CORE-MD

Coordinating Research and Evidence for Medical Devices

6th March 2023

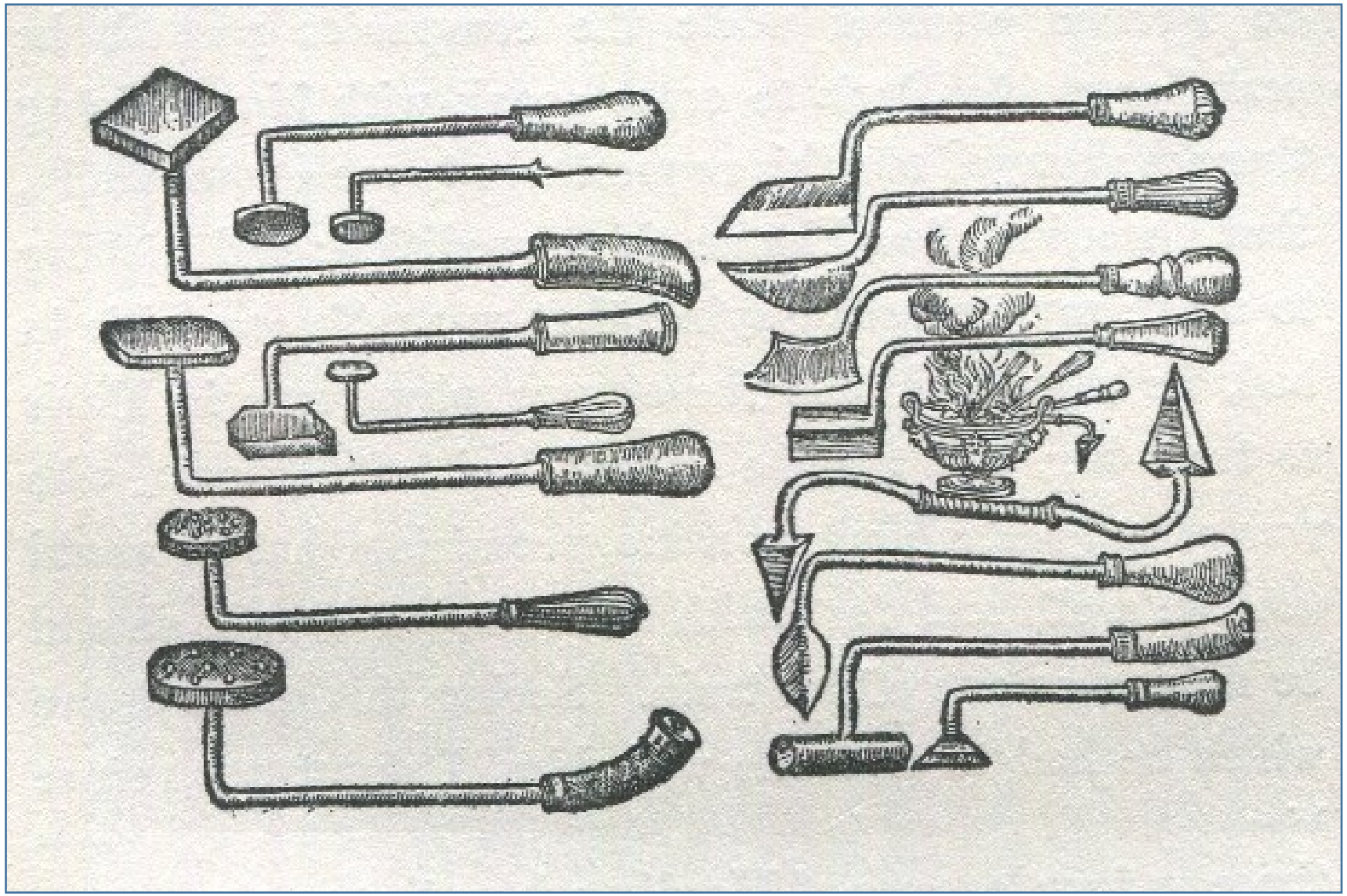
CORE–MD webinar #2

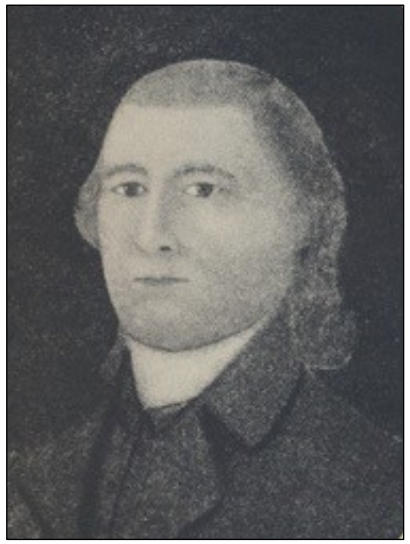
The history of regulation for devices in Europe

Alan G Fraser, European Society of Cardiology

Ambroise Paré

Different sorts of cauteries, 1585





Dr Elisha Perkins (1741–1799)

“ Metallic Tractors ”

- 8 cm
- steel and brass

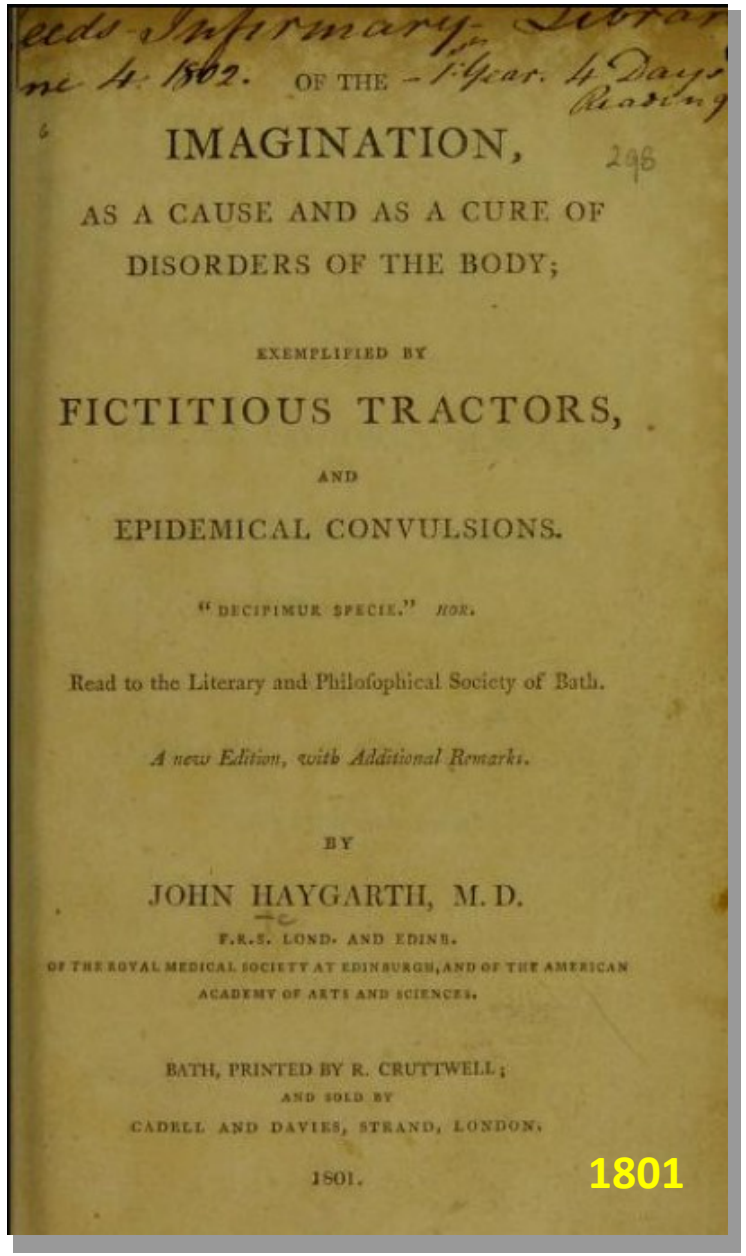
- pain, rheumatism, and inflammation
- drawn downwards for 20 minutes
- “draw off the noxious electrical fluid that lay at the root of suffering”

Miller WS, Yale J Biol Med. 1935; 8: 43

Dr John Haygarth (1740–1827)

“ Fictitious Tractors ”

On the imagination as a cause and as a cure of disorders of the body



Imitation tractors made of wood and painted to look real

- equally wonderful results produced as long as patients believed them to be the real thing
- no effects when patients were aware that imitations

Real tractors had no effects when patients had never heard of them and knew nothing of their wonderful powers

Sitzungs-Berichte
der
Physikalisch-medicinischen Gesellschaft
zu
WÜRZBURG.

Jahrgang 1895. | Der Abonnementspreis pro Jahrgang beträgt ℳ 4.—. Die Nummern werden einzeln nicht abgegeben. Grössere Beiträge erscheinen in Sonderdrucken. | No. 9.

Verlag der Stahel'schen k. Hof- und Universitäts-Buch- und Kunsthandlung in Würzburg.

Am 28. Dezember wurde als Beitrag eingereicht:

W. C. Röntgen: Ueber eine neue Art von Strahlen.

(Vorläufige Mittheilung.)

1. Lässt man durch eine *Hittorf*sche Vacuumröhre, oder einen genügend evacuirten *Lenard*'schen, *Crookes*'schen oder ähnlichen Apparat die Entladungen eines grösseren *Ruhmkorff*'s gehen und bedeckt die Röhre mit einem ziemlich eng anliegenden Mantel aus dünnem, schwarzem Carton, so sieht man in dem vollständig verdunkelten Zimmer einen in die Nähe des Apparates gebrachten, mit Bariumplatincyanür angestrichenen Papierschirm bei jeder Entladung hell aufleuchten, fluoresciren, gleichgültig ob die angestrichene oder die andere Seite des Schirmes dem Entladungsapparat zugewendet ist. Die Fluorescenz ist noch in 2 m Entfernung vom Apparat bemerkbar.

Man überzeugt sich leicht, dass die Ursache der Fluorescenz vom Entladungsapparat und von keiner anderen Stelle der Leitung ausgeht.

2. Das an dieser Erscheinung zunächst Auffallende ist, dass durch die schwarze Cartonhülse, welche keine sichtbaren oder ultravioletten Strahlen des Sonnen- oder des elektrischen Bogenlichtes durchlässt, ein Agens hindurchgeht, das im Stande ist, lebhafte Fluorescenz zu erzeugen, und man wird deshalb wohl zuerst untersuchen, ob auch andere Körper diese Eigenschaft besitzen.

Man findet bald, dass alle Körper für dasselbe durchlässig sind, aber in sehr verschiedenem Grade. Einige Beispiele führe ich an. Papier ist sehr durchlässig:[1]) hinter einem eingebun-

[1]) Mit „Durchlässigkeit" eines Körpers bezeichne ich das Verhältniss der Helligkeit eines dicht hinter dem Körper gehaltenen Fluorescenzschirmes zu derjenigen Helligkeit des Schirmes, welcher dieser unter denselben Verhältnissen aber ohne Zwischenschaltung des Körpers zeigt.

Würzburg Physico-Medical Society, 28.12.1895

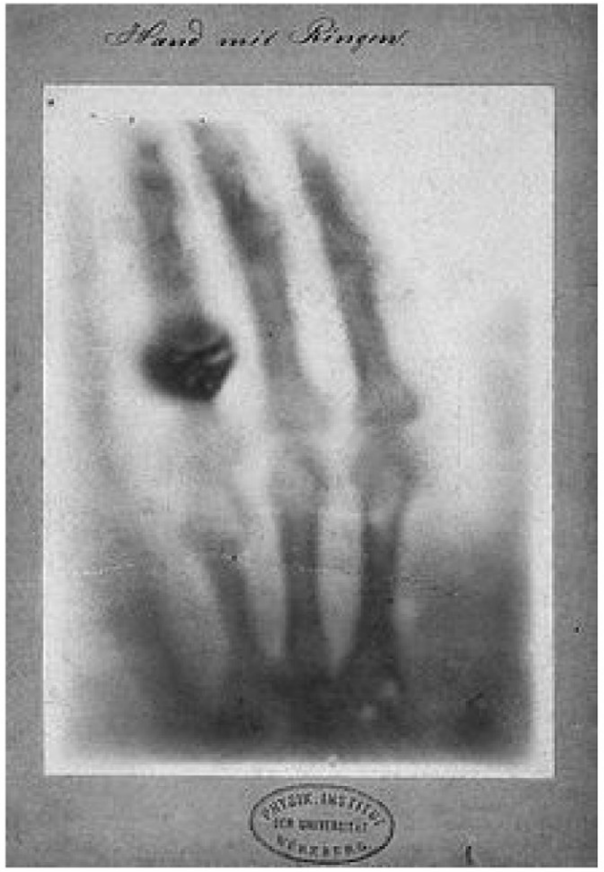
Über eine neue Art von Strahlen

[On a new kind of rays]

22.12.1895

" Hält man die Hand zwischen den Entladungsapparat und den Schirm, so sieht man die dunkleren Schatten der Handknochen in dem nur wenig dunklen Schattenbild der Hand "

Anna Bertha Ludwig:
"I have seen death"



“Chronic dermatitis” after exposure to Roentgen rays

St Bartholomew's Hospital Archives & Museum, Wellcome Collection

X-RAY AND RADIUM PROTECTION.

THE X-ray and Radium Protection Committee, representing various radiological and other scientific bodies in this country, has issued a preliminary report which sets out present knowledge in regard to equipment, ventilation and working conditions of X-ray and radium departments.

The committee proposes to investigate experimentally a number of points which have arisen. Offers of assistance are invited by the committee, and should be sent to the Hon. Secretaries, from whom copies of the preliminary report may be had on application.

The Committee is constituted as follows :—

Chairman : Sir Humphry Rolleston, K.C.B. *Members :* Sir Archibald Reid, K.B.E., C.M.G., St. Thomas's Hospital ; Dr. Robert Knox, King's College Hospital ; Dr. G. Harrison Orton, St. Mary's Hospital ; Dr. S. Gilbert Scott, London Hospital ; Dr. J. C. Mottram, Pathologist, Radium Institute ; Dr. G. W. C. Kaye, O.B.E., National Physical Laboratory ; Mr. Cuthbert Andrews, *Hon. Secretaries :* Dr. Stanley Melville, St. George's Hospital ; Prof. S. Russ, the Middlesex Hospital. *Address :* Care of Royal Society of Medicine, 1, Wimpole Street, W.1.

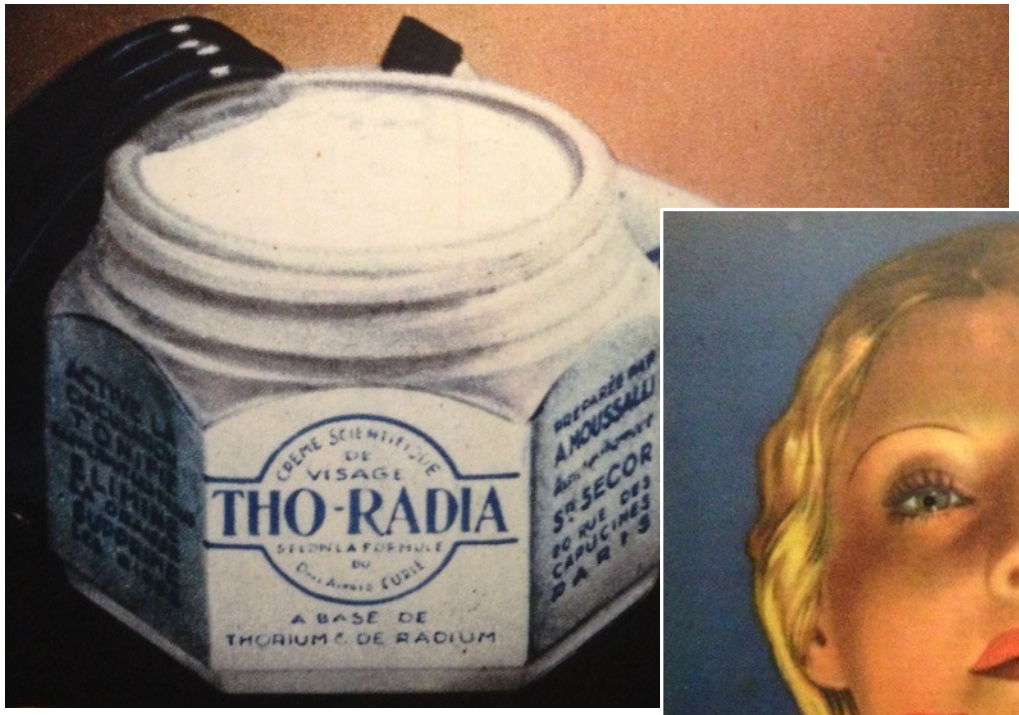
X-RAY AND RADIUM PROTECTION COMMITTEE. PRELIMINARY REPORT.

INTRODUCTION.

The danger of over-exposure to X-rays and radium can be avoided by the provision of efficient protection and suitable working conditions.

INTERNATIONAL RECOMMENDATIONS FOR X-RAY AND RADIUM PROTECTION

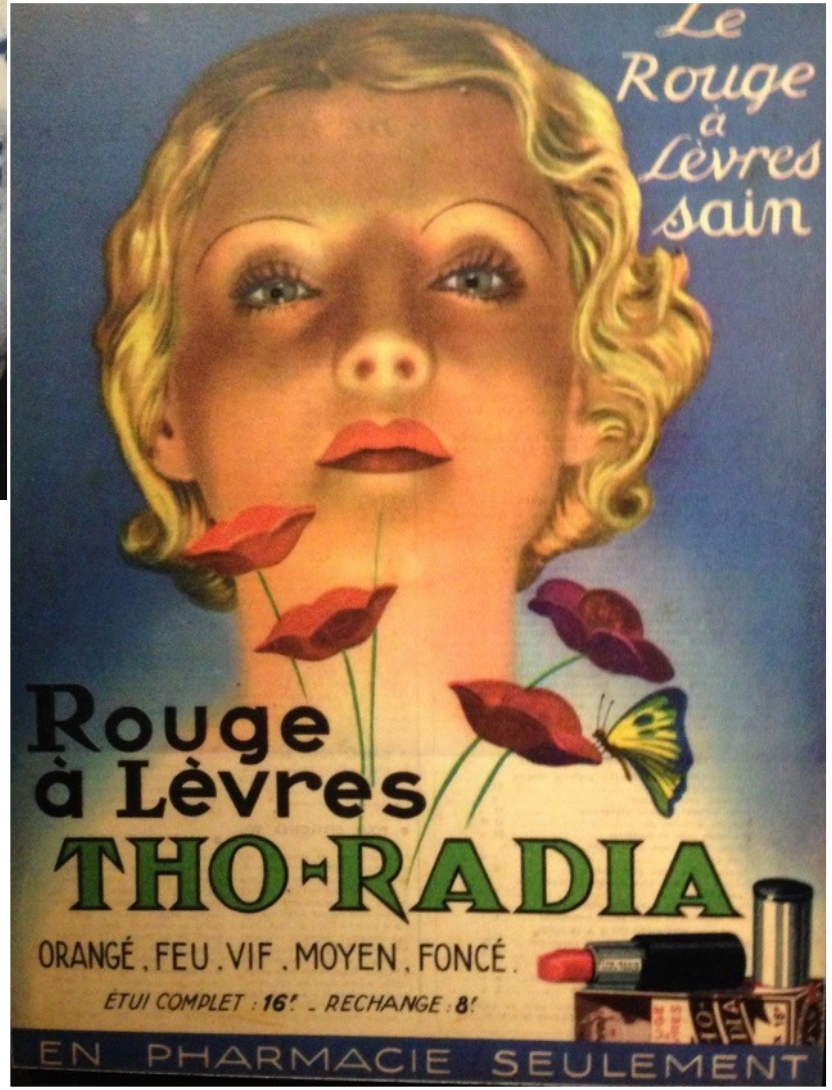
on the proposal of the Radio-Physics Section adopted by the Second International Congress of Radiology in Stockholm, July 27th, 1928



Crème scientifique à base de thorium et de radium

Prohibited late 1930s.

Radiation regulated in EU by DG ENER



High-risk implantable medical devices are a late 20th century phenomenon

Hip arthroplasty

1891 First attempted hip replacement (ivory) / Themistocles Glück, Germany
1925 First molded hip replacement (glass) / Marius Smith-Petersen, USA
1938 First successful total hip replacement / Philip Wiles, UK
1961 "Arthroplasty of the hip: a new operation" / John Charnley, UK
1969 First FDA-approved total hip replacement / Mark Coventry, USA

Cardiac pacemaker

1958 Electrodes, pulse generator, rechargeable battery / Åke Senning, Sweden

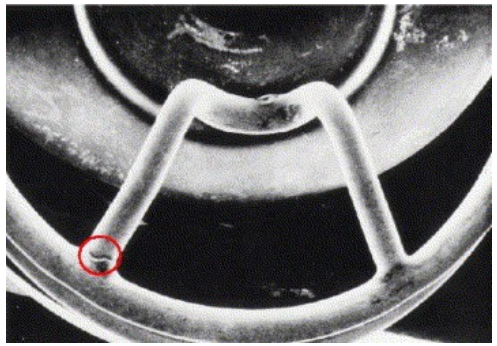
Replacement heart valve

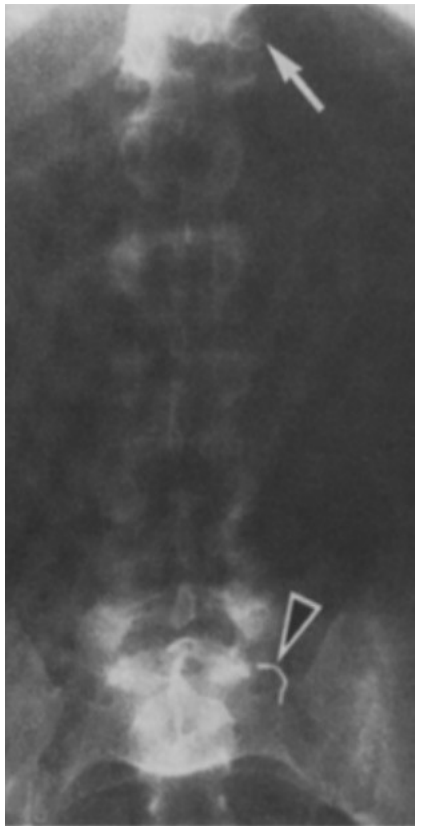
1960 Caged ball in the aortic valve position / Dwight Harken, USA

Coronary stent

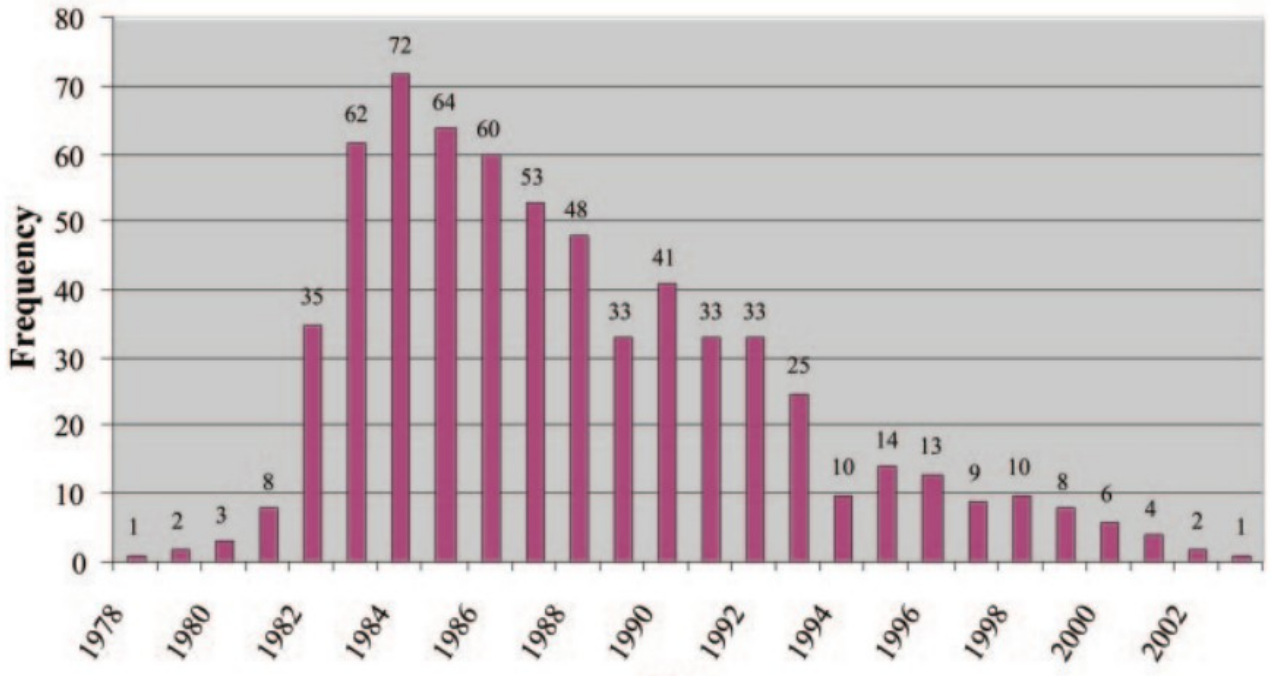
1986 First implantations in patients / Jacques Puel and Ulrich Sigwart

The Björk-Shiley convexo-concave mechanical heart valve, 1978 –





- Outlet strut welded at angle 60 or 70 degrees
- Insufficient bench testing, failure an ‘anomaly’
- Outlet strut fracture in ~1% of 86,000 valves
- 0.6% [60°] / 3.9% [70°; outside US only]
- Acute mechanical complications; 800 deaths?



van Neer P et al, Ultr Med Biol. 2006; 32: 503-12
Hiratzka L et al, J Am Coll Cardiol. 1988; 11; 1130-7
Blot W et al, Circulation. 2005; 111: 2850-7

84/539/EEC [..] relating to electro-medical equipment [..] in human [..] medicine

- **Medical device manufacturers approached the European Commission – 1987**
- Absence of a true common market for medical devices
  - complying with 5 different systems
  - for example clinical criteria in France and type definitions in Germany
  - impacting on the competitiveness of European industry
- Some countries had already delegated assessment to testing houses
- **Opportunity to apply the "New Approach"** = Council Resolution from **1985**

European Economic Community Medical Device Directives

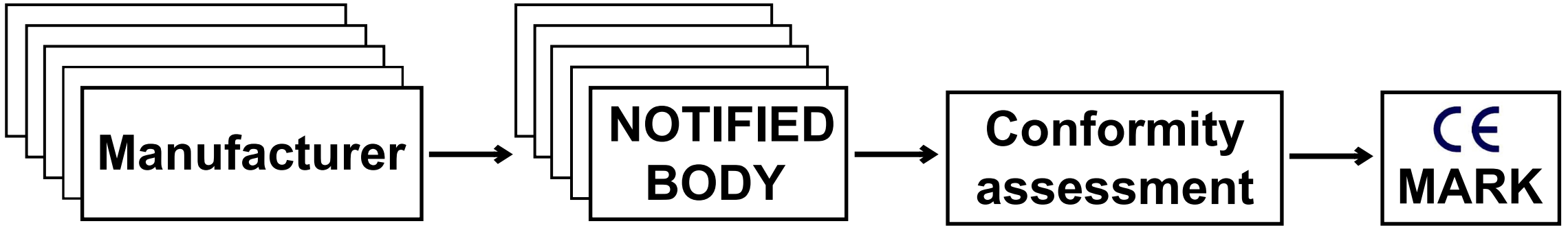
1990 90/385/EEC on Active Implantable Medical Devices (AIMDD)

1993 93/42/EEC on Medical Devices (MDD)

1998 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMD)

85/C 136/01: On a New Approach to Technical Harmonization & Standards

"National bodies authorized to issue marks or certificates of conformity shall be notified by each Member State to the Commission and to the other Member States."



November 1993: **Norbert Anselmann, Principal Administrator, European Commission**

"The Medical Device Directives follow the "New Approach", a methodology to be applied to the harmonization of industrial products. The EC legislation is confined to the setting up of Essential Requirements which are drafted in rather abstract terms. The technical expression of these requirements is ensured by European standards, the application of which is at the discretion of manufacturers."

Freedom of information in the European Union

Regulation EC 1049/2001 on public access to documents

- Wider access should be granted to documents in cases where the institutions are acting in their legislative capacity, including under delegated powers .. **documents should be made directly accessible to the greatest possible extent**.
- .. **all agencies** established by the institutions should apply the principles laid down in this Regulation
- In principle, **all documents** of the institutions should be accessible to the public.

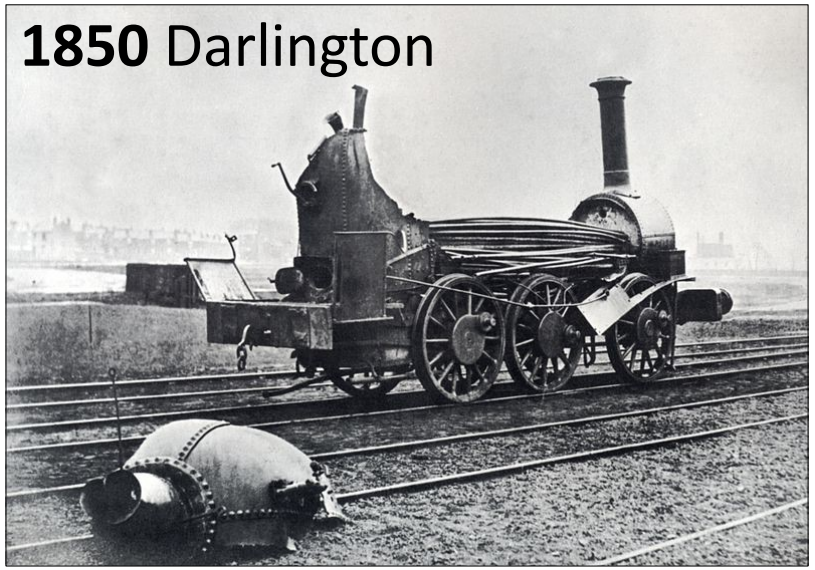
DOES NOT APPLY to Notified Bodies

http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:32001R1049

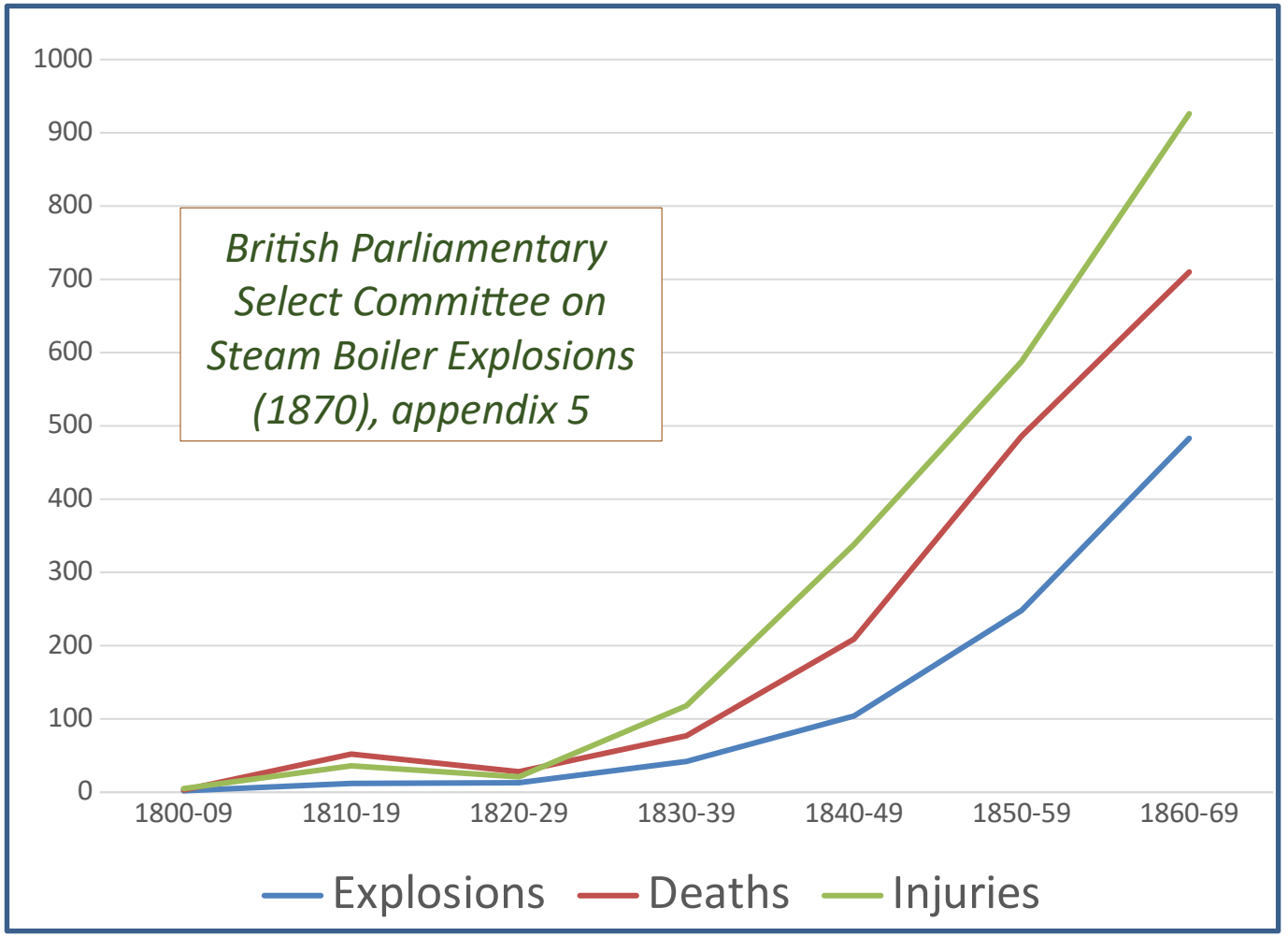
Steam boiler explosions in the 19th century

Technological development increased power output by factor of 40:

- **Horsepower** <50,000 to >2,000,000
- **Kilowatts** 37,000 to 1,500,000



- **Boiler Explosion Act 1882**

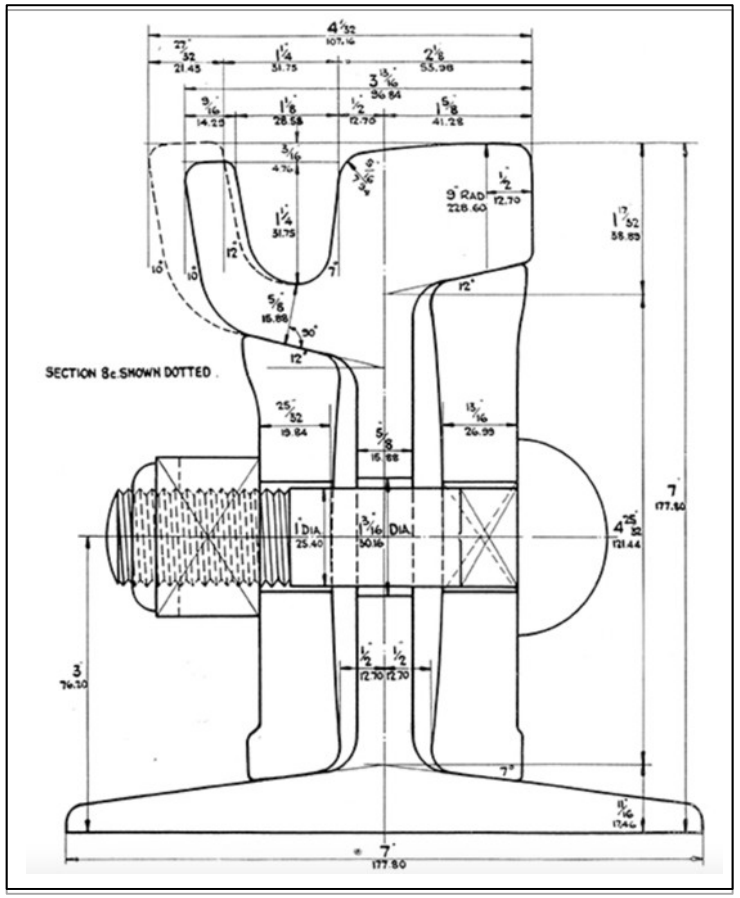


Bartrip PWJ, Int Rev Soc Hist. 1980; 25: 77–105

1901 The Engineering Standards Committee

1931 **The British Standards Institution**

1942 Recognized as the sole organisation for issuing national standards



First British Standard Cross-section of railway and tram tracks

CE

BSI Group The Netherlands B.V. / **NB 2797**

Legislations

- 93/42/EEC Medical devices
- 98/79/EC In vitro diagnostic medical devices
- 90/385/EEC Active implantable medical devices
- 2014/90/EU Marine equipment
- Regulation (EU) 2017/745 on medical devices
- Regulation (EU) 2017/746 on in vitro diagnostic medical devices

https://ec.europa.eu/growth/tools-databases/nando/index

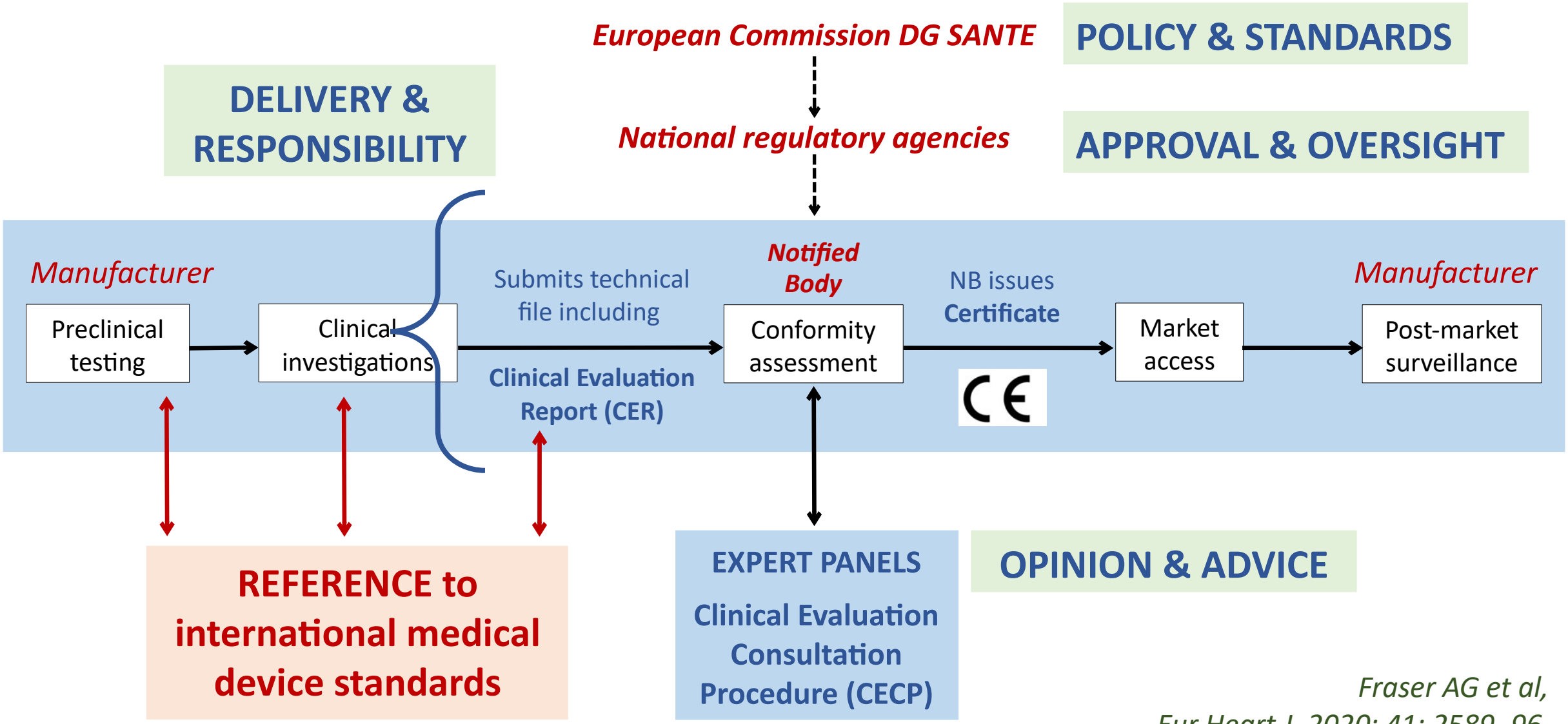
- Gesellschaft zur Überwachung und Versicherung von Dampfkesseln **1866**
  Society for the Supervision and Insurance of Steam Boilers
- Verband von Dampfkesselüberwachungsvereinen **1871**
  Union of Boiler Inspection Associations
- Internationaler Verband von Dampfkesselüberwachungsvereinen
- Bayerische Dampfkessel-Revisions-Verein **1870**
  Bavarian Steam Boiler Inspection Association
- **Technische Überwachungsvereine (TÜV)** **1938**
  14 regional technical inspection associations

TÜV SÜD

TÜVRheinland®

TÜV NORD

Evaluation and approval of high-risk medical devices under (EU) 2017/745



Fraser AG et al,
Eur Heart J. 2020; 41: 2589–96

Origins of international standards

1906 –

International Electrotechnical Commission

".. to secure the cooperation of the technical societies of the world by [..] a representative Commission to consider the question of standardization of the Nomenclature and Ratings of Electrical Apparatus and Machinery"

1926 – 1942

International Federation of National Standardizing Associations (IFA)

- To create standards for mechanical engineering
- To allow fair competition / reduce barriers to international trade

1947 –

International Standardization Organization

- 323 technical committees / >2700 subcommittees / > 22,000 standards
- Members mainly from national standards institutes and manufacturers

1961 –

1972 –

- CEN, ***Comité Européen de Normalisation***
- CENELEC, ***Comité Européen de Normalisation Électrotechnique***
- **On request, harmonize ISO and IEC standards to EU legislation**
- **Listed in Official Journal of EU**
- **Detailed technical standards for particular types of devices**

2011 –

IMDRF International Medical Device Regulators Forum

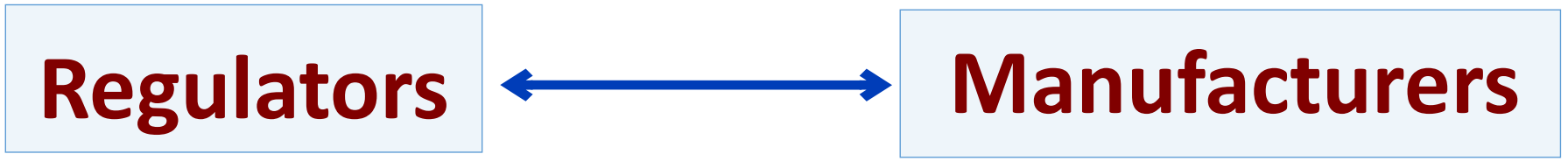
- [succeeded Global Harmonization Task Force, 1993–2012]
- Collaboration of 11 major regulatory jurisdictions
- Working Groups & Task Forces with trade association members
- **Standards for principles and processes**

Competence of EU concerning health care

2007 **<u>The Treaty of Lisbon</u>** (effective 2009): 2 C (k): Shared competence .. applies in .. ***common safety concerns in public health matters***.

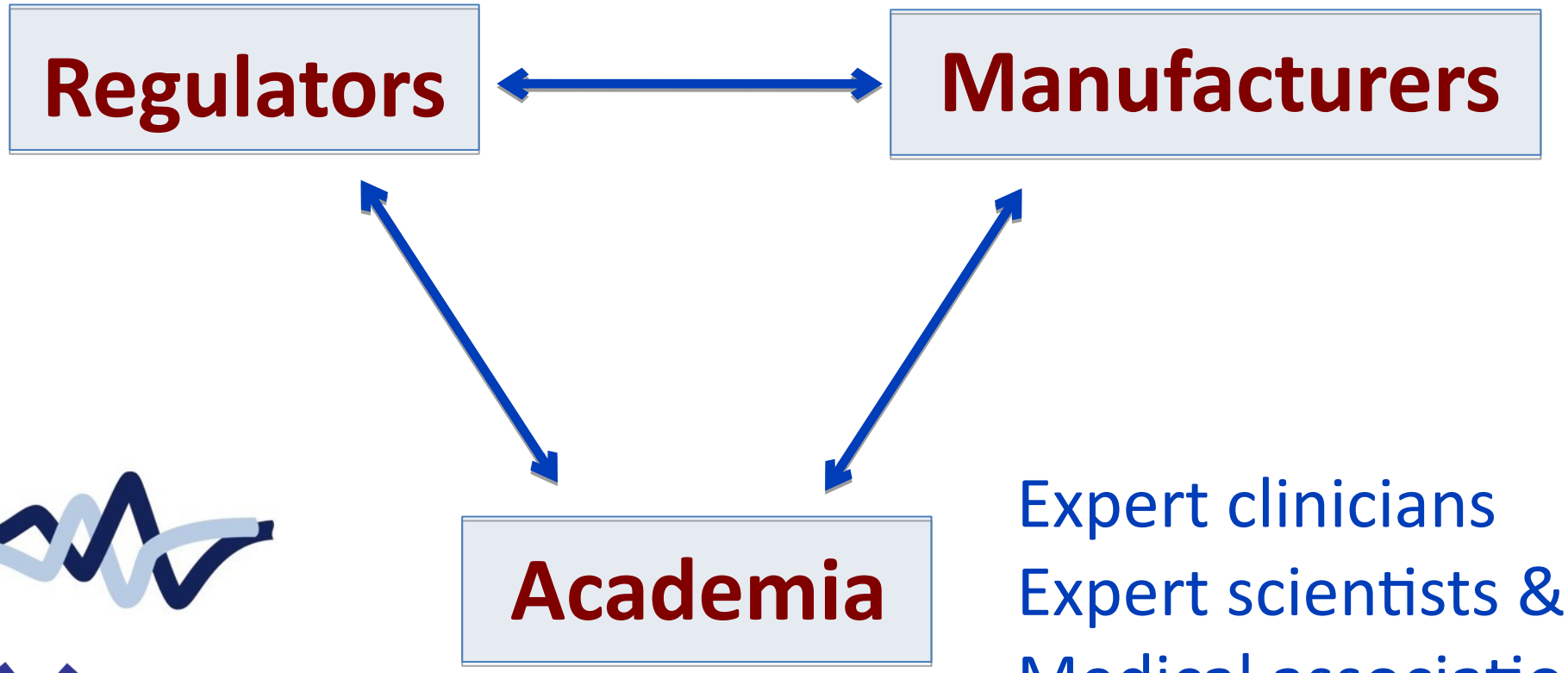
The measures to be adopted .. must .. aim to set high standards of quality and safety where national standards affecting the internal market would otherwise prevent ***a high level of human health protection*** being achieved.

A **reactive** regulatory environment ..?



- **Legislative principles** adapted for medical devices in the EEC / from the **'New Approach'** for manufacturing sectors
- **Notified bodies** / from the voluntary inspection bodies
- **ISO and IEC** / from International engineering standards

An *evidence-based* regulatory environment ..



CORE-MD

Expert clinicians
Expert scientists & engineers
Medical associations
Patients

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945260

For more information, visit: www.core-md.eu

ESC
EFORT
Biomedical Alliance in Europe
European Academy of Paediatrics
Paediatric Section of U.E.M.S
EPF European Patients Forum
LUMC Leiden University Medical Center
University of Oxford
Region Uppsala
RCSI University of Medicine and Health Sciences
INSELSPITAL Universitätsspital Bern Hôpital universitaire de Berne
KU LEUVEN
UMIT TIROL The Tyrolean Private University
University of Gothenburg
Politecnico Milano 1863
HPRA An tÚdarás Rialála Táirgí Sláinte Health Products Regulatory Authority
LÆGEMIDDELSTYRELSEN Danish Medicines Agency
National Institute for Public Health and the Environment Ministry of Health, Welfare and Sport
Istituto Superiore di Sanità
aihta HTA Austria Austrian Institute for Health Technology Assessment GmbH
AETSA
TEAM NB

CORE-MD
Coordinating Research and Evidence for Medical Devices