INTRODUCTIE & DRUG LIFE CYCLE

BRAINFEED

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EVEN VOORSTELLEN

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DUBBELE PETTEN?

- Geen aandelen of belangen in farma-industrie
- Gebruik generieke namen, tenzij specialiténaam functioneel
- Eigen meningen, geen last en ruggespraak andere partijen
- Vergoeding Brainfeed, zonder bemoeienis met inhoud van hun kant

FARMACOLOGIE & VERWACHTINGEN

- Wat is farmacologie?
- Wat zouden deze 2 cursusdagen moeten bieden?

MIJN VOORSTEL

- Uitgangspunt: life cycle van een geneesmiddel

- Universele concepten als basis
  - Farmacokinetiek
  - Farmacodynamiek
  - Als verklaring voor onbewust dagelijks handelen

- Vertaling naar individuele zorg
  - Pitfalls
  - Hoe 'personalised medicine' vorm te geven?

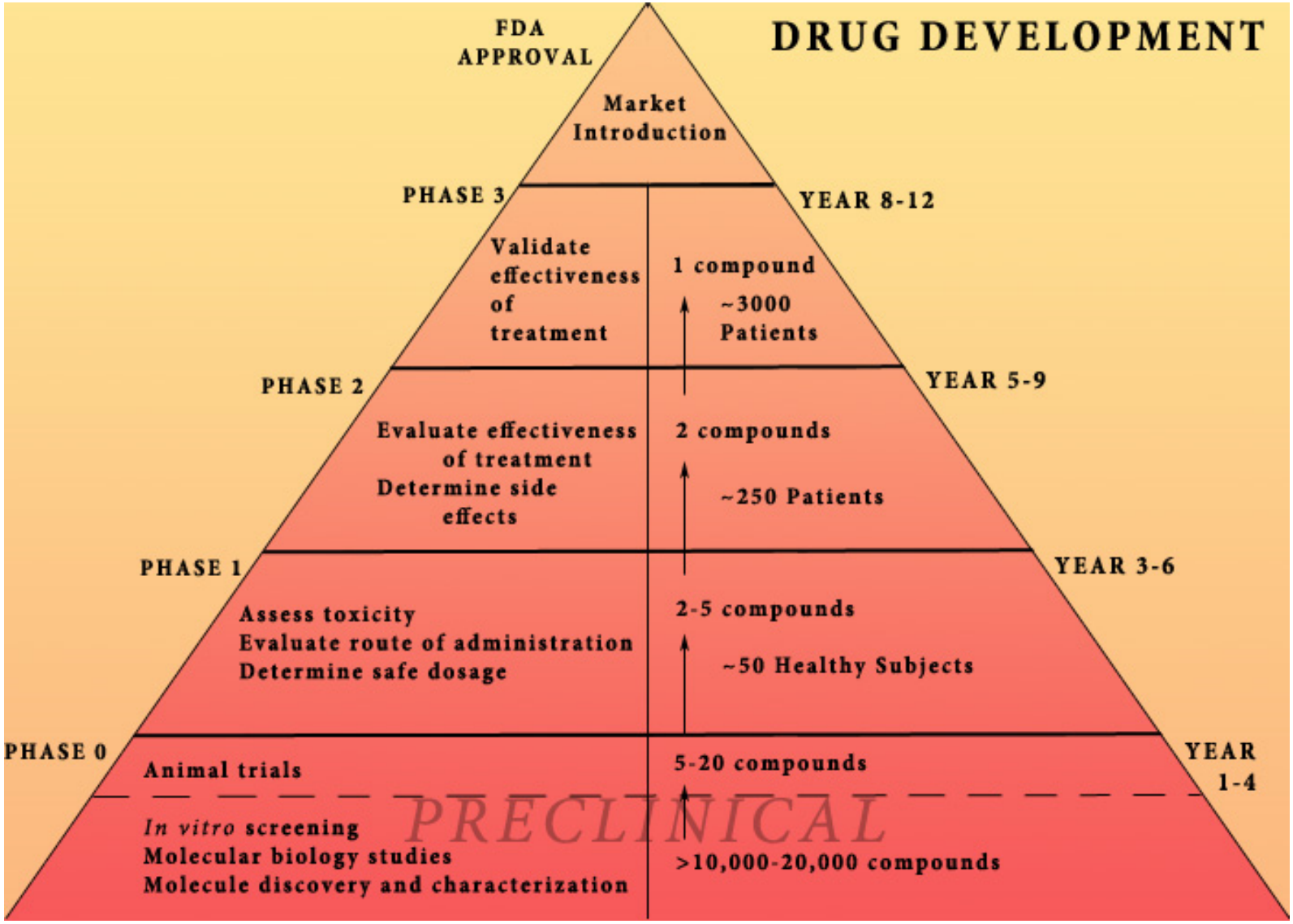
MIJN VOORSTEL

- Aan de hand van de concepten PK en PD
  - De diepte in o.b.v. vignetten
  - Vignetten zijn breed herkenbaar
    - I.v.m. diverse achtergrond aanwezigen
  - Bijv. cholesterolverlaging, NSAIDs, corticosteroïden of antibiotica

- Zo interactief mogelijk
  - Vragen van beide kanten


START

DRUG LIFE CYCLE: PHASE I - IV



http://digitalunion.osu.edu/r2/summer09/jaeger/images/DDevelopment.jpg

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HISTORISCH PERSPECTIEF VAN BIOETHIEK

- Fasen 1 tot en met 4
  - Gebonden aan regels en wetten
  - Continue evolutie van uitgangspunten

- Historisch perspectief om nader te duiden:
  - Binnen welke regels dit (farmacologisch) onderzoek plaatsvindt
  - Waar deze regels hun oorsprong vinden

ETHICS

- Ethics: the discipline dealing with what is good and bad and with moral duty and obligation [1]

1. https://www.merriam-webster.com/dictionary/ethic (Visited July 3 2017

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BIOETHICS

- Application of ethics to the field of medicine, healthcare, biotechnology and ecology
- No absolute standards
- Standards are developed in time

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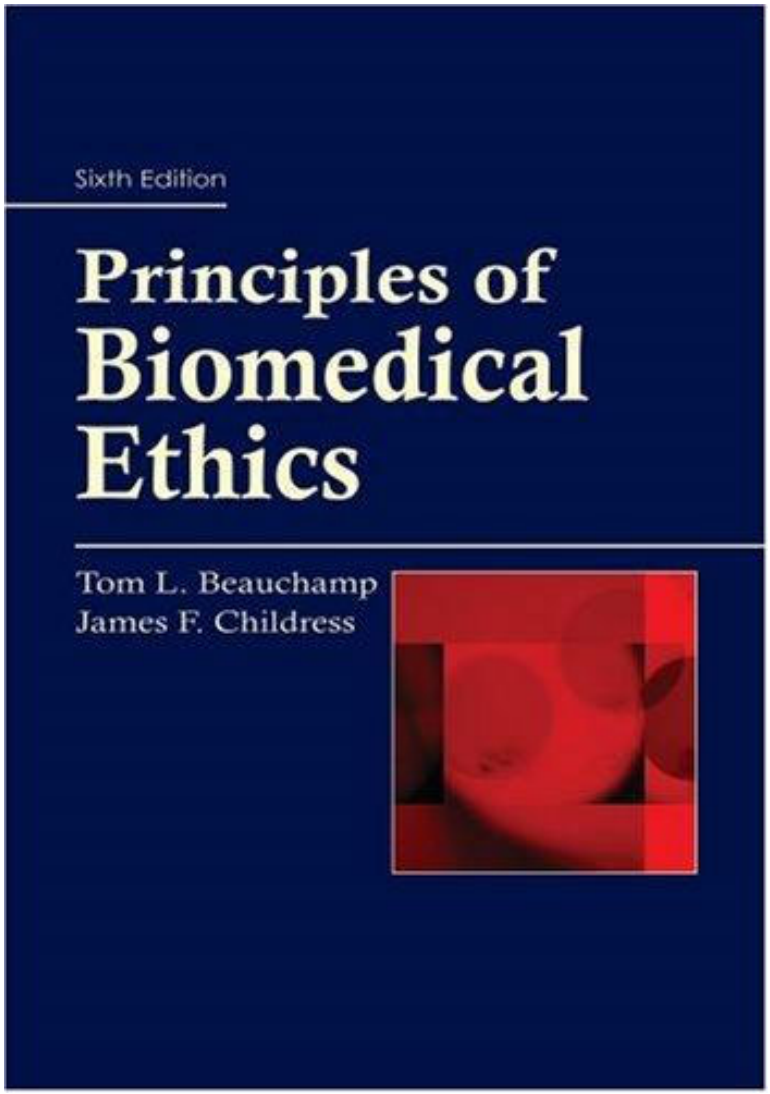
BIOETHICAL PRINCIPLES

- A.k.a. Georgetown mantra

- Respect for autonomy
- Non-maleficence
- Beneficence
- Justice



http://medanth.wikispaces.com/Bioethics (visited July 3 2017)

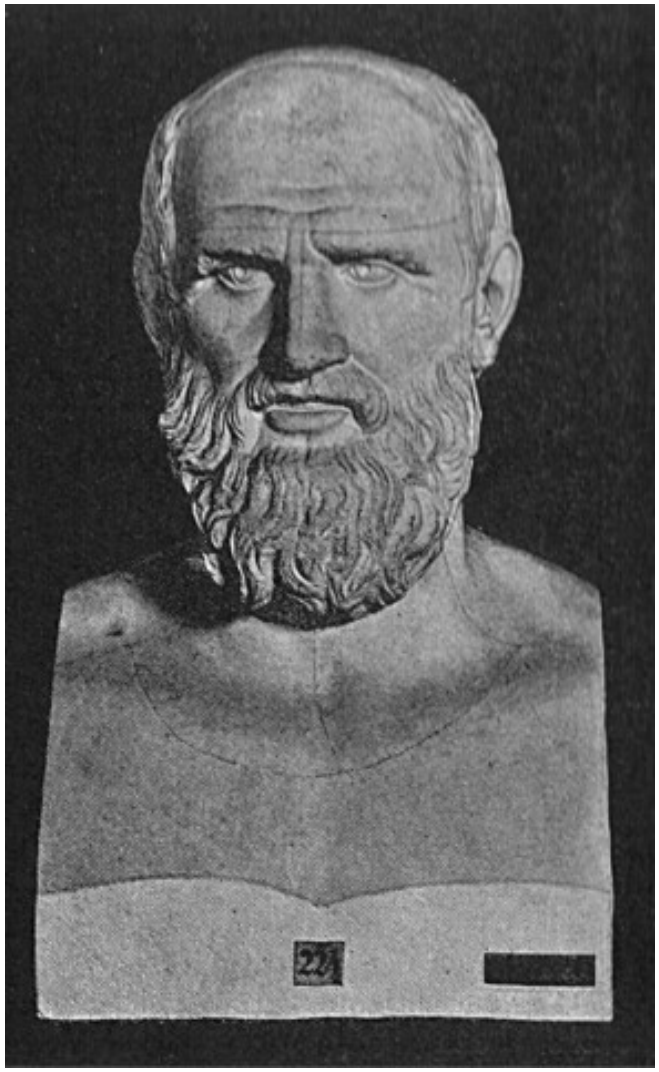
RESPECT FOR AUTONOMY

- Right tot self-rule
- Free from both
    - controlling interference by others and
    - from limitations, such as inadequate understanding, that prevent meaningful choice.
- Respect for autonomy supports other specific actions
    - such as telling the truth,
    - respecting the privacy of others,
    - protection of confidential information,
    - obtaining informed consent, and
    - helping others making important decisions.

NON-MALEFICENCE

- Duty to refrain from causing harm

- Non-maleficence underlies the medical maxim found in the Hippocratic Oath, “above all (or first) do no harm[5] .”



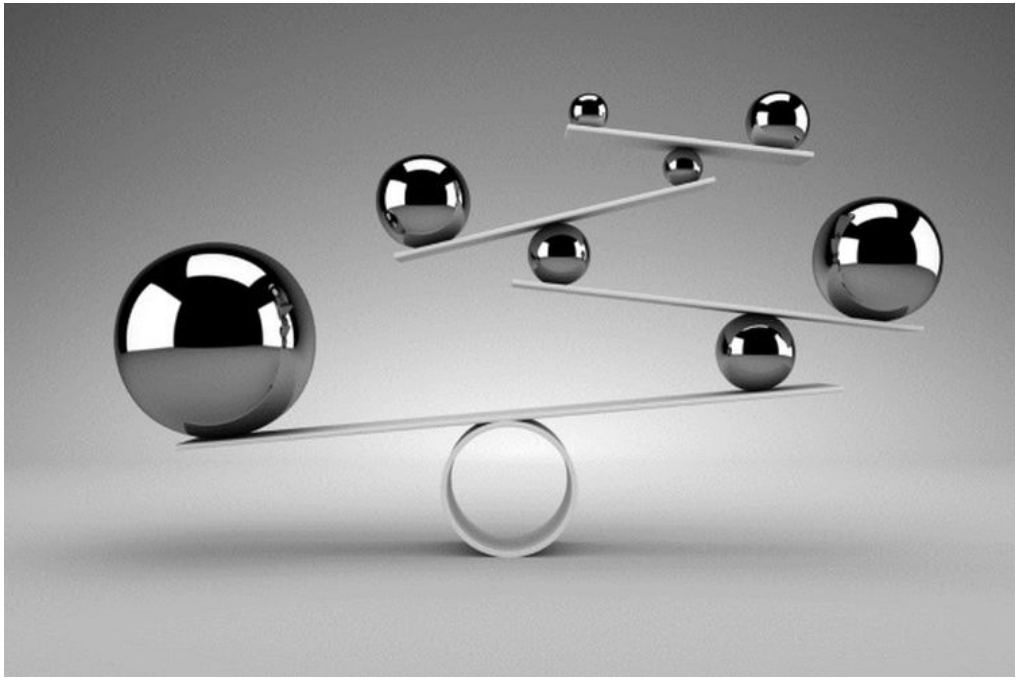
Hippocrate (400 B.C.)

BENEFICENCE

- Beneficence is to bring or create benefit.

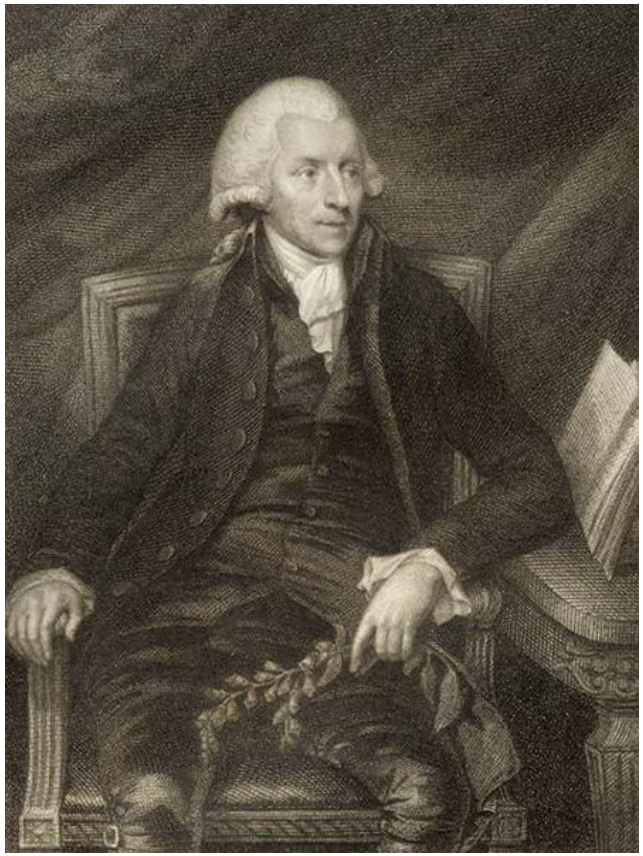
- Under beneficence, one ought to prevent evil or harm, remove evil or harm, and do or promote good.

JUSTICE



- Justice
  - how social benefits and burdens should be distributed

BIOETHICS: THE BEGINNING



William Withering (1741-1799)
English botanist & geologist

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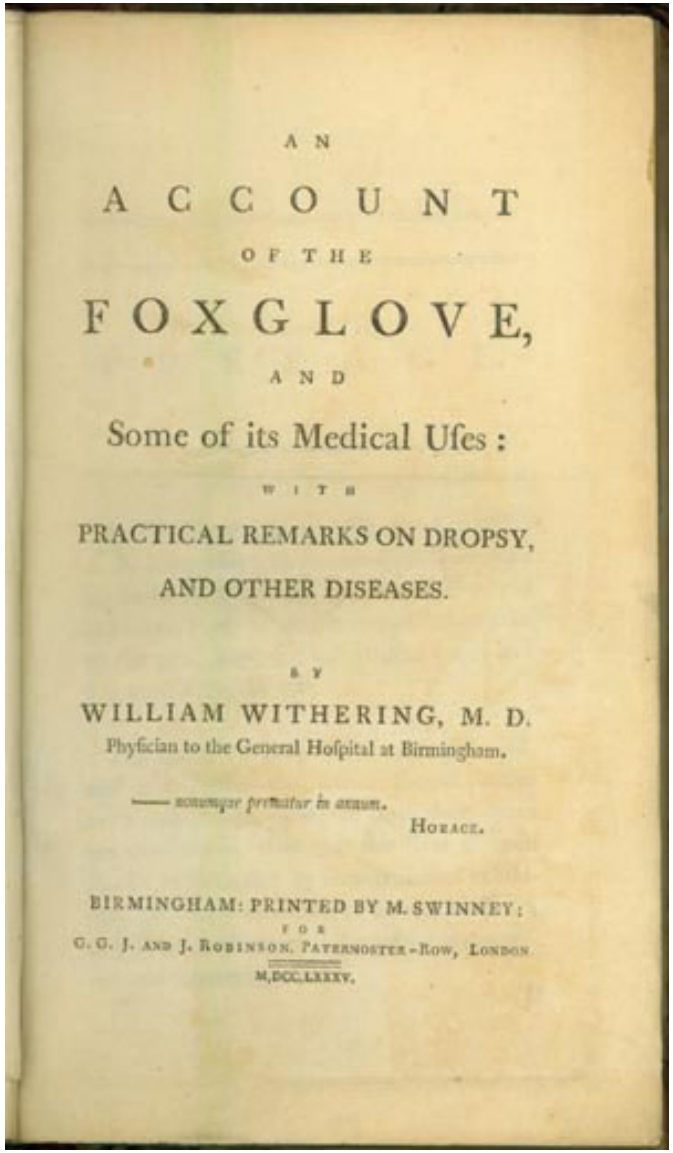
BIOETHICS: THE BEGINNING

- Anecdotal evidence (from 'old mother Hutton') for efficacy of a herbal mixture in 'dropsy' (edema due to congestive heart failure)
- Identified foxglove as principal therapeutic component in the mixture
- Treated 158 patients with dropsy
- Described the efficacy and safety in every case



AN

ACCOUNT

OF THE

FOXGLOVE,

AND

Some of its Medical Uſes:

WITH

PRACTICAL REMARKS ON DROPSY,

AND OTHER DISEASES.

BY

WILLIAM WITHERING, M. D.

Phyſician to the General Hoſpital at Birmingham.

—— *nonumque prematur in annum.*

HORACE.

BIRMINGHAM: PRINTED BY M. SWINNEY:

FOR

G. G. J. AND J. ROBINSON, PATERNOSTER-ROW, LONDON.

M,DCC,LXXXV.

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BIOETHICS: THE BEGINNING

CASE CXXVI.

April 17th. Mr. F——, Æt. 59. A very fat man, and a free liver; had long been ſubject to what was called aſthma, particularly in the winter. For ſome weeks paſt his legs ſwelled, he had great ſenſe of fullneſs acroſs his ſtomach; a ſevere cough; total loſs of appetite, thirſt great, urine ſparing, his breath ſo difficult that he had not lain down in bed for ſeveral nights. Calomel, gum ammoniac, tincture of cantharides, &c. having been given in vain, I ordered two grains of pulv. fol. Digitalis made into pills, with aromatic ſpecies and ſyrup, to be given every night. On the third day his urine was leſs turbid; on the fourth conſiderably increaſed in quantity, and in ten days more he was free from all complaints, and has ſince had no relapſe.

CASE CXXVII.

May 7th. Miſs K——, Æt. 8. After a long continued ague, became hectic and dropſical. Her belly was very large, and ſhe had a total loſs of appetite. Half a grain of fol. Digital. pulv. with 2 gr. of merc. alcalis. were ordered night and morning, and an infuſion of bark and rhubarb with ſteel wine to be given in the day time. Her belly began to ſubſide in a few days, and ſhe was ſoon reſtored to health. Two other children in the family, affected nearly in the ſame way, had died, from the parents being perſuaded that an ague in the ſpring was

was healthful and ſhould not be ſtopped.—I know not how far the recovery in this caſe may be attributed to the Digitalis, but the child was ſo near dying that I dared not truſt to any leſs efficacious diuretic.

CASE CXXVIII.

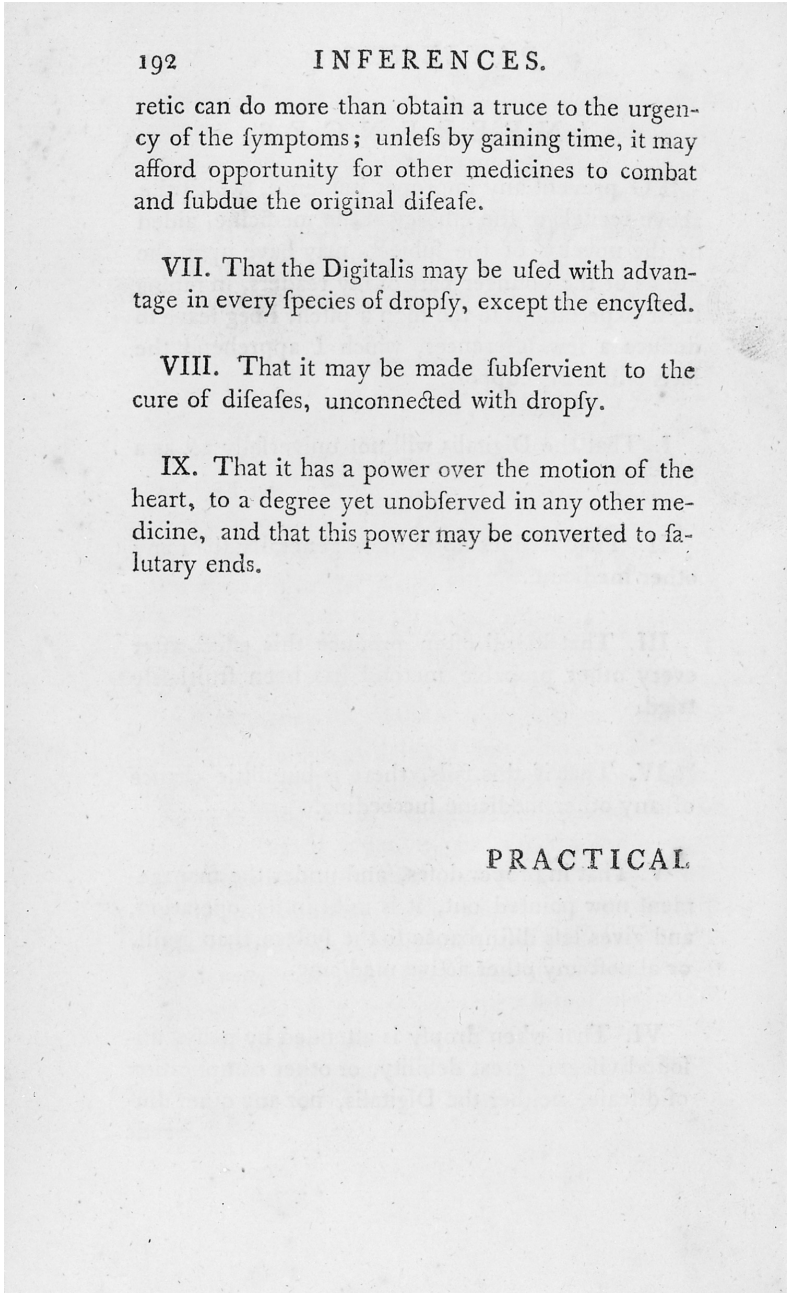
June 13th. Mr. C——, Æt. 45. A fat man, had formerly drank hard, but not latterly: laſt March began to complain of difficult breathing, ſwelled legs, full belly, but without fluctuation, great thirſt, no appetite; urine thick and foul; complection browniſh yellow. Mercurial medicines, diuretics of different kinds, and bitters, had been trying for the laſt three months, but with little advantage. I directed two grains of the fol. Digital. in powder to be taken every night, and infuſ. amar. with tinct. ſacr. twice a day. In three days the quantity of his urine increaſed, in ten or twelve days all his ſymptoms diſappeared, and he has had no relapſe.

CASE CXXIX.

June 17th. Mr. N——, of W——, Æt. 54. A large man, of a pale complexion; had been ſubject to ſevere fits of aſthma for ſome years, but now worſe than uſual. The intermitting pulſe, the great diſturbance from change of poſture, and the ſwelled legs induced me to conclude that the exacerbation of his old complaint was occaſioned by ſerous effuſion. I directed pills with a grain and half of the

BIOETHICS: THE BEGINNING

- Remarkable perspectives
  - Structural assessment of therapeutic value
  - Case reports
  - Formulated general conclusions
  - Admitted to have overdosed patients



192 INFERENCES.

retic can do more than obtain a truce to the urgency of the ſymptoms; unleſs by gaining time, it may afford opportunity for other medicines to combat and ſubdue the original diſeaſe.

VII. That the Digitalis may be uſed with advantage in every ſpecies of dropſy, except the encyſted.

VIII. That it may be made ſubſervient to the cure of diſeaſes, unconnected with dropſy.

IX. That it has a power over the motion of the heart, to a degree yet unobſerved in any other medicine, and that this power may be converted to ſalutary ends.

PRACTICAL

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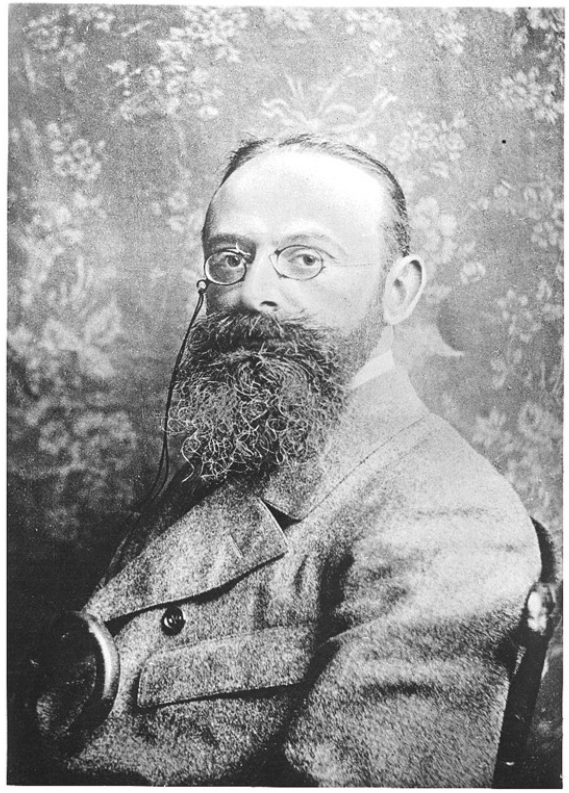
ALBERT LUDWIG NEISSER (1855-1916)



- Discovered Neisseria gonorrhoea
  - Pathogen causing gonorroe
- Injected cell-free serum of syphilis patients in healthy volunteers, mostly prostitutes, as vaccination
- Conclusions:
  - Vaccination is ineffective
  - Syphilis infection is result of the work, not of the serum injection
- Participants were not informed on the trial, nor signed informed consent
  - In 1898 Neisser was fined by the Royal Disciplinary Court for not asking IC

THE AFTERMATH

- 1898: Neisser was fined
    - Not asking informed consent
- 1899: Report of the 'Scientific Council'
    - Experiments have to be useful
    - Participant is autonomous an makes the decision whether or not to engage
- 1900: Prussian Guideline
    - No medical experiments in minors
    - Informed consent obligatory after informing the participant
    - Guidelines on documentation of the experiment
- 1931: ReicksZirkular
    - Guidelines and precautions for 'therapeutical' versus 'non-therapeutical' experiments

Vollmann, et al. BMJ 1996;313:1445-9.

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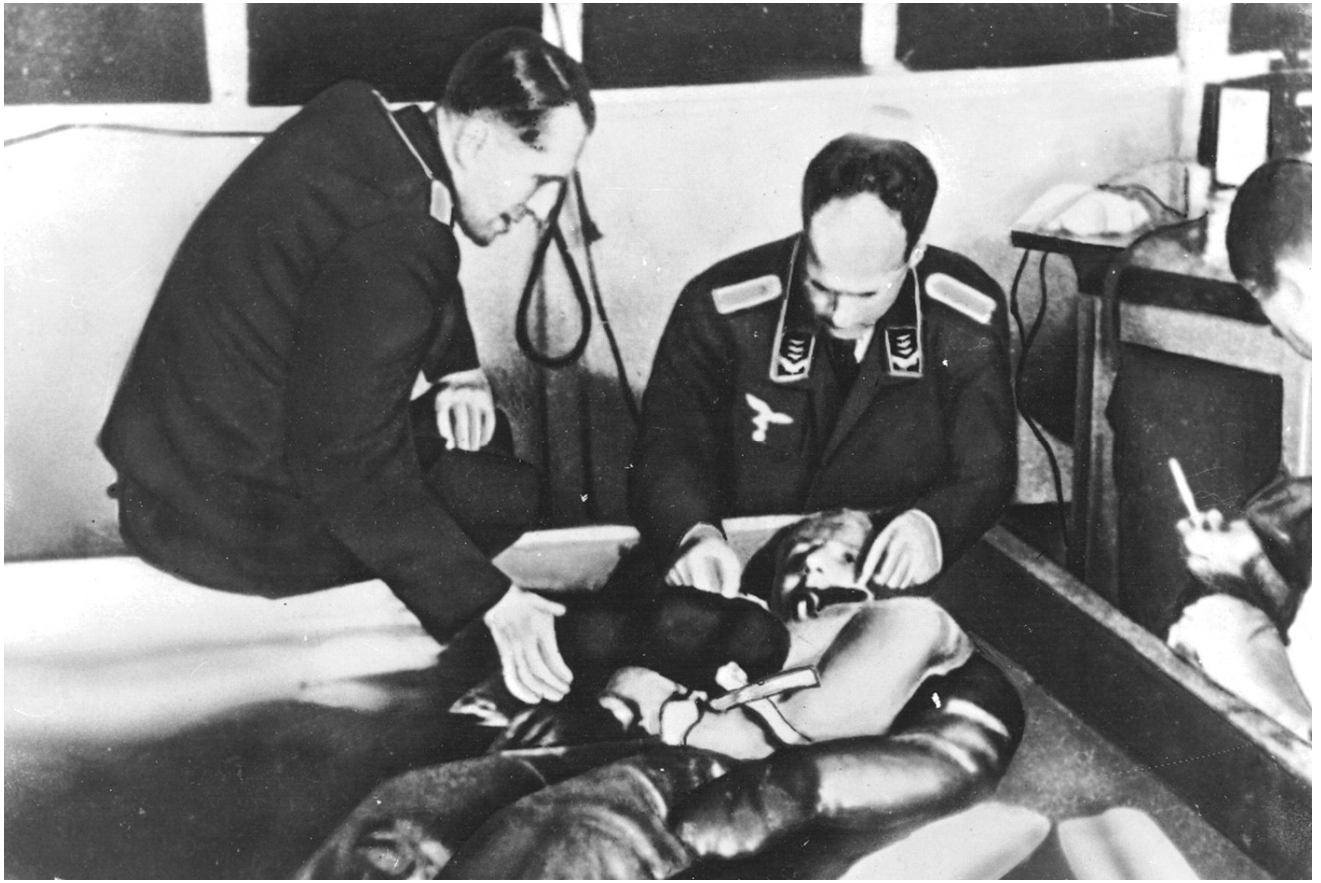
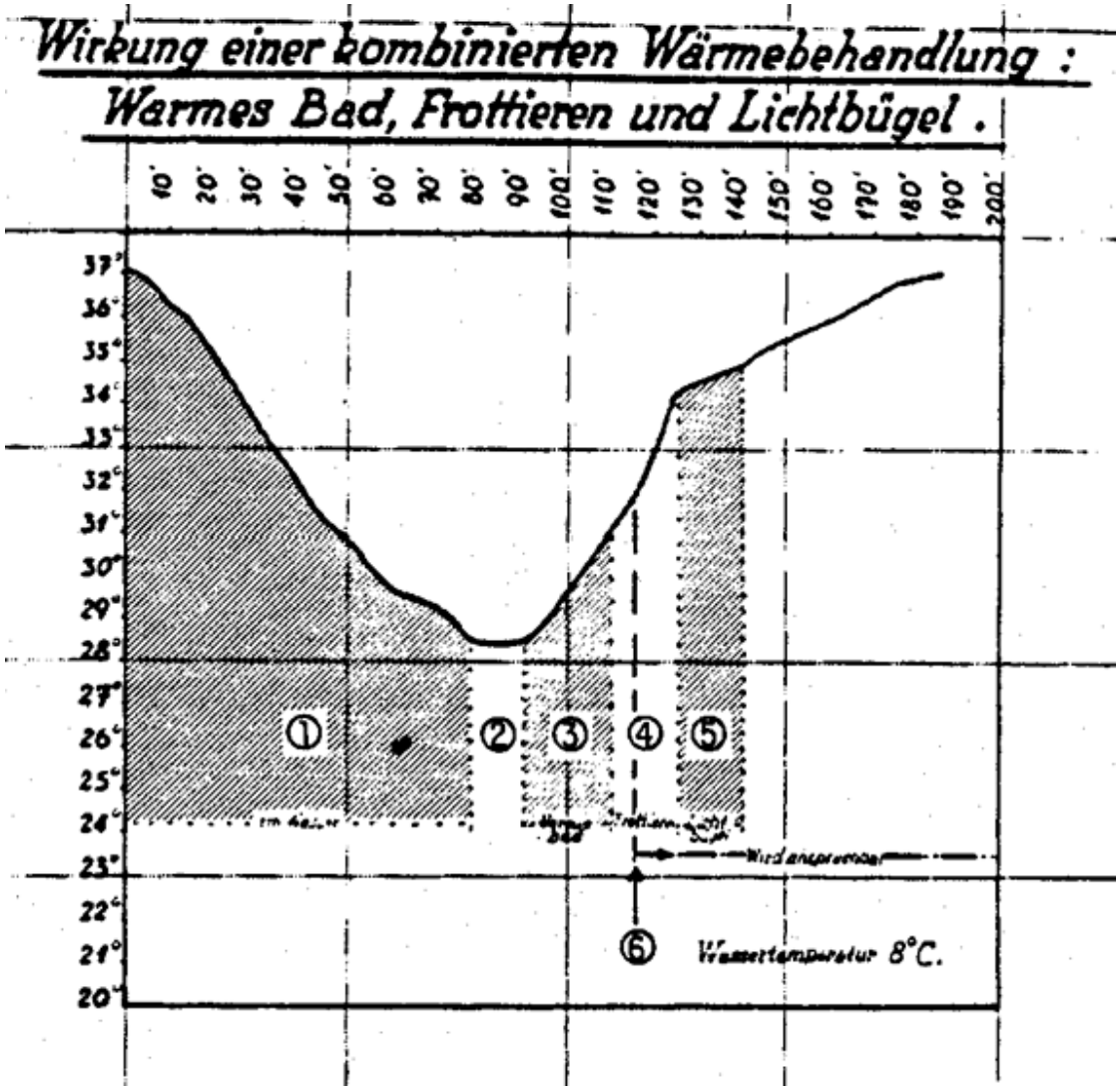
AND THEN . . .



- Rascher & Holzlöhner, 2nd WW, SS physicians
- Experiments on hypothermia in cold water
    - Resembling pilots landing in sea

DO WE USE THESE RESULTS?



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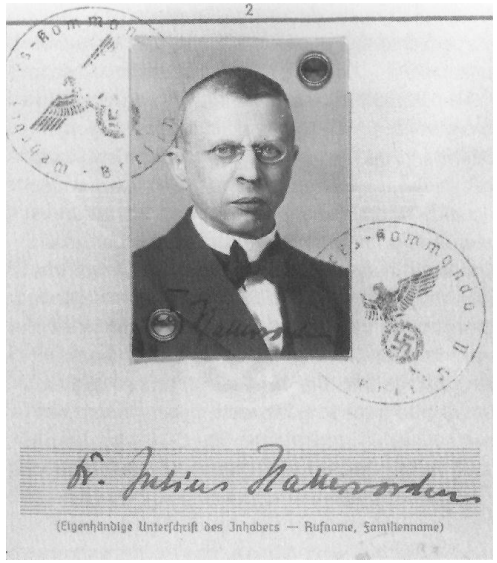
DO WE USE THE RESULTS?



Prof. Dr. Julius Hallervorden ('German physician, neuroscientist; 1882-1965) said in the Nuremberg Trials:

"Look boys, if you feel you have to kill these people please remove the brains so that we can use the material."

"...those brains offered wonderful material, of mentally poor, deformities and early children's diseases. Of course I accepted the brains. It really wasn't my concern where they came from and how they were brought to me."

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THE NUREMBERG CODE 1947: 10 POINTS

1. Required is the voluntary, well-informed, understanding consent of the human subject in a full legal capacity.
2. The experiment should aim at positive results for society that cannot be procured in some other way.
3. It should be based on previous knowledge (e.g. an expectation derived from animal experiments) that justifies the experiment.
4. The experiment should be set up in a way that avoids unnecessary physical and mental suffering and injuries.
5. It should not be conducted when there is any reason to believe that it implies a risk of death or disabling injury.

THE NUREMBERG CODE 1947: 10 POINTS

6. The risks of the experiment should be in proportion to (that is, not exceed) the expected humanitarian benefits.

7. Preparations and facilities must be provided that adequately protect the subjects against the experiment's risks.

8. The staff who conduct or take part in the experiment must be fully trained and scientifically qualified.

9. The human subjects must be free to immediately quit the experiment at any point when they feel physically or mentally unable to go on.

10. Likewise, the medical staff must stop the experiment at any point when they observe that continuation would be dangerous.

DECLARATION OF HELSINKI

WORLD MEDICAL ASSOCIATION

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WHAT WE DO | POLICY | PUBLICATIONS | NEWS & PRESS | WHO WE ARE | JUNIOR DOCTORS | MEMBERS' AREA

Policy / Current Policies / **WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects**

A- A+

WMA DECLARATION OF HELSINKI – ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

19th October 2013

Policy Types

Declaration

Tags

Clinical Study, Ethics, Ethics Committee, Helsinki, Human Subjects, Medical Research, Patient Autonomy, Placebo, Post-Trial Access, Principle, Publication, Register, Review Committee, Risk Assessment, Subject Protection, Vulnerable Populations

Similar Posts

WMA Declaration of

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

The Declaration is intended to be read as a whole and each of its constituent paragraphs should

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https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/ (visited July 3 2017)

DECLARATION OF HELSINKI

- - 37 statements on (among others):
    - Risks, burdens and benefits
    - Vulnerable Groups and Inidividuals
    - Scientific Requirements and Research Protocols
    - Research Ethic Committees
    - Privacy and Confidentiality
    - Informed Consent
    - Use of Placebo

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DOH: SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS

Scientific Requirements and Research Protocols

21. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

22. The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

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DOH: RESEARCH ETHIC COMMITTEES

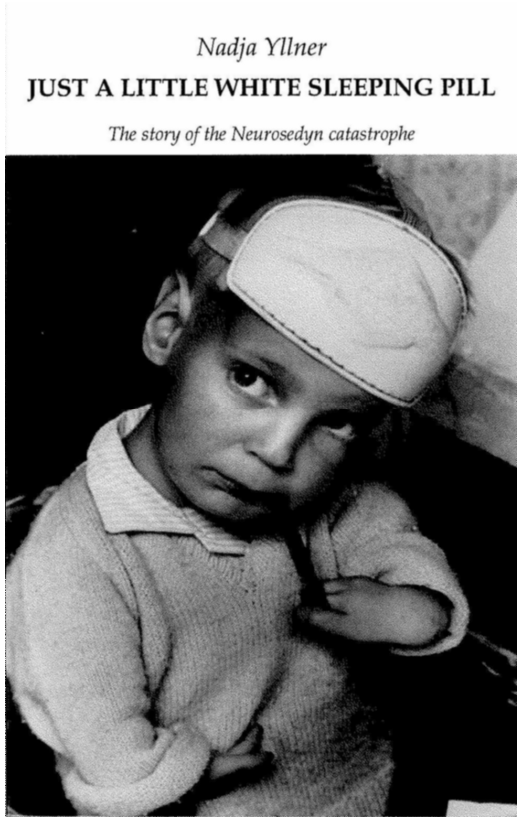
Research Ethics Committees

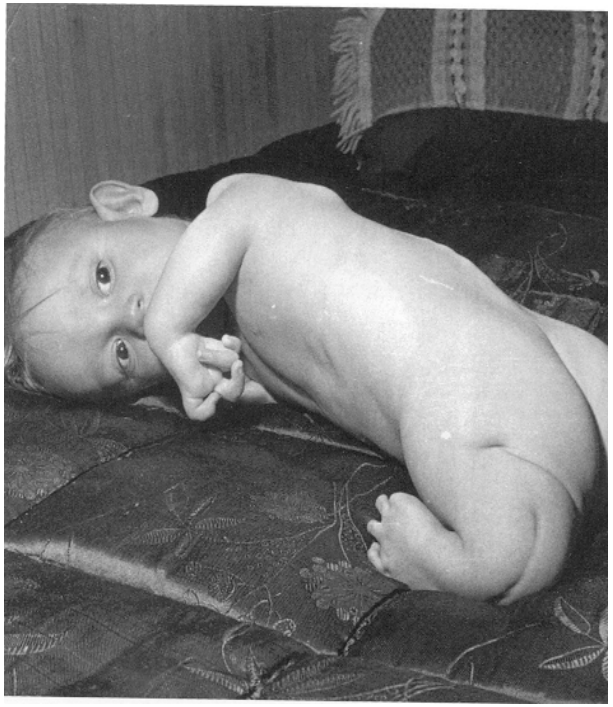
23. The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.

The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.

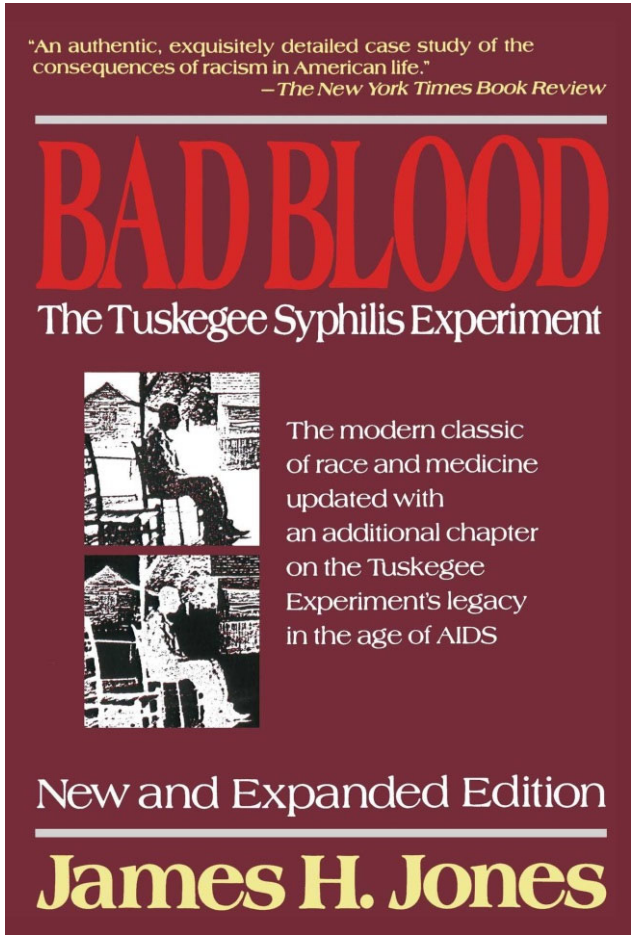
DID ALL GO WELL? THALIDOMIDE

- Consequences of the thalidomide (Softenon®) disaster
  - More attention for safety of drugs in clinical trials
  - More attention on ADR for future generations





TUSKEGEE SYPHILIS STUDY



- 1932 – 1972 (!)
- 399 black men, with syphilis (3rd stage)

- Goals:
  - to discover how syphilis affected blacks as opposed to whites
  - learning syphilis from autopsies

- Methodology: no treatment
  - '..they were thus deliberately left to degenerate under the ravages of tertiary syphilis..'

- Misleading information participants:
  - treatment for 'bad blood' = aspirin
  - 'last chance for free treatment' = spinal tap
  - 'free hospital care' = post mortem

https://www.infoplease.com/us/race-population/tuskegee-syphilis-experiment

TUSKEGEE SYPHILIS STUDY

- Study end:
  - 28 deaths through syphilis
  - 100 deaths due to related complications
  - 40 wives infected
  - 19 children suffered congenital syphilis

The United States government did something that was wrong—deeply, profoundly, morally wrong. It was an outrage to our commitment to integrity and equality for all our citizens. . . . clearly racist.

—President Clinton's apology for the Tuskegee Syphilis Experiment to the eight remaining survivors, May 16, 1997

A New Colonialism? — Conducting Clinical Trials in India

Samiran Nundy, M.Chir., and Chandra M. Gulhati, M.D., D.T.M.&H.

N Engl J Med 2005:352;1633-6.

A Private, "One-Man" Clinic in New Delhi Where Letrozole Was Tested.

Letrozole trials in India

Drugs:	letrozole
Treatment:	Inducing ovulation
Sponsors:	Sun Pharmaceuticals
Period:	2003
Location:	India

Unethical aspects:

Letrozole, which belongs to the group of aromatase inhibitors, was tested by Sun Pharmaceuticals to induce ovulation. The drug has been approved globally for the treatment of breast cancer in post-menopausal women, but it is not approved for any other use in any country. More than 400 women who had been trying in vain to conceive were enrolled in 2003 without their knowledge or consent to take part in clinical trials conducted at nine or more centres across India.

"My antecubital vein was my financial pipeline."

"I was lucky to get into a study, so I could survive financially."

"I do not really understand what a clinical trial means, but we are poor farmers and the most important thing for us is saving money."

The Globalization of Clinical Trials: Testimonies from Human Subjects. December 2010 [1]

Tages-Anzeiger WIRTSCHAFT

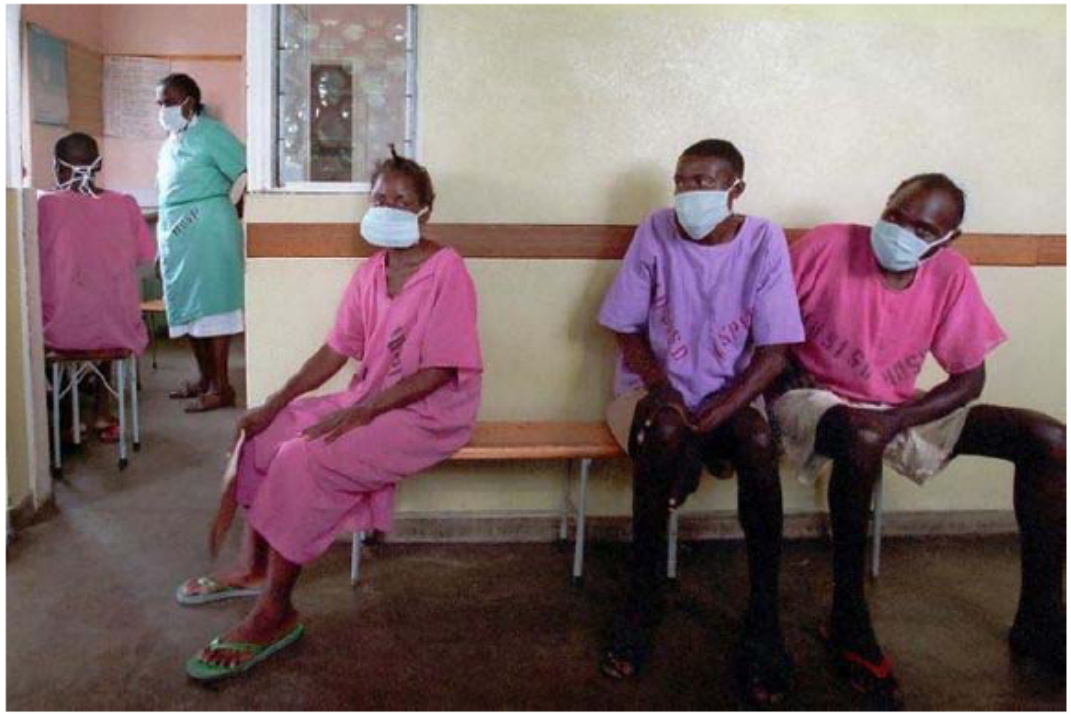
ZÜRICH SCHWEIZ AUSLAND WIRTSCHAFT BÖRSE SPORT KULTUR PANORAMA

Unternehmen **Konjunktur** Geld Karriere Vorbörse Weiterbildung Never Mind The Markets Beruf &

Die Versuchskaninchen der Pharmaindustrie

Von Andreas Möckli. Aktualisiert am 16.06.2011 10 Kommentare Empfehlen 1

Klinische Studien werden immer öfter in Entwicklungs- und Schwellenländern durchgeführt. NGO werfen den Pharmafirmen vor, sich nicht an die ethischen Regeln zu halten.



Aidskranke Tuberkulosepatienten warten in einem Spital in Zimbabwe auf ihre Medikamente. Nur jeder hundertste Kranke im Land hat Zugang zu einer Therapie.

[1] https://www.wemos.nl/wp-content/uploads/2016/07/Testimonies_Wemos.pdf

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GOOD CLINICAL PRACTICE (GCP)

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R1)

Current *Step 4* version
dated 10 June 1996

(including the Post Step 4 corrections)

https://www.ich.org/ And www.ichgcp.net

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GOOD CLINICAL PRACTICE (GCP)

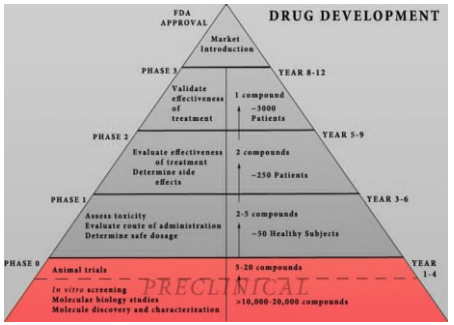
Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

The objective of this ICH GCP Guideline is to provide a unified standard for the European Union (EU), Japan and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

2.1 Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

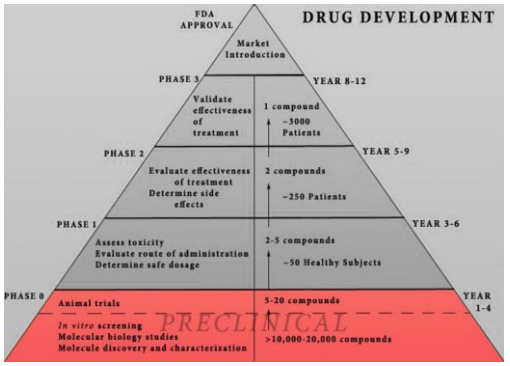
- This GCP-principle states minimal quality demands on biomedical (drug) studies involving humans

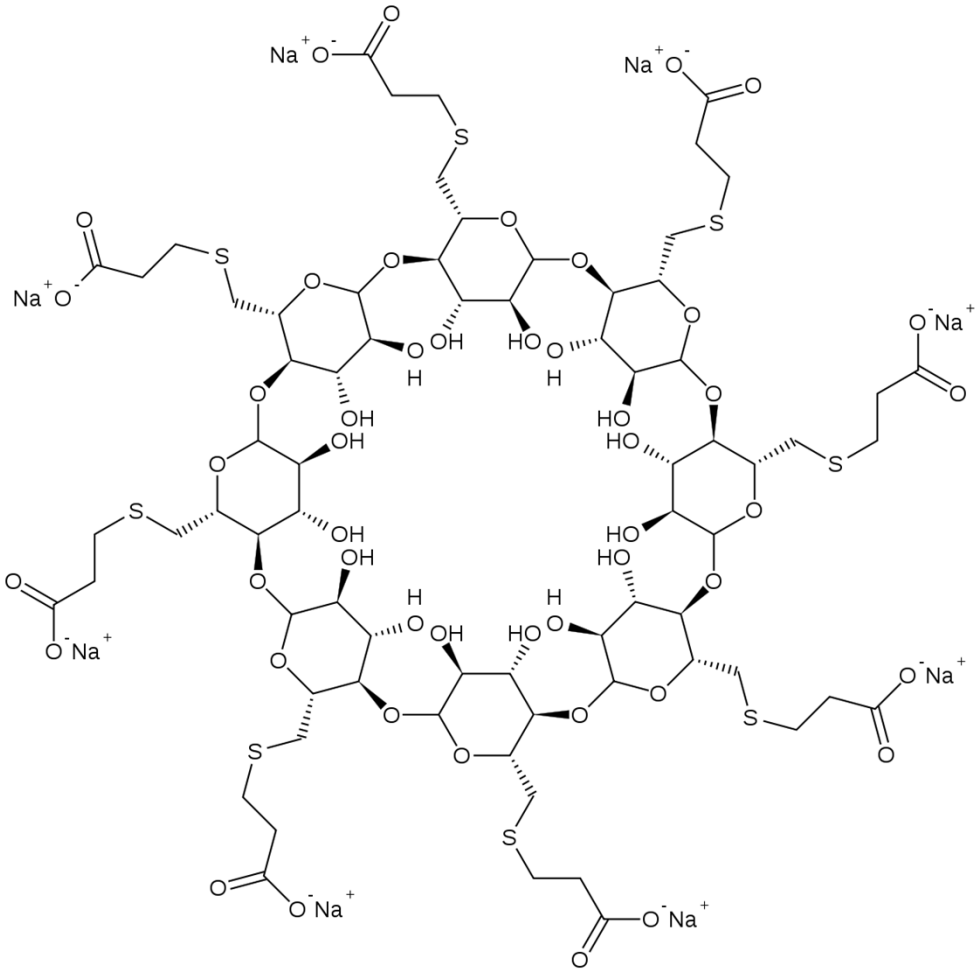
TERUG NAAR DE PYRAMIDE: DRUG DESIGN

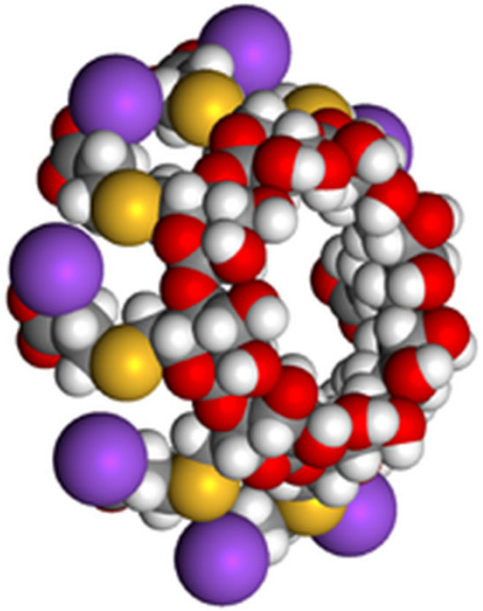


- Focus op invloed op een aangrijpingspunt of model
- In kaart brengen structuur aangrijpingspunt
- In kaart brengen gewenste structuur potentieel nieuw middel
- Voorspellen/toetsen of beide passen

DRUG DESIGN: SUGAMMADEX







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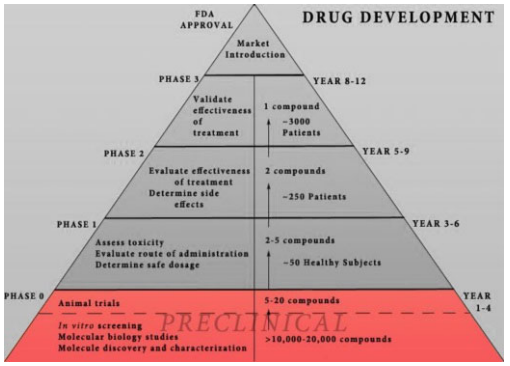
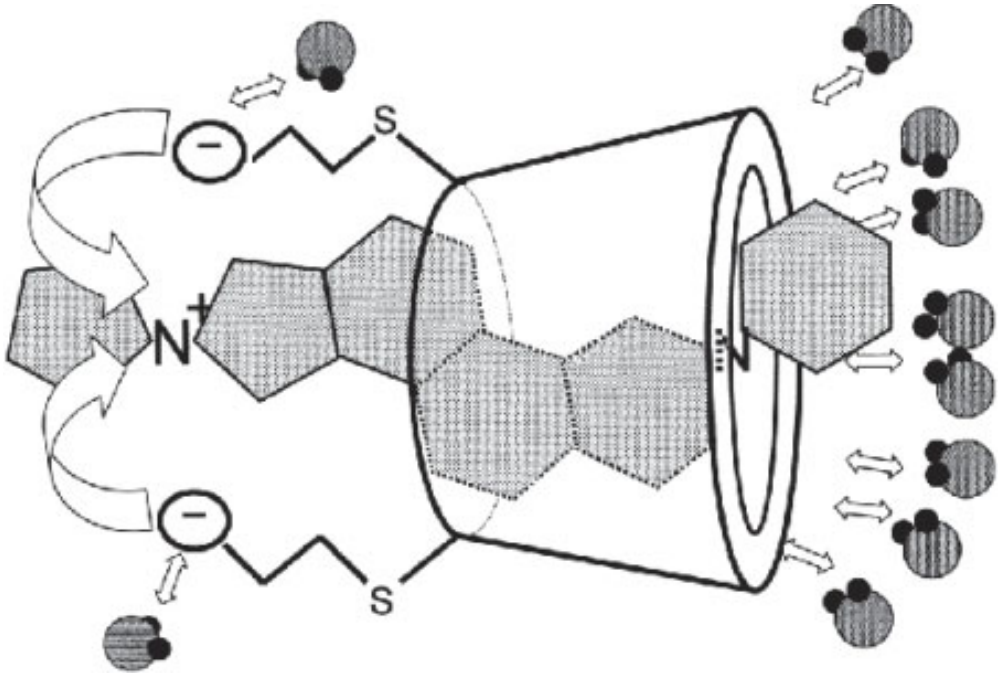
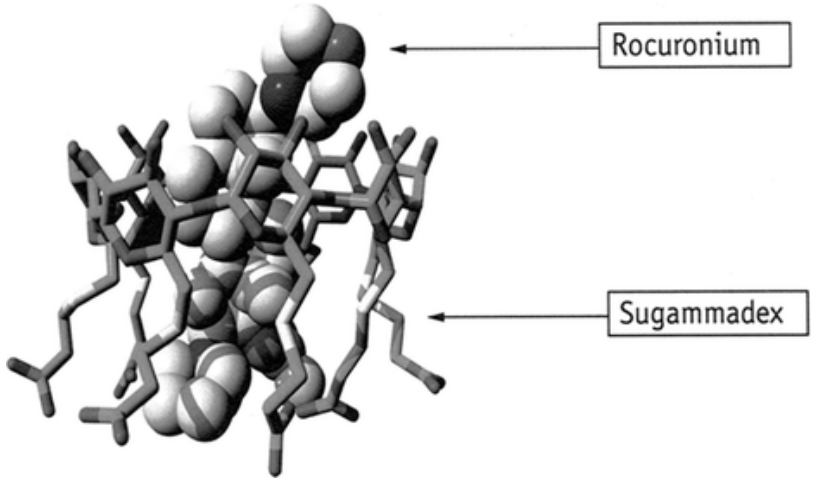
DRUG DESIGN: SUGAMMADEX







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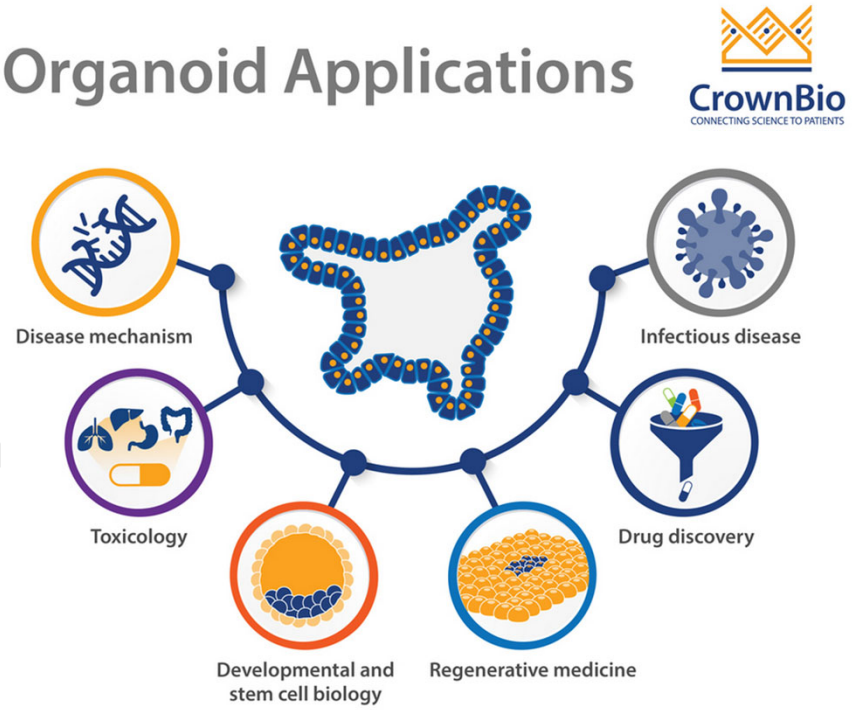
ORGANOÏDEN

- Organs on a desktop
  - Kunstmatig gekweekte miniatuurorganen
  - Gekweekt uit stamcellen



- Alternatief voor (delen van) dierexperimenteel werk?

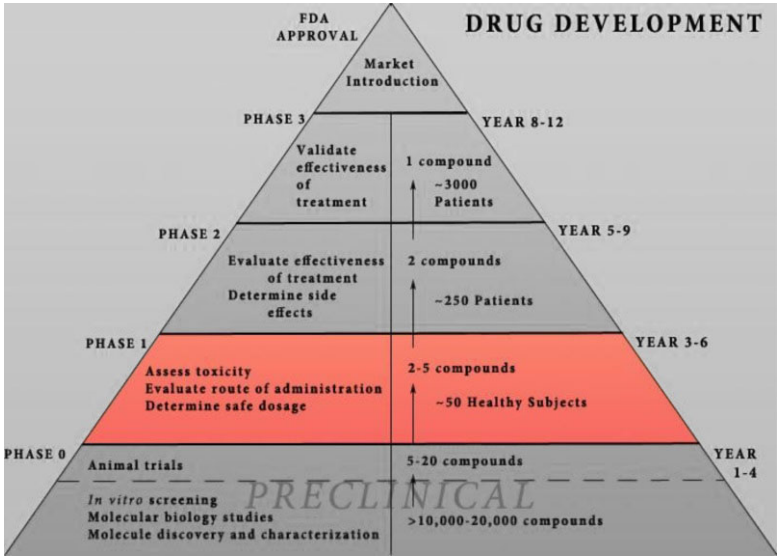
- Vormgeven van ‘personalized medicine’

→ komen we later nog uitgebreid op terug

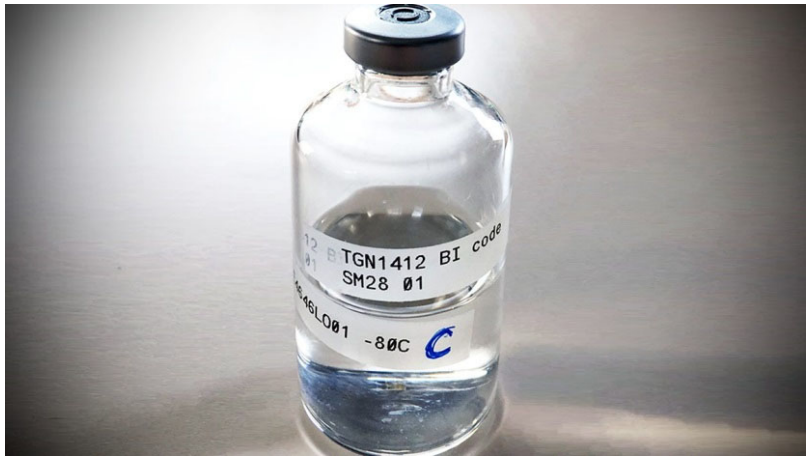
https://blog.crownbio.com/key-organoid-applications

EEN BELANGRIJK MOMENT: FIRST-IN-HUMAN

- Eerste dose level
- Farmacokinetiek
  - Gaan we dieper op in
- Farmacodynamiek
  - Gaan we dieper op in

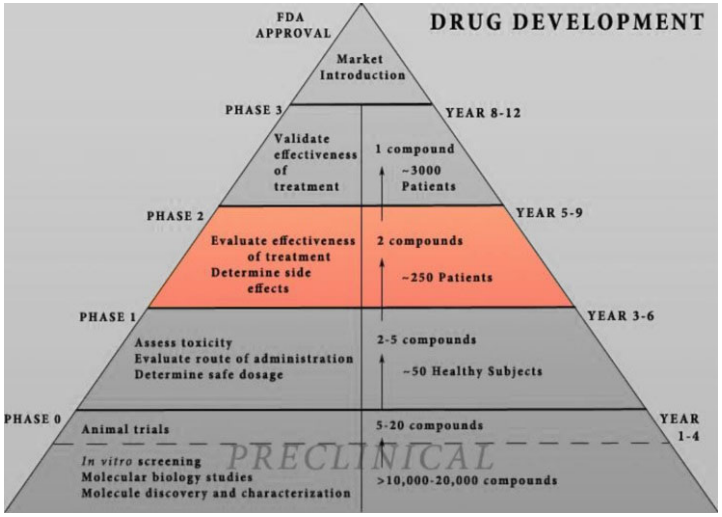


FIH: RECENTE PROBLEMEN



- Tegenero-affaire, Londen 2006
  - TGN1412 = 'superagonistisch' anti-humaan CD28 mAb
  - Activeert immunosuppressieve regulatoire T-cellen
  - Focus: hematologische maligniteiten & inflammatoire ziekten (o.a. RA)
- First-in-human study
  - N = 6 vrijwilligers
  - Binnen 1 uur na toediening: severe systemic inflammatory response ('cytokine storm')
- Lessons learned (among others)
  - Langzamere infusiesnelheid in 'high risk' biological studies (kans op vroegtijdig staken toediening)
  - Sequentiële inclusie i.p.v. alle eerste infusies bij alle vrijwilligers op één moment
  - Aanbeveling: FIH 'high risk' biological studies beschikken over onmiddelijke toegang tot intensieve zorg afdelingen

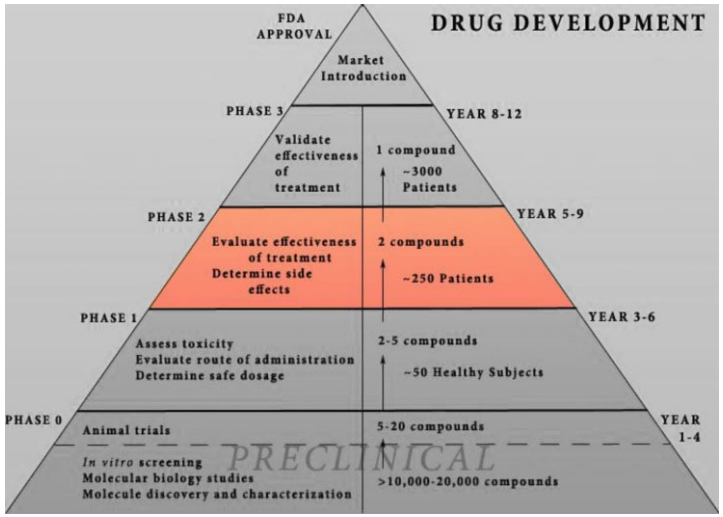
FASE 2



- Dose-finding
  - Toxiciteit

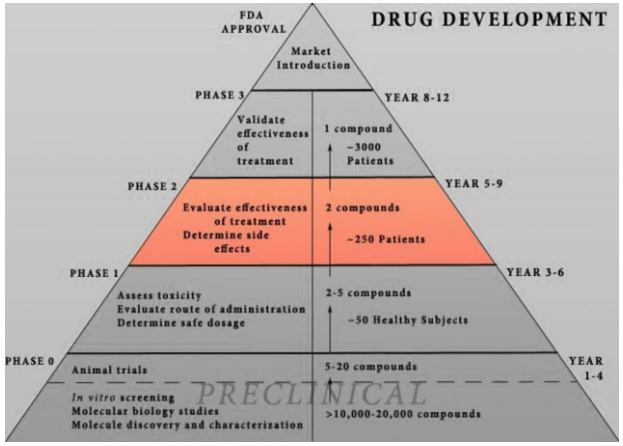
- Eerste indruk effectiviteit

FASE 2



- Bijwerkingen/ADR
  - Type A: gerelateerd aan farmacologisch effect
    - Incidentie: vrij hoog
    - Relatief snel herkend
  - Type B: patiëntgebonden
    - Individuele eigenschappen patiënt bepalen optreden ADR
    - Geen dosis:responsrelatie
    - Allergische/immunologische achtergrond
    - Incidentie: vaak laag, moeilijk herkend
  - Type C: verhoging achtergrondincidentie aandoening
    - Bijv. rofecoxib en verhoogd risico op cardiovasculaire aandoening
    - Bijv. atypische femurschacht # bij bisfosfonaten

FASE 2: CAUSALITEIT

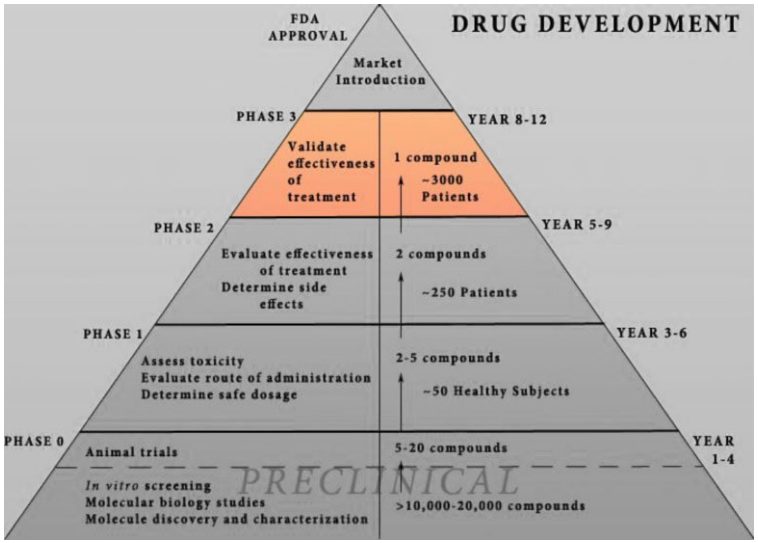


	Yes	No	Do not know
1. Are there previous *conclusive* reports on this reaction?	1	0	0
2. Did the adverse event occur after the suspected drug was administered?	+2	−1	0
3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	+1	0	0
4. Did the adverse reaction reappear when the drug was readministered?	+2	−1	0
5. Are there alternative causes (other than the drug) that could have on their own caused the reaction?	−1	+2	0
6. Did the reaction reappear when a placebo was given?	−1	+1	0
7. Was the blood detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	+1	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0

Naranjo criteria classify the probability that an adverse event is related to drug therapy based on a list of weighted questions. The ADR is assigned to a probability category from the total score as follows: *definite* if the overall score is 9 or greater, *probable* for a score of 5 - 8, *possible* for 1 - 4 and *doubtful* if the score is 0 [1].

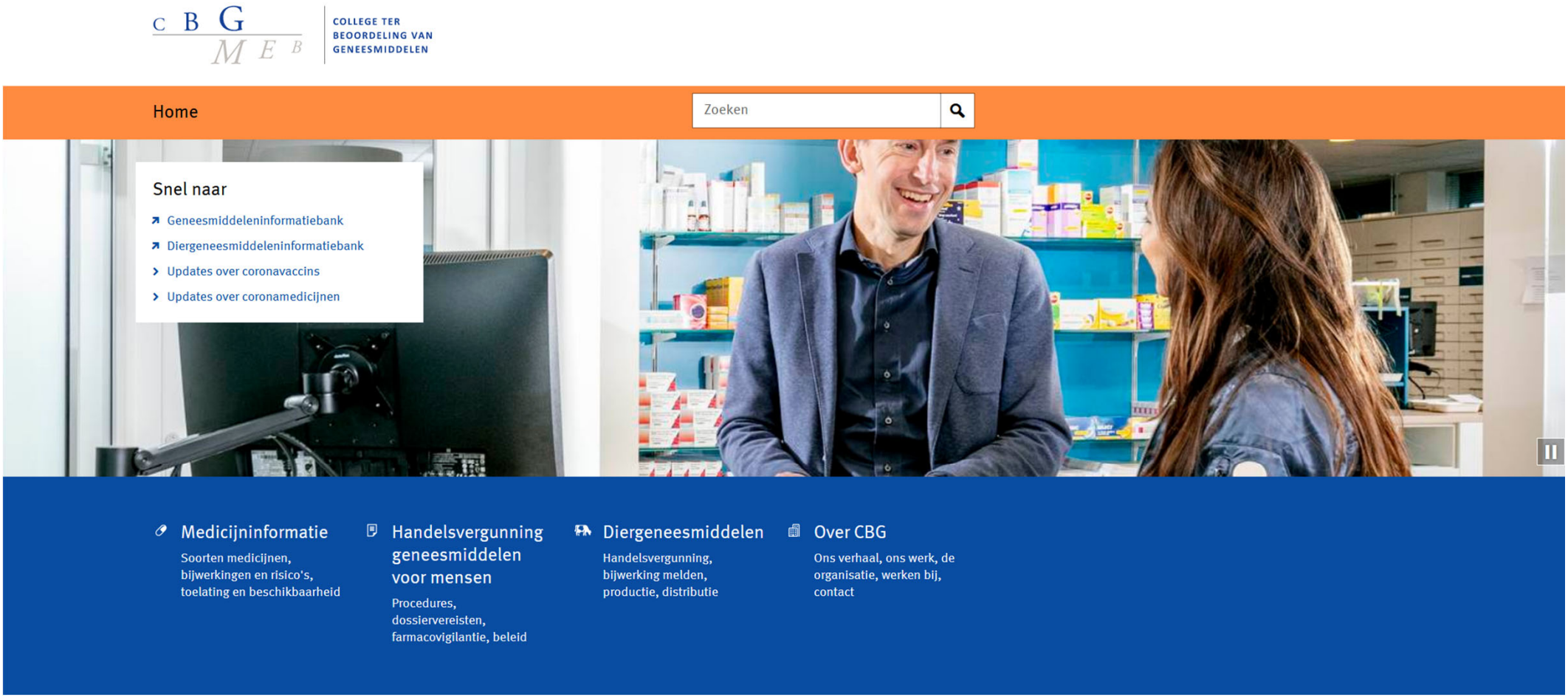
CA Naranjo, et al. Clin Pharmacol Ther 1981;30: 239-45. doi:10.1038/clpt.1981.154

FASE 3



- Vergelijkend onderzoek
  - Gouden standaard behandeling
  - Best supportive care
- Basis voor ‘evidence-based medicine’
- Basis voor registratie en beoordeling balans effectiviteit:veiligheid

VINDEN VAN INFORMATIE: WWW.CBG-MEB.NL



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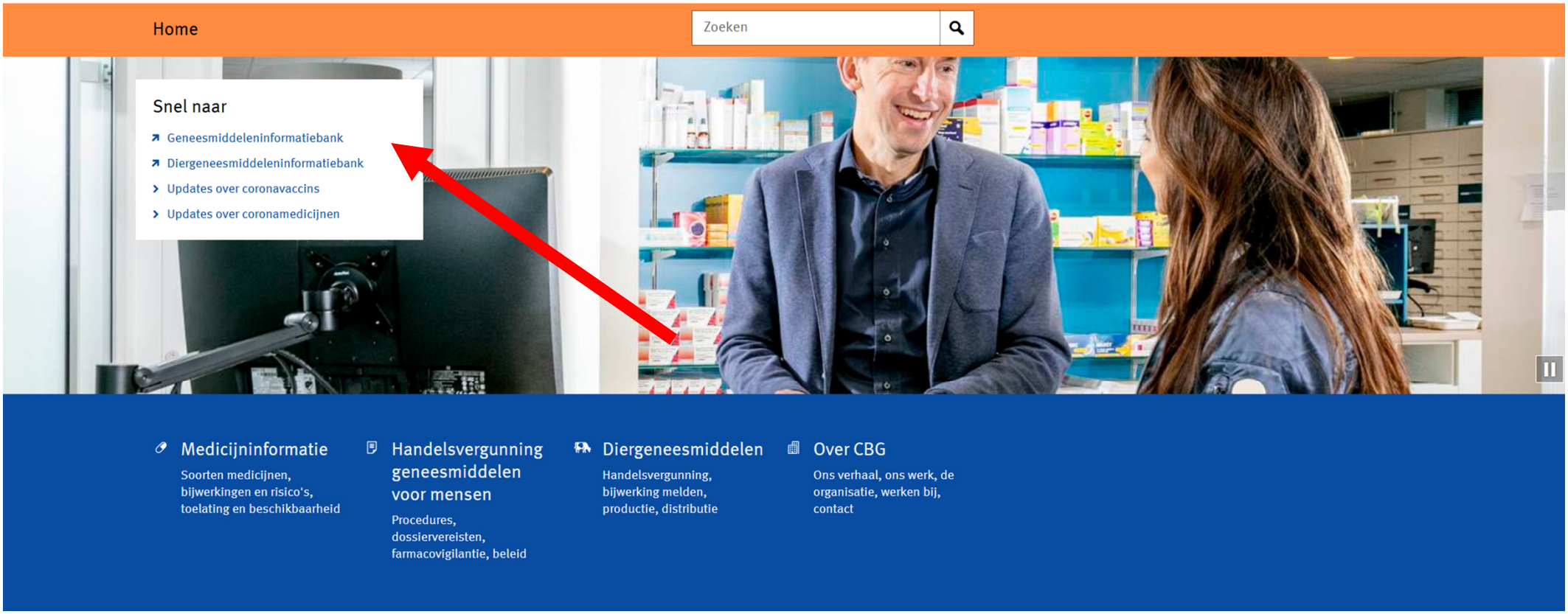

VINDEN VAN INFORMATIE: WWW.CBG-MEB.NL

College ter Beoordeling van Geneesmiddelen

Geneesmiddeleninformatiebank

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Terug naar zoeken

Terug naar resultaatlijst

Bridion

Over dit geneesmiddel | **Details handelsvergunning**

Een uitgebreide beschrijving van de werkzaamheid en mogelijke bijwerkingen van dit geneesmiddel vindt u in de patiëntenbijsluiter en samenvatting van de productkenmerken.

Het kan voorkomen dat uw ziekte/klacht niet wordt genoemd in de gedrukte bijsluiter van het medicijn dat de arts aan u voorschrijft. Dit komt voor bij medicijnen waarvoor een octrooi van een andere vergunninghouder geldt op het gebruik van het middel bij uw ziekte/klacht. De fabrikant van het medicijn mag dit gebruik dan niet vermelden in de gedrukte bijsluiter. In dat geval staat er in de bijsluiter die u hier kunt downloaden een sterretje achter deze ziekte/klacht. Op de pagina Vragen en antwoorden over gebruiksoctrooien en bijsluiters vindt u hierover meer informatie.

SmPC, etiket en patiëntenbijsluiter

Werkzame stof:	SUGAMMADEX NATRIUM SAMENSTELLING overeenkomend met SUGAMMADEX
Hulpstoffen:	NATRIUMHYDROXIDE (E 524) STIKSTOF (HEAD SPACE) (E 941) WATER, GEZUIVERD ZOUTZUUR (E 507)

GOEDGEKEURD

Dit geneesmiddel is goedgekeurd voor gebruik bij de hier vermelde indicatie.

Verkrijgbaarheid: Uitsluitend recept

bijwerkingen centrumlareb

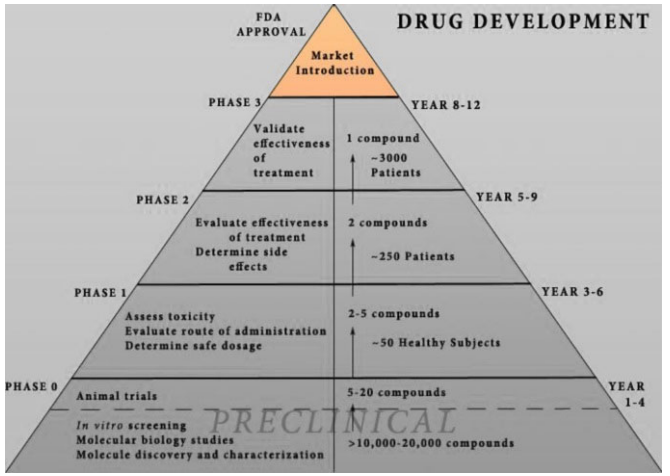
FK Farmacotherapeutisch Kompas

VINDEN VAN INFORMATIE: WWW.CBG-MEB.NL

- SmPC = Summary of Product Characteristics = IB-deel dossier

- Voorbeeld: sugammadex

FASE 4; POST-REGISTRATIE



- Registratiemoment is onderdeel

  continuüm van leren over geneesmiddel

- Wat weten we op het moment van registratie?

- Stel 3000 patiënten blootgesteld aan middel
  - Wat is de maximale incidentie van bijwerking die we hebben kunnen detecteren?

RULE-OF-THREE

- Virtueel
  - Geen specifiek ADR gezien in 3000 patiënten
  - Kans op ADR in patiënt nr. 3001
  - Schatting voorkomen is dan 1/3001 = 0,03%
  - Bovenkant 95CI voor incidentie ADR is dan 3 x 0,03% = plm. 0,1%
  - Stel kans ADR kent altijd fataal beloop

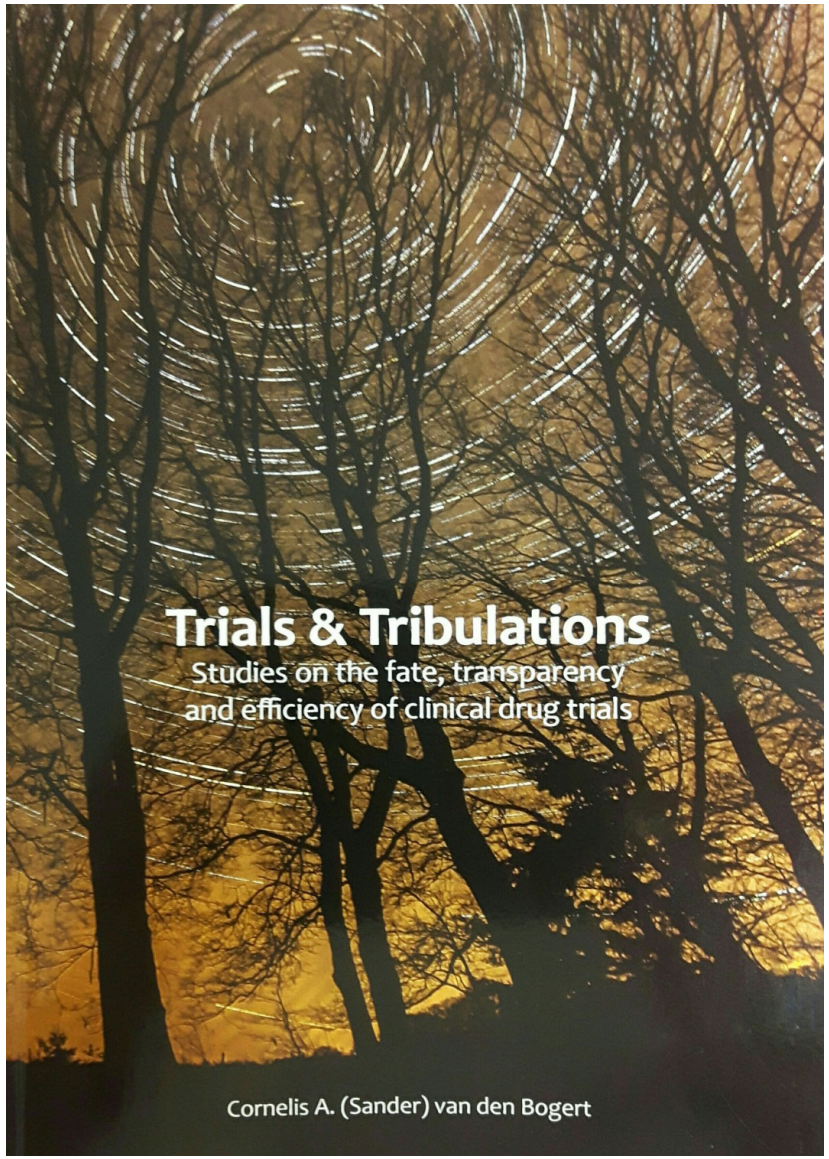
  - Conclusie?

INTERESSANT

- Proefschrift september 2017
- Promotor Bert Leufkens
  - Voorzitter CBG tot medio 2017

- Wat gebeurd er met de klinische geneesmiddelonderzoeken?

- Kader: trials beoordeeld door METCs in 2007
  - N = 558



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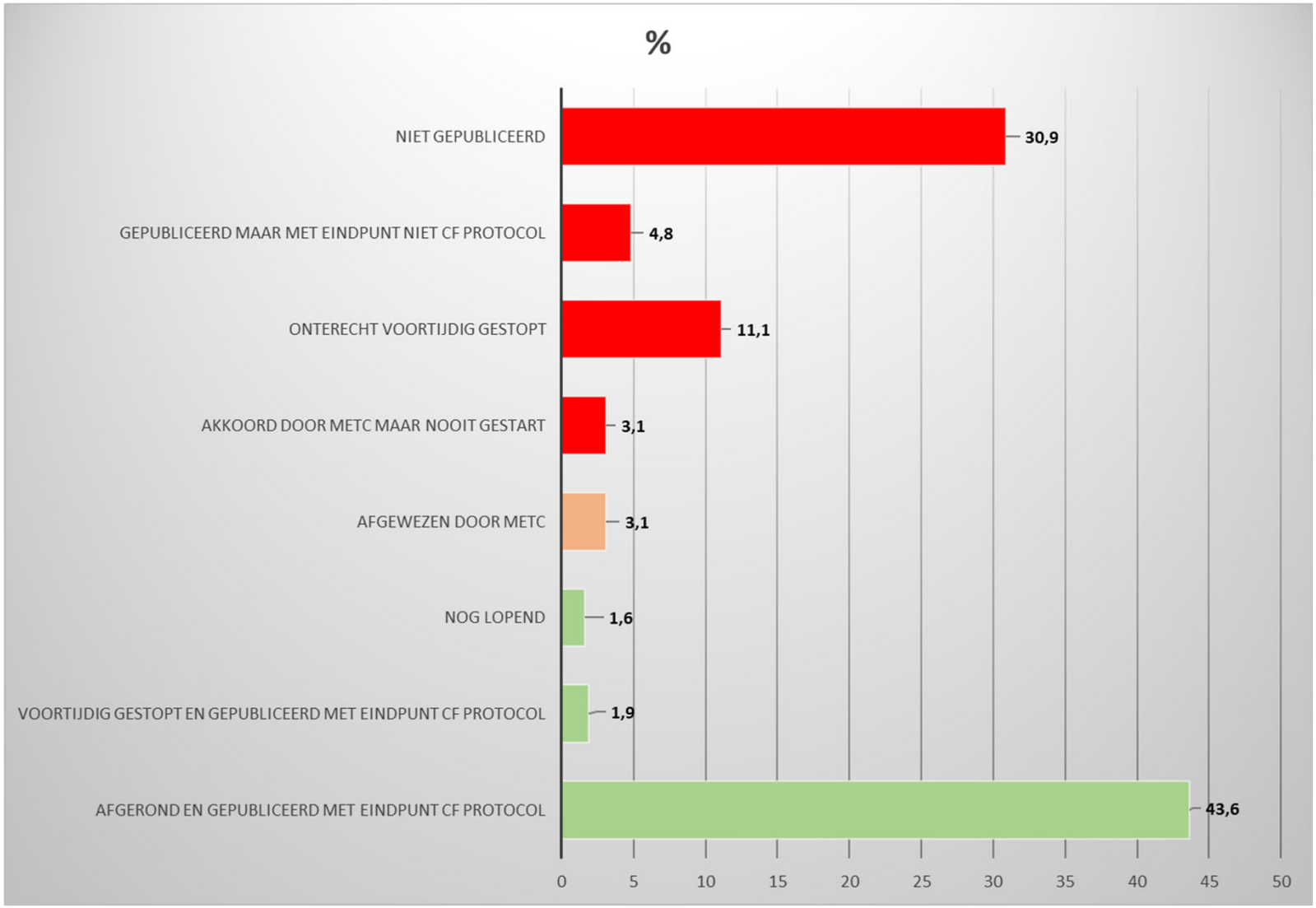
THE FATE OF CLINICAL DRUG TRIALS



General discussion. Thesis CA van den Bogert. UU. Oktober 2017

INFO IN HET DRUG DOSSIER BIJ REGISTRATIE

- 558 trials beoordeeld door METCs
  - 197 (35%) in product dossier (PD)
  - 183 (33%) niet in PD want fabrikant heeft geen licentie in NL
  - 153 (27%) niet in PD want niet gesponsord door fabrikant
  - 14 (3%) niet in PD want indicatie/dosering niet gelicenseerd
  - 11 (2%) niet in PD want informatie al bekend uit ander onderzoek
- Conclusie
  - Alle verplichte informatie is aanwezig in PD
  - Mogelijk ontbreekt relevante informatie in PD

CONCLUSIE

- Op moment registratie (na fase 3)
  - Nog veel onbekend
  - Doorleren in fase 4 → continuüm
    - Verplichting post-marketing surveillance
    - Registratiehouder
    - LAREB
  - Beperkte vertaalbaarheid naar dagelijkse praktijk

EBM EN MBE?

- Evidence-based medicine
- Medicine-based evidence
- Meer en meer gezien als additief/synergistisch
  - Beiden met hun methodologische voorwaarden

BEDANKT VOOR DE AANDACHT
ER ZIJN VAST VRAGEN

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