



Clinical trials: The EU perspective

**Dr Karim Berkouk,
Deputy Head of Unit
DG for Research and Innovation
Health Directorate
European Commission**



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3. Formulating Clinical Trials in Horizon 2020



European
Commission

EU structure



<http://ec.europa.eu/>



<http://consilium.europa.eu/>



<http://europarl.europa.eu/>



The European Commission...

... is Policy Maker

- ✓ **Launches policy debates** (e.g. green paper on Horizon 2020...)
- ✓ **Invite Member States to take action through recommendation, communication** (eg scientific information, cancer screening, European Research Area,...)
- ✓ **Proposes EU legislation through regulation, directive and decisions** (e.g. clinical trial, on cross-border healthcare, data protection..)

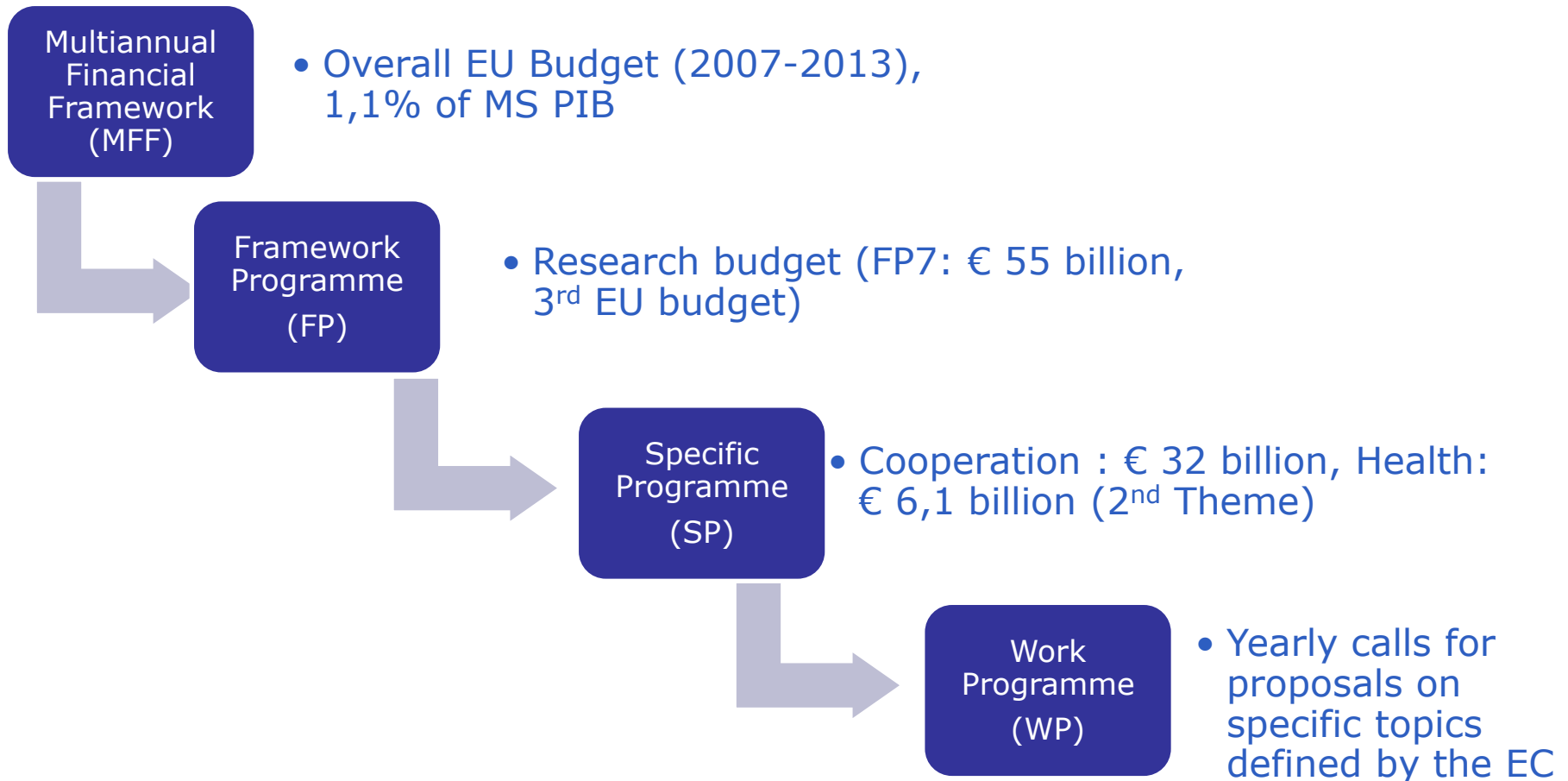


The European Commission...

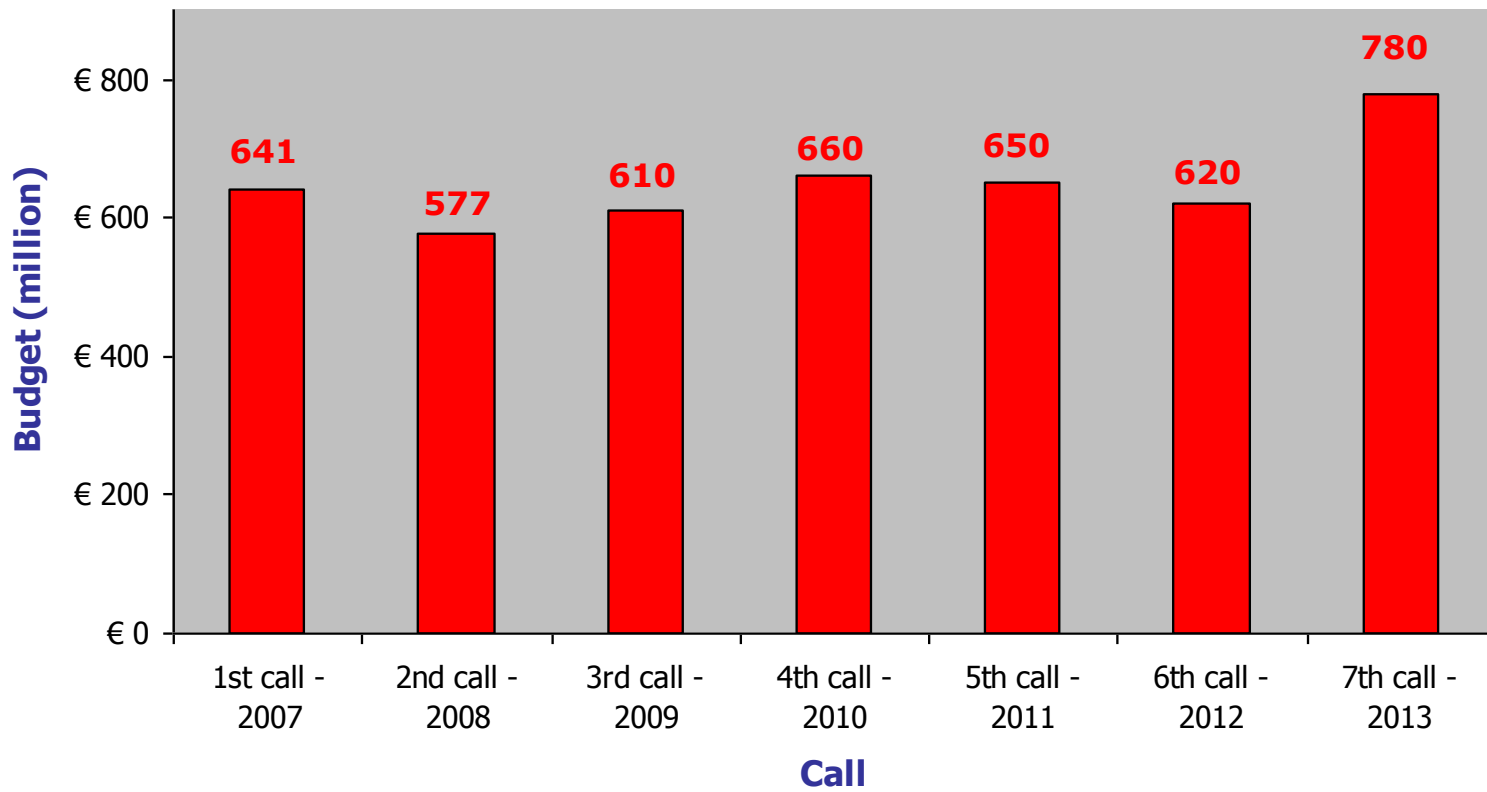
... is Funding Agency

- ✓ E.g. Research& Innovation (through FP7)
- ✓ Infrastructure (e.g. Biobank database)

EU R&I Funding: How does it work?



Annual Budget for Calls for Health



26% increase in the 2013 budget

Challenges in clinical research



**€ 400 million in
clinical trials
(2010-2012)**

- *Investigator-driven CTs*
- *Stratified patient populations*
- *Resistance mechanisms*
- *Innovative technology and devices*
- *Long-term side effects, e.g. cardiotoxicity, second cancers*
- *Co-morbidity, e.g. ageing, obesity*
- *Patient-reported outcomes*
- *Trial participation patients*

Rationale for CT calls in FP7

- European added value:
 - Reach sufficient patient numbers (especially in case of rare diseases and stratified treatment groups)
 - Faster recruitment rate
 - Consolidated expertise
- Emphasis on innovation:
 - CT ultimate validation step for any innovation in Health Research
 - Bringing innovations to markets and patients

Funding – Calls for proposals trend

- Trends over time in successive workprogrammes:
 - Broader topics (with 2-stage submission)
From "Standardisation of immunological assays including surrogate markers for the evaluation of new influenza vaccines in clinical trials" to "Investigator-driven clinical trials for type-1 diabetes"
 - Topics more explicitly focused on clinical trials
2007 call: **No** topic for conduct of clinical trials,
2013 call: **3** topics for investigator-driven clinical trials and **2** topics for comparative effectiveness research

2013 WP: 5 Call topics focused on CTs

- Investigator-driven treatment trials to combat or prevent metastases in patients with solid cancer
- Investigator-driven supportive and palliative care clinical trials and observational studies
- Investigator-driven clinical trials for off-patent medicines using innovative, age-appropriate formulations and/or delivery systems
- Prospective longitudinal data collection and Comparative Effectiveness Research (CER) for traumatic brain injury (TBI)
- Comparative effectiveness research of existing technologies for prevention, diagnosis and treatment of cardiovascular disease



Funding – Projects

- Generally: collaborative projects with a minimum of 3 partners in 3 different EU member or FP-associated states.
- Maximum EU funding per project: varies by topic, typically up to 6 or 12 million EUR
- Projects are selected through independent international peer review (success rate 10-40%)
- Guidelines on CT application

Guidelines for CT Negotiation

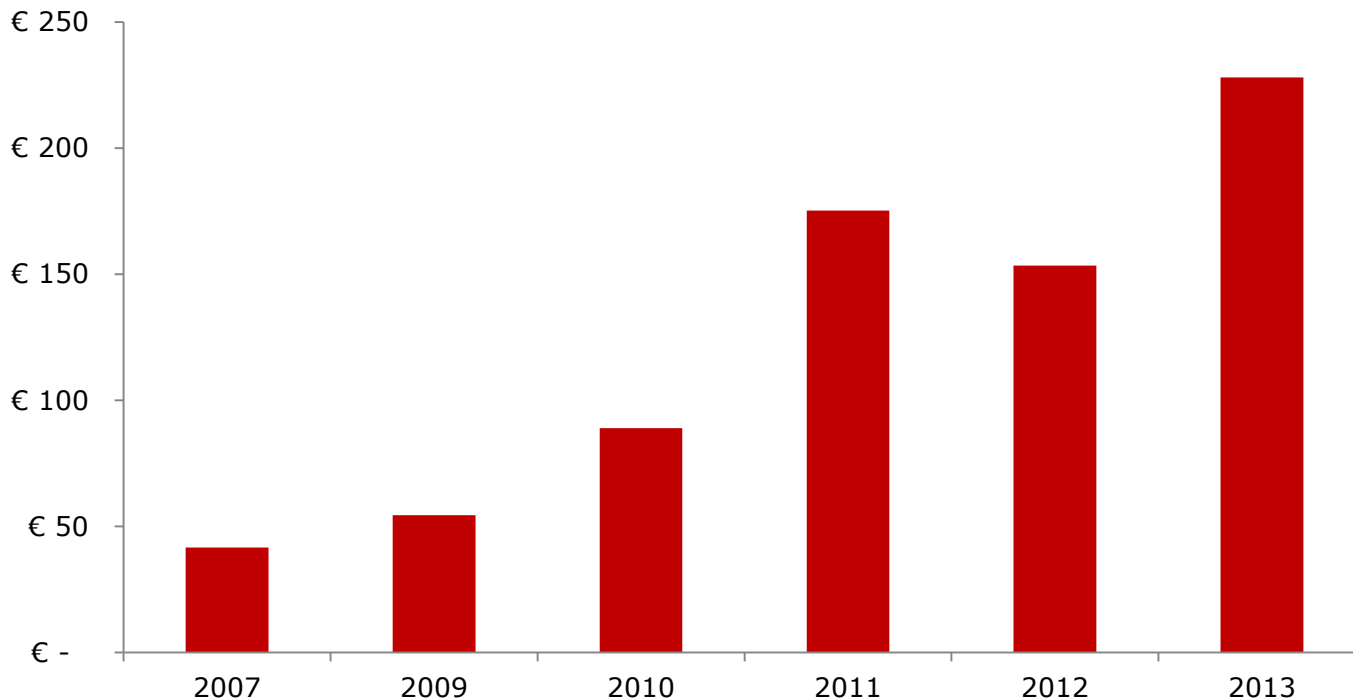
- **Special Clause 16 (applied to all projects with CT)**
- **Structured info on CT in Technical Annex**
- **EU co-funding: 75% of RTD costs, 100% of management and "other" costs, indirect costs: real costs or 20-60% flat-rate**
- **Involvement of "Satellite clinical recruitment sites"**

EU CT Deliverables

Mandatory Deliverables for CT:

- Final version of trial protocol as submitted to regulators/EC (but no need to change deliverable if later amendments)
- Registration number of CT in a WHO- or ICMJE-approved registry
- Ethics + regulatory approvals (takes care of Ethical Review and SC 15!)
- In last month of project: report on the status of the posting of results (to the trial registry)

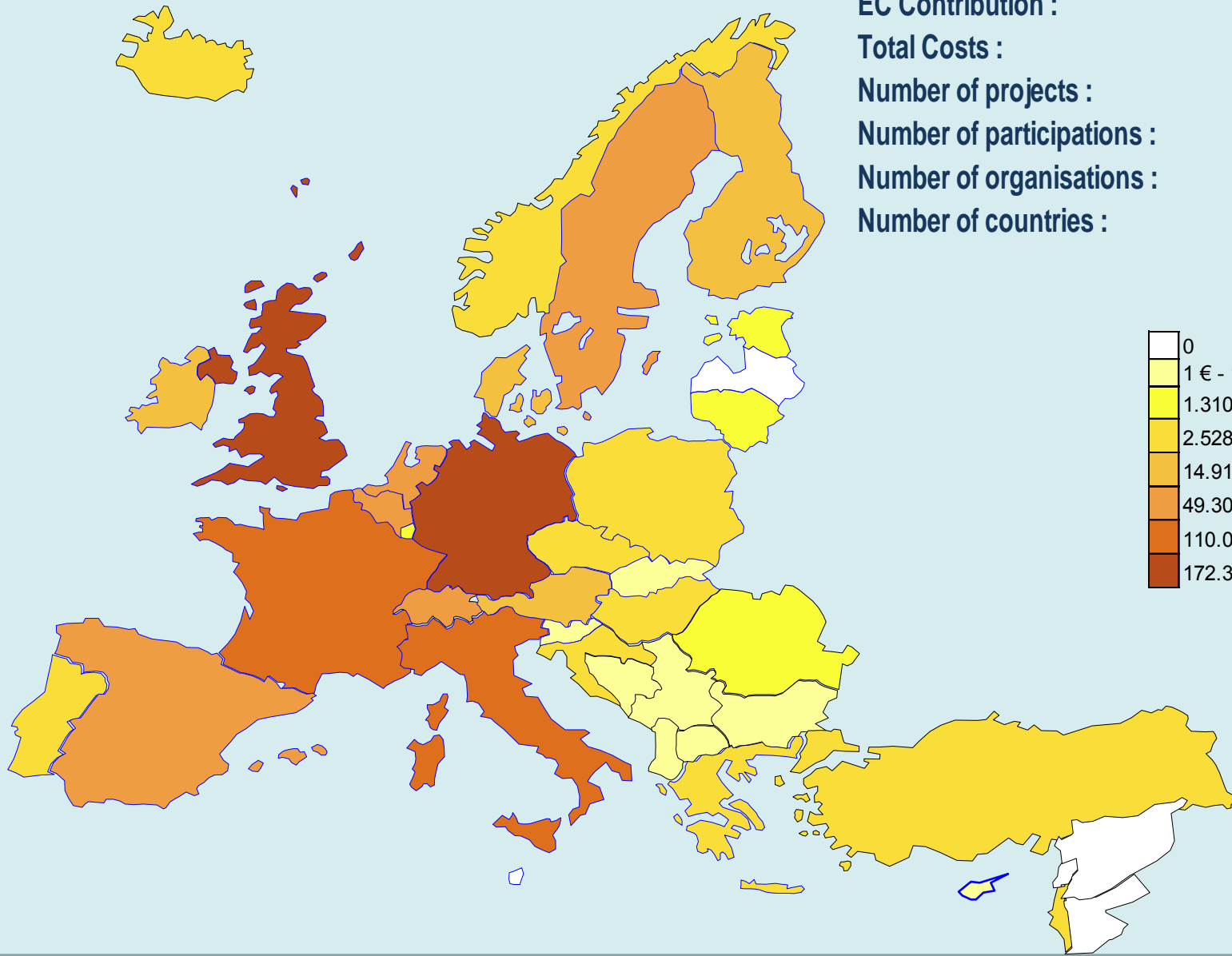
EU Clinical Trials (based on preliminary statistics!)



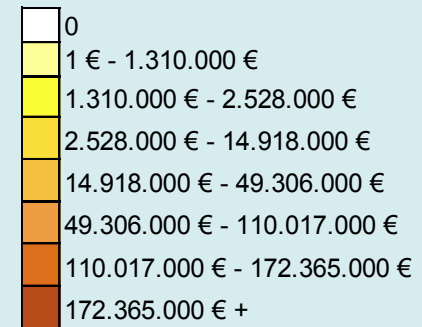
FP7 CT Budget Evolution per year

Clinical Trials – Projects

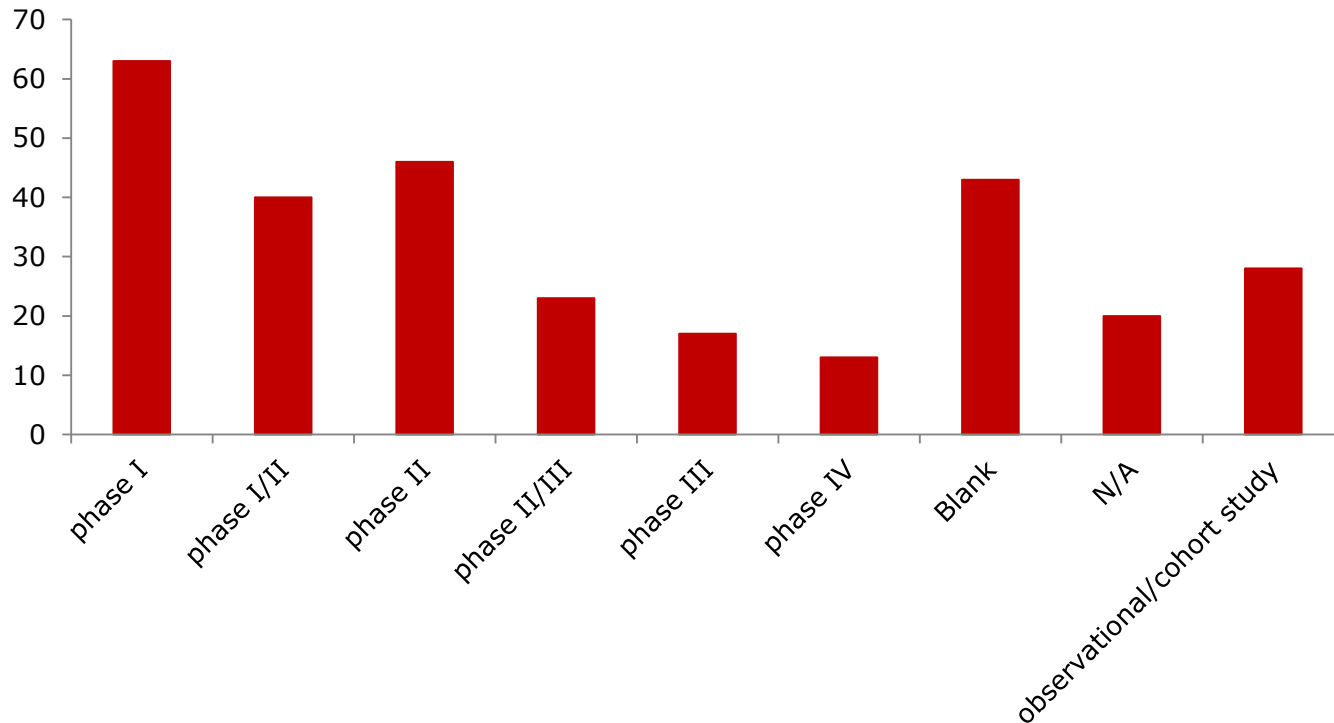
- FP7 HEALTH projects, where clinical trial is included/planned (but not core)
 - >70 projects with more than € 400 million EU contribution
- + additional projects with clinical trial support measures (methodology, ethics, infrastructure etc.)
 - 15 projects with more than € 68 million € EU contribution



EC Contribution :	1.184.534.959
Total Costs :	1.606.748.342
Number of projects :	199
Number of participations :	2.550
Number of organisations :	1.185
Number of countries :	64

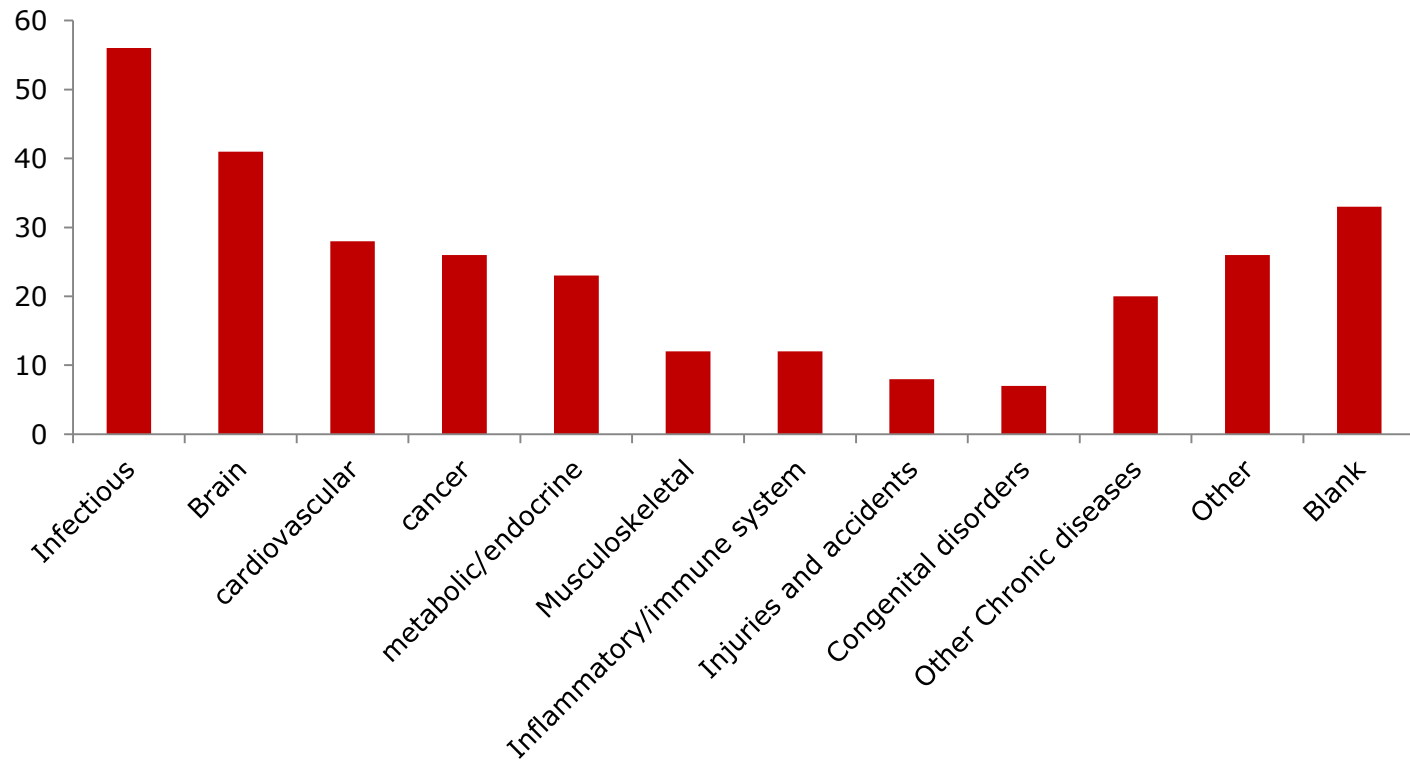


EU Clinical Trials (based on preliminary statistics!)



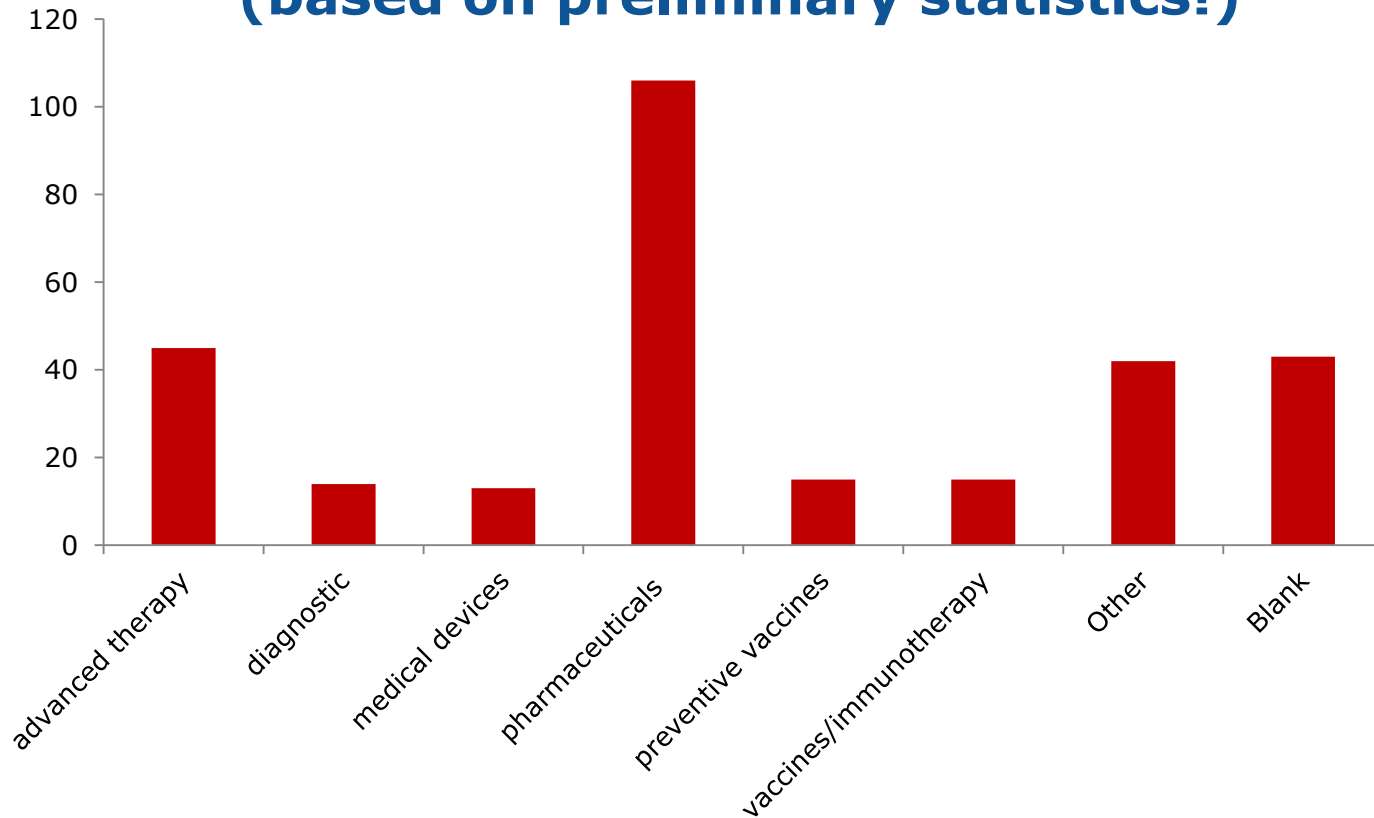
CT funded in FP7 by type of CT
Over 400,000 patients involved

EU Clinical Trials (based on preliminary statistics!)



CT funded in FP7 by type Medical Area

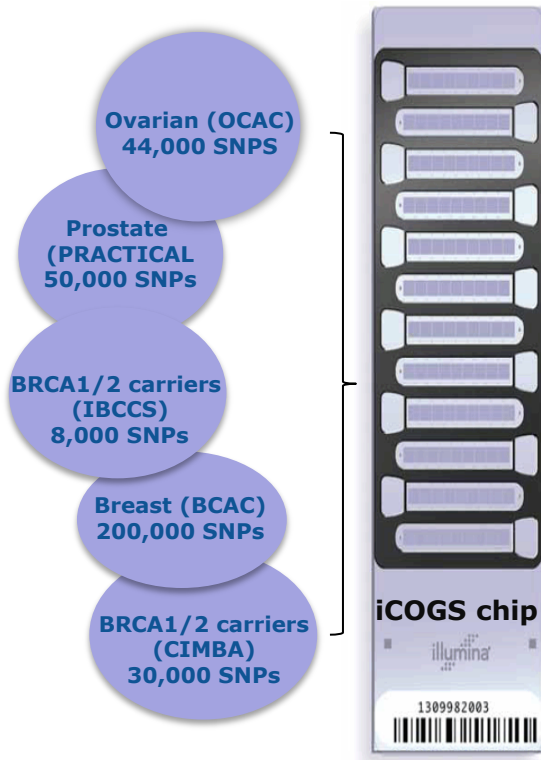
EU Clinical Trials (based on preliminary statistics!)



CT funded in FP7 by type of intervention



COGS: The Collaborative Oncological Gene-environment Study (COGS)



Nature Genetics March 2013 issue

<http://www.cogeu.org/>

- Biggest genotyping consortium in the world with > 200 groups contributing from 3 different continents
- Innovation: creation of **iCOGS** chip
- Identified > 80 novel susceptibility loci breast, ovarian, prostate cancer
- Also identified several multicancer susceptibility loci
- Example: COGS findings likely explain additional 19% of familial breast cancer risk alleles

Leverage: total funding appr € 40-50 million

- ✓ 14 academic partners, 3 SMEs, 2 pharma, 1 patient advocacy
- ✓ 6.5 years
- ✓ € 9.4 million
- ✓ Start date: February 2006



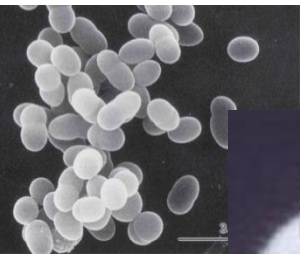


Natural Immunomodulators as
Novel Immunotherapies for
Type 1 Diabetes



Innovative approach to render immune system tolerant to beta-cell

Start in Nov. 2009 (60 months)
14 partners (2 SMEs)
Six countries
EU funding: € 10.9 million



Pilot in humans
to start in 2014



**Clinical trial to start
after end of NAIMIT**

April 2012: Progression of type 1 diabetes **STOPPED IN MICE** by oral administration of *Lactococcus lactis* (an accepted therapy for other diseases) **in combination of low-dose anti-CD3 antibody**, with **NO SIDE-EFFECT**

EU Clinical Trial Directive (CTD)

Why changing?



- ***Overcoming administrative hurdle due to:***
 - ✓ ***divergent implementation of the current CT in different MS***
 - ✓ ***European CT authorised separately by each MS***
- ***Decline of clinical trials in Europe by 25% over the recent years.***
- ***Cornerstone of the Innovation Agenda: To ensure that drugs and products reach patient and the market faster, without reducing the level of patient safety***

EU Clinical Trial Directive (CTD)

What's new?



- ***Regulation => Uniform provisions and direct implementation in MS***
- ***Reduce administrative burden:***
 - ***Single submission portal***
 - ***Joint assessment of applications by all member states involved in the CT***
- ***Tailor the regulatory requirements to the risk of the clinical trials***
- ***Possibility to carry out EC audits of the clinical trials system in third countries***

EU Clinical Trial Regulation(CTD) Next steps?



- ***Adoption of the EC proposal: 16/07/2012***
- ***Co-decision procedure with the European Parliament (EP) and European Council (EC)***
- ***Implementation in MS: 2-3 years after adoption by EP and EC (expected in 2016)***



Clinical Trials – Towards Horizon2020

Report on the Workshop “Clinical Trials in Horizon 2020” 27 February

Main objectives:

- Methodological state of the art
- Bottlenecks
- Financing and economics of CT
- The regulatory and reimbursement

Clinical Trials workshop

Main issues discussed

- Closer interaction between pre-clinical research and CT
- Establishment of targeted treatment strategies (“personalised medicine”)
- Promote quality control and professionalization in CT
- Promoting the full exploitation of animal efficacy data for the design of CTs and meta-analysis review
- Better and early integration of Health Technology Assessment (HTA) into development of new therapeutics
- Continue supporting comparative effectiveness research for evidence-based best care

Horizon 2020: The next Framework Programme for research and innovation

Proposed budget: €80bn, a 46% increase compared to FP7

Europe needs cutting edge research and innovation
Essential to ensure competitiveness, growth and jobs

Vital to tackle pressing societal challenges

3% of GDP invested in R&D: headline target of Europe 2020



The Health Challenge: some of the key features

- Understanding health, wellbeing and disease
 - Preventing disease
 - Treating and managing
 - Active ageing and self-management of health
 - Methods and data
 - Health care provision and integrated care
- Adapting to an ageing population
 - Personalised medicine
 - Translational research
 - **Clinical trials**
 - Private sector competitiveness, capability
 - Coordination of national efforts
 - Reduce costs: **CER**
 - Expanding global cooperation

Renewal of the "European and Developing Countries Clinical Trials Partnership"

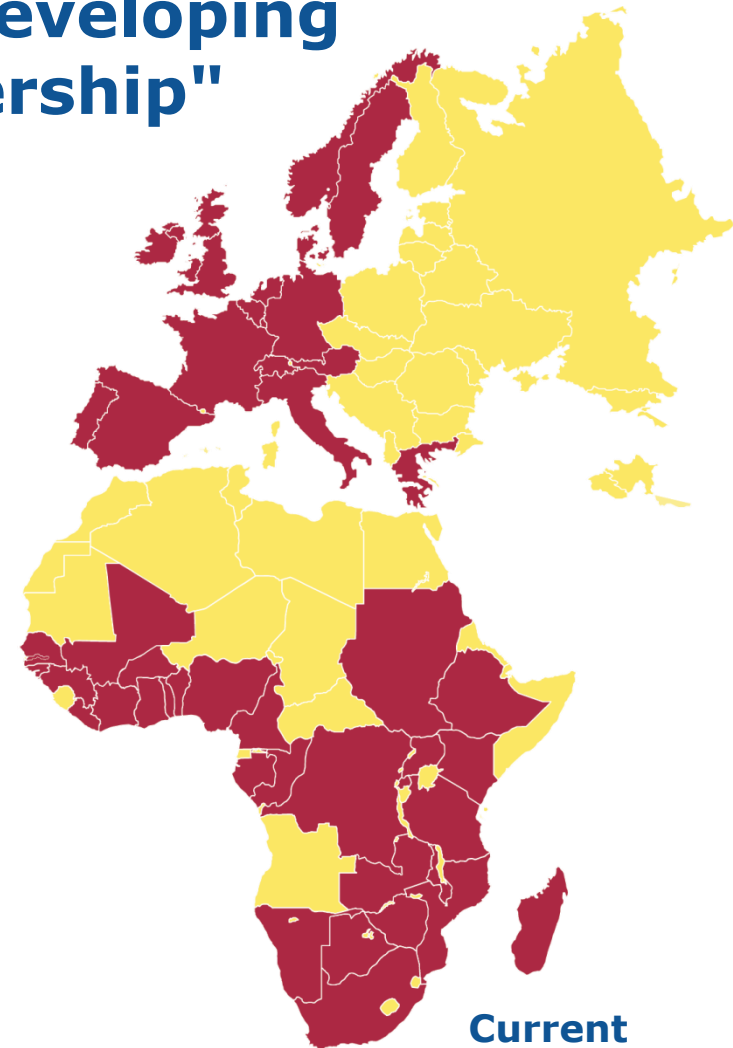
Netherlands the number 3 European participant with 31 projects, after Germany (38) and the UK (40)

Strategic Business Plan to ensure critical level of commitment to EDCTP2

Plans to keep scope and mandate

Proposal for EU legislation on EDCTP2 co-funding under development

High-Level Conference in Cape Town, 5 Nov 2012



**Current
Partnership**



Clinical Trials – Horizon2020

- Clinical trials will be a key element of health research supported in Horizon 2020
- Legal acts not yet adopted!
- Commission legislative proposals 30/11/2011
- "Partial general approach" proposal by Council: General FP 24/05/2012, Specific Programme 12/12/2012
- Adoption of legislative acts by Parliament and Council planned for mid-2013