# *Future Challenges: Relevance of Biobanking to sustain R&D activities of the Pharmaceutical Industry (in Europe)*

*Julie Corfield, Early Clinical Development, AstraZeneca*

*European Science Foundation: Biobanks- Introduction and Next Steps*

*2nd to 6thth November 2008, Saint Feliul Guixols, Spain.*



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# Structure

- Our operating environment
- The AstraZeneca approach to Biobanking……challenges
- Pharma biobanking……..to sustain R&D



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# Our Operating Environment



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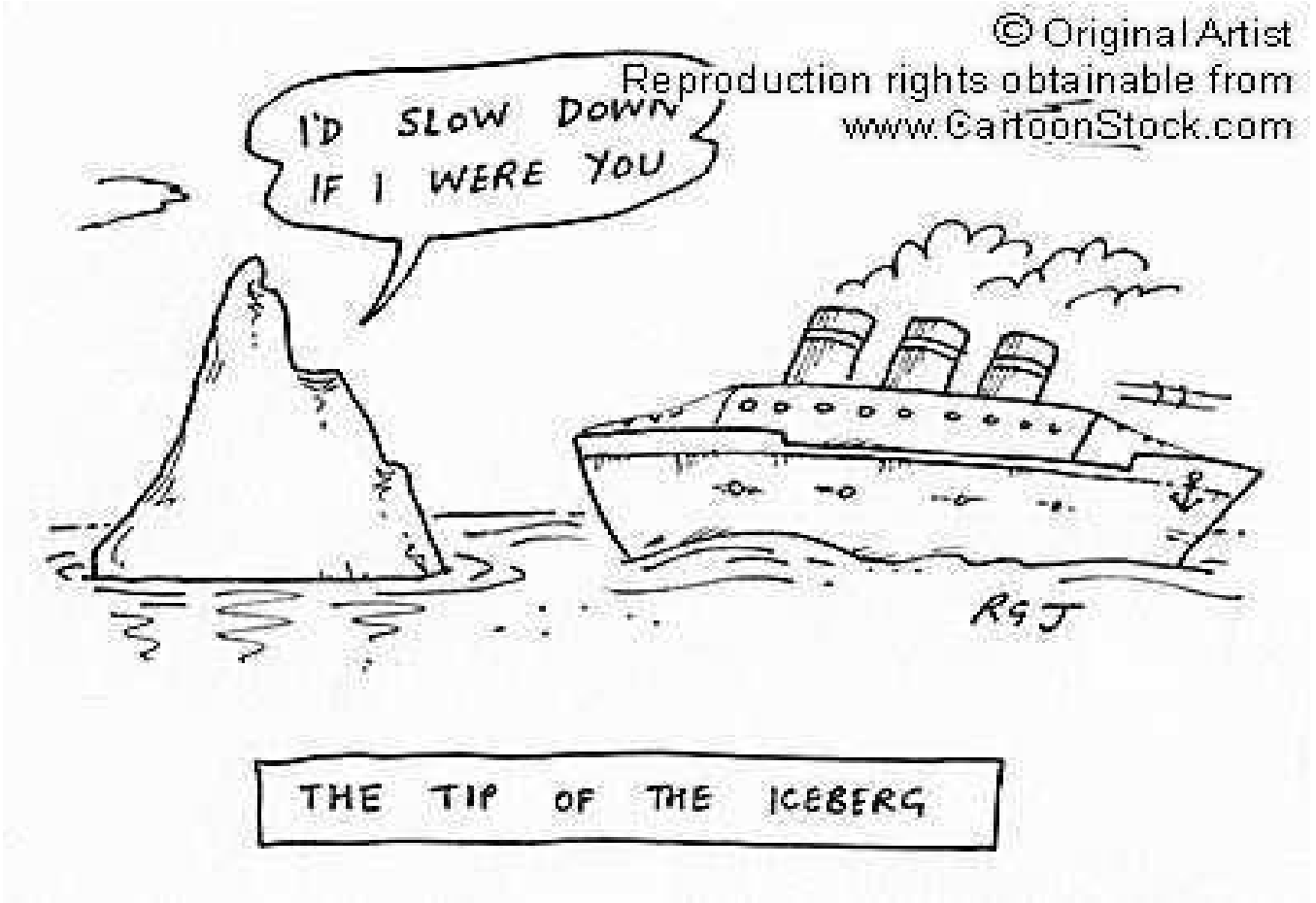


# Simplexity: simple in a complex world?



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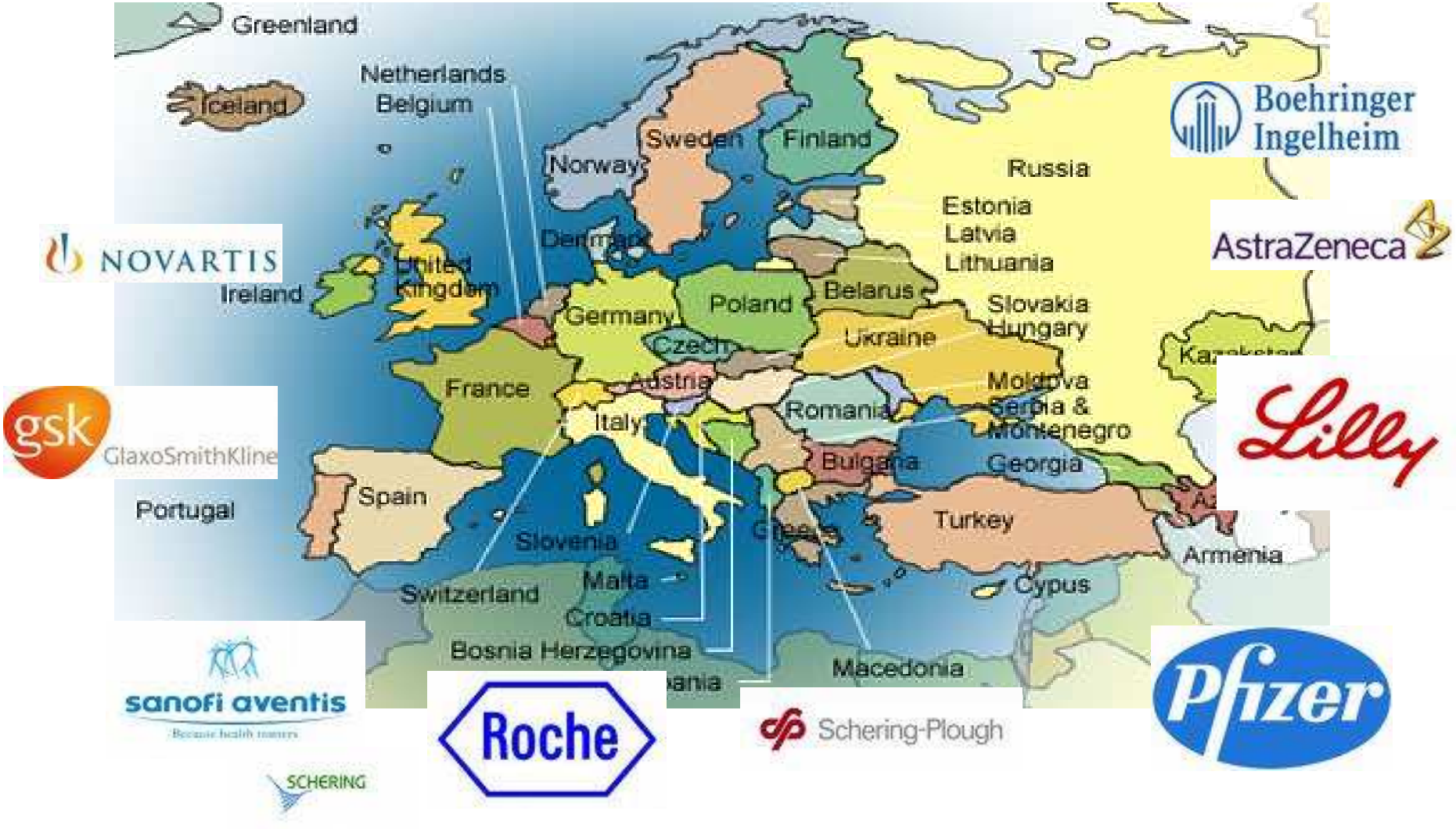
# Belonging to Europe…..sustaining R&D




**PATIENTS; PIPELINE; PATIENTS; PRODUCTS; PATIENTS**

# Sustaining R&D activities in Pharma?

**R&D, provides the foundation for the treatments of today and the cures of tomorrow**:

**Duration**

- An average of 10 to 12 years for a medicine to get from the laboratory to the pharmacy shelf.

**Risk**

- On average, **only** one out of 5,000 to 10,000 promising substances survive testing in the R&D phase to become an approved quality, safe and efficient marketable product.

**Cost**

- R&D costs for a new chemical entity is 600-900 million euros and……70 percent of medicines that reach the market do not recoup their R&D expenditure.

**ROI from a few successful products**

**R&D bottlenecks!**



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# Some views from our operating environment

**The pressure is on those charged with leading discovery.** Effective risk assessment, failing drugs faster and improving productivity a and cost-efficiency are becoming even more important…… a walloping average €895 million on researching and developing a single new medicine.

**LEADERSHIP**

**Is it Time to Revisit the Current R&D Model?** Estimated > 90% of medicines in use today have been discovered or developed by the industry. **Late-stage attrition, with increasing development costs, are now challenging companies and the current R&D model**.

**NEW OPERATING MODEL**

**Industry's best hope for survival lies in innovation**, its traditional strength. The business model of a **vertically integrated approach to developing**, manufacturing and selling drugs **changed in favour of outsourcing.**

INNOVATION, OUTSOURCING

**Biomarkers are playing an increasingly important role** in the development of new drugs to fight disease. 'We're moving …..towards a description for the conditions based on a molecular level. This revolution brings the need for new molecular markers, new assays in order to measure those parameters, which will help us to define new diseases, and to define diseases more specifically, more differentially.' We're in the middle of the realisation of the concept of personalised medicine.:'

**BETTER DEFINED DISEASES, BIOMARKERS, PERSONALISED MEDICINE: BIOBANKS**

Industry is confronting unprecedented challenges that are expected to radically transform the business. Industry's current business model is economically unsustainable and operationally unsuited to act quickly enough to produce the types of innovative treatments that will be demanded. **The industry requires a bold new vision and leaders who have the willingness to embrace a fundamentally new approach to their business**

**NEW APPROACH**



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# Public and private……involving biobanks

- IMI (Innovative Medicines Initiative) EU and EFPIA
  - Removing major bottlenecks (predicting safety/efficacy and bridging gaps in knowledge management and in education and training) in drug development, where **translational research** is key
- BBMRI
  - Research infrastructure/network of existing/*de novo* biobanks and biomolecular resources
- Science and Society
  - Ethical rules for the EC
- European technology platforms
- Innomed integrated project and Ass Neuromed
  - Predictive tox, discovery and validation of new biomarkers, diagnostics, disease progression and efficacy in Alzheimers
- ECDSR
  - Safety biomarkers development and validation
- EORTC, BIG
- CONTICANET
  - Network of excellence for the research and treatment of connective tissue cancers
- EUGENE2
  - Drug targets for obesity

# Translational research /medicine

- Translating scientific discoveries into practical applications " bench" to "bedside."
- Pharma facilitating interactions between basis research and clinical medicine

**TRANSLATIONAL MEDICINE INITIATIVES AT BIG PHARMA**

- **Truly Predictive Power to Boost Efficiency in Research and Development**
- **Questions, Answers, Decisions: a Systematic Translational Research Approach**

**ROI ON ENABLING TECHNOLOGIES IN TRANSLATIONAL MEDICINE**

- **Examining the Scale and Scope of Tools and Programs to Navigate in Translational Oncology Space: Lessons Learned**
- **From Early Discovery to First-in-Human: Realities of the Post-Technology Revolution**

**Translational Research Event - July 2008 Wellcome Trust**

**Translational Research Scheme at KCL:MRC and GSTT funded**

**Focus Areas: Neuroscience or Inflammation/Infection/Immunity**

**Translational Cancer Medicine**

**'Top Ten' Opportunities in Oncology Drug and Diagnostic Development**

**January 26-28, 2009 | Westin San Diego San Diego, California**

MRC's Translational Research Strategy 30th April 2008

**……Dependent on biobanks**



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# Biobanking a new concept??



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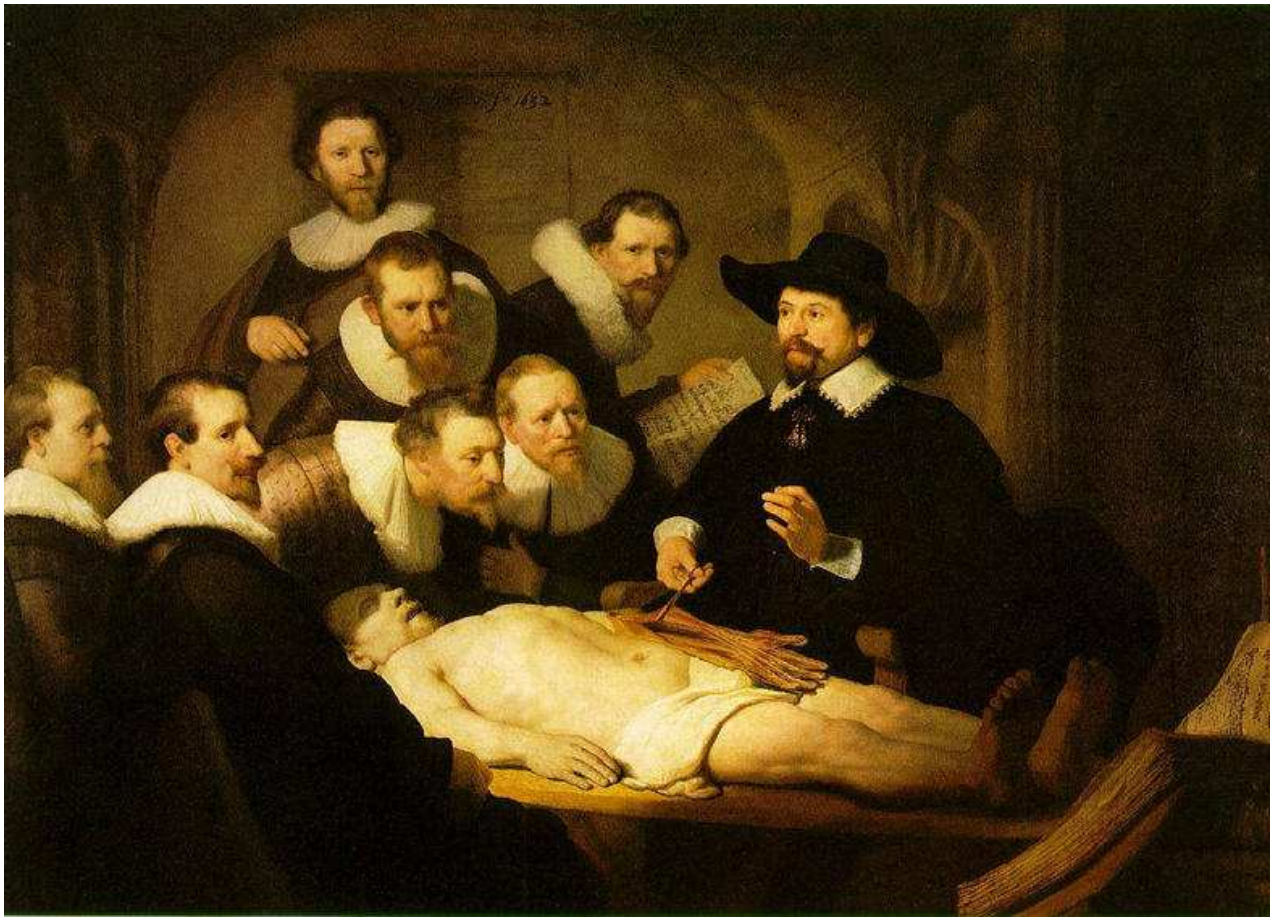

# Biobanking?



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# Biobanking could be a new concept?

| Year | 'Biobank' | Biobank 'consent/ethics' | Biobank/genetics | Biobanks/laws |
|---|---|---|---|---|
| 1998 | 2 | 0 | 1 | 1 |
| 1999 | 2 | 0 | 1 | 1 |
| 2000 | 1 | 0 | 1 | 0 |
| 2001 | 0 | 0 | 0 | 0 |
| 2002 | 3 | 1 | 1 | 1 |
| 2003 | 12 | 5 | 10 | 5 |
| 2004 | 14 | 3 | 10 | 4 |
| 2005 | 19 | 6 | 12 | 8 |
| 2006 | 46 | 10 | 26 | 11 |
| 2007 | 62 | 11 | 22 | 12 |
| 2008 | 62 so far! | 9 | 13 | 7 |



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# Why all these publications?

# A sign of hampering or enabling Biobanking to sustain R&D activities?



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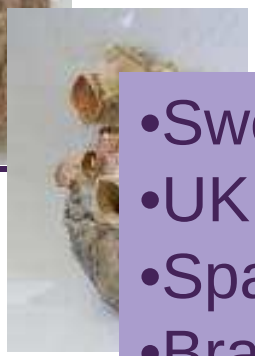
# Due to new legislation?

Cadaver



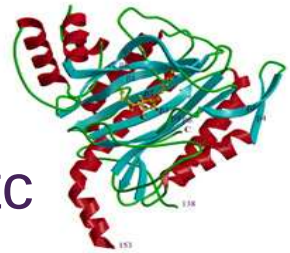
Whole organs

**No consistent definitions**

- Sweden
- UK
- Spain
- Brazil
- Estonia
- Norway

**COMPLEXITY DIFFERENCES**

Bio-fluids, hair



Proteins, lipids, nucleic acids, etc



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# External Drivers….public scandals?

**Tuesday, 30 January, 2001, 17:35 GMT**

## Police to probe Alder Hey


**Practices at Alder Hey Hospital have been condemned**

A pathologist may face criminal charges after a damning report into the "illegal stripping" of thousands of body parts from dead babies.

An official inquiry found that Professor Dick van Velzen was allowed to systematically strip every organ from children who died at Alder Hey hospital in Liverpool, frequently **lying to parents and falsifying medical records.**

A separate report highlighting the scale of the organ scandal in other parts of the NHS, revealed that more than 100,000 body parts have been stockpiled in other UK hospitals - many without the consent of relatives and most of which have never been used for medical researcch

**"At least 16,500 organs and tissues have been retained in apparent contravention of the law because they came about as a result of coroners' post-mortems where the organs should not have been kept beyond the time needed to establish the cause of death"**

**Health secretary, Alan Milburn**

**"Those who did wrong will now be held to account. The pain Caused to the parents by this dreadful sequence of events is unforgivable."**

**Professor van Velzen (1988-1995) lied to parents, lied to other doctors, lied to hospital managers, stole medical records, falsified statistics and reports, and he encouraged other staff to do the same**

**Health secretary, Alan Milburn**

**Hospital executive in US quits amid human-tissue scandal INVESTIGATION: University of Wisconsin's Robert Hoffman was paid by a nonprofit he co-founded that harvested skin and bone.**

**By RONALD CAMPBELL**

**The Orange County Register**

Admitted he took more than $86,000 for sending human skin and bone to two tissue banks.
Robert Hoffmann, 58, had headed the **organ procurement organization** at the University of Wisconsin Hospital in Madison - one of the nation's top suppliers of vital organs - for 25 years.

## Brain Inquiry……BBC News 18th May 2003

***Brain of husband given to researchers at Manchester University without wife's consent***

***Tens of thousands of brains were stripped from corpses 1970-1999***

*Religious factors to consider: as practising jew, would never have consented to having part of body removed, as religious law requires body to be buried intact*

***Husband's brain incinerated after being kept for seven years as it did not meet the researchers' criteria.***

A report by Dr Jeremy Metters, the HM Inspector of Anatomy, condemned the practice of taking organs without consent and recommended it should be made a criminal offence.

**UCLA suspends its Willed Body Program**
**Johnson & Johnson admits buying tissue samples**
Wednesday, March 10, 2004 Posted: 0240 GMT (1040 HKT)
**Henry Reid, the director of UCLA's Willed Body Program, was arrested Saturday.** Director of UCLA program arrested
**LOS ANGELES, California (CNN) -- Top officials at UCLA Tuesday voluntarily suspended the university's Willed Body Program after accusations that its director and others sold body parts for profit, a lawyer for the school said.**

Julie Gerdes
15 Minutes

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# .....and more?




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# Is it due to increased ethics oversight?

- Ethics committees
  - Needing to operate outside traditional area
  - Evolution of research ethics committees….registering biobanks
  - Still variable experience in biobanking
- Approaches to consent
  - broad; blanket; restricted
- Data privacy issues
- Patient/subject engagement/awareness
- Transparency
- Professional ethicists…….in biobanking

## Impact: +ve and -ve



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# Due to emerging science research?

- Changing R&D strategy
- Greater need for biobanks
  - Genetics
  - Pharmacogenetics
  - Personalised medicine
  - Translational science
  - Larger studies……..population cohorts cf case controlled
- Collaboration across countries

**Impact +ve and -ve**



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# Mixed impact on sustaining R&D

- Supply chain
- Ability to recruit subjects/patients
- Complexity
  - Variability not standardisation
- Confusion
- Reputation

- Time and cost to deliver



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# AstraZeneca: approach to Biobanking …….its relevance to sustain R&D



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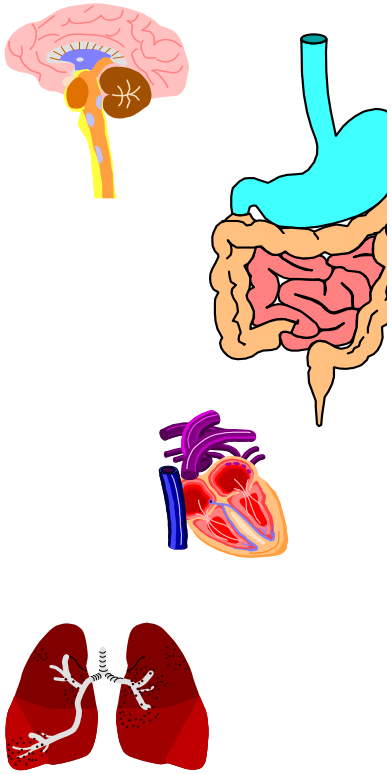
# Human Biological Sample Needs

- Human Biological Samples/Tissue are an essential resource for research and development across all disease areas……

  •Identification of new molecular targets
  •Validation of targets
  •Mapping of target variances
  •Biomarker/Surrogate marker identification and validation; mechanistic, safety and disease
  •Disease stratification
  •Prediction of variance in metabolism
  •Evaluation of drug effect in man (efficacy and safety)
  •Assessment of effect variability in man
  •Diagnostics



**Current and planned research and development processes dictated an increase in human biological sample use**

# Challenges: 1999/2001

- Clinical trial samples
  - Biofluids for safety; DMPK; PD measures
    - Urine
    - Blood
    - Plasma
    - Serum
    - Genetics
  - Biopsies
- Research obtaining some samples
- Research needing more samples
  - New approaches to research…….increasing demand for samples

**Clinical provided a service to Research**

# Approach: collaboration

- **Clinical Drive Acquisition**
  - Approved investigator/supplier
  - Tissue Acquisition Study Protocol; including sample processing
  - Informed Consent Documents
  - Case record forms/clinical data
  - Contract
  - Ethics submission
  - Monitoring
  - Co-ordination of sample delivery
  - GCP

- **Discovery/Investigator Use Samples**
  - Life cycle management of samples
  - Collaboration:
    - share supply
    - additional research

**Increase awareness of ethical/legal requirements**



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# Global Project…….2000 to 2002

**To facilitate best practice in the acquisition banking and use of human tissue**

- Ethical and legal correctness
- Process to acquire tissue and……..
  - Good quality tissues
- Co-ordination of activities
- Provision of tools

**Deliverables**

- Policies; Tissue banking and Genetics
- Position Paper
- Guidelines and templates
- Website
- Pilot tissue/biobanks respiratory and inflammation; 2 R&D sites
- **IS system…….interim solutions**

**Implementation**

## Tactical

# AZ Human Tissue policy

## Framework for processes:

- Approved Suppliers
- Information and consent
- Collection, storage and use of human tissue samples
- Control of banked tissue samples
- Confidentiality and data protection
- Security, safety and quality issues relating to tissue banks
- Intellectual property
- Accountability and audit



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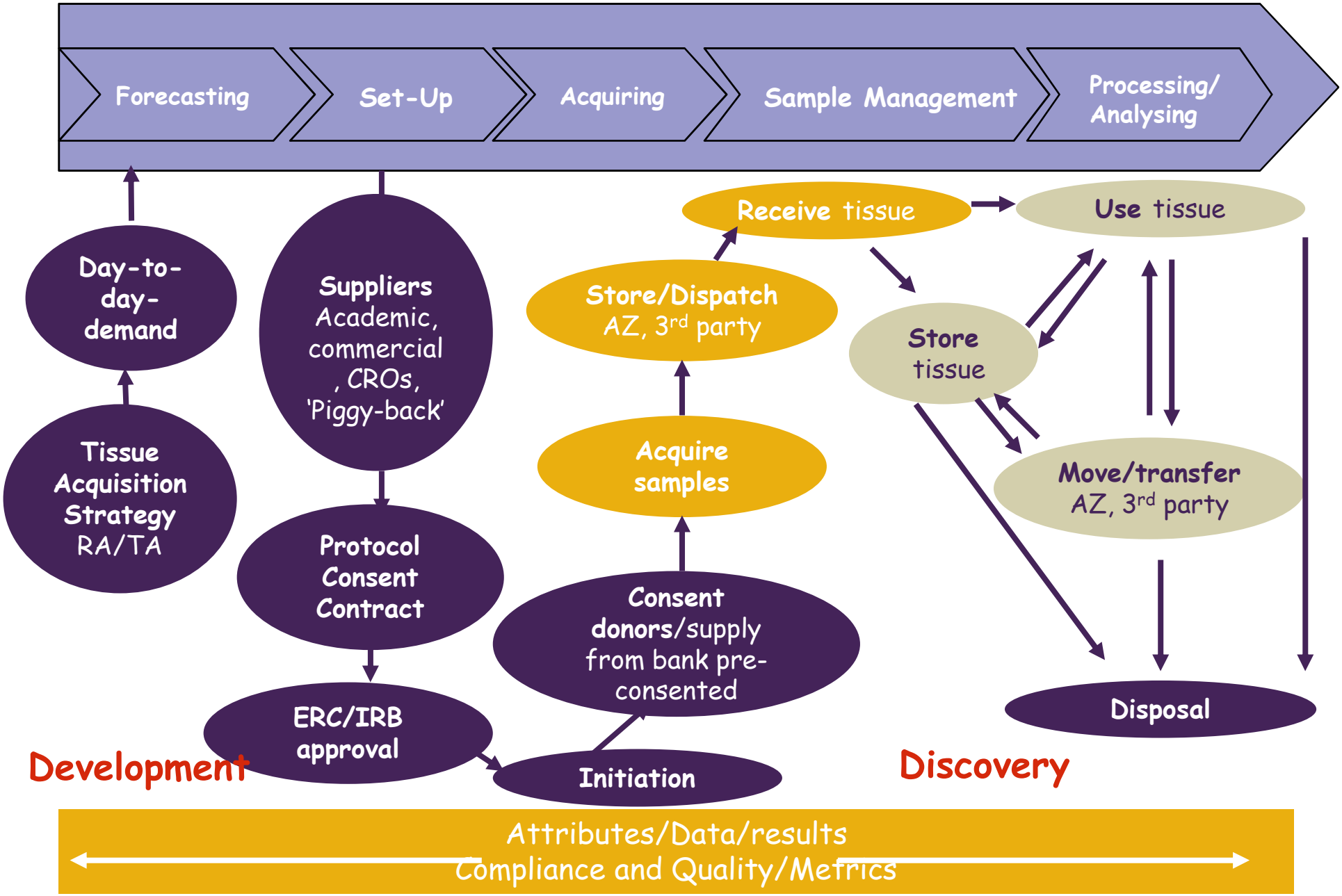
# Operating model



# RA/OA disease area: biobanks: 2001 to 2006

**Profile**

- 2 collaborations in 2000; 12 collaborations in 2006
- 2 physical biobanks; 2 R&D sites

**Research Collaborations**

- UK: RA/OA joint replacement surgery
- UK: Post mortem (knees)
- UK: Case-controlled large joint OA; interaction of genes and environment
- UK and Australia: OA biomarkers
- Sweden: early RA
- Sweden: biomarker validation
- Nederlands: early RA
- US: OA TI/TV, biomarkers
- Commercial suppliers

**Creating and enabling pipeline RA/OA**
**'Humanising Drug Discovery'**



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# Profile

## Biobanks

- Coded samples
- Dynamic not stockpiled
- Controlled release/access; custodians

## Donor characteristics

- Medical history, concurrent disease, current/past medication, MRI, X-ray

  Plus lifestyle/environment

## Sample Types

- Synovium, cartilage, meniscus, bone, tendons, synovial fluid, blood (plasma;serum; DNA), urine;

## Sample Format

- Fresh, arthroscopic samples; paraffin embedded; fresh frozen

## Uses

- Functional assays; IHC; genomics, proteomics, genotyping, biomarker identification and validation; lead optimisation and target validation.

# **R&D** Biobanking Improvement Project 2006

- **Lessons learnt: Successes and failures**
- **All Human Biological Samples**
- **AZ strategy**
  - Benefits of biobanking demonstrated across most Research and Therapeutic Areas
  - Sustaining R&D activities
    - Fostering collaboration internally ad externally; across disease areas
    - Innovation
    - Enabling creation and delivery of pipeline
- **Mitigate risk of non-compliance and conserve reputation**
- **Prioritise and Optimise use of samples**
- **Process improvement**
  - Clarity of R&Rs
  - Less manual data entry; Streamlined process; faster readout
  - Less waste; improved quality
- **Changing operating environment**



**Strategic**

# Deliverables

- Policy and positioning on samples (genetic and non-genetic)
- R&D integrated Process for the life cycle management of samples, with associated information
  - SOPS; templates; Lab manuals; GCP and GLP
  - Structured informed consent
- Global Governance Organisation (10 R&D sites)
- Infrastructure/storage facilities
- Global IS systems…….sample tracking; clinical phenotypic data; common ontologies
- Other tools to enable process/knowledge sharing
  - Biobank laws
  - Biomarker catalogue

## Biggest challenge

- **Implementation**
  - Change programme: stakeholders; communication strategy/plan; education/training
  - Benefit delivery

# AZ Human Biological Sample Research 2008

Governance

Supply Network

Tissue Acquisition Team

A

B

C

Research Tissue Bank

Standard collection, storage, analysis and tracking of samples and consent

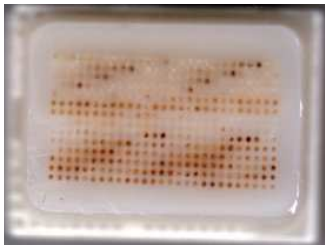
Bioinformatics

High throughput analytical data

Standard histopathological data

Clinical and outcome info from Cancer Registry/ONS and Centre Registry

Clinical and outcome info from clinical trials



- Exploitation of rapid developments of technology and capacity in biomic research

- Improvement in the quality of cancer care through tailored treatment strategies

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# Pharma

# …….biobanking and sustaining R&D



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# Pharma…….challenges in sustaining R&D

- Cost containment……..change programmes
- Different disease strategies, similar disease strategies
- Similar approaches/technologies
- All need access to experts/different skills and knowledge/centres of excellence
- All need human biological samples……need to know what and purpose of use
- All have biobanks…….retrospective samples
- Prospective samples are costly
- Retrospective samples inadequate quality
- Not an unlimited supply of subjects to provide samples……need to engage patient groups
- Visibility/transparency of existing pre-competitive collections
  - Gap analysis



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# Harnessing biobanks……what needs to be done?

- Need for harmonisation of regulations
- Greater standardisation of protocols
- Greater co-ordination of activities across Europe and elsewhere
- More collaboration to provide access to existing biobanks
- Creation of translational and multidisciplinary research collaborations to overcome cultural differences
- Training ‘gap’
- Continuing technology development
- Infrastructure development for large scale population studies…to enable implementation of protocols; collection of data and samples
- Translational research to validate initial findings and explore practical use
- Greater collaboration, public, academia, private sectors……patient groups
- Greater consistency in process for informed consent and ethics committee process…….broad consent



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# Common problems to be addressed

- Data and samples contained in biobanks are variable: content and quality
- Few standardised quality controlled protocols for data collection, sample storage and analysis and access. Difficult to pool data
- Ethical and legal issues……obstacle to collaboration; consent does not routinely allow sharing
- Governance to enable sharing and exchange of material

# Could the Innovative Medicines Initiative Help?

## Aim

Removing major bottlenecks in drug development, where **research** is the key

## Long term goal

Re-invigorate the European bio-pharmaceutical sector and foster Europe as the most attractive place for pharmaceutical R&D; thereby, long term, enhancing access to innovative medicines.

**…for the benefit of patients, scientists and European citizens**



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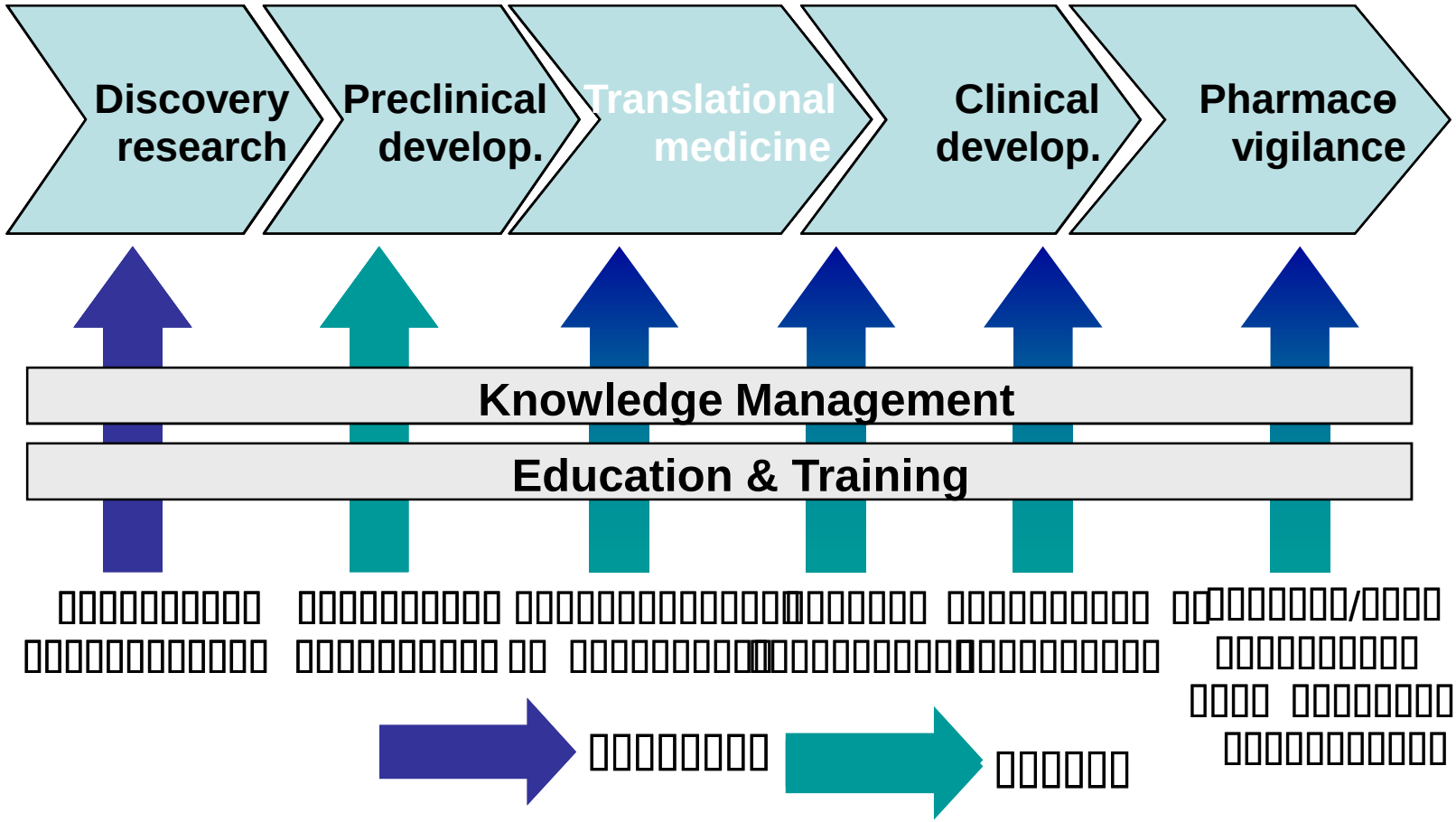
# The Research Focus of IMI – bottlenecks in the Drug development process




**Cancer; brain disorders; inflammatory, metabolic and infectious diseases**



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# What shall the Innovative Medicines Initiative do?

- Support ‘pre-competitive pharmaceutical research and development to accelerate the development of safer and more effective medicines for patients……

- Foster collaboration between all stakeholders, e.g. industry, public authorities (including regulators), Patient organisations, academia, SMEs and clinical centres

- No new medicines will be developed. Focus on delivery of new approaches, methods and technologies, improve knowledge management of research results & data, support training of professionals



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# Call process

- Research agenda
- Annual implementation plan
- Call topics developed by pharma
- Expression of interest by applicant consortia…..1st peer review …….5 months
- If chosen…….invited to submit full project: EFPIA and winning applicant……Scientific excellence
- Full project proposal……2nd peer review…..Feasibility and scientific excellence……..3 months
- Project Agreement/Grant Agreement…….2 months



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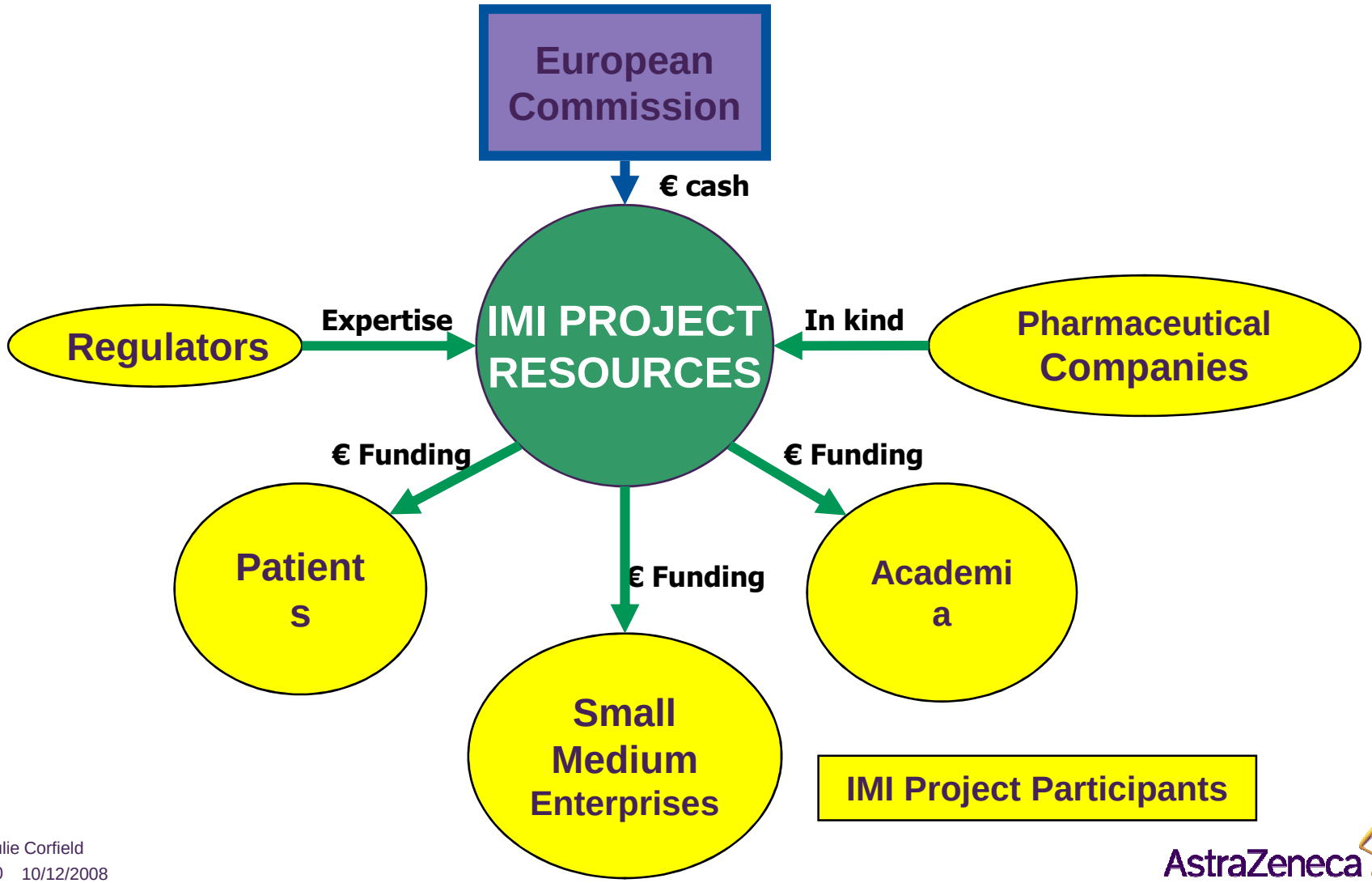
# Project Participants & their Contribution



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# The Future

- Stakeholder engagement
  - Internally/externally
- Collaboration
- Communication
- Well characterised biobanks

**PEOPLE**



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THANK YOU

# Spare slide

# IMI History

2000:
Lisbon strategy

**"Make Europe, by 2010, the most competitive and the most dynamic knowledge-based economy in the world"**
**European Research Area: « internal market » for research**

2004:
European
Technology Platforms

**Informal networks led by industry**
**Strategic research agendas**

2007-2013:
Framework Programme 7
Joint Technology Initiatives

**Roof for all EU-funded research projects**
**Joint Technology Initiatives: new instrument of FP7 for integrated projects (Public-Private Partnership as legal entities)**

2008-2017:
IMI Joint Undertaking

**Public-Private Partnership founded by the European Federation of Pharmaceutical Industries and Associations and the European Commission**



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