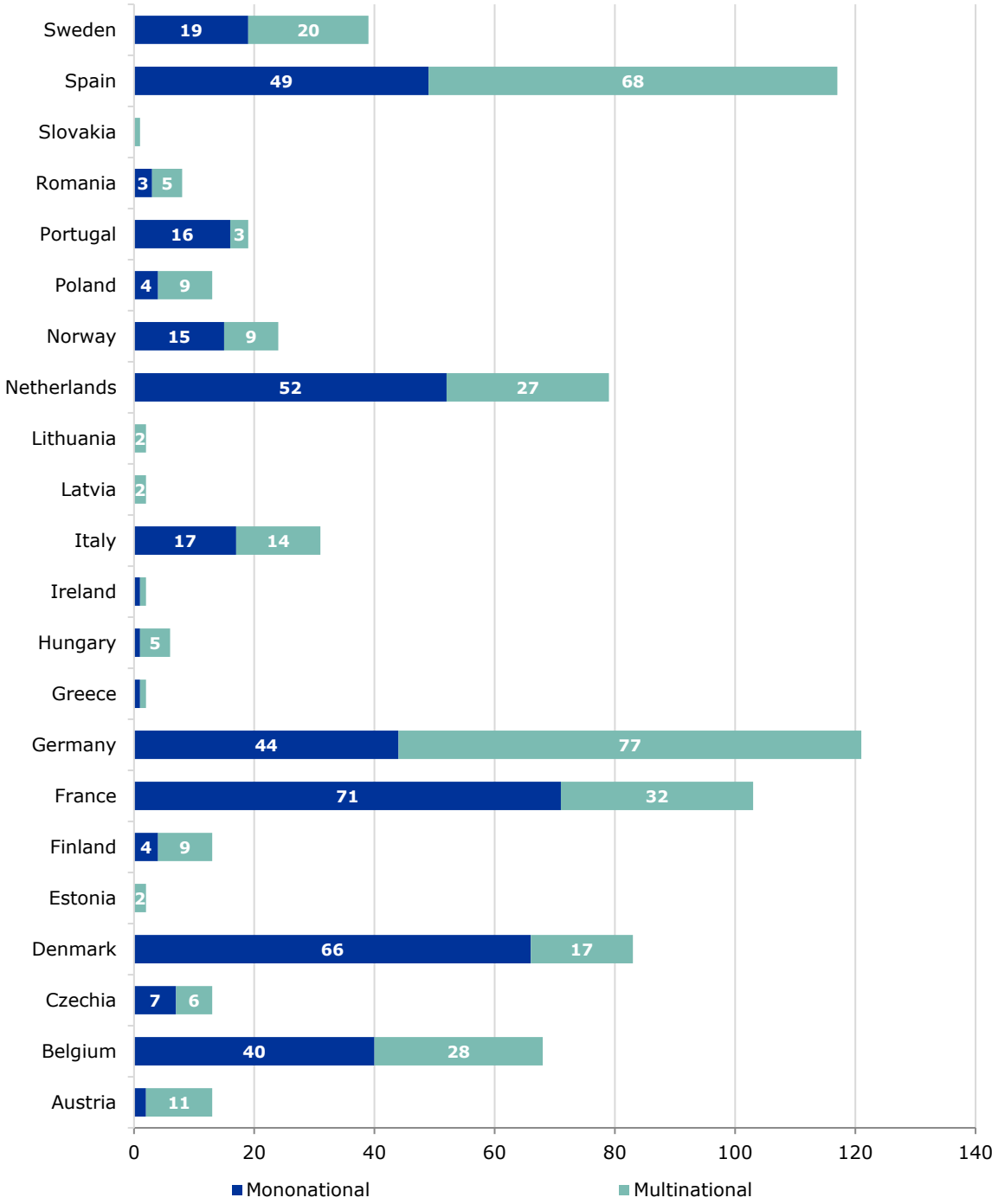
The graph below shows the number of initial clinical trial applications with full dossier, submitted in accordance with Article 5 of CTR since 31 January 2022, per applicable status at the level of the Member States Concerned[18].




[18] In multinational clinical trials the same 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)[19], amongst the applicable Member States Concerned, for clinical trial applications on which a decision has been issued for mono- and multinational trials.

**Reporting Member States**
**Mononational vs Multinational**




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

### *1.16. Number of CTA Article 11 of CTR [partial dossier initial applications with later Part II submission] per applicable trial status during the reporting period, at EU and at MS level*

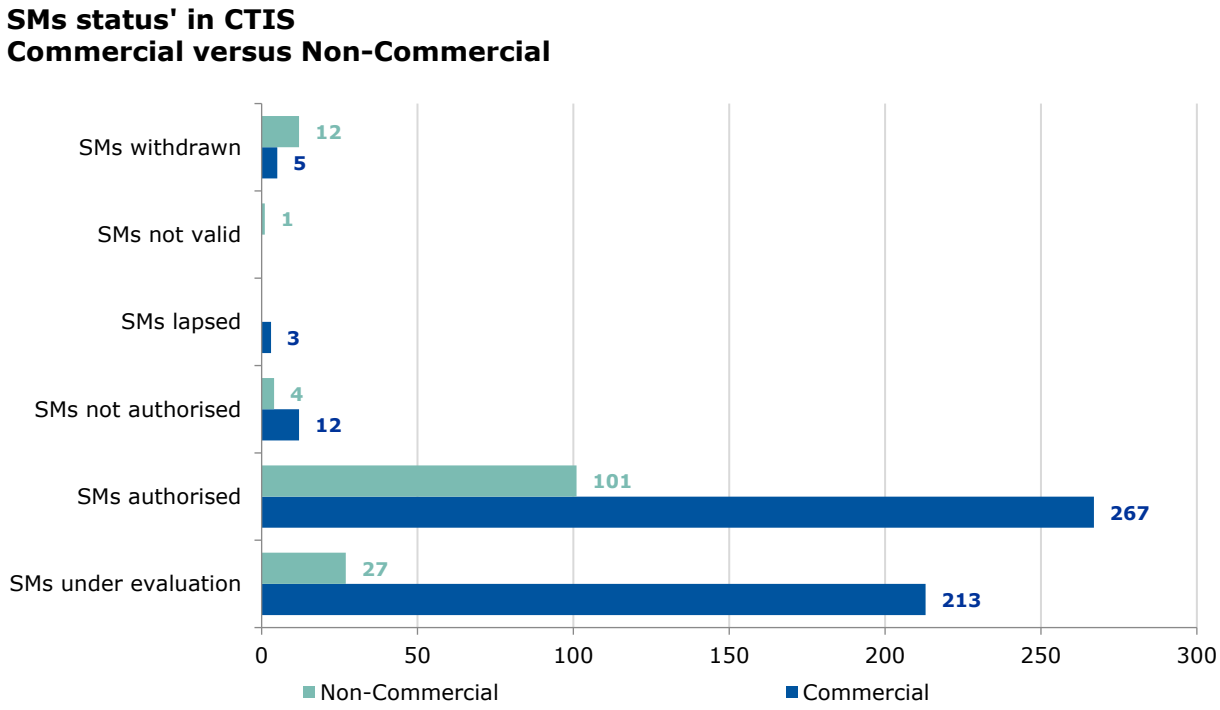
Partial initial applications submitted to CTIS in line with the requirements of Article 11 of the Regulation (EU) No 536/2014 will be considered for future reporting.

### *1.17. Average time from submission to reporting date[20] (Article 11 and Article 5 of CTR), and to first decision (Article 5 of CTR) for initial applications and Substantial Modifications part I or part I and II*

On average it took 90 calendar days to issue a decision, during the selected period, for the 761 initial clinical trial applications.

### *1.18. Number of submitted, validated, authorised, rejected, lapsed and withdrawn Substantial Modification (SM) applications, related to part I / II / I and II, by sponsor type*

Since 31 January 2022, 645 distinct applications for substantial modifications, foreseen in chapter II of Regulation (EU) No 536/2014, were submitted in CTIS for 332 clinical trials.



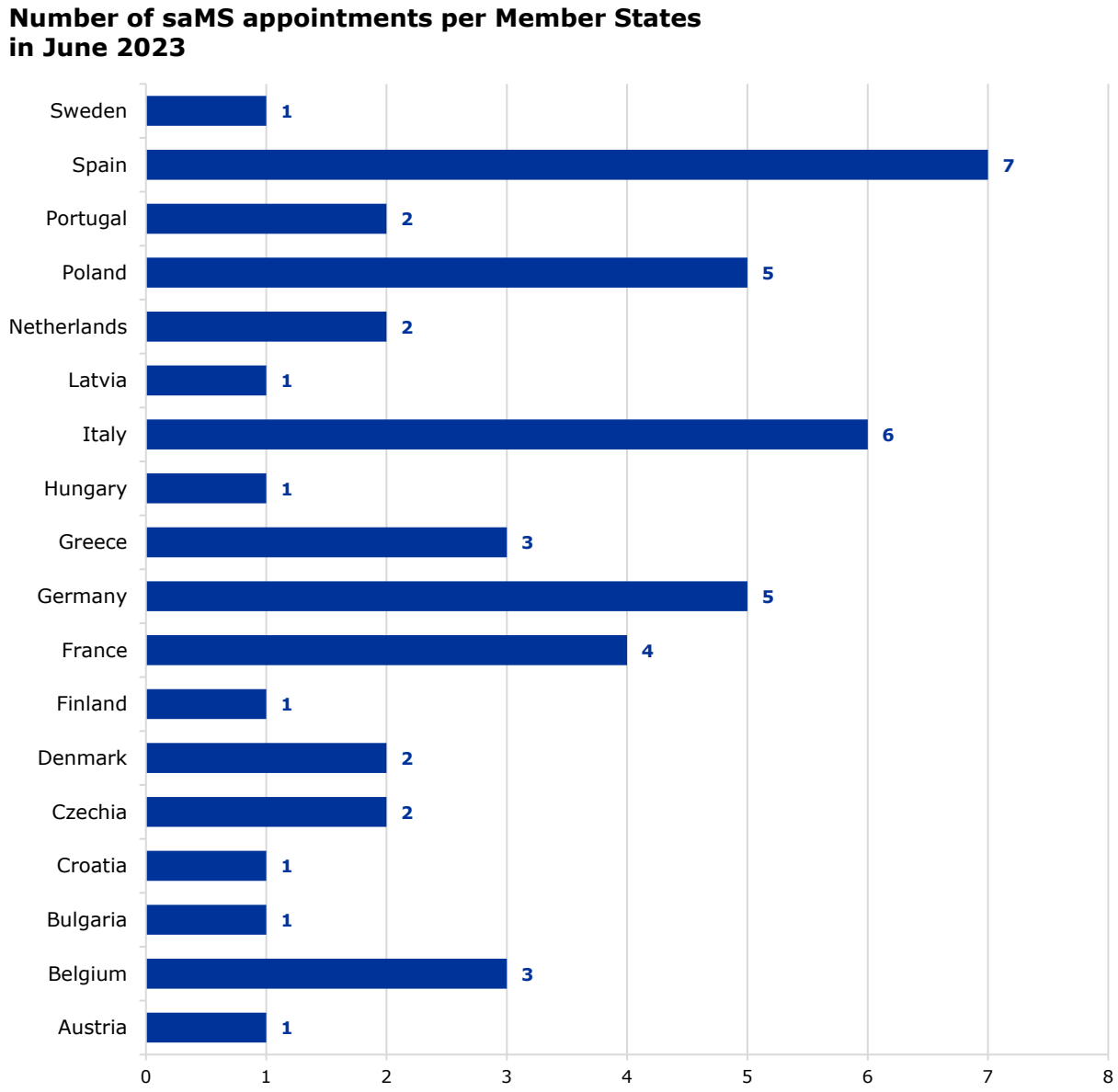

[20] The reporting date is equal to the date of the RMS conclusion on part I assessment

### *1.19. Number of active substances (ASs) in CTR EU trials per safety assessing Member States*

During the reporting period (1-31 May 2023) 18 saMS[21] were appointed for 48 active substances.

The role of safety assessing Member State Concerned (saMS) will be applicable only for active substances investigated in clinical trials in two or more MSC.

The graph below shows the number of saMS appointments per Member States during the reporting period.



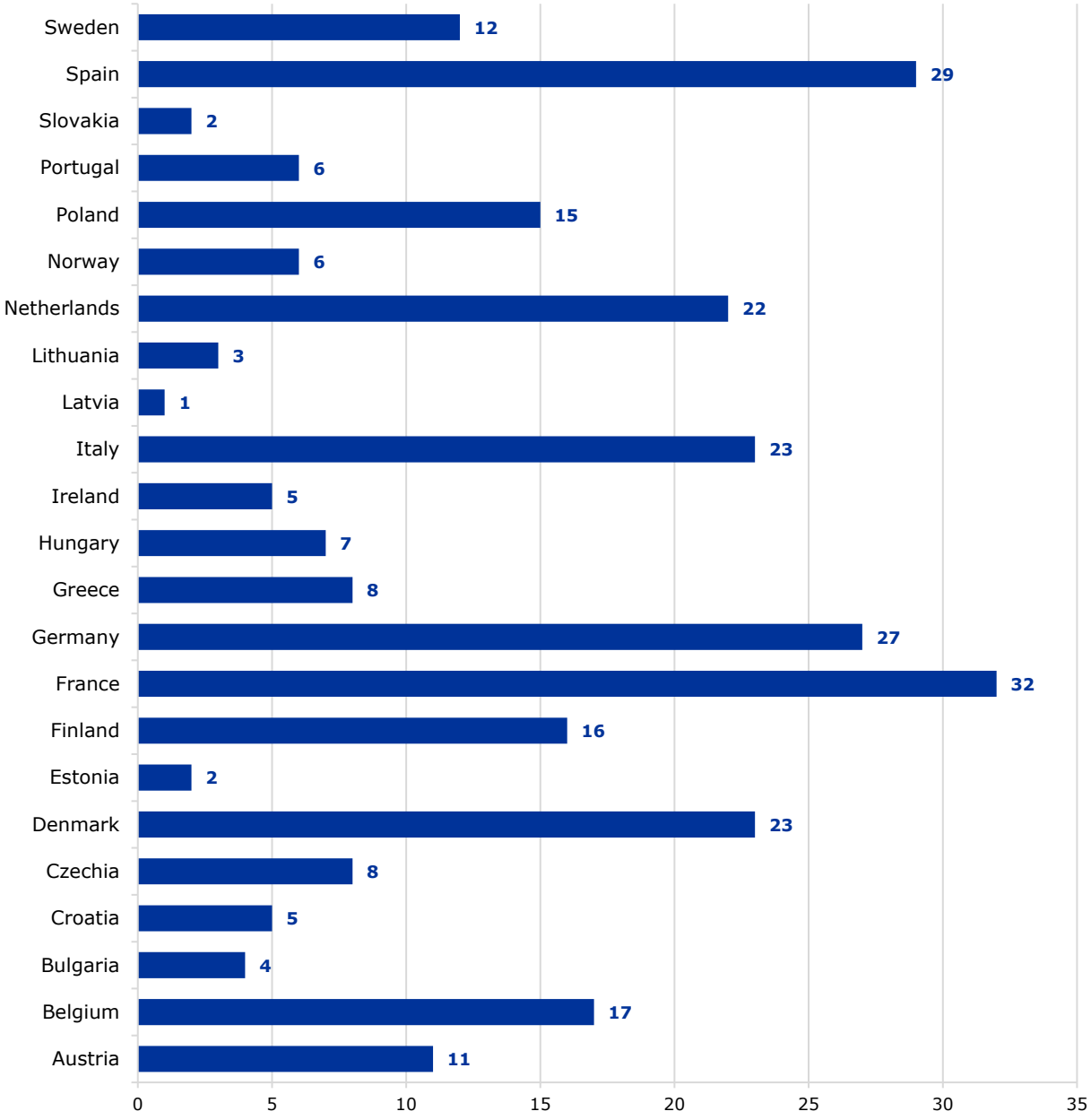

[21] Safety Assessing Member State

Since 31 January 2022, 23 saMS[22] were appointed for 284 active substances.

The role of safety assessing Member State Concerned (saMS) will be applicable only for active substances investigated in clinical trials in two or more MSC.

The graph below shows the total number of saMS appointments per Member States.

**Number of saMS appointments per Member States since 31 January 2022**




[22] Safety Assessing Member State