



# Market Opportunity and Future Industry Trends of Drug-Device and Biologic Combination Products

Roger G. Harrison, PhD.

IIR Life Sciences, Drug/Device and Biologic  
Combination Products

London, November 22/23, 2005

# Outline

- **Introduction**
- **Future Trends and Issues**
  - Technology Convergence
  - Evolution of Combination Products
  - Technical Challenges
  - Regulatory Requirements and Trends
- **Drug-Device Combination Products**
- **Advanced Therapy Products**
  - Tissue Engineering
  - Gene and Cell Therapy
- **Nanotechnology**
- **Summary**

# Introduction

- Historic boundaries existed between devices and drugs
  - Devices – mechanical solutions to structural problems
  - Drugs – impact a biological process to effect an outcome
- Separate language, regulatory pathways, and business models

# Introduction

## Drug-device combinations can

- Improve a device's efficacy and/or safety through the use of a drug coating,
- Enable delivery of a drug to a specific site, or,
- Enhance the ease of delivery of drugs

# Future Trends and Issues

- Medical device companies do not have the expertise to develop drugs
- Pharma companies are still focused on developing drugs
- Partnering will be the short-term solution to innovative device/drug combination products
- New companies are being established to capitalize on future opportunities

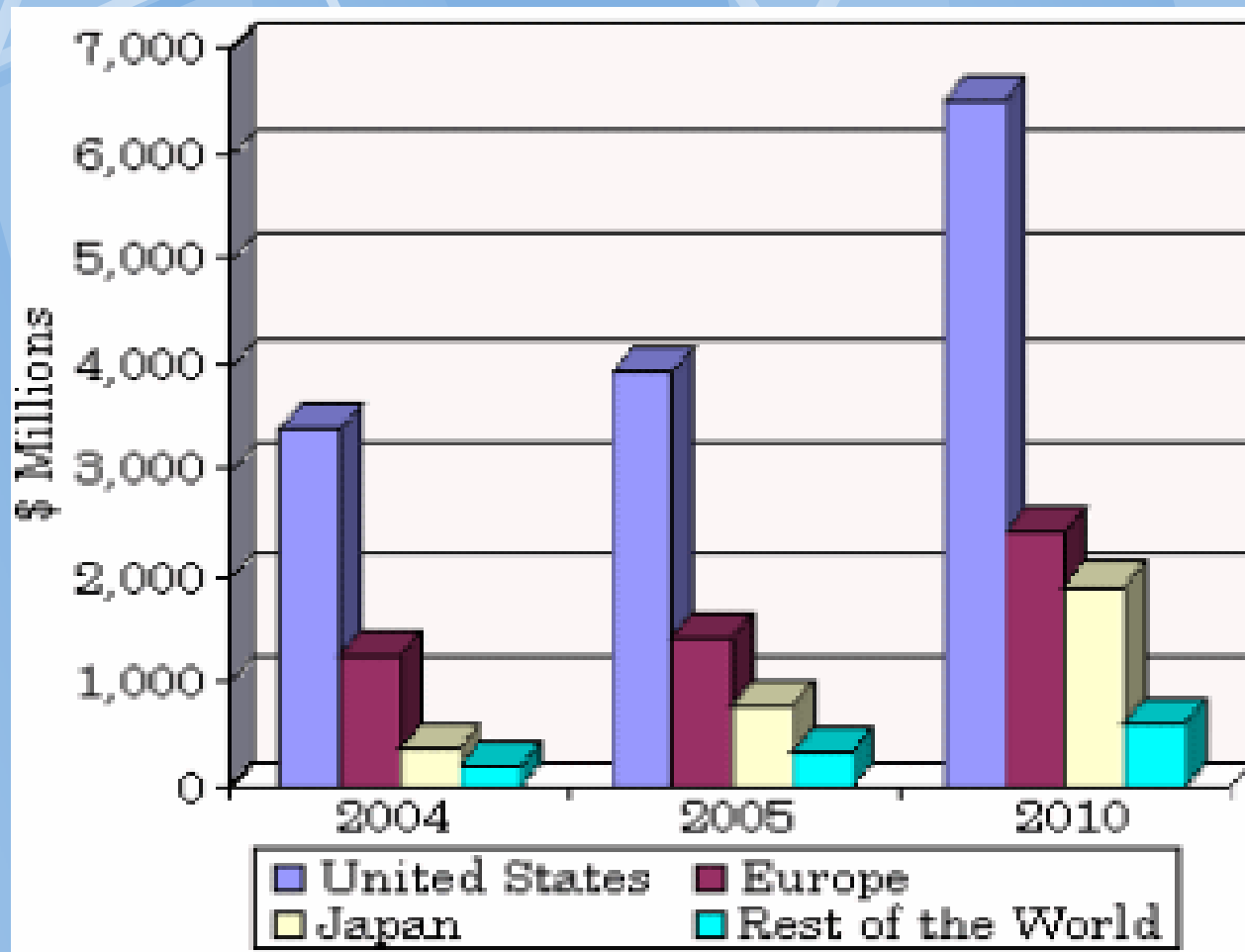
# Technology Convergence in the New Organization?

- Drug design and development
- Device design and engineering
- Proteonomics and genomics
- Polymer science
- Information technology
- Nanotechnology

# Evolution in drug-device combinations

- Inhalation Devices
- Transdermal Delivery Systems
- Prefilled syringes
- Insulin pumps
  - Pharmaceutical companies developed modified insulins more suitable for pumps
- Polymer implants and depot systems (e.g. Gliadel wafers)
- Drug Eluting Stents
  - Account for over 80% of the stents used within 3 years of introduction

# Market for Drug Device Combination Products by Geographic Area, 2004-2010



Source: Business Communications Co, Inc

# Market Projection for Drug-Device Combination Products

- \$5.4 billion in 2004 increasing to \$11.5b in 2010 (13.6 percent annual growth)
- Drug eluting stent market will reach \$8.0b in 2010
- Most categories will show double digit growth
- US dominates market

# Technical Challenges

Combination of products introduces new issues:

- Drug release from polymer materials
- Local safety issues of drug and polymer
- Drug interaction with new contact materials
- Drug-device interactions
- Stability of the drug with the device
- Sterility for combination products
- Dose dumping from implanted systems
- Etc.

# USA: Current Regulatory Process

- Office of Combination Products (OCP)  
Created in 2002
- OCP will determine what are the issues that create potential risk to patient and assign primary review to:
  - CDER if risk of drug outweighs device
  - CDRH if risk of device outweigh those of drug

# USA: Future Regulatory Trends

- **Continuing Development of Rules and Guidelines**
- **Greater Authority for OCP**

# European Current Regulatory Process

- A product is regulated either as a Medical Device or Medicinal Product
- Key applicable Directives are:
  - Medical Device Directive 93/42/EEC
  - Medicinal Products Directive 2004/27/EC
- Assignment depends on intended purpose of the product and the method by which the principal intended action is achieved

# European General Classification

- A device which is intended to deliver a medicinal product is regulated as a device
- The medicinal product in the device must be approved as a medicinal product
- If the device and medicinal product form a single integrated system, and is not reusable, the single product is regulated as a medicinal product (pre-filled syringes, asthma inhalers, transdermal patches)

# European Possible Regulatory Trends

- Greater clarity in how combination products will be reviewed
- Increased requirements for Notified Bodies
- CE mark for medical devices separated from household items

# Company Considerations in Development of a Drug-Device Combination

- Definition of synergistic possibilities
- Rigorous analysis of the market potential and customer acceptance
- Clear development strategy
- Early discussions with Regulatory Authorities
- Outcome benefits to justify reimbursement if associated with additional costs

# Products that Enhance the Performance of Medical Devices

## ● Drug containing stents

- Projected to account for 70% of the combination product market in 2010
- Dramatic impact on restenosis (3% versus >11% requiring revascularization)

## ● INFUSE® bone graft

- Spinal fusion procedures for degenerative disc disease using BMP-2 on an absorbable collagen sponge in titanium fusion cages

# Devices that Enhance Patient Acceptance of Drugs

- Single-use prefilled syringes
- Single-use autoinjectors
- Single-use needle-free injectors
- Inhalation devices to replace injection systems

# Examples of Future Combination Products

- Controlled delivery of anti-arrhythmic drugs from tissue adherent polymeric hydrogel matrices (Genzyme)
- Insulin pump therapy with continuous glucose monitoring (Medtronic)
- Gliasite (Proxima Therapeutics) in cancer treatment – balloon catheter inserted after surgery and filled with a liquid radiation source

# Advanced Therapy Medicinal Products

- **Evolving Opportunities**
  - Human Tissue Engineered products
  - Somatic cell therapy products
  - Gene therapy medicinal products
- **Within the European Community definitions in Article I of Directive 2001/83/EC and Article 3 of Directive 2004/23/EC**
- **Committee for Advanced Therapy Products established within EMEA**

# Tasks for the Committee for Advanced Therapies

- To assess any data generated for an advanced therapy product and formulate an opinion ....
- At the request of the CPMP to formulate an opinion....
- To provide advice on any question related to advanced therapy products....
- To assist scientifically in elaboration of any document.....
- To provide scientific expertise and advice ....

# Combined Advanced Therapy Medicinal Products

- An advanced therapy Medicinal Product which incorporates ..... one or several medical devices within the meaning of Directive 93/42/EC, and which is liable to act upon the human body with action that cannot be considered as ancillary to that of the referred device(s)
- Any medical device which forms part of an advanced therapy medicinal product shall meet the essential requirements as laid down in Annex I to Directive 93/42/EC

# Human Tissue Engineered Products

## ● Tissue Engineering

“The persuasion of the body to heal itself through the delivery to the appropriate sites of cells, molecular signals, and supporting structures” David Williams, 1999

## ● European Regulatory Initiatives

- Currently classified as Medicinal Products
- Human Cells and Tissue Directive (2004/23/EC)
  - Addresses donation, procurement and testing, not route to market
- Proposal for Community Regulatory Framework on Advanced Therapies (EC 04.05.2005)

## ● FDA

- CBER responsibility

# Tissue Engineering Issues

- New development and regulatory challenges
- Organ transplant is not regulated
- Tissue banks not consistently regulated
- Business model to justify company investments

# Commercial Potential for Tissue Engineered Products

- Current market approximately \$75m
- Future projection at \$290 to \$1.2b by 2013
- Challenges of cell sourcing, cell manipulation, tissue expression, implantation and incorporation, immune system response
- Concomitant use of scaffolds, growth factors, or genes?
- Definition of the product and who is the manufacturer will require consideration

# Gene Therapy and Cell Therapy

- The introduction of genetic material into a cell to treat disease
  - Genetic diseases are caused by malfunctioning gene(s) – these can be inherited, occur at birth, or be randomly acquired owing to lifestyle or environmental factors
- Genes can be inserted into the affected tissue outside of the body, which is then returned, or delivered directly, typically using viral vectors

# International Committee on Harmonization (ICH) and Gene Therapy

- **Gene Therapy Discussion Group established with goals of:**
  - Monitoring emerging scientific issues
  - Set out principles that could help in harmonizing regulations
  - Develop new ways of communicating to ensure outcomes of ICH are well understood

# Progress Towards Market for Gene Therapy

- Gendicine for treating head and neck cancer approved in China in late 2003
- Other companies (e.g. Ark Therapeutics) are anticipated applications for market approval of their products in 2007
- Challenges remain in;
  - Gene delivery
  - Durability and integration
  - Immune response
  - Safety of vectors

# Nanotechnologies

- Projected that in 10-15 years, \$1 trillion in products will be affected by nanotechnology
- Most things related to advanced materials, environment, energy conversion, and national security will be affected
- All materials and devices have their basic properties defined at the nanoscale

Mihail Roco, Director US National Nanotechnology Initiative

# Potential Nanotechnology Applications

- *In vivo* “labs on a chip”
  - Nanotech biosensors and microfluidics to continuously monitor temperature, pulse, heart rhythm, blood pressure, oxygenation, glucose levels, detect pathogens, toxins, early tumors, etc.
- Enhancement of Medical Imaging
  - Nanotech particles coated with antibodies that bind to cancer cells
- Stronger artificial bone paste for repair and replacement in load bearing applications

# The Near Future

- MEMS – Micro Electromechanical Systems (silicone wafers packed with information or drugs)
- Closed loop feedback delivery systems
- Nanobots capable of precise drug delivery or other intervention

(September 1999 – Cornell developed a nanobot 100,000X smaller than a grain of sand with small propeller with a segment of ATP attached)

# The Future

- Miniscule particles that can travel through the body to detect and cure disease
- Chemotherapies that can attack individual cancer cells
- Artificial organs (e.g. pancreas)
- Artificial brain cell implants (Alzheimer's disease)
- Ability to repair damaged organs from the inside
- Self replicating machinery and self assembling medical products for eradication of acute and chronic diseases

# Summary

- Numbers and types of combination products will continue to grow
- Earlier partnerships between device and drug companies likely
- Clearer, more predictable regulatory processes will evolve
- New technologies with the potential to revolutionize disease management will challenge current business models and reimbursements systems
- Continuing challenges from a regulatory perspective
- New types of companies likely to be created