

2019-01-24

JMAC Symposium on AMED miRNA Project, International Standards, and Liquid Biopsy

## International Standards and Innovation in Biotech Field

# FIRM pursuing international standardization



FIRM (The Forum for Innovative Regenerative Medicine)

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Convenor: ISO/TC 276/WG 4 (Bioprocessing)

Chair, ISO/TC 276 Japan Mirror Committee

Chair, FIRM Standardization Committee

Board, Standards Coordinating Body

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Secretary, : ISO/TC 276/WG 4 (Bioprocessing)

Vice Chair, ISO/TC 276 Japan Mirror Committee

Vice Chair, FIRM Standardization Committee

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3-1) Developing standards

3-2) Leveraging use of standards

3-3) Planning standards

### 4) FIRM pursuing standardization

The contents of the presentation are thoughts of Tatsuo Heki / Yutaka Yanagita, and do not represent consensus of Japan industry and/or regulation community.

# FIRM

Forum for Innovative Regenerative Medicine

## About FIRM

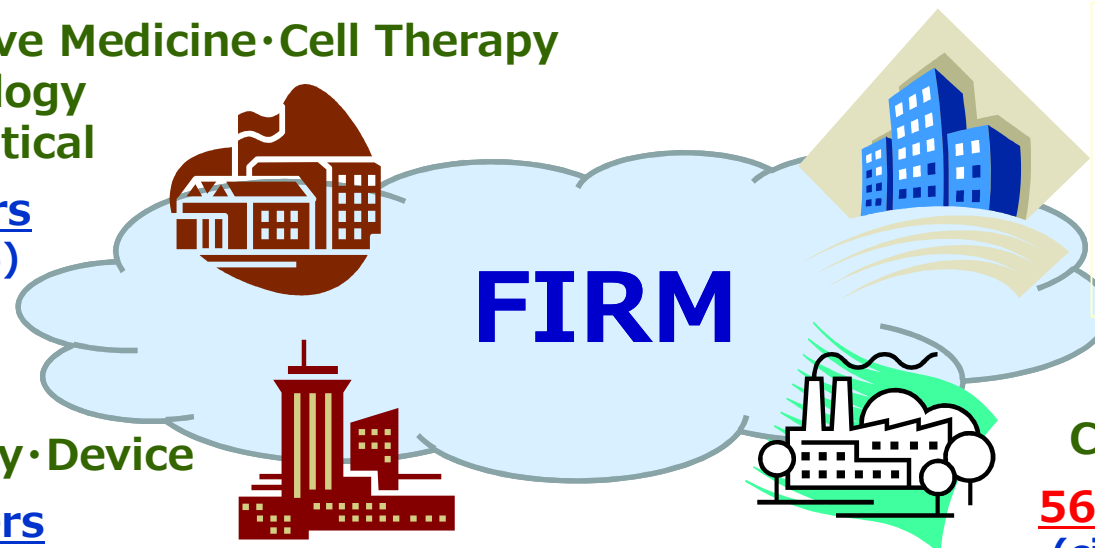
- Established on June 17, 2011
- Regenerative Medicine Industrial Association in Japan
- FIRM consists of **238** members, as of **Apr. 2018**
- To accelerate Industrialization Regenerative Medicine in Japan

Regenerative Medicine·Cell Therapy  
Bio-technology  
Pharmaceutical

**50** members  
(circa. 20%)

Machinery·Device

**37** members  
(circa. 15%)



Logistics  
Insurance  
Consulting, etc.

**95** members  
(circa. 40%)

Chemical·Material

**56** members  
(circa. 25%)

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1) FIRM

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# Innovation

- FIRM (Forum for **Innovative** Regenerative Medicine)
- Session 1: International standards and **innovation** in biotech field

What is **innovation**?

# Innovation

- **Innovation** is production or adoption, **assimilation, and exploitation of a value-added novelty in economic and social spheres**; renewal and enlargement of products, services, and markets; development of new methods of production; and the establishment of new management systems. It is both a process and an outcome. (Wikipedia)
- The process of **translating an idea or invention into a good or service that creates** value or for which customers will pay. (Business Dictionary)

# イノベーションとは

「再生医療の産業化と標準化－イノベーションの社会実装に向けて－」、JMAC第115回定例会(2018.11.22)、柳田豊

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- The process of translating an idea or invention **into a good or service that creates value or for which customers will pay**. (Business Dictionary) <http://www.businessdictionary.com/definition/innovation.html>
- イノベーションは単なる技術革新ではありません。革新的なアイデアが、**製品、サービス、組織、制度などとして実現して、それらが社会に受け入れられて初めてイノベーションと認識されます**。それゆえイノベーションの創出過程は、多くの人々を巻き込んだ、すぐれて社会的な過程です。(一橋大学イノベーション研究センター 青島矢一 センター長)  
<http://www.iir.hit-u.ac.jp/pages/about/index>
- 「**創新普及**」(玉田俊平太・関西学院大学経営戦略研究科教授)  
<https://business.nikkeibp.co.jp/atclbdt/15/258677/063000009/?ST=print>

# Innovation

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◆ Innovation is not only a progress in science/technology itself, but adoption of products, service, systems and rules by the community.

◆ **Multiple stakeholders with different backgrounds must support each other** in order to bring novel value of regenerative medicine into the society.

**creates** value or for which customers will pay.  
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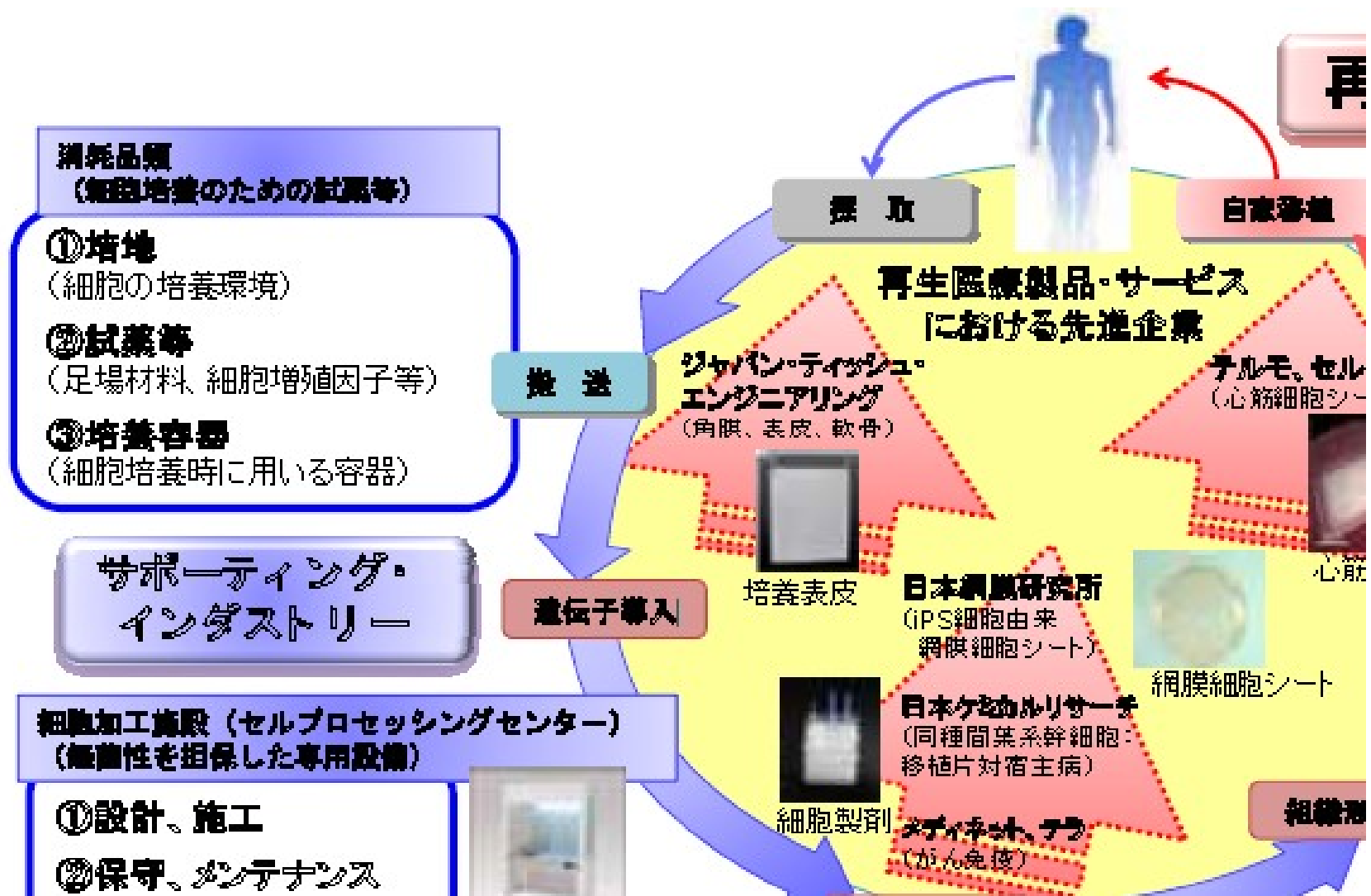
# Ecosystem

# Ecosystem

- An economic community supported by a foundation of **interacting organizations and individuals**—the organisms of the business world. The economic community produces goods and services of value to customers, who are themselves members of the ecosystem. The member organisms also include suppliers, lead producers, competitors, and other stakeholders. Over time, they coevolve their capabilities and roles, and tend to align themselves with the directions set by one or more central companies. Those companies holding leadership roles may change over time, but the function of ecosystem leader is valued by the community because it enables members to move toward shared visions to align their investments, and to **find mutually supportive roles** (James F. Moore)

- ◆ The ecosystem will consist of **multiple stakeholders** with different backgrounds .
- ◆ These **multiple stakeholders** must support each other in order to make the ecosystem workable.

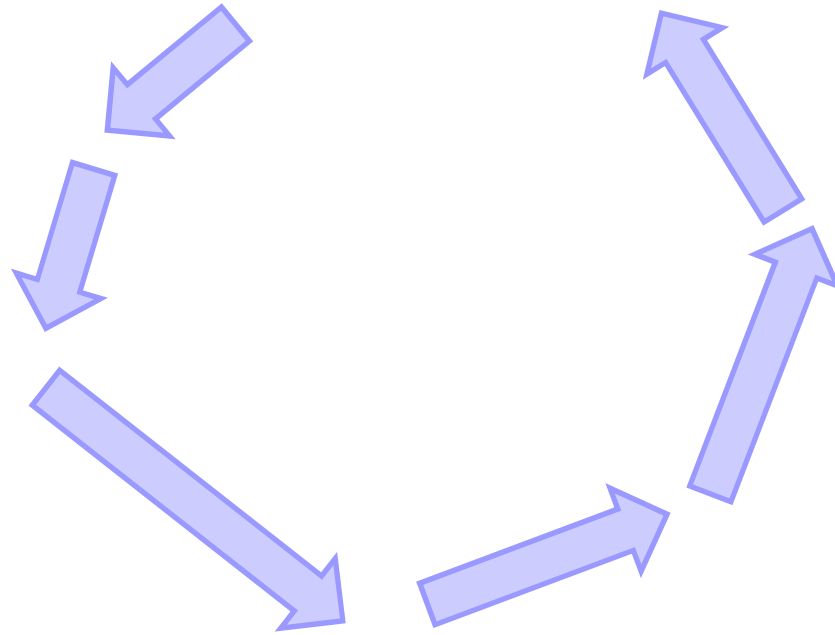
# The value chain



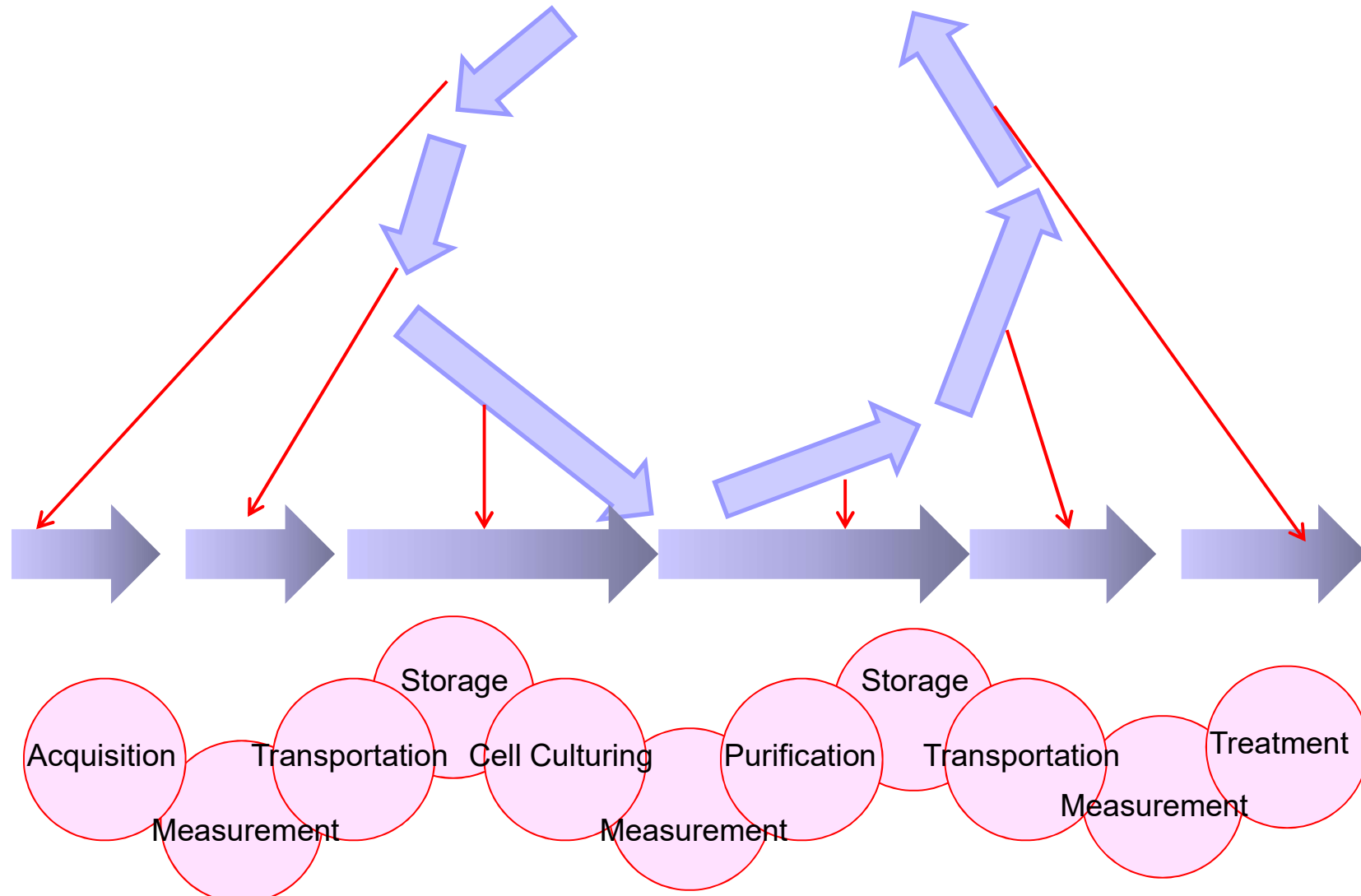
再生医療の実用化・産業化に関する報告書 最終とりまとめ 平成25年2月 再生医療の実用化・産業化に関する研究会

<http://www.meti.go.jp/press/2012/02/20130222004/20130222004-2.pdf>

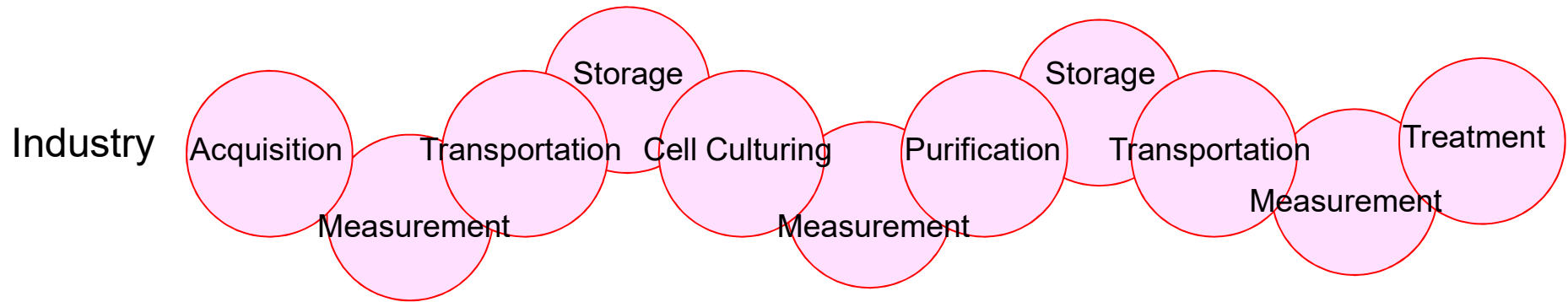
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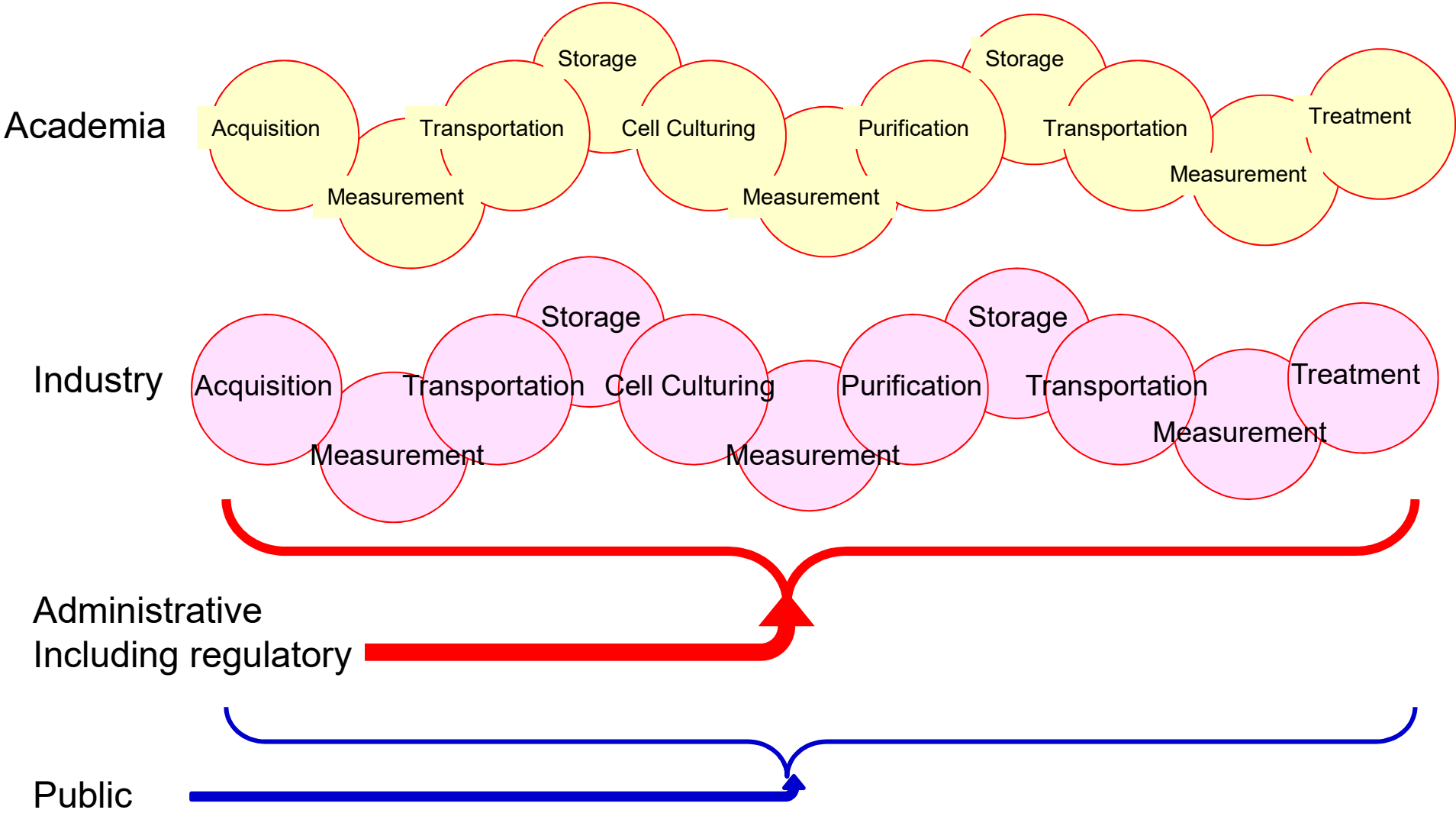
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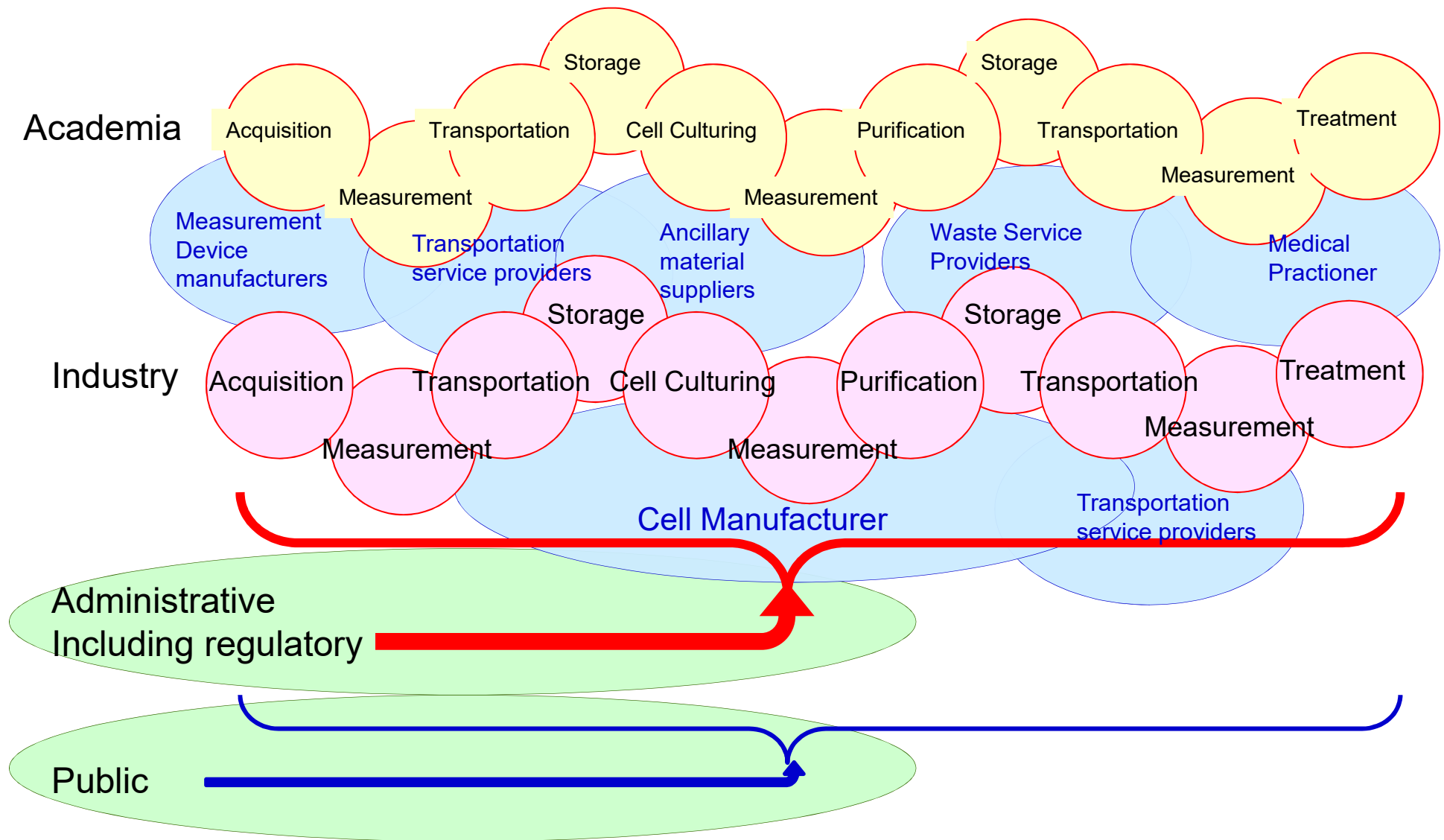
# Multiple stakeholders



# Multiple stakeholders

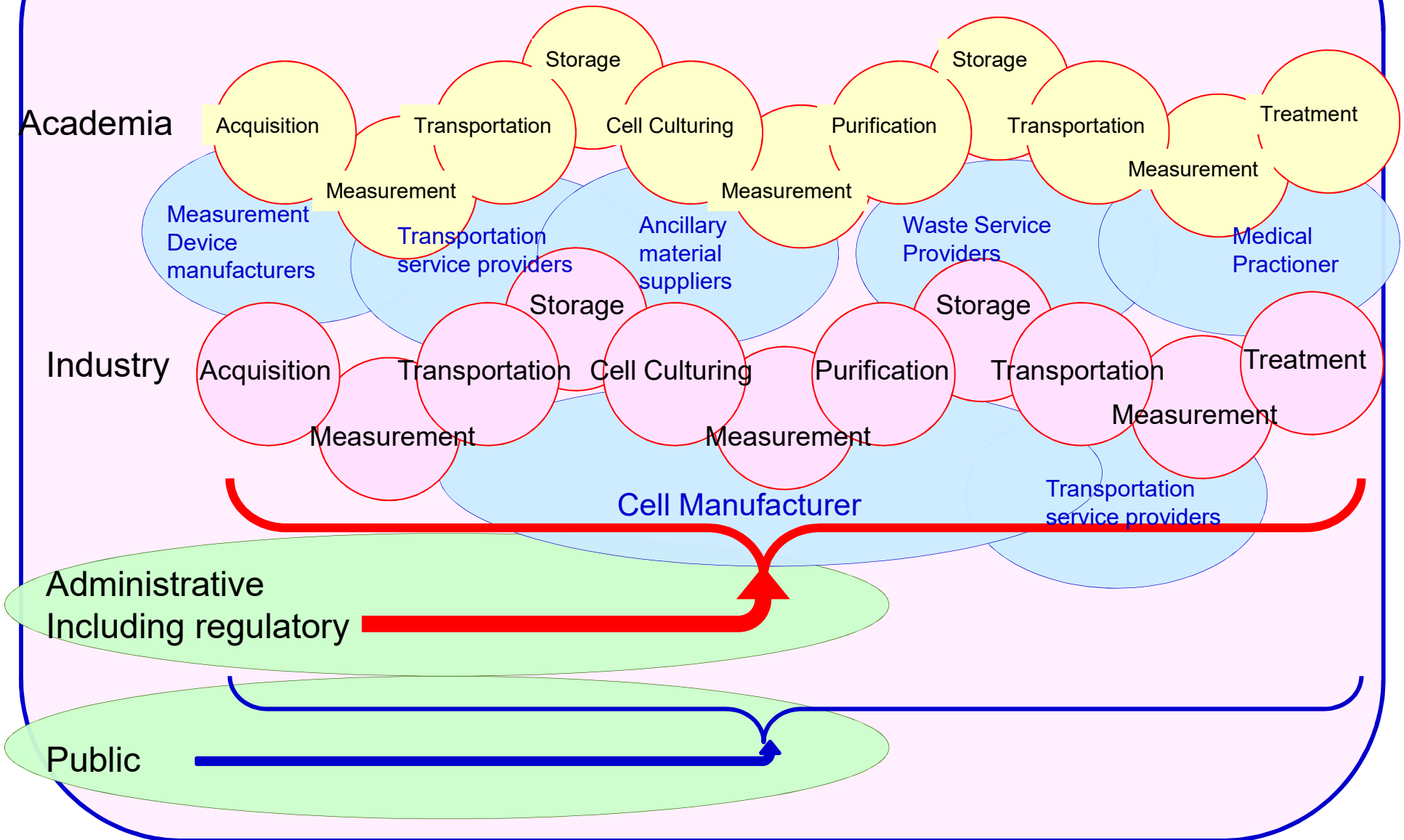


# The value chain – the stakeholders

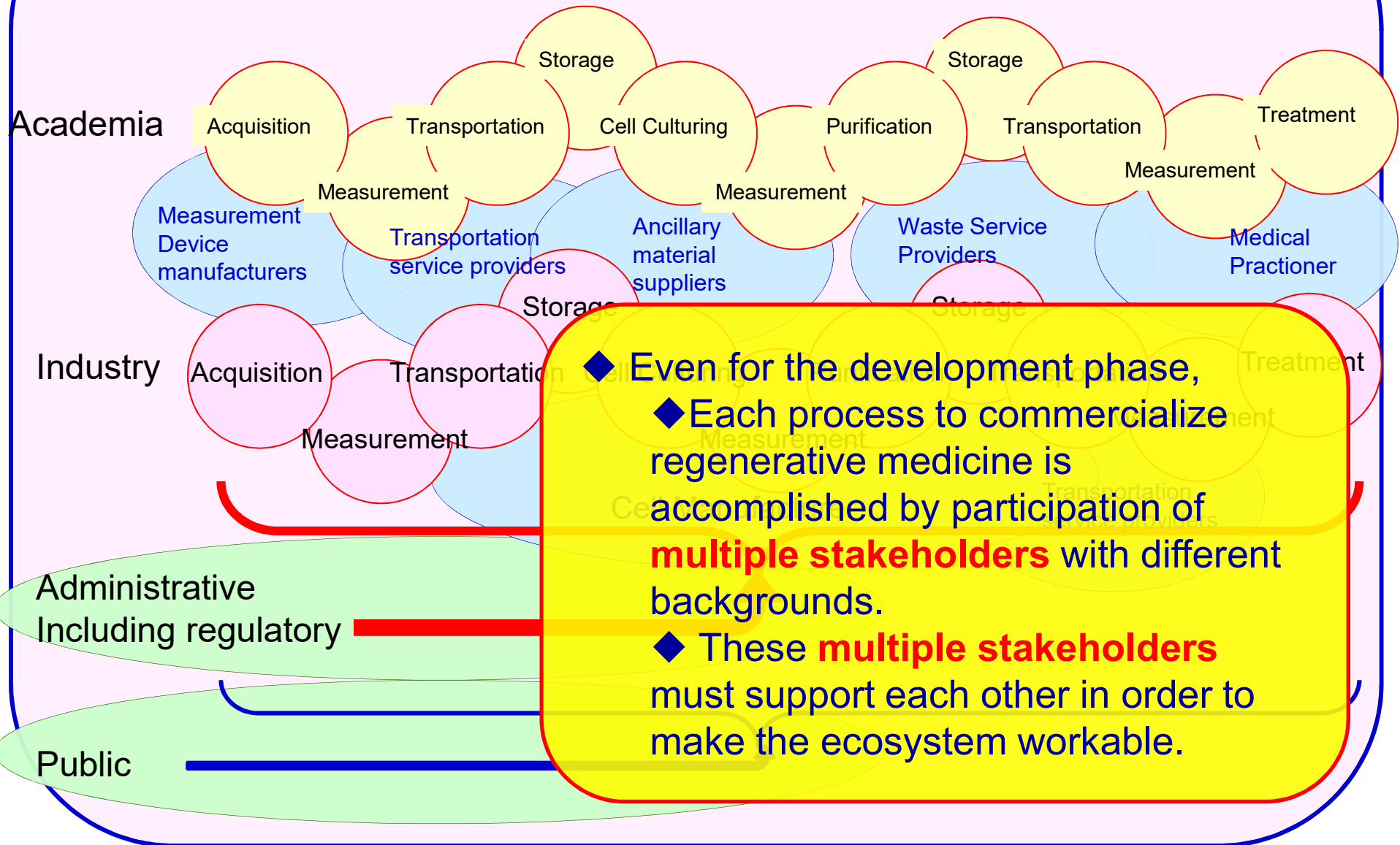




# The Ecosystem for regenerative medicine



# The Ecosystem for regenerative medicine

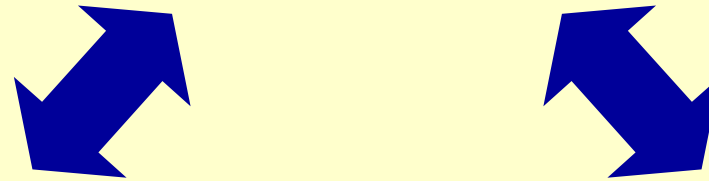


# Needs in regenerative medicine

- ◆ Multiple stakeholders with different backgrounds must support each other in order to bring novel value of regenerative medicine into the society.
- ◆ Transition of science into therapy is the goal.

What is needed? It is,

**Common language**



Rules, conventions

Objective references

**Common language** promotes/assures **common understanding** among individuals involved

# Needs in regenerative medicine

- ◆ Multiple stakeholders with different backgrounds must support each other in order to bring novel value of regenerative medicine into the society.
- ◆ Transition of science into therapy is the goal.

What is needed? It is,

共通言語

**Common language**

ルールや用語

Rules, conventions

客観的参照物

Objective references

**Common language** promotes/assures **common understanding** among individuals involved

# Contribution by common language – How?

“Chain store fast food” – a benchmark for industrialization

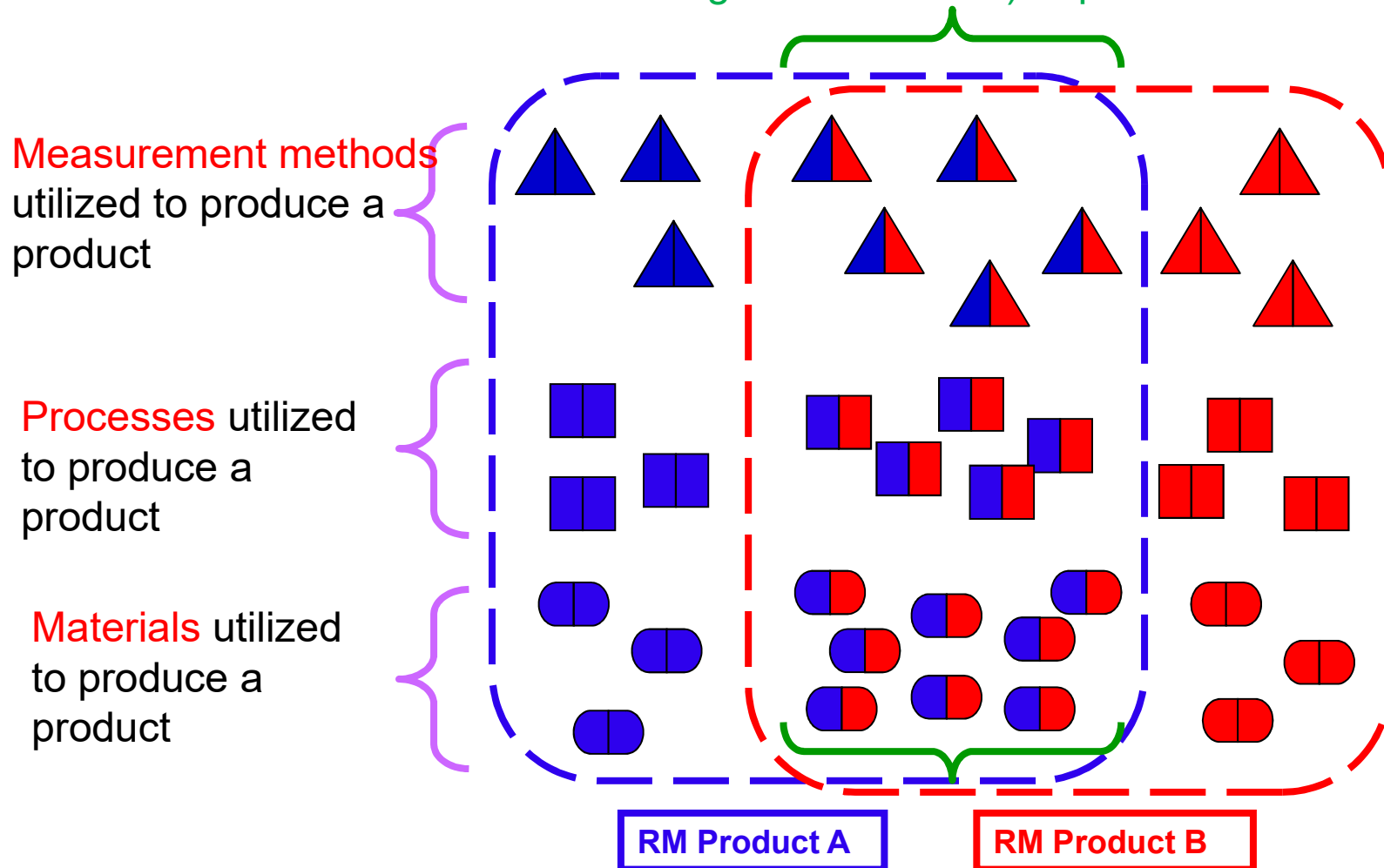
- Provides service/product with aimed quality  
**ANYTIME, ANYWHERE, and by ANYBODY** (and at an acceptable cost)
  - Comparable/ reproducible taste, price, serving time among WW shops.

- Enabled by their common language – the company’s internal standards (ex. SOPs, spec for raw materials)

# Regenerative Medicine (RM)

## What can be **common languages** ?

Measurement, materials and processes utilized to produce RM products, which are **common** (and not be acknowledged as common) at present.



# Regenerative Medicine (RM)

## What can be **common languages** ?

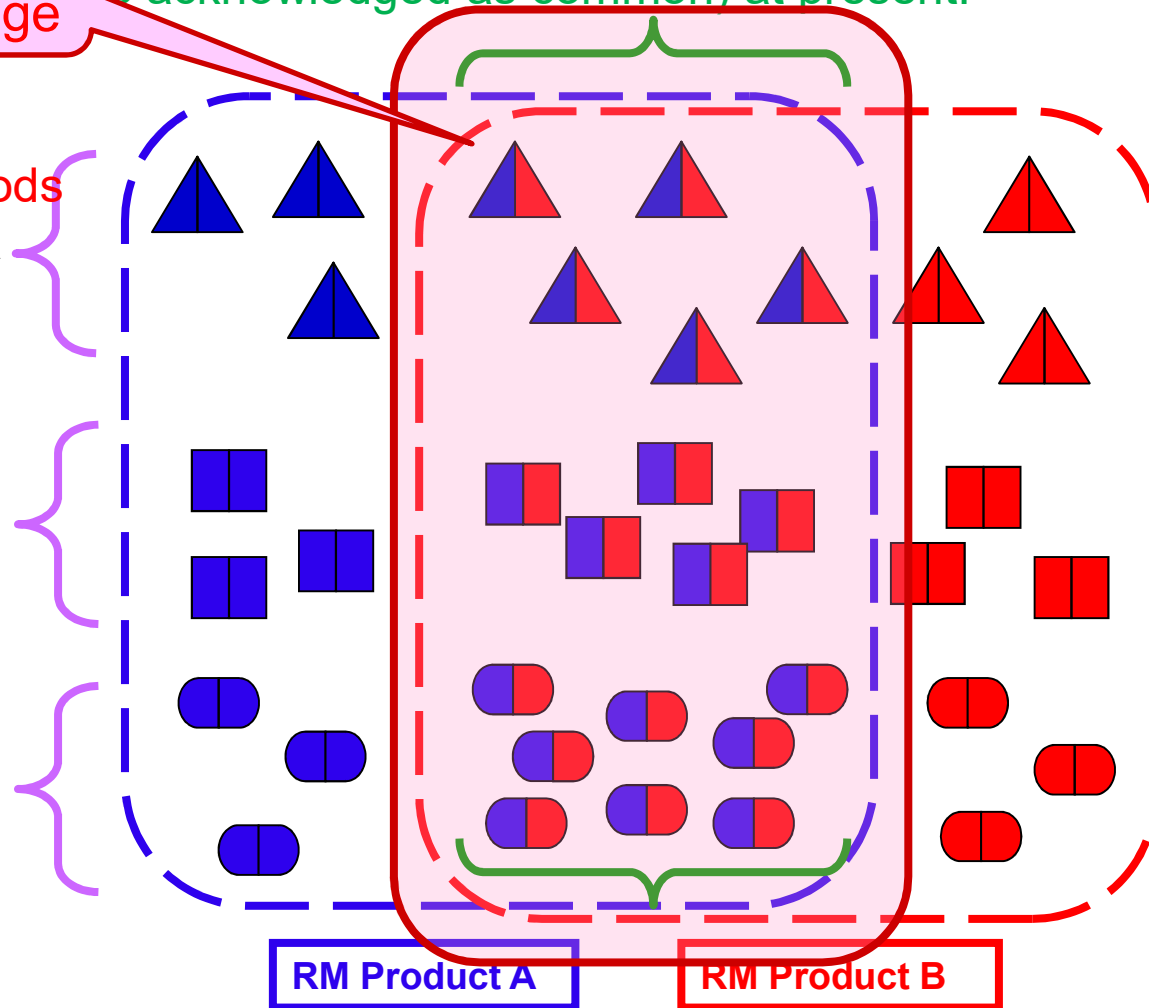
Measurement, materials and processes utilized to produce RM products, which are **common** (and not be acknowledged as common) at present.

Possible area for common language

Measurement methods utilized to produce a product

Processes utilized to produce a product

Materials utilized to produce a product



# Regenerative Medicine (RM)

## What are **common languages** ?

Measurement, materials and processes utilized to produce RM products, which are **common** (and not be acknowledged as common) at present.

Possible area to standardize

Measurement methods utilized to produce a product

Processes utilized to produce a product

Materials utilized to produce a product

Published standards and ongoing projects in **ISO/TC 276** in the field of regenerative medicine

Measurement methods:

- **Cell counting (ISO 20391 published)**
- Cell characterization

Processes

- Transportation of cells for therapeutic use

Materials

- Ancillary materials present during production of cells (published in December 2018 as the 1<sup>st</sup> achievement)
- Equipment systems for manufacturing of cells

RM Product A

RM Product B



## Definition of “standards” in ISO

- ①Common language, ②Made Open, ③Authority

- established by consensus and
- approved by a recognized body,

③Authority

②Made open

- that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context

ISO Directives Part 2

①Common language

ISO

③Standards with authority

②Standards made open

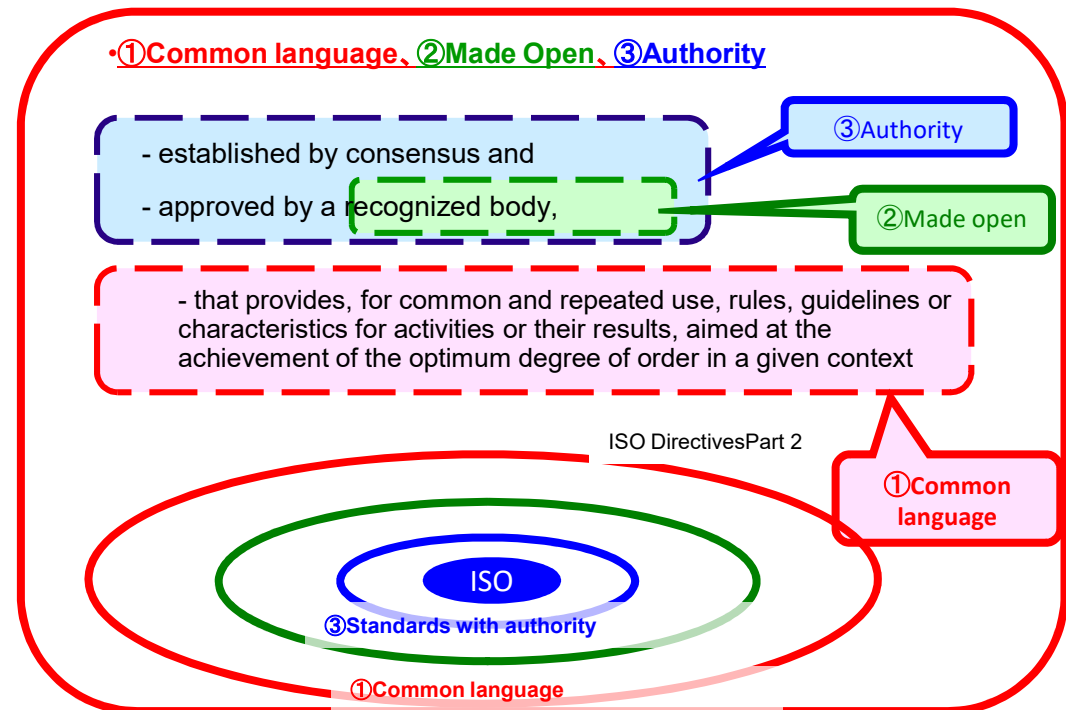
①Common language

## Definition of “standards”

- ◆ ① Common language should be
  - ◆ ② made open
  - ◆ ③ acquire authority
- to be recognized as “standard”



ISO/IEC Worlds Standards Day (2015)



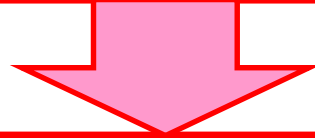
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  - 3-2) Leveraging use of standards**
  - 3-3) Planning standards**
- 4) FIRM pursuing standardization

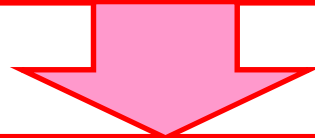
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# How shall we make this happen

#1: Planning standards



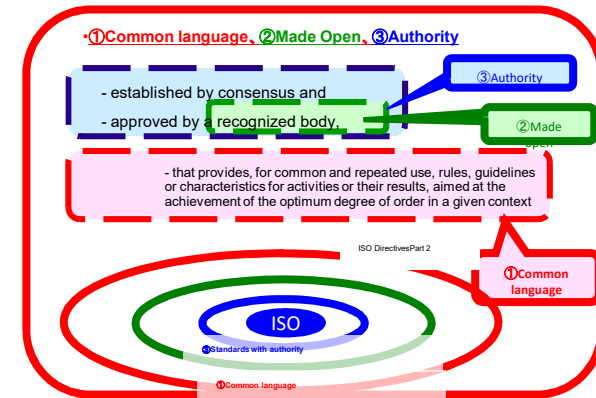
#2: Developing standards



#3: Leveraging use of standards

# ISO is the organization that provides open standards with authority

- ISO (International Organization for Standardization) is a well recognized body.
- ISO is of global relevance.
  - Consensus of
    - All the countries across the world.
    - All relevant stakeholders participate
      - Experts from industry, academia and government participate in its development.
- ISO works under impartial process.
- Standards are developed by contributions of experts.



ISO Central Secretariat in Geneva, Switzerland.  
Photo taken by Yutaka Yanagita

# How can we make use of standards

#1: Planning standards

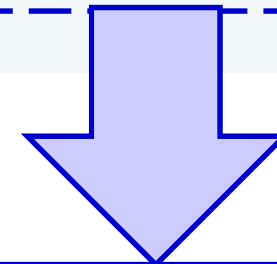
```
graph TD; A["#1: Planning standards"] --> B["#2: Developing standards"]; B --> C["#3: Leveraging use of standards"]; style C fill:#ffff00,stroke:#ff0000,stroke-width:2px
```

#2: Developing standards

#3: Leveraging use of standards

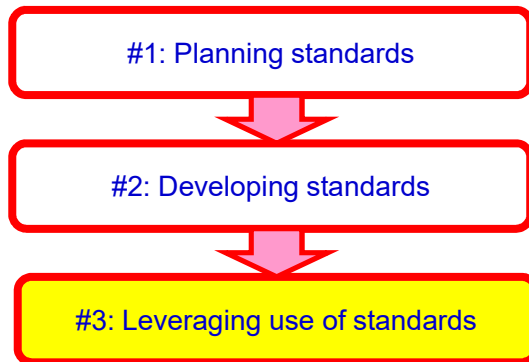
# ISO vs. fastfood

	Fast food standard	ISO standard
Common language	YES	YES
Made open	NO	YES
Authority	YES (only within company)	YES (World wide)
Stakeholder engagement	as User (for most employees)	as Developer (contributor) and User
Stakeholder usage	Mandatory (within company)	Voluntary (unless mandated by contract or regulation)



Challenge to open standards including ISO

# #3: Leveraging use of standards



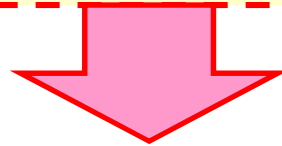
- Standards (including ISO standards) are, essentially voluntary.
- The standard will not be used, unless there is a need (or rational) to use it.
  - Note: Keep in mind there is a need for a common language in regenerative medicine.



## Needs of Common languages in Regenerative Medicine

- Potential need of common languages in regenerative medicine.
  - Common language to address safety
  - Common language to address efficacy

– Common language to address reliability of process / measurement



Significant opportunity for these standards to be commonly use

This the scope for **ISO/TC 276**

Standardization in the field of **biotechnology processes** that includes the following topics:

Terms and definitions;  
biobanks and bioresources;

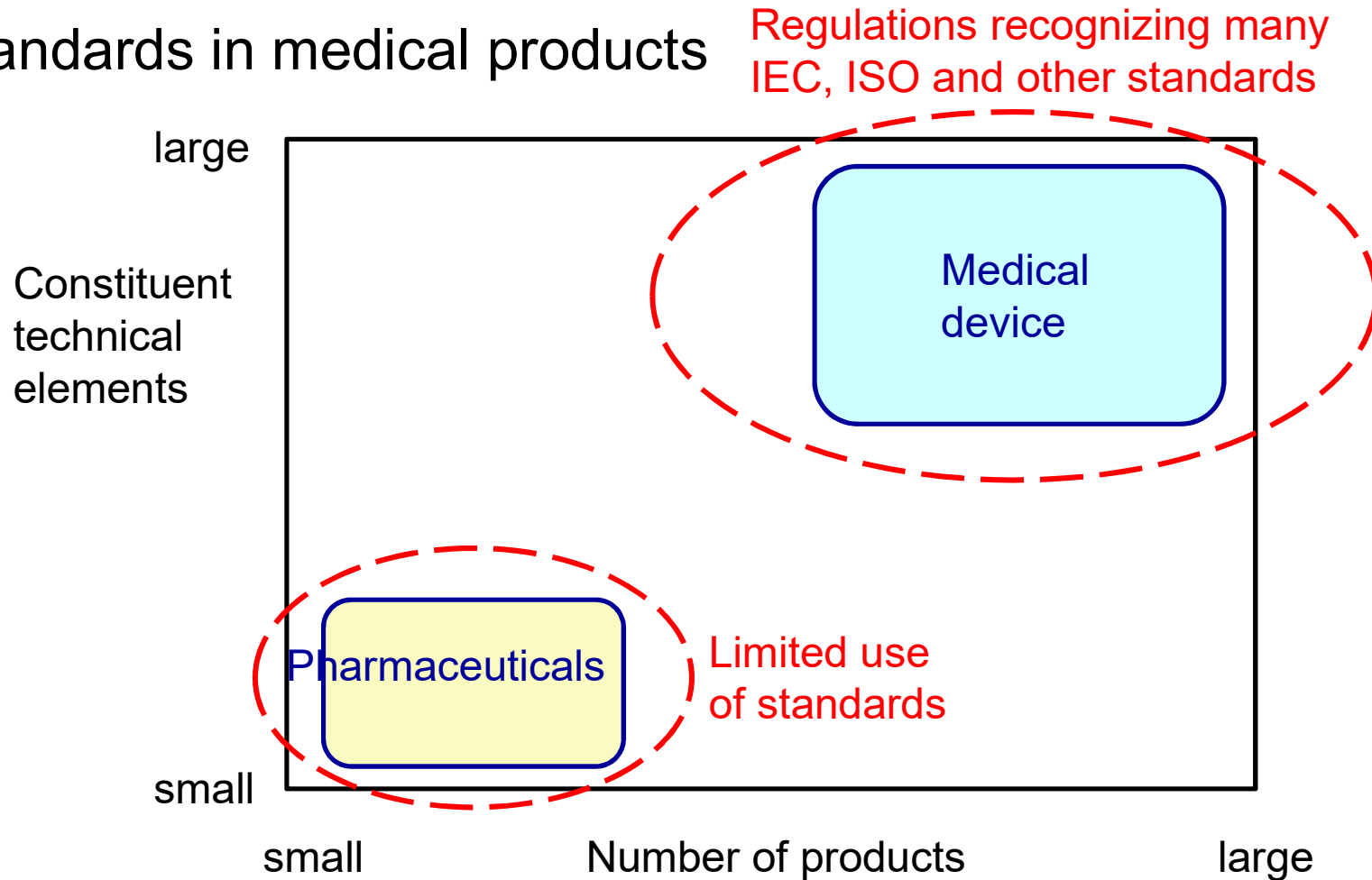
**analytical methods;**

**bioprocessing;**

data processing including annotation, analysis, validation, comparability and integration;  
metrology.

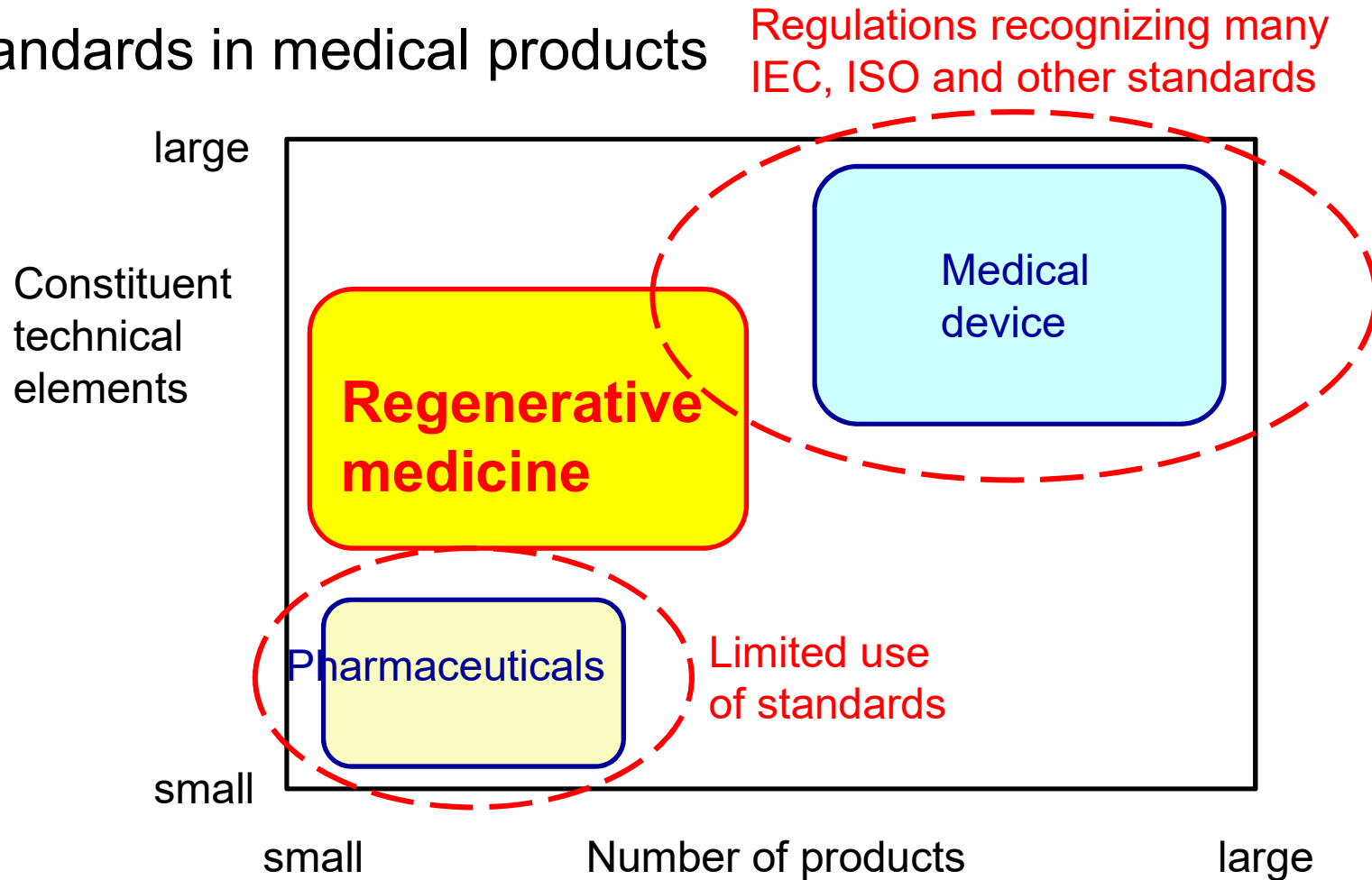
# Standards contributing to regenerative medicine – How we envision it

Standards in medical products

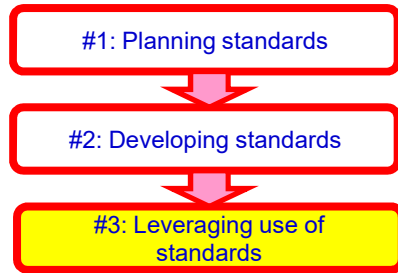


# Standards contributing to regenerative medicine – How we envision it

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# Standards contributing to regenerative medicine – How we envision it

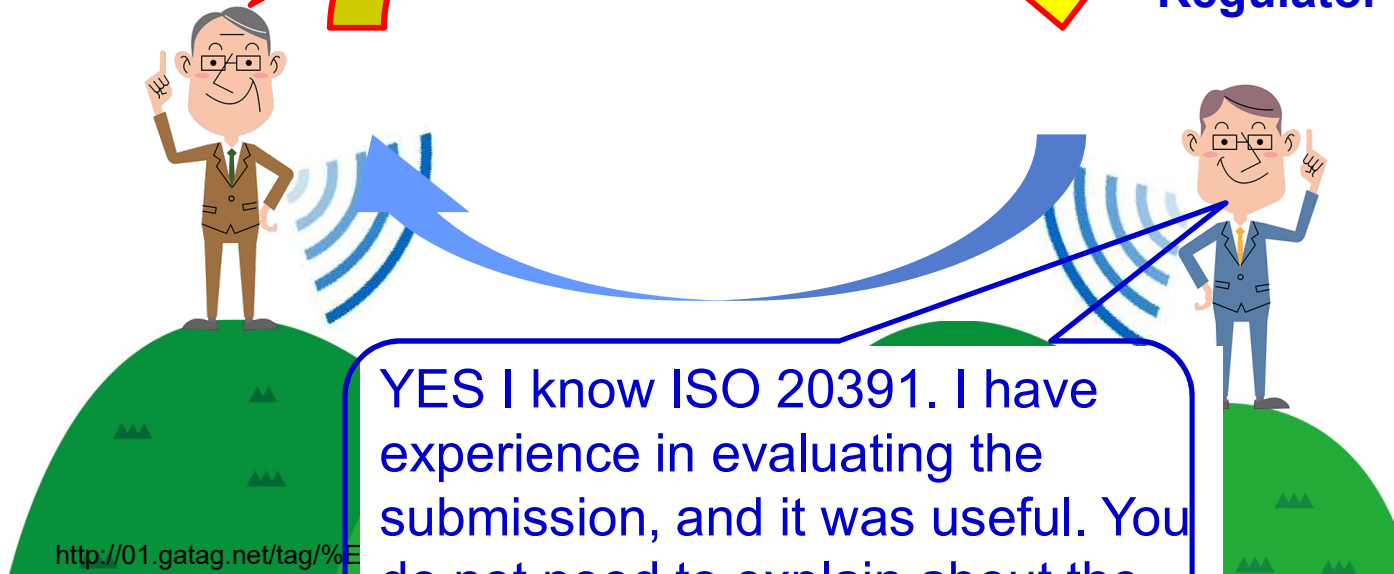


Dialog between regulators and sponcers

I measured cell count complying to ISO 20391

Sponcer

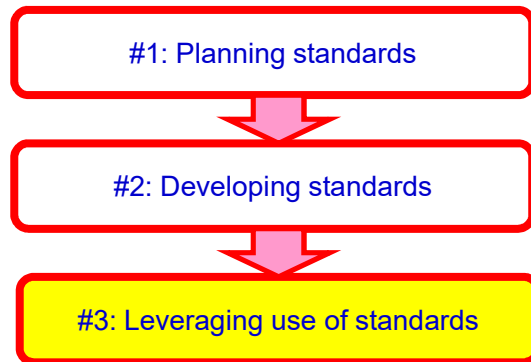
Regulator



YES I know ISO 20391. I have experience in evaluating the submission, and it was useful. You do not need to explain about the details.

<http://01.gatag.net/tag/%E>

# Positive message from FDA



- FDA is
  - In the direction to make use of standards
  - FDA is actively participating in ISO/TC 276 activities

## **Standards Development and Standards in Regulatory Review Reviewed in the Center for Evaluation and Research**

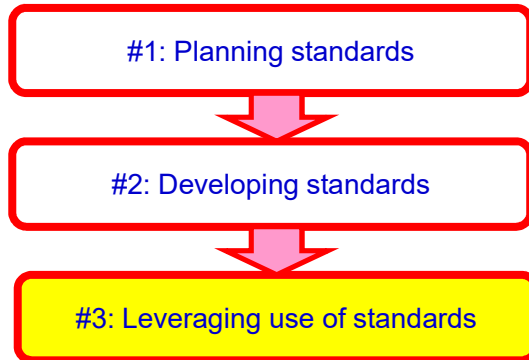
### **Draft Guidance for Industry and Drug Administration**

This guidance document is for comment purposes.

Submit one set of either electronic or written comments on this draft provided in the *Federal Register* notice announcing the availability. Submit electronic comments to <https://www.regulations.gov/>. Submit comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 1061, Rockville, MD 20852. You should identify all comments with the notice of availability that publishes in the *Federal Register*.

Additional copies of this guidance are available from the Office of

# Positive message from FDA



## Standards Development and Standards in Regulatory Review Reviewed in the Center for Evaluation and Research

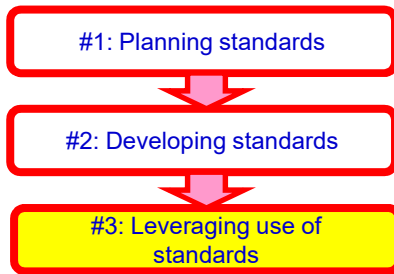
- FDA is actively participating in ISO/TC 276 activities
  - What is needed to have the standards be “accepted”?
  - Standards should have proven records and/or experience in using it

### Draft Guidance for Industry: Standards in Regulatory Review

This guidance document is for comment purposes only.

Submit the set of either electronic or written comments on this draft provided in the *Federal Register* notice announcing the availability of this draft guidance to the Regulatory Information Systems (RIS) web regulations.gov. Submissions should be made to the Regulatory Information Systems (RIS) web regulations.gov. Submissions should be made to the Regulatory Information Systems (RIS) web regulations.gov. Submissions should be made to the Regulatory Information Systems (RIS) web regulations.gov. You should identify all comments with the notice of availability that publishes in the *Federal Register*.

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## What is needed to have the standards accepted

- Example action to promote disclosure of sufficient proven records
  - **NIST-FDA Cell Counting Workshop**: Sharing practices in cell counting measurements
  - April 10, 2017
  - **NIST Organizers**: Sheng Lin-Gibson, Sumona Sarkar, Clare Allocca  
**FDA Organizers**: Judith A. Arcidiacono, Steven S. Oh, Steven Bauer
  - NIST and FDA are actively collaborating on projects that address regulatory and measurement challenges for regenerative medicine products and advanced therapies. These collaborations leverage NIST expertise in measurement sciences to address specific analytical scientific challenges as well as FDA regulatory science, research and review expertise in regenerative medicine products to ensure that the science and standards developed address significant regulatory challenges that recur across the field. One of the fundamental challenges for manufacturers of regenerative medicine products is the counting of cells for manufacturing and dosing purposes. This workshop will focus on approaches for selecting appropriate cell counting methods and overcoming gaps in obtaining sufficient measurement assurance for cell counting. The expected outcome of the workshop is a Workshop Summary/Whitepaper to be published in a peer reviewed journal as well as input into standards for cell characterization.

# How shall we make this happen

**#1: Planning standards**



**#2: Developing standards**

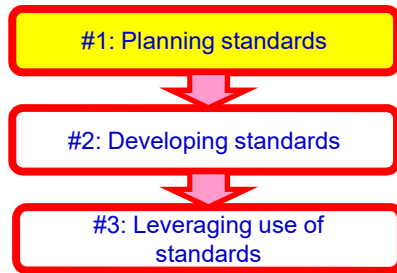


**#3: Leveraging use of standards**





# #1: Planning standards



What is current landscape for standards?

Report (2018-02) by the Standards Coordinating Body (SCB)

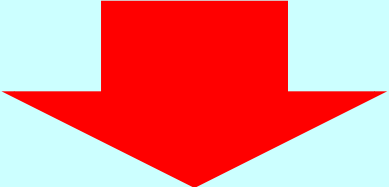
- 1) Current landscape
- 2) Needs and opportunities

- The Standards Coordinating Body for Gene, Cell, and Regenerative Medicines and Cell-Based Drug Discovery (SCB) brings together product developers, tools and service providers, professional societies, government entities, and academic centers with the intent to support standards development for the global regenerative medicine community.

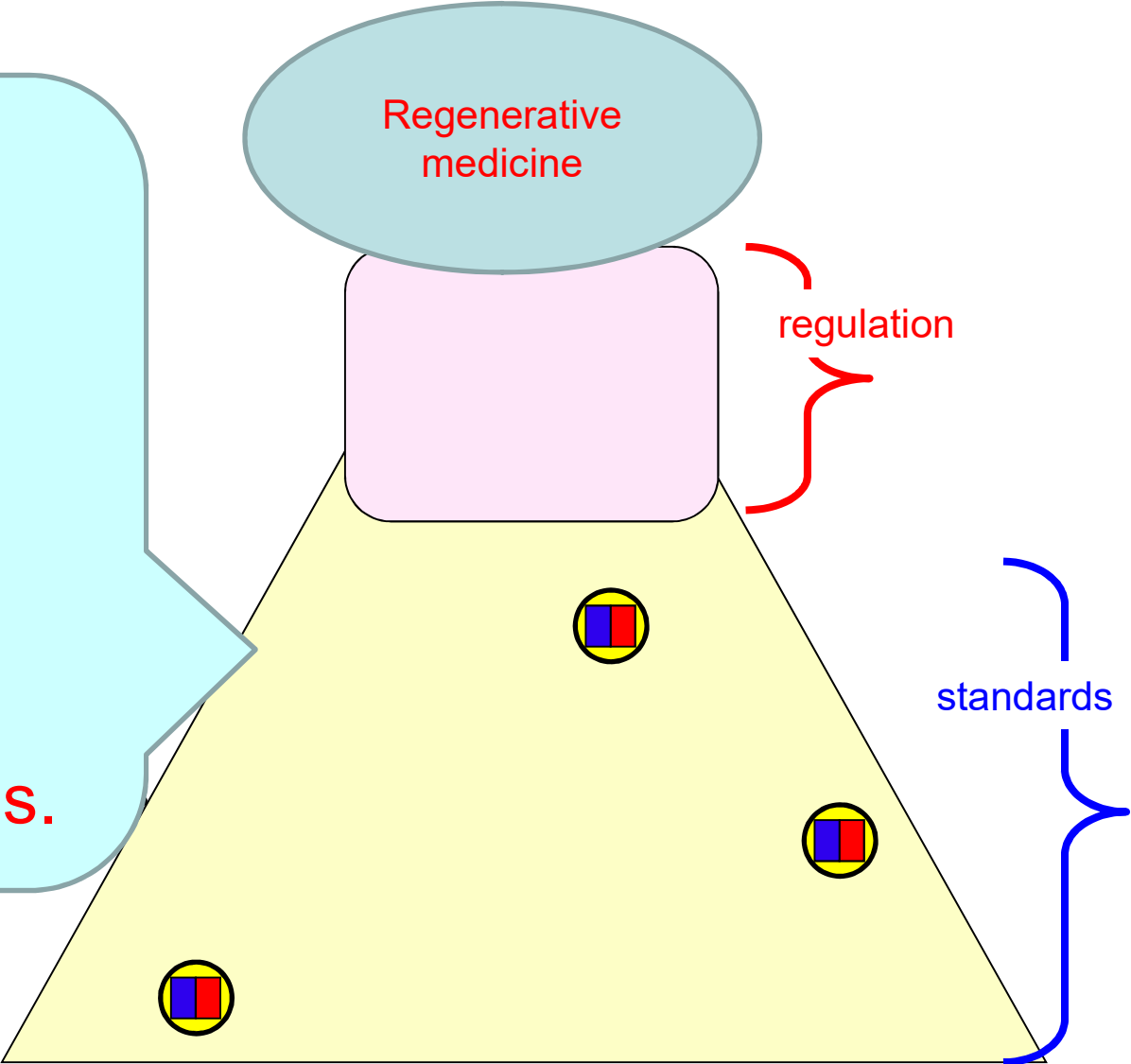


# Currently

Not so many work on standards.

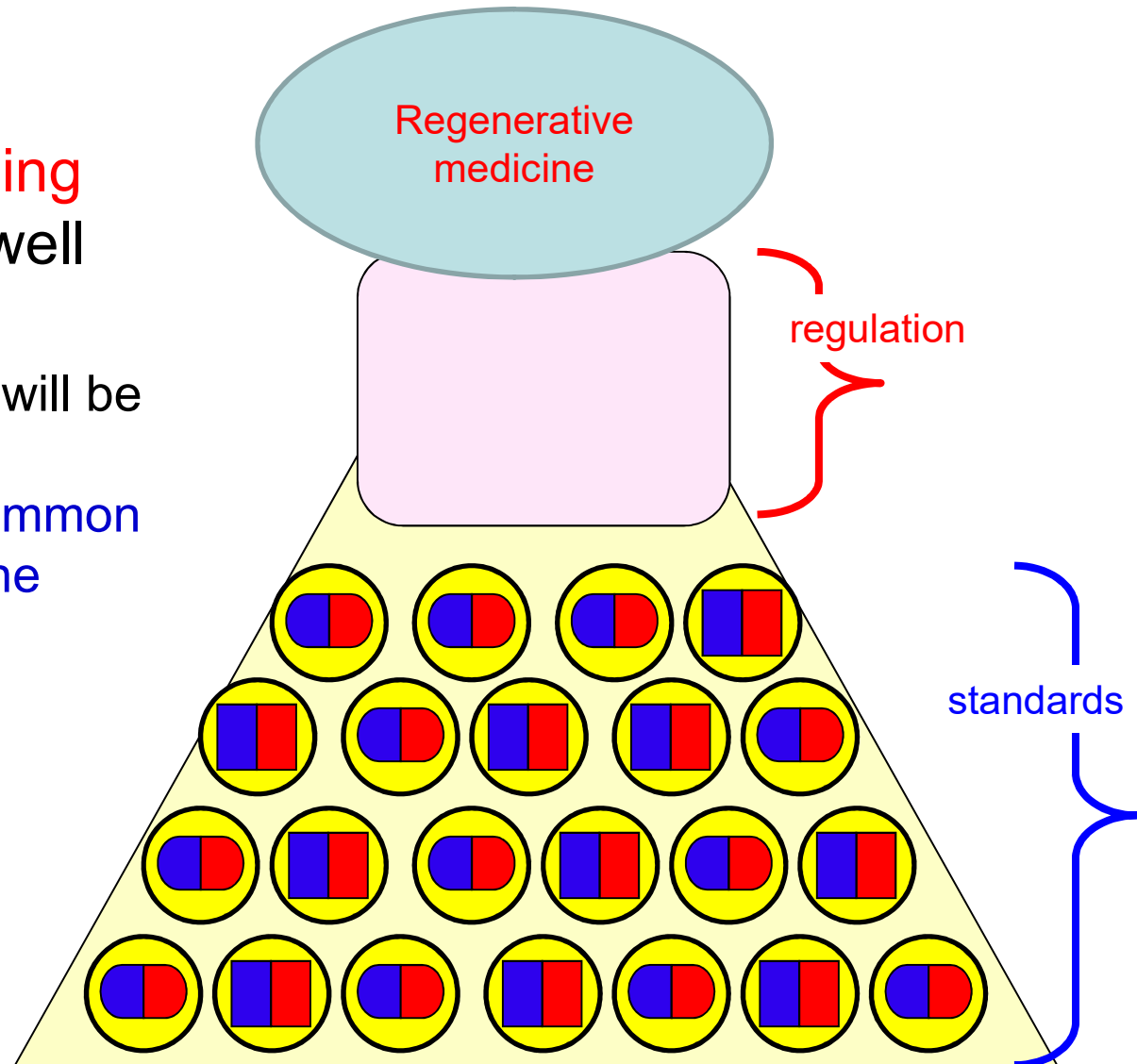


Big “frontier” of standards lies right in front of us.



# Our goal

- To provide “Building Blocks” that are well organized.
  - “Building Blocks” will be the foundation to promote/assure common understanding in the ecosystem

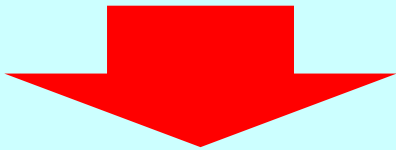


# Next Step

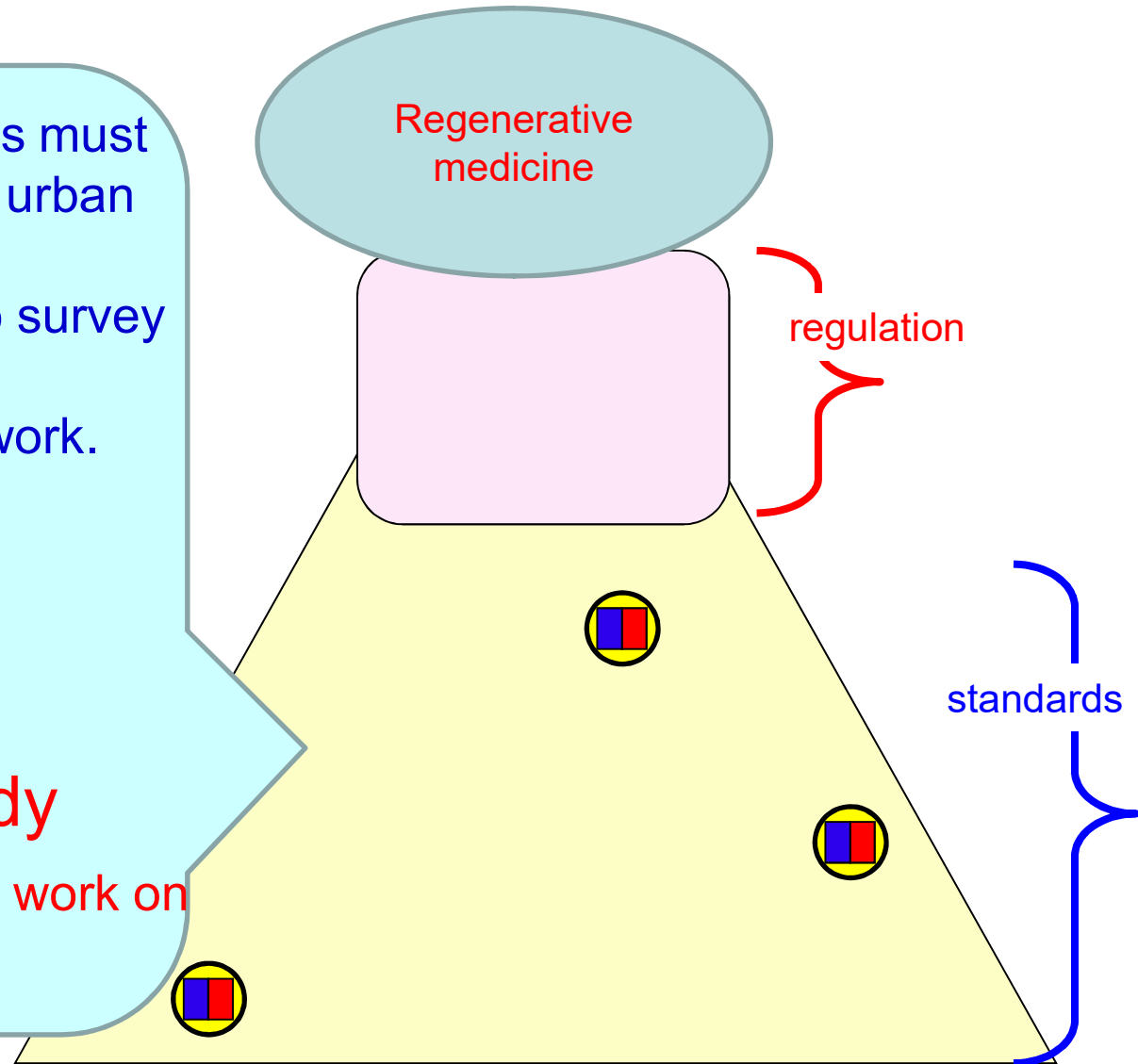
Draft page to be worked

The frontier of standards must be developed under an urban planning that:

- minimizes workload to survey existing standards, and
- avoids duplication of work.



**The Standards Coordinating Body (SCB)** is expected to work on this activity.



# SCB (Standards Coordinating Body)

- [Realizing the Benefit of 21st Century Cures through Standards Development: A Workshop Convened by FDA, NIST, SCB, and Nexight Group](#)

- Mon, Jan 14, 2019 8:30 AM 08:30 Tue, Jan 15, 2019 4:30 PM 16:30
- NIST National Cybersecurity Center of Excellence (NCCoE)

Postponed

- [Poll for Needed Regenerative Medicine Therapies Standards](#)

- Please complete a poll about needed regenerative medicine therapy standards at this link before Wednesday, December 12, 2018. The poll should take less than 20 minutes to complete and contains questions on the following areas:
  - Needed Standards? Which areas would standards development most benefit the cell, gene therapy, and tissue engineering fields?  
Impact and Urgency? What is the impact a standard could have on the availability of safe and high-quality regenerative medicine therapies?  
What is the level of urgency with which a needed standard should be pursued to mitigate risk and realize opportunities?

Looking forward to receive the report

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# FIRM Leveraging standard activities

- Standards Coordinating Body
  - Board member from FIRM
- ISO/TC 276
  - Organizes Japan mirror committee

# ISO/TC 276 activities

**FIRM** organizes Japan Mirror Committee for ISO/TC 276 and Committee to Standardize Foundation for Cell Characterization and Cell Production. Experts from academia, government and industry are actively participating in these committees.

ISO/TC 276 is expected to be the centerpiece for the process of regenerative medicine. More than 100 experts from worldwide gathered at the ISO/TC 276

Plenary and Working group meetings held in Beijing this June. **FIRM** will organize its next meetings in 2019 to be held in Nihonbashi, Tokyo.



Beijing 2018-06

**ISO/TC 276  
The 7th plenary  
meeting**

**Tokyo, Japan  
June 10<sup>th</sup>-15<sup>th</sup>, 2019**



**New ideas will start here**



## ISO/TC 276における日本

FIRM organizes Japan Mirror Committee for ISO/TC 276 and Committee to Standardize Foundation for Cell Characterization and Cell Production. Experts from academia, government and industry are actively participating in these committees.

IRMはISO/TC 276の国内幹事団体として国内委員会を運営するとともに経産省受託事業を進めるための「細胞評価及び製造基盤標準化委員会」を運営している。両委員会には産官学の専門家が積極参画している。

# Summary

- **Innovation** in regenerative medicine needs an **ecosystem** where multiple stakeholders with different backgrounds communicate by a **common language** to each other.
- Efforts to make use of standard, as well as efforts to orderly develop the standards are important to have is used as **common language** in the **ecosystem**.
- Need of a **common language** is the **driver for current and potential standards efforts**.

Thank you for your attention  
ご清聴ありがとうございました。