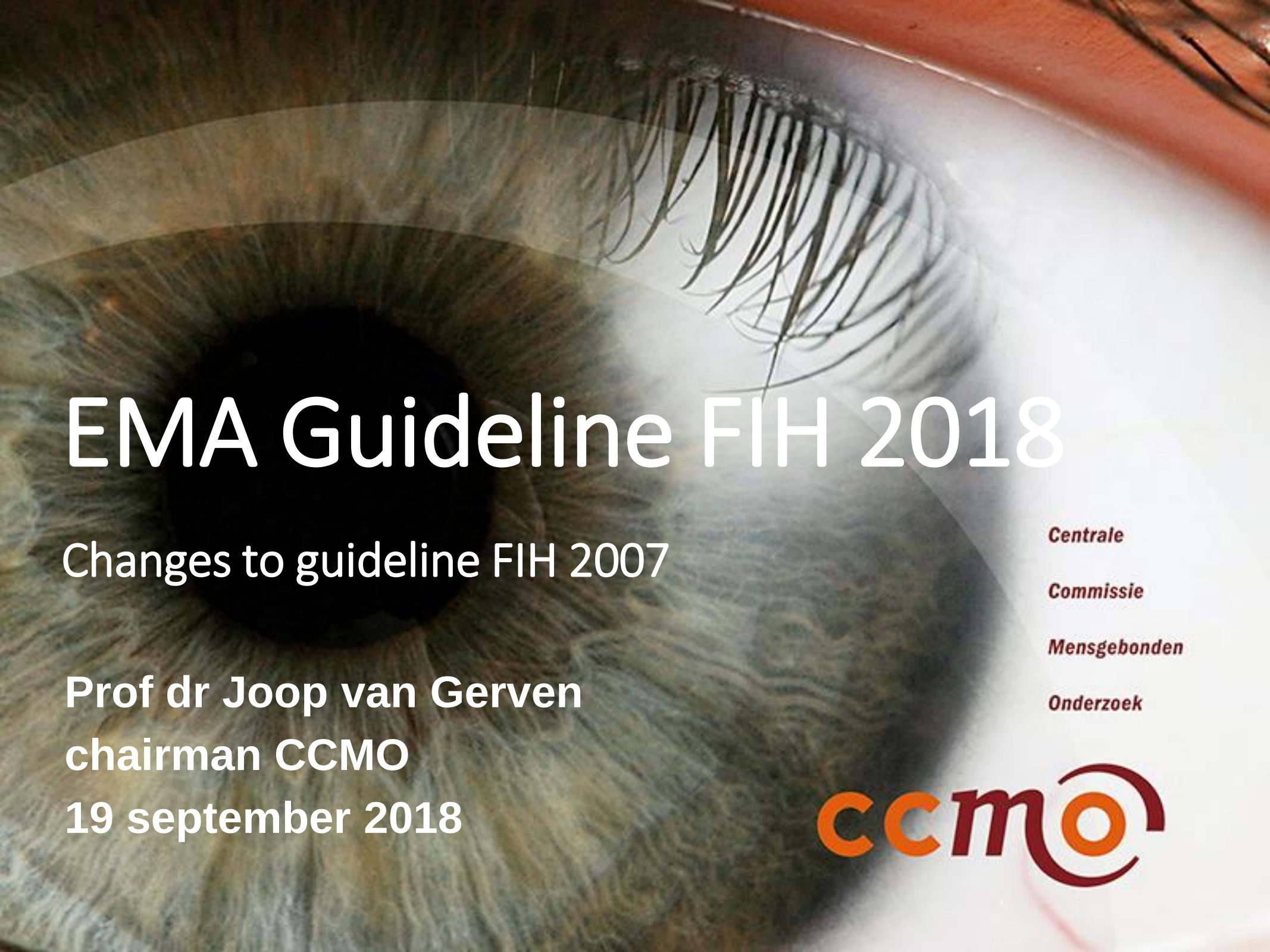


EMA Guideline FIH 2018

Changes to guideline FIH 2007

Prof dr Joop van Gerven
chairman CCMO
19 september 2018

Centrale
Commissie
Mensgebonden
Onderzoek

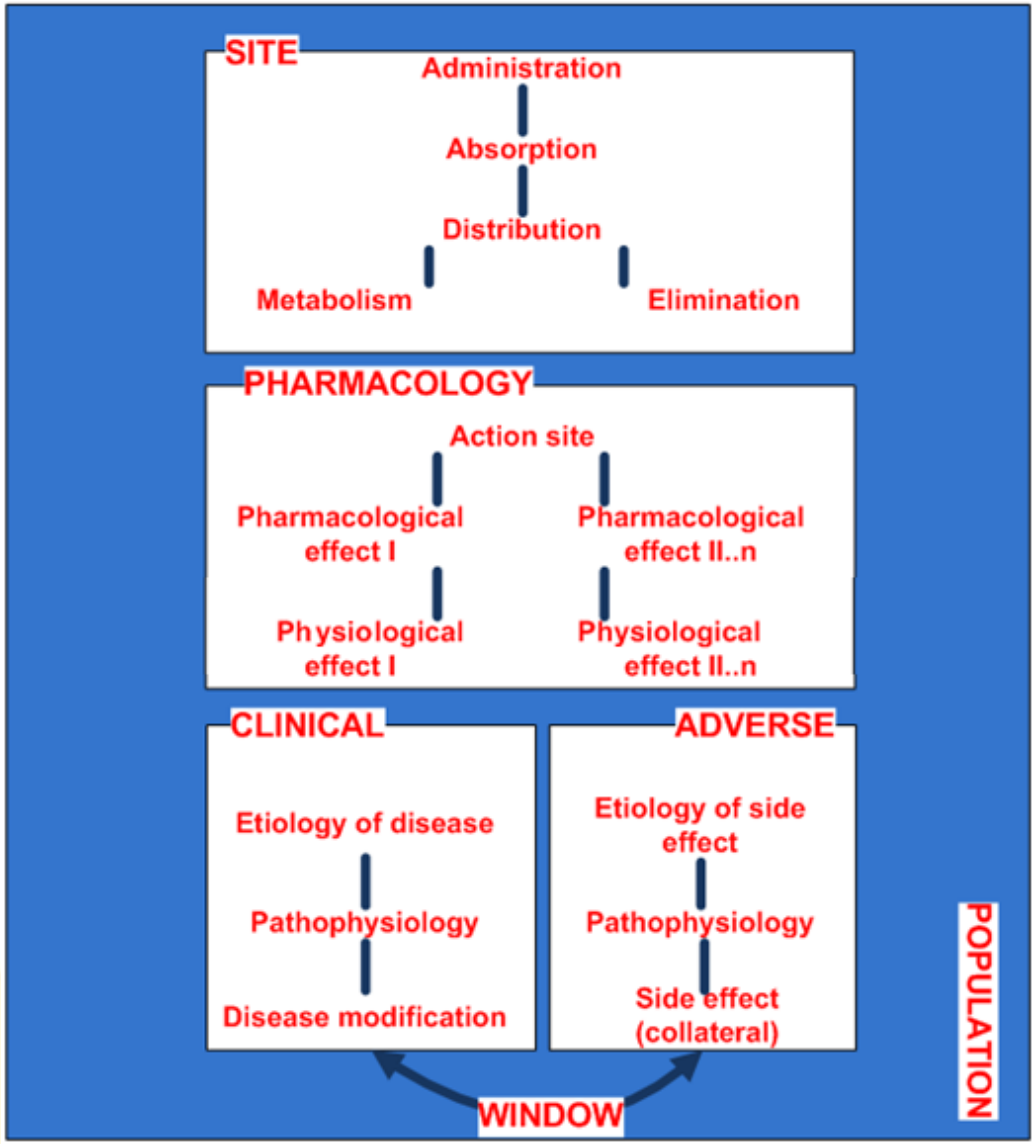
ccmo

Essential Changes

- **More emphasis on pharmacology and action mechanism**
  - MABEL, PK, PD, PAD, ATD (no MTD)
  - primary / secondary pharmacology
  - PK- and PD-monitoring
  - dosing limits

- **More emphasis on protocol arrangements**
  - rationale / justification
  - predefined expectations
  - amendments
  - stopping rules
  - responsibilities

- **More emphasis on 'totality of evidence'**
  - structured IB-assessment (ib-derisk.org)
  - translational models, PD/PD
  - decisions based on integration of emerging data



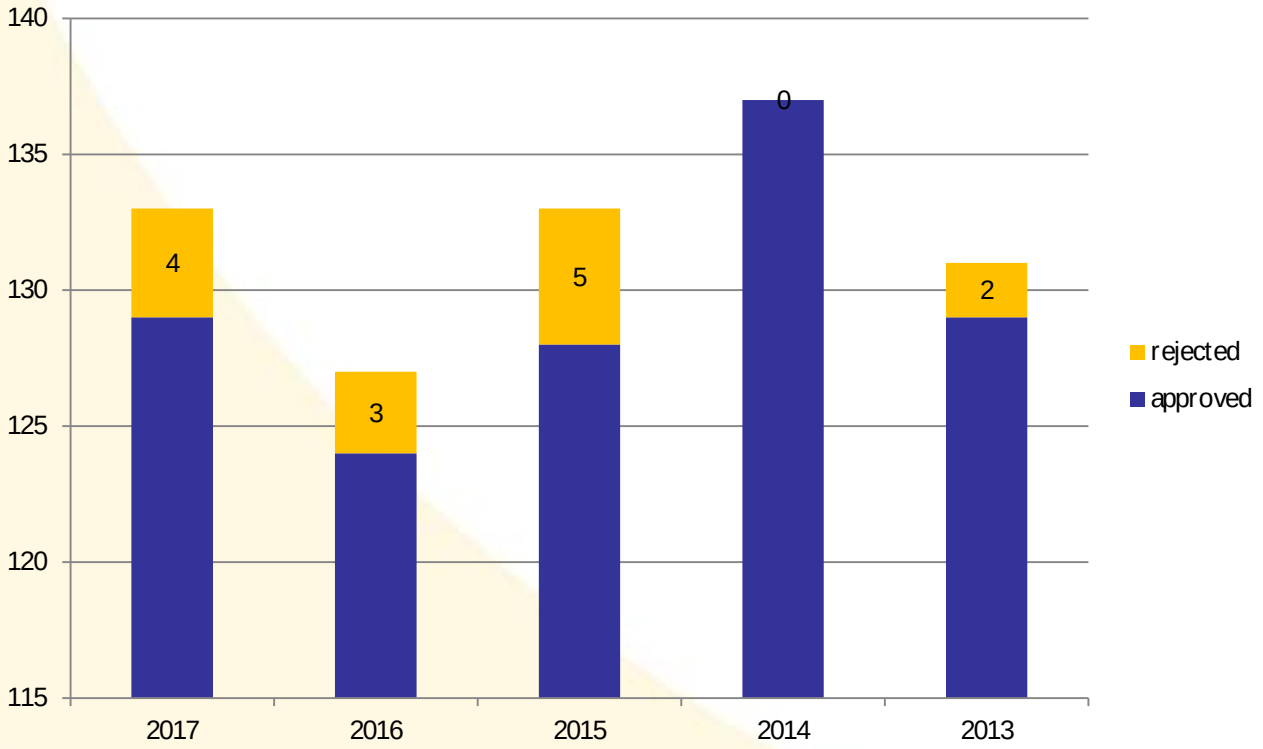
Bonelli M, Van Gerven JMA. Commentary on the EMA Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products (EMEA/CHMP/SWP/28367/07 Rev. 1). Br J Clin Pharmacol 2018;84(7):1401-1409

Cohen AF. Developing drug prototypes: pharmacology replaces safety and tolerability? Nat Rev Drug Discov. 2010;9:856-65

Van Gerven JMA, Cohen AF. Integrating data from the IMPD/IB. A new tool for translational integration of preclinical effects. Br J Clin Pharmacol 2018 Jul;84(7):1457-1466.

Cohen AF, Burggraaf J, Gerven JM, Moerland M, Groeneveld G. The Use of Biomarkers in Human Pharmacology (Phase I) Studies. Annu Rev Pharmacol Toxicol. 2015; 6;55:55-74

Phase I Studies in the Netherlands



jaar	fase I	negatief	Totaal beoordelingen CCMO	Negatief CCMO	Negatief andere TC
2017	133	4	13	3	1 (METC Brabant)
2016	127	3	7	3	
2015	133	5	10	4	1 (UMCU)
2014	137	0	10		
2013	131	2	5	1	1 (AMC)

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