



27 October 2022
EMA/799170/2022

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

Metrics on the Clinical Trials Regulation and Clinical Trials Directive

1 – 30 September 2022, edition 6

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 EudraCT¹ as of 30 September for Clinical Trial applications (CTA) submitted between 1-30 September 2022² 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

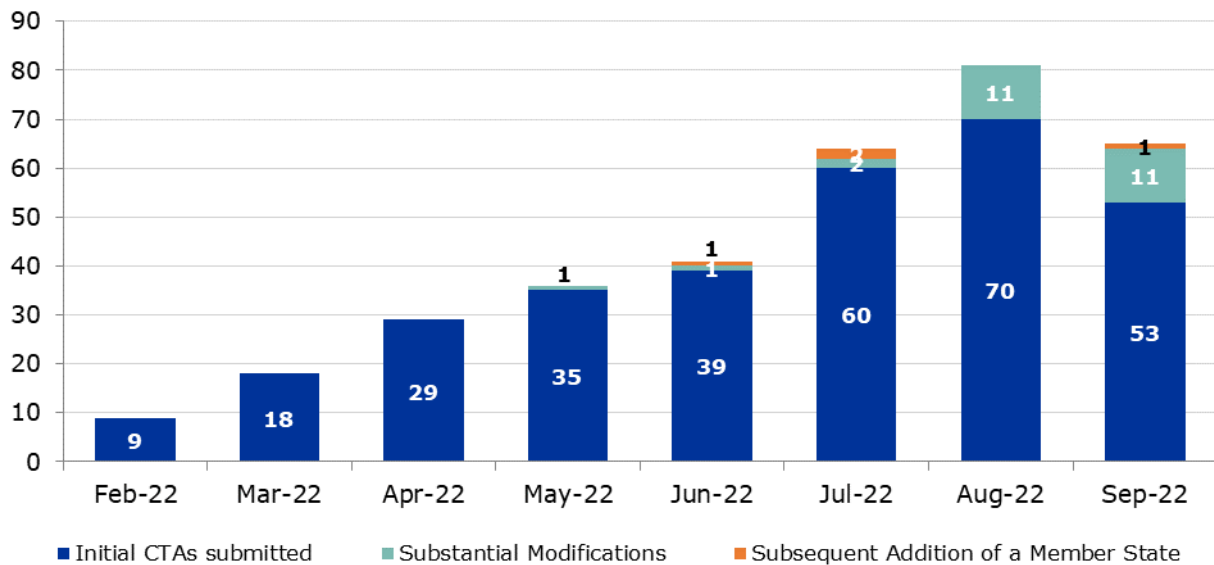
This report shows the key performance indicators (KPIs) generated from the two databases containing information on clinical trials in the EU/EEA, namely CTIS and EudraCT.

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 September 2022 include initial clinical trial applications³, substantial modifications⁴ and addition of a new Member State Concerned⁵ applications in the selected period.⁶

CTAs submitted in CTIS per month



Overall, 343 clinical trial applications have been submitted in CTIS since the launch of the system on 31 January 2022, of which 313 are initial clinical trial applications, 26 are substantial modification applications and 4 are applications for the addition of a new Member State Concerned.

Of the submitted applications during September 2022, 5 are re-submissions, 1 of previous lapsed application, 3 of previously withdrawn applications and 1 of previously not-authorized application.

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

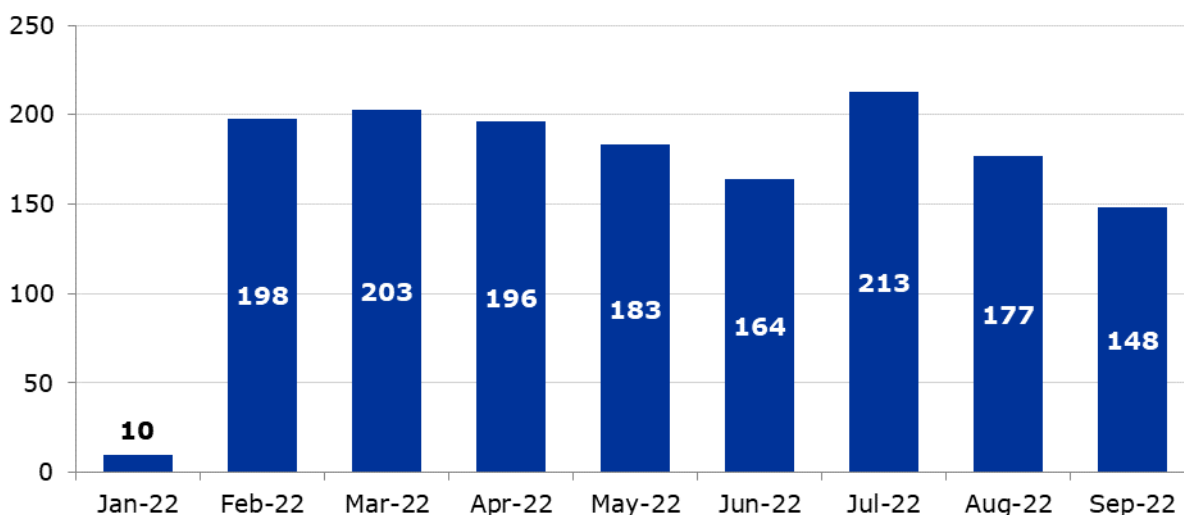
⁵ Applications to add a new Member States Concerned are submitted in accordance with the requirements of Article 14 of Regulation (EU) No 536/2014

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 shows⁷ the number of CTAs uploaded by the Member States in EudraCT as individual clinical trial protocol⁸, per month during the selected period⁹.

CTAs uploaded by Member States in EudraCT (CTAs are counted as individual trial protocol)



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 sites¹⁰.

As of 30 September 2022, 17 clinical trials were reported as ongoing.

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 deferral¹¹ for the protocol

There were 8 clinical trials for which a decision has been issued in September 2022, with deferrals¹² of the protocol, therefore the protocols have not been published.

⁷ Corrigendum: the graph shows the corrected figures for initial clinical trial applications submitted in EudraCT. The incorrect calculations reported in previous editions of this document were due to an error in the reporting system.

⁸ The figures presented below are based on distinct counts of CTA, if the same protocol is submitted to more than one MSC it is counted only once, based on the first Member State that had uploaded the application in EudraCT.

⁹ The data for January that appear in the graph below refers to CTA uploaded by the Member State on the 31 January only

¹⁰ Details on recruitment status are based on the information reported by the trial sponsor in CTIS

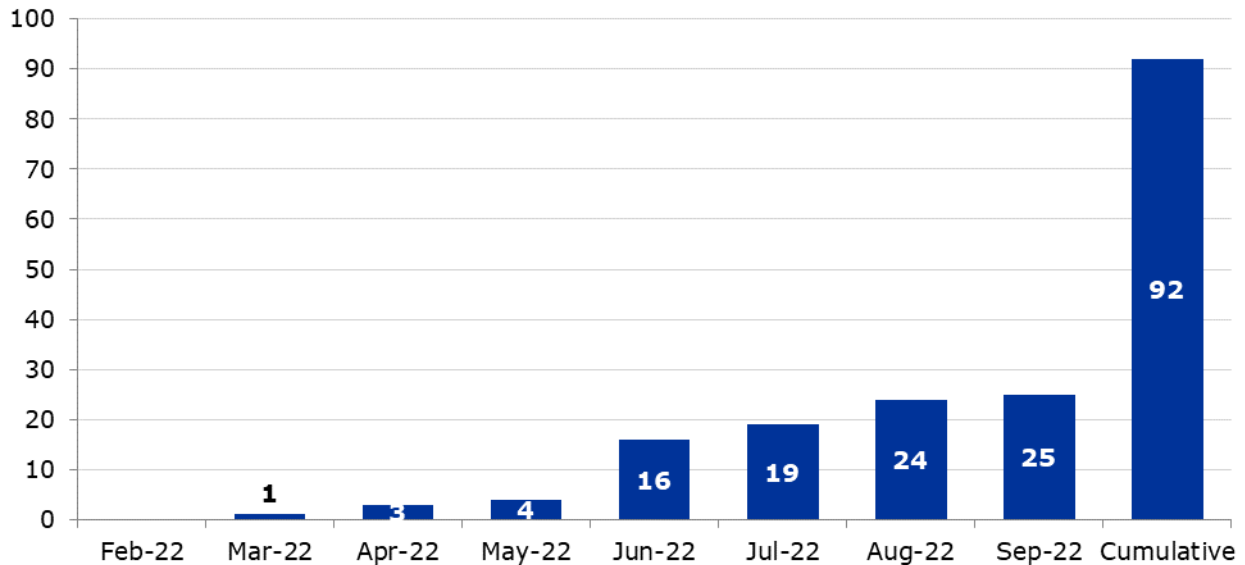
¹¹ The option to defer the protocol is only available in CTIS.

¹² 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 MSCs¹³

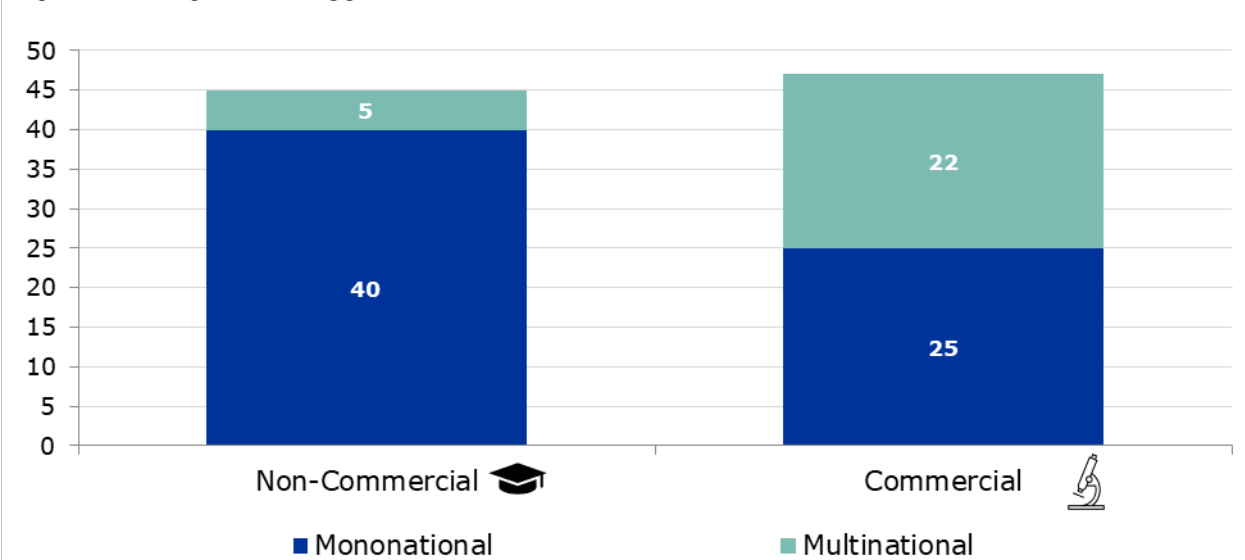
The graph below shows the number of trials for which a decision has been issued in CTIS by the Member State Concerned, per month, since 31 January 2022. The trials reflected in the graph below have been authorised, authorised with conditions and not authorised.

CTs with a decision in CTIS



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.

**CTs with a decision in CTIS
Split into Sponsor Type and Mono- vs Multinational**



¹³ 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.

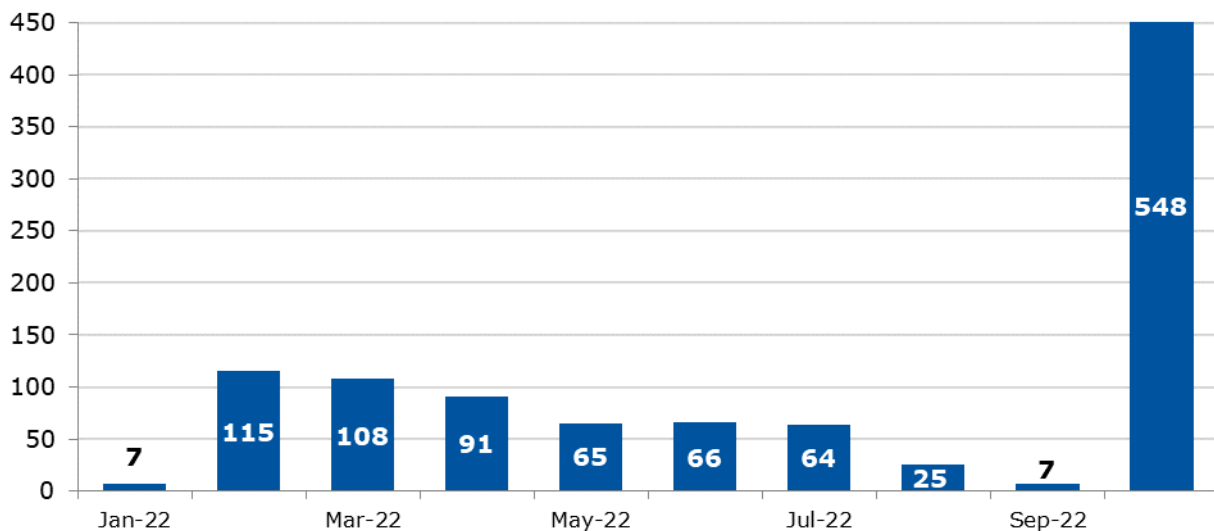
Currently 27 multinational clinical trial have a decision in CTIS with an average of 6 Member States Concerned.

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, 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 2022¹⁴ 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.

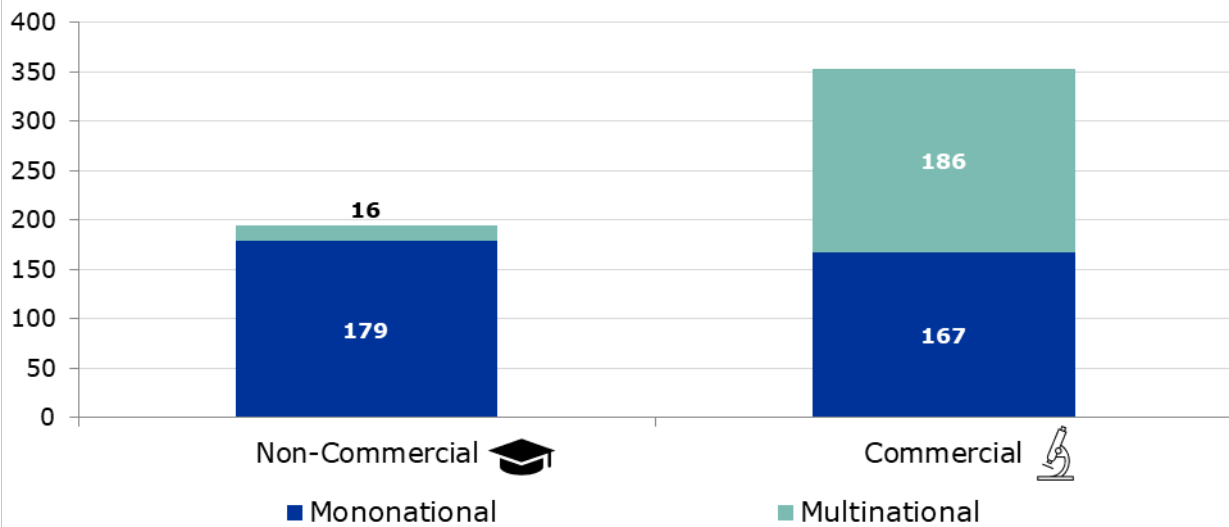
CTs in EudraCT



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.

¹⁴ The data for January that appear in the graph below refers to CTA loaded in EudraCT the 31st January having a subsequent decision by the national Competent Authority and Ethic Committee opinion loaded in EudraCT..

CTs in EudraCT Split into Sponsor Type and Mono- vs Multinational

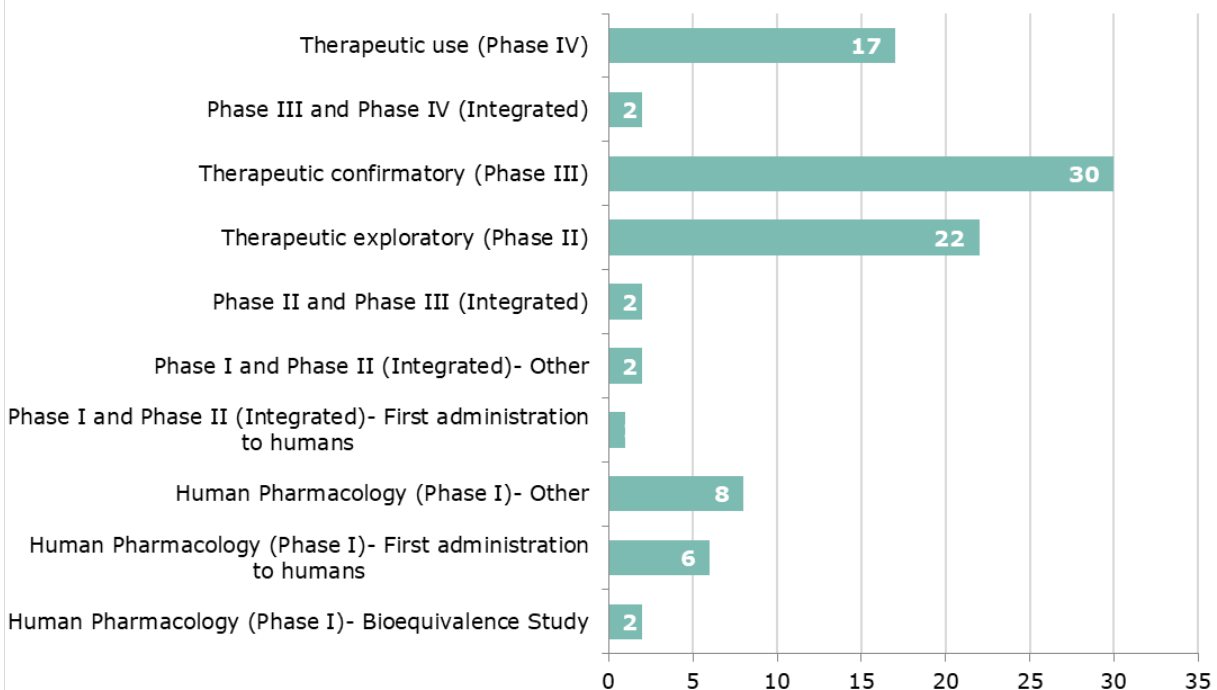


Considering clinical trials for which a decision and an opinion have been issued, on average 3 Member States are involved in multinational trials.

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 CTR¹⁵

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

CTs with a decision in CTIS per phase

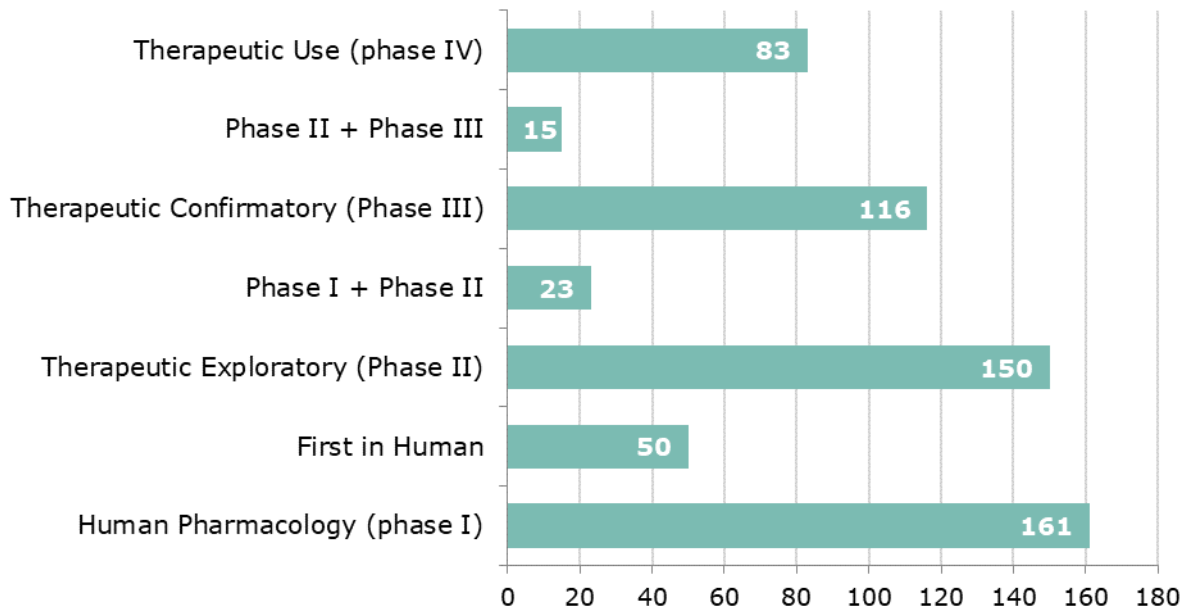


¹⁵ More than one trial phase can be selected for a single trial and it is counted in each trial. The graph shows the applicable trial phases in the selected period.

1.8. 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

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

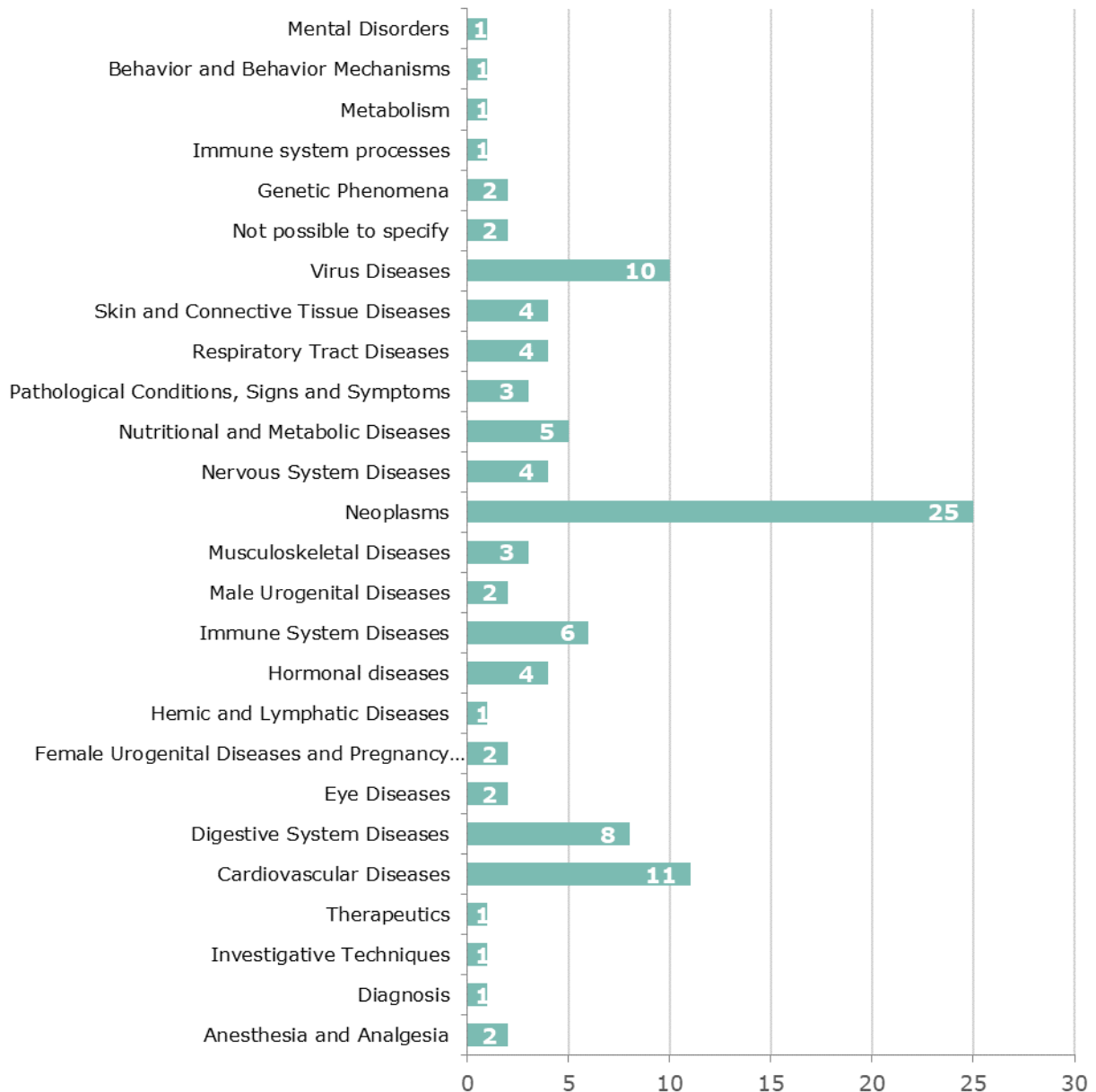
CTs in EudraCT per phase



1.9. Number of trials for which a decision has been issued under CTR, per therapeutic area¹⁶

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

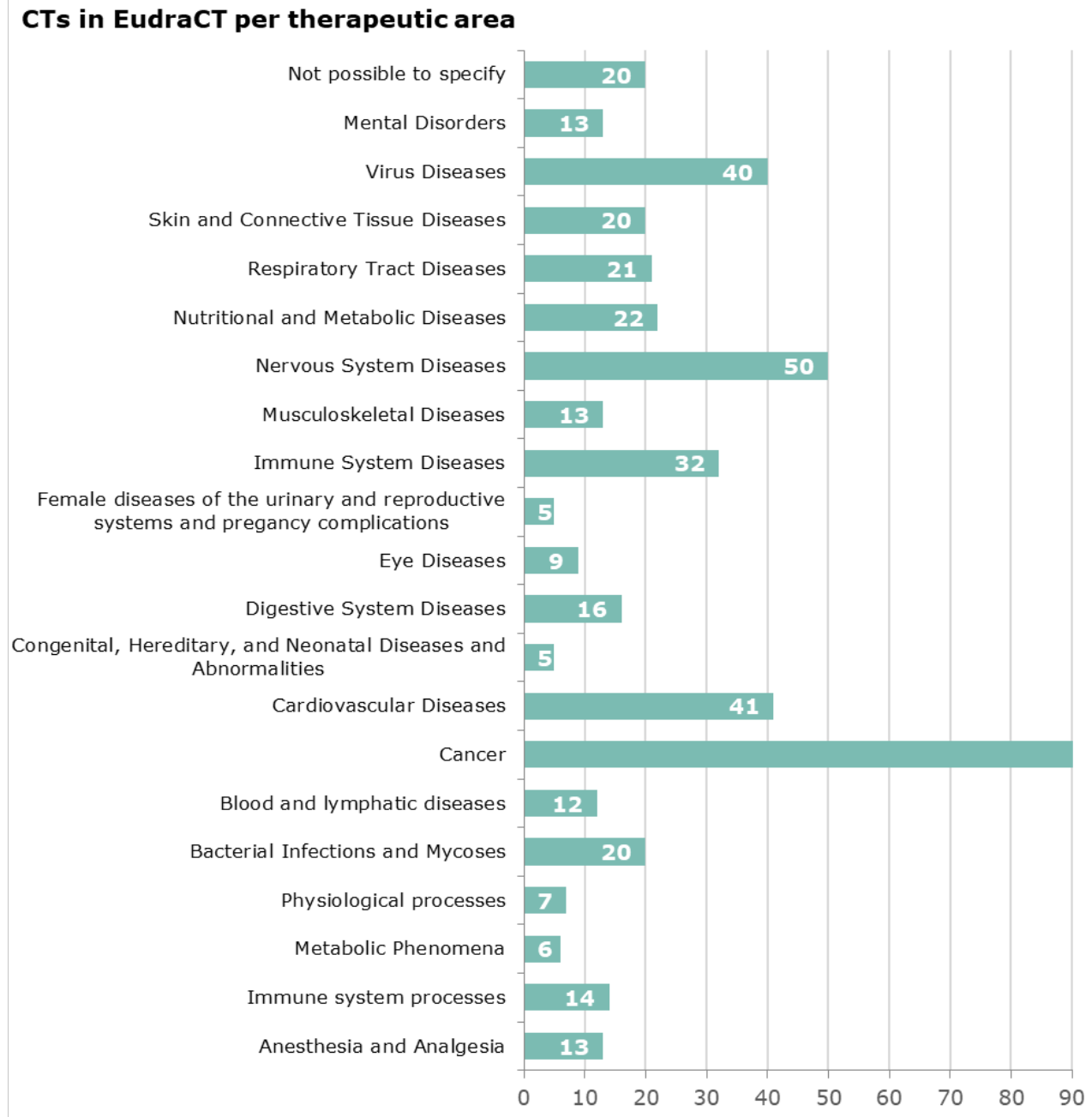
CTs with a decision in CTIS per therapeutic area



¹⁶ In case a clinical trial investigates several therapeutic areas, it is counted in each of such identified therapeutic areas.

1.10. Number of trials for which a NCA decision and an Ethics Committee opinion have been issued under CTD, per therapeutic area¹⁷

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, broken down per therapeutic area.¹⁸



¹⁷ In case a clinical trial investigates several therapeutic areas, it is counted in each of such identified therapeutic areas. 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.

¹⁸ 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

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

One of the clinical trials for which a decision has been issued in CTIS includes an Advanced Therapy Medicinal Product in the area of Tissue Engineered Therapy.

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

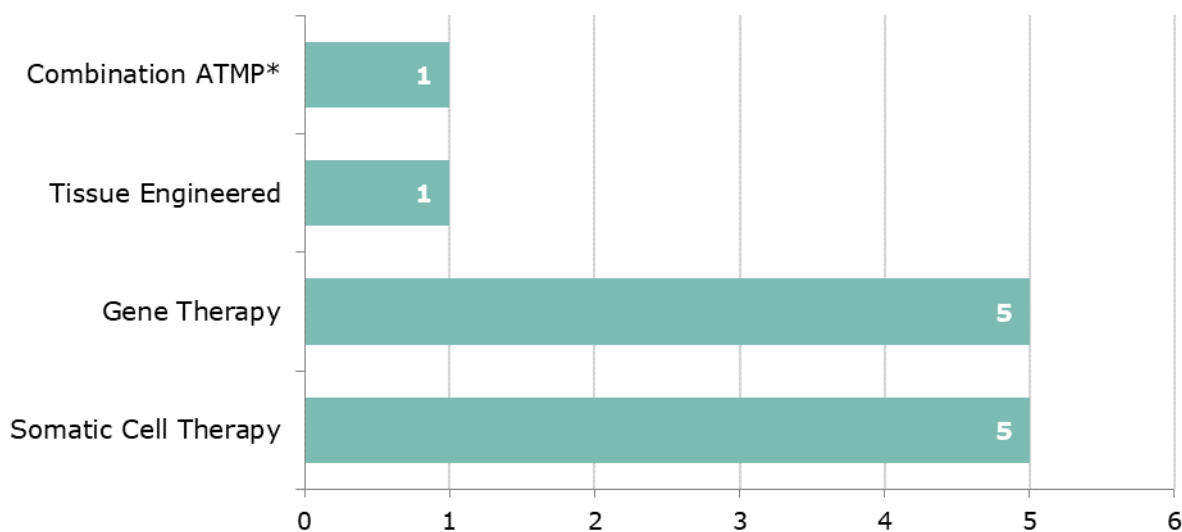
One of the clinical trials for which a decision has been issued in CTIS includes an Advanced Therapy Medicinal Product in the area of Tissue Engineered Therapy.

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 12 clinical trials in EudraCT since 31 January 2022, with a decision and an opinion issued by 30 September 2022 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.

CTs in EudraCT per ATMP type

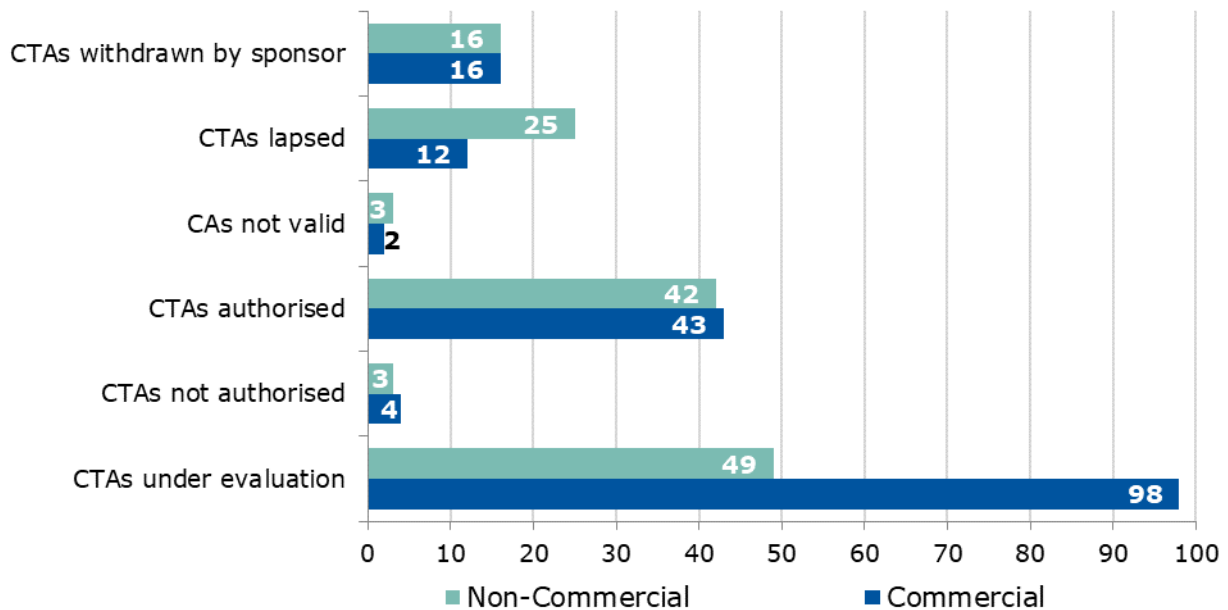


* Combination ATMP with a medical device.

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 status¹⁹ and information of sponsor type submitted in CTIS since 31 January 2022.

**CTAs per Trial status in CTIS
Commercial versus Non-Commercial**



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

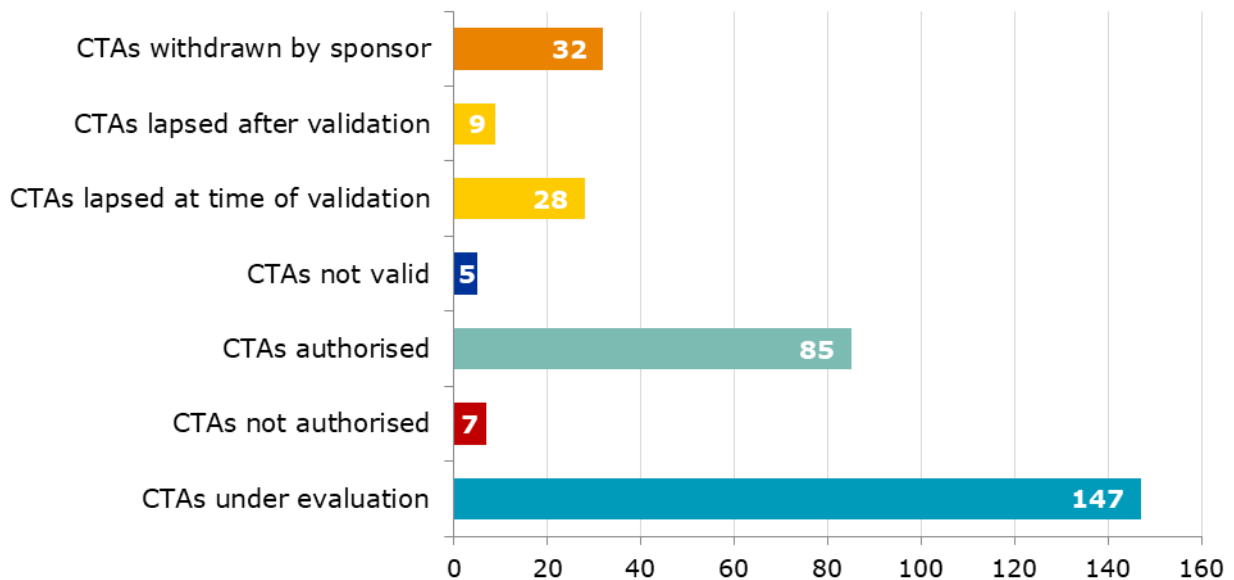
As of 30 September 2022 4 clinical trial applications for the addition of a new MSC, foreseen under Article 14 of Regulation (EU) No 536/2014, have been submitted in CTIS for 3 clinical trials.

¹⁹ Overall trial status is the status per application and not per individual Member State Concerned.

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.

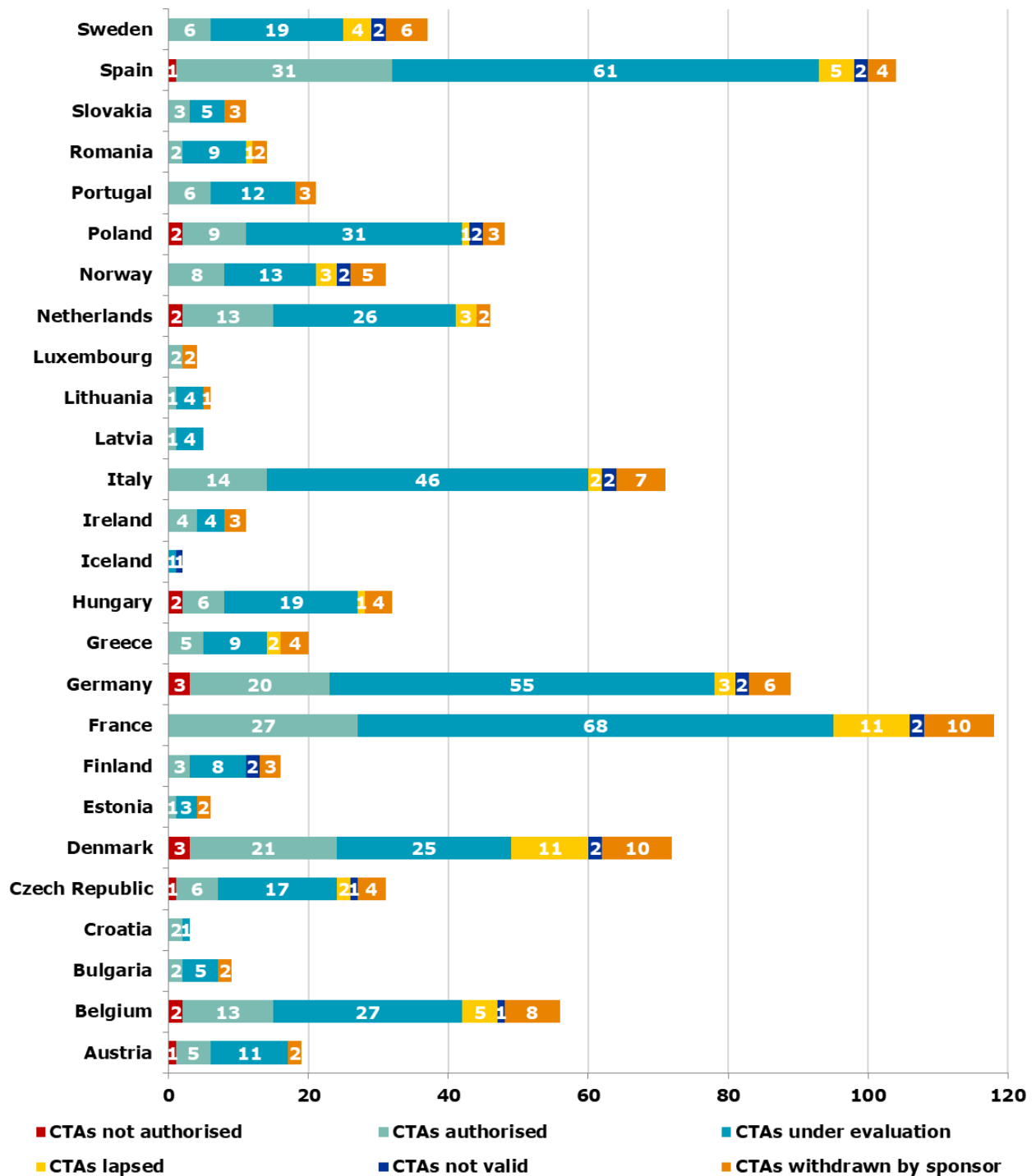
CTAs in CTIS per Status



It can be noted an increase of 10% of clinical trial applications under evaluation and authorisation of clinical trial applications have increased by 35% 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 Concerned²⁰.

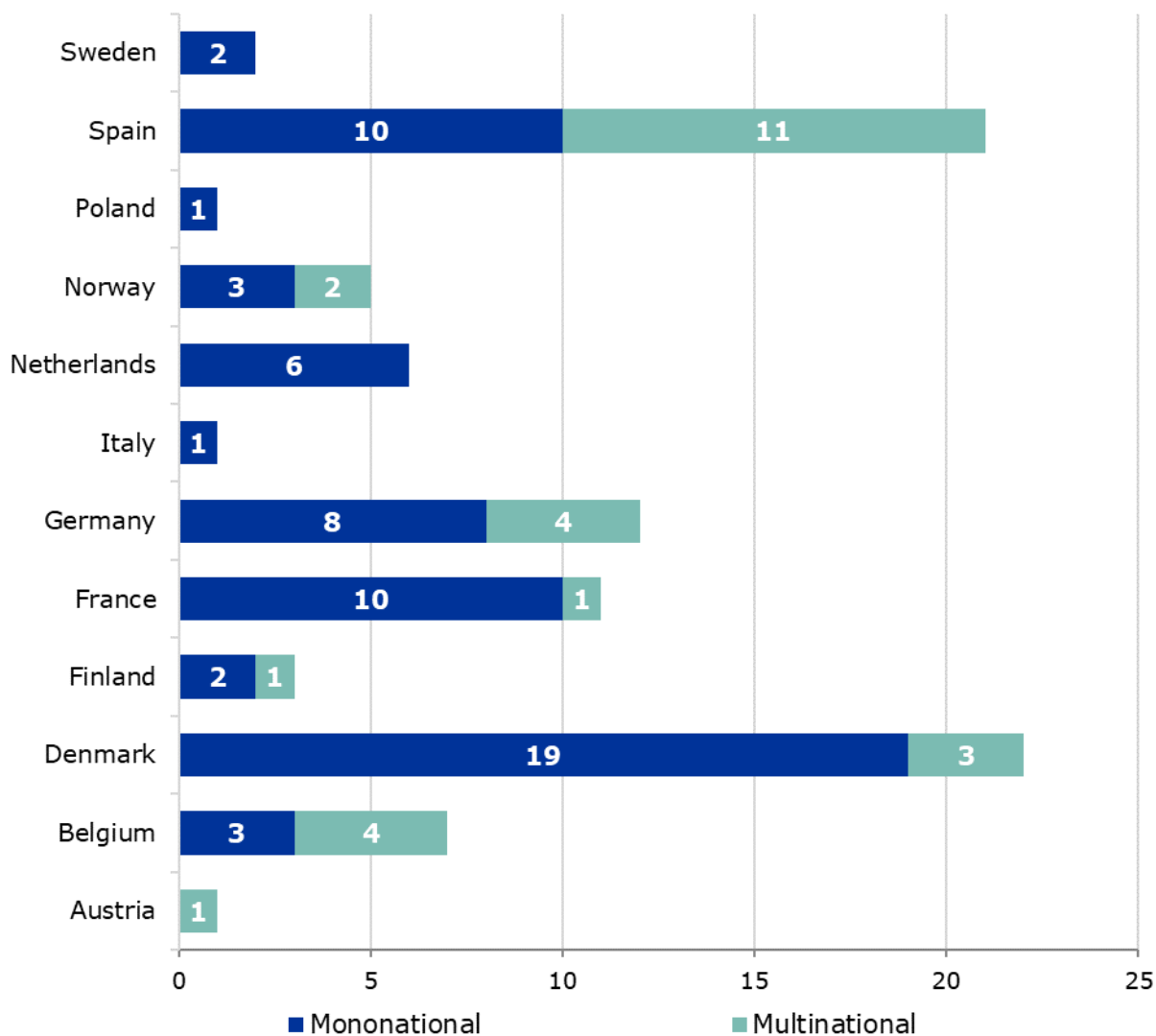
Member States Concerned



²⁰ 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)²¹, 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



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.

²¹ RMS is the Reporting Member State appointed in line with the requirements of Article 5 of the Clinical Trials Regulation (EU) No 536/2014

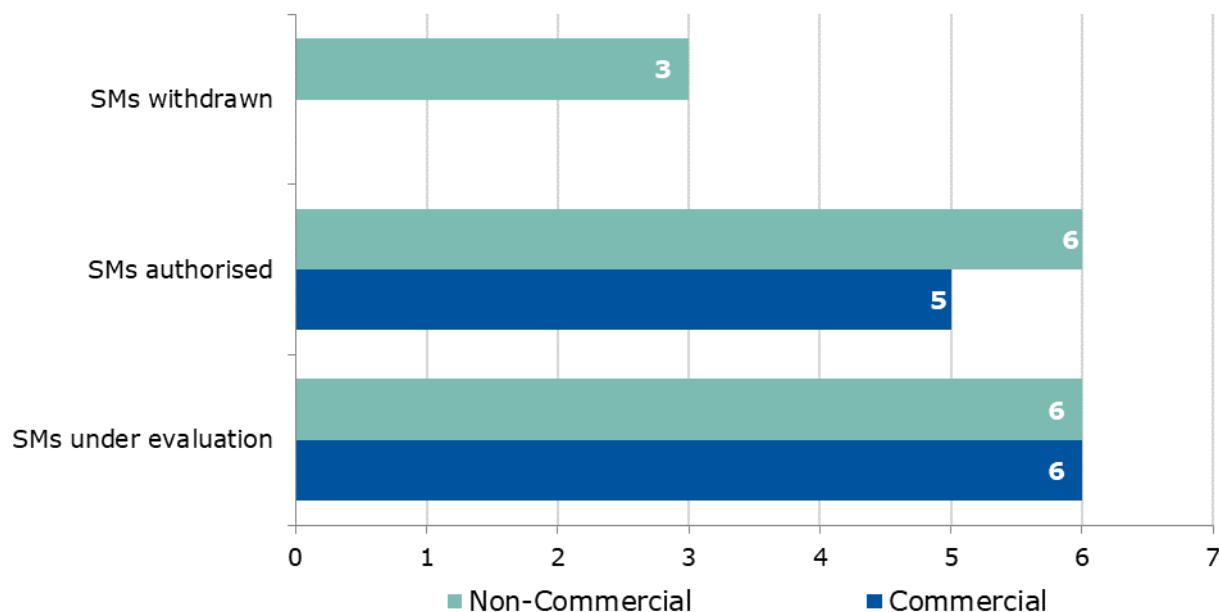
1.18. Average time from submission to reporting date²² (Article 11 and Article 5 of CTR), and to first decision (Article 5 of CTR) for initial applications and Substantial Modifications part I or part I and II

On average it took 81 calendar days to issue a decision, during the selected period, for the 92 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

As of 30 September 2022 applications for substantial modifications, foreseen in chapter II of Regulation (EU) No 536/2014, were submitted in CTIS for 20 clinical trials and correspond to 26 distinct substantial modifications.

**SMs status' in CTIS
Commercial versus Non-Commercial**



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

During the reporting period saMS²³ were appointed for the following 8 active substances: Abemaciclib, Florbetaben (18F), Fulvestrant, Marstacimab, Pembrolizumab, RLY-2608, Ruxotemitide, and Sibeprenlimab.

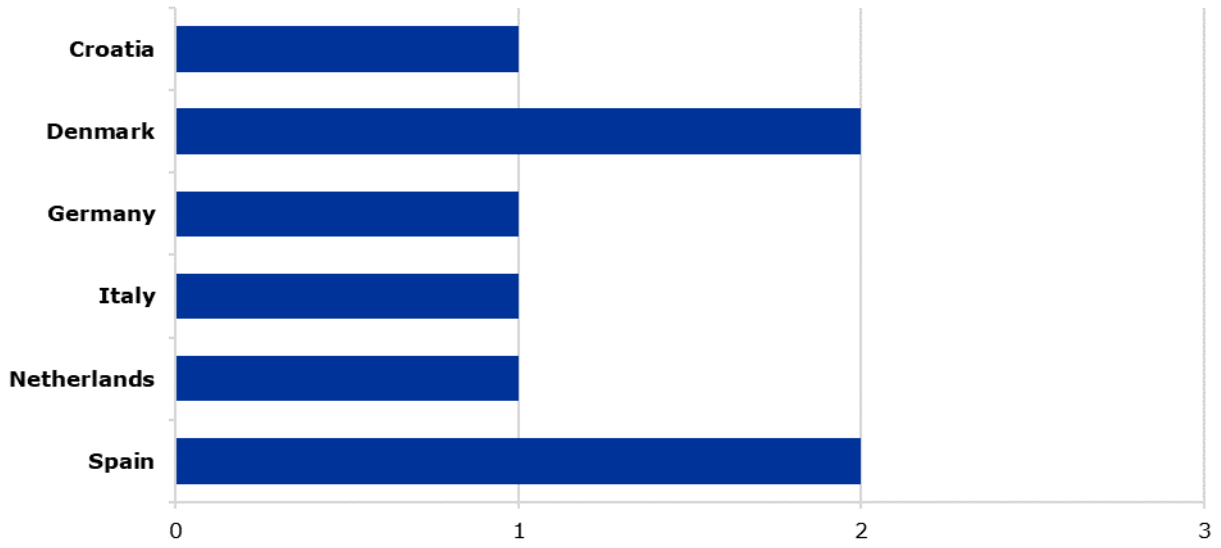
1.21. Number of safety assessing Member State (saMS)-ships per MS

The role of safety assessing Member State Concerned (saMS) will be applicable only for active substances investigated in clinical trials in two or more MSC. During the selected reporting period, 6 saMSs (Croatia, Denmark, Germany, Italy, the Netherlands and Spain) have been appointed for the active substances listed in point 1.20 above.

²² The reporting date is equal to the date of the RMS conclusion on part I assessment

²³ Safety Assessing Member State

Number of saMS appointments per Member States



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.

Please consider that due dates for tasks completion, including decision, in CTIS takes into account rules such as: allowing 2 consecutive working days, the due date cannot fall on weekend nor on a bank holiday in addition to counting the calendar days.

The list of clinical trials below include resubmitted applications.

#	Submission date	Decision date	Days to Decision
1	15/02/2022	02/06/2022	107.00
2	24/02/2022	16/06/2022	112.00
3	07/03/2022	28/06/2022	113.00
4	20/02/2022	30/05/2022	99.00
5	08/04/2022	28/06/2022	81.00
6	01/04/2022	01/06/2022	61.00
7	03/03/2022	27/06/2022	116.00
8	09/02/2022	07/04/2022	57.00
9	10/05/2022	04/08/2022	86.00
10	12/05/2022	31/08/2022	111.00
11	29/04/2022	05/08/2022	98.00
12	31/03/2022	26/07/2022	117.00
13	03/05/2022	24/08/2022	113.00
14	04/03/2022	31/05/2022	88.00
15	24/03/2022	30/06/2022	98.00
16	05/04/2022	18/07/2022	104.00
17	22/04/2022	28/07/2022	97.00
18	15/02/2022	27/04/2022	71.00
19	28/02/2022	28/03/2022	28.00
20	20/05/2022	08/07/2022	49.00
21	22/04/2022	05/08/2022	105.00
22	24/03/2022	14/06/2022	82.00
23	28/04/2022	24/08/2022	118.00
24	20/07/2022	22/09/2022	64.00
25	14/04/2022	28/07/2022	105.00
26	16/03/2022	27/06/2022	103.00
27	06/04/2022	12/07/2022	97.00
28	19/04/2022	03/08/2022	106.00
29	10/05/2022	26/07/2022	77.00
30	17/05/2022	09/09/2022	115.00
31	28/04/2022	16/08/2022	110.00
32	06/05/2022	23/06/2022	48.00
33	18/05/2022	01/09/2022	106.00

#	Submission date	Decision date	Days to Decision
34	09/05/2022	18/07/2022	70.00
35	10/03/2022	19/05/2022	70.00
36	03/06/2022	21/09/2022	110.00
37	29/03/2022	22/06/2022	85.00
38	04/03/2022	21/06/2022	109.00
39	19/04/2022	05/07/2022	77.00
40	18/04/2022	27/05/2022	39.00
41	15/03/2022	27/04/2022	43.00
42	28/03/2022	19/07/2022	113.00
43	05/05/2022	01/08/2022	88.00
44	14/04/2022	28/07/2022	105.00
45	31/05/2022	23/09/2022	115.00
46	12/05/2022	01/09/2022	112.00
47	30/05/2022	06/09/2022	99.00
48	09/06/2022	23/08/2022	75.00
49	14/06/2022	15/09/2022	93.00
50	30/05/2022	22/06/2022	23.00
51	22/04/2022	08/07/2022	77.00
52	02/06/2022	10/08/2022	69.00
53	13/05/2022	26/08/2022	105.00
54	25/05/2022	11/08/2022	78.00
55	16/06/2022	09/09/2022	85.00
56	03/06/2022	26/09/2022	115.00
57	22/04/2022	01/08/2022	101.00
58	04/05/2022	04/07/2022	61.00
59	02/05/2022	07/06/2022	36.00
60	26/04/2022	28/06/2022	63.00
61	20/05/2022	25/08/2022	97.00
62	29/04/2022	08/08/2022	101.00
63	13/06/2022	09/08/2022	57.00
64	21/04/2022	28/07/2022	98.00
65	19/06/2022	03/08/2022	45.00
66	12/07/2022	28/07/2022	16.00
67	18/05/2022	28/06/2022	41.00
68	08/05/2022	04/07/2022	57.00
69	09/06/2022	11/08/2022	63.00
70	05/05/2022	08/07/2022	64.00
71	03/06/2022	01/08/2022	59.00
72	03/06/2022	01/08/2022	59.00
73	23/06/2022	26/09/2022	95.00
74	08/06/2022	27/09/2022	111.00
75	05/08/2022	16/09/2022	42.00

#	Submission date	Decision date	Days to Decision
76	07/06/2022	27/09/2022	112.00
77	24/06/2022	12/09/2022	80.00
78	25/05/2022	16/09/2022	114.00
79	04/07/2022	12/09/2022	70.00
80	15/06/2022	12/08/2022	58.00
81	24/06/2022	12/09/2022	80.00
82	03/06/2022	27/09/2022	116.00
83	11/07/2022	23/08/2022	43.00
84	22/06/2022	12/08/2022	51.00
85	05/07/2022	26/09/2022	83.00
86	22/06/2022	08/07/2022	16.00
87	23/06/2022	15/09/2022	84.00
88	28/07/2022	19/09/2022	53.00
89	09/07/2022	26/09/2022	79.00
90	15/07/2022	12/09/2022	59.00
91	18/07/2022	29/09/2022	73.00
92	21/07/2022	26/07/2022	5.00