Nanomedicines Challenges and Opportunities in a Global Development Environment

Rogério Sá Gaspar

Faculdade de Farmácia da Universidade de Lisboa e
Current positions

- Full Professor, Faculty of Pharmacy University of Lisbon - **FFUL** (Portugal)
- Coordinator of Nanomedicine & Drug Delivery Systems research group at the Research Institute for Medicines and Pharmaceutical Sciences (**iMed.UL**), since 2007
- Member of the General Council at the **University of Lisbon** (Portugal), since 2008
- Member of the Medicines Evaluation Committee at **INFARMED** and different positions in European regulatory affairs (1995-2002 and since September 2008, Portugal)
- Member of adhoc expert group in nanomedicines at **European Medicines Agency** (since April 2009)
- Member of the coordination of MScs in Regulatory Affairs (since 2001), in Advanced Pharmacotechnics (since 2006) and in Pharmaceutical Engineering (since 2007) at FFUL
- Doctoral Programme in BioNanotechnology (University Lisbon, approved 2009, to be started)
- Member of the Executive Committee of **EUFEPS** since 2009 (liaison with Network in Pharmacogenetics/Pharmacogenomics, chair of Network in Regulation & Science 2010, currently establishing Network in Nanomedicine)
- **Controlled Release Society (CRS)**, Adhoc group in Regulatory Affairs, since 2010
- Member of Board, Portuguese Society for Pharmaceutical Sciences (**SPCF**) since 2005
• The views and opinions hereby expressed reflect only my personal opinion and not the views of institutions or organisations with which I’m or have been affiliated in the past or present.
International Standards: Cooperative Research and Regulation: Lessons and Challenges

Nanotechnology and Oncology

What policies support cooperative research internationally?

RESEARCH
- how to increase the probability of viable candidates for clinical evaluation

What lessons can US regulators learn from regulation of nanotechnology in other countries?

DEVELOPMENT
- how to increase the probability of successful and timely product development

What policies support product development and regulation internationally?
A Converging Approach Across Disciplines….

Understanding fundamental nanoscale processes

Developing new analytical tools

- visualization of nanostructures
- characterisation
  and characterisation
  of dynamic (fast) changes
- synthesis/fabrication

Nanoscience

Basic
Applied Science

Nanobiotechnology

Nanotechnologies

Manufacturing Processes and Materials

Nanomaging

Nanoengineering

Nanoelectronics

Computing and Information Technology

Nanomedicine

Aerospacce

Defence
Build On Existing European Landscape?

The ETP Nanomedicine, an initiative led by industry and set up together with the European Commission is addressing the application of nanotechnology to achieve breakthroughs in healthcare.

Diagnostics
- in vivo imaging
- In vitro diagnostics

Drug Delivery
- Nanopharmaceuticals
- Nanodevices

Regenerative Medicine
- Smart Biomaterials
- Cell Therapies
Evolution of Nanomedicines - drug targeting and controlled release

1970s
- Liposomes
- Polymer-protein and -drug conjugates
- Antibody conjugates
- Nanoparticles
- Controlled Release Depot Formulations

1980s
- Polymer micelles

1990s
- Dendrimers
- Doxil
- Neulasta
- Mylotarg
- SP1049C
- Zoladex
- Leupron Depot
- Gliadel

2000s
- PEG-interferon α
- XYOTAX
- Abraxane
- nanocrystals for oral use

2009
European regulatory scenario

• Therapeutics
  – Medicinal Products are covered by national and European agencies, within a networking system, under currently existing four procedures
    • national,
    • mutual recognition,
    • decentralised
    • and centralised (this one managed by EMA)

• Imaging
  – In vivo imaging agents are classified as medicinal products

• Diagnostics
  – Diagnostic agents have a different and complex regulatory frame, overlapping with a number of existing medical devices
## Nanocrystals: Current Status

<table>
<thead>
<tr>
<th>TRADENAME</th>
<th>DRUG</th>
<th>INDICATION</th>
<th>TECHNOLOGY</th>
<th>COMPANY</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapamune®</td>
<td>Rapamycin</td>
<td>Immunosuppressive</td>
<td>Nanocrystal®</td>
<td>Wyeth</td>
<td>Marketed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Elan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emend®</td>
<td>Aprepitant</td>
<td>Anti-emetic</td>
<td>Nanocrystal®</td>
<td>Merck</td>
<td>Marketed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Elan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricor®</td>
<td>Fenofibrate</td>
<td>Hypercholesterolemia</td>
<td>Nanocrystal®</td>
<td>Abbott</td>
<td>Marketed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Elan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Megace ES®</td>
<td>Megestrol</td>
<td>Anti-anorectic</td>
<td>Nanocrystal®</td>
<td>Par Pharm.Co.</td>
<td>Marketed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Elan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglide®</td>
<td>Fenofibrate</td>
<td>Hypercholesterolemia</td>
<td>IDD-P®</td>
<td>Sciele Pharma Inc.</td>
<td>Marketed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Skyepharma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semapimod®</td>
<td>Guanylyhydrazone</td>
<td>TNF-α inhibitor</td>
<td>own</td>
<td>Cytokine Pharmasciences</td>
<td>Phase II</td>
</tr>
<tr>
<td>Paxceed®</td>
<td>Paclitaxel</td>
<td>Anti-inflammatory</td>
<td>unknown</td>
<td>Angiotech</td>
<td>Phase III</td>
</tr>
<tr>
<td>Theralux®</td>
<td>Thymectacin</td>
<td>Anti-cancer</td>
<td>Nanocrystal®</td>
<td>Celmed</td>
<td>Phase II</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Elan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nucryst®</td>
<td>Silver</td>
<td>Anti-bacterial</td>
<td>own</td>
<td>Nucryst Pharm.</td>
<td>Phase II</td>
</tr>
</tbody>
</table>
Doxil/Caelyx: Stealth® Liposomes

Caelyx is indicated:

- As monotherapy for patients with metastatic breast cancer, where there is an increased cardiac risk.

- For treatment of advanced ovarian cancer in women who have failed a first-line platinum-based chemotherapy regimen.

- For treatment of AIDS-related Kaposi’s sarcoma (KS) in patients with low CD4 counts (< 200 CD4 lymphocytes/mm3) and extensive mucocutaneous or visceral disease.
  - Caelyx may be used as first-line systemic chemotherapy, or as second line chemotherapy in AIDS-KS patients with disease that has progressed with, or in patients intolerant to, prior combination systemic chemotherapy comprising at least two of the following agents: a vinca alkaloid, bleomycin and standard doxorubicin (or other anthracycline).
Myocet, in combination with cyclophosphamide, is indicated for the first line treatment of metastatic breast cancer in women.

<table>
<thead>
<tr>
<th></th>
<th>Myocet/CPA (60/600 mg/m²) (n=142)</th>
<th>Dox 60/CPA (60/600 mg/m²) (n=155)</th>
<th>Myocet/CPA (75/600 mg/m²) (n=80)</th>
<th>Epi/CPA (75/600 mg/m²) (n=80)</th>
<th>Myocet (75 mg/m²) (n=108)</th>
<th>Dox (75 mg/m²) (n=116)</th>
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</thead>
<tbody>
<tr>
<td>Tumour response rate</td>
<td>43%</td>
<td>43%</td>
<td>46%</td>
<td>39%</td>
<td>26%</td>
<td>26%</td>
</tr>
<tr>
<td>Relative Risk (95% C.I.)</td>
<td>1.01 (0.78-1.31)</td>
<td></td>
<td>1.19 (0.83-1.72)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median PFS (months)²</td>
<td>5.1</td>
<td>5.5</td>
<td>7.7</td>
<td>5.6</td>
<td>2.9</td>
<td>3.2</td>
</tr>
<tr>
<td>Risk Ratio (95% C.I.)</td>
<td>1.03 (0.80-1.34)</td>
<td></td>
<td>1.52 (1.06-2.20)</td>
<td></td>
<td>0.87</td>
<td>0.66-1.16</td>
</tr>
</tbody>
</table>

Abbreviations: PFS, progression-free survival; Dox, doxorubicin; Epi, epirubicin; Relative Risk, comparator taken as reference; Risk Ratio, Myocet taken as reference

² Secondary endpoint

EMEA, European Public Assessment Report (EPAR), Summary of Product Characteristics (SmPC), 2007

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iMed.UL (Research Institute for Medicines and Pharmaceutical Sciences)
<table>
<thead>
<tr>
<th>TRADENAME</th>
<th>DRUG</th>
<th>INDICATION</th>
<th>COMPANY</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AmBisome®</td>
<td>Amphotericin B</td>
<td>fungal infections</td>
<td>Astellas Pharma</td>
<td>Marketed</td>
</tr>
<tr>
<td>ABELCET®</td>
<td>Amphotericin B</td>
<td>fungal infections</td>
<td>Sigma-Tau Pharmaceutical</td>
<td>Marketed</td>
</tr>
<tr>
<td>DOXIL/Caelyx®</td>
<td>Doxorubicin</td>
<td>cancer</td>
<td>Schering-Plough</td>
<td>Marketed</td>
</tr>
<tr>
<td>Daunoxome®</td>
<td>Daunorubicin</td>
<td>cancer</td>
<td>Gilead Sciences</td>
<td>Marketed</td>
</tr>
<tr>
<td>MEPACT®</td>
<td>MTP</td>
<td>cancer</td>
<td>Takeda</td>
<td>Marketed</td>
</tr>
<tr>
<td>Visudyne</td>
<td>Verteporfin</td>
<td>age related macular degeneration</td>
<td>Novartis</td>
<td>Marketed</td>
</tr>
<tr>
<td>Definity®</td>
<td>Octafluoropropane</td>
<td>Ultrasound imaging</td>
<td>Dupont Merck</td>
<td>Marketed</td>
</tr>
<tr>
<td>Myocet®</td>
<td>Doxorubicin</td>
<td>cancer</td>
<td>Cephalon</td>
<td>Marketed</td>
</tr>
<tr>
<td>Depocyt®</td>
<td>Cytarabine</td>
<td>cancer</td>
<td>Sigma-Tau Pharmaceuticals</td>
<td>Marketed</td>
</tr>
<tr>
<td>DepoDur®</td>
<td>Morphine</td>
<td>pain relief</td>
<td>Flynn Pharma</td>
<td>Marketed</td>
</tr>
<tr>
<td>Octocog alfa®</td>
<td>Factor VIII</td>
<td>haemophilia</td>
<td>Bayer Schering</td>
<td>Marketed</td>
</tr>
</tbody>
</table>
Abraxane®

- Albumin binds to caveolin-1 receptors and causes the formation of caveolae, to transport albumin across the endothelial membrane.
- Transcytosis is the transport of albumin across the endothelial barrier from within the blood vessel to the tumor's interstitium.
- SPARC is then secreted by the tumor to attract and retain albumin-bound nutrients within the tumor cell.

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iMed.UL (Research Institute for Medicines and Pharmaceutical Sciences)
## Nanoparticles pipeline (overview)

<table>
<thead>
<tr>
<th>Type of carrier and mean diameter (nm)</th>
<th>Drug entrapped or linked</th>
<th>Current stage of development</th>
<th>Type of cancer (for clinical trials)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymer–drug conjugates (6–15)</td>
<td>Doxorubicin, Paclitaxel, Camptothecin, Platinale, TNF-470</td>
<td>12 products under clinical trials (Phases I–III) and in vivo</td>
<td>Various tumours</td>
</tr>
<tr>
<td>Liposomes (both PEG and non-PEG coated) (85–100)</td>
<td>Doxorubicin, Paclitaxel, platinum compounds, Annamycin</td>
<td>Several products in clinical trials (Phases I–III) and in vivo</td>
<td>Solid tumours, renal cell carcinoma, mesothelioma, ovarian and acute lymphoblastic leukaemia</td>
</tr>
<tr>
<td>Polymeric nanoparticles (50–200)</td>
<td>Doxorubicin, Paclitaxel, platinum-based drugs, Docetaxel</td>
<td>Several products are in clinical trials (Phases I–III) and in vivo</td>
<td>Adenocarcinoma of the oesophagus, metastatic breast cancer and acute lymphoblastic leukaemia</td>
</tr>
<tr>
<td>Polyethersomes (–100)</td>
<td>Doxorubicin, Paclitaxel</td>
<td>in vivo</td>
<td></td>
</tr>
<tr>
<td>Micelles (lipid based and polymeric) (5–100)</td>
<td>Doxorubicin</td>
<td>Clinical trials (Phase I)</td>
<td>Metastatic or recurrent solid tumours refractory to conventional chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Paclitaxel</td>
<td>Clinical trials (Phase I)</td>
<td>Pancreatic, bile duct, gastric and colonic cancers</td>
</tr>
<tr>
<td></td>
<td>Platinum-based drugs (carboplatin/cisplatin), Camptothecin, Tamoxifen, Epinicubic</td>
<td>in vivo and in vitro</td>
<td></td>
</tr>
<tr>
<td>Nanoshells (Gold-silica) (–130)</td>
<td>No drug (for photothermal therapy)</td>
<td>in vivo</td>
<td></td>
</tr>
<tr>
<td>Gold nanoparticles (10–40)</td>
<td>No drug (for photothermal ablation)</td>
<td>in vivo</td>
<td></td>
</tr>
<tr>
<td>Nanocages (30–40)</td>
<td>No drug</td>
<td>Chemistry, structural analysis and in vitro</td>
<td></td>
</tr>
<tr>
<td>Dendrimers (6)</td>
<td>Methotrexate</td>
<td>in vitro/in vivo</td>
<td></td>
</tr>
<tr>
<td>Immuno-PEG-liposomes (100)</td>
<td>Doxorubicin</td>
<td>Clinical trials (Phase I)</td>
<td>Metastatic stomach cancer</td>
</tr>
<tr>
<td>Immunoliposomes (100–150)</td>
<td>Doxorubicin, platinum-based drugs, Vinblastin, Vinorelin, Topotecan, Paclitaxel</td>
<td>in vivo</td>
<td></td>
</tr>
<tr>
<td>Immunotoxins, immunopolymers, and fusion proteins (3–15)</td>
<td>Various drugs, toxins</td>
<td>Clinical trials (Phases I–III)</td>
<td>Various types of cancer</td>
</tr>
</tbody>
</table>

**Nanocarriers as an emerging platform for cancer therapy,**
<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
<th>Application</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polymer-Protein Conjugates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinostatin Stimamer*</td>
<td>SMANCS</td>
<td>Hepatocellular carcinoma (local administration via hepatic artery infusion)</td>
<td>Market (Japan)</td>
</tr>
<tr>
<td>Oncaspar*</td>
<td>PEG-asparaginase</td>
<td>Acute lymphocytic leukaemia</td>
<td>Market</td>
</tr>
<tr>
<td>PEG-Intron*</td>
<td>PEG-Interferon alpha 2b</td>
<td>Hepatitis C</td>
<td>Market</td>
</tr>
<tr>
<td>PEG-Asys*</td>
<td>PEG-Interferon alpha 2a</td>
<td>Hepatitis C</td>
<td>Market</td>
</tr>
<tr>
<td>Neulasta™</td>
<td>PEG-Human-GCSF</td>
<td>Chemotherapy-induced neutropenia</td>
<td>Market</td>
</tr>
<tr>
<td><strong>Polymer-drug Conjugates</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xyotax™/Opaxio</td>
<td>PGA-paclitaxel</td>
<td>NSCLC and various others</td>
<td>Phase III</td>
</tr>
<tr>
<td>Prolindac*</td>
<td>HPMA copolymer-Pt</td>
<td>Melanoma, Ovarian</td>
<td>Phase II</td>
</tr>
<tr>
<td>CALLA01</td>
<td>polymer-cyclodextrin-siRNA</td>
<td></td>
<td>Phase I</td>
</tr>
<tr>
<td>NKTR-105</td>
<td>PEG-paclitaxel</td>
<td></td>
<td>Phase I</td>
</tr>
<tr>
<td>XMT 1001</td>
<td>polymer-CPT</td>
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<td>Phase I</td>
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</table>
# Superparamagnetic Iron Oxide Imaging Products

<table>
<thead>
<tr>
<th>TRADENAME</th>
<th>INDICATION</th>
<th>COMPANY</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feridex™</td>
<td>liver imaging i.v.</td>
<td>Bayer Healthcare Pharmaceuticals</td>
<td>Marketed</td>
</tr>
<tr>
<td>Endorem™</td>
<td>liver imaging i.v.</td>
<td>AMAG Pharmaceuticals Guerbet S.A.</td>
<td>Marketed</td>
</tr>
<tr>
<td>GastroMARK®</td>
<td>GI imaging oral</td>
<td>AMAG Pharmaceuticals</td>
<td>Marketed</td>
</tr>
<tr>
<td>Lumirem®</td>
<td>GI imaging oral</td>
<td>AMAG Pharmaceuticals</td>
<td>Marketed</td>
</tr>
<tr>
<td>Sinerem®</td>
<td>lymph node imaging - infusion</td>
<td>AMAG Pharmaceuticals</td>
<td>Phase III</td>
</tr>
<tr>
<td>Resovist®</td>
<td>small liver lesions iv</td>
<td>Bayer Healthcare Pharmaceuticals</td>
<td>Marketed</td>
</tr>
</tbody>
</table>

- (SPIO) Relatively new types of MRI contrast agents are superparamagnetic iron oxide-based colloids
- Median diameter > 50 nm
- Nonstoichiometric microcrystalline magnetite cores coated with
  - dextrans (in ferumoxide)
  - siloxanes (in ferumoxsil)
Regulation of Nanomedicines under appropriate control

- Current regulation provided adequate frame for existing first generation of nanopharmaceuticals
Diagnostics & Therapeutics
Personalized Medicine & the integration of diagnostics and therapeutics

The Path to Personalized Medicine
Margaret A. Hamburg, M.D., and Francis S. Collins, M.D., Ph.D.

The success of personalized medicine depends on **having accurate diagnostic tests** that identify patients who can benefit from targeted therapies. Increasingly, however, the use of therapeutic innovations for a specific patient is contingent on or guided by the results from a diagnostic test that has not been **independently reviewed for accuracy and reliability by the FDA.**

The agency's goal is an **efficient review process that produces diagnostic–therapeutic approaches that clinicians can rely on** and allows companies that invest in establishing the validity and usefulness of tests to make specific, FDA-backed claims about benefits.

http://content.nejm.org/cgi/content/full/NEJMp1006304
Future developments

In vivo nano-imaging of membrane dynamics in metastatic tumor cells using quantum dots.


Cell in bloodstream

1s
17s
41s

In vivo

A 0.072X10^3
B 0.8X10^3
C 2.2X10^3
D 3.6X10^3
E 8.2X10^3
F 8.2X10^3
G 8.2X10^3
H 8.2X10^3
I D=8.2X10^4nm/s
D=3.9X10^4nm/s
D=3.6X10^4nm/s

PAR1 diffusion
Blood Flow

Screw
Handmade aluminum stage

Laser (488nm) (532nm)

Objective
Confocal unit

Computer

EM-CCD
The Regulatory Gap

Legislation

Medical Devices
93/42/EEC

?

Medicinal Products
2001/83/EC

Advanced Therapies

Medical Devices

Tissue Engineering

Cell Therapy

Gene Therapy

Biotech

Chemicals
Key factors for design of new nanomedicines
(in respect of specific medical use)

• Materials Science and Formulation (Technology)
• Understanding underlying basic molecular mechanisms
• Integrating anatomo-physiological issues with pathology or disease state and its progression
• Changes in biological interactions
• Impact in toxicity and efficacy
• Relevance of animal models (In vitro ??! In vivo !!?)
• Differences both in Pharmacokinetics and Pharmacodynamics
• Translational models adapted to specific questions with “nano” (PK/PD versus specific organ toxicity and differential uptake of particles – translocation)
• Important issues in clinical development: How to move faster and safer? Comparability towards specific therapeutic indication?
Issues

• **Materials Science**
  – Challenges arising from new materials (inorganic nanoparticles, non-biodegradable/ non-biocompatible materials, quantum dots, cationic particles and dendrimeric structures, carbon nanotubes)

• **Formulation / Technologies**
  – Adapting existing technologies to new opportunities (e.g. Quality by Design, Process Analytical Technologies)

• **Translational Research**
  – Adequacy of non-clinical methodology before first in man use (relevance of, appropriate toxicityfficacy biomarkers and barriers related to disease phase and different routes of administration)

• **Clinical development**
  – Comparability: non-inferiority versus superiority (risk-benefit management)

• **Market Access**
  – Comparative pharmacoeconomic assessment
Current and future regulatory challenges

• combination therapy
  – The trend for reformulation of old APIs, with advantages of combined administration on the same delivery system (issues on quality/stability, PK/PD, clinical, IP, market access)

• potential theranostic approaches
  – Combined system that is able to localize to the target pathophysiology and deliver an appropriate therapeutic agent (both diagnostic and therapeutic functions)

• “follow-on” products
  – A number of unresolved problems will arise if preventive action is not taken on matters related to old products, previously not classified as nanoparticles that are in fact colloidal nanoparticulate systems
Iron oxide similars / Iron nanoparticles

- A number medicinal products containing iron oxide nanoparticles have been approved as “follow on” products (controversial data published in the literature)

Roth et al, Translational Research 2008;151:36-44 (BfArm)

Toblli et al, Arzneimittelforschung 2009;59(4):176–190

Fig. 2. Mean liver iron content (in % of control ± SEM) after administration of FeD, FeS, and FeG that contains 8-mg Fe^{3+} to fertilized turkey eggs. Egg white injection, incubation time was 22 days. Statistical significance in comparison with control is shown.

Fig. 6: Bar charts and micrographs showing Prussian blue staining for iron deposits and ferritin immunostaining for stored iron in liver samples taken from the ISS test 1, ISS test 2, reference and control groups on day 28.

Toblli et al, Arzneimittelforschung 2009;59(4):176–190
Risk management
(personal view presented previously
during OECD Working Party in Nanotechnology, Vienna September 2009)

• What are the criteria used to decide that risk management actions are required?
  – In the medicinal products sector well defined and implemented, not in the medical devices or other borderline areas...

• How is scientific evidence and uncertainty reflected in subsequent risk management actions?
  – In the medicinal products area integrated in the product life cycle permanent assessment

• How are decisions taken? - and how transparent and predictable are they?
  – Under established regulation framework for medicinal products, with well defined competences and enforcement modalities

• To what extent is risk management science-based?
  – Science-driven, based on data on medicinal products compiled with appropriate rules established under globally harmonized (USA, EU, Japan – ICH) guidelines; need care with situation regarding new engineered materials and combination products
Current trends in the pharma/bio model for DDD

Innovative Medicines Initiative (IMI): addressing pre-competitive bottlenecks in pharmaceutical R&D

http://www.imi-europe.org/
Current trends in the pharma/bio model for DDD
Innovative Medicines Initiative (IMI): addressing pre-competitive bottlenecks in pharmaceutical R&D

http://www.imi-europe.org/

Room for Pharmaceutical Sciences
U.S.A. versus E.U. trends

**FDA Critical Path**
- Biomarkers & disease models
- Clinical trial streamlining
- Bioinformatics
- Manufacturing
- Develop products of urgent public health need (e.g., anthrax Rx)
- At risk populations-pediatrics

**EU Innovative Medicines Initiative**
- Prediction of Safety
- Early indication of Efficacy
- Knowledge Management
- Education & Training
How to move in a global environment?

• **Learn with ICH cooperation**
  – Regulators and stakeholders, working groups, guidance documents and maintenance procedures

• **Improve efficiency of procedures**
  – Predictive Safety Testing Consortium (PTSC)

• **Establish institutional mechanisms for cooperation based on specific goals**
  – PPPs with limited and timed objectives (IMI-JTU)

• **Act global as soon as possible – R&D phase**
  – Scientific advise and increase cooperation between scientists and regulators
Need for global cooperation
Need for integrated routine collaboration

Quality

Safety

Efficacy

Regulators

Industry

Academia
Scope:
The proposed workshop will focus on key features of nanomedicines and the emerging scientific knowledge in the field.

Objective:
Explore scientific aspects specific to nanomedicines and share experience at an international level, to anticipate future needs.

Outcome:
Report on identified issues and emerging science aspects, which may assist future developments in the field and may be relevant to future regulatory considerations.