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SCIENCE MEDICINES HEALTH

Clinical trials in the EU

How European Reference Networks can add value to clinical research

Presented by Laura Pioppo on 29 May 2018
Scientific Administrator at Committees and Inspections Department

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EudraCT database

- The current legal framework for authorisation and supervision of clinical trials in the EU is the Directive 2001/20/EC
- Article 11 of the same Directive foresees the establishment of a European Database containing information on clinical trials in the EU –> EudraCT
- EudraCT database is only accessible to the Competent Authorities, European Commission and EMA. It contains information shared between national authorities as part of the oversight of CTs in the EU. Information contained includes:
  - ❑ Clinical trials applications (i.e. protocol information)
  - ❑ Clinical trial results
  - ❑ Alerts- warning of suspension of trial or temporary halt
  - ❑ Analysis of data via the data warehouse
- Part of the information contained in EudraCT is published via the EU CTR (public register) https://www.clinicaltrialsregister.eu/

EudraCT database

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Sponsors and PIP addresses

- Create Clinical Trial Applications & substantial amendments
- Create Submission Packages
- Create and post directly CT results in EudraCT since October 2013

EudraCT DATABASE

EU Clinical Trial Register

EU CTR provides public information on CTA and summary of results

National Competent Authorities (NCAs)

- Upload in EudraCT the CTA & substantial amendments since May 2004
- Record NCA & Ethics Committee Decision
- Record End Of Trial (EoT) Notification

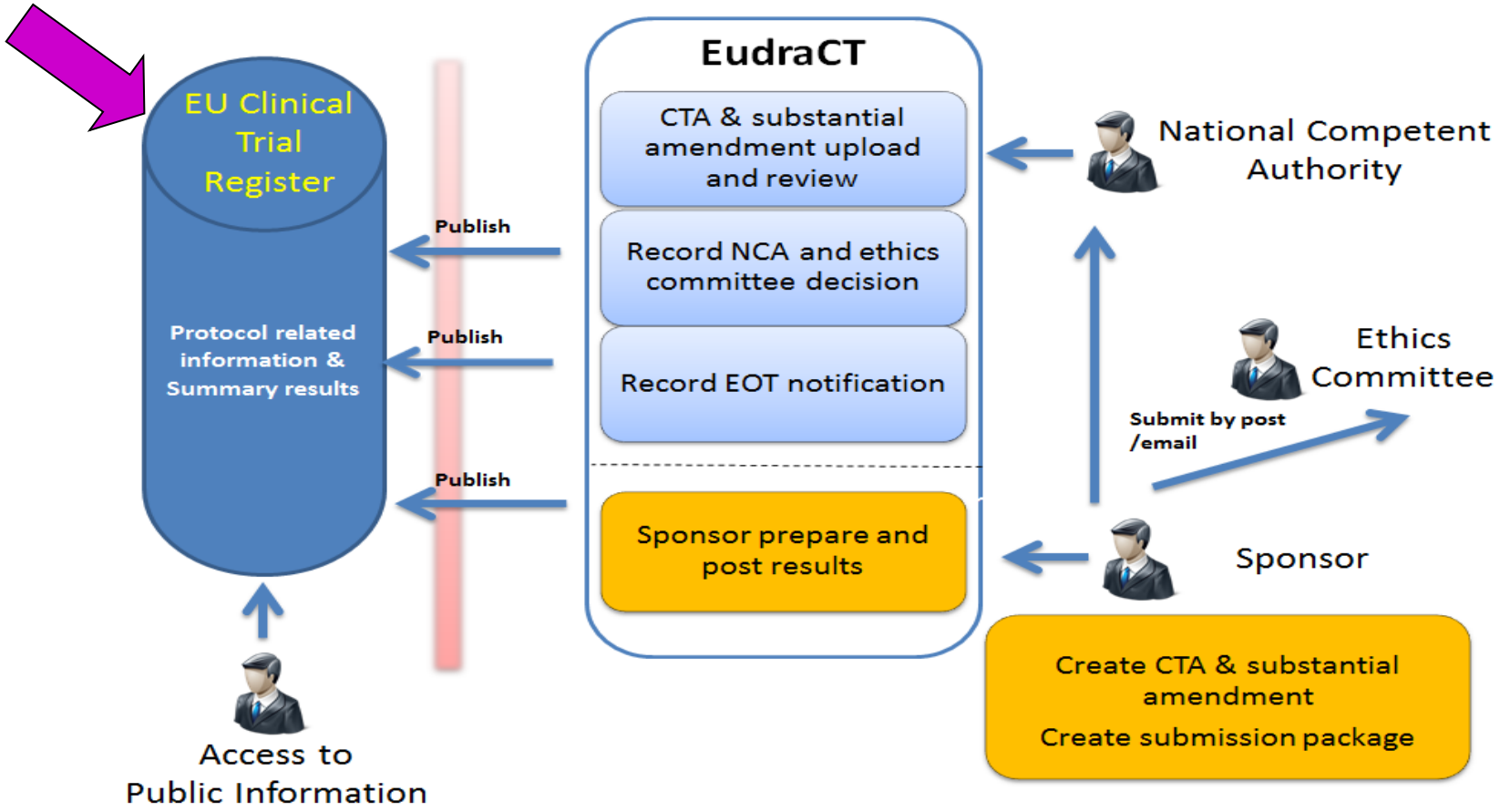
Sponsor

Sponsors provide NCA and Ethics Committee outside the system with a submission package containing several documents, including the clinical trial application dossier, substantial amendment,
end of trial notifications during the trial life cycle

NCA and Ethics Committees

Notify decision/opinion on the authorisation of the trial to sponsor outside the system. NCAs are responsible to enter the information into the EudraCT database

EudraCT database



Standardisation

- Significant degree of **standardisation of data elements** and alignment of standards used for clinical trials

- This is in relation to the standard used for capturing **protocol and results** related information between EudraCT/EU CTR, WHO ICTRP, ICMJE and ClinicalTrials.gov

EU CTR landing page

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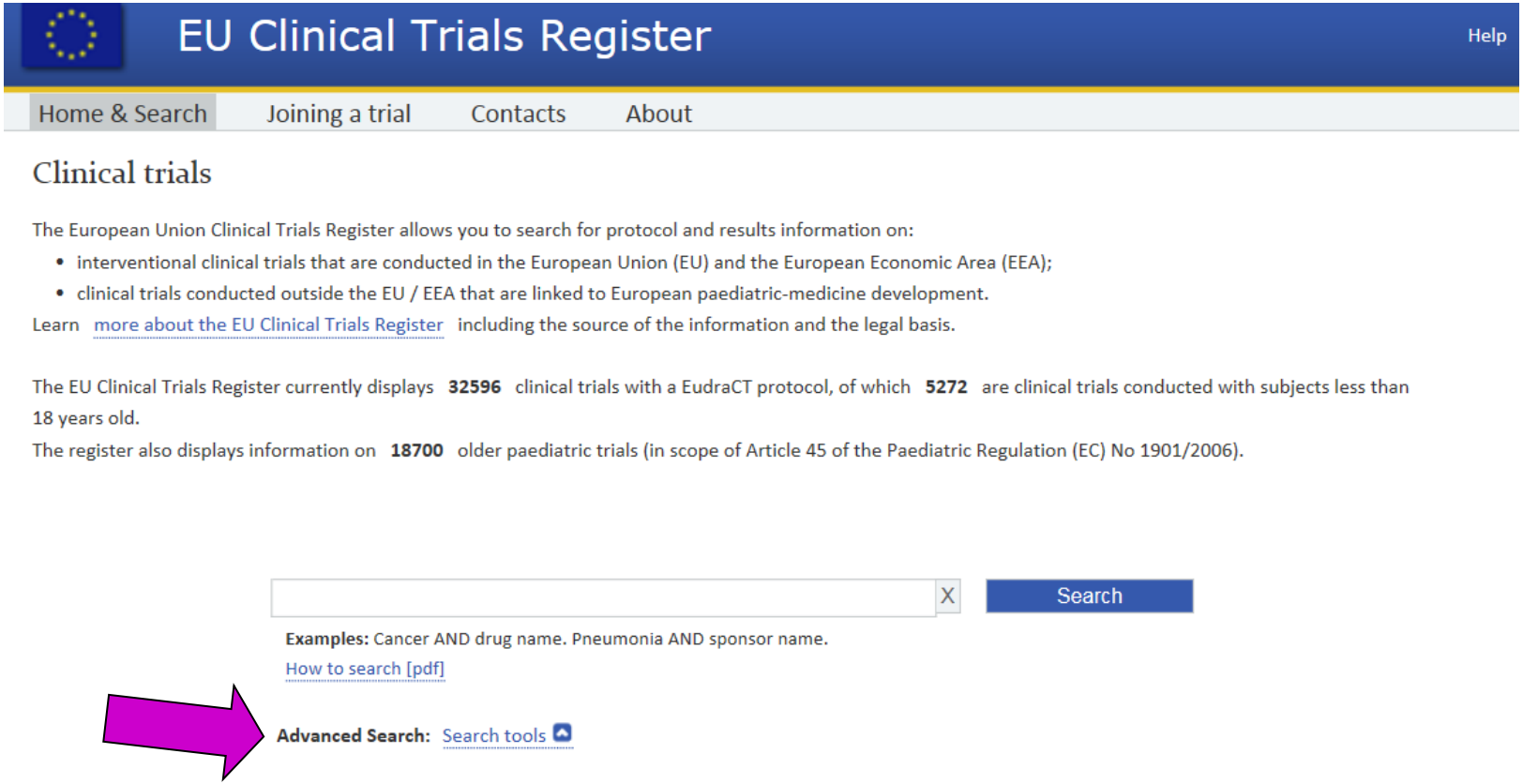
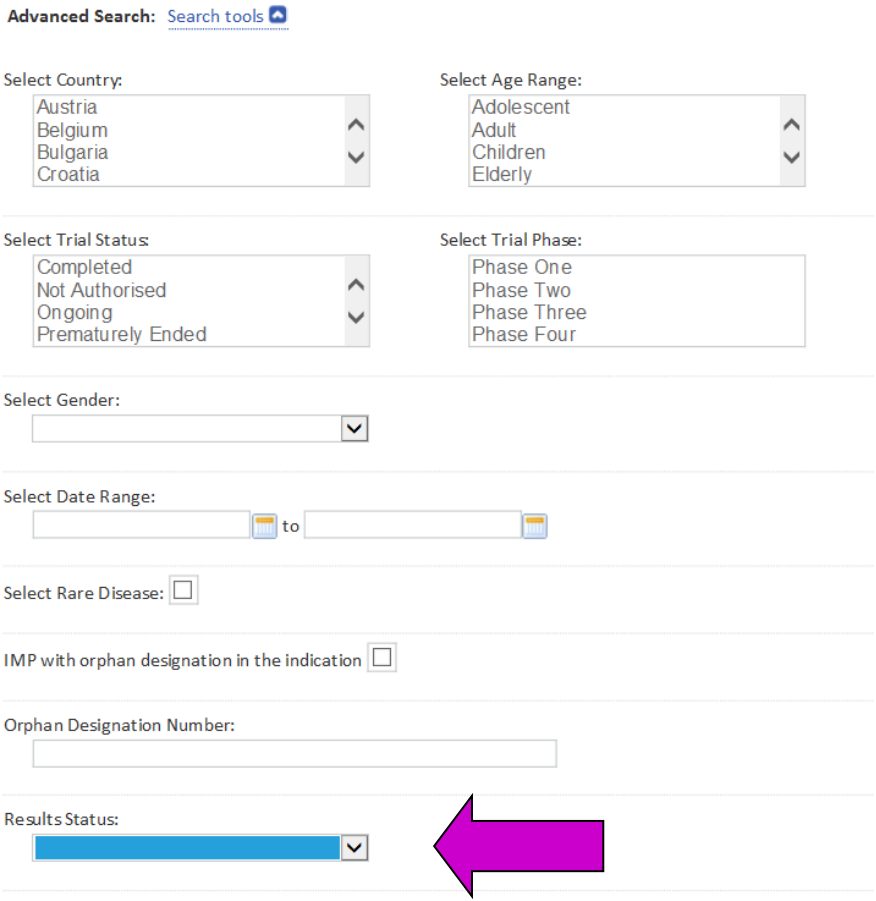


https://www.clinicaltrialsregister.eu/ctr-search/search

EU CTR advanced search



EU CTR advanced search

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EudraCT Number: 2010-024000-10	**Sponsor Protocol Number:** 101MS206	**Start Date*:** 2011-06-28
Sponsor Name: Biogen Idec Limited		
Full Title: A Randomized, Blinded, Parallel-Group, Phase 2 Study Exploring the Safety, Tolerability, and Efficacy of Multiple Regimens of Natalizumab in Adult Subjects With Relapsing Multiple Sclerosis		
Medical condition: Relapsing-Remitting Multiple Sclerosis		

Disease:	Version	SOC Term	Classification Code	Term	Level
	14.1	10029205 - Nervous system disorders	10063399	Relapsing-remitting multiple sclerosis	PT

Population Age: Adults	**Gender:** Male, Female
Trial protocol: BE *(Completed)* DE *(Completed)* ES *(Completed)* IT *(Completed)*	
Trial results: View results	

Trial search results

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< Back to search results

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Clinical Trial Results:
A Randomized, Blinded, Parallel-Group, Phase 2 Study Exploring the Safety, Tolerability, and Efficacy of Multiple Regimens of Natalizumab in Adult Subjects With Relapsing Multiple Sclerosis

Summary	
EudraCT number	2010-024000-10
Trial protocol	BE DE ES IT
Global end of trial date	03 Oct 2014
Results information	
Results version number	v1(current)
This version publication date	04 Feb 2016
First version publication date	15 Jul 2015
Other versions	

Trial Information
Subject Disposition
Baseline Characteristics
End Points
Adverse Events
More Information

EU CTR view for trial results

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Subject disposition

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Recruitment	
Recruitment details	-
Pre-assignment	
Screening details	Subject eligibility for the study was determined within approximately 4 weeks prior to study entry.
Period 1	
Period 1 title	Randomized Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator
Arms	
Are arms mutually exclusive	Yes
Arm title	Natalizumab 300 mg IV every 4 weeks
Arm description	Natalizumab 300 mg intravenous (IV) every 4 weeks for 60 weeks.
Arm type	Active comparator
Investigational medicinal product name	Natalizumab for IV Infusion
Investigational medicinal product code	BG00002
Other name	Tysabri
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details	All subjects received study treatment every 4 weeks. Subjects receiving natalizumab every 12 weeks received matching placebo during the intervening 4-week periods.

Statistics from EudraCT database

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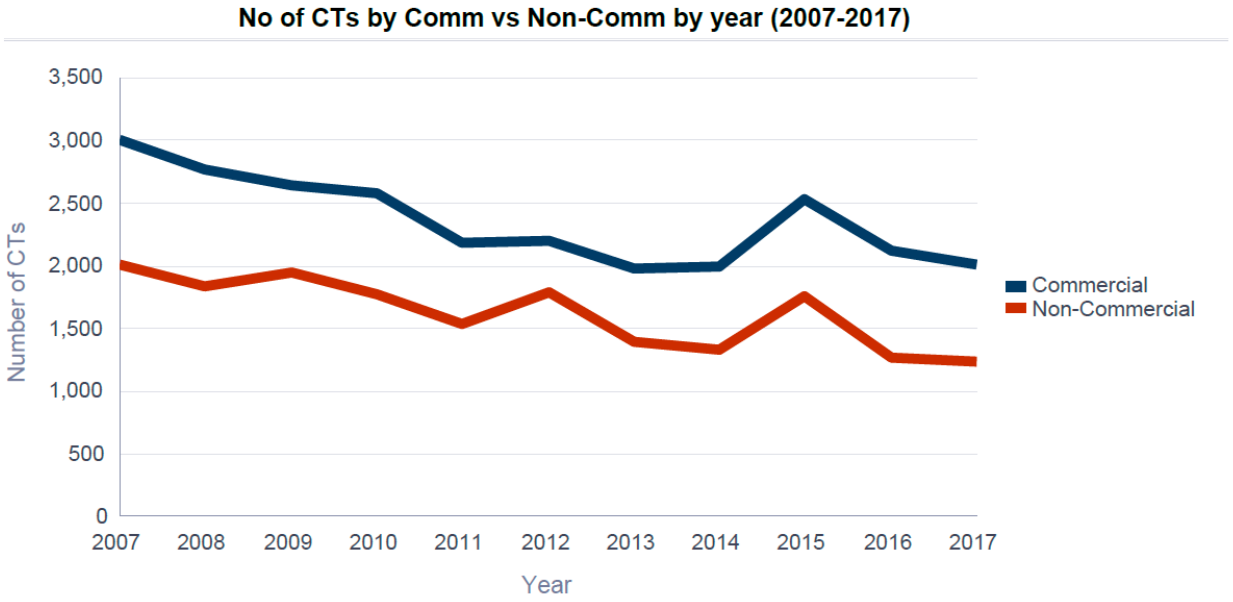
B.3.1 and B.3.2 Sponsor Status is equal to **Commercial** , **Non-Commercial**
and CTA Created Year is between **2007** and **2017**
and First Past the Post(FPP) Flag is equal to / is in **Y**



Statistics from EudraCT database

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Clinical Trials per Number of Member States Involved and Year, Commercial Sponsor

Time run: 25/05/2018 12:19:04

	Number of Member States Involved																								Total
Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	
2007	1,935	238	159	137	94	87	70	69	50	34	34	27	20	21	15	6	2	7	1	2	2	1		1		**3,012**
2008	1,757	226	153	118	98	85	67	59	47	39	31	29	19	14	11	7	6	5	3	3		3	2	3		**2,785**
2009	1,664	201	175	110	96	92	64	52	48	25	28	18	26	8	19	3	7	3	3	4	1				1	**2,648**
2010	1,565	193	156	92	117	85	73	57	59	36	38	19	23	12	11	7	11	8	7	7	3	2	1		1	**2,583**
2011	1,225	196	141	99	118	74	67	65	64	37	27	21	15	14	13	6	6	3	2		1		1			**2,195**
2012	1,276	167	121	120	89	85	64	66	40	41	33	20	20	13	15	15	6	3	2	1		2	1	1	1	**2,202**
2013	1,056	163	117	123	72	78	75	73	54	35	24	19	13	16	15	12	11	2	4	5	4	1	1	2		**1,975**
2014	1,068	176	110	122	96	75	69	65	45	39	37	27	12	19	14	7	1	4	4	5		3	2		1	**2,001**
2015	1,521	197	146	125	109	80	67	49	48	47	30	25	23	13	11	13	6	6	4	3	2	2	3	2		**2,532**
2016	1,185	197	131	126	108	86	58	60	44	36	19	18	15	11	7	9	7	4	3	2	2			1		**2,129**
2017	1,102	207	155	134	92	71	63	52	39	24	19	16	10	9	4	3	3	5	4	2		1				**2,015**
Grand Total	**15,354**	**2,161**	**1,564**	**1,306**	**1,089**	**898**	**737**	**667**	**538**	**393**	**320**	**239**	**196**	**150**	**135**	**88**	**66**	**50**	**37**	**34**	**15**	**15**	**11**	**10**	**4**	**26,077**

Clinical Trials per Number of Member States Involved and Year, Non-Commercial

Time run: 25/05/2018 12:19:51

	Number of Member States Involved																Total
Year	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
2007	1,903	56	33	16	2	1	4	1	1	1	2		1				**2,021**
2008	1,766	33	22	14	8	3	1			1							**1,848**
2009	1,871	45	19	11	4	4		3	1	2		1				1	**1,962**
2010	1,703	39	19	10	2	4	3		4	1	1	1	1	1	1		**1,790**
2011	1,458	31	16	11	6	5	7	4	1	1	2	1					**1,543**
2012	1,688	46	22	13	6	5	8	4	3	1	3	1		2			**1,802**
2013	1,285	38	15	13	17	4	9	3	4	3	1		1				**1,393**
2014	1,217	46	19	13	10	9	4	3	3	1			1		1		**1,327**
2015	1,649	49	17	10	11	4	7	7	1	2	1		2				**1,760**
2016	1,176	43	19	6	6	8	5	4	1		1	2					**1,271**
2017	1,157	31	22	13	5	6	2	2									**1,238**
Grand Total	**16,873**	**457**	**223**	**130**	**77**	**53**	**50**	**31**	**19**	**13**	**11**	**6**	**6**	**3**	**2**	**1**	**17,955**

Statistics from EudraCT database

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Planned Patients by Year by Phase by Sponsor Status (2017)

This report contains the number of Planned Patients by Year, by Phase and by Sponsor Status in the EEA (section F.4.2.1) and in the whole clinical trial (section F.4.2.2)

Time run: 25/05/2018 12:16:49

	B.3.1 and B.3.2 Sponsor Status	2017
Phase I_EEA	Commercial	16,864
	Non-Commercial	1,760
Phase I_EEA Total		**18,624**
Phase II_EEA	Commercial	43,252
	Non-Commercial	12,846
Phase II_EEA Total		**56,098**
Phase III_EEA	Commercial	117,882
	Non-Commercial	18,905
Phase III_EEA Total		**136,787**
Phase IV_EEA	Commercial	10,730
	Non-Commercial	19,927
Phase IV_EEA Total		**30,657**

Statistics from EudraCT database

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Query 07 - Number of Clinical Investigator Sites by Year by Phase and by Sponsor Status

This report contains the number of Clinical Investigator Sites anticipated in the EEA (section E.8.5.1) by year, by phase and by Sponsor Status (Commercial/Non-Commercial)

Time run: 25/05/2018 12:12:37

First Past the Post(FPP) Flag is equal to / is in **Y**

and B.3.1 and B.3.2 Sponsor Status is equal to **Commercial** , **Non-Commercial**

and CTA Created Year is equal to / is in **2017**

	B.3.1 and B.3.2 Sponsor Status	2017	**Grand Total**
PHASEI_EEA	Commercial	2,384	**2,384**
	Non-Commercial	98	**98**
PHASEI_EEA Total		**2,482**	**2,482**
PHASEII_EEA	Commercial	9,029	**9,029**
	Non-Commercial	1,029	**1,029**
PHASEII_EEA Total		**10,058**	**10,058**
PHASEIII_EEA	Commercial	20,531	**20,531**
	Non-Commercial	1,528	**1,528**
PHASEIII_EEA Total		**22,059**	**22,059**
PHASEIV_EEA	Commercial	1,080	**1,080**
	Non-Commercial	388	**388**
PHASEIV_EEA Total		**1,468**	**1,468**

Upcoming Clinical Trial Regulation: what is new?

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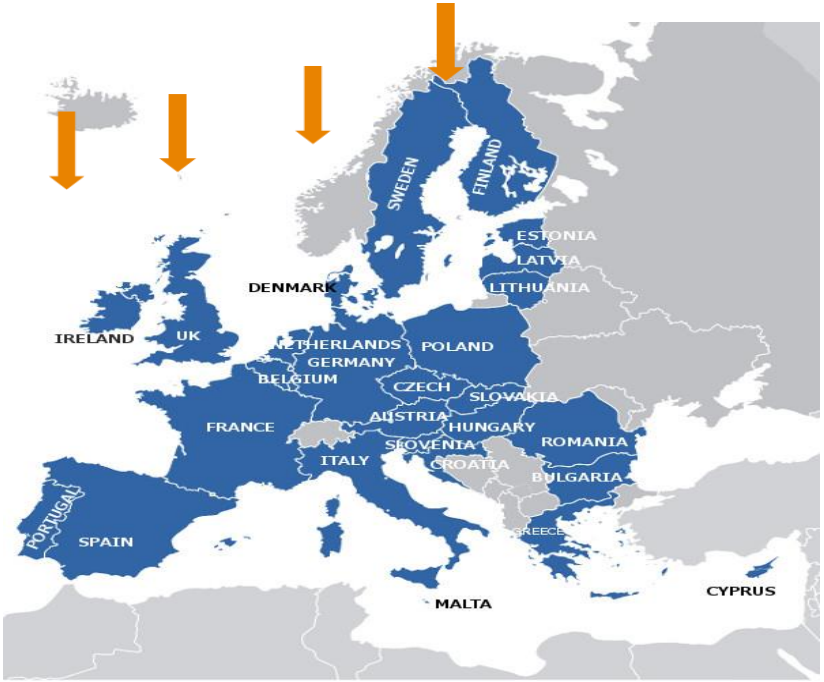
Directive versus Regulation

Implemented in national laws*



*with EEA relevance and applicable in EEA countries: Norway, Iceland and Liechtenstein

Directly applicable*

Objectives of new CTR

- To protect the rights, safety, dignity and well-being of subjects and the reliability and robustness of the data generated in the CT;
- To foster innovation and simplify the clinical trial application process**, in particular for multistate trials;**
- To increase transparency, keeping the balance between protecting public health and fostering the innovation capacity of European medical research while recognising the legitimate economic interests of the sponsors.
- Overall objective: Make EU attractive for R&D.

Summary of key changes from Directive to Regulation

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Unchanged scope: Interventional clinical trials with medicinal products for human use

As-is (Directive 2001/20) – EudraCT	To be (CT Regulation) - The EU portal and database (EU PD)
• Multiple submissions for one trial (1 submission per each Member State Concerned (MSC) /no harmonized dossier	• Single e-submission via EU PD to all Member States Concerned (MSC) including NCA and EC/harmonized dossier for one trial (content described in Annex I)
• Double submission within a MSC: to NCA and to Ethics Committees (EC)	
• Individual assessment by each MSC with no IT collaboration tool available	• Joint assessment for Part I of the dossier facilitated by collaboration tools via the EU Portal and Database IT system
• No single MSC decision (NCA & ECs)	• Single MSC decision for NCA and Ethics Committees
• Limited EudraCT data availability to the public : structured data from the application (CTA) and summary of results	• View extensive CT related information via the public version of the EU PD

EU Portal and database project

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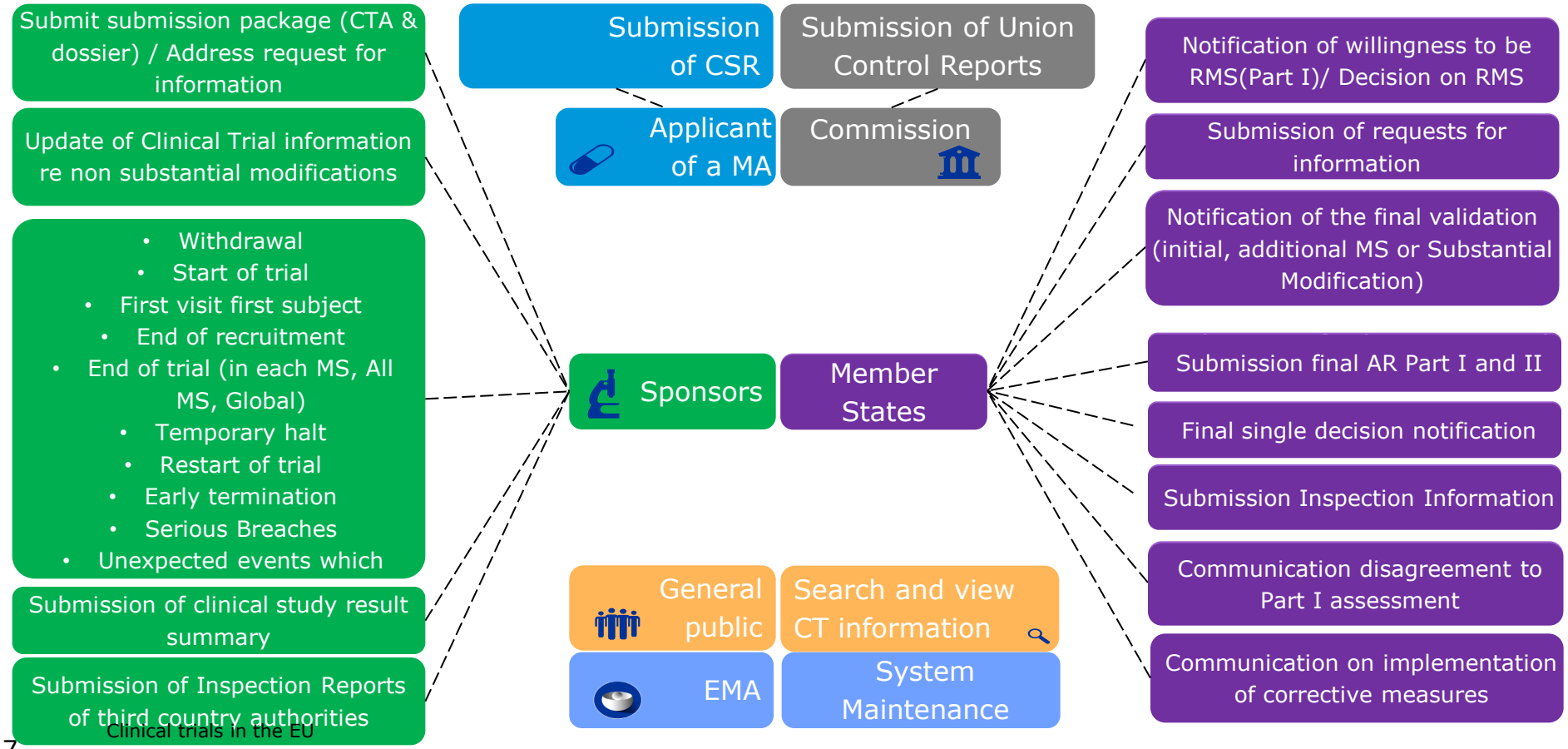

What will be published?*

- Clinical trial protocol details
- Product details (including IMPD S&E, IB/SmPC)
- Sponsor contact details in the EU
- Principal investigator details, including clinical investigator sites address
- Statement on the suitability of the facility
- Clinical trial summary of results
- Clinical study reports for trials provided as part of a marketing authorisation applications
- Notifications of start of trial/ start of recruitment/ temporary halt/end of trial
- Notifications of serious breaches/ unexpected events/urgent safety measures
- Member State Assessment reports
- Member State inspection reports

This is not an exhaustive list

Objectives of the public disclosure of clinical trial information

- Is there a trial in which I could participate?
- What was the outcome of the trial I did participate in?
- What trials were the basis of the marketing authorisation, what were their results?
- What is known about the medicine I am taking/prescribing?
- Can we review the data used to support the marketing authorisation?
- Has the trial we are designing already been conducted? Were there problems with similar trials?

Conclusions

- **Harmonisation**: One single submission for authorisation of a clinical trial, irrespective of the number of Member States involved, to National Competent Authority & Ethics Committee and for public registration (primary register of clinical trials);
- **Member state collaboration**: Facilitate cooperation among MSCs in assessing a request for authorisation of a clinical trial;
- **One single decision** per Member State within the same timelines;
- **IT maintenance**: EMA in charge maintain and update the IT platforms;
- **Public data** and information about medicines, their development
  - To generate trust – information is available
  - To build confidence – I understand what is happening
  - To empower – knowledge enables decision-making

Any questions?

Further information

laura.pioppo@ema.europa.eu

European Medicines Agency
30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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