



The Benefits of a Simplified and Coherent Clinical Trials Framework in Europe

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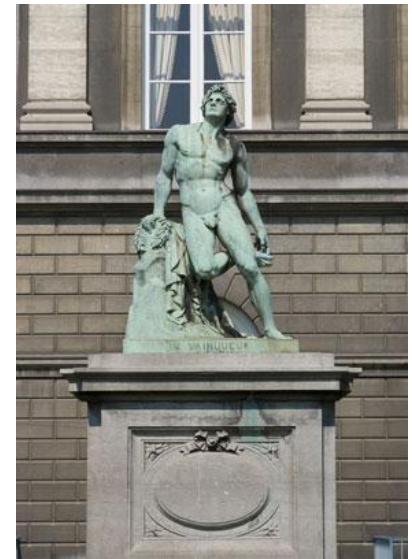


Photos Luc Schrobiltgen



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- **Brussels-based network of 13 European Academies of Medicine**
- **Independent from vested interests, multidisciplinary**
- **Collective evidence-based advice to European and national decision-makers on European public health issues**
- **August 2010 statement: *Opportunities and Challenges for Reforming the EU Clinical Trials Directive: an Academic perspective***



Le vainqueur, Jean Greefs (1825-1860), bronze.

FEAM's VIEW

- **Value of medical research**
- **Consistency in regulation of clinical research in EU**
 - **Objectives**
 - **Benefits**
 - **Problems**
- **Analysis of current Directive**
- **Options for reform of policy and legislation**

MAJOR ACHIEVEMENTS IN EUROPEAN BIOMEDICAL RESEARCH

Nobel Prize Winners

Legacy of success in combining curiosity-driven/ clinical/ translational research

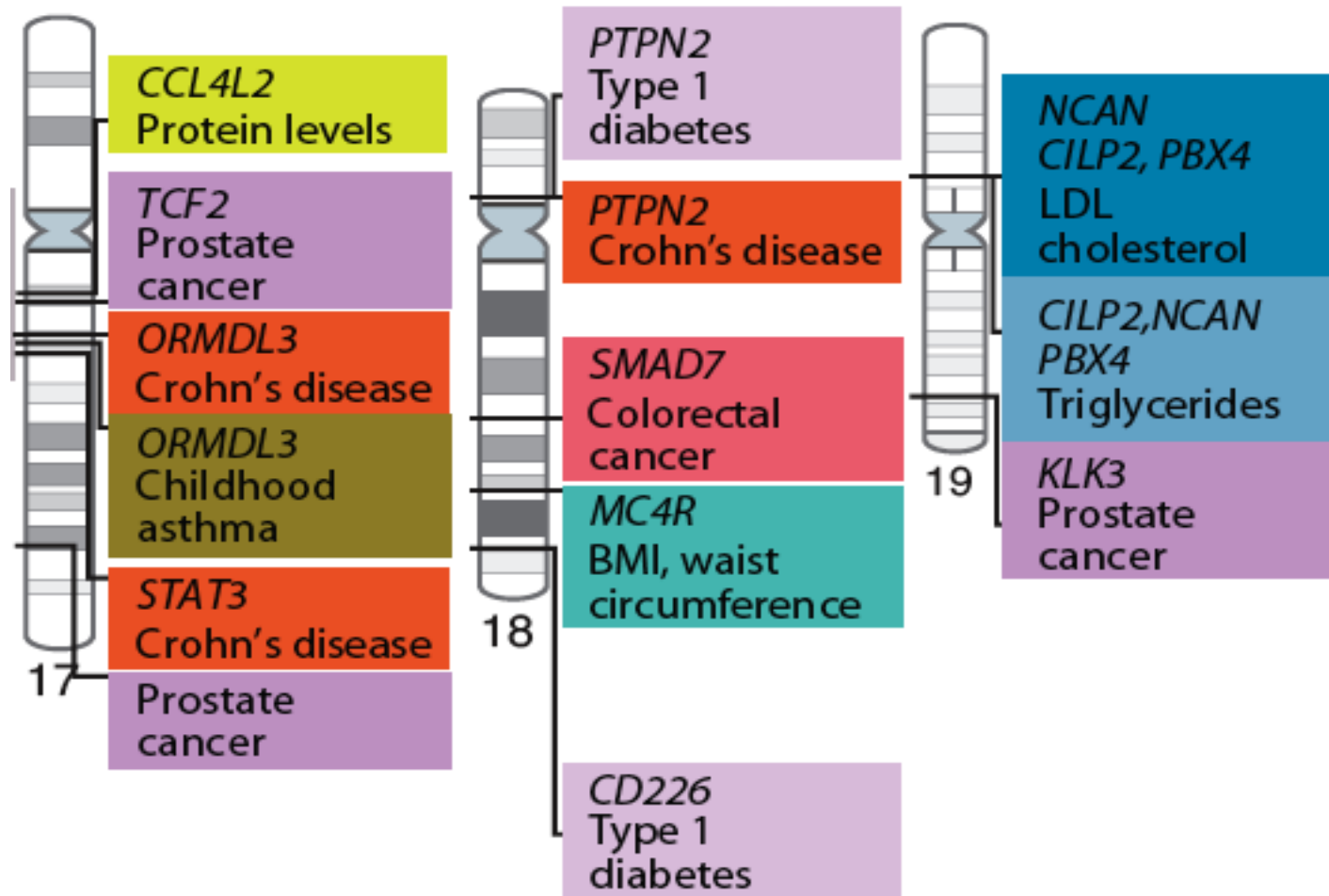
- 2011 Hoffmann (France) - basic immunology
- 2008 zur Hausen (Germany) - HPV
- 2008 Barre-Sinoussi, Montagnier (France) - HIV
- 2001 Nurse, Hunt (UK) - cell cycle control
- 2000 Carlsson (Sweden) - nervous system signal transduction
- 1995 Nüsslein-Volhard (Germany) - embryonic development

VALUE OF BIOMEDICAL/ ACADEMIC CLINICAL RESEARCH

- **Understanding disease pathogenesis**
 - Frequent diseases
 - Rare diseases
- **Improved health care**
 - Diagnosis
 - Treatment
 - Prevention
- **Translation into commercial innovations**
- **Major socio-economic benefits**
 - UK academy study: up to 40% annual rate of return on public investment in cardiovascular and mental health research
- **Personalized/ individualized Medicine**

GENOME-WIDE ASSOCIATION ANALYSES

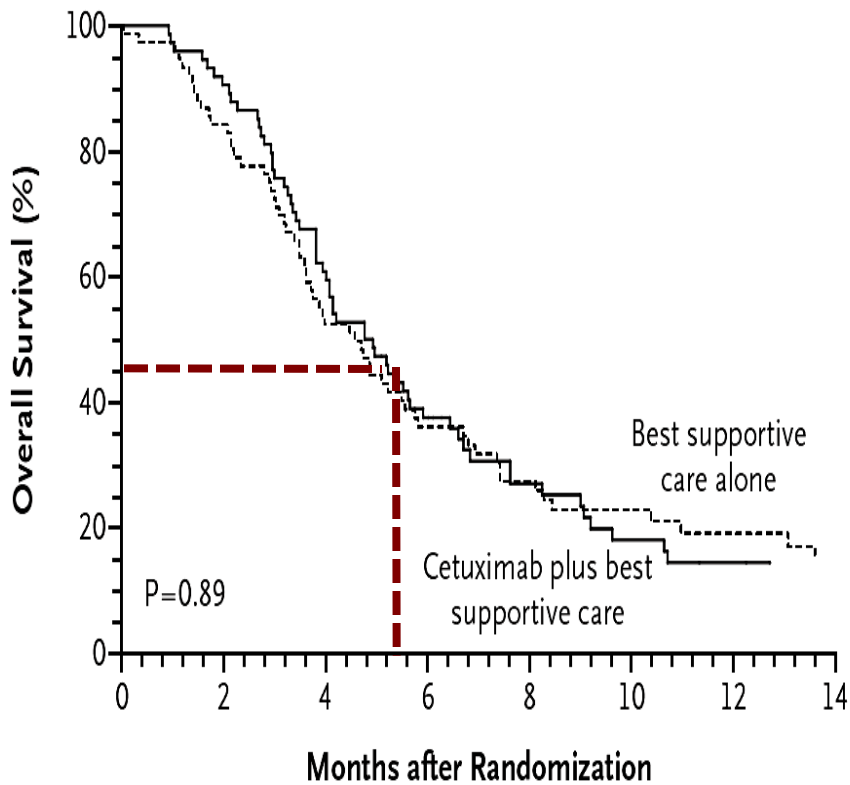
Single Nucleotide Polymorphisms (SNPs)



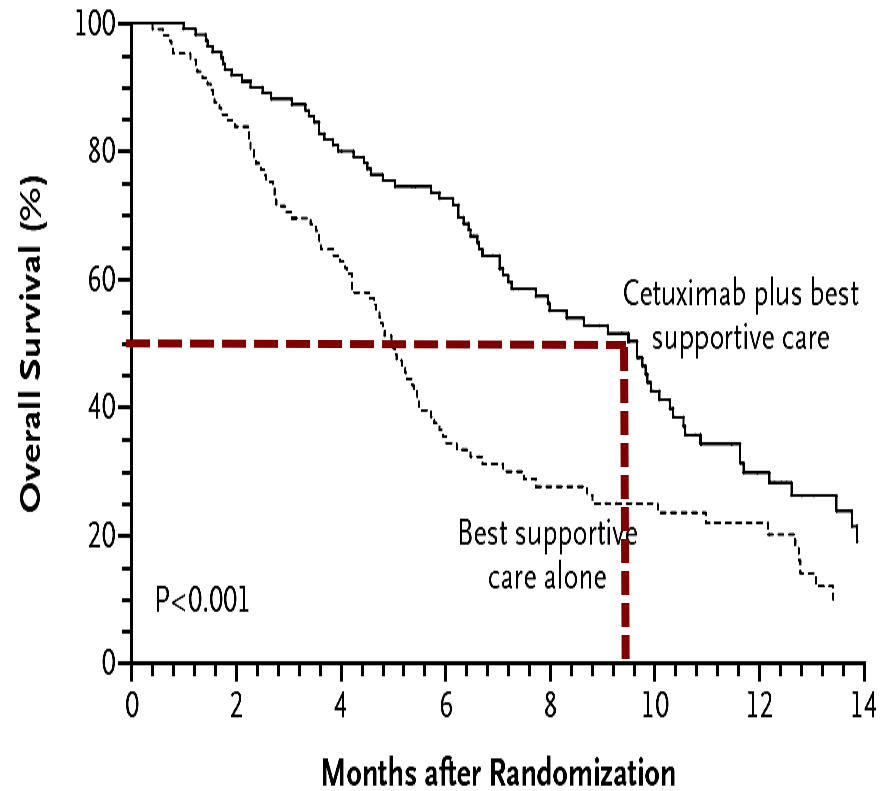
COLORECTAL CANCER

K-ras Status of Tumor and Response to Cetuximab

K-ras mutated



K-ras wild-type



CENTRAL ROLE OF CLINICAL TRIALS (CTs)

- **Research and health care delivery are interdependent**
 - **Drug discovery**
 - **Commercial development**
- **CTs test novel therapeutics**
 - **Efficacy**
 - **Safety**
- **Multicenter CTs frequently involve different Member states with different regulations**

THE EU CLINICAL TRIALS DIRECTIVE (CTD) 2001/20/EC

- **CTD implemented in 2004 with the aim**
 - to harmonise authorisation procedures for trials on medicinal products
 - to improve acquisition of reliable patient data
 - to increase protection of health and safety of participants
 - to ensure ethical soundness of trials

- **FEAM's view in 2004**
 - welcomed the CTD for its potential benefits for multi-national collaboration
 - predicted problems to academic research in case of inflexible application

PROBLEMS AFTER CTD IMPLEMENTATION

- **Continuing inconsistencies in regulatory standards and uncertainties in practice**
- **Increased administrative burden and costs for academia (and other researchers)**
- **EU became less attractive - deterrent effect on clinical research**
- **No good evidence to show improved patient protection or ethical soundness**

NEGATIVE IMPACT - FACTS (1)

- **Reduction of planned number of participants in EU trial applications (DG Sanco statistics)**
 - **2007: 535,000**
 - **2009: 358,000**
- **Reduction of proportion of world's pharmaceutical CTs in UK (BMJ 2009)**
 - **2000: 6%**
 - **2009: 2%**
- **EU trials (ICREL statistics)**
 - **More costly**
 - **More difficult to plan, start and conduct**

NEGATIVE IMPACT - FACTS (2)

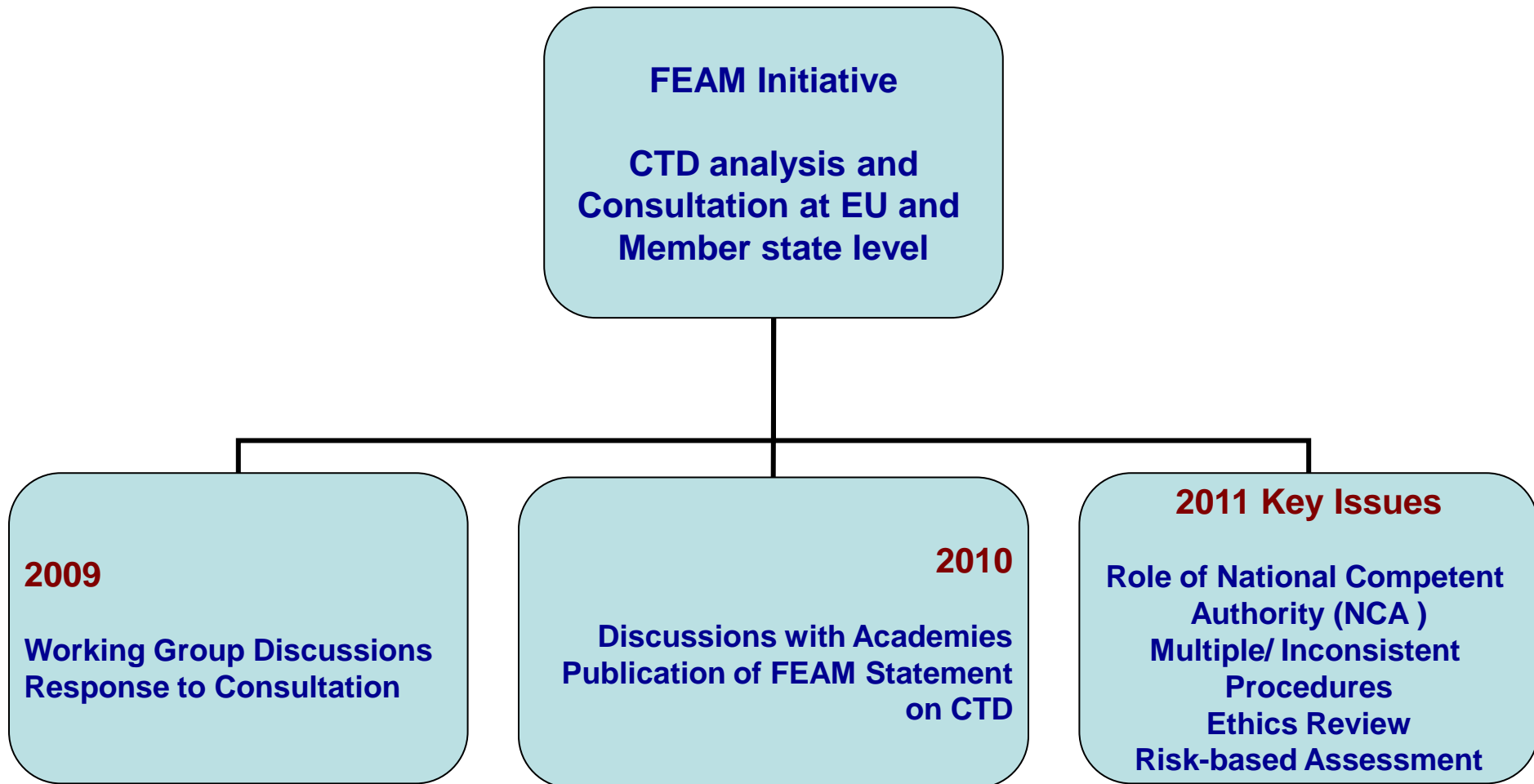
- **Particular problems in multi-national, non-commercial trials (PLoS Medicine 2009)**
 - **Cancer**
 - **Paediatrics**
 - **Organ transplantation**

- **Striking decrease in new drug development companies in Europe (EuropaBio 2010)**

CTD - WHERE ARE WE NOW?

- **2008 Collection of evidence on impact**
- **2009 EC consultation on issues; pharmaceutical policy moves from DG Enterprise to DG Sanco**
- **2010 Consultation responses published with Commission Roadmap**
- **2011 Proposed options for legislative reform, involvement of European Parliament and Council of Ministers**

FEAM ACTIVITIES



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GUIDING PRINCIPLES FOR REGULATING CLINICAL RESEARCH (1)

- **Research must be recognised as part of the mission of health care systems**
- **Patient safety**
 - is highly important
 - regulation of a trial should be proportionate to risk to patient
- **Clarifications of roles**
 - **Researcher/ scientists**
 - **Sponsors**
 - **National competent authorities (NCAs)**
 - **Ethics reviewers**

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GUIDING PRINCIPLES FOR REGULATING CLINICAL RESEARCH (2)

- **Aims of CTD reform**
 - **Reduce administrative burden**
 - **Streamline review procedures**
 - **Prevent duplication**

- **Before adoption of CTD reform**
 - **Pilot studies**
 - **Rigorous evaluation**
 - **Evidence-based changes**

REFORMING NCA ROLES IN MULTINATIONAL STUDIES

- **Burden on trials based within single Member State (70% of total) must not further increase**
- **Streamlining of multinational trial reviews**
 - **Further potential for NCA voluntary cooperation**
 - **Explore option of ‘common agreement’ where lead NCA reviews approved trials from other NCAs**
 - **No new centralised body**

RESOLVING PROBLEMS IN TRIAL SUPPORT AND REPORTING

- OBJECTIVES -

- **Insurance System needs to be**
 - **Consistent**
 - **Flexible**
 - **Risk-based**
 - **EU-wide insurance system**
- **Substantial Amendments to Research**
 - **'Substantial' needs to be clearly defined**
 - **Needs to be agreed between countries**
- **Suspected Unexpected Serious Adverse Reactions**
 - **Need to be clearly defined**
 - **Need to be agreed between countries**
 - **Reporting needs to be simplified**

REFORMING ROLES OF ETHICS COMMITTEES

- **Clarify responsibilities**
- **Train committee members**
- **Improve efficiency**
- **Create centralised ethics opinion at Member state level**
- **Increase consistency across EU**
 - **Common template for consent**
 - **Mutual recognition**
- **Single Ethics review for all multi-national trials difficult**
 - **National differences in ethical views**
 - **National differences in regulations/ laws (e.g., embryonic and stem cell research)**

ADOPTING A RISK-BASED APPROACH

- **Central weakness of current CTD**
 - **Regulations not proportionate to expected risks**
- **Regulatory flexibility needed**
 - **Handle different types of current and future trials**
 - **Focus on benefit-risk, not safety alone**
- **Consider implications for**
 - **Ethics**
 - **Safety**
 - **Monitoring**
 - **Insurance**
 - **Quality**

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- CONCLUSIONS AND MAIN MESSAGES -

- **Clinical research is vital for Europe**
- **Administrative burden can be lessened without risk for safety**
- **CTD procedures must be urgently reformed - key issues:**
 - **Clarifications - Definitions**
 - **Simplification**
- **Discussion of regulatory reforms and building supportive infra-structure must include:**
 - **Patients**
 - **Academia**
 - **Funding agencies or partners**
 - **Industry**



A European Academic Network 13 European National Academies

- Austria
- Belgium
- Czech Republic
- France
- Germany
- Greece
- Hungary
- Italy
- Portugal
- Netherlands
- Romania
- Spain
- United Kingdom

- Collaborations with EASAC, EuropaBio, ESF....

