Centrale Commissie Mensgebonden Onderzoek

ACT EU PA05 – Data analytics workshop

Session: Clinical Trials Data – Present and Future
Use case from ethics perspective*

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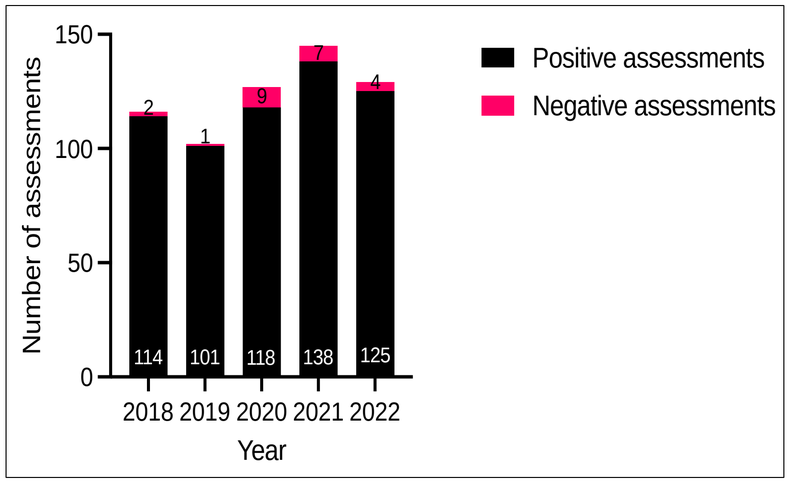
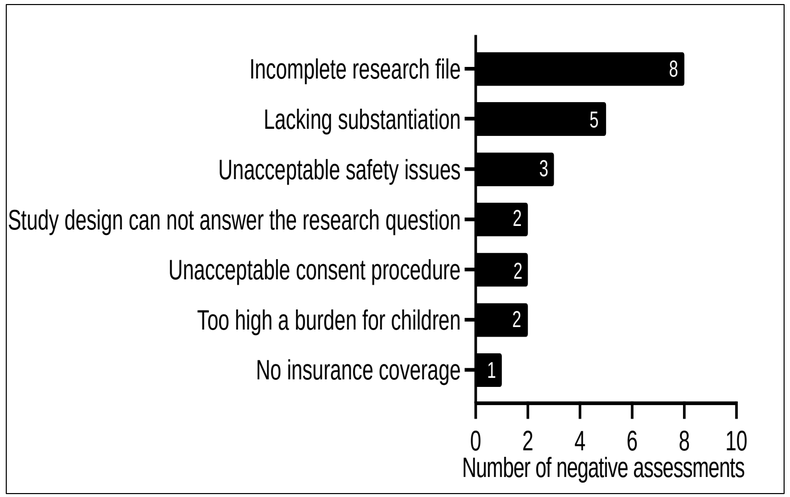
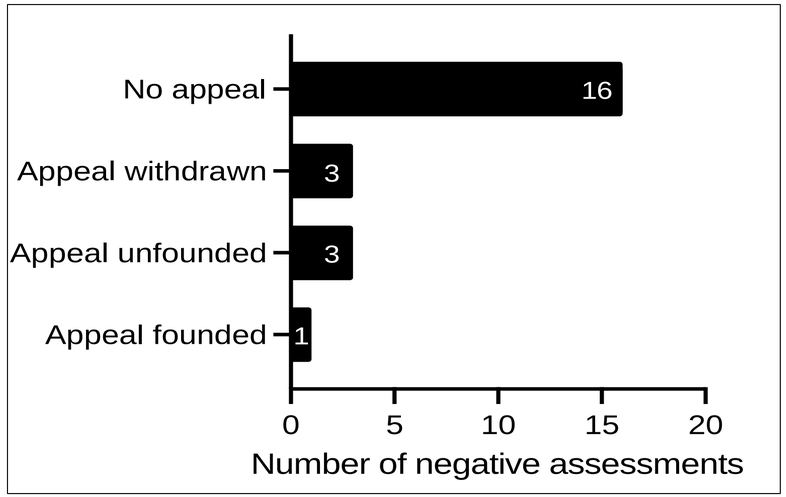
Use Case (1): MREC ‘NEDMEC’ negative decisions (23/596 dossiers ~4%)







Central ethics committee: 1.7% negative decisions in the NL

Analyses of reasons to reject clinical trials may provide info/guidance to investigators, sponsors and regulators

Heinsbroek et al, In press, Journal of Trial and Error

Use Case (2): Number of clinical trials with antisense nucleotides/oligonucleotides and products on the market/in development

Data sources:

- ToetsingOnline (Database with structured and open text fields on studies in NL submitted for review by MRECs : https://english.ccmo.nl/about-ccmo/toetsingonline (not active anymore for clinical trials: CTIS and national collaboration platform for clinical trials)
- EMA database: https://www.ema.europa.eu/en/medicines
- FDA databases: https://www.fda.gov/drugs/drug-approvals-and-databases/resources-information-approved-drugs

Outcome:

	ASO ('..rsen')		siRNA ('...siran')		other*	
Number of Studies	83		38		9	
Rejections/Withdrawals	13	(16%)	3	(8%)	1	(11%)
Number of Compounds	49		16		6	
Development Stopped/Uncertain	21	(41%)	1	(6%)	1	(17%)
Development Ongoing	22	(47%)	9	(56%)	5	(83%)
Registration Pending/Completed (EMA/ *FDA*) *(italics: no studies in NL)*	3 nusinersen (SMA-1) volansorsen (FHC) *fomivirsen (CMV retinitis)* 7 mipomersen (FHT) viltolarsen (DMD) casimersen/golodirsen eteplirsen (DMD) *inotersen (TTA-P/C)* *tofersen (SOD1-ALS)*	(6%) *(14%)*	6 givosiran (porphyria) inclisiran (FHC) lumasiran (PH-1) patisiran (TTA-P/C) vutrisiran (TTA-P/C) teprasiran (graft protection)	(38%)	-	-

Analyses of reasons for rejection of clinical trials, product development program, and obtained marketing authorisation → potential consequences for next CTs with these compounds

Use Case (3): Evaluation ethical considerations paediatric clinical trials: direct benefit, group benefit, no benefit, group relatedness and risk and burden for the trial participants

Data sources:

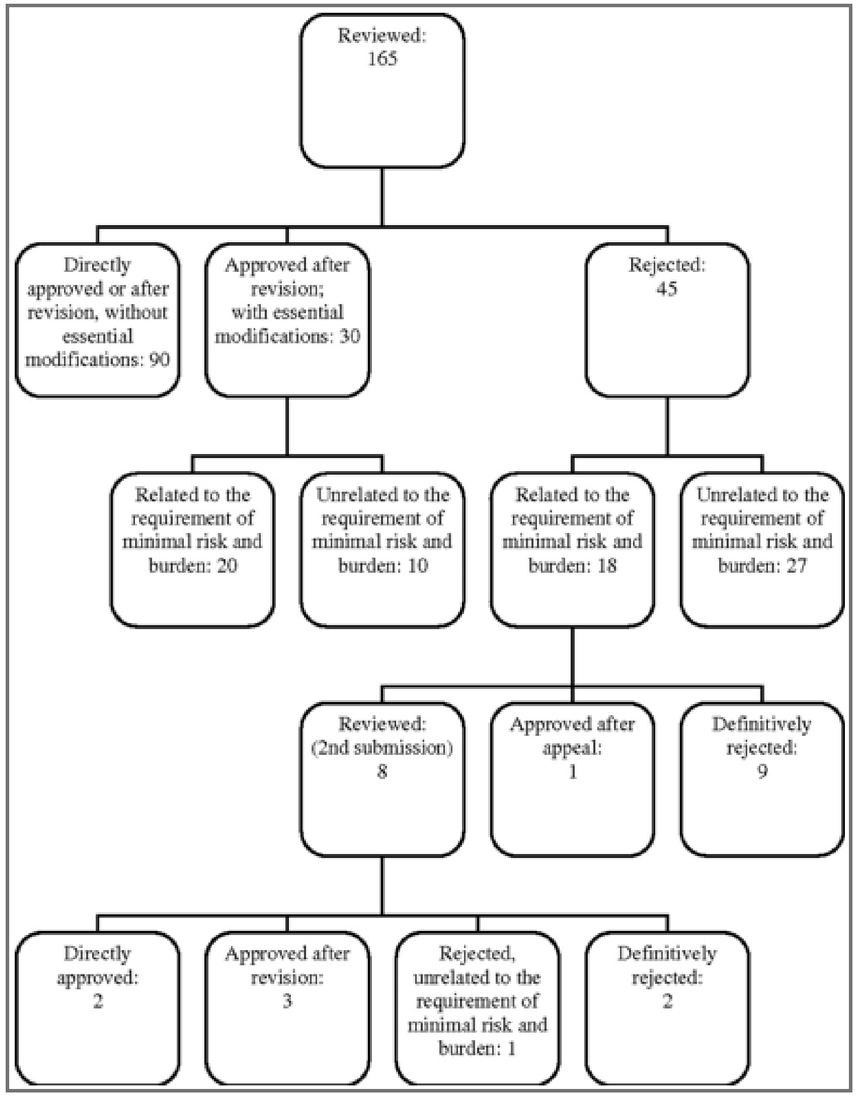
- ToetsingOnline (Database with structured and open text fields on studies in NL submitted for review by MRECs : https://english.ccmo.nl/about-ccmo/toetsingonline (not active anymore for clinical trials: CTIS and national collaboration platform for clinical trials)
- CCMO/MREC document management system (local, not public)

Outcome: report with in-depth analysis: Rapport Westra Evaluatie CCMO-beoordelingen niet-therapeutisch onderzoek met minderjarigen | Rapport | Centrale Commissie Mensgebonden Onderzoek

In CTIS no structured data fields for easy selection on clinical trials in paediatric population (or other populations) without direct benefit.

Evaluation of ethical considerations used for national legislation, recommendation paper, and harmonised approach on assessing paediatric clinical trials.

The committee's decisions on the 165 protocols.

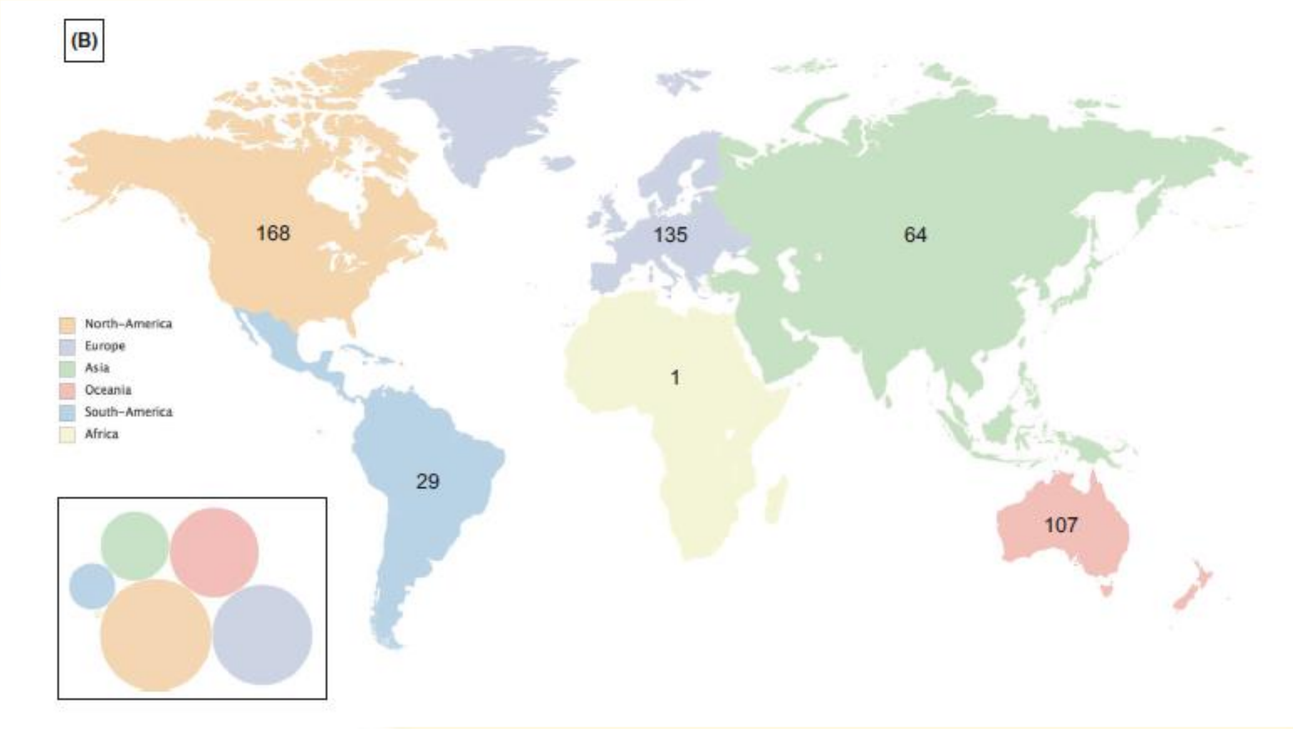


Anna E Westra et al. J Med Ethics 2010;36:420-424

Use Case (4):

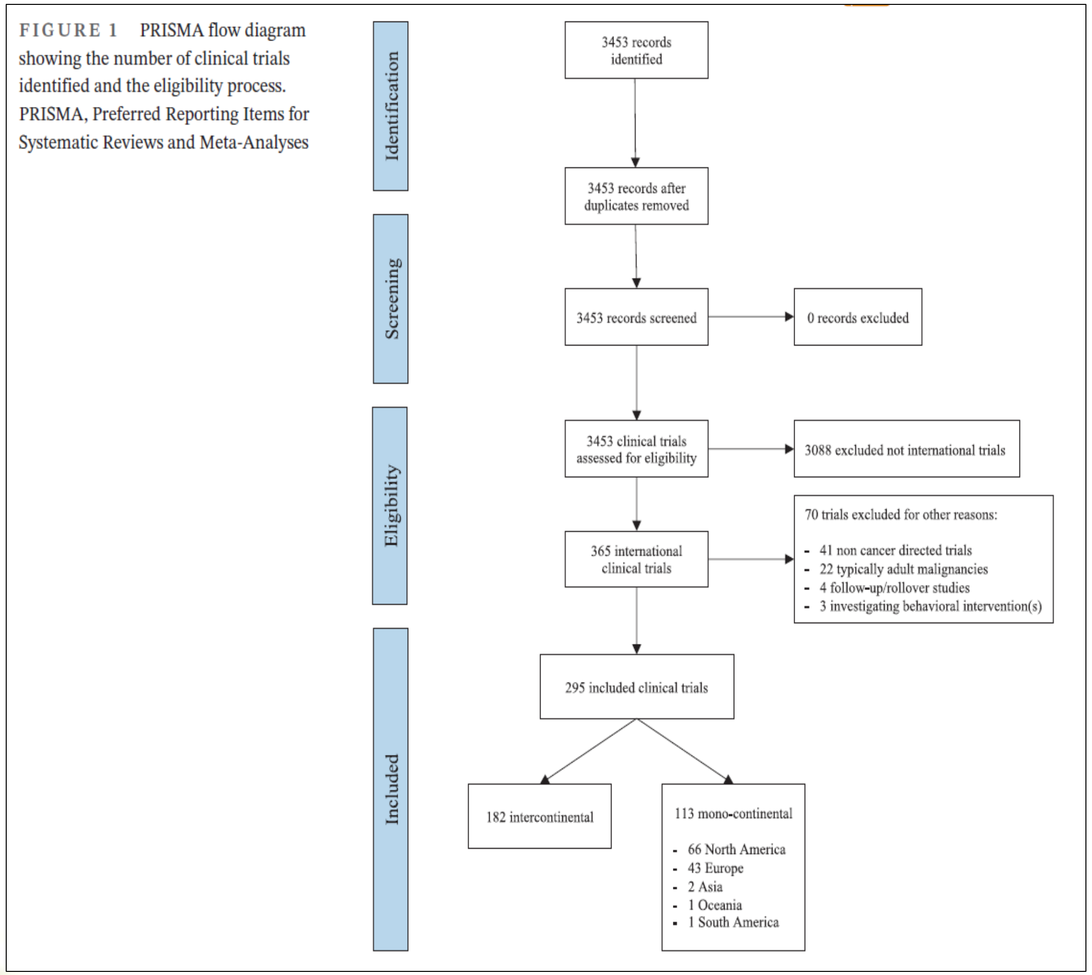
Transatlantic Ped Oncology studies

Only Clin Trials.gov was used – lack of European standard database



Intercontinental collaboration in clinical trials for children and adolescents with cancer—A systematic review by ACCELERATE

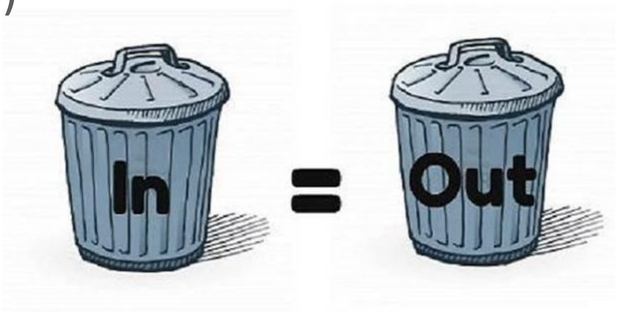
Teresa de Rojas[1] | Andrew J. Pearson[1] | Nicole Scobie[2] | Leona Knox[3] | Darshan Wariabharaj[4] | Pamela Kearns[5] | Gilles Vassal[1,6] | Gregory Reaman[7]



Global footprint: standardisation and easy access to datasources worldwide

Data analytics: potential topics of interest for data collection

- **Clinical trials rejected:** how many and reasons
- **Clinical trials authorised and number of products on the market:** how many and reasons
- **Clinical trials with vulnerable populations:** minors, incapacitated persons, pregnant and lactating women, emergency situations and specific requirements (CTR chapter V): analysis of the specific requirements for guidance development
- **Are considerations of CAs/ethics committees** taken into account by the RMS?
- **Addition of MSs in an authorised clinical trial**: percentage of clinical trials with MS added later, number of opt-outs, number of MSs involved in the first authorisation: an acceptable strategy?
- **Number of clinical trials on hold** with premature end or re-start including the reasons
- **Number of clinical trials withdrawn and re-submitted** including the reasons (reason: no structered data field)
- **Number of clinical trials** with a “drop the age” approach
- **Number of clinical trials** (prematurely) ended and the **publication of results** (public databases: clinicaltrials.gov, clinicaltrialregister.eu, Dutch trial register, Pubmed)
- **Post-trial access** (structured data field!)



Crucial:
- Standardisation and generating of reliable data
- Central monitoring

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THANK YOU!

Questions?

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