28 July 2022
EMA/620032/2022

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

Metrics on the Clinical Trials Regulation and Clinical Trials Directive

1 – 30 June 2022, edition 3

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 is published on a monthly basis starting in May 2022. The previous report 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.

ACT EU seeks to transform how clinical trials are initiated, designed and run. 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 2022 for Clinical Trial applications (CTA) submitted between 1 – 30 June 2022[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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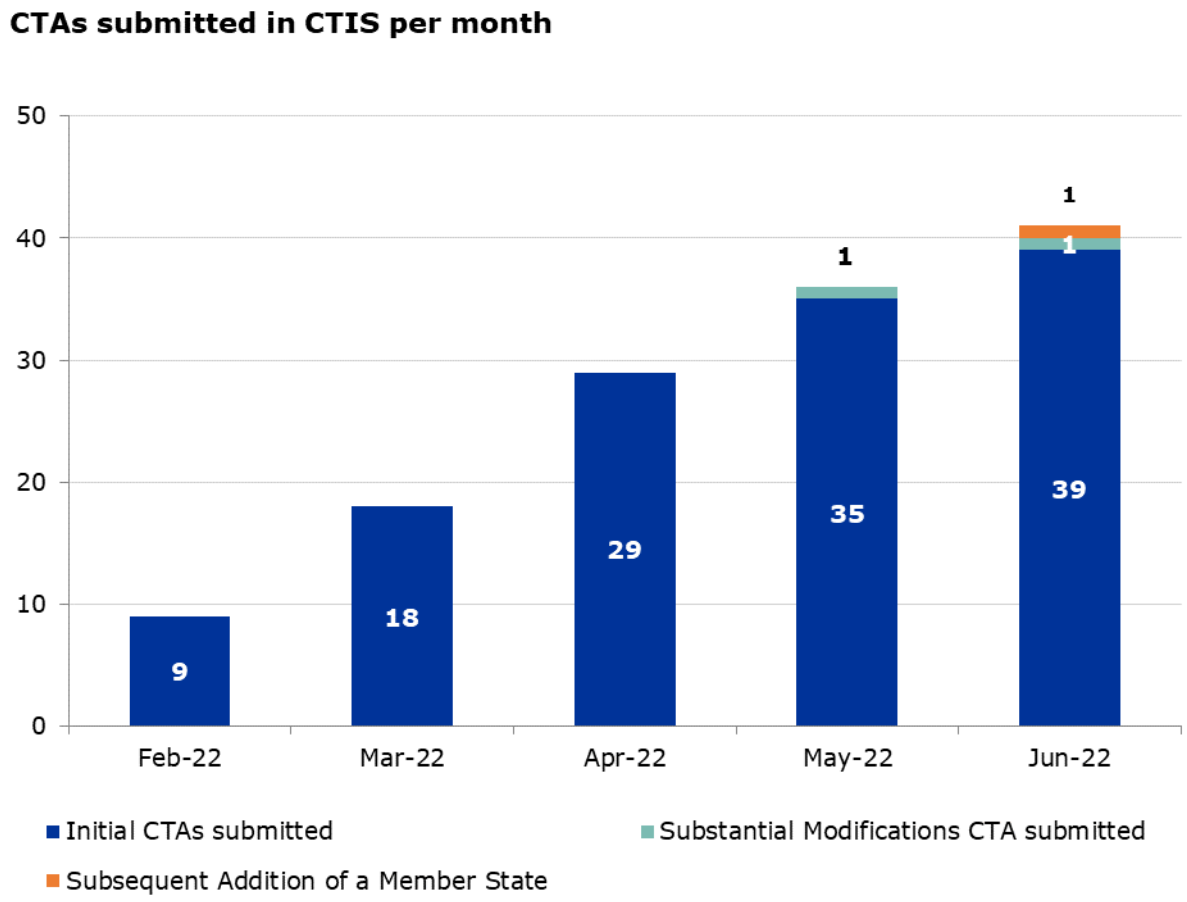
Clinical Trial Information System (CTIS) and EudraCT metrics

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

1.1. Number of clinical trial applications (CTAs) submitted under the Clinical Trials Regulation in CTIS

The graph below shows the cumulative number of clinical trial applications that have been submitted to CTIS since the launch on 31 January 2022.

Specifically, the applications submitted in June 2022 include initial clinical trial applications[3], one substantial modification[4] and one addition of a new Member State Concerned[5].



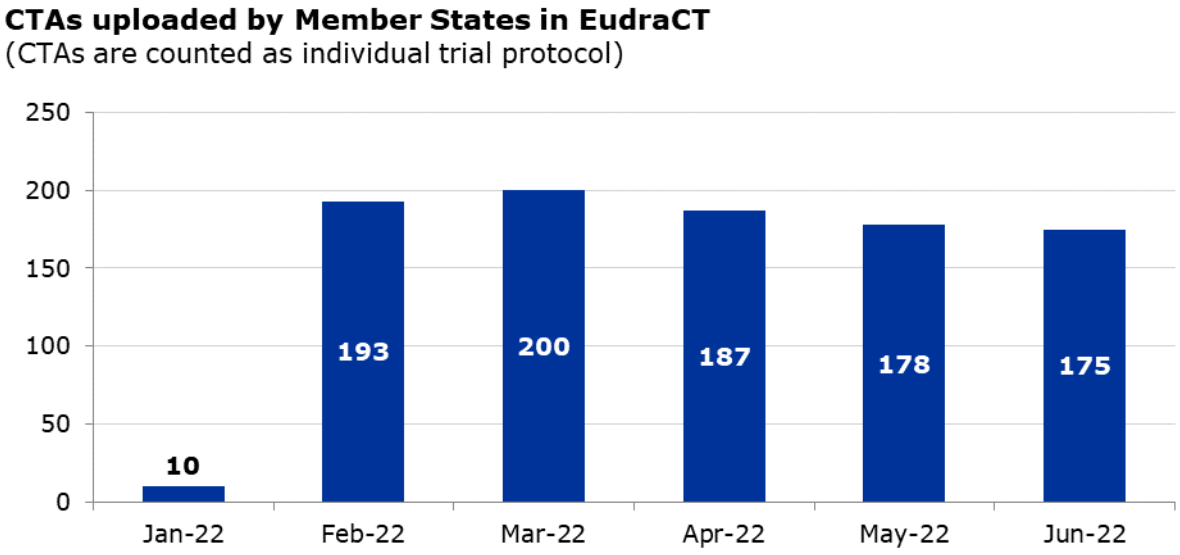
Overall, 133 clinical trial applications have been submitted in CTIS during the first 5 months since the launch of the system on 31 January 2022, of which 130 are initial clinical trial applications, 2 are substantial modification applications and 1 is the addition of a new Member State Concerned.

[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

Of the submitted applications during June 2022, 1 is a re-submission of previous lapsed application.

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[6], per month during the selected period[7].



1.3. Number of ongoing clinical trials (CTs)

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

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[8].

Three clinical trials were reported as ongoing with recruitment started as of 30 June 2022.

CTs under the CTD

In EudraCT there are no fields available to capture recruitment status at the site.

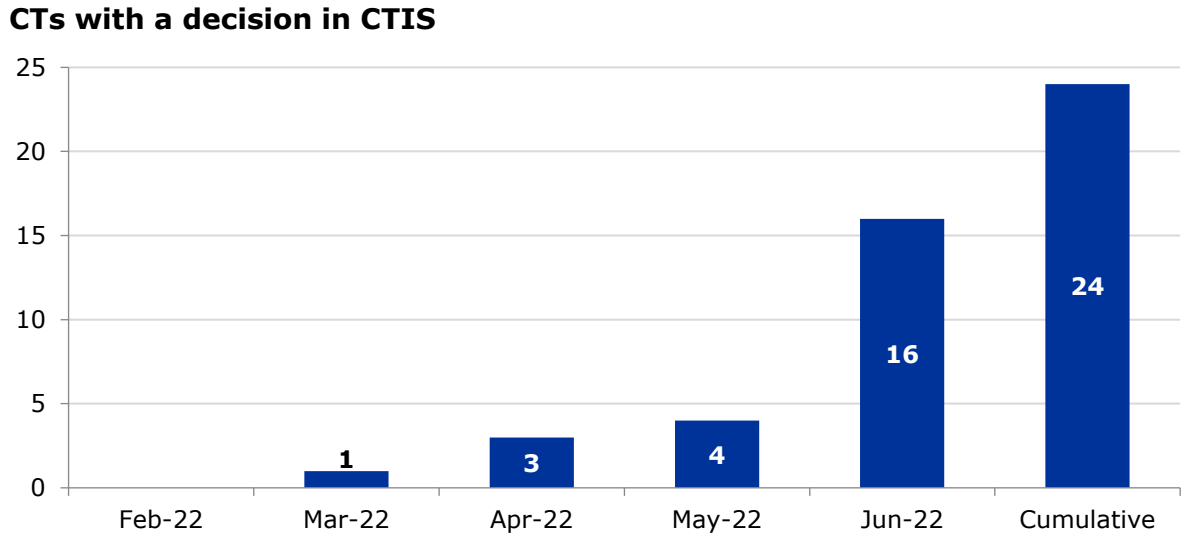
1.4. Number of trials for which a decision has been issued under the CTR with/without deferral[9] for the protocol

There were nine clinical trials for which a decision has been issued in June 2022, with deferrals[10] of the protocol, therefore the protocols have not been published.

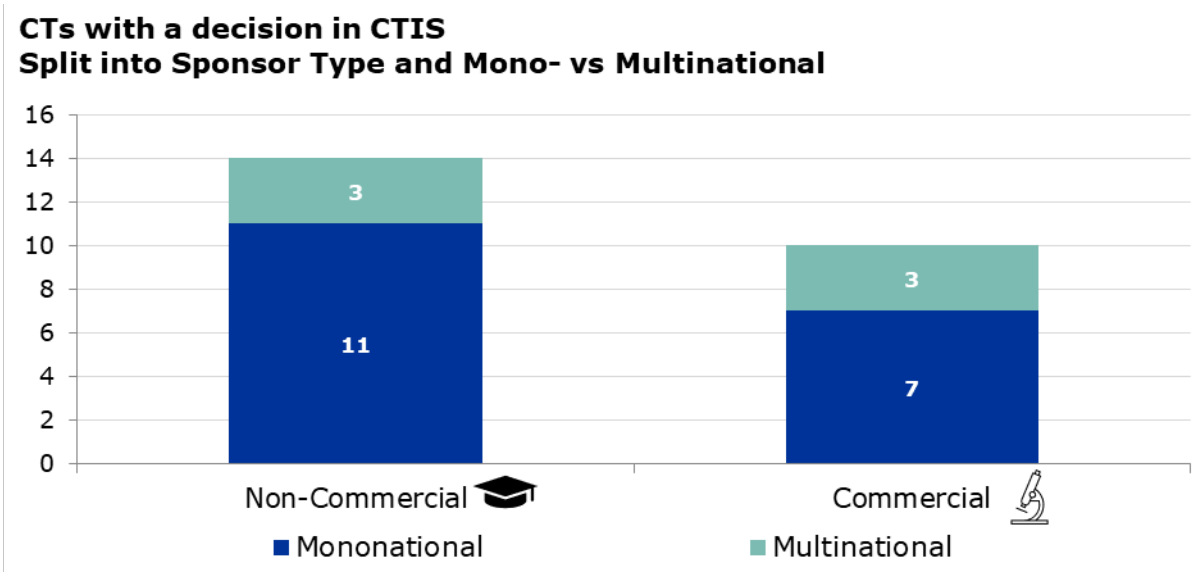
[6] The figures presented below are based on distinct counts of CTA, if the same protocol is submitted to more than one MSC is counted once.
[7] The data for January that appear in the graph below refers to CTA uploaded by the Member State on the 31 January only
[8] Details on recruitment status are based on the information reported by the trial sponsor in CTIS
[9] The option to defer the protocol is only available in CTIS.
[10] Deferral is a functionality implemented in CTIS that has been introduced to reduce the burden of redaction (deletion) of commercially confidential information (CCI) in the documents uploaded in CTIS. More information on deferrals can be found in the Appendix on disclosure rules

1.5. Number of mononational-multinational trials for which 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[11]

The graph below shows the number of trials for which a decision has been issued in CTIS by the Member State Concerned, per month, since 31 January 2022. The trials reflected in the graph below have been authorised, authorised with conditions and not authorised.



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



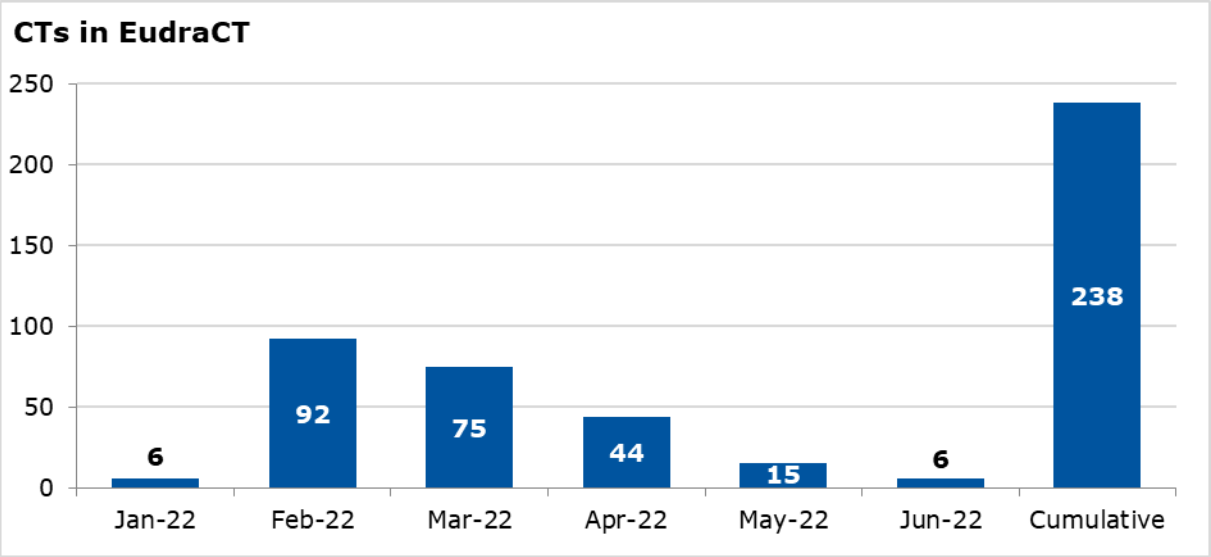
Currently six multinational clinical trial have a decision in CTIS with an average of 6 Member States Concerned.

[11] 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.

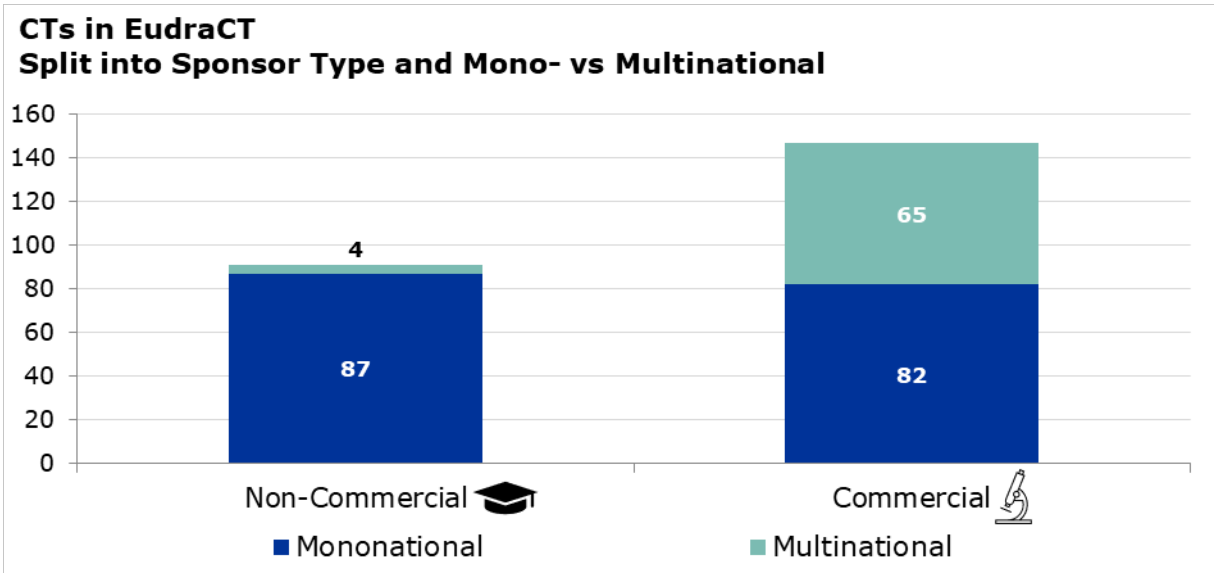
1.6. Number of mononational-multinational trials for which a NCA decision and an Ethics Committee opinion have been issued by the Member States under the Clinical Trials Directive, broken down per sponsor type (commercial vs. non-commercial) and average number of MSs

The graph below shows the number of trials that received a National Competent Authority decision and an Ethics Committee opinion from the Member States, per month, since 31 January 2022[12] 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 for which a decision and an opinion have been issued, with information whether the trial is a mono- or multinational and in relation to sponsor type.

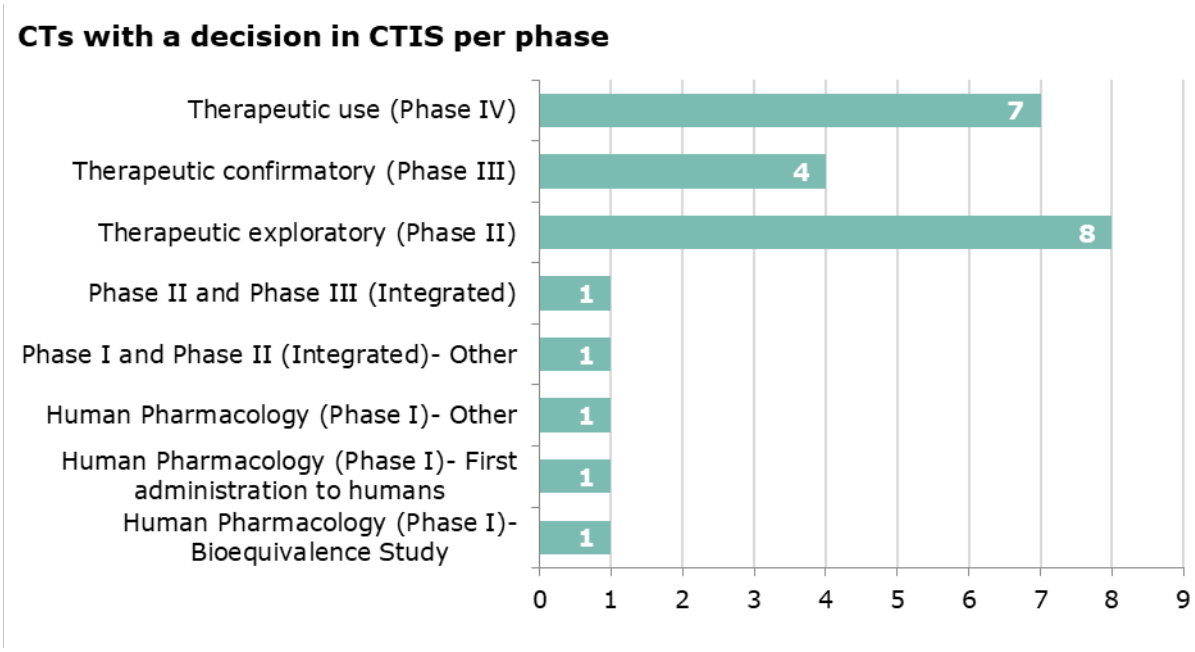


[12] The data for January that appear in the graph below refers to CTA with a decision for the 31 January only.

Considering clinical trials for which a decision and an opinion have been issued, on average 2 Member States are involved in multinational trials.

1.7. Number of clinical trials for which a decision has 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 CTR[13]

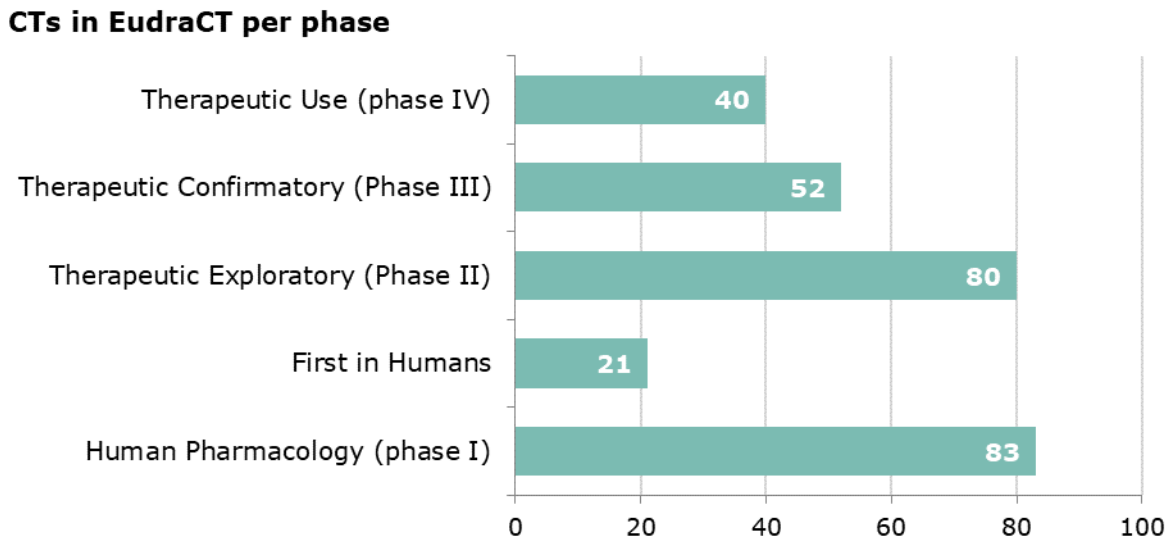
The graph below shows the number of clinical trials for which a decision has been issued, broken down per trial phase.



1.8. Number of 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[14]

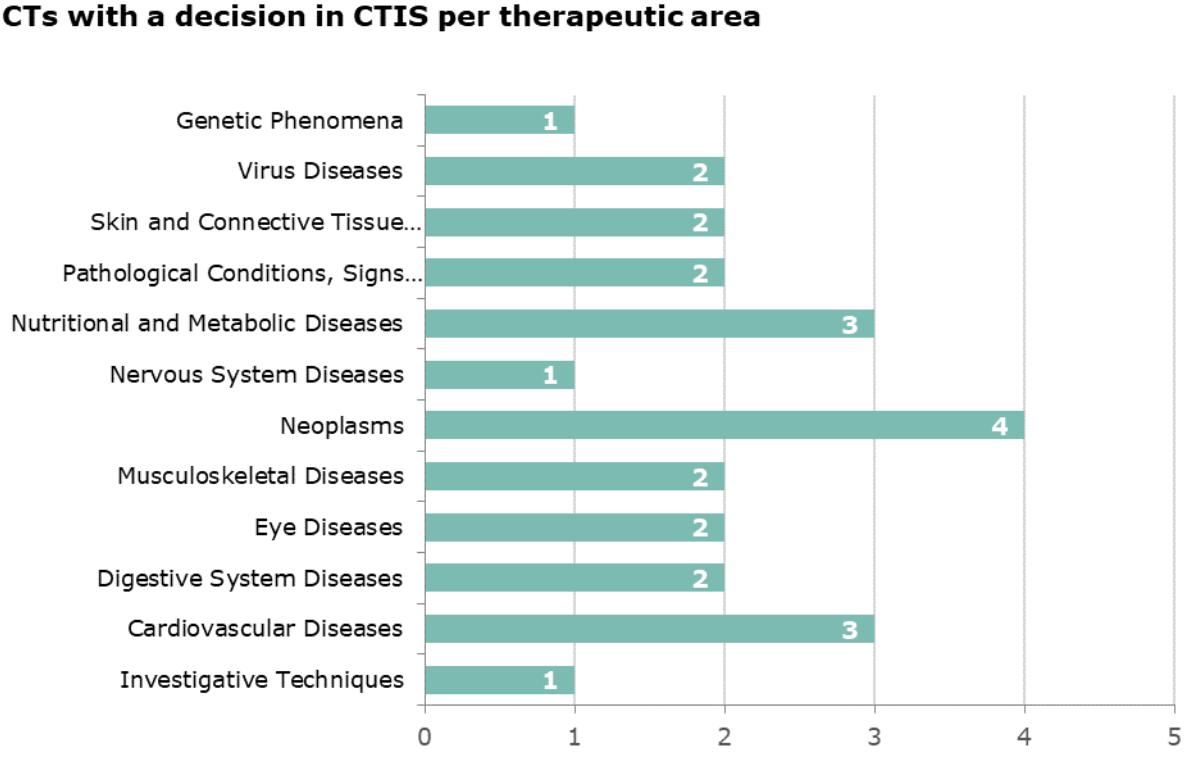
The graph below shows the number of clinical trials, as individual clinical trial protocol, for which a decision and an opinion have been issued by the Member States in EudraCT, broken down per trial phase.

[13] 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.
[14] 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. Number of trials for which a decision has been issued under CTR, per therapeutic area[15]

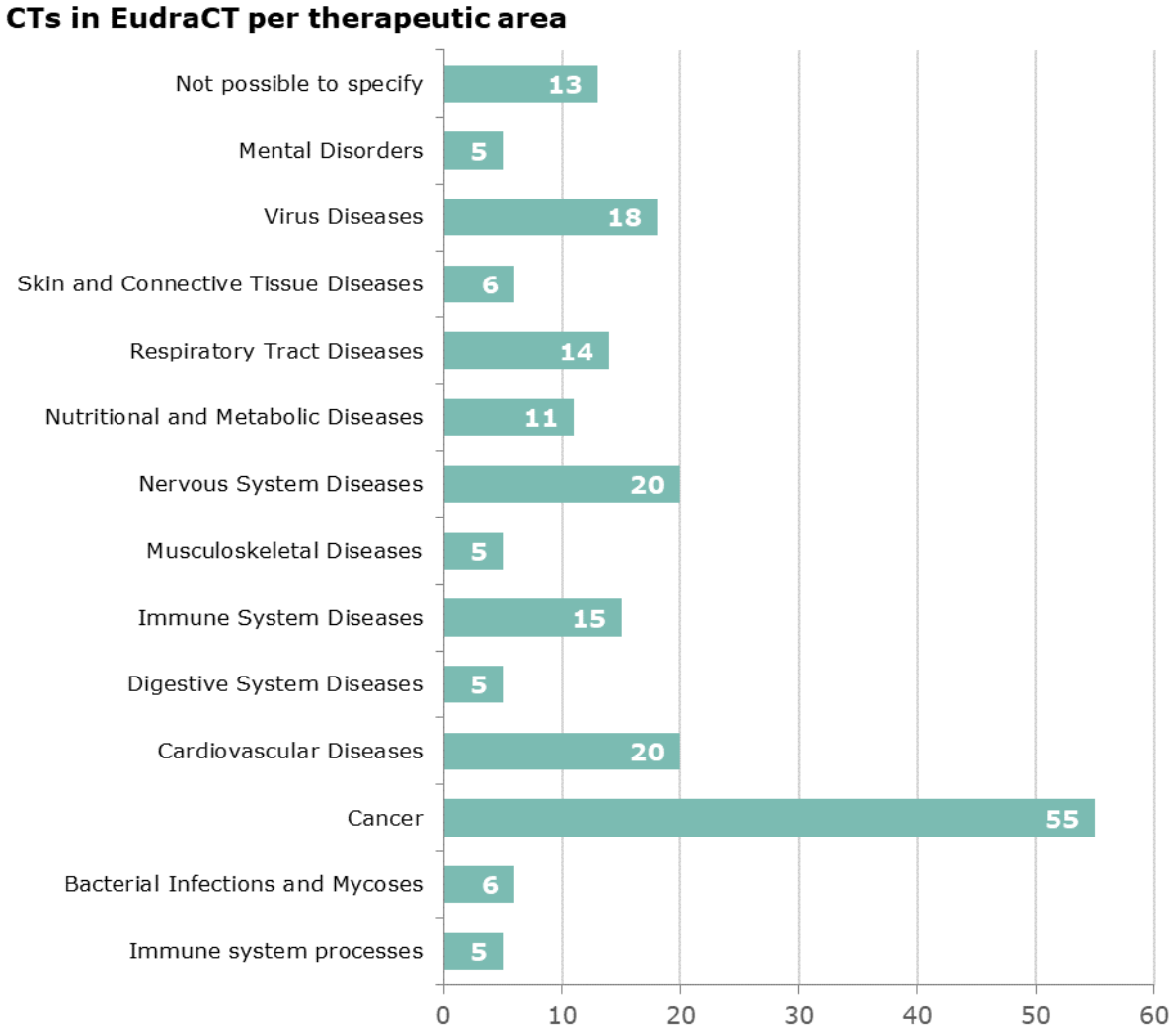
The graph below shows the number of clinical trials for which a decision has been issued in CTIS, broken down per therapeutic area.



[15] More than one therapeutic area can be selected for a single trial and it is counted in each trial. The graph shows the applicable trials therapeutic areas in the selected period.

1.10. Number of trials for which a NCA decision and an Ethics Committee opinion have been issued under CTD, per therapeutic area[16]

The graph below shows the number of trials, as individual clinical trial protocol, for which a decision and an opinion have been issued by the Member States in EudraCT, broken down per therapeutic area.[17]



1.11. Number of trials for which a decision has been issued on Advanced Therapy Medicinal Products (ATMP) under CTR

None of the clinical trials for which a decision has been issued in CTIS during the selected period includes an Advanced Therapy Medicinal Product.

[16] It should be noted that more than one therapeutic area can be selected for a single trial and it is counted in each trial. The graph shows the applicable trials therapeutic areas in the selected period displaying only therapeutic areas selected in 5 or more clinical trials, but not less.

[17] 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

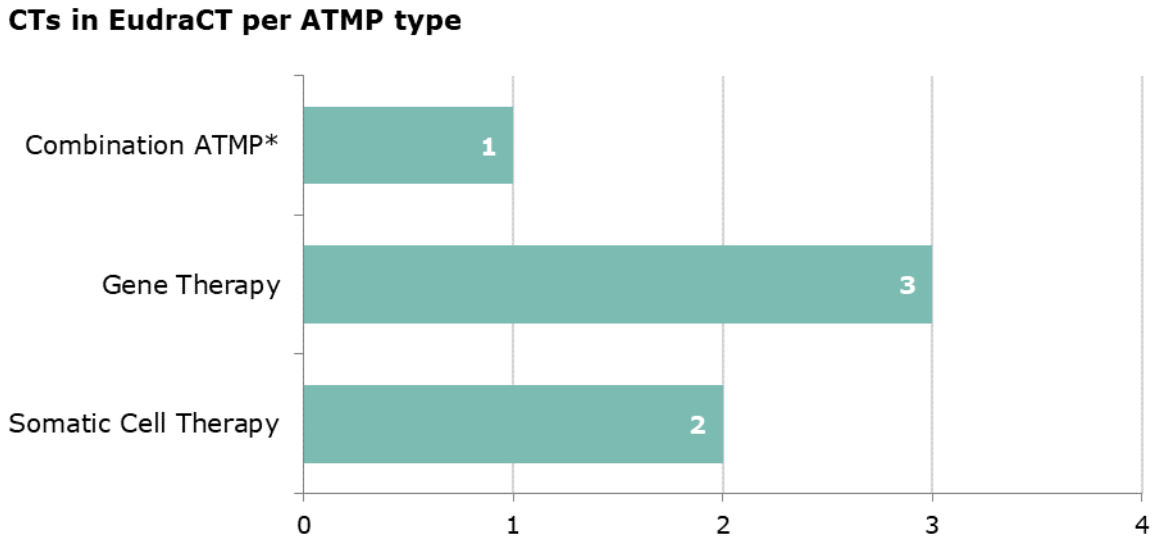
1.12. Number of trials for which a decision has been issued, with ATMP of type "gene therapy", "somatic cell therapy" and "tissue engineered therapy" under CTR

None of the clinical trials for which a decision has been issued in CTIS during the selected period includes an Advanced Therapy Medicinal Product of type: gene therapy, somatic cell therapy and tissue engineered therapy.

1.13. Number of trials for which a NCA decision and an Ethics Committee opinion have been issued, with ATMP of type "gene therapy", "somatic cell therapy" and "tissue engineered therapy" under CTD

There were six clinical trials with a decision and an opinion issued by 30 June 2022 including an advanced therapy medicinal products.

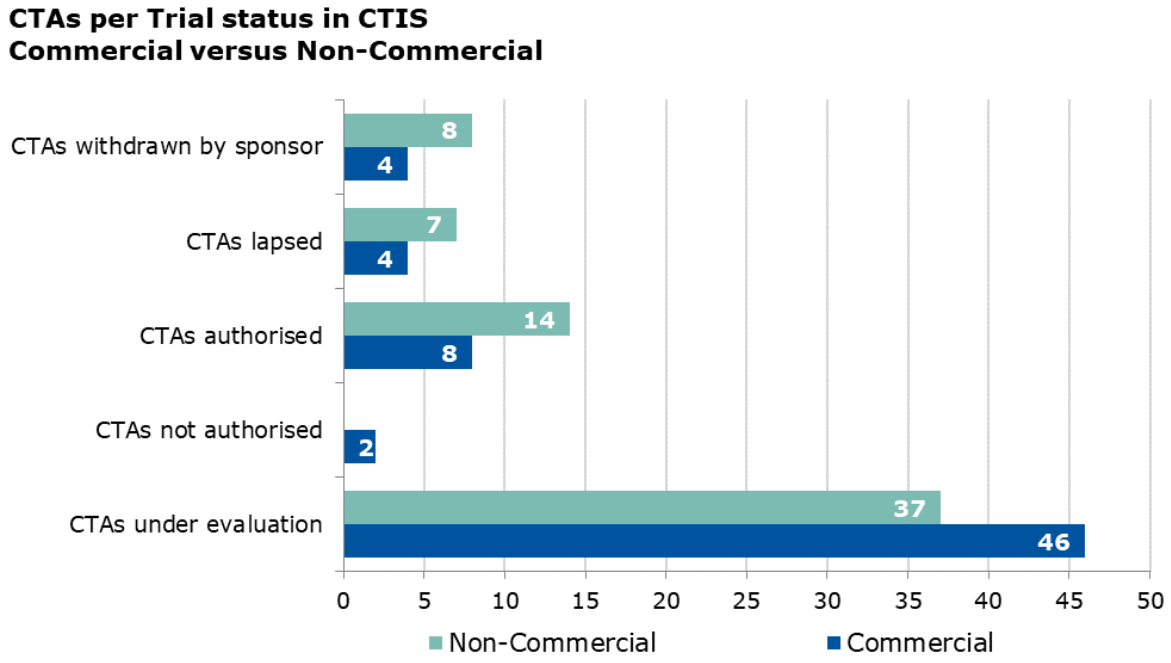
The graph below shows the number of clinical trials per ATMP type as reported in EudraCT.



* Combination ATMP with a medical device.

1.14. Number of 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[18] and information of sponsor type submitted in CTIS since 31 January 2022.



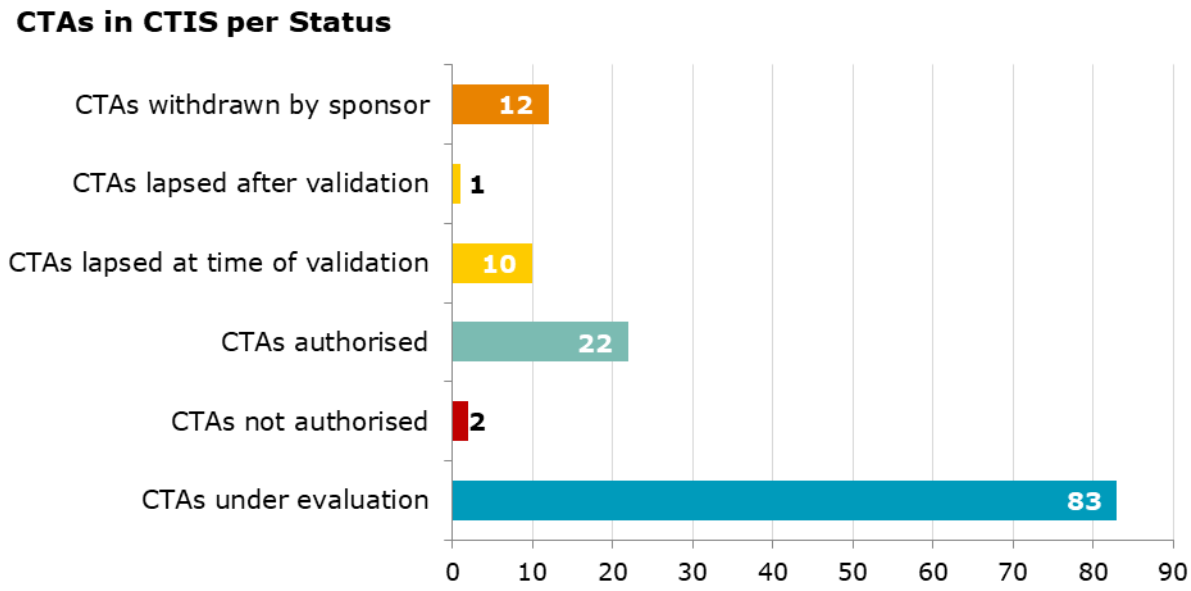
1.15. Art 14 applications: (re-)submission, authorisation, rejection, lapsed and withdrawn dossiers

One clinical trial application has been submitted in CTIS as of 30 June 2022, for the addition of a new MSC foreseen under Article 14 of Regulation (EU) No 536/2014.

1.16. Number of CTAs Article 5 of CTR [full dossier initial applications] per applicable trial status during the reporting period, at EU, at MS level and with Reporting Member State (RMS) details

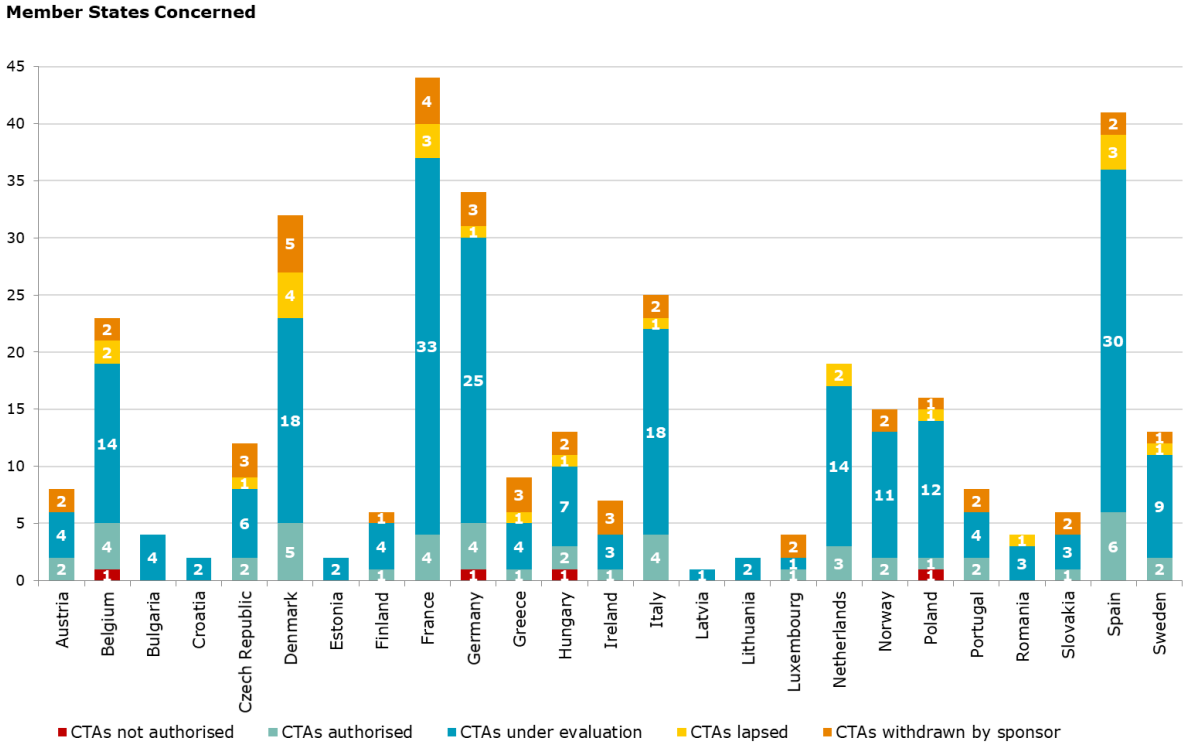
The graph below shows the number of initial clinical trial applications with full dossier, submitted in accordance with Article 5 of CTR since 31 January 2022, per applicable overall status at EU level.

[18] Overall trial status is the status per application and not per individual Member State Concerned.



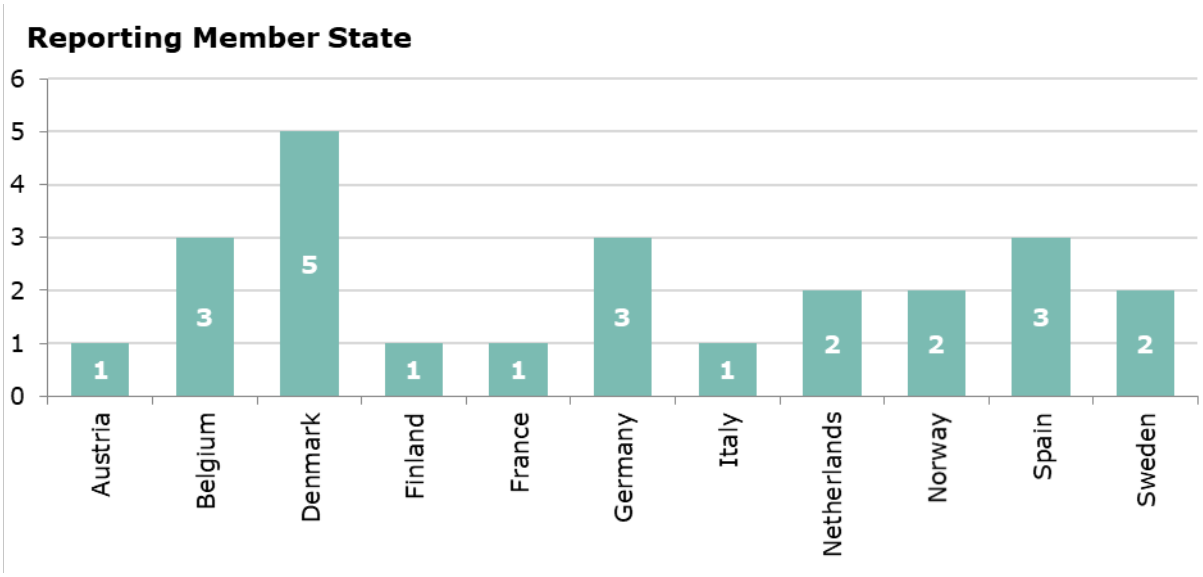
It can be noted an increase of 20% of clinical trial applications under evaluation and authorisation of clinical trial applications have nearly tripled compared to the previous reporting period.

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[19].



[19] 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)[20], amongst the applicable Member States Concerned, for clinical trial applications on which a decision has been issued.



1.17. 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.

1.18. Average time from submission to reporting date[21] (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 74 calendar days to issue a decision, during the selected period, for the 24 initial clinical trial applications. More details can be found in Annex I.

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

There were two applications in CTIS related to submission of substantial modifications as foreseen in Chapter II of the Regulation (EU) No 536/2014. The applications were both under evaluation as of 30 June 2022.

1.20. Number of active substances (ASs) in CTR EU trials (mononational and multinational AS)

A saMS has been appointed during the reporting period for the following substances:

Giredestrant, Trastuzumab, Pertuzumab.

[20] RMS is the Reporting Member State appointed in line with the requirements of Article 5 of the Clinical Trials Regulation (EU) No 536/2014
[21] The reporting date is equal to the date of the RMS conclusion on part I assessment

1.21. Number of safety assessing Member State (saMS)-ships per MS

The role of safety assessing Member State Concerned (saMS) will be applicable only for multinational clinical trials. One saMS (Germany) has been appointed during the selected reporting period for the active substances listed in point 1.20 above.

Annex I –Average time from submission to decision for initial CTAs

The table below shows the number of calendar days since the submission of the initial clinical trial application to CTIS up to the time of the first decision of the Member States Concerned.

Submission date	Decision date	Days to Decision
15/02/2022	02/06/2022	107
24/02/2022	16/06/2022	112
07/03/2022	28/06/2022	113
20/02/2022	30/05/2022	99
08/04/2022	28/06/2022	81
01/04/2022	01/06/2022	61
09/02/2022	07/04/2022	57
04/03/2022	31/05/2022	88
24/03/2022	30/06/2022	98
15/02/2022	27/04/2022	71
28/02/2022	28/03/2022	28
24/03/2022	14/06/2022	82
06/05/2022	23/06/2022	48
10/03/2022	19/05/2022	70
29/03/2022	22/06/2022	85
04/03/2022	21/06/2022	109
18/04/2022	27/05/2022	39
15/03/2022	27/04/2022	43
30/05/2022	22/06/2022	23
02/05/2022	07/06/2022	36
26/04/2022	28/06/2022	63
18/05/2022	28/06/2022	41
16/03/2022	27/06/2022	103
03/03/2022	27/06/2022	116