EUDAX®

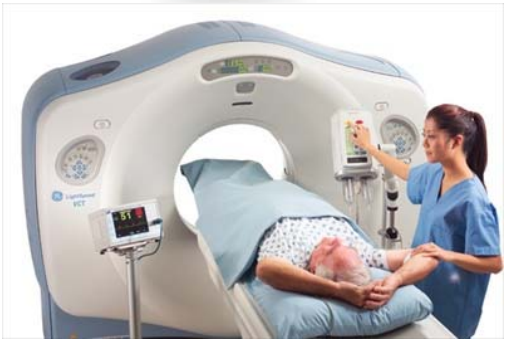
Borderline medical devices and combined products

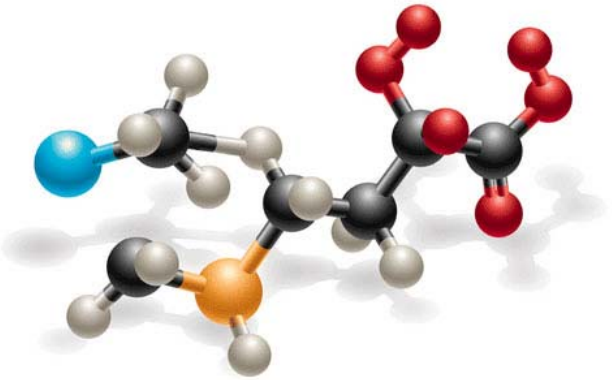
Enrico Perfler – Eudax s.r.l.

Summary

- Medical devices vs. drugs
  - Market data (EU)
  - Technical features
- Borderline medical devices and combination products: a regulatory perspective
- Conclusions

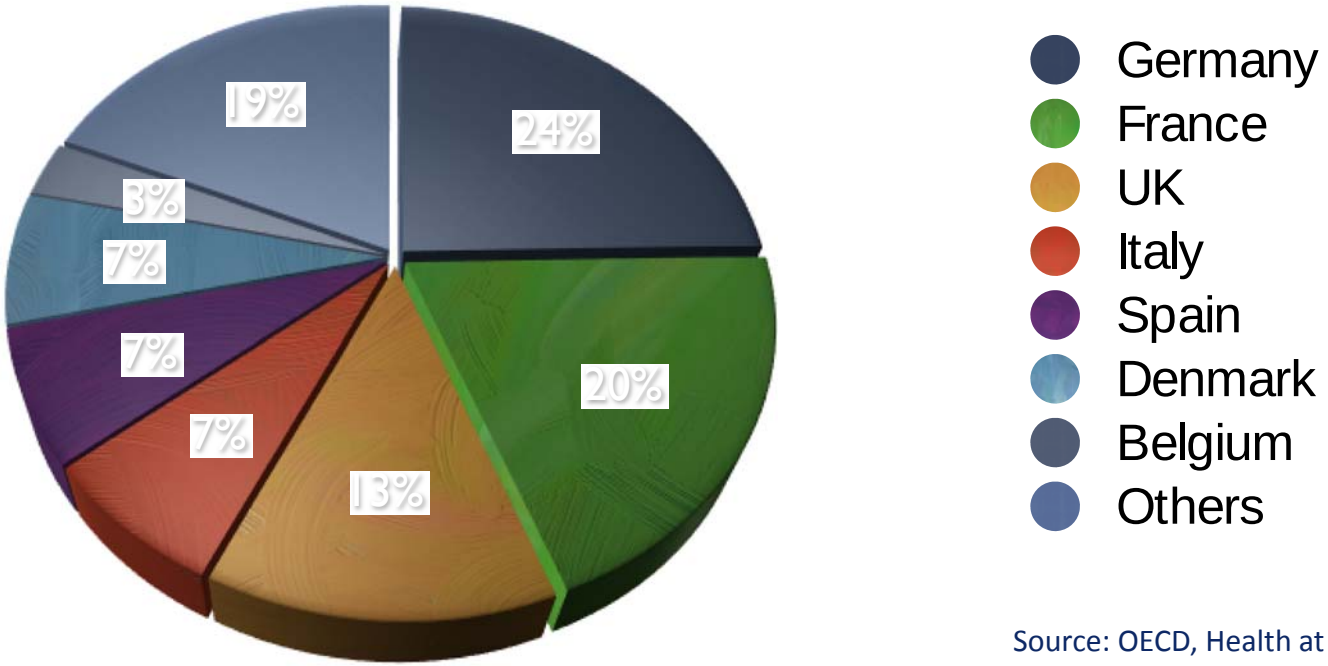
MD vs. Drug





Medical Device EU Market

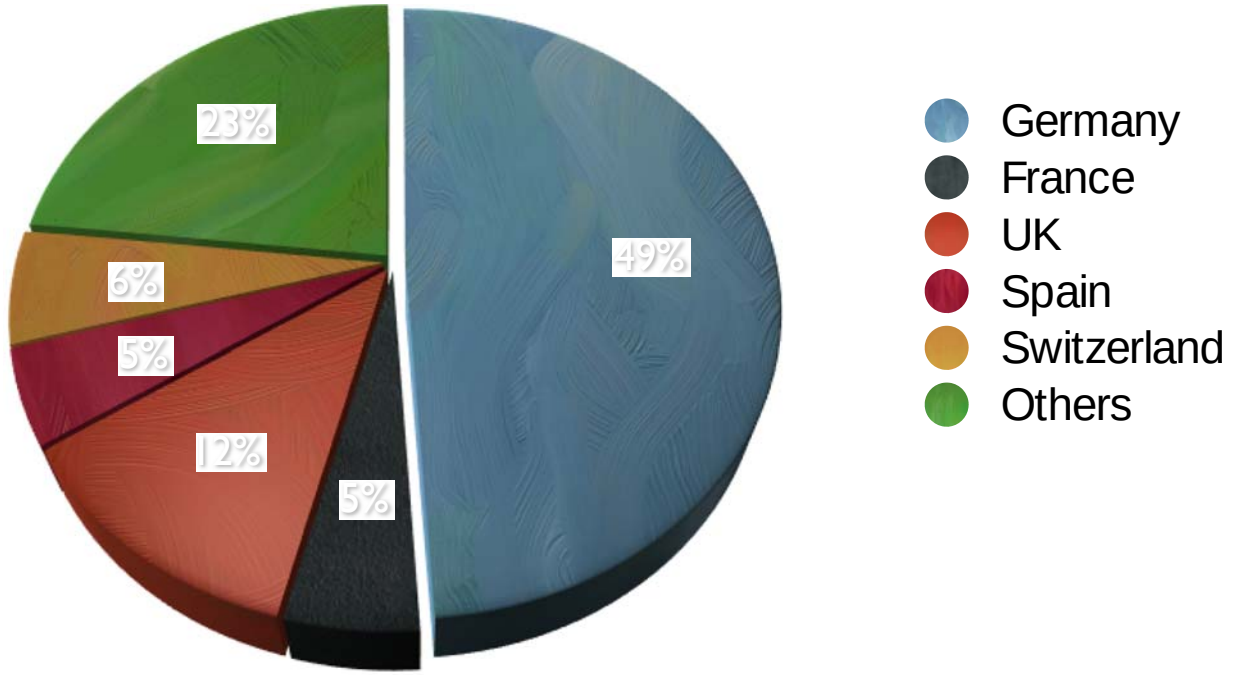
- € 95 billion (30% of worldmarket)
- Annual growth: 5%
- 8% of reinvestment in R&D



Source: OECD, Health at a Glance - 2011

Medical Devices

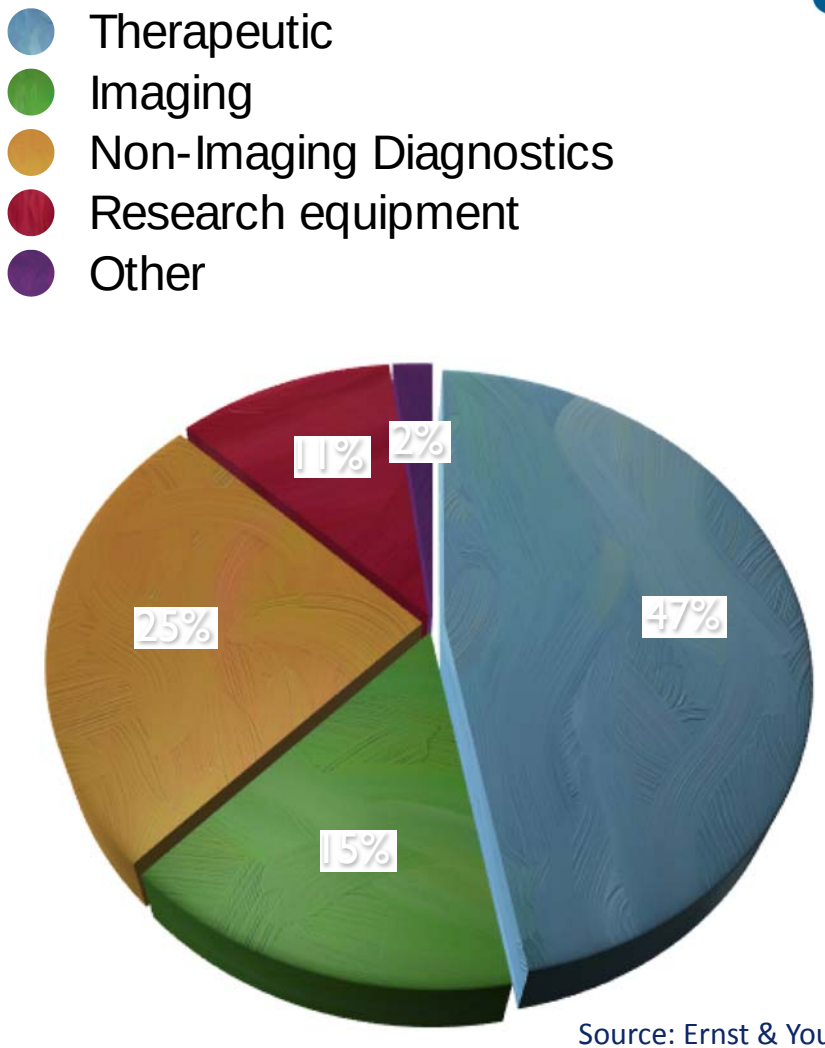
- 22.500 companies (80% SMEs)
- 10.000 very small companies < 10 employees



Source: World Bank, EDMA, Espicom and Eucomed Calculations, 2009

Medical Devices

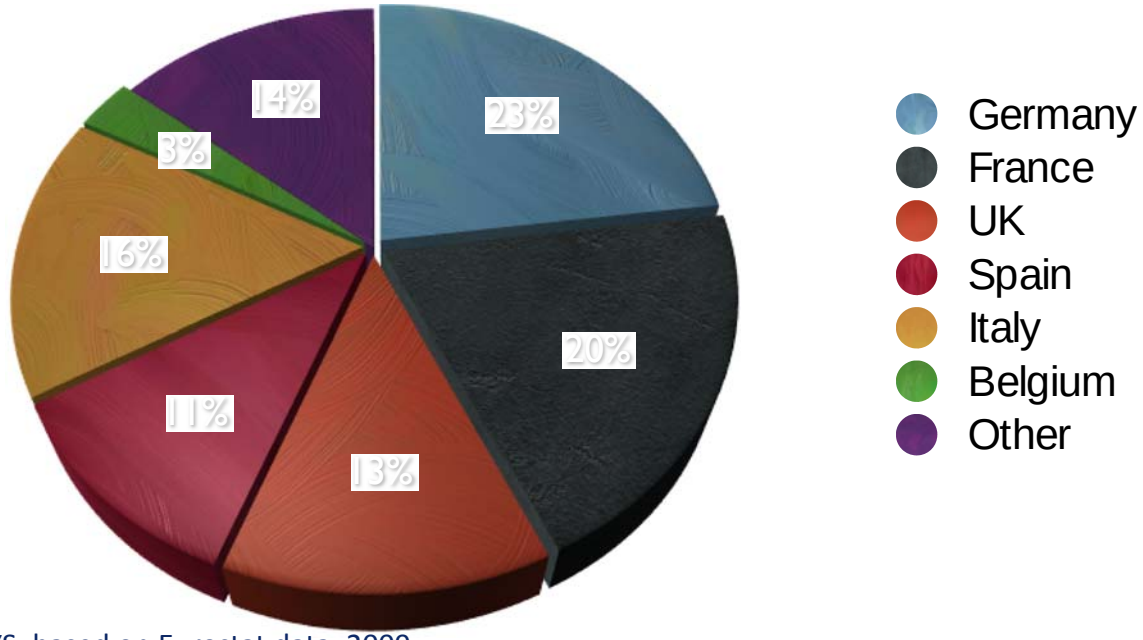
%	Therapeutic devices
19	Orthopaedics
15	Cardiovascular/vascular
14	Non disease specific
8	Multiple
7	Ophtalmic
7	Dental
6	Wound Care
5	Oncology
4	Aesthetics
3	Neurology
12	Other



Source: Ernst & Young, 2008

Drugs

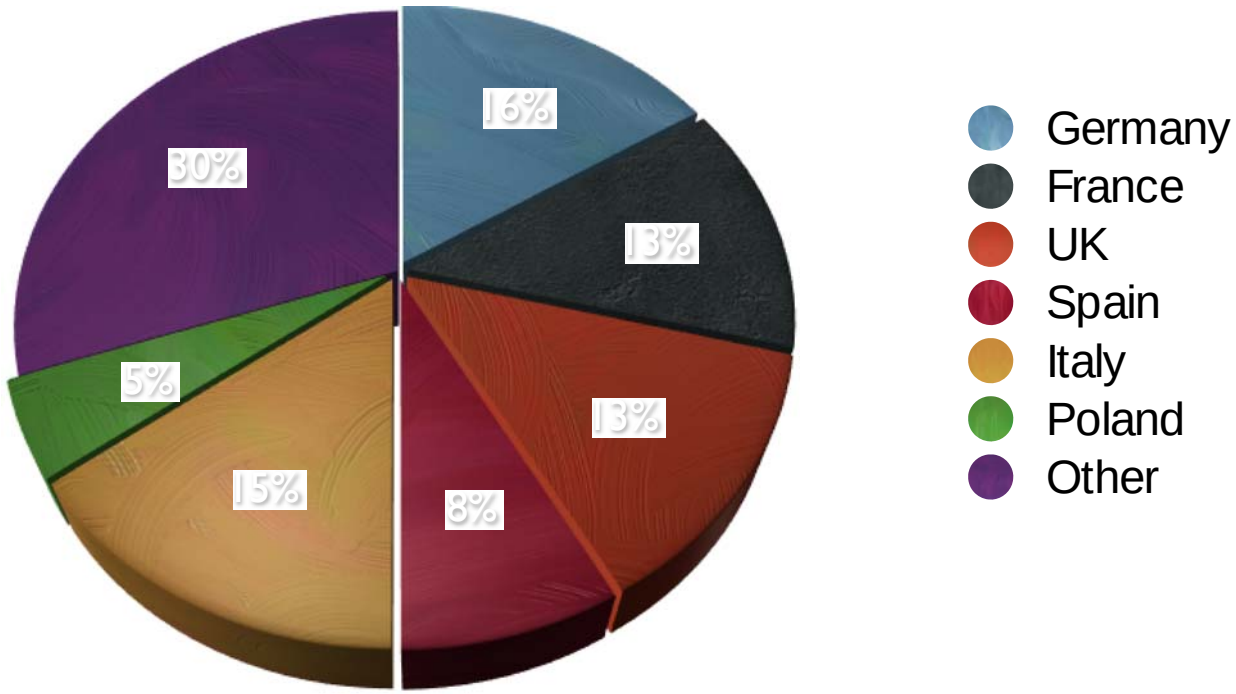
- € 180 billion (30% of world market)
- Annual growth: 4%
- 3,5% is reinvested in R&D



Source: ECORYS, based on Eurostat data, 2009

Drugs

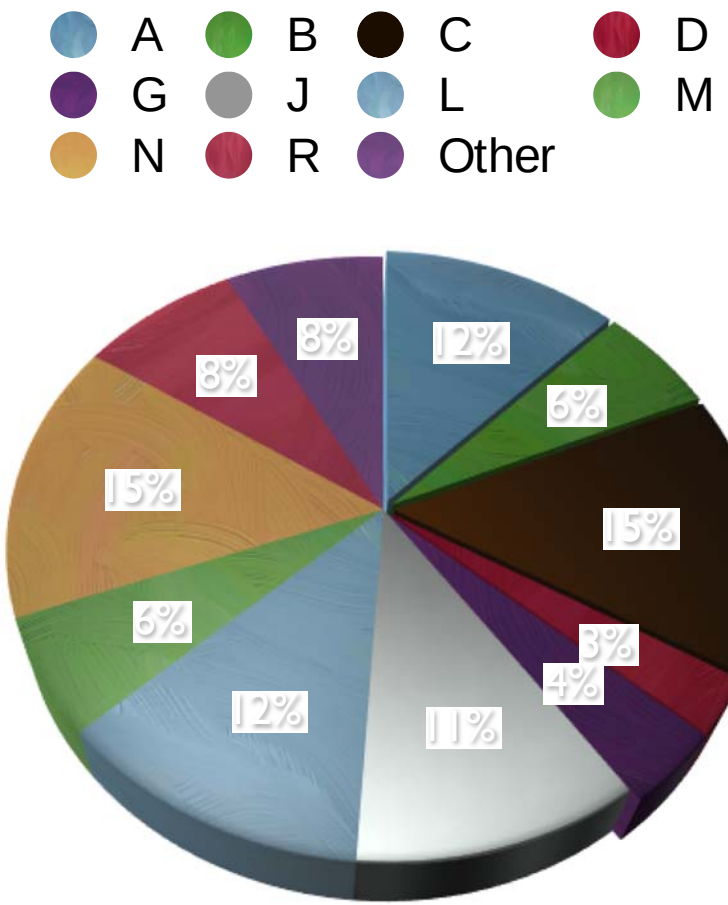
- 4.460 companies (90% PMI)
- 2.073 companies < 10 employees



Source: ECORYS, based on Eurostat data, 2009

Drugs

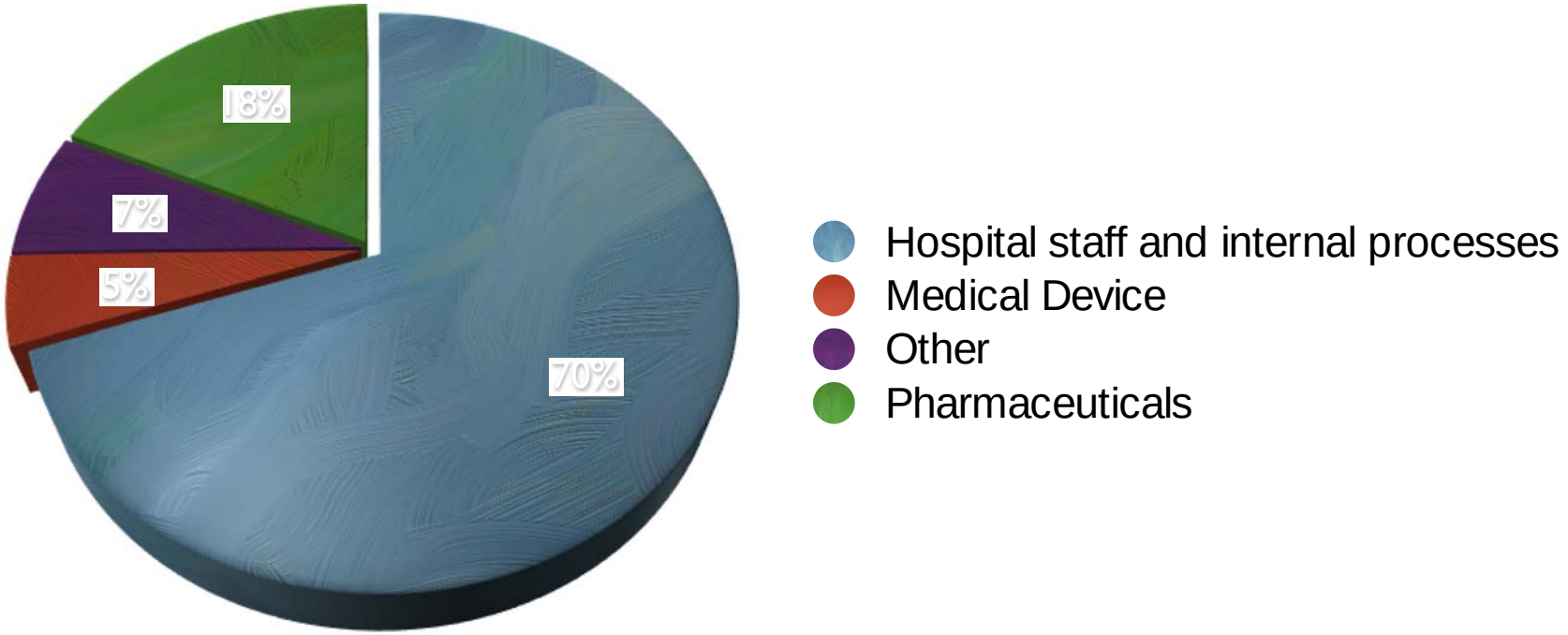
ATC	ATC Description	%
A	Alimentary tract, metabolism	12
B	Blood + B.forming organs	6
C	Cardiovascular	15
D	Dermatologicals	3
G	G.U. System & sex hormons	4
J	Systemic anti-infectives	11
L	Antineoplast + immunomodul	12
M	Muscolo-skeletal system	6
N	Nervous system	15
R	Respiratory system	8
H+K+P+S+T+V		8



Source: IMS Health Data, 2009

Healthcare expenditures

- Medical devices represents 5% of global healthcare costs



Comparison MD vs. Drug

	Medical Device	Drug
Mechanism of action	Mechanical, physical	Chemical, metabolic
Delivery Treatment	Strictly dependent on the physician (the medical device affect the procedure i.e. percutaneous heart valves, etc.) Training is very important!	Less dependent on the physician. Learning curve is shorter. Treatment delivery is more standardized.
Effect	Local, direct	Local, direct sistemic
Mean lifecycle	Prouct turnover is around 18-24 months	Several years/decades

Confronto DM - Farmaco

	Medical Device	Drug
Preclinical validation	Bench test Animal studies (not always)	In-vitro studies Animal studies
Authorization process	Depends on the class of risk of the MD, it may take between 1-5 years for CE mark	For a new chemical entity is burdensome!
Clinical Evaluation	Mandatory. For MD with a low class of risk a premarket study could be done using retrospective data.	Mandatory.

Drugs

Acute to
Pharma
Chronic
Phase I
Phase II
Phase III
Registration

R&D costs are the highest in the industry!

Supplementary Protection Certificate
max +5 years

Source: World Health Organization, 2006

Medical Device

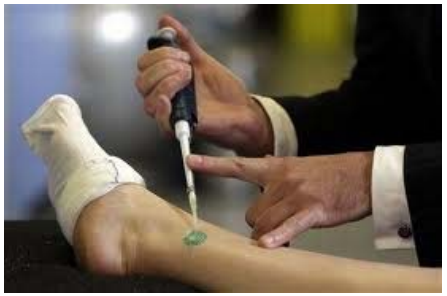
Bench Te
Preclinica
FIM clini
Registrat

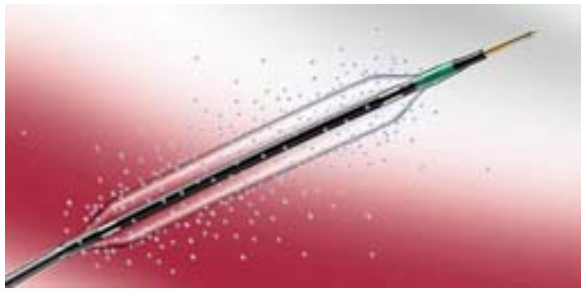
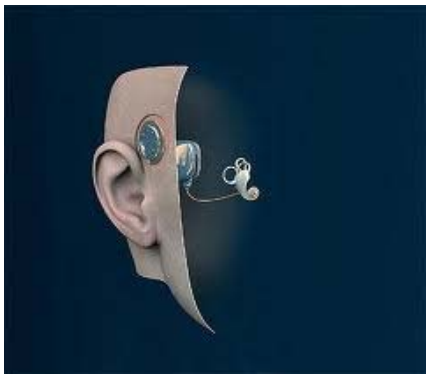
Patent Duration
≠
Product Lifecycle

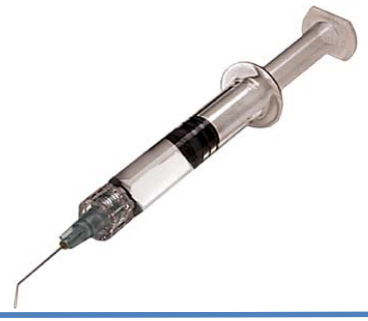
Borderline medical devices



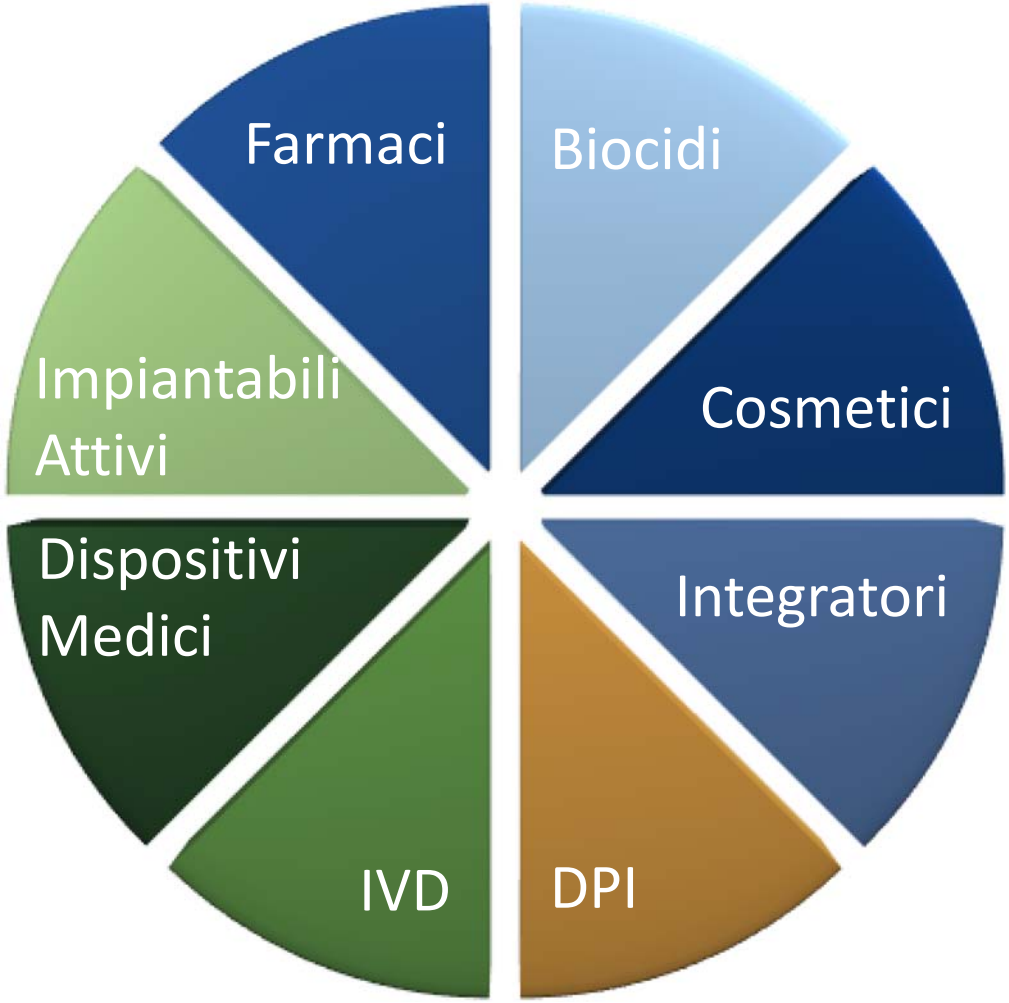






Definition of borderline MD



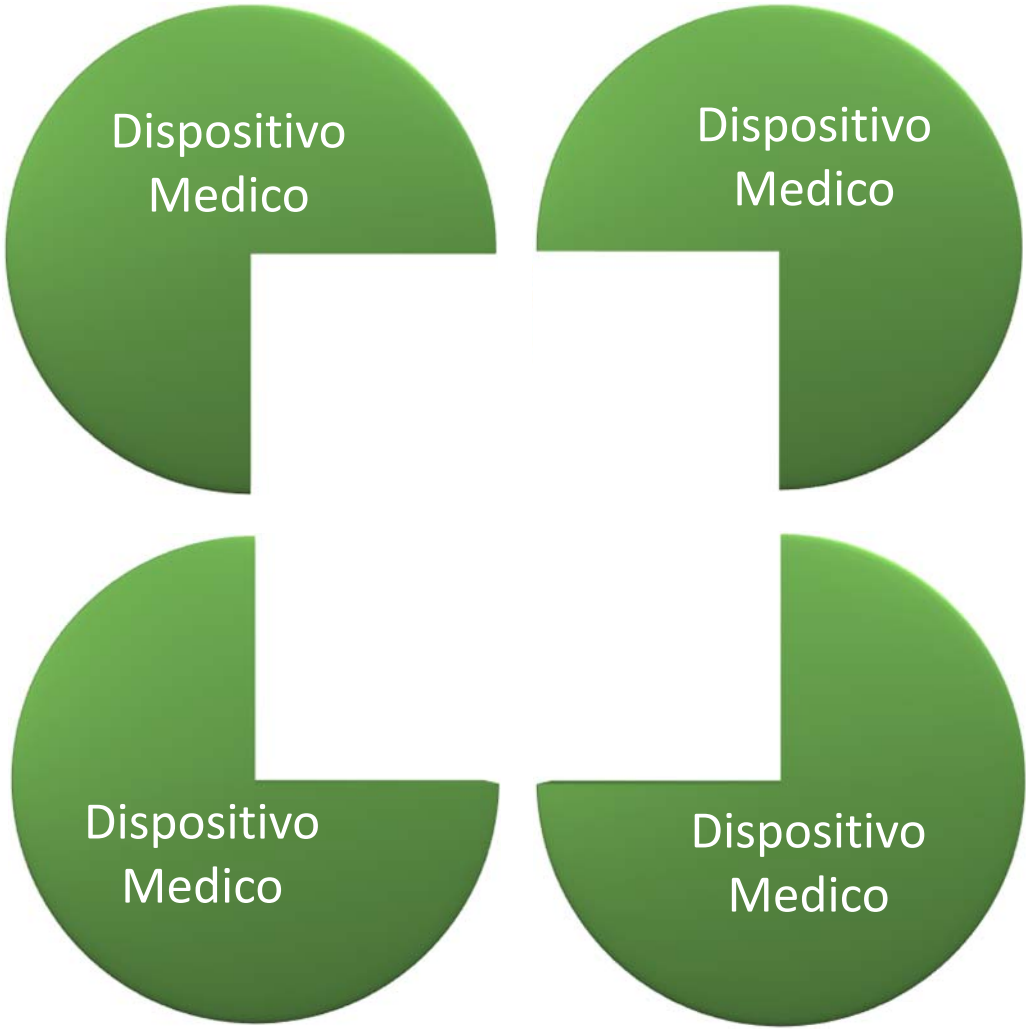
Definition of borderline MD

Definition of borderline MD

MANUAL ON BORDERLINE AND CLASSIFICATION IN THE COMMUNITY REGULATORY FRAMEWORK FOR MEDICAL DEVICES - Version 1.16 (07-2014)

"Borderline cases are considered to be those cases where it is not clear from the outset whether a given product is a medical device, an in vitro diagnostic medical device, an active implantable medical device or not. Or alternatively, borderline cases are those cases where the product falls within the definition of a medical device but is excluded from the Directives by their scope"

Definition of borderline MD



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Quale Direttiva applicare?

Procedura Autorizzativa
Tempi!
Costi!

2-6

R&D A

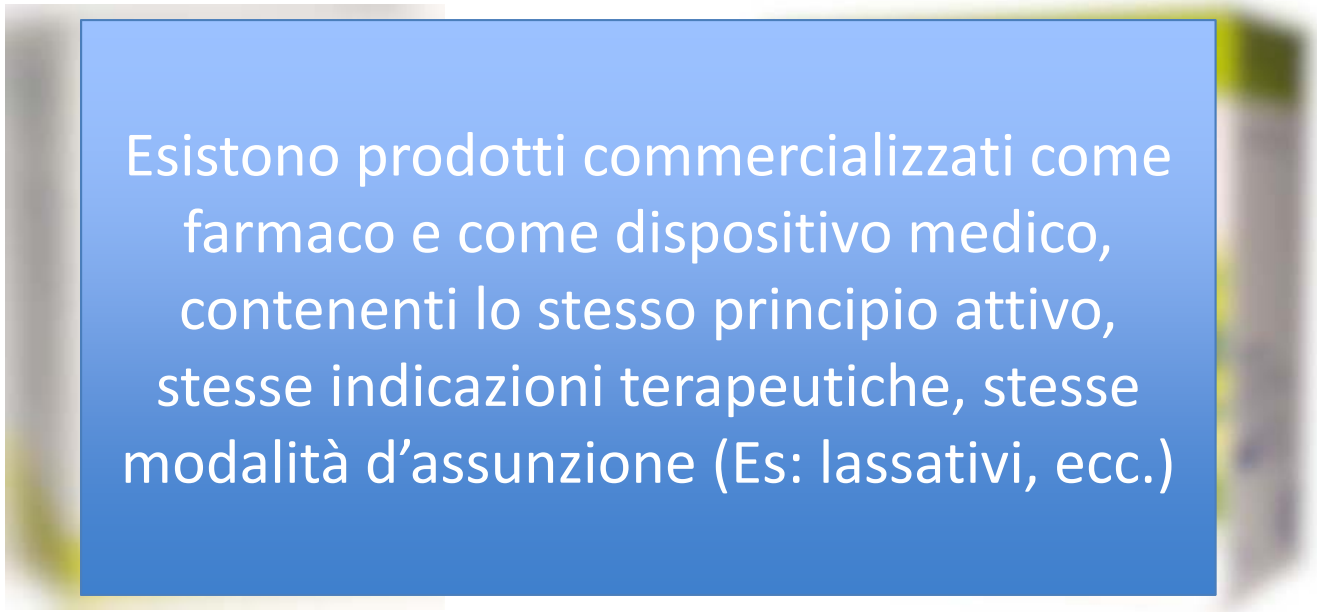
Definition of borderline MD

La Direttiva 93/42/CEE emendata dalla Direttiva 2007/47/CE nella definizione di dispositivo ammette che:

"(…) la cui azione principale voluta nel o sul corpo umano non sia conseguita con mezzi farmacologici né immunologici né mediante metabolismo, ma la cui funzione possa essere assistita da questi mezzi".

Definition of borderline MD

Problemi di interpretazione



Definition of borderline MD

Direttiva 2007/47/CE sui dispositivi medici al punto (13) dei “considerando”:

“L’istituzione di una procedura decisionale per stabilire se un prodotto rientri nella definizione di dispositivo medico è nell’interesse della sorveglianza dei mercati nazionali e della salute e dell’incolumità delle persone, ai fini di un corretto ed efficace funzionamento della direttiva 93/42/CEE in materia di consulenza normativa su questioni inerenti alla classificazione a livello nazionale, in particolare in merito all’applicabilità della definizione di dispositivo medico a un determinato prodotto”.

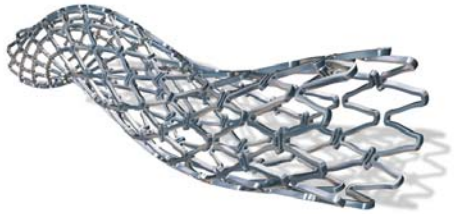
Definition of borderline MD

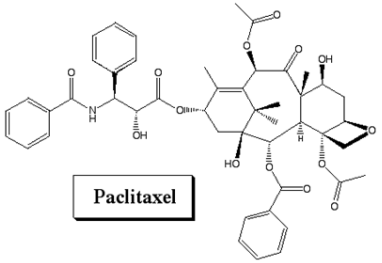
- Evidenze convincenti su meccanismo d'azione rispetto alla destinazione d'uso prevista
- Modalità con cui si ottiene l'effetto desiderato

Definition of borderline MD

- MEDDEV 2.1/3 rev.3 2009 Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative
- MEDDEV 2.4/1 rev.9 2010 Classification of medical devices
- Manual on borderline and classification in the Community Regulatory Framework for medical devices version 1.14 (03-2013)
- Ministero della Salute - Circolari della Direzione Generale

Sinergie DM e Farmaco





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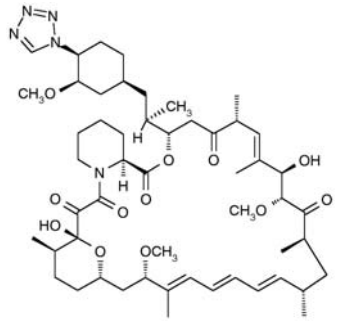
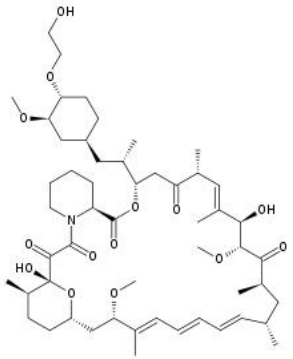


Zotarolimus



Everolimus

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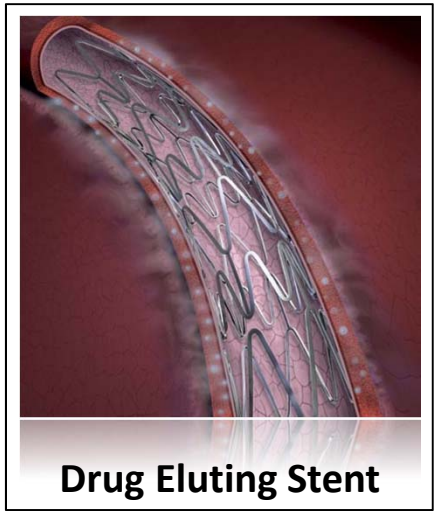

Sinergie DM e Farmaco

Circulation

American Heart

Nature Reviews Card

Interventiona
are superior t
patients

Alexandra King

Original article

Douglas, P. S. *et al*
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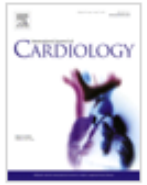
International Journal of Cardiology

Available online 13 May 2011

In Press, Corrected Proof — Note to users



Drug-eluting stents perform better than bare metal stents in small coronary vessels: A meta-analysis of randomised and observational clinical studies with mid-term follow up

Bernardo Cortese[a], Alessandra Bertoletti[b], Sara De Matteis[c, d], Gian Battista Danzi[b], Adnan Kastrati[e]

[a] Interventional Cardiology, Ospedale Humanitas Gavazzeni, Bergamo, Italy

[b] Cardiologic Department, Ospedale Maggiore Policlinico, Milano, Italy

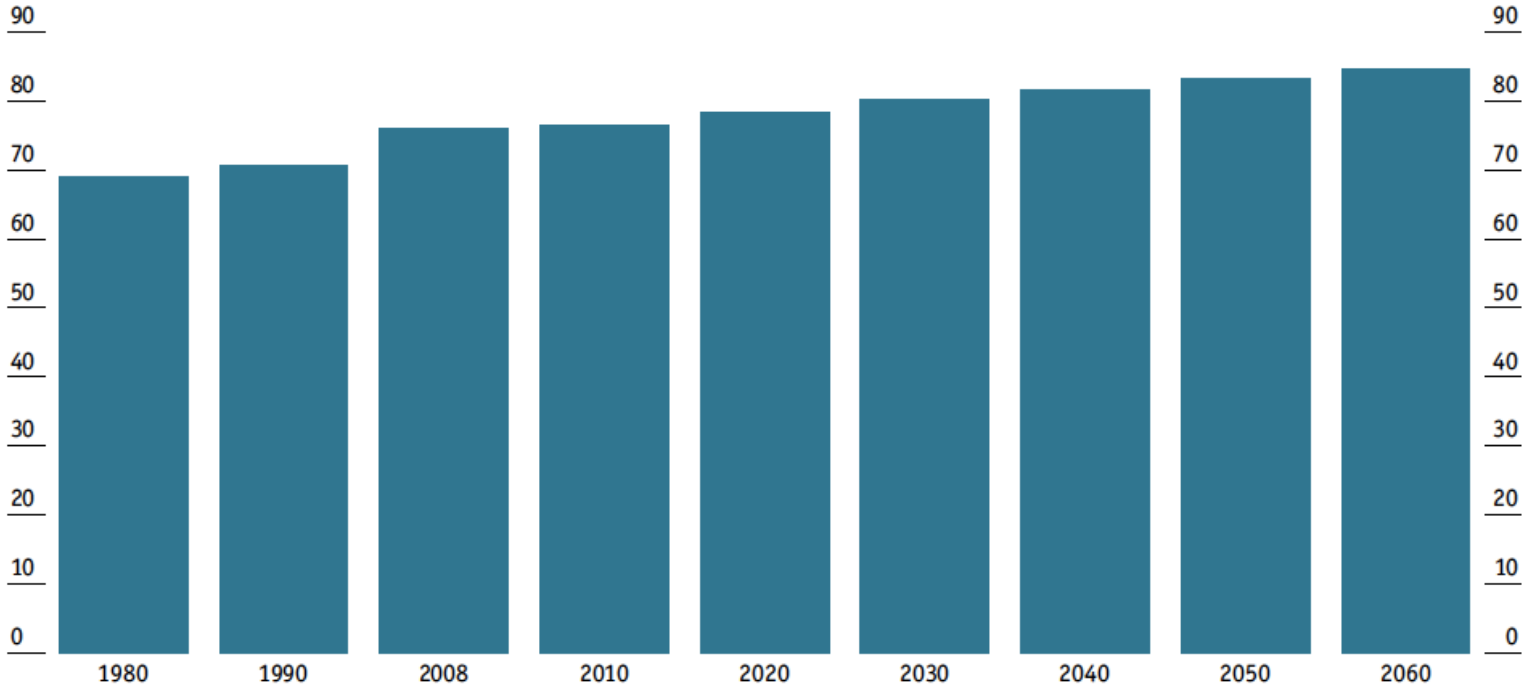
[c] Unit of Epidemiology, Department of Preventive Medicine, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Italy

[d] EPOCA Research Center, Department of Occupational and Environmental Health, Università degli Studi di Milano, Milan, Italy

[e] Department of Cardiology, Deutsches Herzzentrum, Technische Universität, Munich, Germany

Sinergia DM e Farmaco

- Quali sono le opportunità?
- Quali sono le prospettive?



Source: Eurostat

Opportunità

- Sviluppo di nuove soluzioni terapeutiche che permettano prestazioni (efficacia e sicurezza) non altrimenti ottenibili da un'applicazione separata di prodotti farmaceutici o di dispositivi medici.
- Innovazione economicamente sostenibile

Opportunità – Drug Delivery Devices

Esempio 1: Drug Eluting Stent

Riduce la probabilità di recidiva e di conseguenza i costi di gestione della patologia

J Am Coll Ca
Cost ef
revascu
Bakhai A, S
TAXUS-IV I
Harvard Clini

Applied Health Economics & Health Policy:
1 March 2009 - Volume 7 - Issue 1 - pp 19-29
doi: 10.2165/00148365-200907010-00003
Original Research Articles

Cost Effectiveness of Sirolimus-Eluting Stents Compared with Bare Metal Stents in Acute Myocardial Infarction: Insights from the TYPHOON Trial

Canoui-Poitrine, Florence[1 2]; Jeanblanc, Grégoire[1]; Alberti, Corinne[3 4]; Armoogum, Priscilla[3]; Cebrian, Ana[5]; Carrié, Didier[6]; Henry, Patrick[7]; Teiger, Emmanuel[1]; Slama, Michel[8]; Spaulding, Christian[9 10]; Durand-Zaleski, Isabelle[1]

Opportunità – Drug Delivery Devices

Esempio 2: Rivestimento per impianti endossei

Rilascio controllato di farmaci per migliorare la stabilità degli impianti, l'osteointegrazione e ridurre la formazione di biofilm

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Bone

Volume 50, Issue 5, May 2012, Pages 1148–1151

Original Full Length Article

A bisphosphonate-coating improves the fixation of metal implants in human bone. A randomized trial of dental implants

Jahan Abtahi[a, b], Pentti Tengvall[c], Per Aspenberg[b]

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Received 31 October 2011. Revised 23 January 2012. Accepted 2 February 2012. Available online 10 February 2012. Edited by: Thomas Einhorn.

Opportunità – Drug Delivery Devices

Esempio 3: Microchip per rilascio di farmaci

MicroCHIPS Announces Clinical Results for First Successful Human Trial Of Implantable, Wireless Microchip Drug Delivery Device

- *Study Validates Microchip Approach to Multi-Year Drug Delivery Without Injections*
- *Novel Technology Supports Improved Patient Outcomes and Remote Medicine*

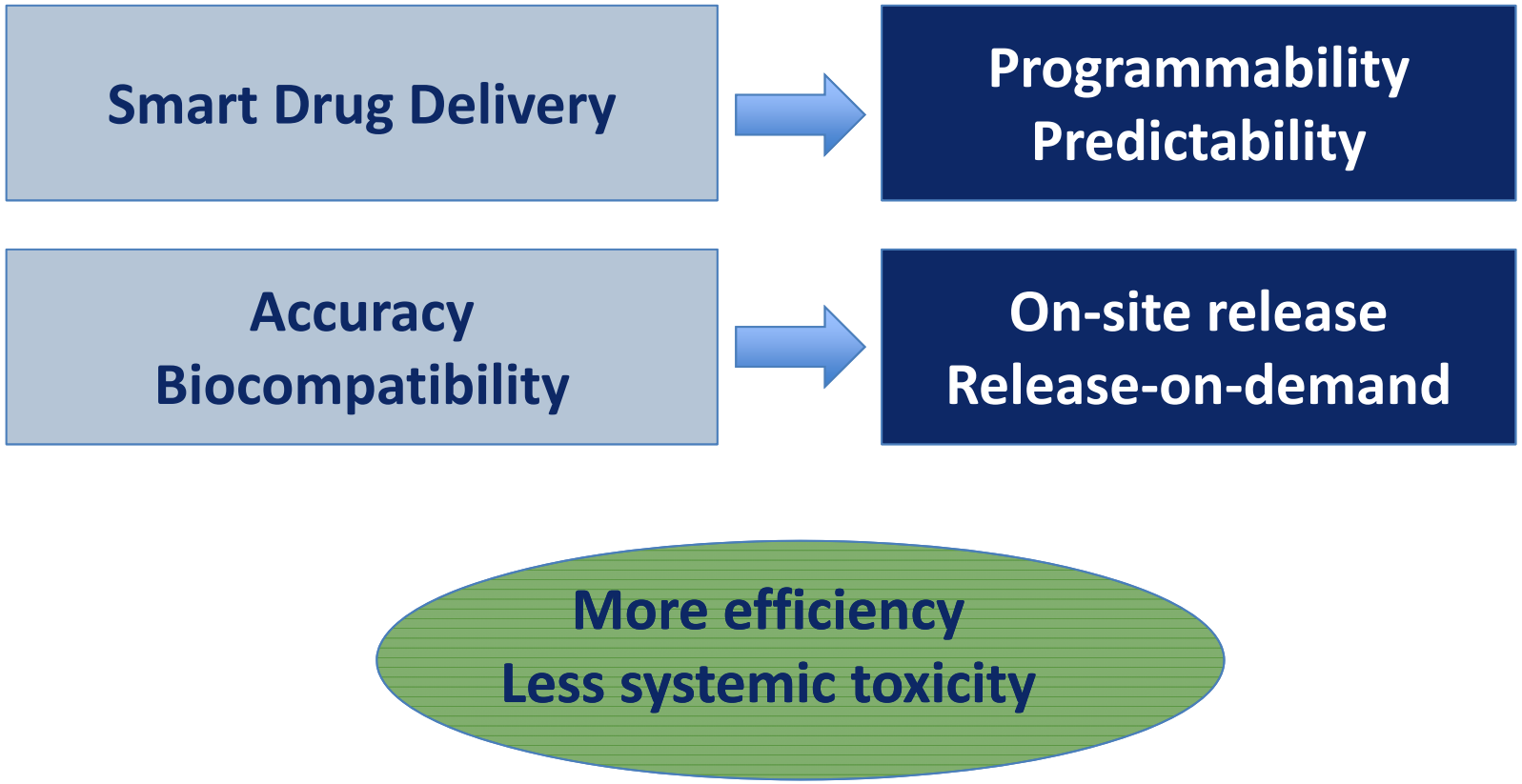
Editors Note: Digital Images/Video of MicroCHIPS device available.

WALTHAM, Mass – February 16, 2012 – MicroCHIPS, Inc., a developer of implantable drug delivery devices and biosensors, announces today the results of the first successful human clinical trial with an implantable, wirelessly controlled and programmable microchip-based drug delivery device. The MicroCHIPS study was published in today's online edition of the journal *Science Translational Medicine*.

"These data validate the microchip approach to multi-year drug delivery without the need for frequent injections, which can improve the management of many chronic diseases like osteoporosis where adherence to therapy is a significant problem," said study lead author Robert Farra, MicroCHIPS President and Chief Operating Officer. "We look forward to making further progress to advance our first device toward regulatory approvals, as well as developing a range of products for use in important disease areas such as osteoporosis, cardiovascular disease, multiple sclerosis, cancer, and chronic pain."

Opportunità – Drug Delivery Devices

Esempio 4: Nanotech



Opportunità – Drug Delivery Devices

Nanotechnology drug delivery market
$ 136 billion entro il 2021

	Daunoxome			
	Myocet			
	Epaxal			
	Inflexal V			
	DepoDur			
	Visudyne			
	Doxil		Kaposi's sarcoma	USA
	Caelyx	Doxorubicin	Ovarian cancer, Kaposi's sarcoma & breast cancer	Schering-Plough, Kenilworth, NJ, USA
	Estrasorb	Estradiol	Menopausal – Hot flushes	Novavax, Rockville, MD, USA
	Survanta	Beractant (bovine lung homogenate)	Respiratory distress syndrome	Abbott Laboratories, IL, USA
Liposomes	Alveofact	Bovactant(bovine lung lavage)	Respiratory distress syndrome	Boehringer Ingelheim GmbH, Ingelheim, Germany
	Curosurf	Poractant alfa (porcine lung homogenate)	Respiratory distress syndrome	Chiesi Farmaceutici SpA, Parma, Italy
Polymeric micelles	Genexol-PM	Paclitaxel	Cancer chemotherapy	Samyang Pharmaceutical, Daejeon City, Korea

Source: Trop J Pharm Res, june 2009
Cientifica Ltd., 2011

Conclusions

- Rapporto vincente tra farmaco e dispositivo medico
- Numerose opportunità per creare soluzioni innovative – drug delivery devices
- In questo contesto lo sviluppo delle nanotecnologie rappresenta un segmento estremamente promettente

Thank you for your kind attention!

Enrico Perfler

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