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Difference of Clinical Trial Result Disclosure Between ClinicalTrials.gov and EudraCT

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Meet the Speaker

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- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

Agenda

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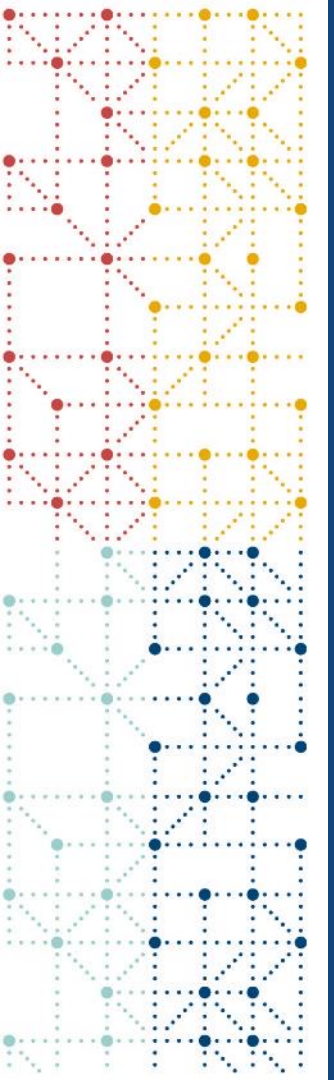
2. The Whole Picture of Result Part
3. Difference in Detail
4. Conclusion



Clinical Trial Disclosure Overview

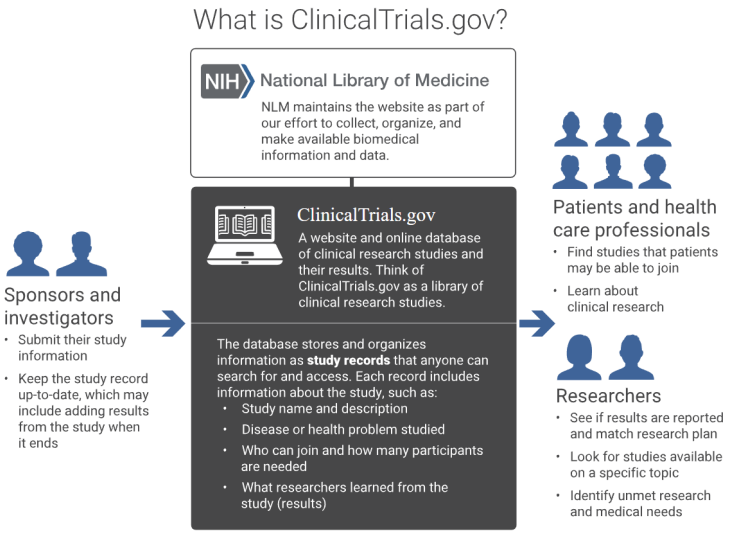
What is Clinical Trial Disclosure?

- Begins with registering a clinical trial with governmental registries
- Continues with posting of study protocols and results
- Makes them accessible to public

What is Clinical Trial Disclosure? (cont'd)

- Approximately 90 countries have disclosure requirements on over 30 registries

What is ClinicalTrials.gov?



- Scope of Trials Under the US Final Rule
  - All applicable clinical trials (ACTs) with a primary completion date on or after January 18, 2017
  - Regardless of approval status

ClinicalTrials.gov *ClinicalTrials.gov is a service of the National Institutes of Health.*

Checklist for Evaluating Whether a Clinical Trial or Study is an Applicable Clinical Trial (ACT) Under 42 CFR 11.22(b) for Clinical Trials Initiated on or After January 18, 2017[1] (NOT FOR SUBMISSION[2])

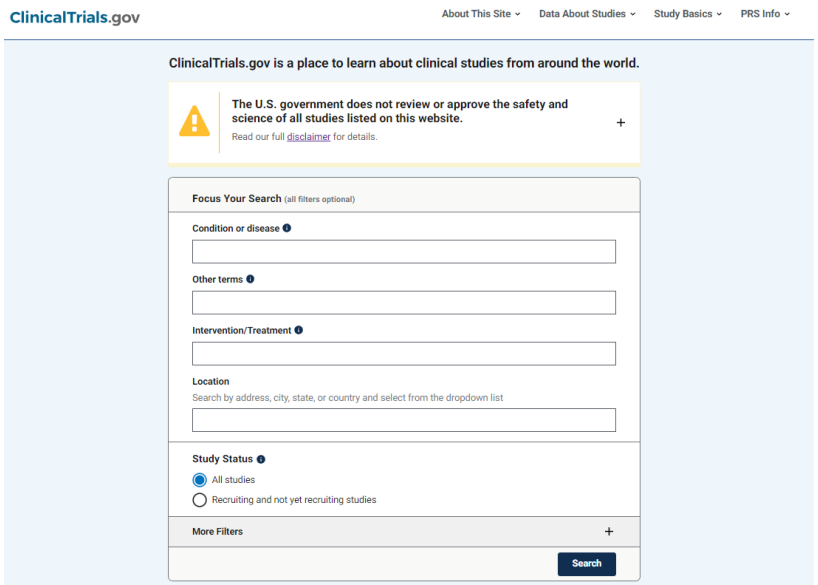
Instructions: Answer the following questions to evaluate whether the study is an applicable clinical trial (ACT). Use the accompanying "Elaboration" for additional information to help answer the questions.

Question	Yes	No
1. **Is the study interventional (a clinical trial)?** *Study Type* data element is "Interventional"	☐	☐
2. **Do ANY of the following apply (is the answer "Yes" to at least one of the following sub-questions: 2a, 2b, OR 2c)?** a. **Is at least one study facility located in the United States or a U.S. territory?** *Facility Location – Country* data element is "United States," "American Samoa," "Guam," "Northern Mariana Islands," "Puerto Rico," "U.S. Virgin Islands," or other U.S. territory. b. **Is the study conducted under a U.S. FDA Investigational New Drug application (IND) or Investigational Device Exemption (IDE)?** *U.S. Food and Drug Administration IND or IDE Number* data element is "Yes." c. **Does the study involve a drug, biological, or device product that is manufactured in and exported from the U.S. (or a U.S. territory) for study in another country?** *Product Manufactured in and Exported from the U.S.* data element is "Yes."	☐	☐
3. **Does the study evaluate at least one drug, biological, or device product regulated by the United States Food and Drug Administration (U.S. FDA)?** *Studies a U.S. FDA-regulated Device Product* data element is "Yes" and/or *Studies a U.S. FDA-regulated Drug Product* data element is "Yes."	☐	☐
4. **Is the study other than a Phase 1 trial of a drug and/or biological product or is the study other than a device feasibility study?** For drug product trials, *Study Phase* data element is NOT "Phase 1" and for device product trials, *Primary Purpose* is NOT "Device Feasibility."	☐	☐

If "Yes" is answered to all 4 questions, and the study was initiated on or after January 18, 2017, the trial would meet the definition of an ACT that is required to be registered under 42 CFR 11.22.

What is ClinicalTrials.gov? (cont'd)

- More than 460,000 studies in this database

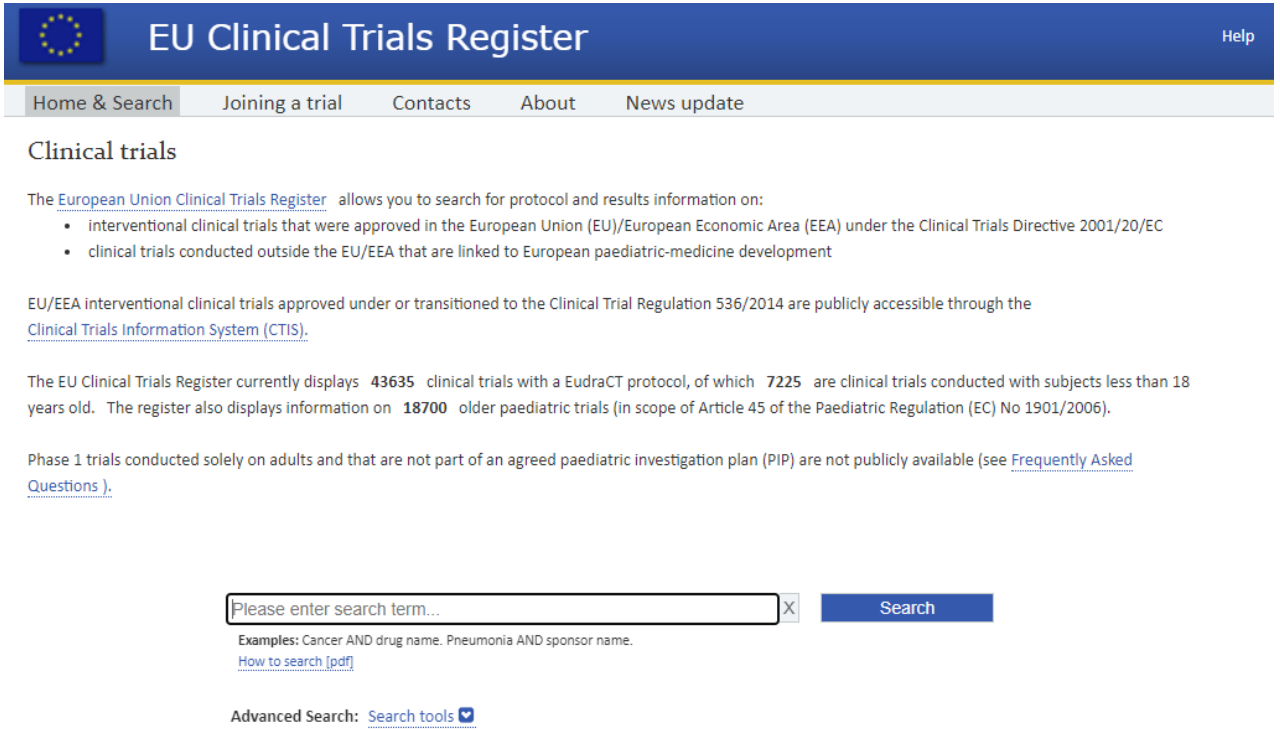


What is EudraCT?

EudraCT (European Union Drug Regulating Authorities Clinical Trials Database) is the database for all interventional clinical trials of medicinal products submitted to the European Union (EU)/European Economic Area (EEA)

- Scope of Trials
  - All Interventional Clinical Trials of Medicinal Products conducted in EU
  - Part of an EU Pediatric Investigation Plan (PIP)
- As of 31 January 2023, all initial clinical trial applications in the European Union (EU)/European Economic Area (EEA) must be submitted through the Clinical Trials Information System

What is EudraCT? (cont'd)



The Whole Picture of Result Part

Results Data Element

Content	ClincalTrials.gov	EudraCT
Trial Information		√
Participant Flow / Subject Disposition	√	√
Baseline Characteristics	√	√
Outcome Measures / End Points	√	√
Adverse Event Information	√	√
Limitations and Caveats	√	√
Certain Agreements	√	
Results Point of Contact	√	√
Document Upload Information	√	
More Information		√

Result Disclosure Timeline

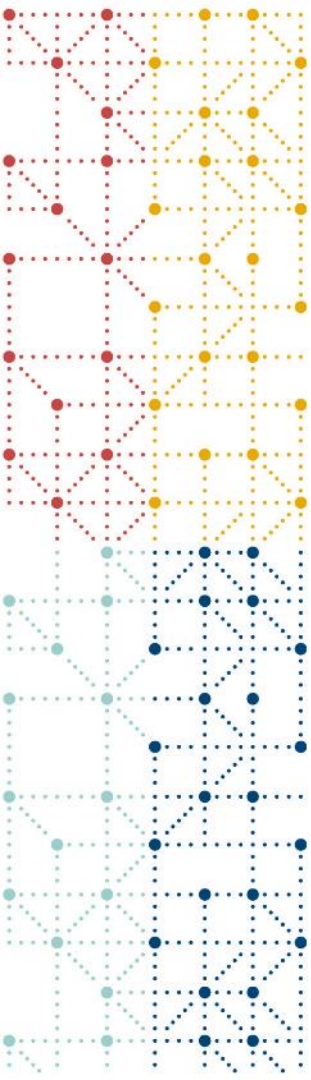
- ClinicalTrials.gov: No later than 12 months after primary completion date
  - Primary completion date refer to completion date.

COMPLETION DATE

In the NPRM, we defined "completion date" in § 11.10(a) to mean "for a clinical trial, the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated. In the case of clinical trials with more than one primary outcome measure with different completion dates, this term refers to the date upon which data collection is completed for all of the primary outcomes."

- EudraCT
  - Non-pediatric trials: No later than 12 months from the end of trial date
  - Pediatric trials: No later than 6 months from the end of trial date

a clear and unambiguous definition of the end of the trial in question. In most cases this will be the date of the last visit of the last patient undergoing the trial. Any exceptions to this should be justified in the protocol; and



Difference in Detail

Different Part: Trial Information in EudraCT

From Protocol Info:

- Trial identification
- Additional study identifiers
- Sponsor details
- General information about trial

Specific Info:

- Results analysis stage
- Pediatric regulatory details
- Population of trial subjects
- Age group breakdown for trial

Different Part: Additional Information

- EudraCT:

Section	EudraCT UI (user interface) field name
Substantial protocol	
	Were there any global substantial amendments to the protocol?
	Add global substantial protocol amendment
	Amendment date
	Amendment description
Interruptions (globally)	
	Were there any global interruptions to the trial?
	Add global interruption
	Interruption date
	Interruption description
	Restart date
Limitations and caveats	
	Limitations and caveats applicable to this summary of the results
Online references	
	PubMed identifier (PMID)
	N/A

- ClinicalTrials.gov:
  - Certain Agreements
  - Document Upload Information

Difference in Participant Flow / Subject Disposition

Period details
Is this the baseline period
Allocation method
Blinding used
Roles blinded
Blinding implementation details

Products
IMP name
IMP code
Other names
Route of Administration
Pharmaceutical forms
Dosage and administration details

Subject joining reasons
Subject joining reason
Number of subjects

Difference in Baseline Characteristics

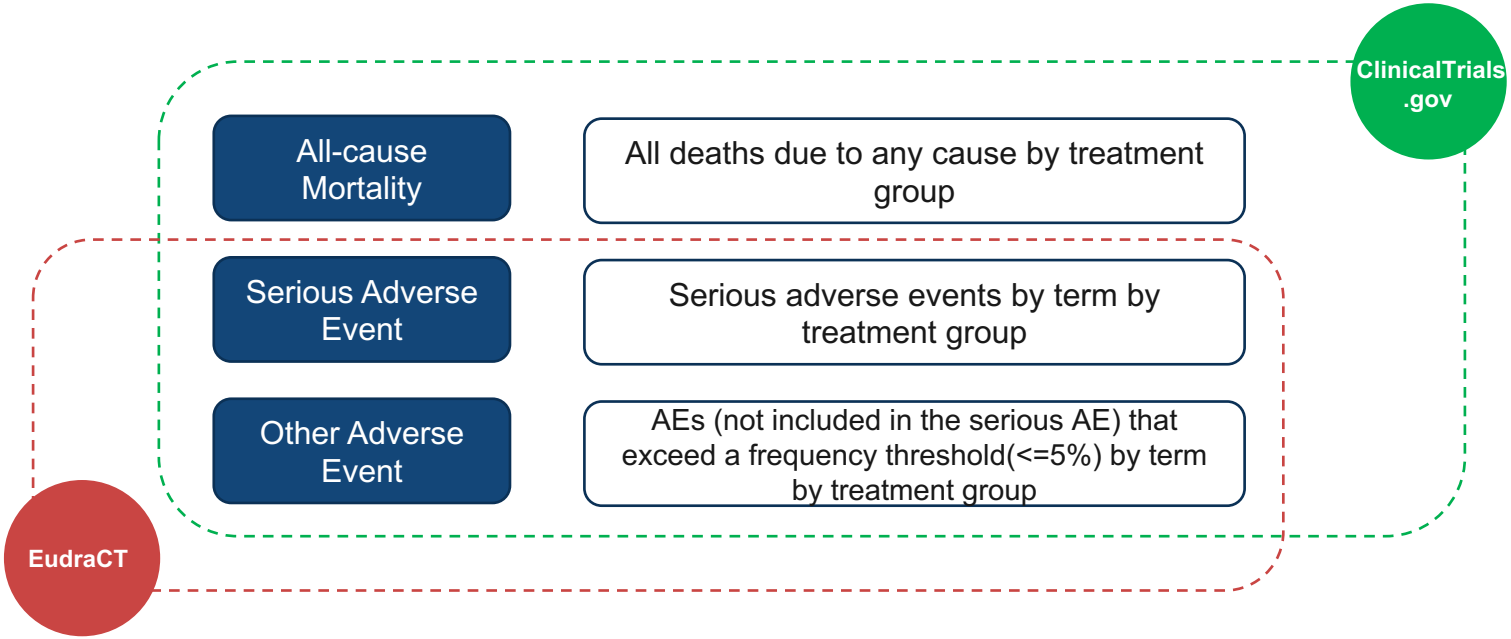
- Continuous Variables
  - Mean (SD)
- Categorical Variables
  - Only **frequency** is shown in EudraCT
  - **Frequency and percentage** are shown in ClinicalTrials.gov
  - Age category is specific in EudraCT

Age Category in EudraCT
In utero
Preterm newborn - gestational age < 37 wk
Newborns (0-27 days)
Infants and toddlers (28 days-23 months)
Children (2-11 years)
Adolescents (12-17 years)
Adults (18-64 years)
From 65 to 84 years
85 years and over

Difference in Outcome Measures / End Points

- Most are same
- Except only frequency is shown in EudraCT when frequency and percentage are shown in ClinicalTrials.gov

Difference in Adverse Events



Difference in Adverse Events (cont'd)

- Serious Adverse Event

- ClinicalTrials.gov

ALL-CAUSE MORTALITY

Arm/Group Title	TRT A	TRT B
	Affected / at Risk (%)	Affected / at Risk (%)
Total	0/58 (0.00%)	0/59 (0.00%)

SERIOUS ADVERSE EVENTS

Arm/Group Title	TRT A		TRT B	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	12/58 (20.69%)		8/59 (13.56%)	
Blood and lymphatic system disorders				
Neutropenia †1	0/58 (0.00%)	0	2/59 (3.39%)	2

- EudraCT

Serious adverse events	TRT A	TRT B
Total subjects affected by serious adverse events		
subjects affected / exposed	12 / 58 (20.69%)	8 / 59 (13.56%)
number of deaths (all causes)	0	0
number of deaths resulting from adverse events		
Blood and lymphatic system disorders		
Neutropenia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 58 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 0	2 2
deaths causally related to treatment / all	0 / 0	0 0

Specific

Difference in Adverse Events (cont'd)

- Other Adverse Event

- ClinicalTrials.gov

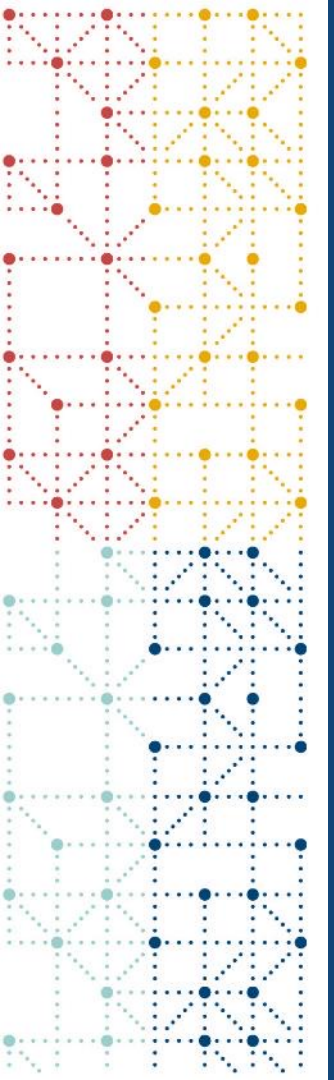
OTHER (NOT INCLUDING SERIOUS) ADVERSE EVENTS

Frequency Threshold for Reporting Other Adverse Events	5%			
Arm/Group Title	TRT A		TRT B	
	Affected / at Risk (%)	# Events	Affected / at Risk (%)	# Events
Total	42/58 (72.41%)		42/59 (71.19%)	
Blood and lymphatic system disorders				
Increased Tendency To Bruise [†1]	4/58 (6.90%)	4	4/59 (6.78%)	4
Leukopenia [†1]	0/58 (0.00%)	0	4/59 (6.78%)	4
Neutropenia [†1]	0/58 (0.00%)	0	7/59 (11.86%)	9

- EudraCT

Frequency threshold for reporting non-serious adverse events: 5%

Non-serious adverse events	TRT A	TRT B
Total subjects affected by non serious adverse events		
subjects affected / exposed	42 / 58 (72.41%)	42 / 59 (71.19%)
Blood and lymphatic system disorders		
Increased Tendency To Bruise		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	4 / 58 (6.90%)	4 / 59 (6.78%)
occurrences all number	4	4
Leukopenia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 58 (0.00%)	4 / 59 (6.78%)
occurrences all number	0	4
Neutropenia		
alternative dictionary used: MedDRA 24.0		
subjects affected / exposed	0 / 58 (0.00%)	7 / 59 (11.86%)
occurrences all number	0	9



Conclusion

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- Result disclosure has a positive impact of pharmaceutical industry
- Have a clear understanding of each regulation
- Keep the consistency and distinguish the discrepancy when simultaneous disclosure

Thank You!