

'Session 1: Nanotechnologies today and tomorrow

Health applications of nanoscience and nanotechnologies

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Head of the European Medical Research Councils (EMRC)

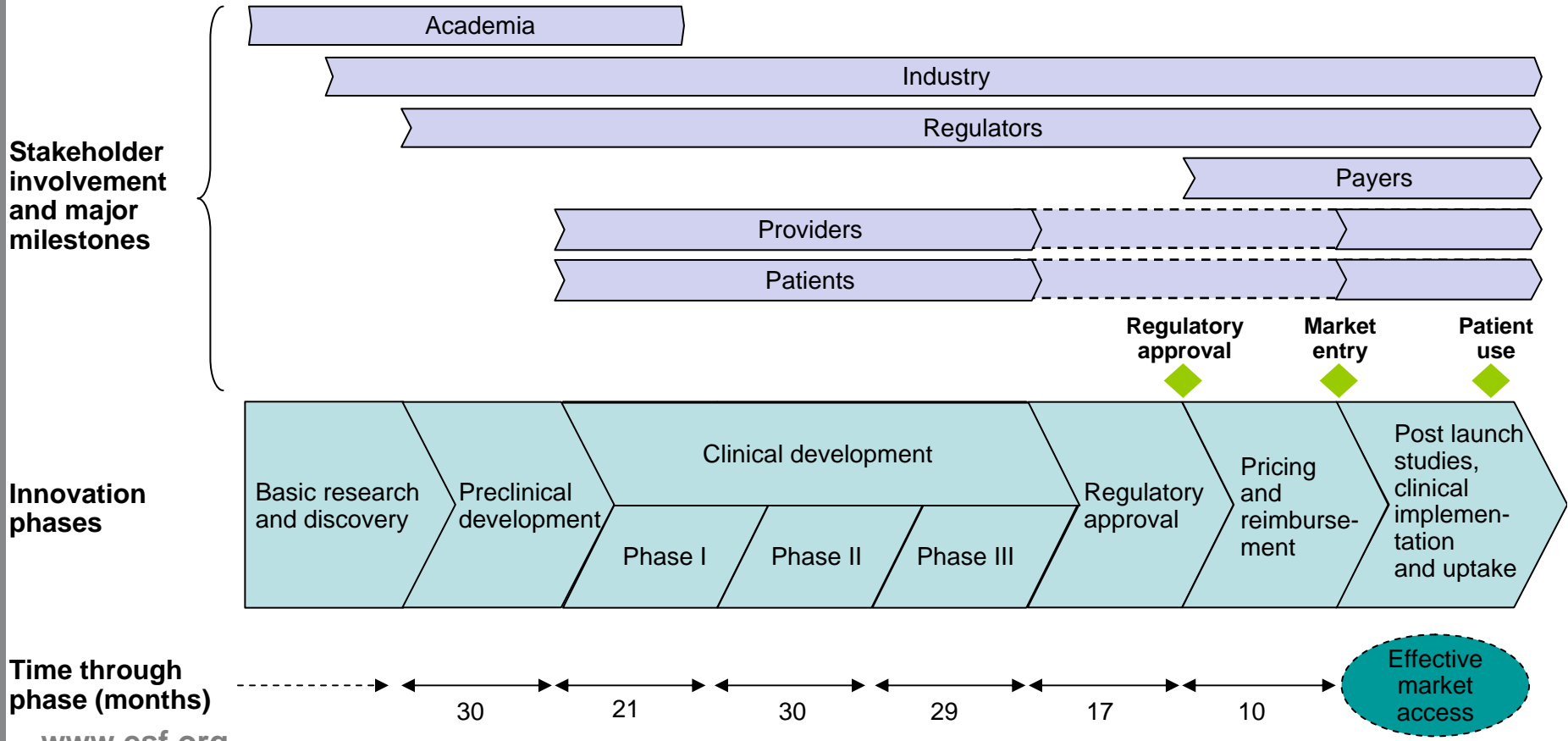
1. Medical Innovation: Paradigm shift and patients unmet needs
2. Nanomedicine: Convergence of nanosciences and systems biology
3. Health applications today: examples
4. Health applications tomorrow: challenges

Medical Innovation: Paradigm Shift

- Paradigm shift from large markets to personalized/individualized medicine and need for knowledge transfer across disciplines and research sectors (e.g., academia & industry)
- Patient centered process
- Patients unmet needs (WHO, 2004)

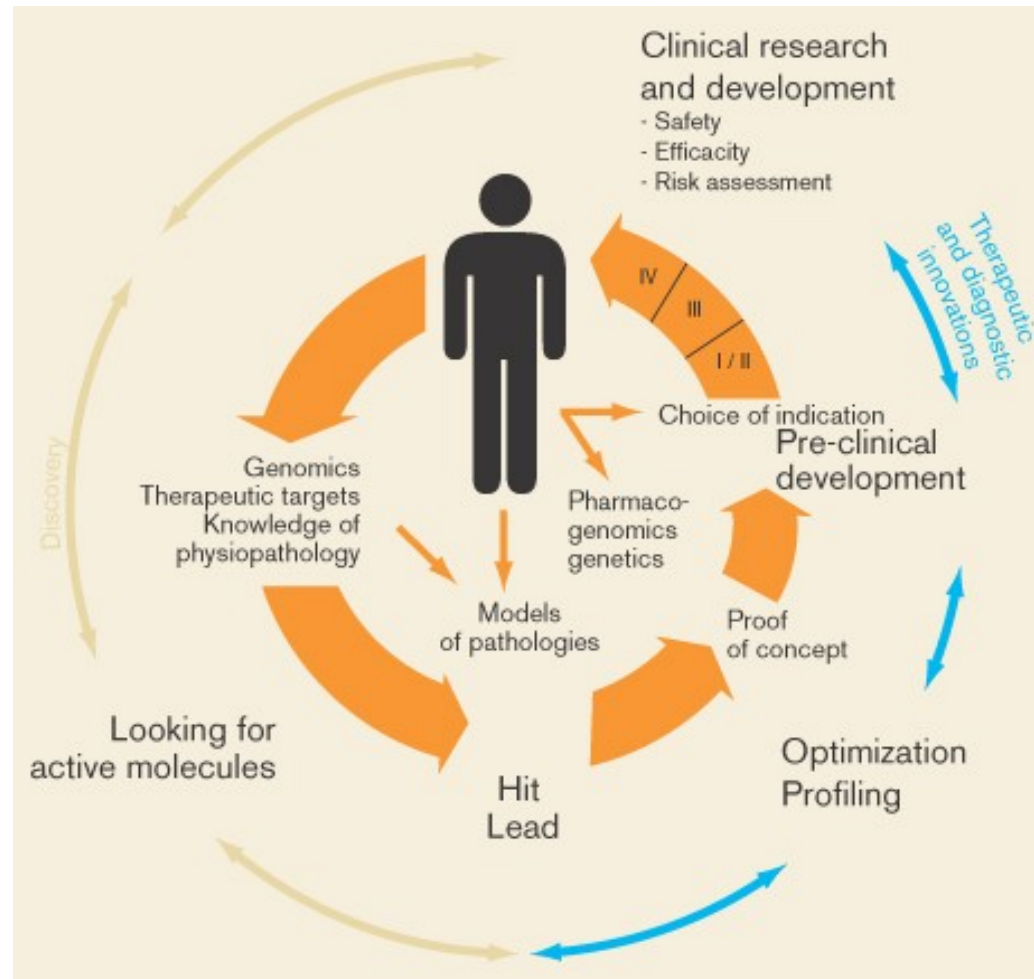
Medical Innovation: Paradigm Shift

Current process for the development and commercialization of drugs in Europe
(EBC EFNA)



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Patient Centered Process



Priority diseases for Europe (WHO, 2004)

EUROPE

- Tuberculosis
- Osteoarthritis
- Diabetes
- Alzheimer disease
- Cardiovascular diseases
- Acute stroke (cerebro-vascular accident)
- Alcohol dependence and alcoholic liver disease
- Antimicrobial resistance as it relates to infectious diseases
- Influenza (primarily related to vaccines to counter the pandemic threat)
- Depression
- Chronic Obstructive Pulmonary Disease
- HIV/AIDS
- Cancers

THE WORLD

- Malaria
- Postpartum Haemorrhage
- Neglected Diseases including Trypanosomiasis, Leishmaniasis and Buruli Ulcer

ESF - ZON-MW - WHO (Nov. 2004)

'Priority medicines for the citizens of Europe'

Priority diseases for Europe

(WHO, 2004)

17 priorities

- Diseases for which **basic and applied research is required**: cancer; acute stroke
- Diseases for which **biomarkers are absent**: Alzheimer disease; osteoarthritis
- Diseases for which **better formulations** are required: cardiovascular disease (secondary prevention); diabetes; postpartum haemorrhage; paediatric HIV/AIDS; depression in the elderly and adolescents
- **Neglected diseases** or areas: tuberculosis; malaria and other tropical infectious diseases such as trypanosomiasis, leishmaniasis and Buruli ulcer, HIV vaccine
- Diseases for which **prevention** is particularly effective: chronic obstructive pulmonary disease including smoking cessation; alcohol use disorders: alcoholic liver diseases and alcohol dependency
- **Future public health threats**: infections due to antibacterial resistance; pandemic influenza

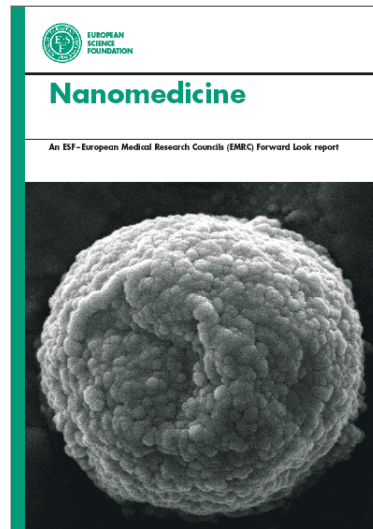
Special concerns

- Children
- Elderly (ageing population in Europe)
- Rare diseases

Nanomedicine: Convergence of nanosciences and systems biology

'The field of Nanomedicine is the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.'

ESF-EMRC
Forward Look Report
Nanomedicine
November 2005

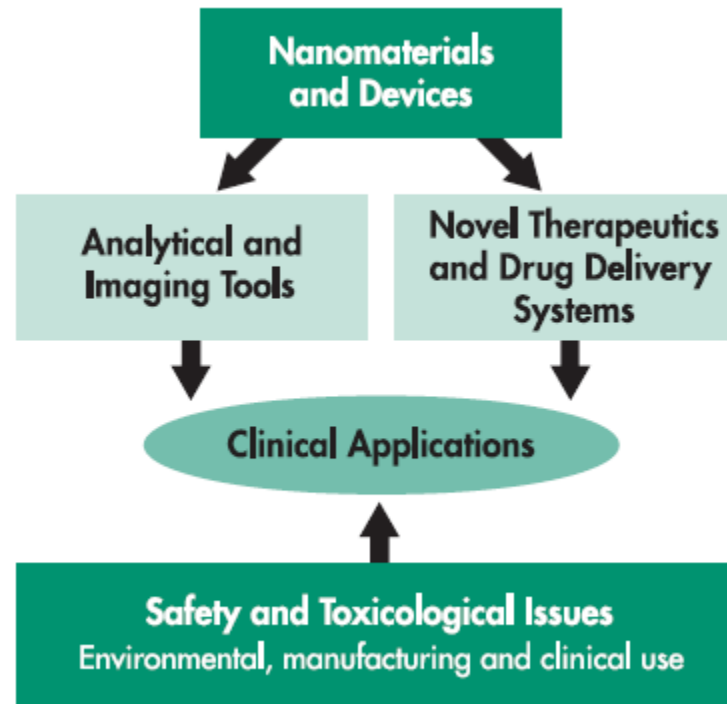


ESF
Forward Look
Systems Biology
September 2007



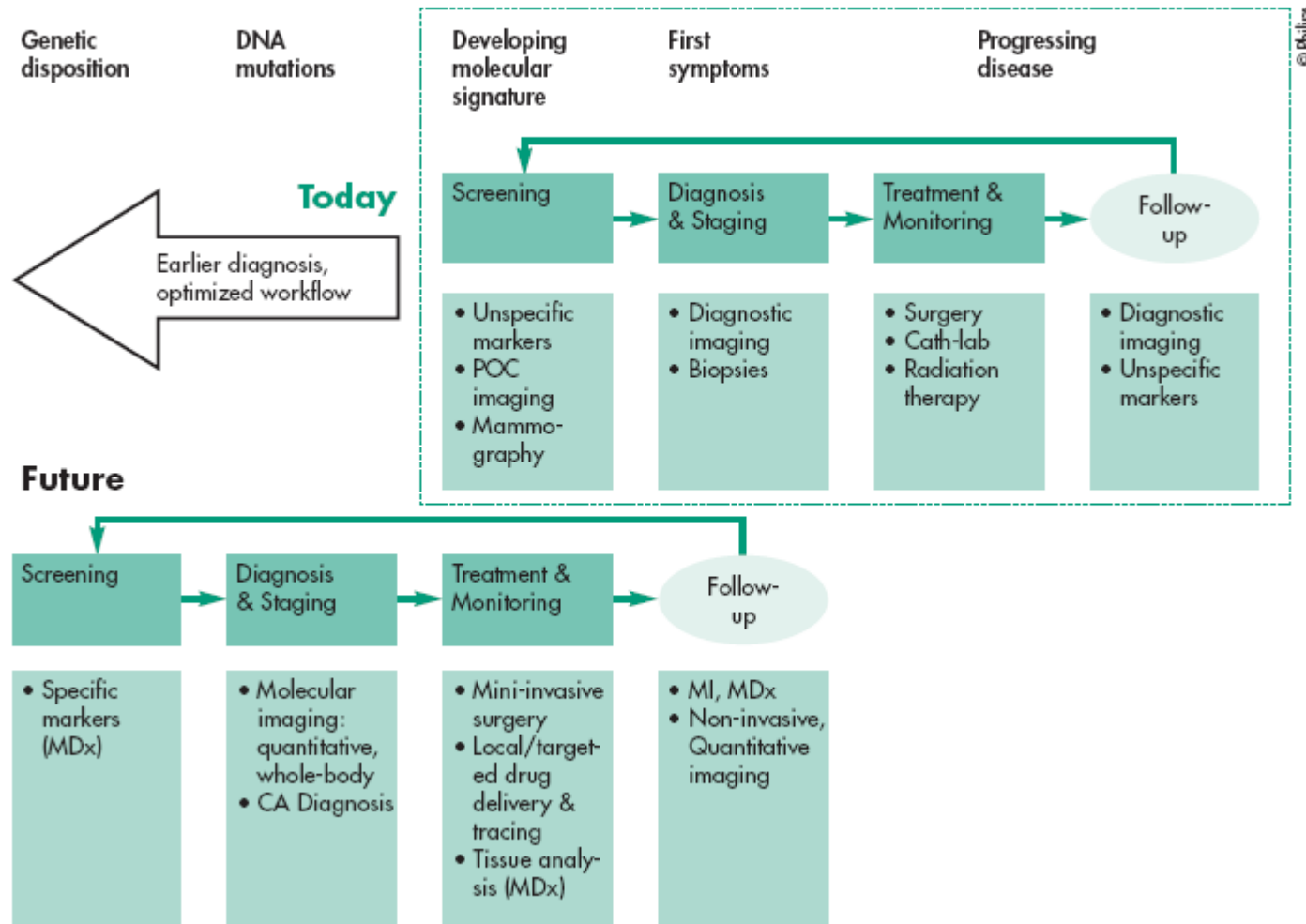
Nanomedicine: Convergence of nanosciences and systems biology

The field of nanomedicine is perceived as embracing five main sub-disciplines:



Paradigm shift curative towards preventive and predictive medicine

Molecular Imaging Diagnostics (MDx): Impact on healthcare in the future



Biological Applications:

- **Definition of target and pathway and network identification**
 - Via multiple, co-assembled biomolecules
- **Definition of mechanisms of signalling and signal transduction**
 - Via artificial assemblies in vitro

Medical Applications:

- **Drug targeting**
 - Whole body, cellular, sub-cellular localisation of drugs, proteins and genes
- **Drug discovery**
 - High Throughput Screening technology with biomolecular or cellular read-outs
 - Novel bioactives, obtained through nanotechnology
 - Novel drug delivery systems
- **Diagnostics and sensing**
 - In vitro (multiple analyte detection) and in vivo
- **Regenerative medicine**
 - Materials to regulate cell signalling and differentiation, and also controlling morphogenesis thus helping to bring functional integration

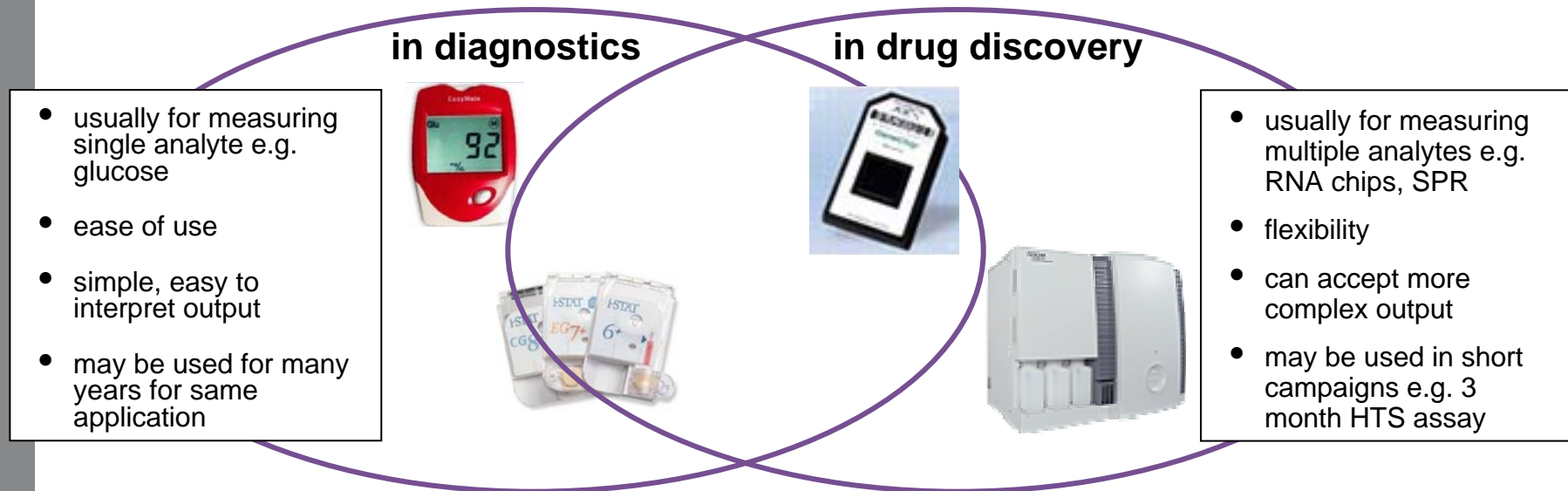
Nanomaterials and nanodevices

Medical devices and diagnostics: e.g., Biosensors (J. Deacon, UK MNT)

Regenerative medicine: bioresponsive materials for tissue engineering
(J.A. Hubbell, CH; J. Planell, IBEC, ES)

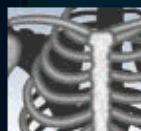
Role of biosensors diagnostics vs drug discovery (AstraZeneca)

- An **analytical tool** consisting of a **biologically active material** used in close conjunction with a device that will convert a biochemical signal into a **quantifiable physical signal** (current, light etc.)
- Most people associate the term biosensor with an integrated device (e.g. glucose sensor), but Pharma looking to stress in-situ transduction system and external detector (e.g. telemetry probe)



THE NEW ERA OF REGENERATIVE MEDICINE

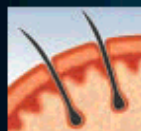
Dozens of biotech companies and university labs are developing ways to replace or regenerate failed body parts. Here are a few of the projects:



BONE

Bone-growth factors or stem cells are inserted into a porous material cut to a specific shape, creating new jaws or limbs. A product that creates shinbones is in clinical trials.

COMPANIES: Creative Biomolecules, Orquest, Sulzer Orthopedics Biologics, Genetics Institute, Osiris Therapeutics, Regeneron.



SKIN

Organogenesis' Apligraf, a human-skin equivalent, is the first engineered body part to win FDA approval, initially for leg ulcers. Other skins are in the works for foot ulcers and burns.

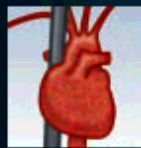
COMPANIES: Organogenesis, Advanced Tissue Sciences, Integra LifeSciences, LifeCell, Ortec International.



PANCREAS

Insulin-manufacturing cells are harvested from pigs, encapsulated in membranes, and injected into the abdomen. The method has been tested in animals and could be in human trials in two years.

COMPANIES: BioHybrid Technologies, Neocrin, Circe Biomedical



HEART VALVES, ARTERIES, AND VEINS

A 10-year initiative to build a heart has just started. Genetically engineered proteins have been successfully used to regrow blood vessels.

COMPANIES: Organogenesis, Advanced Tissue Sciences, Genentech, LifeCell, Regeneron.

DATA: BUSINESS WEEK, DRUG & MARKET DEVELOPMENT REPORTS



SALIVA GLANDS

Proteins called aquaporins that allow cells to secrete water are used to recreate saliva glands damaged by disease or radiation. Glands are also being engineered to secrete healing drugs. The technique has proven successful in mice.

COMPANIES: None yet.



URINARY TRACT

Cartilage cells are taken from the patient, packed into a tiny matrix, and injected into the weakened ureter, where they bulk up the tissue walls to prevent urinary backup and incontinence. The method is in late-phase clinical trials.

COMPANIES: Regeneration, Integra LifeSciences.



BLADDER

Doctors at Children's Hospital in Boston have grown bladders from skin cells and implanted them in sheep. They are about to try the same process on a patient.

COMPANIES: Regeneration.



CARTILAGE

A product is already on the market that regrows knee cartilage. A chest has been grown for a boy and a human ear on a mouse.

COMPANIES: Genzyme Tissue, Biomatrix, Integra LifeSciences, Advanced Tissue Sciences, ReGen Biologics, Osiris Therapeutics



TEETH

Enamel matrix proteins are used to fill cavities. It works in dogs; human trials are a few years away.

COMPANIES: Biora, Atrix Laboratories, Creative BioMolecules.



BREAST

In preclinical studies, several companies have been able to create a cosmetic nipple by inserting a ball of cartilage. Researchers are now trying to grow a whole cosmetic breast.

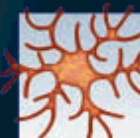
COMPANIES: Regeneration, Integra LifeSciences.



LIVER

A spongy membrane is built up and then seeded with liver cells. Organs the size of a dime have been grown, but a full-size liver could take 10 years due to its complexity.

COMPANIES: Advanced Tissue Sciences, Human Organ Sciences, Organogenesis.

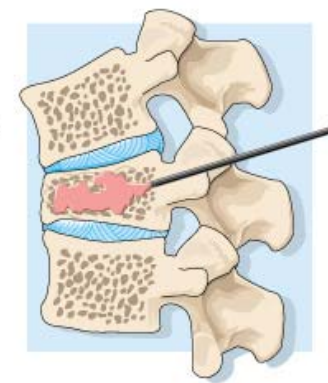
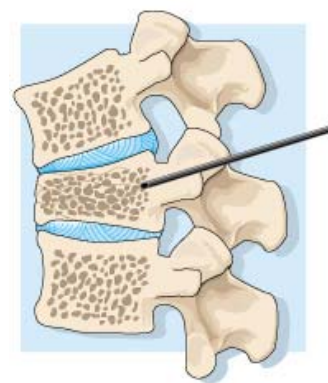
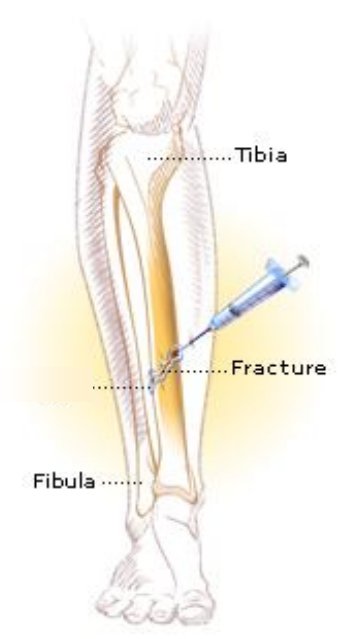


SPINAL CORD NERVES

Scientists are investigating nerve-growth factors, injecting them at the site of damage to encourage regeneration or seeding them along biodegradable filaments and implanting them. Rats have been made to walk again.

COMPANIES: Acorda, Regeneron, CytoTherapeutics, Guilford Pharmaceuticals.

*Candidates for bone repair and regeneration
in minimally invasive surgery*



Injectable
Porous
Calcium
Phosphate
Cements
(J. A. Planell, IBEC,
Barcelona, ES)

Molecular and Patient Imaging

Targeted therapeutics and molecular imaging in cancer

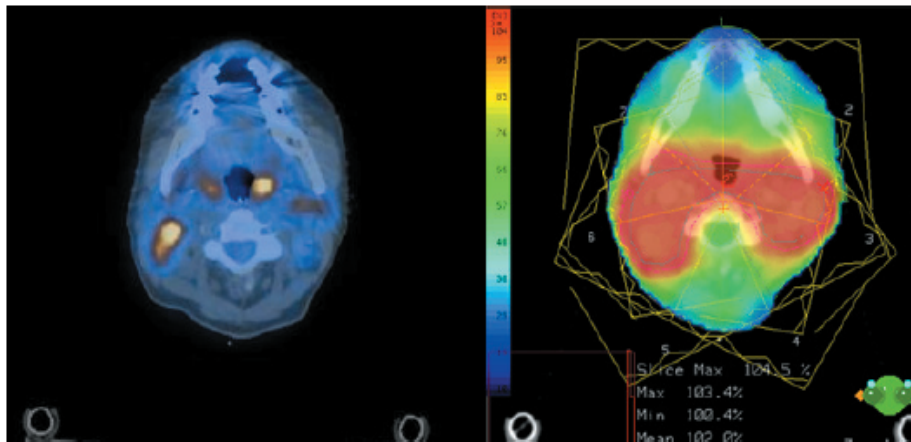


Figure 5: Radiation treatment planning (right) of head/neck cancer based on fusion of morphologic and functional information obtained with PET-CT (left) (courtesy of Prof. Liselotte Højgaard)

EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

SCIENCE POLICY BRIEFING • September 2007 28

Medical Imaging for Improved Patient Care

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1 - Foreword & Introduction
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Foreword
The rapid development in medical research produces a continuous stream of new knowledge about disease processes, how therapies target, and the complex relationship between a patient's genome and his/her related risk for disease. New technology is being developed for all aspects of patient care and the potential benefits of personalised medicine is gaining acceptance. Medical imaging can now play a central role in the global healthcare system as it contributes to improved patient outcome and more cost-efficient healthcare in all major disease entities. More and better research in medical imaging is needed in Europe to increase our knowledge about disease processes and therapy management with the long-term goal of improving the health of European citizens.

The European Science Foundation's medical section, the European Medical Research Council (EMRC), organised in this science policy activity because medical imaging plays a role of ever-increasing importance at all levels of the healthcare system. EMRC assembled a group of European high-level experts in this field and conducted a Strategic Workshop in November 2006 to put a focus on research in the wide area of medical imaging, to analyse the status quo of medical imaging in Europe and to develop a policy for optimal use of research resources at the European level. Their recommendations are summarised in this policy briefing. To strengthen Europe's position in this truly global scientific field, emphasis has to be put on an increased collaboration, in particular between different universities, between imaging scientists and clinicians, between academia and industry and between different imaging modalities. The establishment of interdisciplinary research groups or sufficient size provided with access to long-term funding is a prerequisite to ensuring further development of this research area in Europe.

The aim of this science policy activity is to develop research-based knowledge on how to use medical imaging for the benefit of improved patient outcome, sustainable healthcare systems and increased competitiveness in the European medical industry.

John Miles
Chair, EMRC, ESP

Liselotte Højgaard
Chair, EMRC

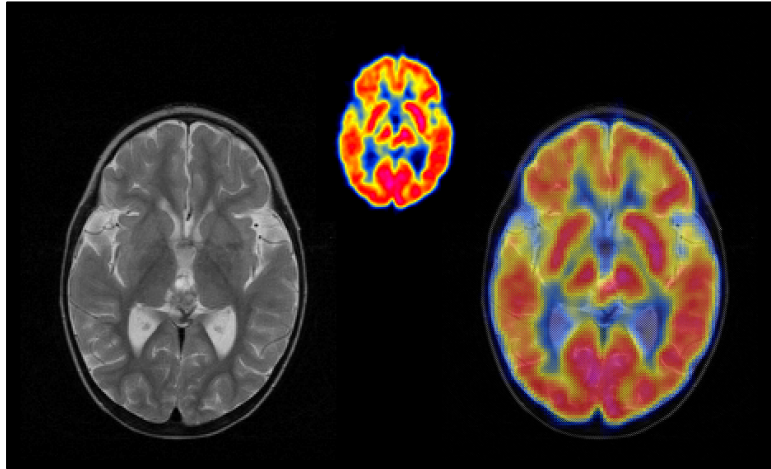
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Introduction
Medical imaging is one of the fastest growing areas with medicine at present, both in the clinical setting in hospitals and in research and development (R&D). Some important benefits from an increased research effort in medical imaging are expected in:
Improved Patient Care
• personalised medicine with individually tailored treatment
• more evidence-based decision making within healthcare
• less complications during and after surgery
• better understanding of the effect of treatments on diseases

Figure 4: Multiparametric post-processing procedure and results of brain tumour PET and MRI data. The image shows four brain slices with different color-coded regions representing different imaging parameters.

Improved Health of European Citizens
• screening of an entire population, e.g. for breast cancer, or targeted subpopulations with increased risk of specific disease entities
• better assessment of risk factors and better prevention of disease
• earlier time to cure for improved treatment efficacy
• less recurrence of disease
• increased mortality and morbidity

ESF-EMRC
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Medical Imaging
September 2007



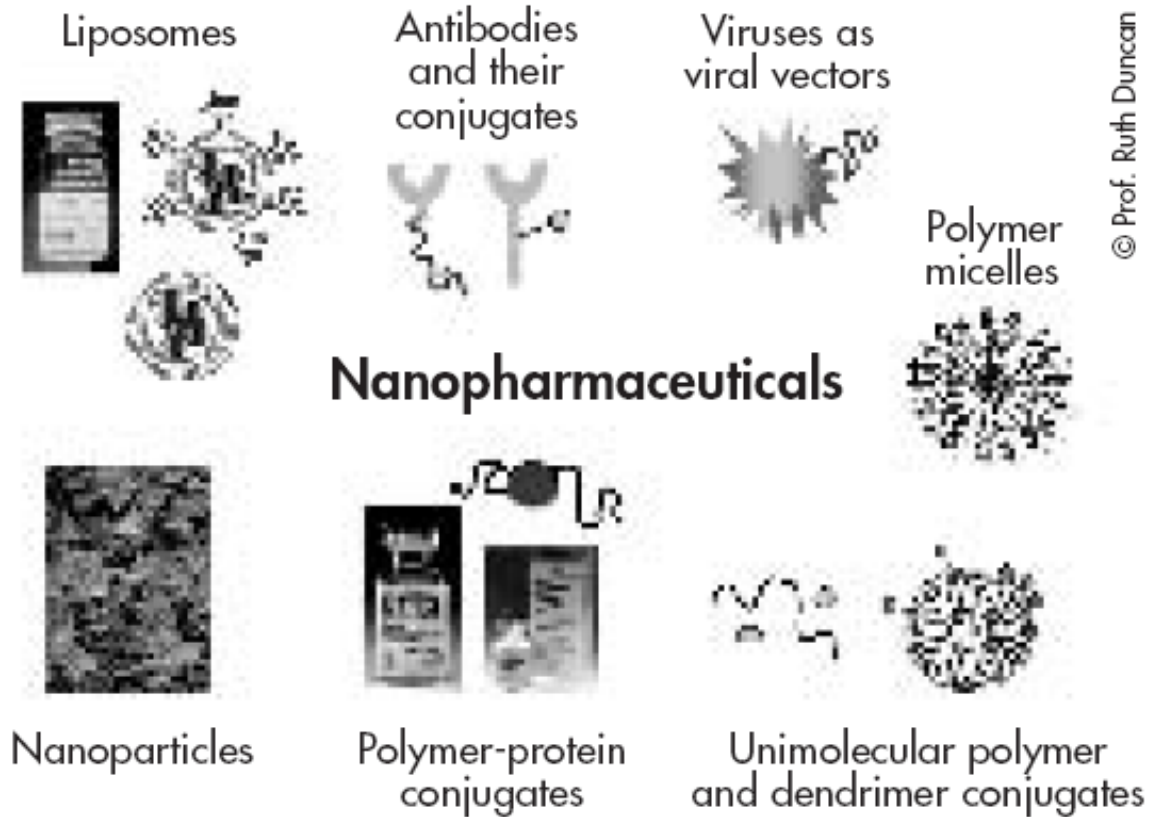
Imaging is crucial for the concept of personalised medicine

For treatment tailored to the individual patient's disease biology and in the future combined with genetic make-up.

Prof. Liselotte Højgaard, Chair of EMRC

Various types of nanopharmaceuticals

Novel therapeutics and Drug delivery systems (R&D)



Novel therapeutics and Drug delivery systems (R&D)

- Mylotarg: an Antibody-Drug conjugate (M. Eaton, UCB, BE)
- Polymer conjugates: e.g., Paclitaxel Poliglumex (Xyotax) as therapeutic in NSCLC (J. Singer, Cell Therapeutics, USA); for delivery of combination therapy (endocrine and chemotherapy); PEG-protein conjugates as anticancer agents
- Gene therapy: gene delivery based on biodegradable polyesters (T. Kiessel, DE)

Health applications tomorrow: challenges

- **Safety and Toxicological Issues** (environmental, manufacturing and clinical use): proactive risk assessment (EuroNanoPar project)
- **Categories and Design of Clinical Trials**
- **Regulatory and Legal issues, IPR and Data sharing**
- **Funding and Models of Partnerships**
- **Management and Logistics of Clinical Trials**
- **Education and Training, Career and Authorship**

Health applications tomorrow: challenges

- **Regulatory and legal status:** was mainly targeted to address large Pharma R&D, need to support Academia and Biotech and to establish early dialog with Competent Authorities
 - 1/ Actual references in Europe for medicinal drug on human use: First in place at the international level (US, EU, JP) ICH E6 for GCP (1996)
 - EU Directives: 2001/20/EC (and guidelines) enforced by 1 May 2004 and completed by 2005/28/EC
 - 2003/94/EC for GMP
 - EU Directive for medical devices 93/42/EC
 - EU Directive for personal data 95/46/EC
 - EU Regulation for paediatrics and rare diseases and thoughts are given in US to develop specific regulation for women and ethnic groups

Health applications tomorrow: challenges

2/ Other guidelines incl. draft for specific cases and new situations:

- Draft guidance on 'specific modalities' for Non-Commercial Clinical Trials referred to in Commission Directive 2005/28/EC laying down the principles detailed guidelines for good clinical practices
- Draft guideline on requirement for first-in-man clinical trials for potential high risk medicinal products (EMA/CHMP/SWP/28367/2007): including chemical and biological medicinal products. It covers the first administration of a single dose of high-risk medicinal product and the initial single ascending dose phase of clinical development

To be developed?

- Diagnosis
- Theranostics
- Population survey and biobanking
- Physiology and physiopathology
- Surgery
- Socio-Economic Studies

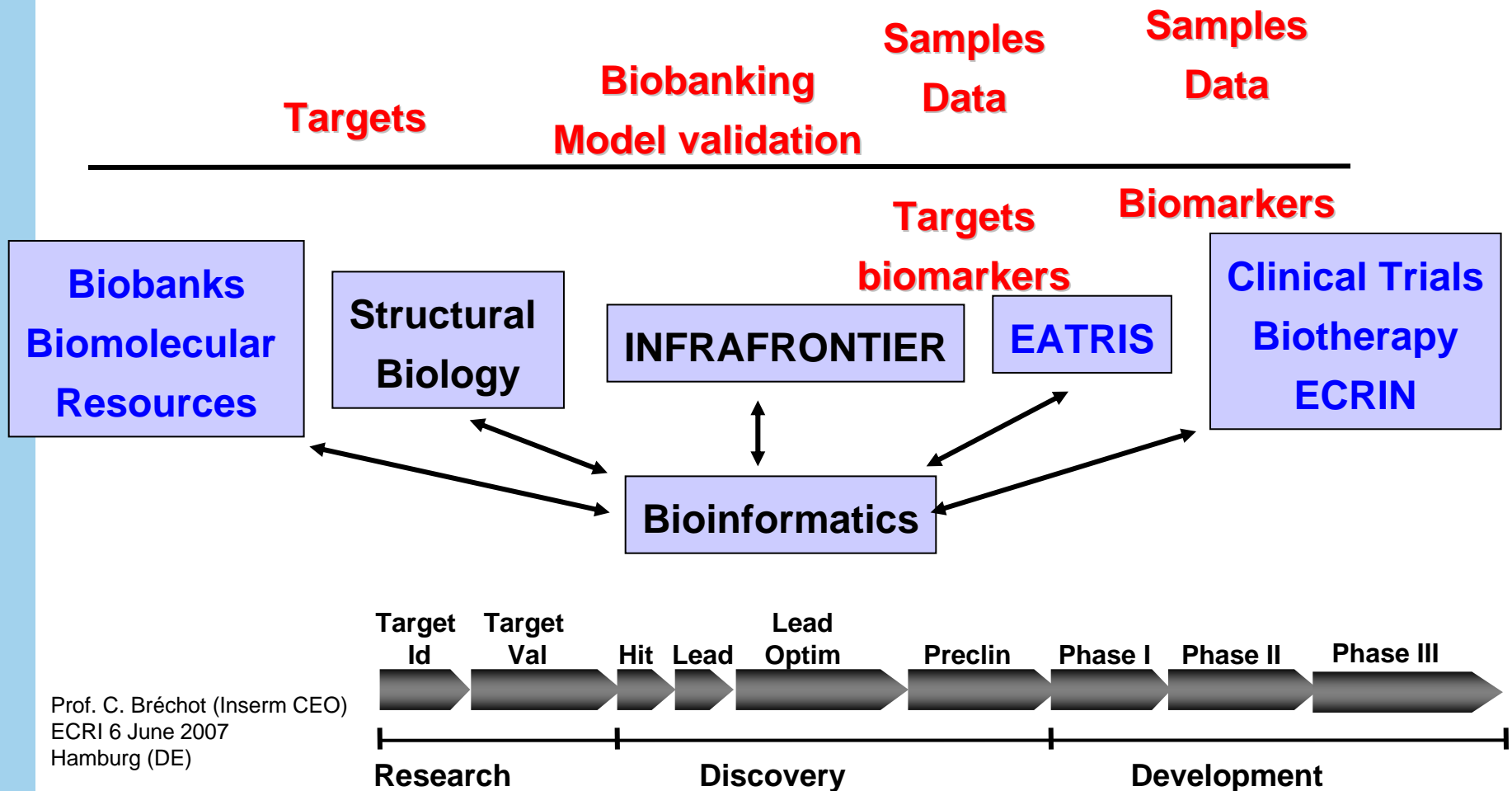


It is necessary to create **true multi- and interdisciplinary research environments** where medical doctors, pharmacists, physicists, chemists, mathematicians, molecular biologists, computer scientists can work together

Long-term funding of large research projects, collaboration between universities and major research centres

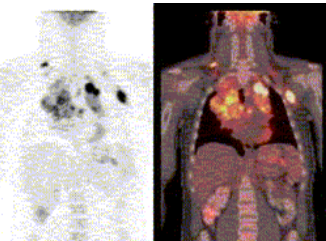
European coordination and collaboration.

Synergies between BMS ESFRI Infrastructures : *Concerted approach*



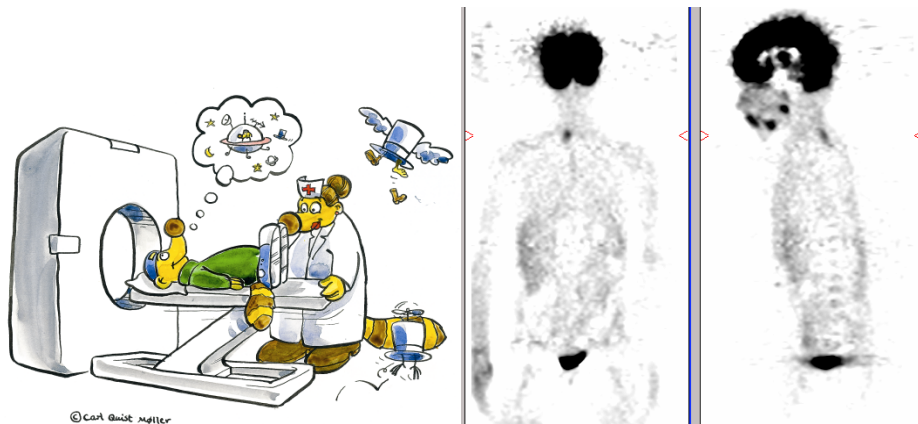
Prof. C. Bréchet (Inserm CEO)
 ECRI 6 June 2007
 Hamburg (DE)

"The special case of medicine"



The **University Hospitals** produce the majority of research in health & lifesciences in Europe.

Need for **GMP facilities**



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On the European level there is a need to develop, coordinate and adopt better systems for **evidence-based medicine** and **health technology** assessment for recommendations of standard practice in patient care.

In conclusion



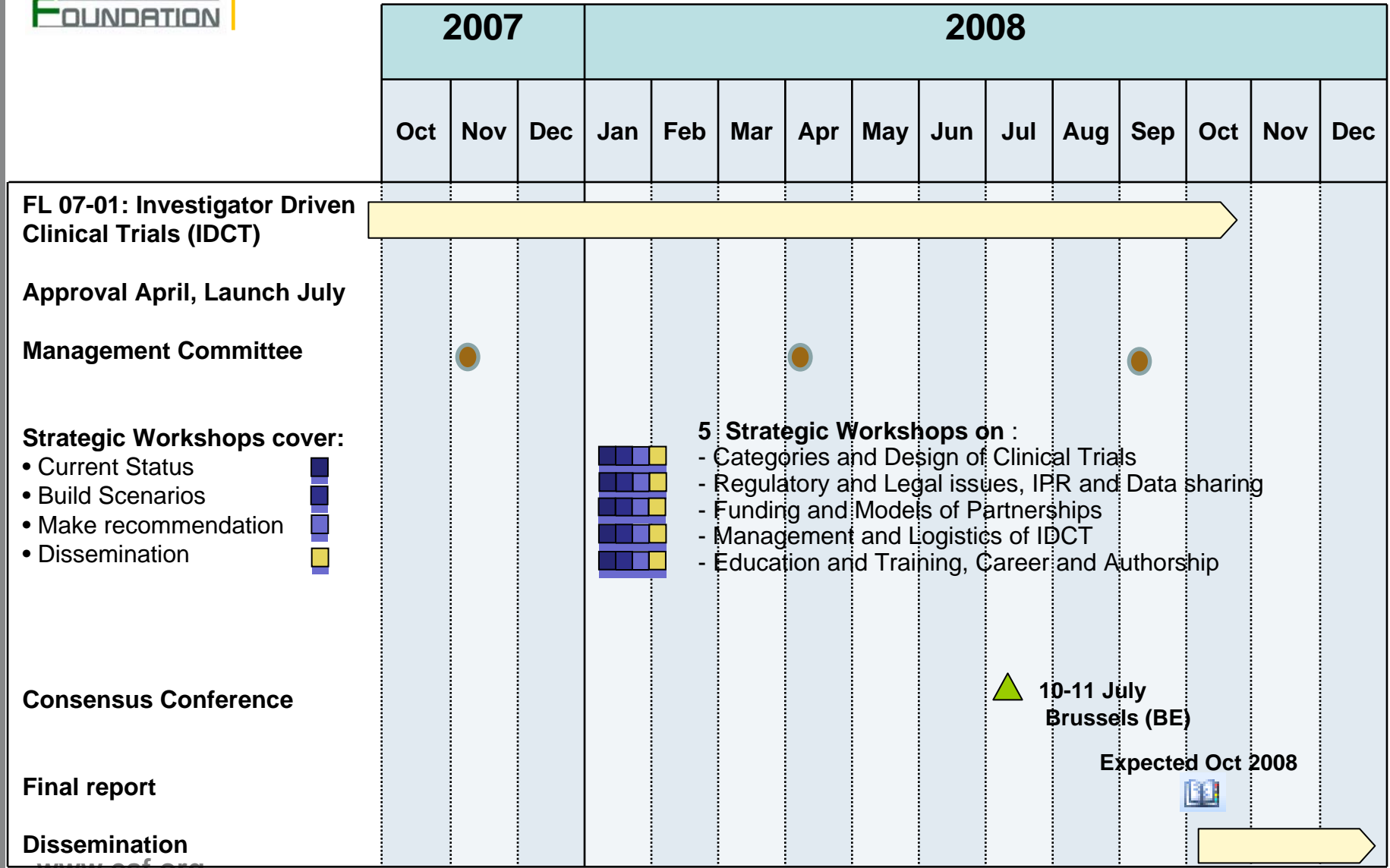
EMRC: Clinical and Translational research should be strengthened in Europe

NIH in USA: Clinical and Translational research very important focus areas

Launch in 2007 of the ESF-EMRC Forward Look on

“Investigator-Driven Clinical Trials”

Chair: Prof. Jurgen Schölmerich (Vice-President DFG) in collaboration with NIH and FDA



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European Medical Research Councils

www.esf.org/EMRC

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SETTING SCIENCE AGENDAS FOR EUROPE

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