Leids Universitair Medisch Centrum

Challenging the Status Quo:
towards a Global Approach for managing Traceability in Laboratory Medicine

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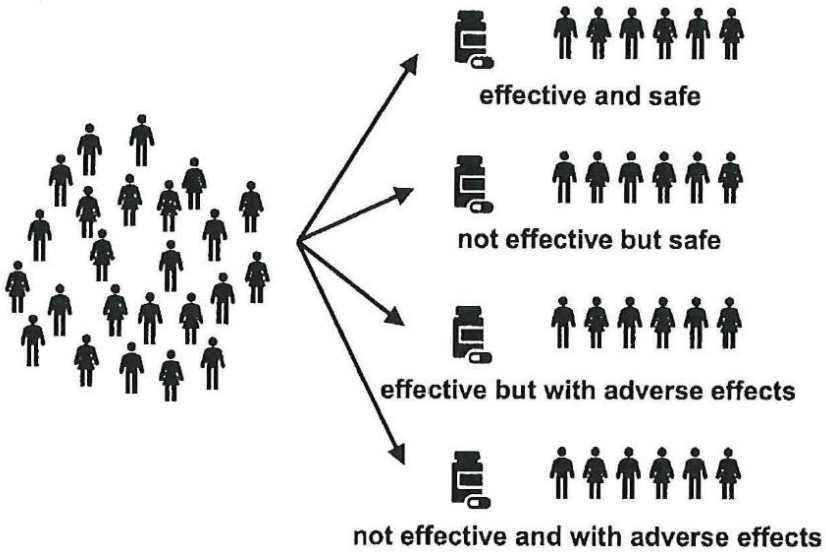
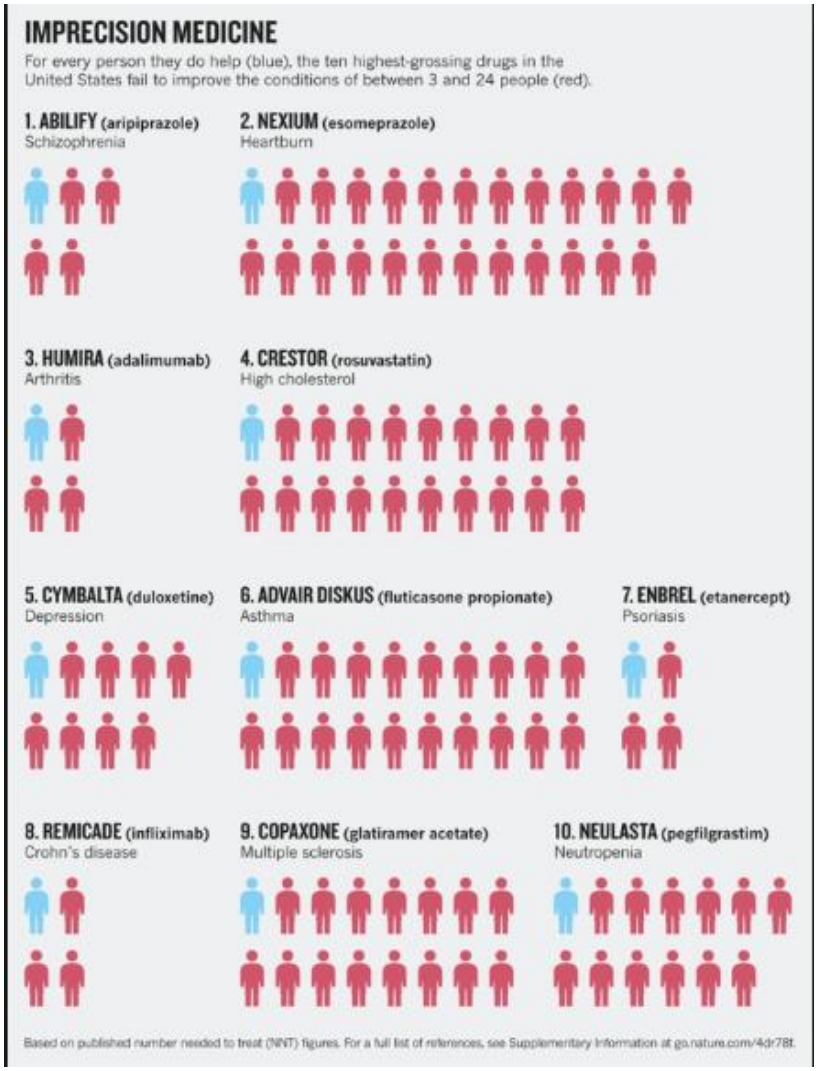
Content

Disclosures: lecture content reflects my personal viewpoint!

I. Healthcare systems' development

Current practice:
targeting the hypothetical average





Healthcare systems' development

Current practice:

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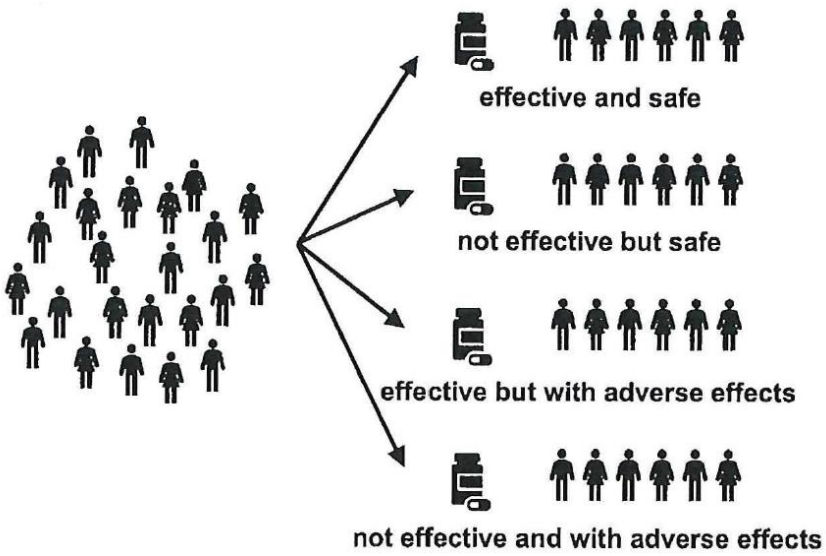
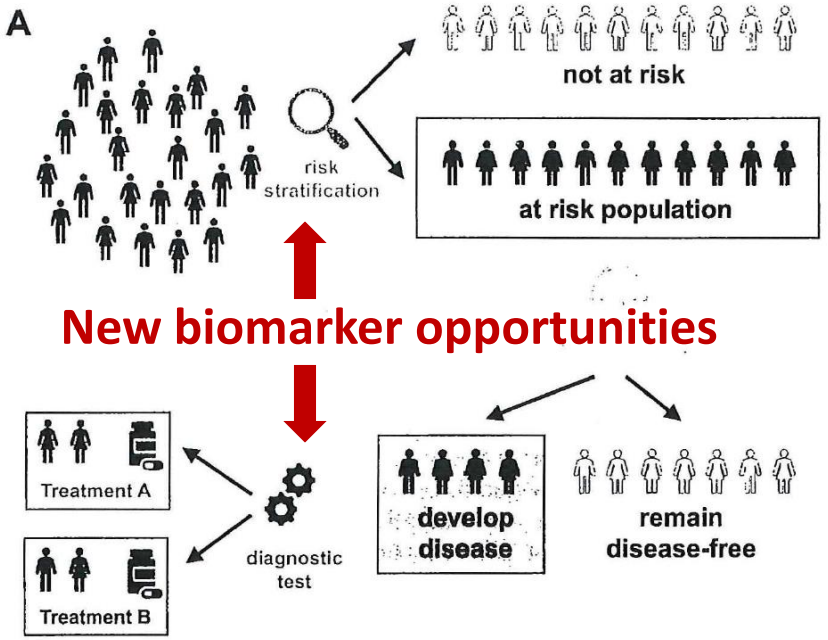


Evolving practice:

Precision Medicine



More precise definitions of disease & more precise characterization of patients/ populations are needed with potential to translate into targeted therapeutics with improved response rate.

Technological advances

New technologies change the ways health status can be assessed!

Mobile health (m-health) devices and sensors

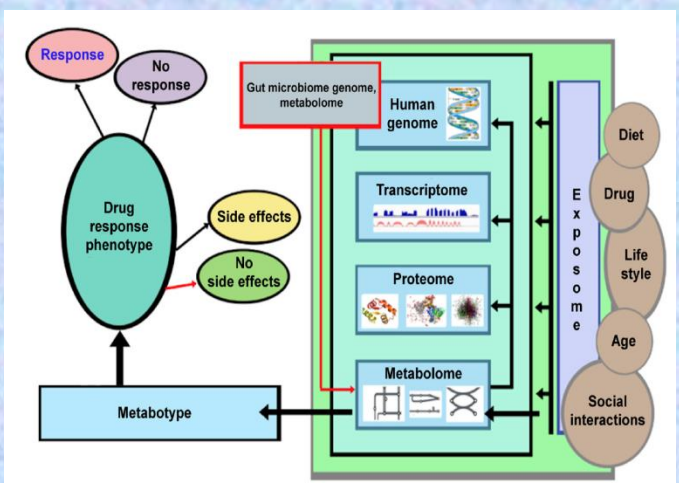
revolutionized the measurement of human dynamic physiology

e.g. BP, heart rhythm, brain waves, air quality…

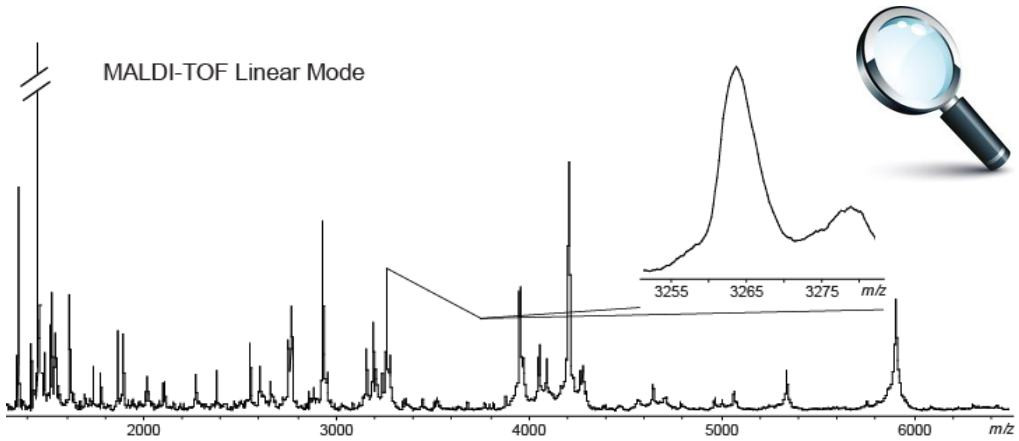
Deriving a phenotypic repertoire at scale

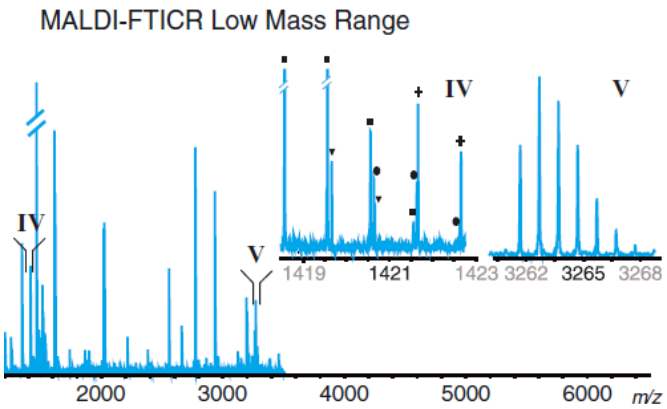
Finding novel pathways by leaving empirical science's tendency to mostly build on known paradigms.

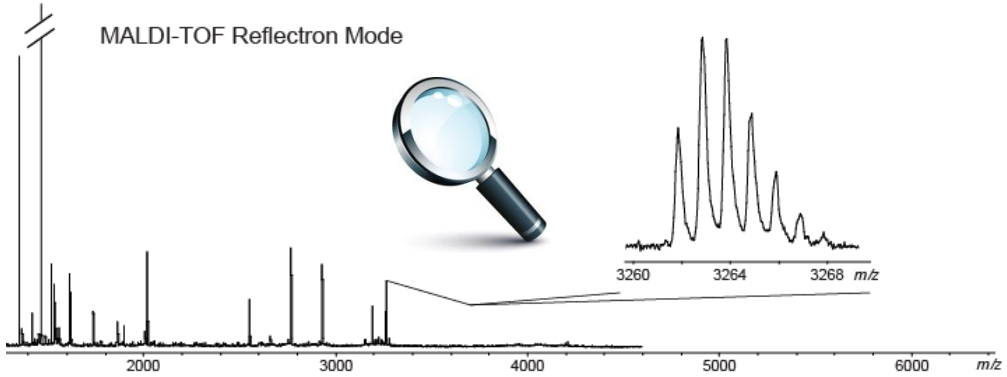
To fully redeem the promise of precision medicine, we should integrate data on all fronts from genomes to phenomes.

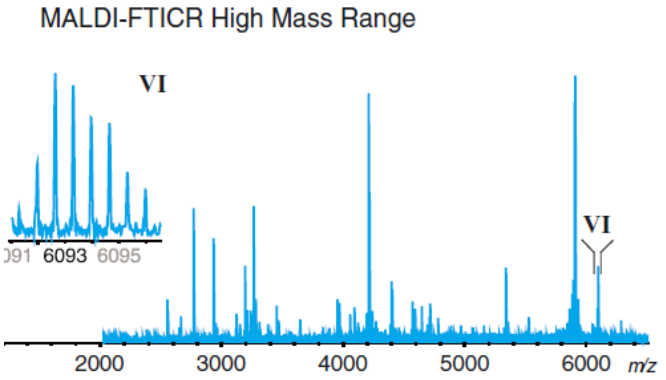


Zoom in *mass spectrum* provides new views









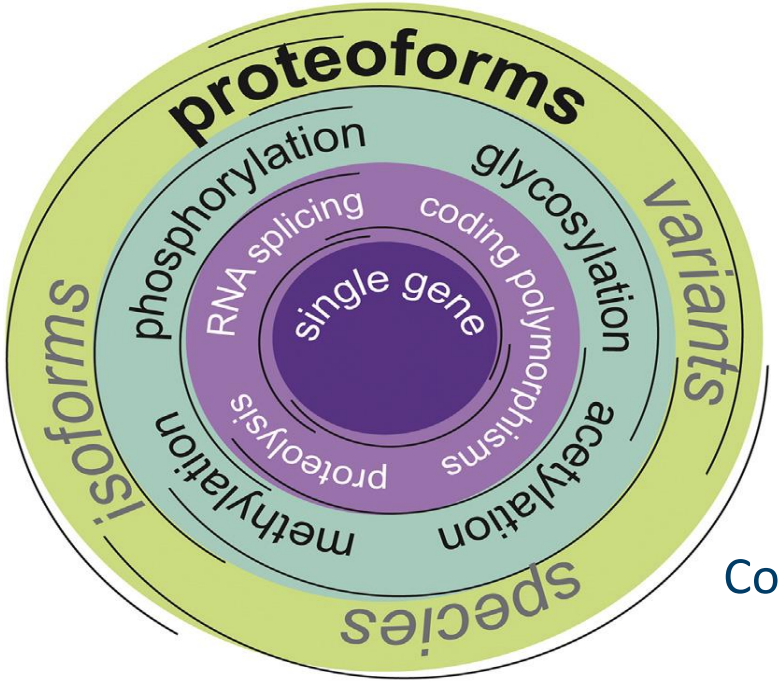
Resolving power of a mass spectrometer:
From early day hundreds (1980s) to state-of-the-art millions

Zoom provides detail and new views

from the Netherlands, to Leiden, to the LUMC, to our routine lab…

Proteoform Hypothesis

The term proteoform was proposed in 2012 "**to designate all of the different forms in which the protein product of a single gene can be found**" (Neil Kelleher)



Cobbaert et al. Clin Lab Med 2018

followed in 2014 by the hypothesis that "**intact proteoforms represent a class of molecules for use as biomarkers of disease states**"

Current Technology
is BLIND for Proteoforms

Biomarker (R)Evolution

Biomarker qualification at PRESENT	Biomarker qualification in the FUTURE
Identified in **observational studies**	**Large data**, **open-discovery approach with *-omics*, big data and PM**
Association with disease	**Inter-related Molecular Alterations**, organized into **mechanistic pathways**
Unimarker tests, with heterogenous mixture of measurands.	**Multimarker PANELS** with well characterized molecular forms.
Surrogate measures at best with weak or unclear relation to patient outcome.	**Molecular Markers** reflect disease course, give mechanistic insight, or are usable as therapeutic target*.

***The closer a test is related to the pathophysiology of disease and to the mechanism of action of the proposed therapy, the better will be its precision and thereby its usefulness as stratification tool or to inform personalized approaches.**

II. The Fundamentals of Standardisation

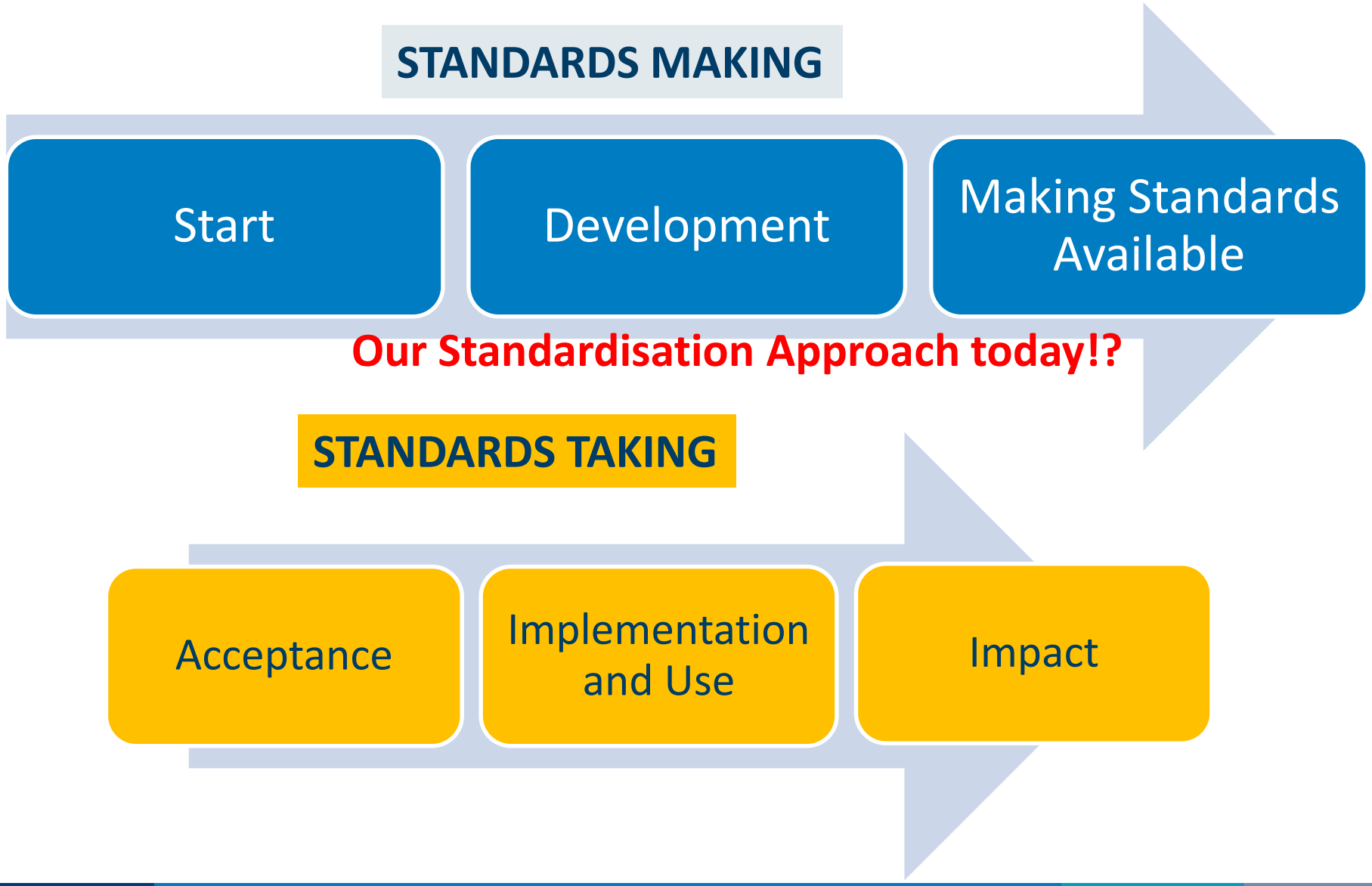
Generic definition:

STANDARDISATION *is the activity of establishing and recording a limited set of solutions to actual or potential* ***MATCHING PROBLEMS****, directed at benefits for the party or parties involved, balancing their needs, and intending and expecting that these solutions will be repeatedly or continuously used, during a certain period, by a substantial number of the parties for whom they are meant.* HJ de Vries, 1997.

A **matching problem** is a problem of interrelated **entities** that do not harmonise with each other. Solving it means determining one or more features of these entities in a way that they harmonize with one other or determining one or more features of an entity because of its relationship(s) with one or more other entities.

Most **STANDARDS** are related to **products, services or processes**, whereas **management system standards** impact entire organisations.

Standardisation Process Model



Standardisation Process Model

It starts with an **idea**.

Standard development and approval is **often** done by **formal standardisation organisations**, such as national standards bodies.

Challenge: to have a **balanced stakeholder representation**.

Literature tends to focus on **battles** between competing standards. E.g. e-purse battle between Chipper and Chipknip.

Use of standards in **innovation management**/ technical design activities **AND governance & management of standards within companies**.

Investigate the **impact** of standards/ standardisation on innovation!

Standardisation Process Model

It starts with an **idea**.

Development and approval often by formal standardisation organisations.

Investigate the **impact** of standards/ standardisation on innovation!

1. How can standardisation be integrated in innovation management?
2. To what extent can the innovation process itself benefit from standardisation?

- ❑ Standardisation is **enabler of globalisation**!
- ❑ Impact of **participation** in standardisation!
- ❑ Standards may relate to **regulation** by laying down essential requirements in legislation, whereas more detailed requirements are in voluntary standards.

Successful example of a barcode icone

Mr Albert Heijn, CEO and owner of the biggest chain of supermarkets in the Netherlands, **introduced the barcode* on the package of any product in 1976** and became its global promoter. We cannot imagine retail and supply chains without such universal product codes anymore.

- Scanning barcodes allows the physical flow of products to interconnect with the information flow and facilitates process improvements such as automatic ordering and self-scan checkouts.
- It decreases handling costs enormously for all retailers, yet bigger retailers have relatively more advantages than small ones (competitive advantage).

*American invention

Findings from Standardisation Research

A. MANAGEMENT OF STANDARDS & STANDARDISATION

1. Companies' management of standardisation

- ✓ Mostly not managed systematically.
- ✓ Integration of standardisation in innovation projects tends to be operational rather than strategic!

2. Management of inter-organizational standardisation projects

- ✓ Investigate impact of standards and standardisation and relate to stakeholders, as a starting point for improvement!

3. Management of standardisation systems

- ✓ Egg product has 10 different seals of conformity to requirements for the environment and for animal welfare in NL

At each level special attention is needed to the RELATIONSHIP WITH INNOVATION MANAGEMENT & SUSTAINABILITY.
Standards will be instrumental when taking SOCIETAL ISSUES AS THE STARTING POINT.

Findings from Standardisation Research

A. MANAGEMENT OF STANDARDS & STANDARDISATION

Lack of professional standardisation management

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2. **Manageme…**
   …stakeholders, as a starting point

3. **Ma… …ion systems**
   - ✓ …s 10 different seals of conformity to requirements for the environment and for animal …ure in NL

At each level special attention is needed to the relationship with innovation management and sustainability.
Standards will be instrumental when taking societal issues as the starting point.

B. EDUCATION ABOUT STANDARDISATION

What is EURAS ?

EURAS, the European Academy for Standardisation e.V., was founded in Hamburg in 1993 by researchers from various academic fields (i.e. economics, engineering, social sciences, law, and information sciences). It is a registered society under German civil law, and a non-profit organization. The foundation of EURAS was prompted by a common desire to promote and achieve progress in the academic treatment of standardisation, involving the widest possible range of disciplines.

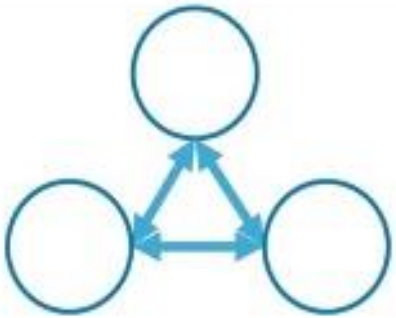
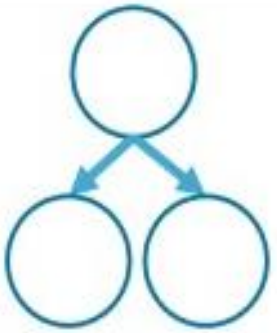
Objective: "EURAS' objective is to promote research, education and publication in the field of standardisation."

H. De Vries, president

EURAS education objectives

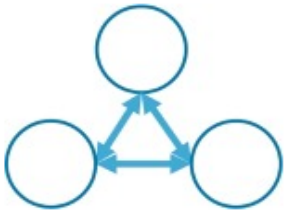
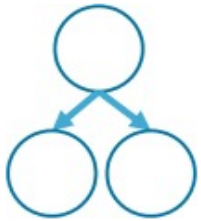
Standardization is a much neglected topic in higher education. EURAS wants to help change this situation and supports the development of standardization curricula by providing a platform and opportunities for the discussion, development and exchange of teaching material.

III. Typical modes of Standardisation 1/3

	Committee-Based Standardisation	Market-Based Standardisation	Government-Based Standardisation
Relationships between actors			

Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Typical modes of standardisation – characteristics 2/3

	Committee-Based Standardisation	Market-Based Standardisation	Government-Based Standardisation
Relationships between actors			
Coordination mechanism	Coordination through *cooperation* between stakeholders. Standards are developed in committees and only diffused if members agree on a common solution.	Solutions intended as a standard can be developed by anyone. Coordination through *competition* between solutions in the market, leading often (but not always) to one de-facto standard.	Solutions intended as a standard can come from various sources. Coordination through governments using their *hierarchical position* to impose these standards' use on others.
Timing of coordination	Coordination takes place during standard *development* – only one solution is chosen to enter the market.	Coordination takes place during *diffusion* – different standards are developed and compete with each other.	Governments can intervene in development or mandate using an already developed standard.

Typical modes of standardisation – characteristics 3/3

	Committee-Based Standardisation	Market-Based Standardisation	Government-Based Standardisation
Main actors driving the standardisation process	Predominantly private	Predominantly private	Predominantly public
	Stakeholders cooperating in committees; SDOs providing a platform for standard development.	Individual market actors influencing the outcome of the market competition with their actions.	Governmental bodies developing standards and/or enforcing their use.
Avenues of influence	Participating in committees to influence standards' contents.	Engaging in the market to influence battles' outcomes by influencing decisive factors.	Influencing government decision-making through lobbying or parliamentary representatives.
Inclusiveness in standard development	High, any interested party can join a committee.	Varies, some standard development venues are open; access to others is restricted.	Medium, lobbying may require high effort.

Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Becoming the industry standard when standardisation is not standardised

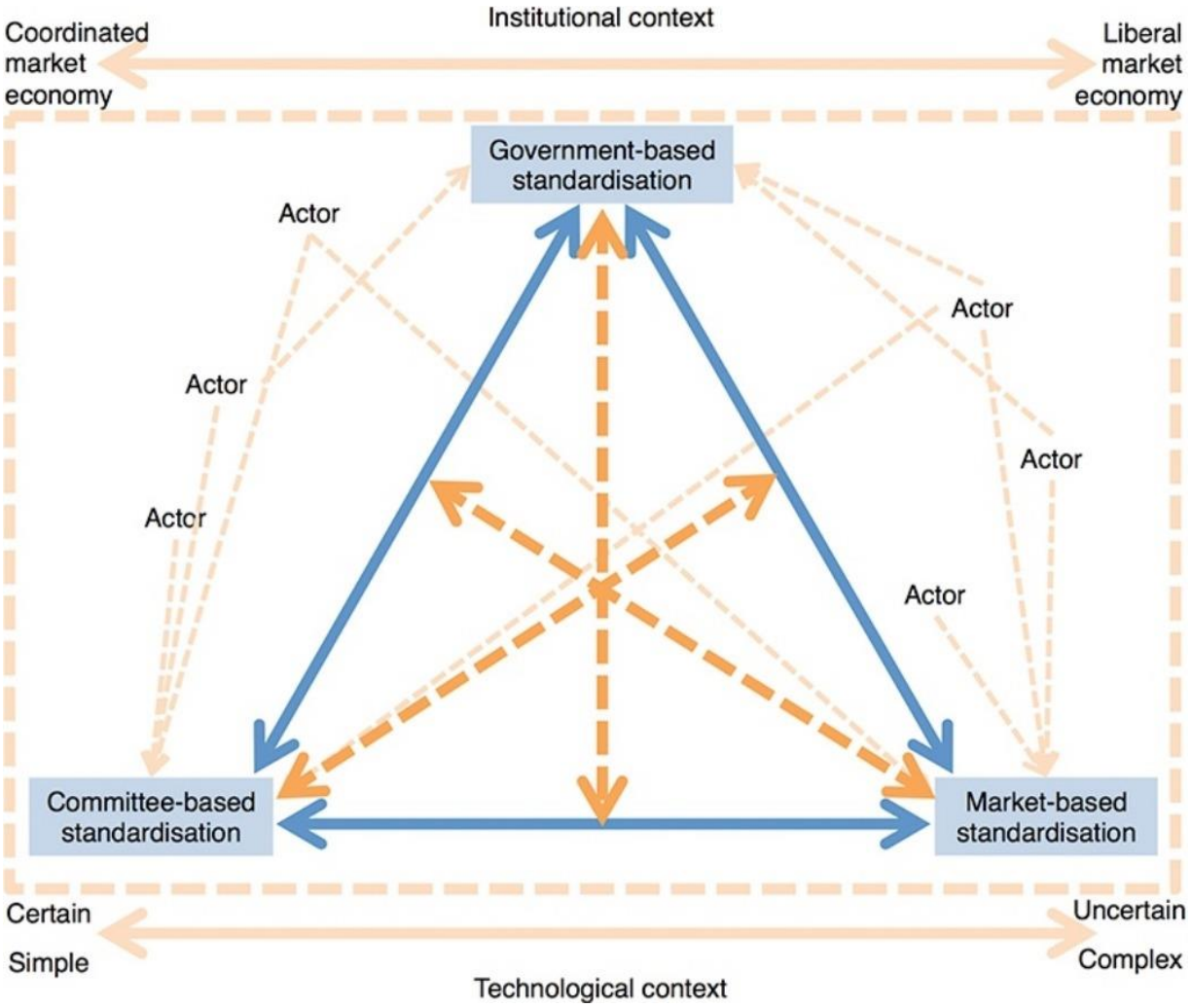
- Wi-Fi and 4G internet connections, central heating, direct debit bank cards,… have been through a process of standardisation and contain standard technologies that are used across many products in each sector.
- **Making things "smart" relies on standardisation!** Without standardisation, many technological developments simply wouldn't be possible.
- **Standardisations's key aim is to allow those options that meet essential requirements.**

Video format battle between Betamax cassette (top) and a VHS cassette (bottom).

Beta sales dwindled away and VHS emerged as the winner of the format war. The **video format war** is now a highly scrutinized event in business and marketing history, leading to a plethora of market investigations into why Betamax failed.

Bankcard and biofuel standardisation

IV. Multi-mode standardisation



Due to increasing complexity: smart cities, IoT, …., medical test standardization?

Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Highlights of multi-mode standardisation research

1. Finds that multi-mode standardisation is **key to big technological and societal changes**.

2. Reviews and recombines **evidence** on multi-mode standardisation to develop new theory.

3. Establishes **conditions** under which modes can be activated in standardisation processes.

4. Identifies underlying **dynamics** in multi-mode standardisation.

5. Finds that multi-mode standardisation is an **ongoing process**, with no clear end-point.

Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Example of multi-mode standardisation

Three standardisation modes had been used **strategically** by the winning company!

https://www.youtube.com/watch?v=cmUxuLtW0HU

V. Making Standardisation happen …

Lack of professional standardisation management

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At each level special attention is needed to the relationship with innovation management and sustainability.

Standards will be instrumental when taking societal issues as the starting point.

How can we improve this situation?

Start bottom-up by analysing standardisation projects

- ✓ **Cross-case analysis** may reveal patterns in current project management that relate to the processes and governance of standardisation -
  - at the global, regional and national levels
  - and related not only to standard bodies but also to trade associations, NGOs and governments.

- ✓ A **better understanding of processes and governance** may form the basis for improvement initiatives followed by impact assessment and measurement.

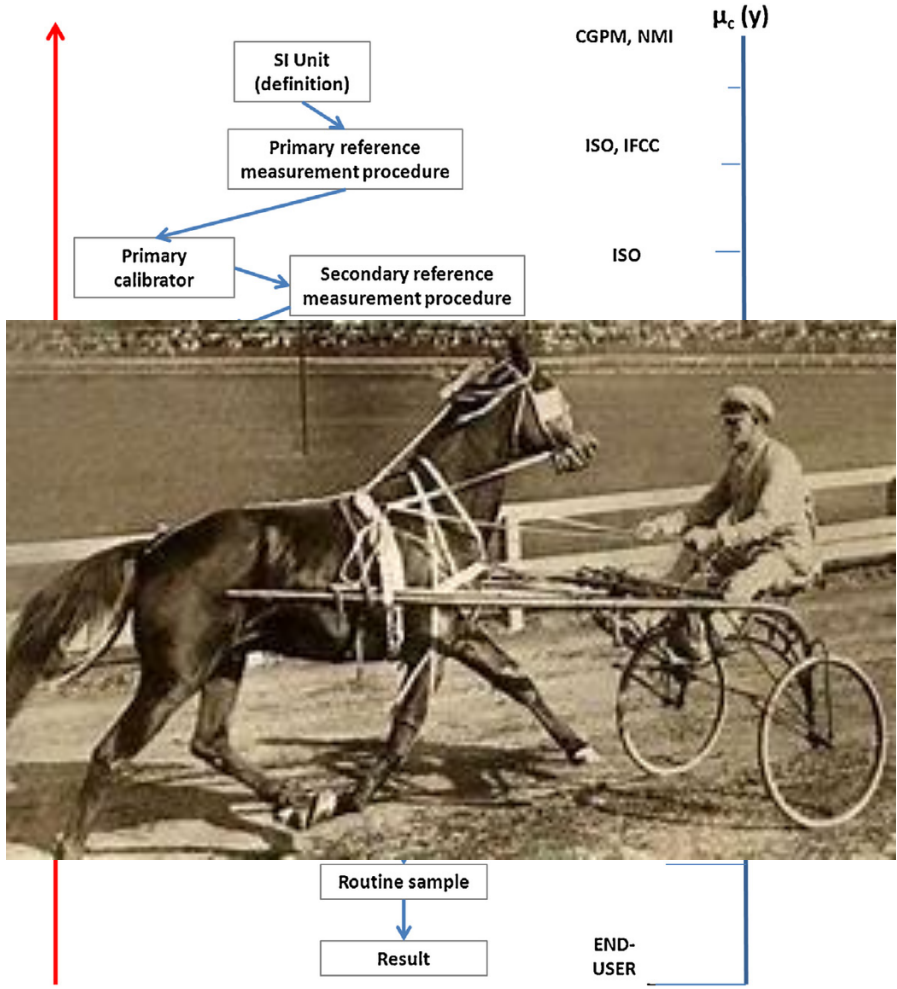
Making Standardisation happen in Lab Medicine!?

Medical Test Standardisation anno 2019

1. Often no “up-front” standardisation process when new tests are introduced.

2. No overall governance but a process handled in silo’s in different ways by multiple stakeholders.

3. IFCC SD leaves responsibility for the global standardisation process to IFCC WGs or Cs. Median standardisation process takes 6-10 years per test.

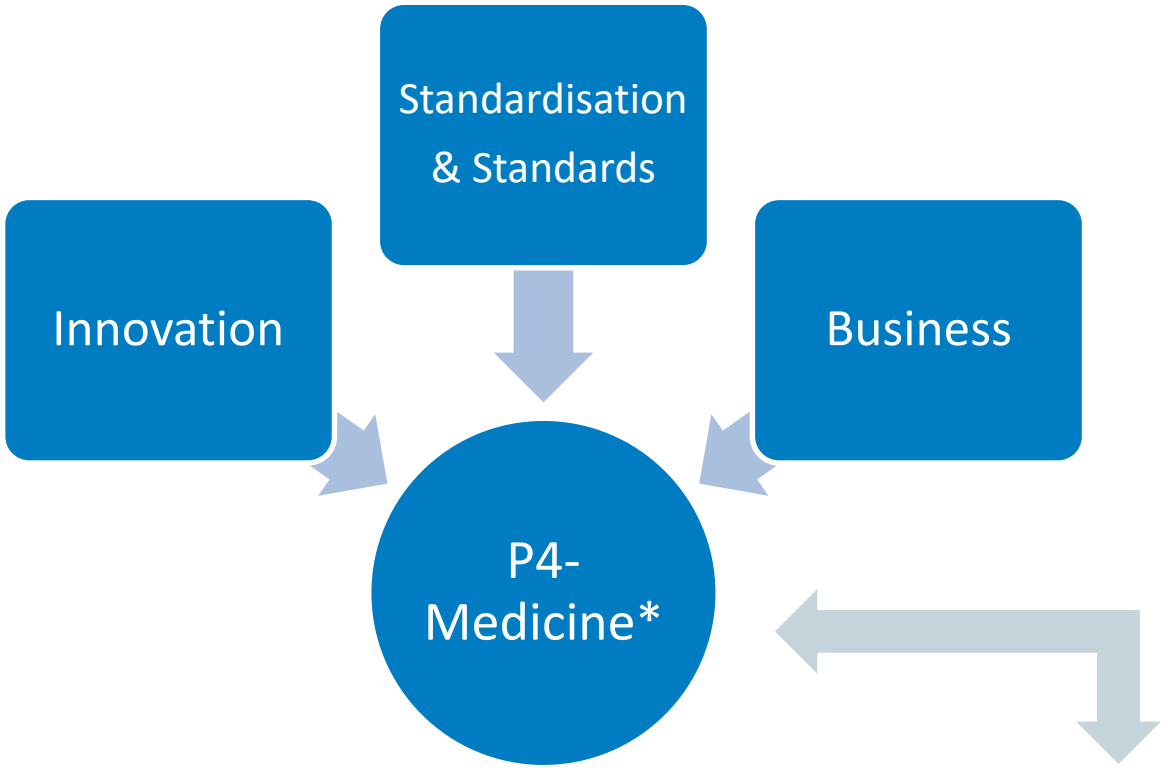


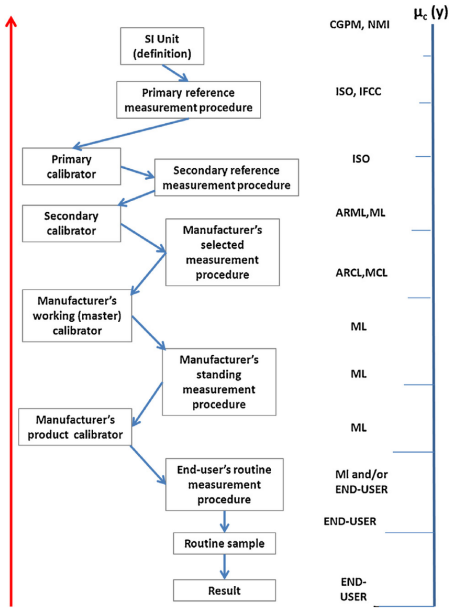
Suboptimal Standardisation Process

ISO 17511:2003

Making Standardisation happen in Lab Medicine

Medical Test Standardisation demands a JOINT PATIENT-CENTRIC MISSION / VISION!





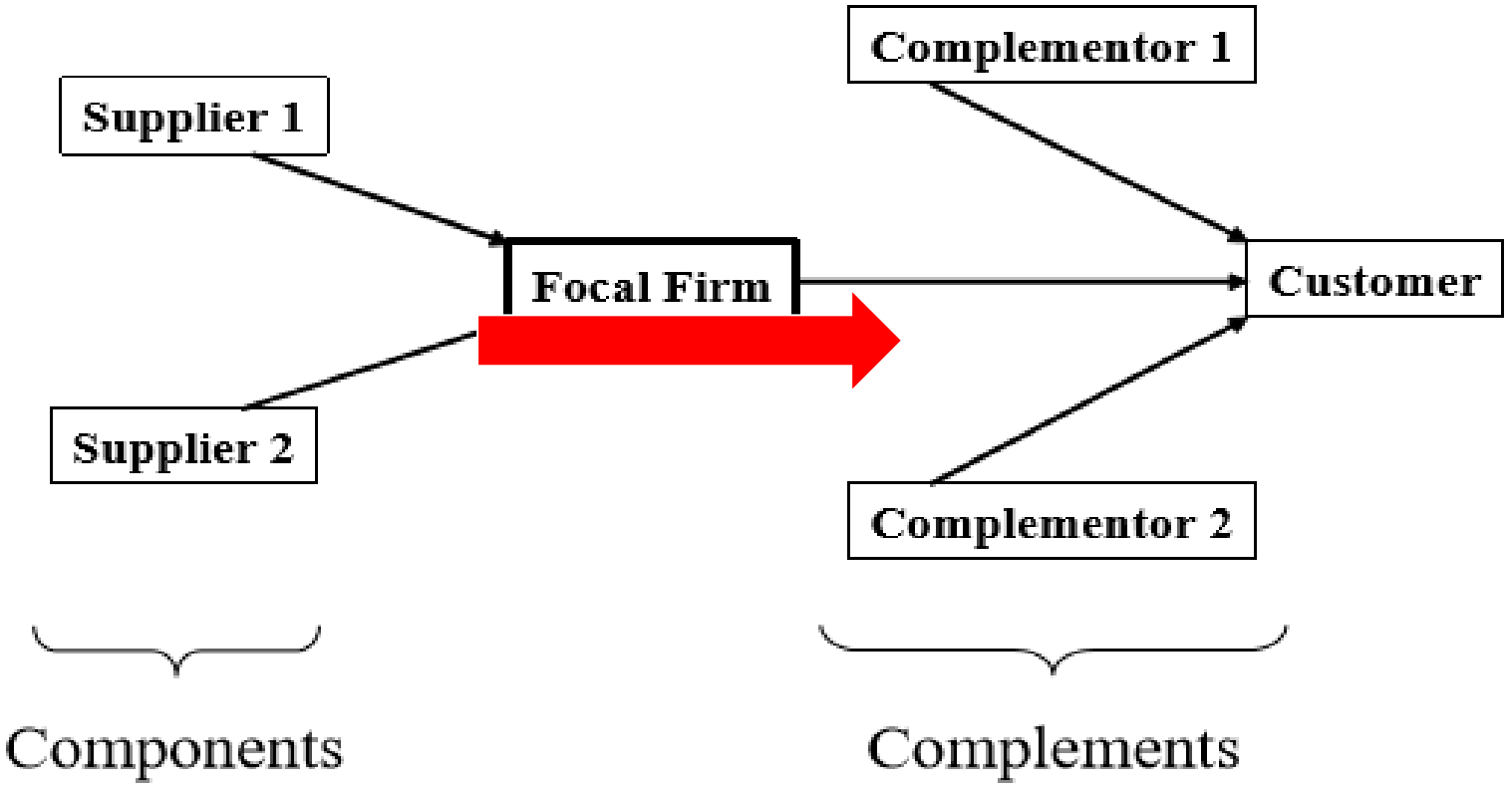
ISO 17511:2003

*P4 medicine: **P**revention, **P**rediction, **P**ersonalized **and with Participation of the patient**

Value Creation in Innovation Ecosystems – generic scheme

The value for users is generated by interplay of all stakeholders.

All actors have to contribute to the same mission, e.g. standards, regulation, mutual agreements, …



Adner and Kapoor, 2010

CONCLUSIVE THOUGHTS

Standards are Instruments of Power!!!

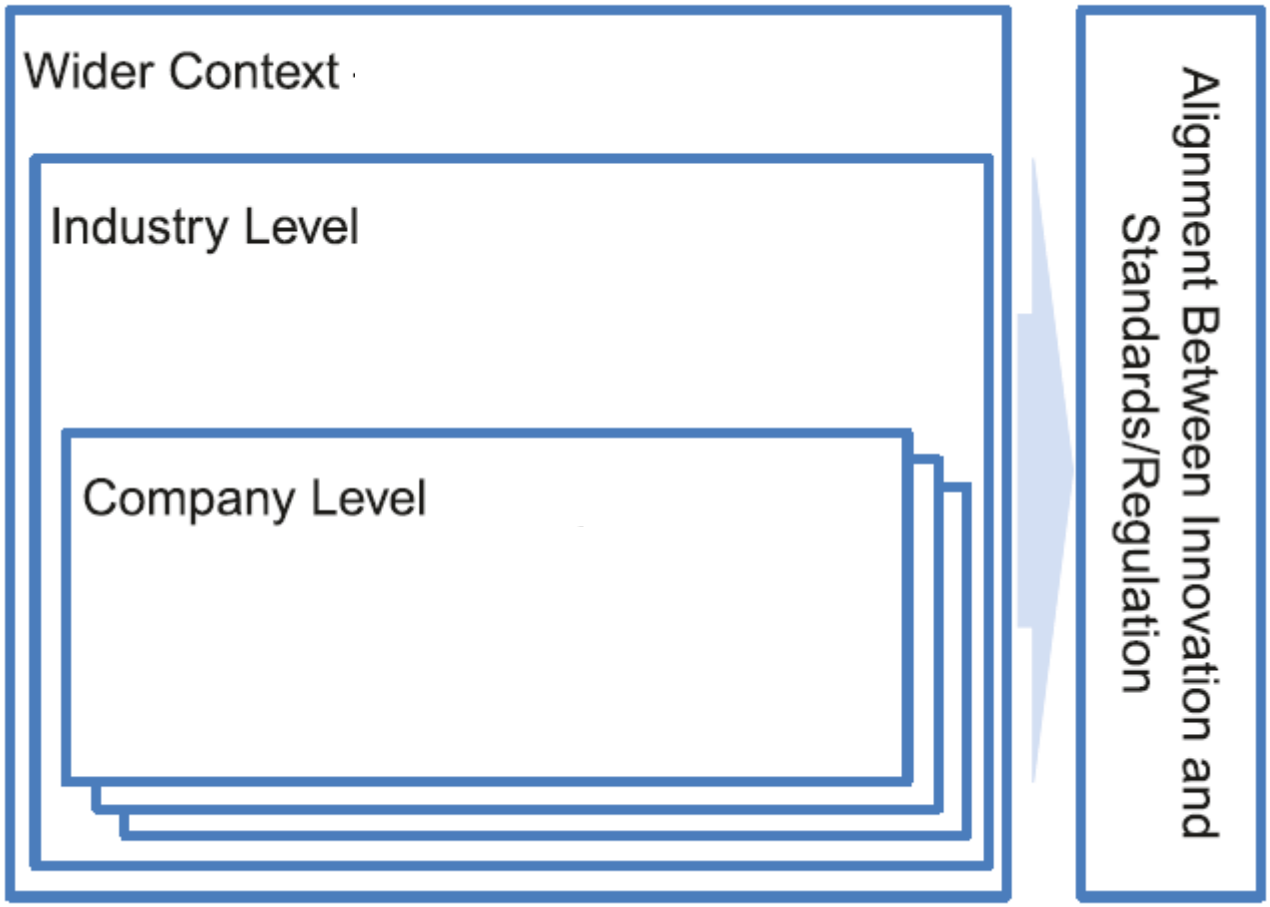
1. **Standards shape technology, business and to an increasing extent also society, and this makes the SHAPING of standards and their IMPACT a topic of utmost importance**!

2. We have **limited knowledge** about this hidden and powerful instrument of standardisation!

3. **Scientific Research** is limited and most of us focus on certain aspects rather than on the phenomenon as a whole.

4. **Standardisation Education** in academic curricula is negligible.

Framework for managing standards in innovation contexts



For global test standardization we have to fill in the blanks by looking closely at each level and identifying the factors which eventually lead to such an outcome. We have to build detailed theory about the company level and the industry level. Finally, we have to consider how all of this relates to developments and the associated processes that occur in the wider context of test/healthcare innovation.

Adapted from Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Lets start with a joint Patient-Centric Mission

START WITH A MISSION & INVOLVE VISIONARY ACTORS (personal view):

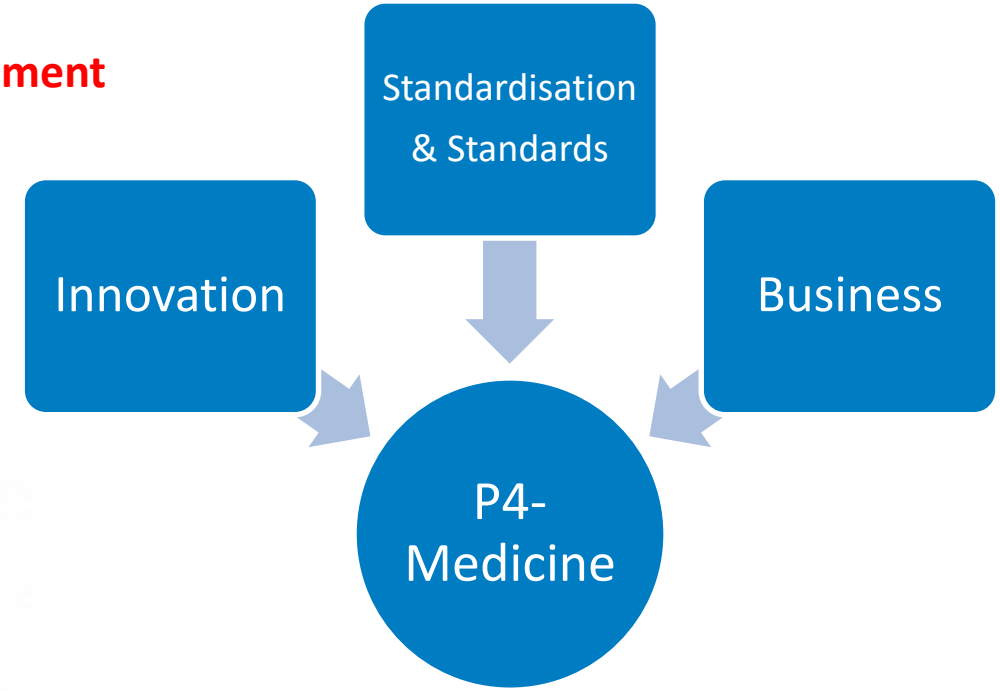
1. **Keeping populations healthier with P4-medicine** by means of innovations, enabling technology & standards/ standardisation.

2. **Standardisation of medical tests** -and even combined with standardisation of test processes and underlying IT- should go hand in hand with healthcare innovations, **right from the start** (cave: huge (cost) impact on society!)

3. Stakeholders of the metrological traceability chain should have a **less conservative mindset** and **make normalisation and standardisation more INCLUSIVE** in 21st century healthcare system. Learn from (un)succesful experiences on standardisation management and governance from other sectors…. and think big!

Questions?

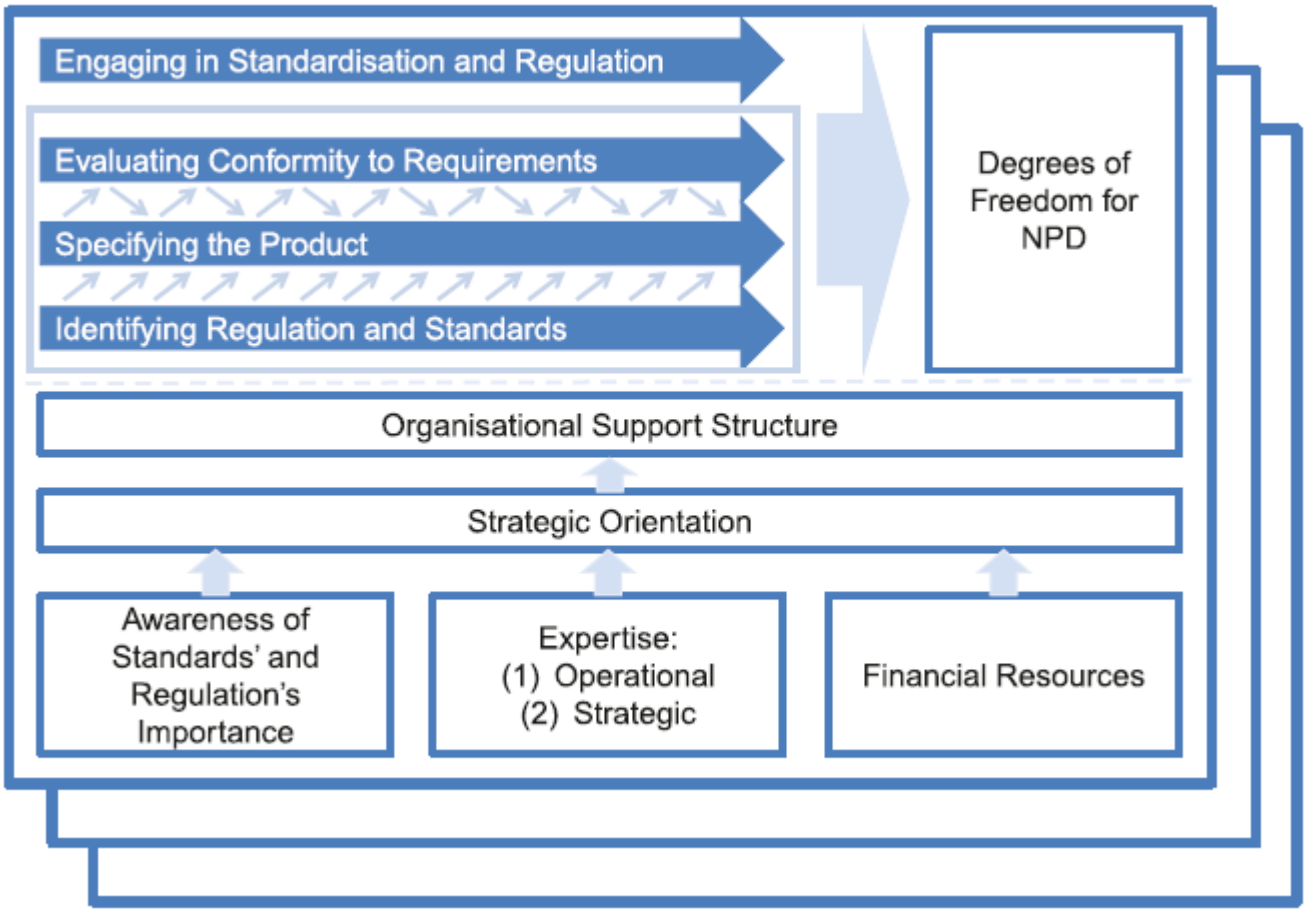
STRATEGIC THINKING on innovation & standardisation management and governance is key!



Including involvement of patient foundations

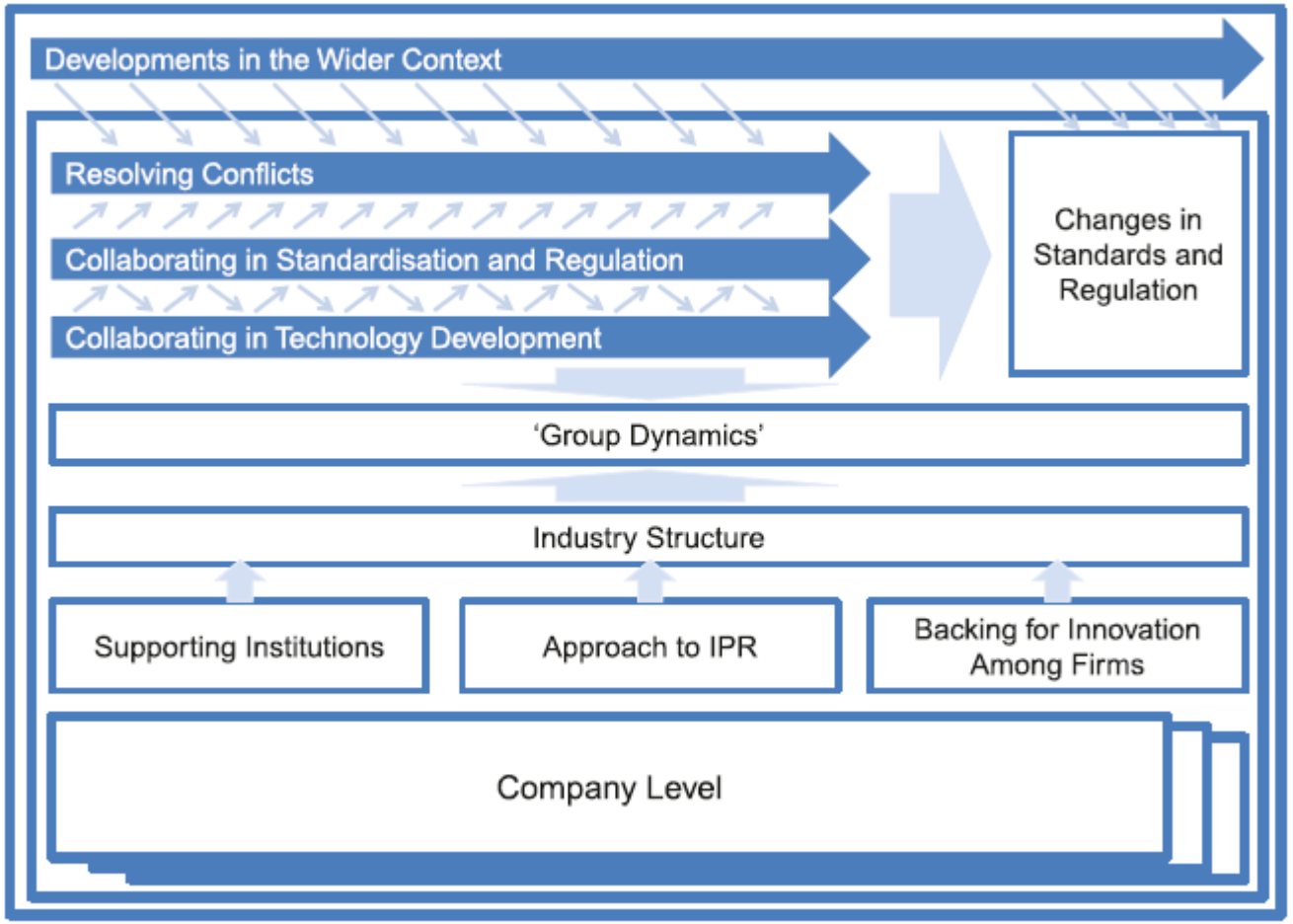
Email: c.m.cobbaert@lumc.nl

Company-level management of standards and regulation in NPD contexts



Wiegmann PM et al., Research Policy, 2017, 46: 1370-86.

Industry-level structure and processes for addressing standards and regulation



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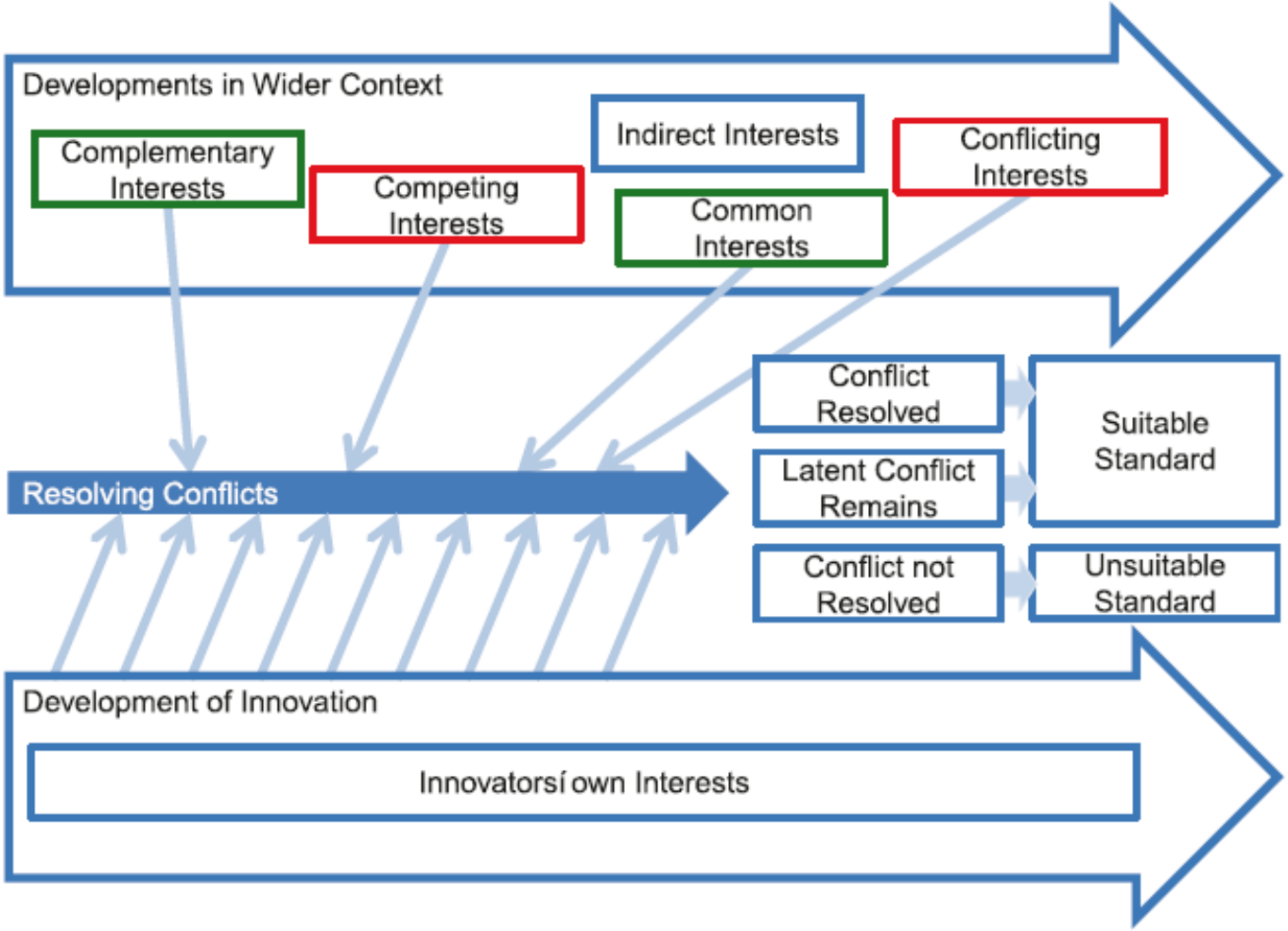
Interactions between the innovation and developments in the wider context



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