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V Conferencia Anual de las Plataformas Tecnológicas de Investigación Biomédica: Medicamentos Innovadores, Nanomedicina Tecnología Sanitaria y Mercados Biotecnológicos
Fomentando la *Open Innovation*

International Rare Diseases Research Consortium

Josep Torrent-Farnell

COMP and SAWP, EMA, London

Barcelona Autonomous University - UAB

Barcelona, 14 y 15 de febrero de 2012

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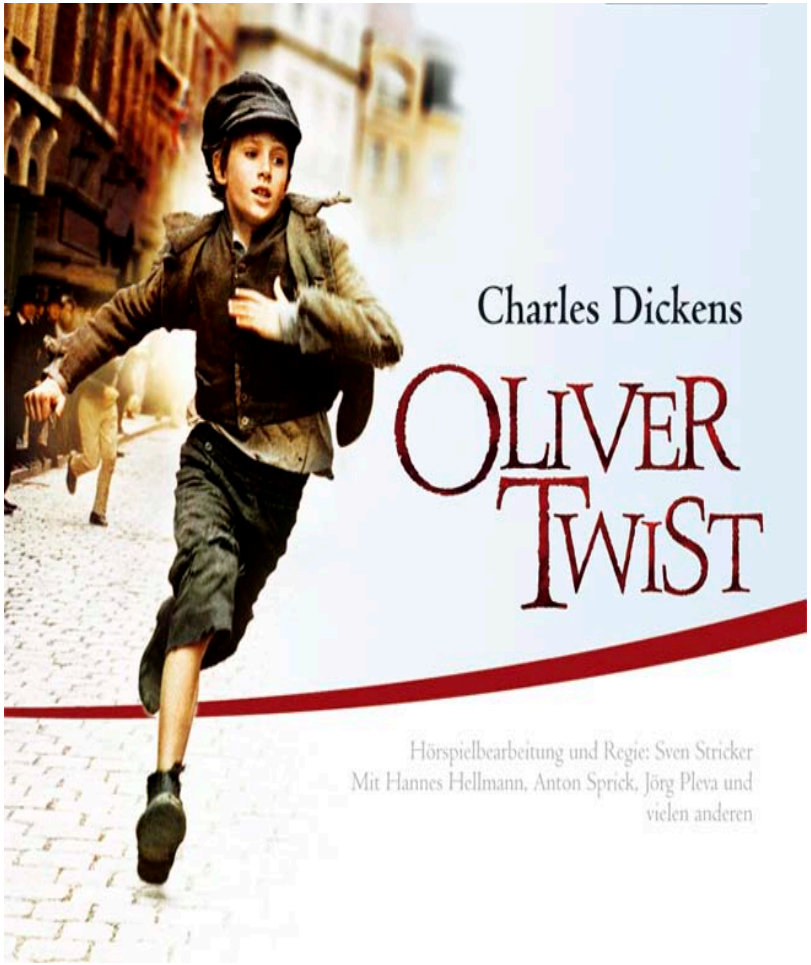

1. The current Rare Diseases framework: COMP/ EMA achievements / challenges

2. They way forward: a new international cooperative platform: IRDiRC

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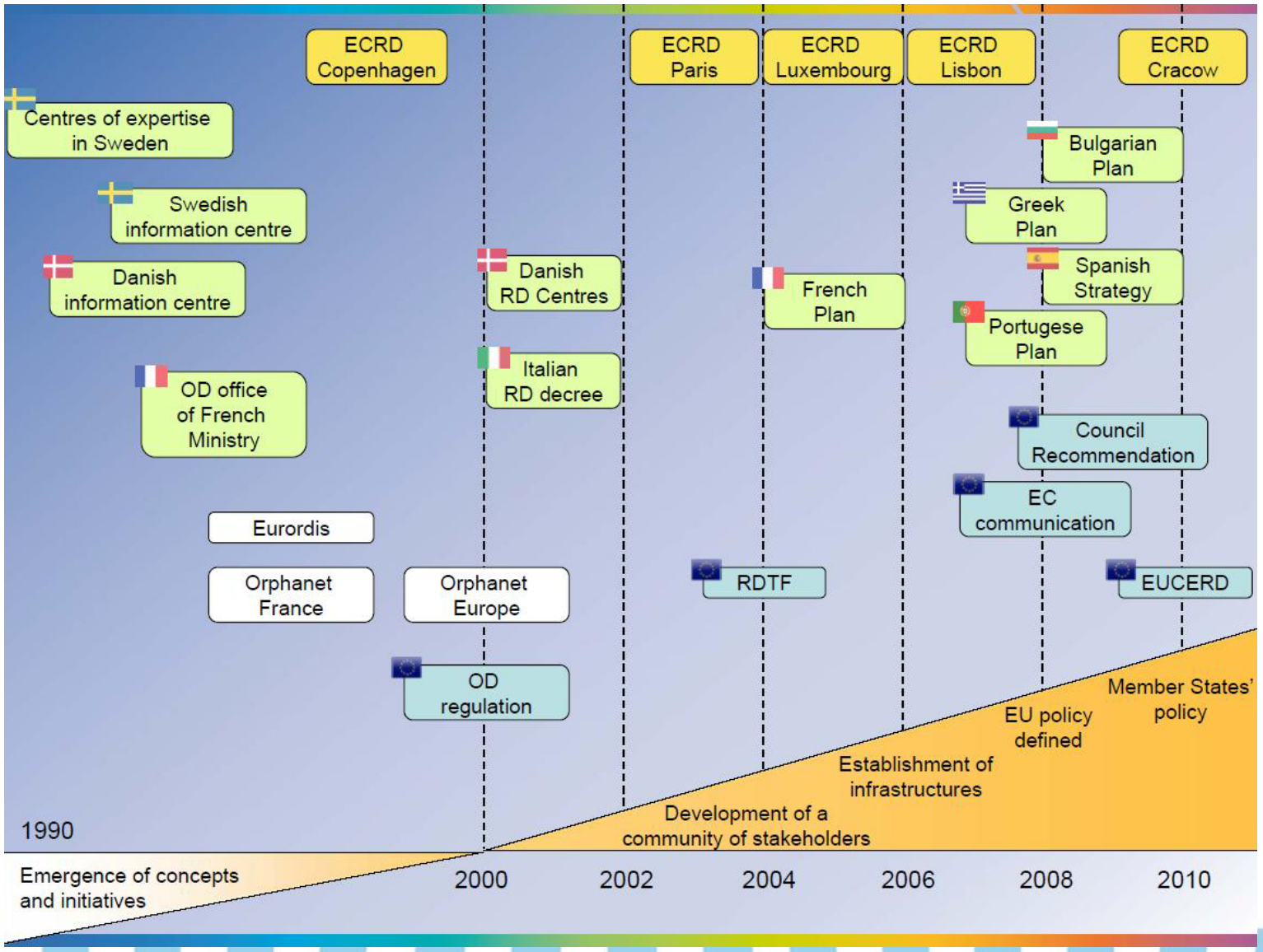
Why a regulation for Orphan Medicines is needed?

Some conditions occur so infrequently that the cost of developing a medicinal product would not be recovered by the expected revenues. Therefore the pharmaceutical industry is unwilling to develop these medicines under normal market conditions.

Patients suffering from rare conditions should be entitled to the same quality of treatment as other patients

(EC Regulation No 141/2000)

Growing rare disease actions



A patient-centered regulatory agency

EMA Scientific Committees

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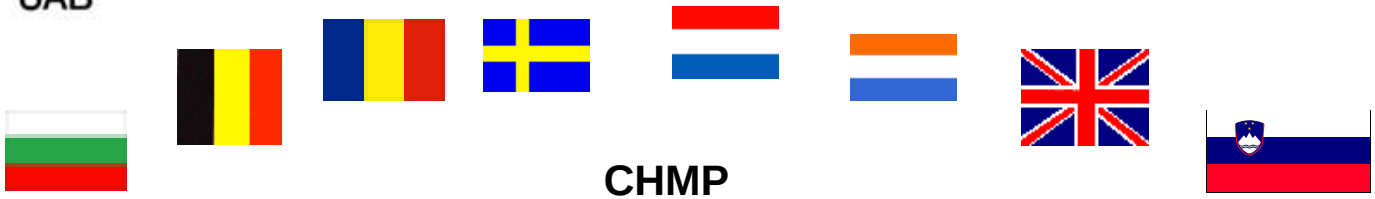
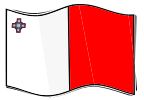


CHMP

(Committee for Human Medicinal Products) Chair : Dr E. Abadie

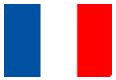


CVMP

(Committee for Veternary Medicinal Products): Chair Dr. A. Holm

HMPC

(Committee for Herbal Medicinal Products) Chair: Dr W. Knoss



COMP

(Committee for Orphan Medicinal Products) Chair : Prof K. Westermark

CAT

(Committee for Advanced Therapy Medicinal Products) Chair: Dr C. Schneider

PDCO

(Paediatric Committee) Chair: Dr D. Brasseur

+ PRAC (July 2012)

(PhVig Risk Assessment Committee) Chair: xxx

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COMP

Composition

Chair and Vice Chair

+

1 member/MS

+

3 patient reps

+

3 EMA reps

Dr. Westermark,
COMP Chair

+ 3 patient organisations

+ 3 EMEA

…the level of evidence…

CHMP

evidence

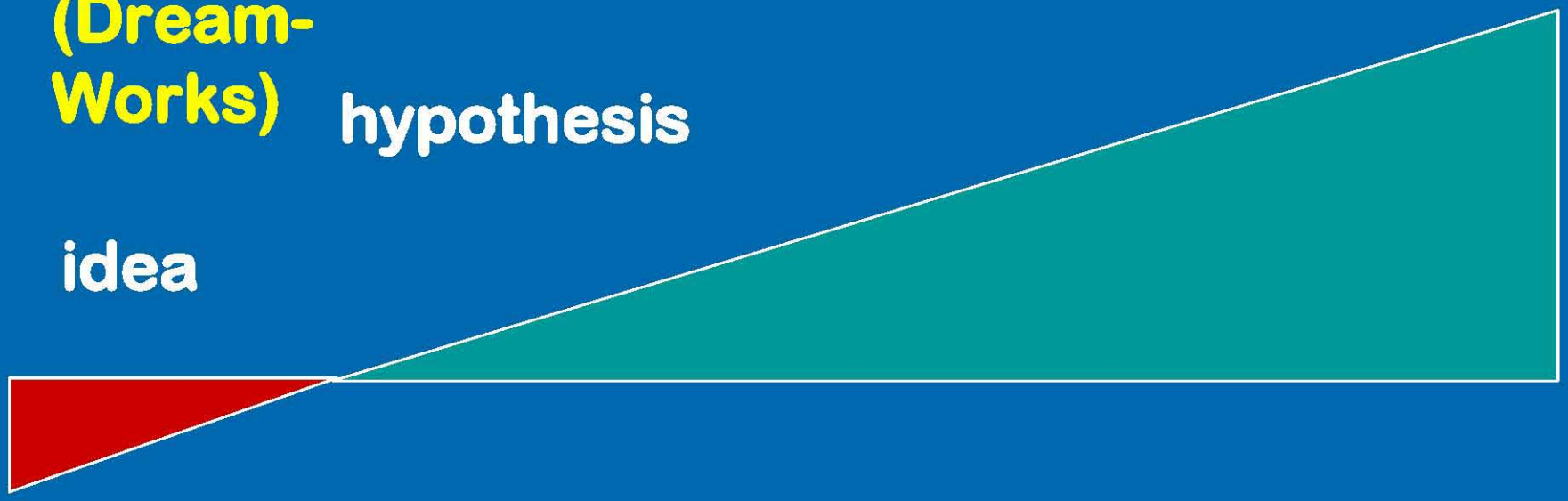
COMP

plausible
assumption

(Dream-
Works)

hypothesis

idea



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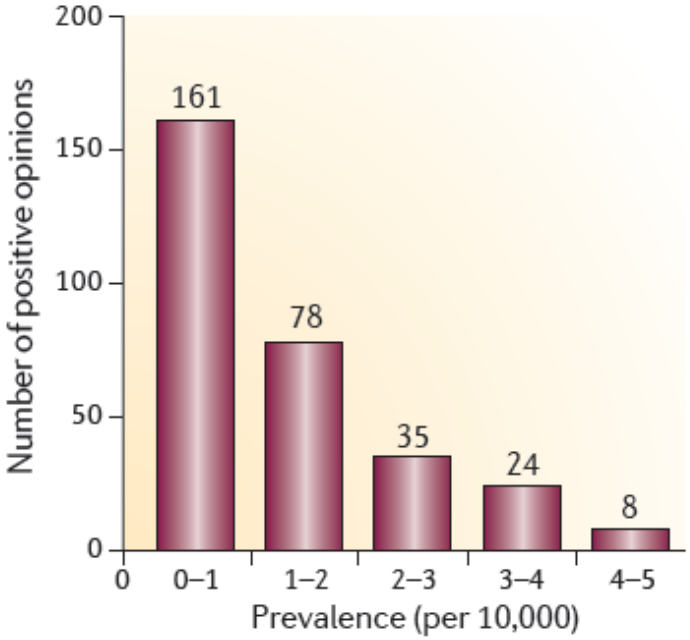
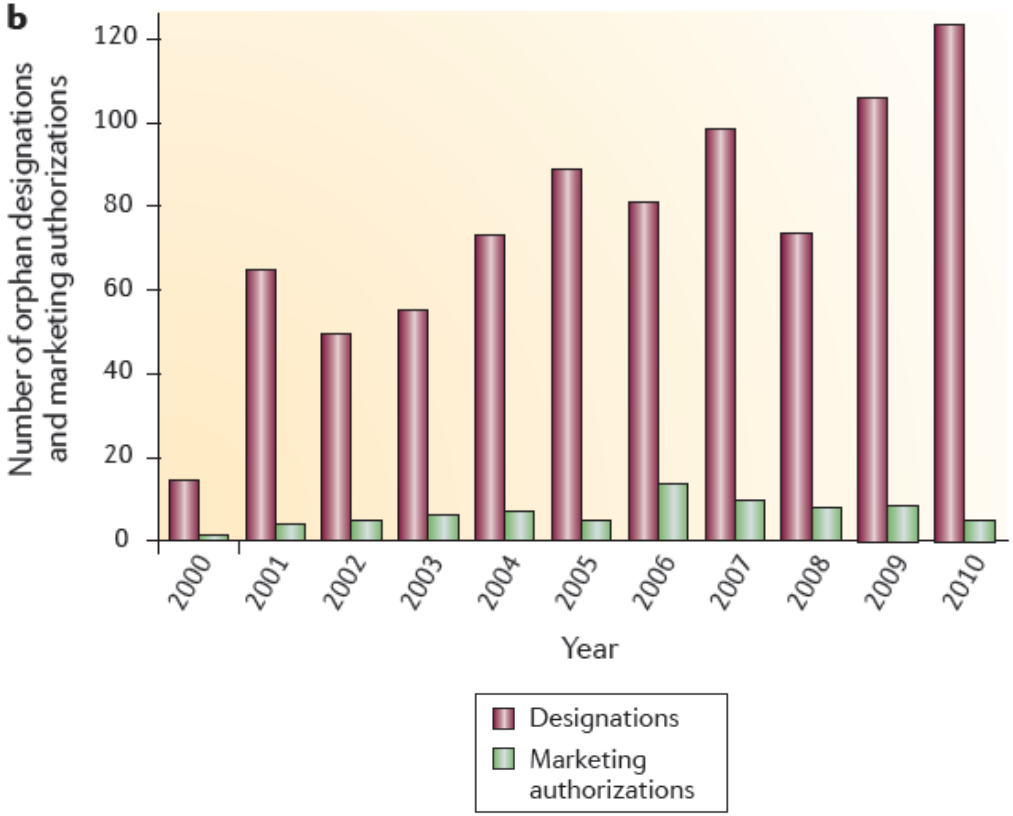
EU Orphan Designation (2000-2010)

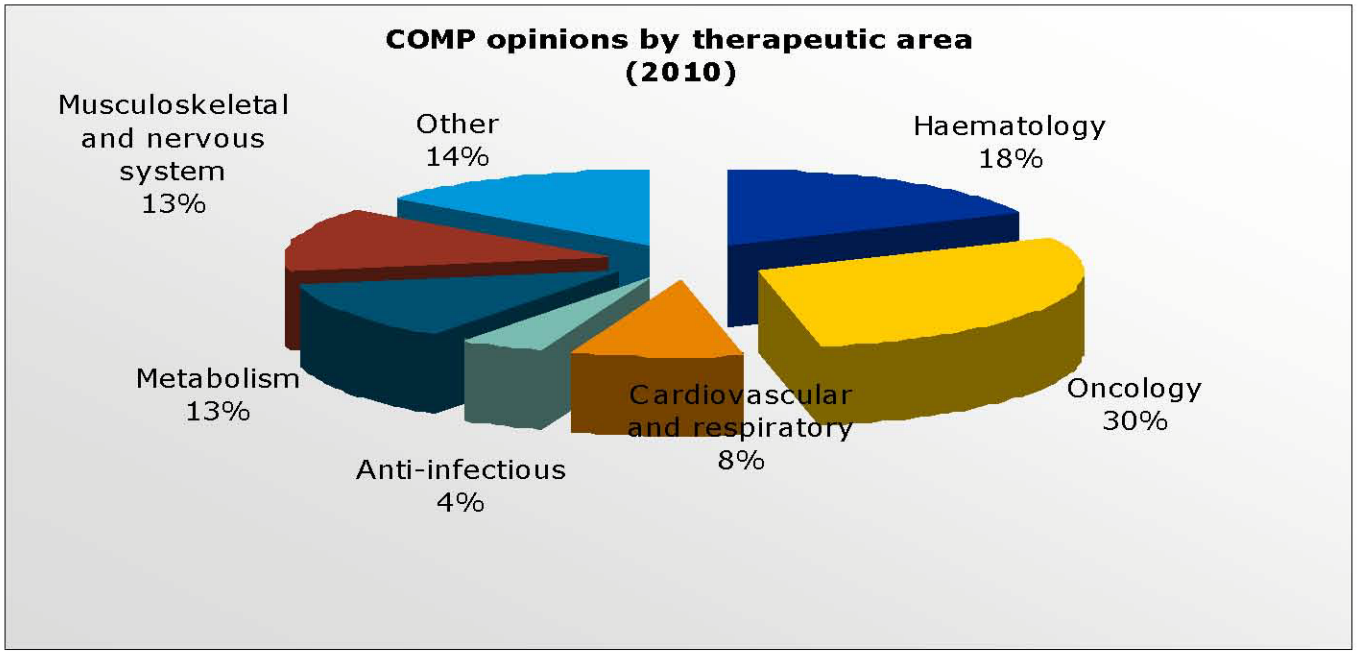


≈300 RD



Committee for Orphan Medicinal Products and the European Medicines. European regulation on orphan medicinal products: 10 years of experience and future perspectives. Nat Rev Drug Discov. 2011 May;10(5):341-9.

OD by therapeutic field



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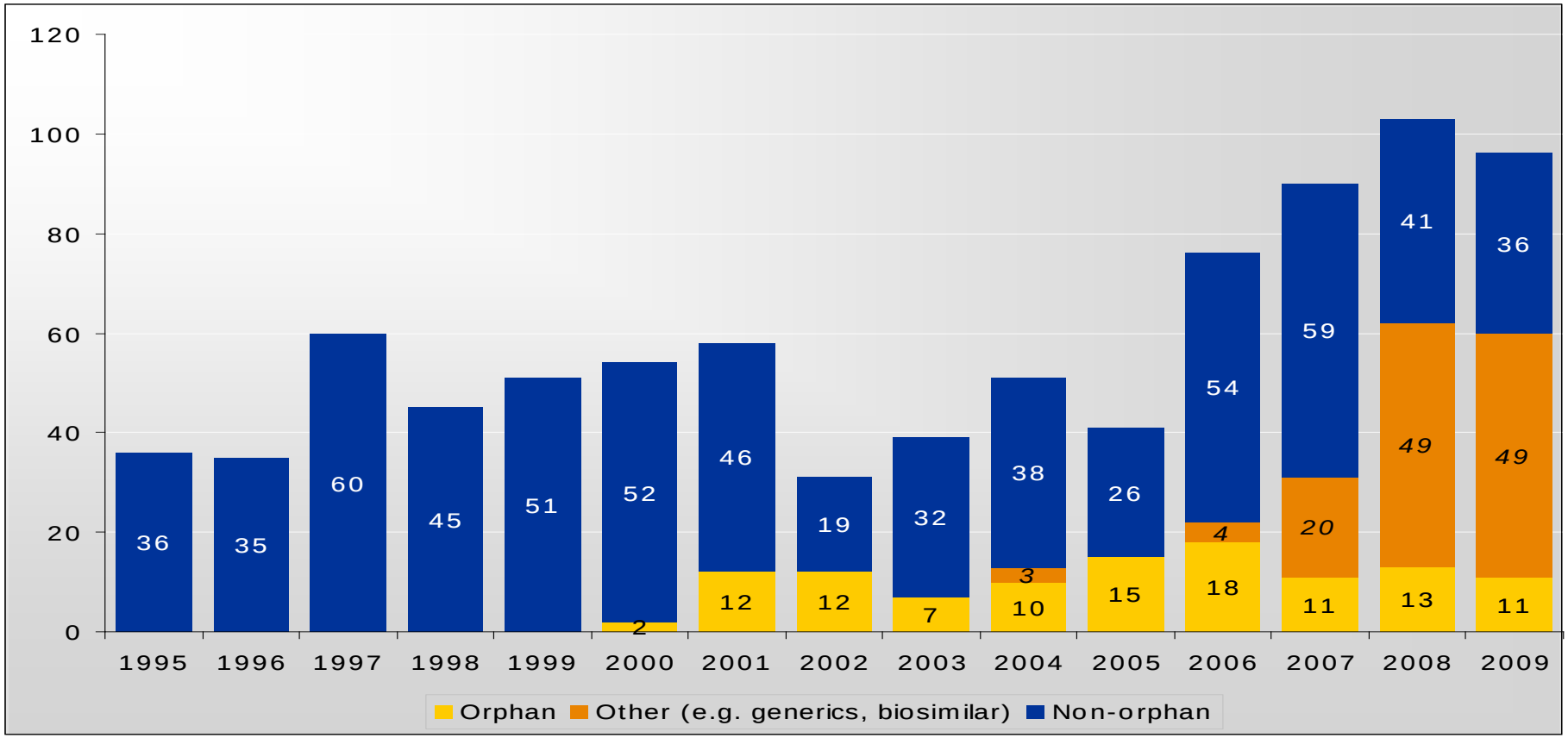
EMA: New MA Applications 1995-2009



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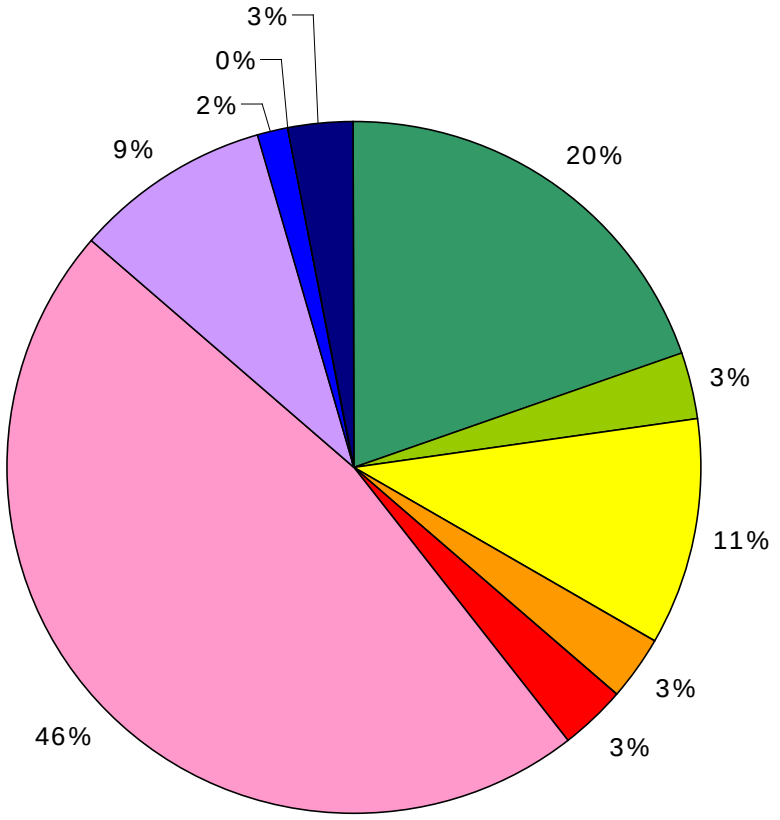
Therapeutic areas –marketing authorisations (n=66)



Number of conditions: 50 (+9 variations not included in graph)

COMP 10 year outcome

> 1200 orphan designation applications

- > 800 orphan designations: c:a 30% innovative products (fusion proteins, monoclonal antibodies, oligonucleotides), 7% advanced therapies (cell/gene/tissue)
- 66 marketing authorizations (41% with prevalence < 1/10,000), 41% 'under exceptional circumstances'; 5% 'conditional approval'

- **Public Health Impact – General:** drugs for children and for diseases rare in the EU (e.g. tropical diseases)

  Public Health Impact – Examples: 1/3 of authorised ODS for rare cancers (e.g. Tyrosine kinase inihibitors for chronic myeloid leukaemia; Endothelin receptor antagonists for pulmonary arterial hypertension; Enzyme replacement therapies for lysosomal storage diseases)

European rare diseases research landscape

4 770 ongoing research projects, covering 2121 diseases, excluding clinical trials

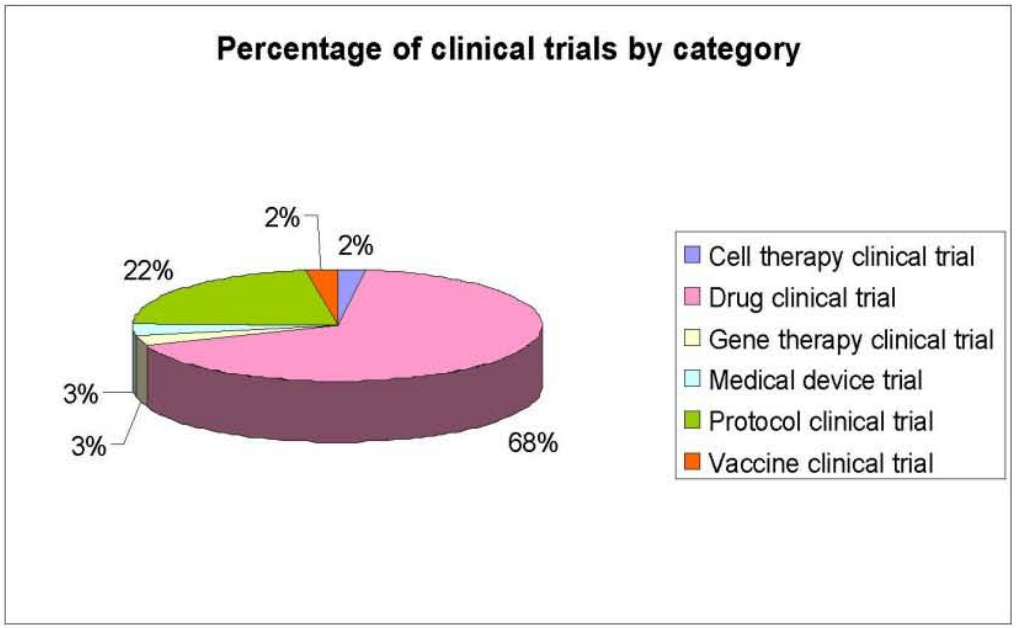
524	Gene search
701	Mutation search
255	Gene expression profile
346	Animal model creation/study
353	Genotype/phenotype correlation
313	Diagnostic tool/protocol dvpt
89	Biomarker development
228	Epidemiological studies
174	Observational clinical studies
57	Preclinical cell therapy
121	Preclinical gene therapy
128	Preclinical drug therapy

Source: S. Aymé – Orphanet (Oct. 2010)

COOPERATION

European rare diseases research landscape

666 ongoing national or international clinical trials for 312 diseases

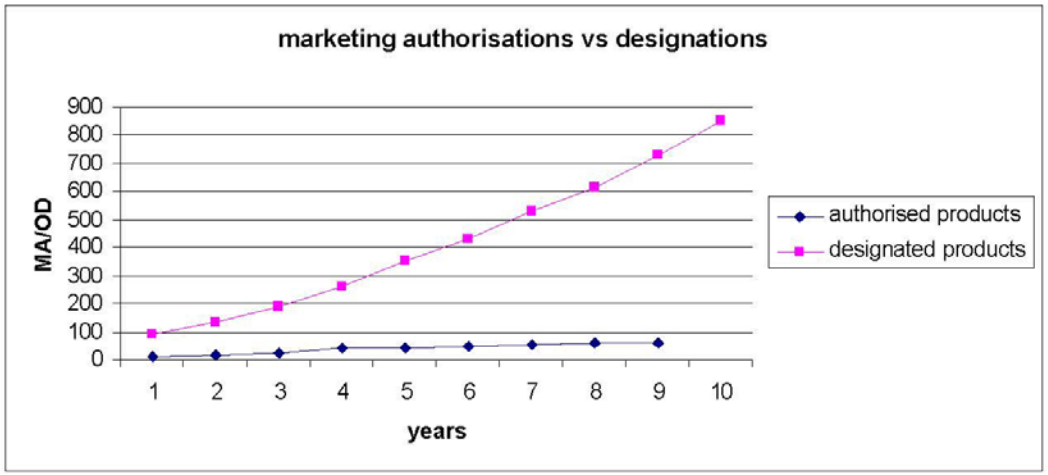


Source: S. Aymé – Orphanet (Oct. 2010)

Still remaining - around 5000-7000 different rare conditions – around 3500 treatable with pharmaceutical products

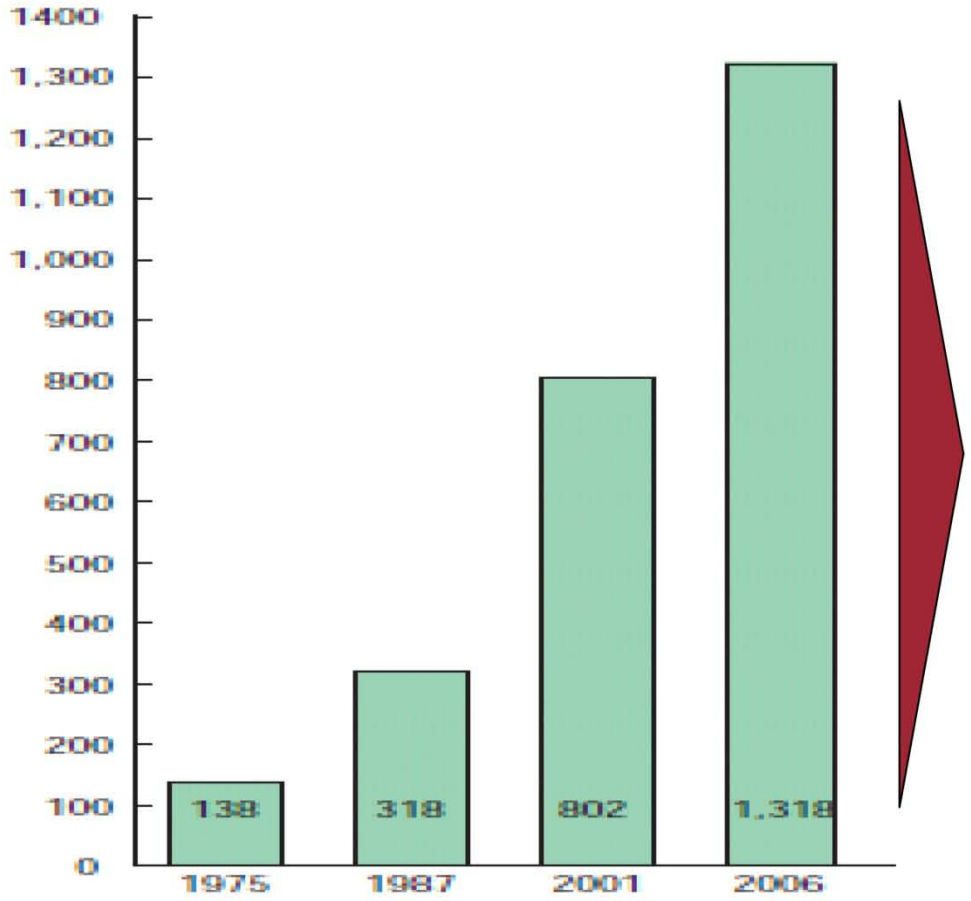
Unmet medical needs!

A growing gap?



- Need to analyse research needs that can narrow the gap
- Particularly worrying in some neglected areas

Estimated cost of bringing New Molecular Entity to market: ($ Million – Year in 2005 $)

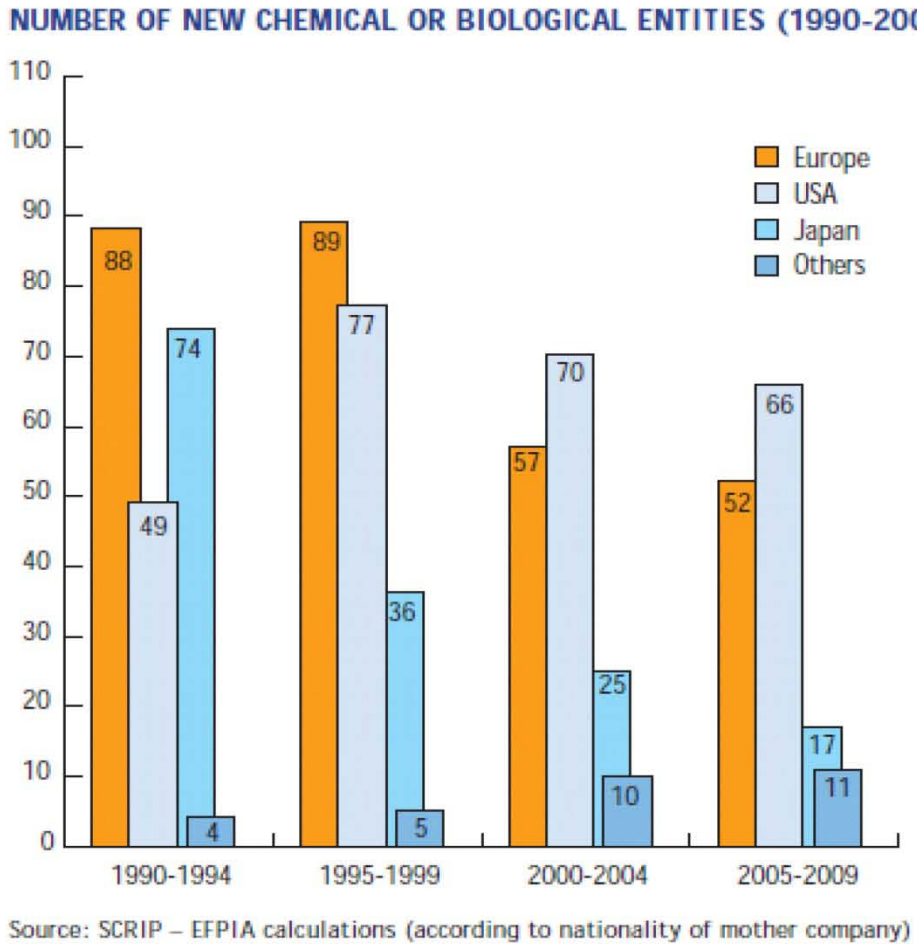


- Average cost to develop a new drug now ~1.3B USD
- Cost continues to rise given many factors (e.g., greater focus on safety, increased trial complexity, etc.)
- The industry only has 5-10 years to recoup the R&D investment for a new drug
  - 5 year data exclusivity for non-orphan drugs in US

Sources: Tufts CSDD; DiMasi and Grabowski, Managerial and Decision Economics, 2007

NOVARTIS

...but the number of New Molecular Entities is not increasing



NOVARTIS

European Commission

IRDiRC

International Rare Diseases Research Consortium

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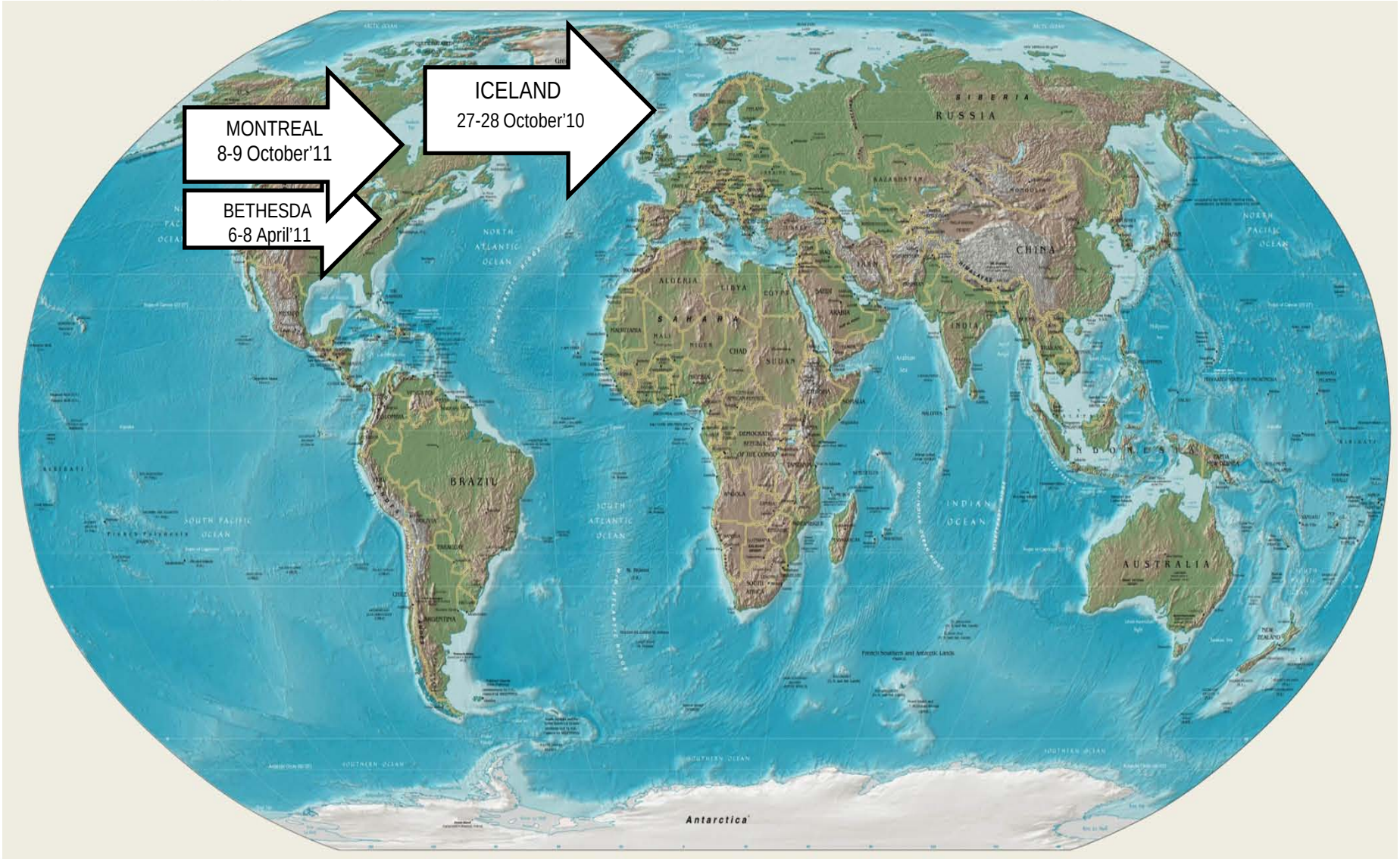
IRDiRC PREPARATORY MEETINGS



What is the problem?

- **Huge unmet medical needs**

- life-threatening, chronically debilitating diseases

- ~30 million of Europeans are affected or will be affected during their lifetime

- doctors often lack knowledge and tools to do correct diagnosis

- lack of specific treatments: up to ~90% drug use for rare conditions is off-label

- **Small patient populations are challenging for the development of diagnostic/therapeutic tools:**

- challenge of (standardized / harmonized) data/sample gathering

- challenge for clinical trials, due to difficult identification of cases and small patient samples (classic double blinded, placebo-controlled multi-centered, multi-national clinical trials cannot be envisioned…)

- **Research resources** (patients, experts, budget) are scarce and scattered

How do we want to solve it?

- Increase research volume
- Improve co-ordination to maximize research investments
- Speed up the uptake of research efforts into clinical practice

How do we want to solve it ?

Cooperation: the way forward

Let's set research on rare diseases to music!

COOPERATION

Advantages of international program level cooperation

- Economy of scale as treatments and cures are universal
- Allowing to set and faster reach ambitious goals
- Easier to mobilize the necessary critical mass of expertise and resources
- Avoid overlaps in research allowing for more diseases to be tackled

Why now?

Timely reflection in the context of:

- The set up of similar research programs throughout the world and involving various funding agencies and organizations
- "-Omics" technologies bringing new opportunities and are getting ripe to demonstrate their clinical utility
- Rare diseases could and should be seen as models for developing personalized medicine approaches
- Increased number of orphan drug designations that need further research for reaching the patients (« crossing the valley of death »)

COOPERATION

The European Union: a major player in funding rare diseases research

What did we do so far?

- EU has been investing in research on rare diseases for more than 2 decades
- **50 FP7 collaborative projects** relevant to rare diseases
- **€ 237 million (~ $ 334 million)** invested on RD research in the 4 first calls for proposals (2007-2010) of the current framework programme, FP7 (2007-2013)

COOPERATION

Cooperation: successful examples

International Cancer Genomics Consortium (ICGC)

International Cancer Genome Consortium

To obtain a comprehensive description of genomic, transcriptomic and epigenomic changes in 50 different tumor types

NIH, EU Commission, and 11 other countries (DE, UK, Aus, etc)

Total investment > $250 million

www.icgc.org

International Human Epigenome Consortium (IHEC)

IHEC
International Human Epigenome Consortium

Coordinate the production of reference maps (at least 1000 epigenomes) of human epigenomes for key cellular states relevant to health and diseases. (in preparation)

NIH, EU Commission, CIHR (Canada), 10 other countries

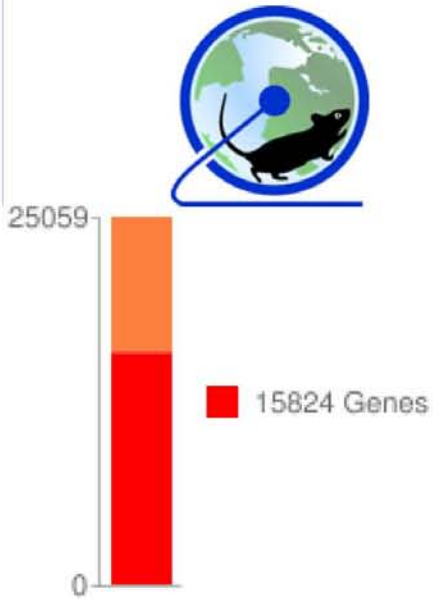
Total investment foreseen> $100 million

www.ihec-epigenomes.org

COOPERATION

Cooperation: successful examples

International Mouse Knockout Consortium (IKMC)



- Mutate all protein-coding genes in the mouse
- NIH, EU Commission, Genome Canada
- Total investment: $100 million
- www.knockoutmouse.org
- 63 % of the work done
- >15000 targeted ES lines available
- 1000 K.O. mouse lines already generated and freely available
- The resource should be completed by 2012-2013

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Goals of IRDiRC

200 new therapies for rare diseases by 2020

Means to diagnose most rare diseases by 2020

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International Rare Disease Research Consortium (IRDiRC)

- International co-operation to stimulate, co-ordinate and maximise output of rare disease research efforts around the world
- Research funders with relevant programmes >$10 million US over a 5-year period can join & work together
- Funded projects adhere to a common framework
- Scientists will join thematic working groups such as sequencing, natural history, biomarkers, or clinical research

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IRDiRC objectives & milestones

Objectives

200 new therapies

Means to diagnose most rare diseases

YEAR	Diagnostics	Therapies
2012	Mapping of sequencing & characterisation efforts Identified & prioritised gaps in sequencing & diagnostics	Prioritisation of 100 new or repurposed therapies
2015	5000 sequenced / characterised 3000 diagnostics	50 new applications for market authorizations for new or repurposed therapies
2020	6000 diagnostics	200 new market authorizations given for new or repurposed therapies

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IRDiRC committed funding bodies February 2012

European Commission, EU

Agence Nationale de la Recherche, France

Association Française contre les Myopathies, France

Bundesministerium für Bildung und Forschung, Germany

Telethon Foundation, Italy

Istituto Superiore di Sanita, Italy

The Netherlands Organisation for Health Research and Development, the Netherlands

Prosensa, the Netherlands

Instituto de Salud Carlos III, Spain

National Institute for Health Research, UK

Western Australian Department of Health, Australia

Canadian Institutes for Health Research, Canada

Genome Canada, Canada

Office of Rare Diseases, US

National Human Genome Research Institute - Mendelian Disorders Genome Centres, US

National Human Genome Research Institute - National Centre for Translational Therapeutics, Library programme, US

National Cancer Institute, US

National Institute of Neurological Disorders and Stroke, US

National Institute of Arthritis and Musculoskeletal and Skin Diseases, US

National Institute of Child Health and Human Development, US

National Eye Institute, US

Sanford Research, US

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IRDiRC Governance

Executive Committee

- 1 representative per funding body
- 1 representative per group of funders (accumulative funding)
- the chairs of the Scientific Committees

Scientific Committees

Diagnostics | **Interdisciplinary** | **Therapies**

15 members with balanced representation of scientists, patients, industry, etc.

Working Groups

Sequencing | Ontologies | Model systems | Clinical

Registries | Natural history | Biomarkers | Etc.

Representatives of funded projects

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IRDiRC Governance

- **Executive Committee**
  Represents the IRDiRC funding bodies; develops policy and guidelines , coordinates research funding, and nominates Scientific Committee members

- **Scientific Committees**
  Each with 15 members to represent stakeholders in a balanced way; propose research priorities to the Executive Committee, assess progress, and agrees on procedures and standards..

- **Working groups**
  Represent all IRDiRC projects; ensure synergies, propose standards for best data/research results use

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IRDiRC next steps

Setting up Scientific Committees

Members to be appointed 29 February 2012, first meetings spring 2012

Policy Document

Consolidation and consultation of IRDiRC policies and guidelines

Executive Committee meeting

Next meeting September 2012 date and venue to be confirmed

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Being a part of IRDiRC

Want to become an Executive Committee member?
Required research investment: $10 million US over a 5 year period including funding from 2010 forward; application template available on the IRDiRC website

http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html

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Rare Disease Day®

29th February 2012