

Challenges Posed by Combination Medical Products
By Scientia Advisors

Contacts: Harry Glorikian
Managing Partner

Email: hglorkian@scientiaadv.com

Office: 617-401-2330 - Ext 1382

Mobile: +1-617-407-5093

Fax: +1-617-812-0315

1 Broadway, 14th Floor
Kendall Square
Cambridge, MA 02142

Combination Medical Products (CMP)

High value products that can transform healthcare

Combination medical product consists of two or more regulated medical products that are marketed as single unit



- CMP consists of the following different combinations
 - » **Drug-device**
 - » **Biologic-device**
 - » **Drug-biologic**
 - » **Drug-device-biologic**
- These combinations can be physically or chemically combined or co-packaged in a kit or separate, cross-labeled products

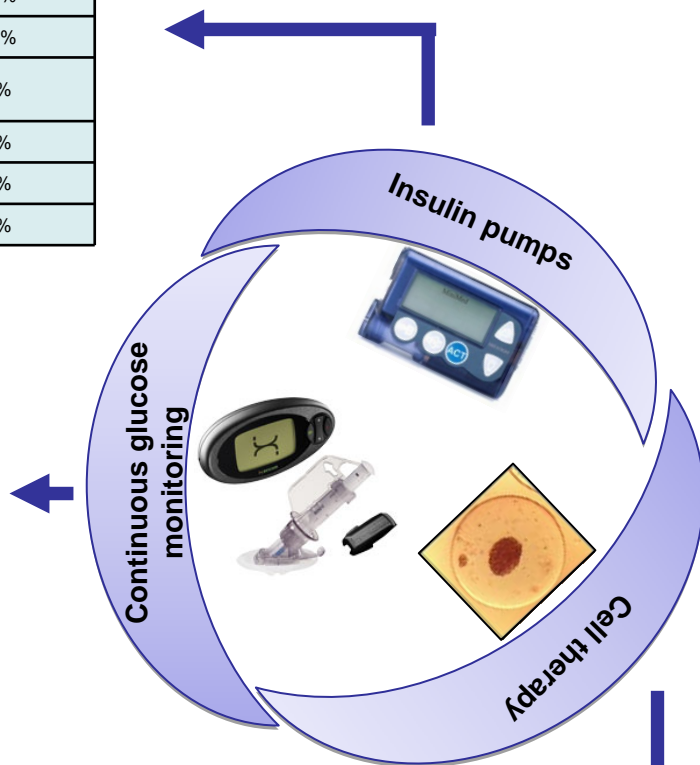
Future Diabetes Circle of Care

Artificial pancreas is the “holy grail” of diabetes care

	% Mkt Share
Medtronic	72%
Roche/Disetronic	15%
Smiths Medical/Deltec	4%
Insulet	1%
Animas-J&J	7%
Other ^A	1%

	Status
ABT	PMA filed
DexCom	IDE trial ongoing
Medtronic	Approved w/o CGM label
Cygnus-J&J	Approved
Roche	In development
Other*	In development

	Status
Amcyte	Phase II
Transition therapeutics	Phase II
Microislet	Preclinical
Novocell	Preclinical



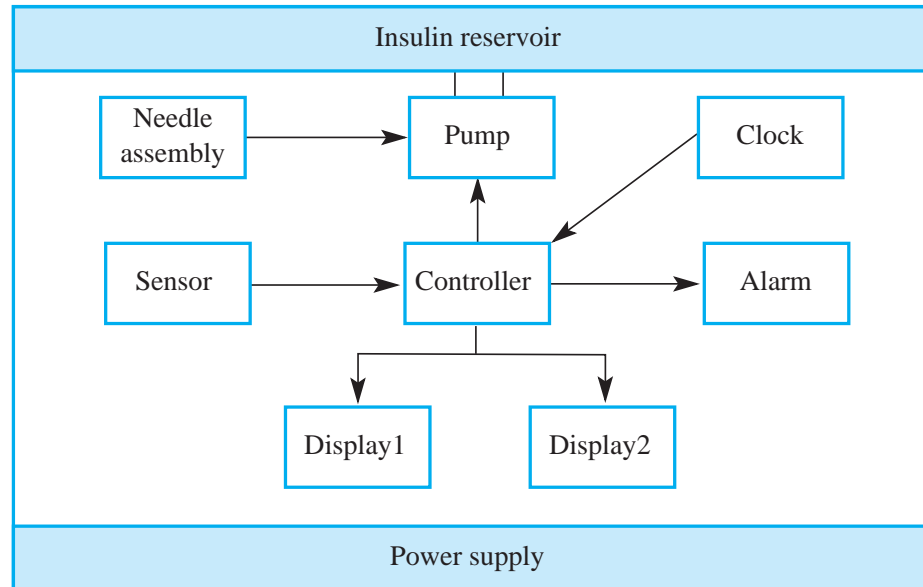
Key Take-Aways

- Continuous glucose monitoring (CGM) is the next big thing in glucose monitoring
 - Medtronic, DexCom, Abbott-TheraSense, and J&J-Cygnus appear to be in a close race to develop the first patient-friendly CGM system
- Combination of an implantable CGM sensor and an insulin pump will automate the process of insulin delivery and close the loop of an artificial pancreas
 - Medtronic, dominates the market, followed by Roche/Disetronic, Animas-J&J, Smiths Medical, and Insulet
- Bio-artificial pancreas, islet cell therapy, and stem cells are targeting preservation and/or replacement of β -cells. This will serve as the ideal artificial pancreas but commercialization and availability of a real product is at least 5-10 years away

^{*} Includes: A.Menarni, BodyMedia, Cybersensors, Cybiocare, Diabetes Sentry, GlucoLight, iSense, M-Biotech, Sentek Group, Sontra Medical, SMSI®, and other emerging companies

^A includes: Debiotech, Eksigent, HEI, Nipro Diabetes Systems, SOOIL Development, TheraFuse, and other emerging companies

- Challenges associated with developing a CMP:
 - » Difficult product development (High R&D costs)
 - » Difficult manufacturing process
 - » No specific regulations or regulatory submissions unique to CMP
 - » Organizational challenge: Disparate industries need to work together (eg. Device companies with engineering expertise and Drug companies with biology expertise)
 - » Commercial challenges: Cross-industry partnerships-Licensing products vs. direct involvement



- >20 years in the making! (First pump was from BioStar in 1980) with current best being an alarm at 3 Units of insulin, for a pediatric patient or a patient with high insulin sensitivity this means up to 15 hours before an alarm
- Complex design: Flow control coupled to advanced sensors for intelligent drug delivery without bubbles, flow without damaging the insulin (shear, hydrophobic surfaces, sharp corners, etc.)
- No reliable, inexpensive method for flow control in pumps is available yet

- Key to ensure adequate sterility and shelf life of the drug. Coatings can flake off or the product can deposit too much drug into the body; leading to reduced safety and efficacy
 - » Boston Scientific issued three recall notices in July and August 2004 because of manufacturing problems that caused the catheter systems' balloons to fail to deflate after stent deployment on rare occasions.

The Boston Globe

Cordis gets FDA warning letter of GMP

agency reports on new tests on computerized systems added to the high cost of U.S. health care.

In the first study of its kind, a Pennsylvania state agency has found that 11,000 hospital-acquired infections were associated with an additional 1,110 deaths, 260,000 extra hospital days and

list prices similar to antiretroviral drugs, as the actual payments to health insurers and individuals are generally much lower.

Nevertheless, the Pennsylvania agency believes that the data submitted by the state's hospitals account for only



U.S. Food and Drug Administration



Disetronic Medical Systems, Inc. Announces a Voluntary Nationwide Recall Of All ACCU-CHEK™ Ultraflex Infusion Sets

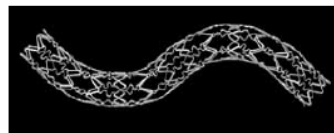
Contact:
Joel Reuter
317-521-7431

FOR IMMEDIATE RELEASE -- Fishers, IN -- April 3, 2006 -- Disetronic Medical Systems, Inc. (Disetronic) of Fishers, Ind. announced today a voluntary nationwide recall of all ACCU-CHEK™ Ultraflex Infusion Sets, because of a potential that tubing could fully or partially separate at the luer lock-tubing connection. In the event that a full or partial separation occurs, it is possible that insulin could leak from the infusion set tubing causing an interruption of insulin delivery, which can cause hyperglycemia.

- The Office of Combination Products (OCP), established by FDA in 2003, is responsible for the prompt assignment of a new combination product to the lead FDA review center (CDRH or CDER or CBER) based on the PMOA.
 - » Based on the intricacy of the underlying components and their interface, combination products can be classified into four increasingly sophisticated categories: traditional drug-delivery systems, novel drug-delivery systems, drug-enhanced devices, and regenerative medicinal products

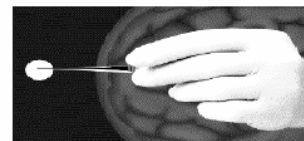
PMOA Examples

Drug Eluting Stent



- Primary Mode of Action:
 - Stent opens artery
- Secondary Action:
 - Drug prevents inflammation and restenosis of artery
- Regulated as a Device (PMA)

Drug Eluting Disk



- Primary Mode of Action:
 - Cancer chemotherapy for brain tumor
- Secondary Action:
 - Local drug delivery of drug by device
- Regulated as a Drug (NDA)

Disparate Industries

Devices	Drugs
Engineering, materials	Biology, chemistry
Local effects	Systemic effects
Technology development	Research
Systematic & rapid product development	Slow, trial & error product development
Engineers	Scientists
Product lifetime usually short	Product lifetime usually long

Source: Scientia analysis, devicelink

- While biotechnology products are marketed directly to patients (much like traditional pharmaceuticals), medical device marketing requires specialized knowledge of sales channels within the healthcare industry. Will doctors be making the decision to use the device or will a hospital board be making that call?
- The need for constant innovation in the medical device sector is more critical than in the pharmaceutical industry and devices patent protections are not as far reaching as pharma patents

Science, Knowledge and Skill for your competitive advantage.



Scientia Advisors is an international strategy and management consulting firm with a concentration in life sciences. We have one mission, to ensure that our clients consistently outperform the market and their competitors.

CONTACT INFORMATION

Harry Glorikian
Managing Partner

hglorkian@scientiaadv.com

Office: +1-617-583-1382

Mobile: 617-407-5093

Fax: +1-617-812-0315

1 Broadway, 14th Floor
Kendall Square
Cambridge, MA 02142

THIS PRESENTATION IS MEANT TO BE ACCOMPANIED BY COMMENTARY &
VIEWPOINTS BY SCIENTIA ADVISORS

THIS IS NOT MEANT TO BE A STANDALONE DOCUMENT ON WHICH TO BASE THE
FINAL VIEWPOINTS OF SCIENTIA ADVISORS OR ON WHICH TO BASE THE
FINAL AND DEFINITIVE GO-FORWARD DECISIONS

 Scientia Advisors