Single Dossier: will national early stage trials suffer or benefit?

The Dutch approach;

Consequences of the new EU Directive on the National Level

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Medical ethical review system in the Netherlands:

decentral controlled & integrated peer review system

Decentral:

review by 24 **accredited** MECs

Controlled:

oversight by the CCMO

Integrated:

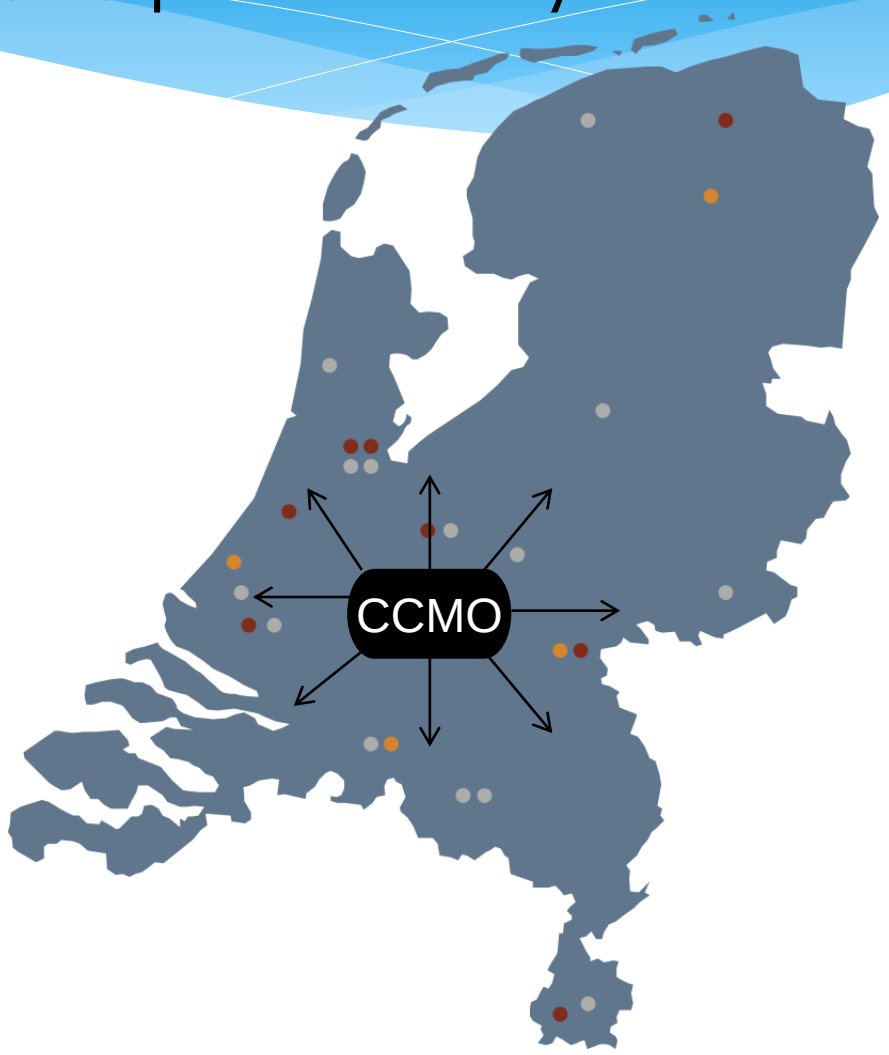
all documents in one review

Peer review:

review by experts in accredited MECs

Limited central review:

by CCMO (e.g. gene therapy)



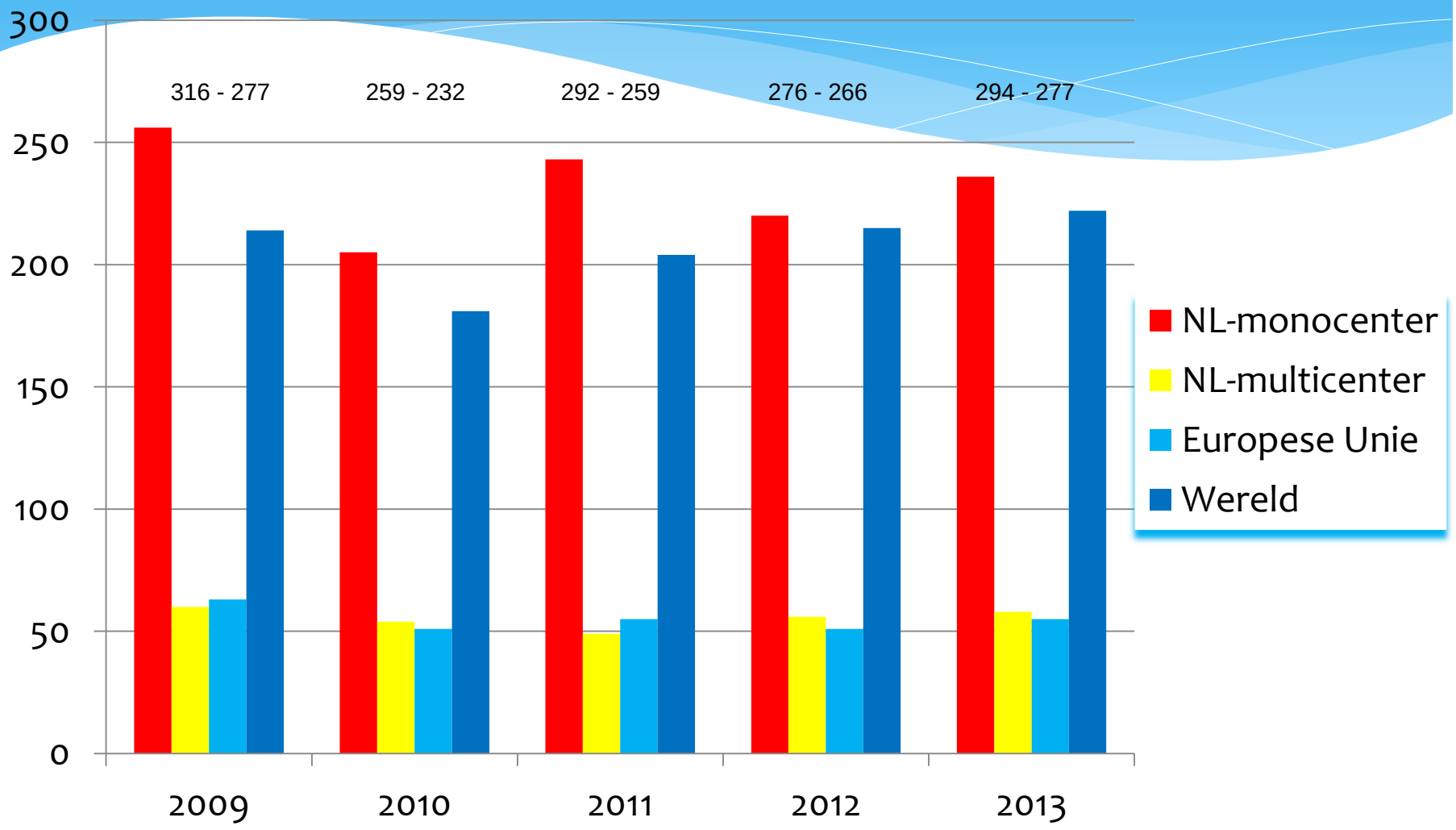
Tasks of the Central Committee

* Overseeing the operations of MEC's (accreditation)
* Reviewing Committee for specific fields of research (e.g. cell therapy, gene therapy etc.)
* Competent Authority (CA); marginal role
* Registration of Medical Research with human subjects
* Administrative Body
* Information

Number of trials in the Netherlands

* About 1800 trials yearly
* About 3% negative decisions
* 60% intervention studies (rest is observational research)
* Around 30% is research with medicinal products, more than 50% sponsored
* Figures are quite the same each year

Number of trials with medicinal products in the Netherlands



Accreditation is given to MEC when:

minimal requirements for the MEC-composition are fulfilled

- ✓ one physician
- ✓ one ethical expert
- ✓ one lawyer
- ✓ one research methodologist
- ✓ one lay person
- ✓ one clinical pharmacologist
- ✓ one pharmacist

For all disciplines criteria have been established.

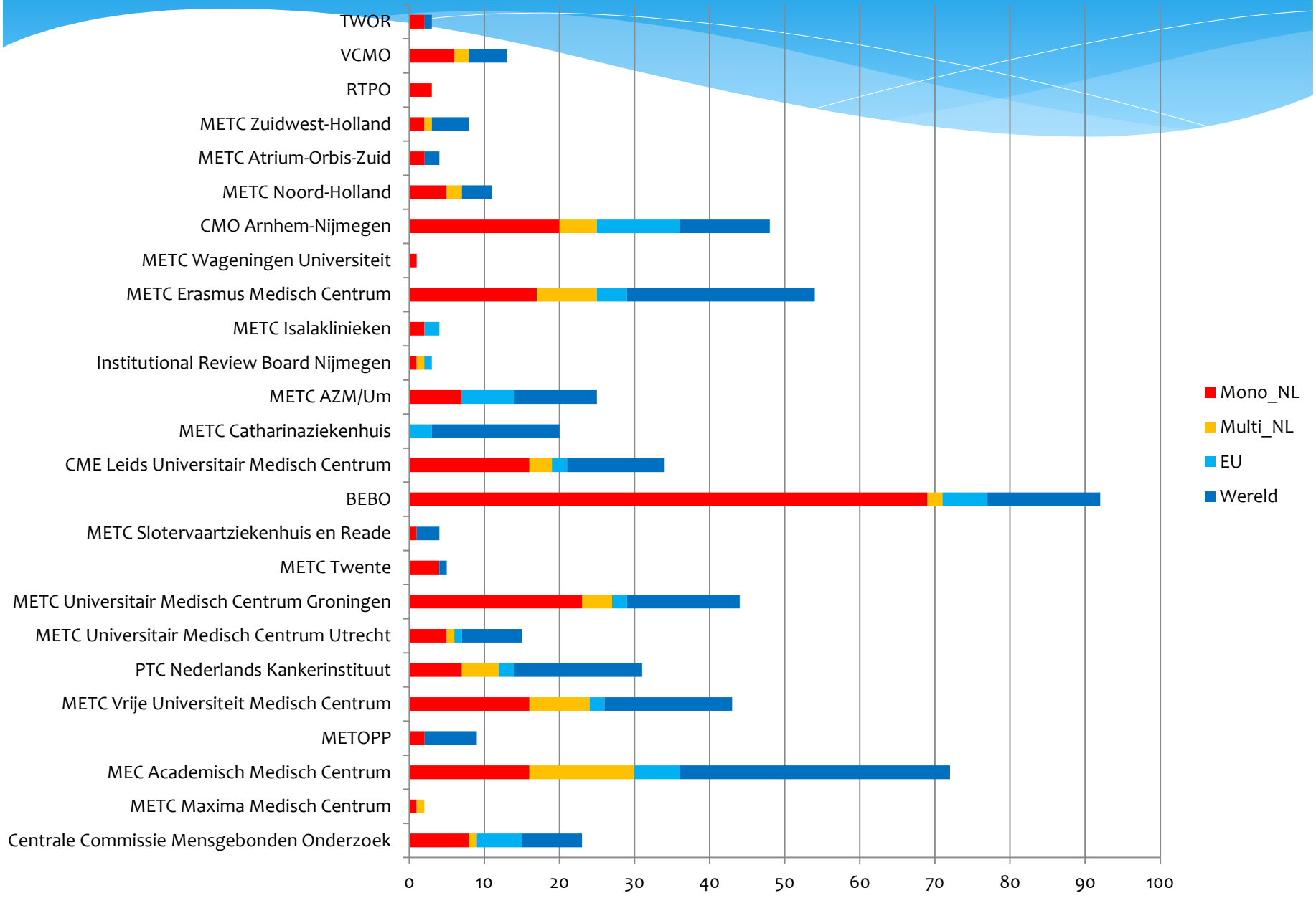
All members have to be approved by the CCMO.

Independent and no conflict of interest

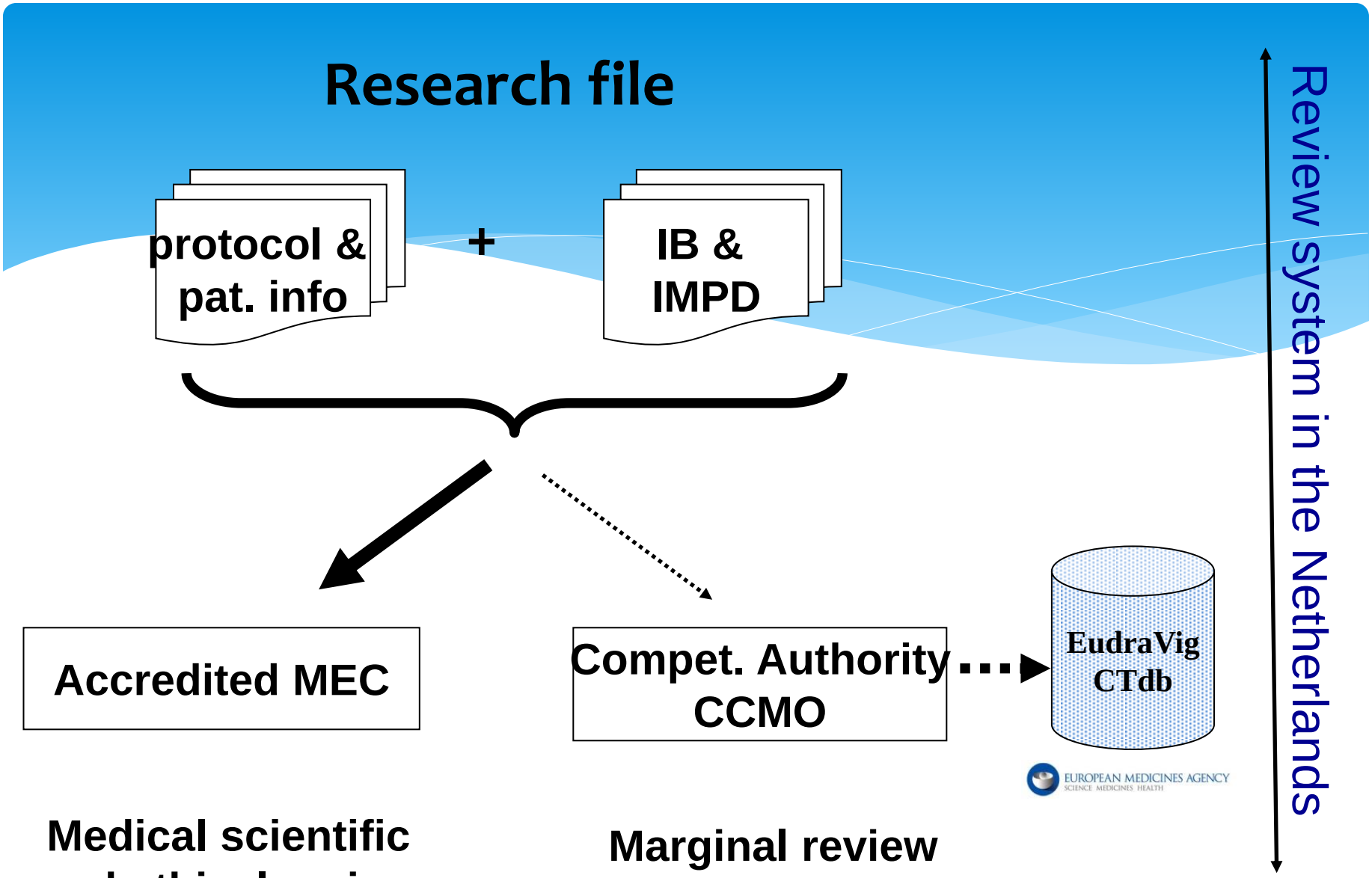
* MEC has proper regulations
* a minimum number of research dossiers is reviewed
* MEC has a quality assurance system (e.g. SOPs)

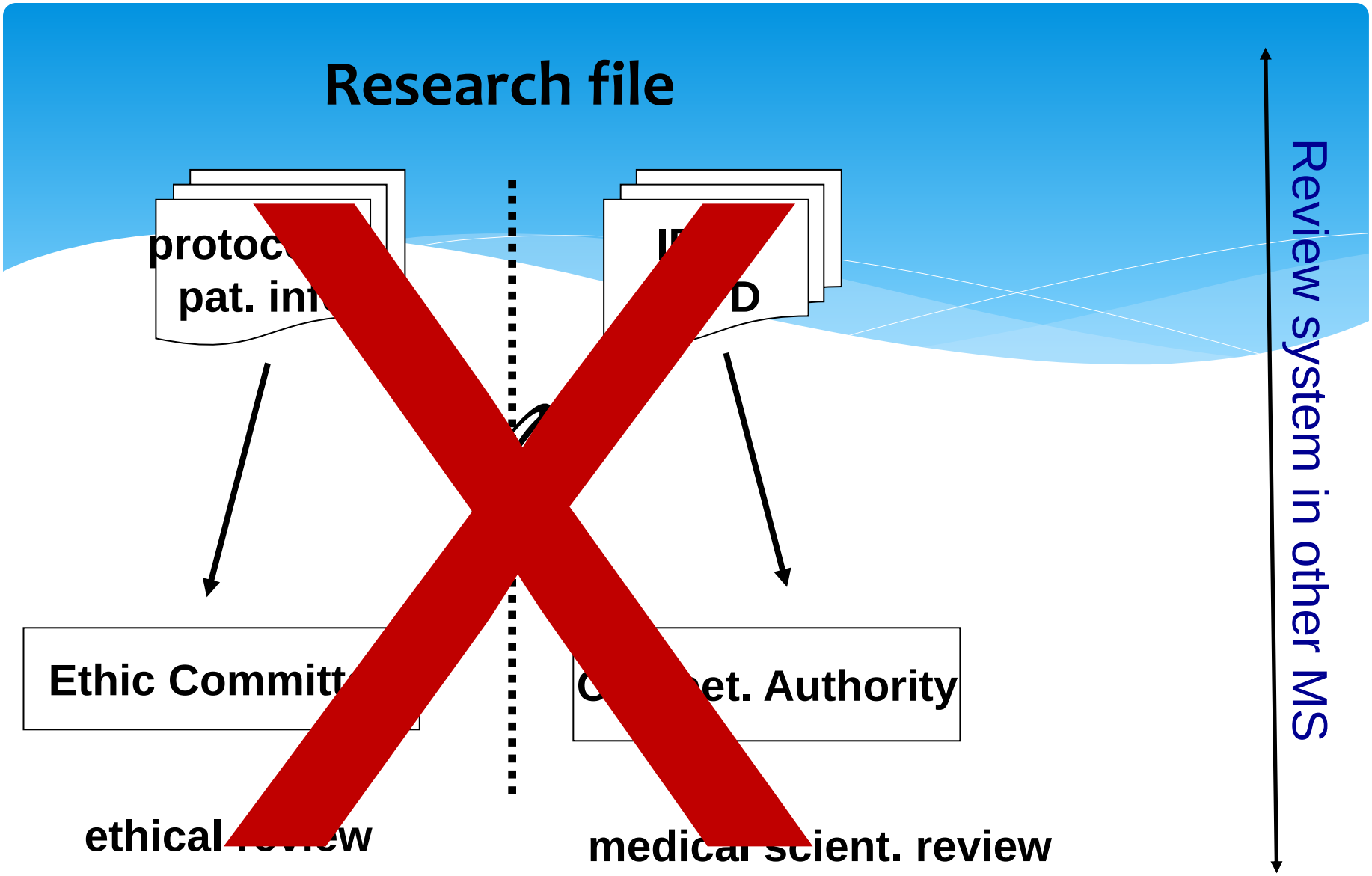
Number of trials with medicinal products in 2013 per MEC

monocenter in NL, multicenter in NL, in Europese Unie en Wereld



Research file

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Review system in other MS

An accredited MEC in the Netherlands has the expertise and fulfils the criteria for:

- part 1 assessment
- part 2 assessment
- ethical review

One committee – one **integrated assessment**!

Dutch approach

1. The Dutch Ministry of Health (VWS) installed a working Party with representatives of:

- The minister of Health (public health/ethics and medicinal products and medical technology)
- Central Committee (CCMO)
- Dutch Association of RECs (NVMETC)
- Inspectorate ('Inspectie')
- College of assessment of medicinal products (CBG)

2 options

I Remaining the decentral system with new national Secretariat? (only a limited of the present MEC's will be allowed to act as a RMS)

II Create a central system with one MEC. Members of the current MEC's and with new national Secretariat?

- Total change of the Dutch system!!!

- Both options; national Secretariat of the CCMO
- Financial consequences of both options are not clear yet
- Existing MEC's anticipate on the future changes by merging into new bigger MEC's.

Approach

- 2. Advise expert SWOT analyse (central or decentral model?)
  Definitive version February 2015.
- 3. Back to the initial working party to work this out
- 4. The Dutch minister of Health takes a decision
- 5. Start preparations for the new system

➢ **Chance** to further improve the current system

SWOT analysis

➔ Investigate which model is better (central or decentral).

Take into account:

- Maintain the current integrated review of scientific and ethics by one REC
- The ambition level (NL rMS of min. 25%)
- The expected efficacy of model I or II
- Maintain the decentralised review for national research
- Weaknesses and risks of both models
- Organizational consequences of both models

Starting points

* Ambition; active role as reporting Member State
* Efficient and payable system
* Efficient review system: quality and uniformity are guaranteed, that meets the requirements of the EU Directive

- For other research the current Dutch law will apply.
- The Dutch law will be adjusted, with extra regulation about tasks for the assessment of research with medicinal products.

SWOT Advice

* Maintain the current **integrated review** of science and ethics **by one MEC**
* Maintaining the current Dutch system of decentralisation, but **concentration** of (specialised) MEC's for medicinal products. The number of MEC's for medicinal products will be limited!!!
* Quality & efficiency will be further improved
* Support by a " **Central Coordination Point"** (to be approved by the Ministry of Health)
* This will change the MEC landscape

Role of Central Coordination Point

- Validation of about 550 trials with medicinal products
- Oversee the review of 275 nation trials by MEC's
- Draft the assessment report of multinational trials (70) part 1 and 2 (including amendments) (discussion point)
- Coordination role for the review of safety information and serious breaches
- Communication with/between MS and sponsor via the EU portal
- The use and support of the EU portal in the Netherlands

➢ Biggest change: **One contact point for communication**

Early stage trials; changes?

- Only a few MEC's review phase 1 (including Central Committee for specialized trials)
- One specialised committee for early stage trials: BEBO
- Own applicants
- Central coordination point selects (e.g. expertise of METC, request of applicant, agenda of MEC)
- Expect these specialised MEC's will continue to receive the phase 1 trials
- Remain its applicants after implementation of the EU directive
- No big changes

Remarks and conclusion

- Potentially pitfalls:
- **Communication via EU Portal** (Central coordination point) in stead of direct contact with applicants. Delay?
- Possible delay if assessment report by and via Central coordination point. Discussion point.
- However: we need a professional coordination point in order to meet the requirements of the EU directive. Experience with the VHP in the Netherlands.
- Financial issues
- My conclusion: marginal changes for phase 1 national trials expected in the Netherlands because of already integrated system (part I&II/ethical review). Other countries might have more struggle.
- Remark: timelines to respond (10 days) could be a problem for CRO's of international trials. (They need time to tune with sponsor in the US for example.)

Sources:

- CCMO: www.ccmo.nl
- Report of P. Driebergen (Dutch)

We don’t have mountains in the Netherlands…