Choose certainty.
Add value.

Product Service

Klinische Bewertung und Design von Zulassungsstudien

Doz. Dr. Gerold Labek

Wien, 2018-11-06

Disclaimer

This presentation is based on information available as of today and prepared to my best knowledge.

This presentation presents my personal understanding of the medical device requirements in Europe.

Background Gerold Labek and References

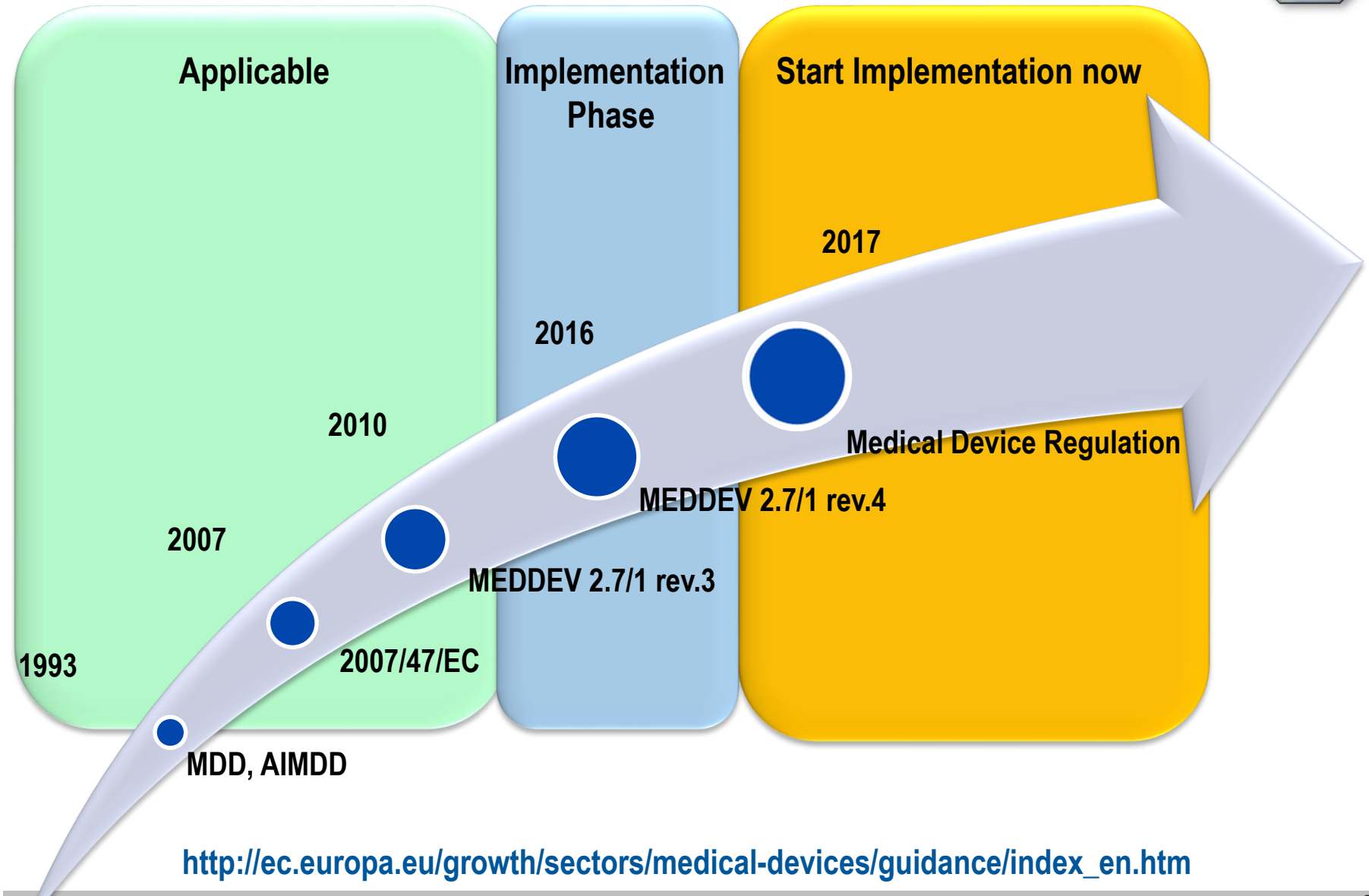
- From 1999: Registries and Research

- From 2006: EUPHORIC-Project,
  QoLA Project

- 2011: PIP, ASR
  ➔ EU Commission,

- MDR
- MEDDEV 2.7.1 and others
- IMDRF, Registry working Group, 2 Papers

Major Regulatory Updates in EU relevant for Clinical Evaluation



http://ec.europa.eu/growth/sectors/medical-devices/guidance/index_en.htm

Timelines

Grace Period

MDR

- Publication
- 20 Days Entry into force
- 6 Month Allowance to apply for designation
- Joint Assessment
- 0 - 6 Month Closure of potential Non-Conformities
- 0 - 6 Month Recommendation to the EU Commission and designation
- Publication on NANDO Webpage
- 1- 2 Years Remaining for application of Manufacturers

MDR – Art. 61.5 Equivalence

A manufacturer of a device demonstrated to be equivalent to an already marketed device not manufactured by him, may also rely on paragraph 4 in order not to perform a clinical investigation provided that the following conditions are fulfilled in addition to what is required in that paragraph:

- **the two manufacturers have a contract** in place that explicitly allows the manufacturer of the second device **full access** to the **technical documentation** on an ongoing basis
- the **original clinical evaluation** has been performed in compliance with the requirements of **this regulation**
- the manufacturer of the second device provides **clear evidence there of to the notified body**

Equivalence Route

MDD - In the case of implantable devices and devices in Class III ***clinical investigations*** shall be performed **unless it is duly justified to rely on existing clinical data**. If demonstrated, equivalence is possible.

I NEED:
- full access to your TD
- your clinical investigation to be reviewed by our NB
- you to sign this in a

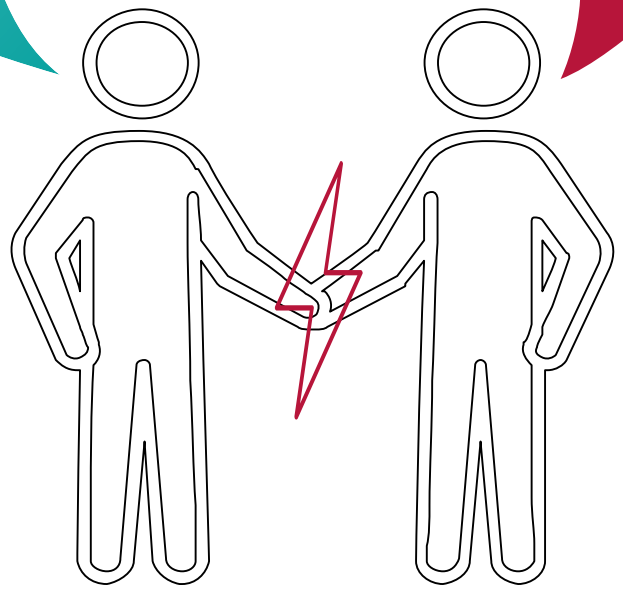
MDR

?!?
Surely not!

EU Regulation - Article (61)

Device Iteration or

…



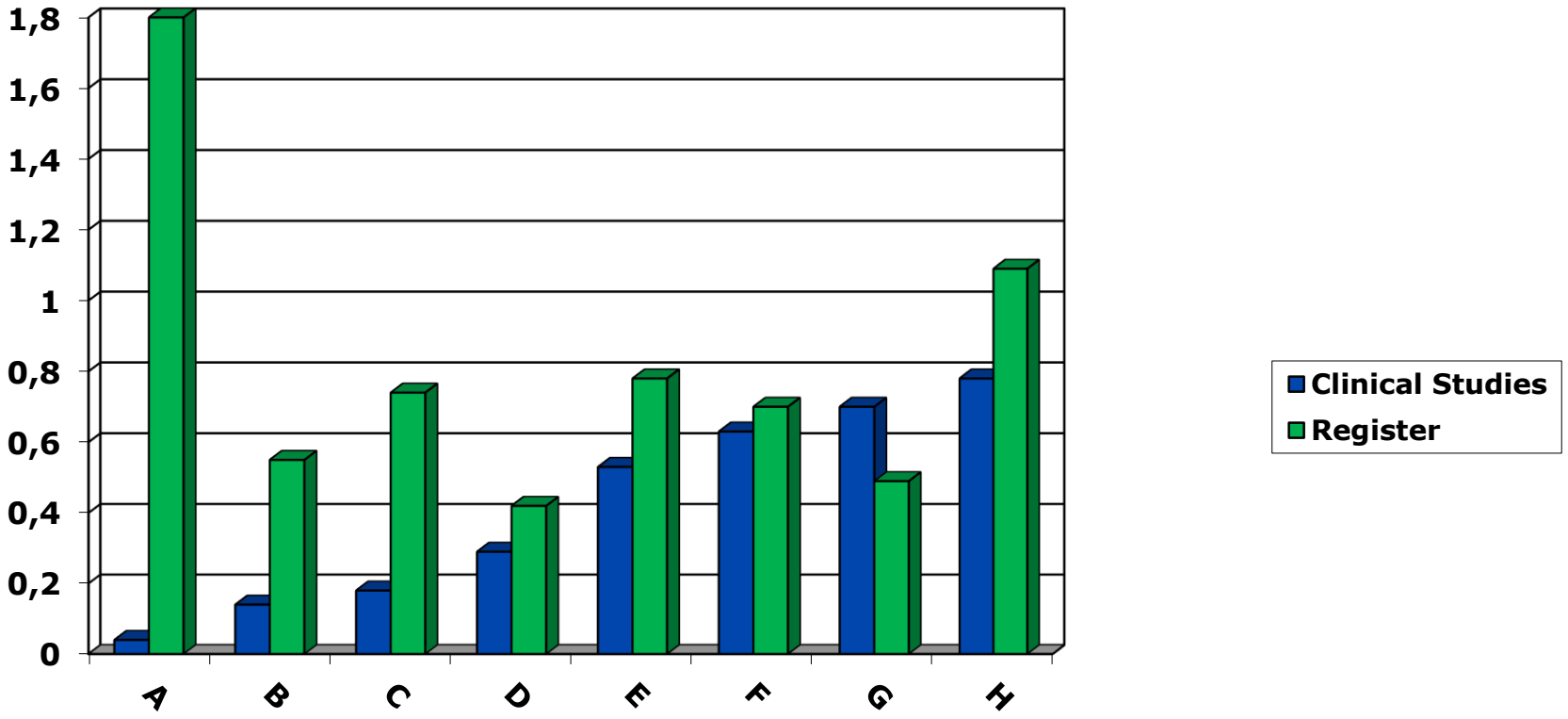
Manufacturer A Manufacturer B

EU Regulation - Article (61) 6.a

The requirement to perform clinical investigations pursuant to previously presented requirements shall not apply to implantable devices and devices falling into class III:

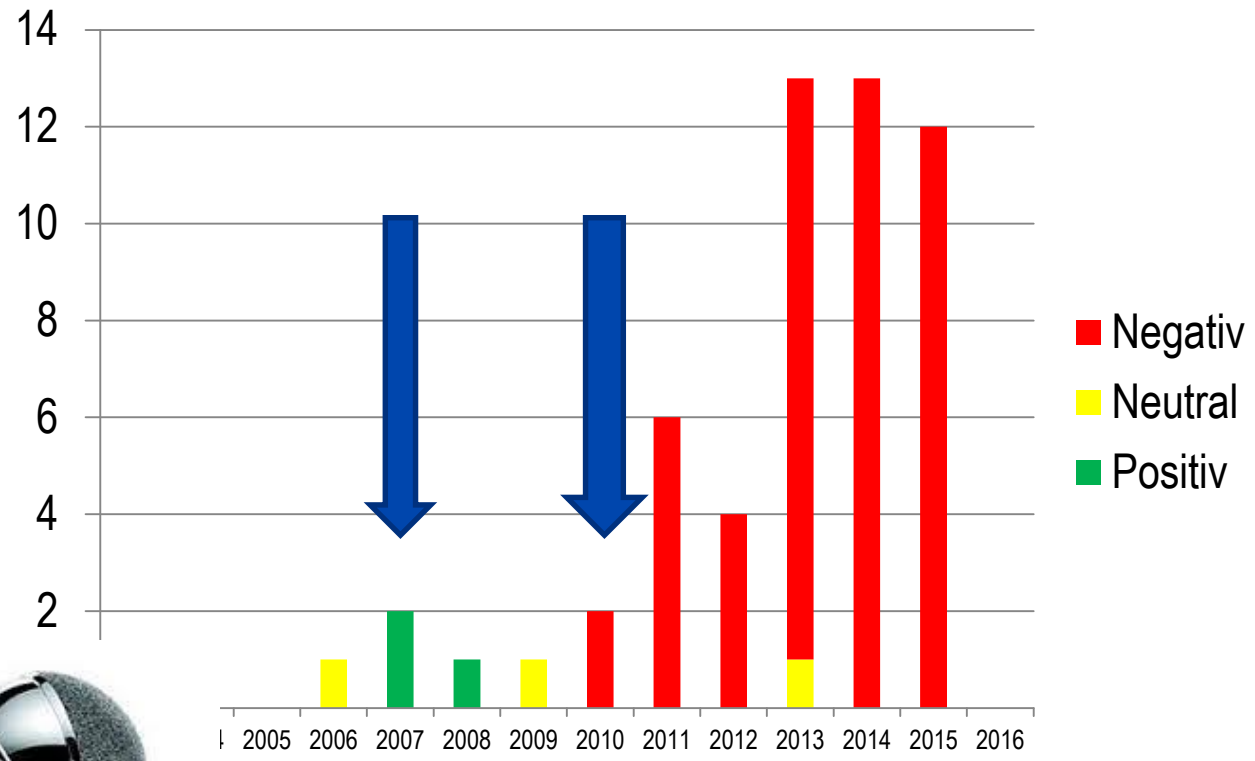
- which have been lawfully placed on the market or put into service in accordance with Directive 90/385/EEC or Directive 93/42/EEC and for which the clinical evaluation
- is based on **sufficient clinical data**
- is in compliance with the relevant product-specific common specification for the clinical evaluation of that kind of device, where such a common specification is available

Validity of Clinical Studies



ASR Publications

- 58 Articles with clinical outcome data



Reporting Incidences

	FUP-periode	Revision rate	Primary cases	Revision cases	Observed component years	Revisions per 100 observed component years	CI	factor Difference to Register 2007
immer-Data post marketing surveillance	1,00	0,63	480	3	480,00	0,63	0,21-1,82	3,2
Zimmer ponsored study	4,50	0,00	386	0	1737,00	0,00		
Total market monitoring		0,35	866	3	2217	0,14	0,05-0,4	14,78
Examination immer USA best centres	1	0,6	1300	8	1300,00	0,62	0,31-1,21	3,25
Examination Zimmer USA all centres	1	1,5	1300	20	1300,00	1,54	1,0-2,36	1,3
Australian Arthroplasty Register 2007		2,3	341	8	408	2	0,85-3,86	
2014 Global		8,79	4541	399	33270	1,2	1,09-1,32	

Revision rate increased at the Zimmer-Investigation at a ratio of **11**

Clinical Data Sources

- Clinical Studies (any kind, systematic search strategy)
- Systematic Reviews
  - Cochrane
  - HTA
  - Metaanalyses
  - Guidelines, Consensus Papers

Clinical Studies

- Implant Registry Reports

Market Experience / Real World Evidence

Starting Position

Medical Devices ➔ highly regulated Business

Processes are defined by law ➔ Requirements

Sometimes legal processes are not ahead of the trend and have long transation periodes

Loan


ZZz
Kredit ohne Stress.
OK
OK – der Online-Kredit.
Bis 30.000 € rund um die Uhr bequem online beantragen.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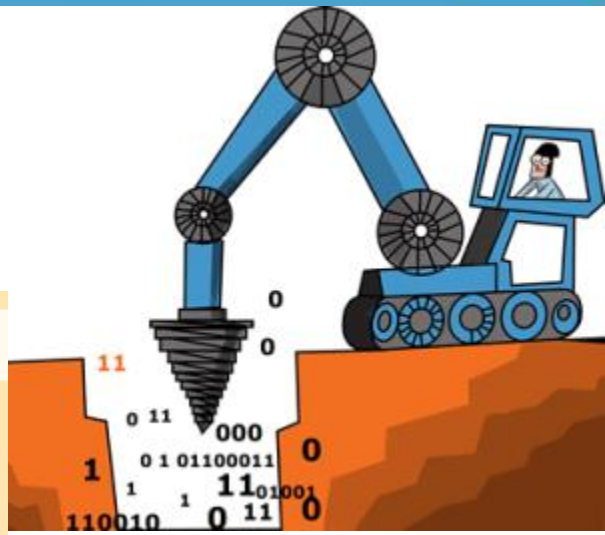
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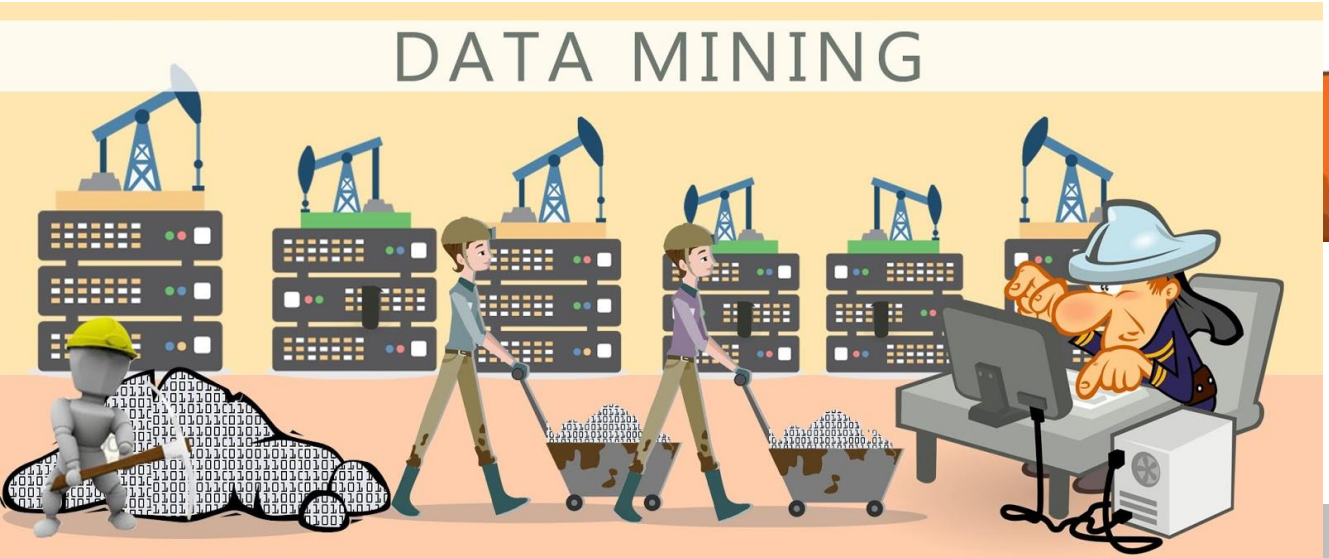
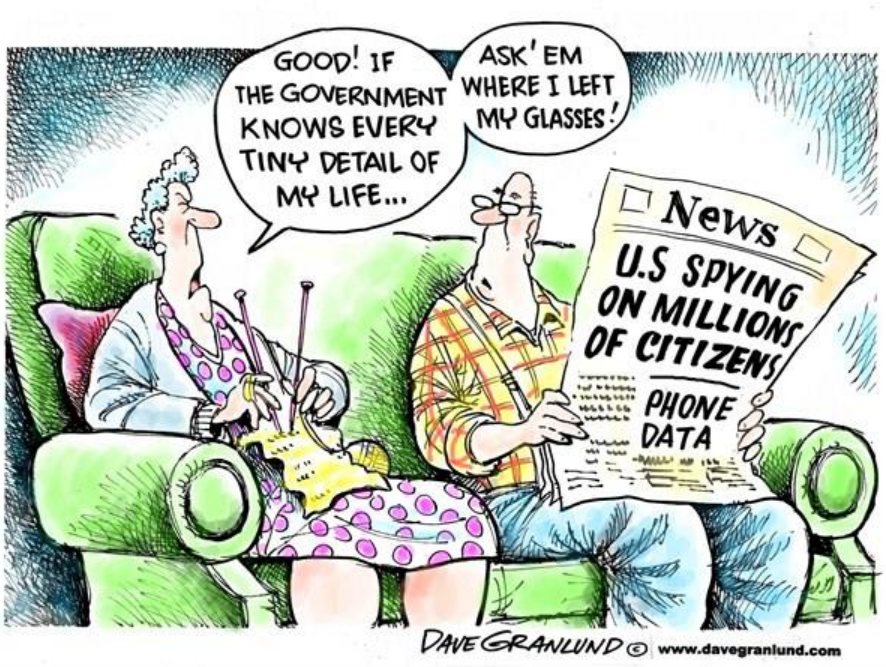

DATA MINING



Is this the place to learn about mining?


MAKE DATA GREAT AGAIN
"BIG" DATA IS SO SAD. WITH ME, YOU WILL GET "YUGE" DATA, AND WE WILL MAKE DATA GREAT AGAIN!

R.I.P.

There were no clinical data


SIMPLE. ALL WE DO NOW IS CONNECT THEM!
U.S. INTELLIGENCE AGENCIES
CARLSON 07.10
UNIVERSAL UCLICK
CARLSONTOONS.COM

Another highly regulated business

- Aircraft engines:
  - 250.000 Parameter at operation
  - Part real time transfer
  - Safety, Maintenance, Performance

- 9.000 Business Jet Engines
- 24x7 support by „Business Aviation Centre“ Dahlewitz/Berlin
- 350.000.000 datasets

Register - AHRQ Definition

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Registries

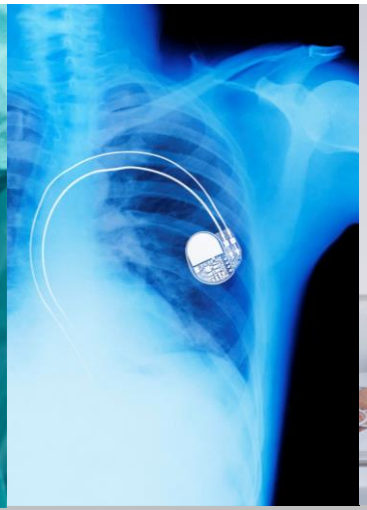
- **In fact any data collection without defined termination**
- Examples:
  - Quality/Patient Registries (well known in arthroplasty, cardiology, others in development)
    - National
    - Regional
    - Local, institutional (hospital routine documentation)
    - By Manufacturers
  - Reimbursement and discharge data
    - „Sick funds“
    - Internal quality monitoring at public health institutions
  - Data generated by active medical devices
  - Telemedicine related to medical devices/diagnostics
    - In development (apps)
    - Monitoring of pacemakers
    - Monitoing of diagnostic measures by physicians
  - Cohort studies
  - …….

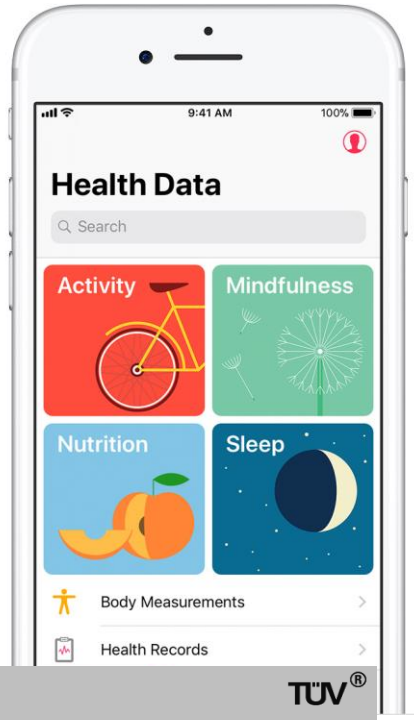
Examples

- Non Active Devices ➔ Quality Registries, Customer Feedback like stuctured Surveys,
- Active Medical Devices ➔ Data from the devices use/framework (ICU)
- Software ➔ generate data by use

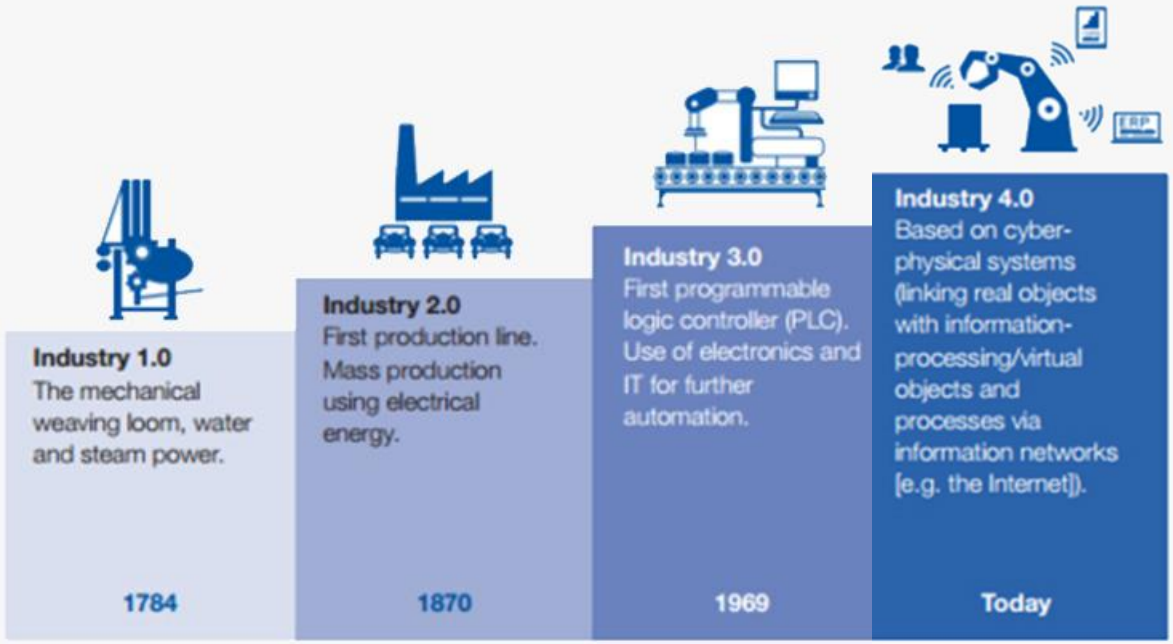
- All devices:
  - Discharge records
  - Hospital internal system
  - Payers (Sick Funds, AOK, Medicare)

- **Every Company/Device need it´s own solution**





The general perspective



Why Clinical Data are a Top Issue?

Design | Production | Risk Management | Use of Device | Patients

Health System/Access to Device | ……

Clinical Data provide information on the outcome of the entire treatment chain
➔ „final validation“

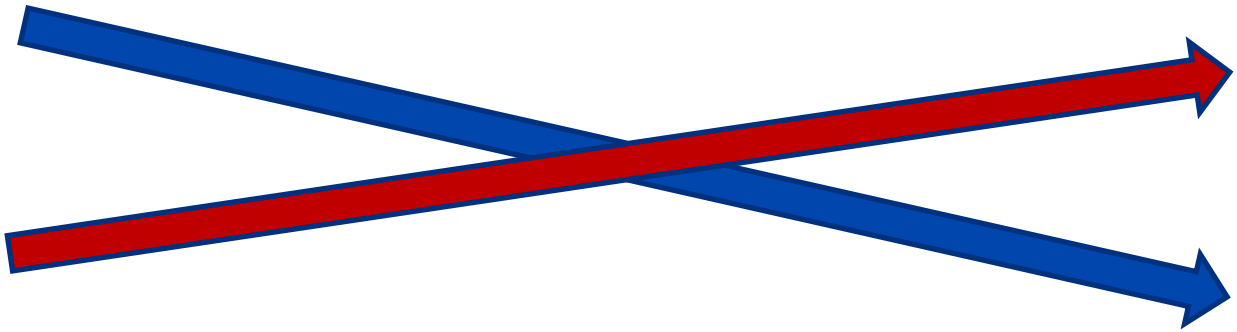
Evaluation of Clinical Data

Confounders

Statistics
(N Patients, Data – Nominal, ordinal. Metric,.)

Methodology
(Selection Bias, Documentation Bias,…)

Treatment Outcome
(Users, Patients, Implantation,…)



RCT

Registries

Pharma

Med. Dev.

Follow Up Studies

EU Regulation – Post-Approval

Limited Data → Big Data

EU Regulation – Post-Approval

The manufacturers should:

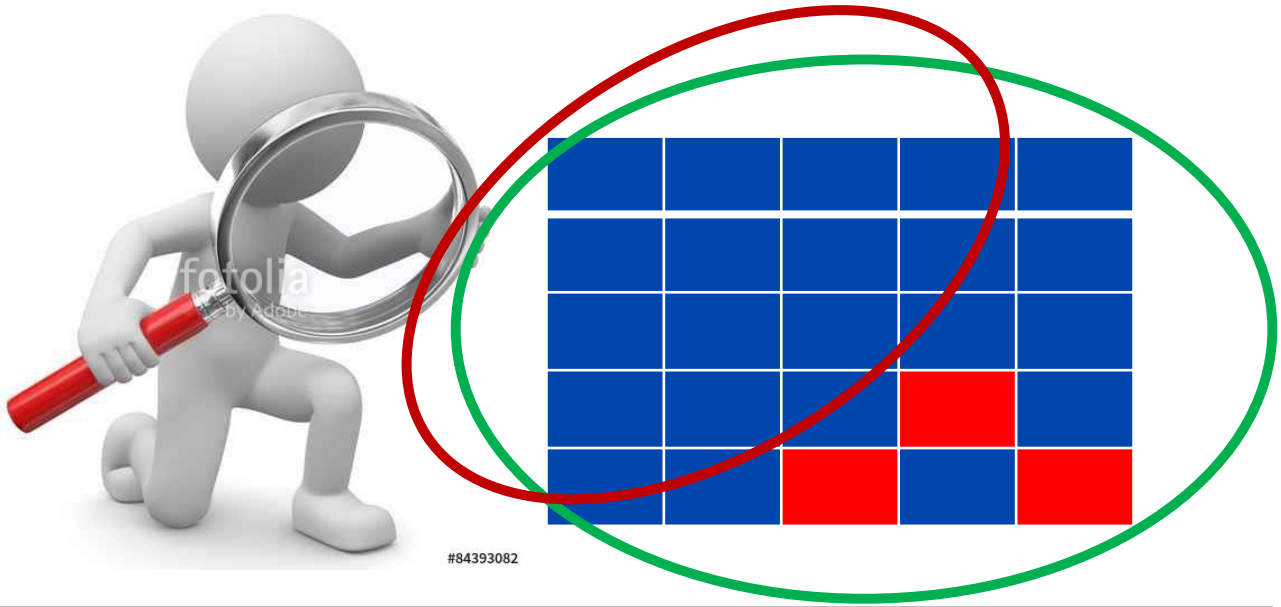
- establish a comprehensive post-market surveillance (PMS) system
- set up under the quality management system
- and based on a PMS plan.

*

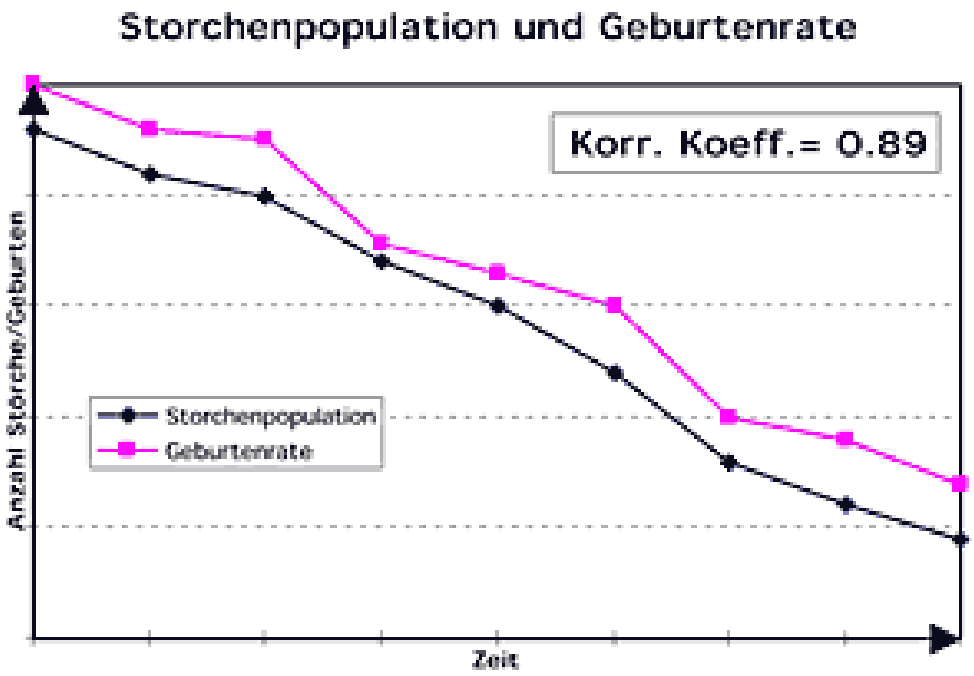
Dead to Head Comparative Studies

- Sample based Clinical Study
  - Inclusion/Exclusion Criteria
  - Statistical Power

- Register



Stork Population and Birth Rate in Europe



- RWE:
- good tool to detect Correllation

- Causality
  ➔ process assessment insufficient
  ➔ expert know how in medical field

- US TVT-Registry + EU Registry Data
- Inoperable Patients
- Alternative approach

- Approval based only on RWE-data without any study

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

THE CHANGING FACE OF CLINICAL TRIALS

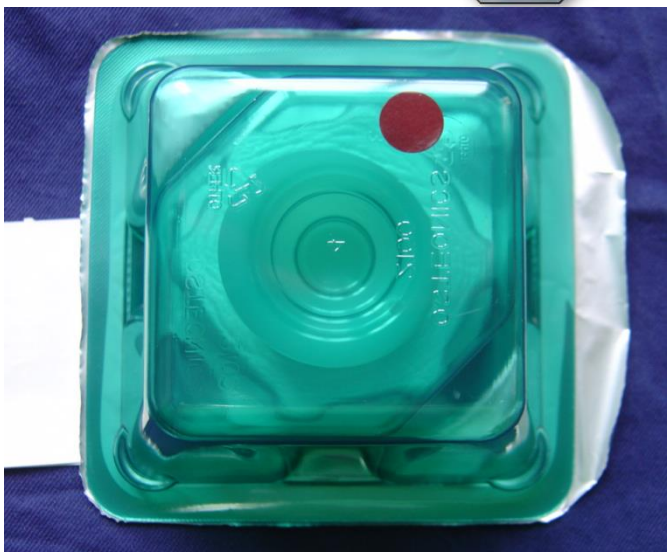
Jeffrey M. Drazen, M.D., David P. Harrington, Ph.D., John J.V. McMurray, M.D., James H. Ware, Ph.D., and Janet Woodcock, M.D., *Editors*

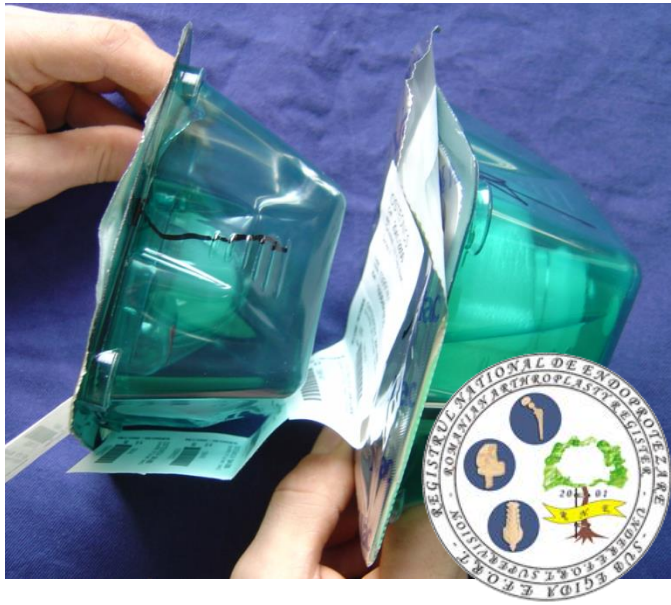
An FDA Viewpoint on Unique Considerations for Medical-Device Clinical Trials

Owen Faris, Ph.D., and Jeffrey Shuren, M.D., J.D.

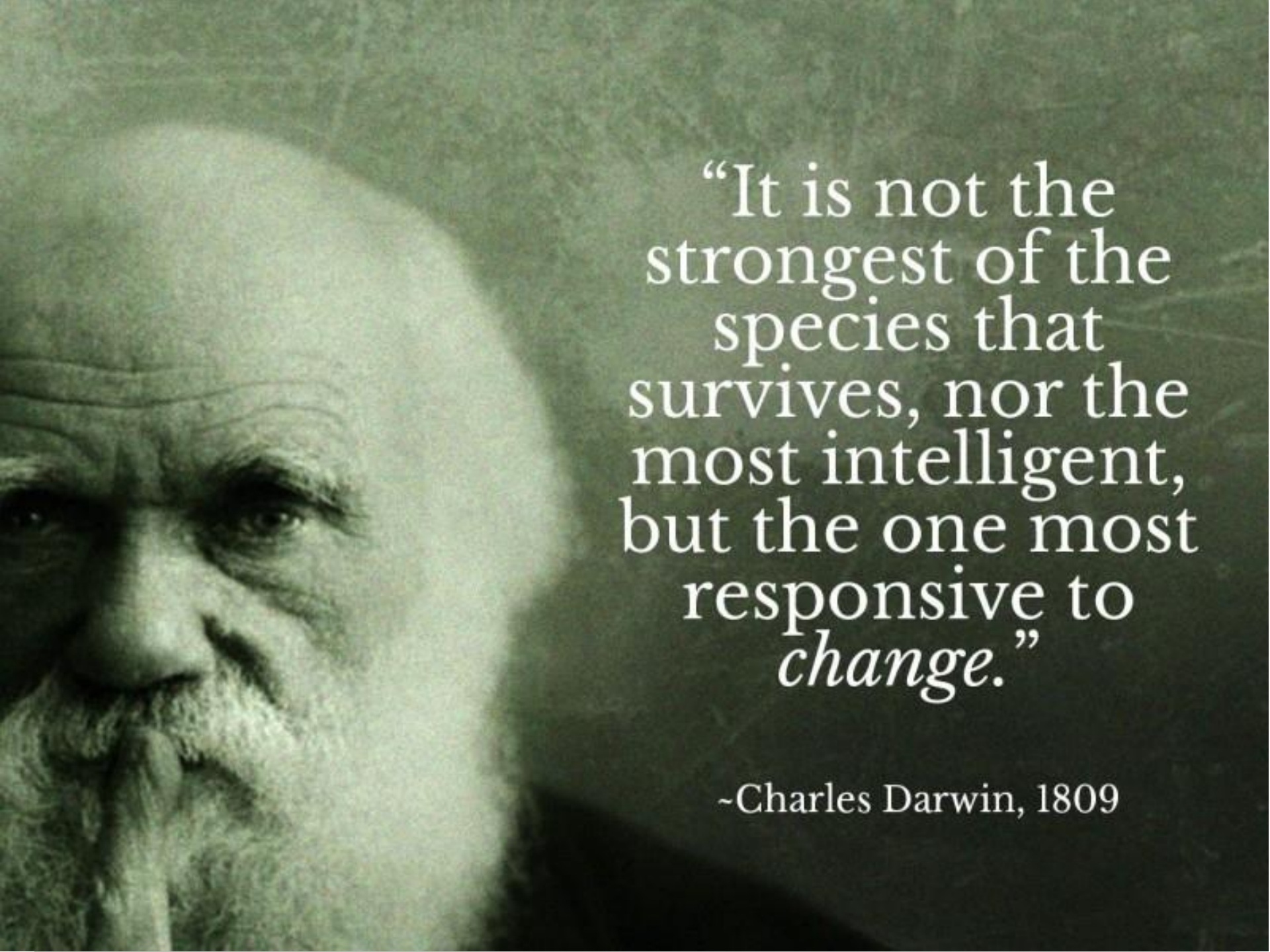
MEDICAL DEVICES PLAY A CRITICAL ROLE IN THE LIVES AND HEALTH OF millions of people worldwide. From everyday household items such as oral thermometers to complex implantables such as deep-brain stimulators,

Registries are Communication Networks






DISRUPT
SHAKE UP
CHALLENGE
EVOLVE
CHANGE


"It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to *change*."
~Charles Darwin, 1809

LISAvienna life science austria

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Michael Fürsch, Chief Compliance Officer & Co-Founder, mySugr GmbH und
Martin Schmid, Geschäftsführer, en.co.tec Schmid KG – Consulting & Akademie für Medizinprodukte & IVD

E) Testing & Post Market Surveillance

1. Block: Testing von aktiven Medizinprodukten

Rouven Rosenheimer, Senior Account Manager Active Medical Devices, TÜV SÜD Product Service GmbH

2. Block: Post Market Surveillance

Gerold Labek, Director Clinical Market Surveillance, Clinical Centre of Excellence, TÜV SÜD Product Service GmbH

Choose certainty.
Add value.

Product Service

Questions?

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gerold.labek@tuev-sued.de