2019-01-24

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

A Summary of Current Standardization Activities in ISO/TC 276 *Biotechnology*

FIRM (The Forum for Innovative Regenerative Medicine)

Yutaka Yanagita

Astellas Pharma Inc.

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

Vice Chair, ISO/TC 276 Japan Mirror Commitee

Vice Chair, FIRM Standardization Committee

Table of contents

0. はじめに

- Clare Alloccaさん
  - Standards Coordination Office, NIST
    - The National Institute of Standards and Technology (NIST) was founded in 1901 and is now part of the U.S. Department of Commerce. NIST is one of the nation's oldest physical science laboratories.
  - Secretary of ISO/TC 276/WG 3
  - Secretary of the US Mirror Committee

Table of contents

ライフサイエンスやバイオ技術等の生物分野で標準化の議論が少なかった理由

- 生物が関係する分野の先端技術はあまりにも基礎的な科学と近く、
- また、多くの学問分野がそれぞれ独自の体系を作っていること、
- 測定方法や評価のやり方がそれぞれ個別の特性を持っていること
- 個々の優れた医療技術、あるいは特別な技能を持った人に特化したノウハウに依存する自己完結した技術である
- 医薬品は化学構造が特定でき、特許で研究成果を確実に保護でき、機器類と異なり多くの技術との組合せとの整合性を図るインターフェースについて心配する必要のない技術であった。

「幹細胞技術の標準化」－再生医療への期待
堀友繁　監修／田中正躬　編著　日本規格協会2012
終章　再生医療における技術標準の役割
（田中正躬）より

Table of contents

ISO/TC 276の経緯：（1）前史

- 2008年　ISO内でバイオテクノロジー分野の国際標準化に関するタスクフォース（TF）設立
- 2009年　TF、新規専門委員会(Technical Committee, TC)の設立を勧告
- 2011年　ワークショップ” International Standards for Biotechnology ”で新たなTCの骨格を検討
  - 基本的にHorizontal（分野横断的）な課題を扱う
  - Vertical（各産業分野に特化した技術）な課題は、それぞれのステークホルダー（利害関係者）と連携する
  - 進展が早く、標準化ニーズの高い分野の一つとして、”Regenerative Medicine”を例示した
- 出典
  - http://www.iso.org/sites/biotechnology2011/index.html
  - 「幹細胞技術の国際標準化」 堀友繁　監修/田中正躬　編著、日本規格協会、2012年

（2015年6月4日　SKIPセミナー「ISO国際標準化ー幹細胞との関わり『2. ISO/TC 276 (Biotechnology)の状況』柳田豊」より）

ISO Workshop “International Standards for Biotechnology” (Geneva, 25-26 October 2011)

- “**New ISO work in the biotechnology field**”**のscopeを提案**
- On one axis, horizontal issues concerning the set-up, undertaking and results of assays, such as:
  - Sample preparation
  - Sample processing and handling
  - Experimental methodologies
  - Data structuring and processing
  - Reporting
- On the other axis, bioscience/biotechnology disciplines and their characterization in relation to specific applications, such as:
  - Genomics (e.g. for health care, …)
  - Proteomics (e.g. for biopharmaceutical, …)
  - Functional genomics (e.g. for cell characterization, …)
  - Metabolomics (e.g. for toxicogenetics, food safety, …)

ISO/TC 276の経緯 （2）設立以降

- 2012年
  - 7月　新規TC設立を提案（ドイツ）
- 2013年
  - 2月　ISO/TC 276設立（日、英、独、韓など10か国が積極参加）
  - 5月　FIRMが日本国内幹事団体となる
  - 8月　日本国内委員会立ち上げ
  - 12月　第1回全体会議（ベルリン）（米、仏が積極参加）
- 2014年
  - 1月　中国が積極参加
  - 5月　第2回全体会議（ベルリン）
  - 10月　ワーキンググループ1～4を設立、活動開始
  - 12月　合同ワーキンググループ会議（ベルリン）
- 2015年
  - 4月　第3回全体会議（中国・深圳）、ワーキンググループ5を設立
  - 10月　合同ワーキンググループ会議（日本・東京）←国立がん研究センター）

↓第3回全体会議（深圳）

（2015年6月4日　SKIPセミナー「ISO国際標準化ー幹細胞との関わり『2. ISO/TC 276 (Biotechnology)の状況』柳田豊」より）

再生医療に関連するISO専門委員会(technical committee)と分科委員会(subcommittee)

- ISO/TC 150: Implants for surgery
  - ISO/TC 150/SC 7: Tissue-engineered medical products（ファインセラミックス国際標準化推進協議会）
- ISO/TC 194: Biological and clinical evaluation of medical devices
  - ISO/TC 194/SC 1: Tissue product safety（日本医療器材工業会）
- ISO/TC 198: Sterilization of health care products（日本医療機器学会）
- ISO/PC 271: Compliance management systems
- ISO/PC 272: Forensic sciences
- ISO/PC 273: Customer contact centres
- ISO/TC 274: Light and lighting
- ISO/TC 275: Sludge recovery, recycling, treatment and disposal
- ISO/TC 276: Biotechnology（再生医療イノベーションフォーラム）
- ISO/PC 277: Sustainable procurement
- ISO/PC 278: Anti-bribery management systems
- ISO/TC 279: Innovation management
- ISO/PC 280: Management Consultancy

（括弧内は国内審議団体名）

http://www.iso.org/iso/home/standards_development/list_of_iso_technical_committees.htm

ISO/TC 276の経緯 （3）今日まで

- 2016年
  - 5月　　第4回全体会議（米国・ワシントンDC）←農務省研修施設
  - 10月　　合同ワーキンググループ会議（アイルランド・ダブリン）
- 2017年
  - 5月　　第5回全体会議（韓国・ソウル）
  - 11月　　合同ワーキンググループ会議（イタリア・ローマ）
- 2018年　　ISO/TC 276の成果物（標準）5点が発行された
  - 6月　　第6回全体会議（中国・北京）
  - 7月　　Xun Xu氏（中国）、副議長に就任
  - 12月　　合同ワーキンググループ会議（ドイツ・ポツダム）
- 2019年（予定）
  - 6月　　第7回全体会議（日本・東京）←日本橋ライフサイエンスハブ
  - 12月　　合同ワーキンググループ会議（カナダ・トロント）

合同WG会議（ポツダム）→

Table of contents

ISO/TC 276 - Structure

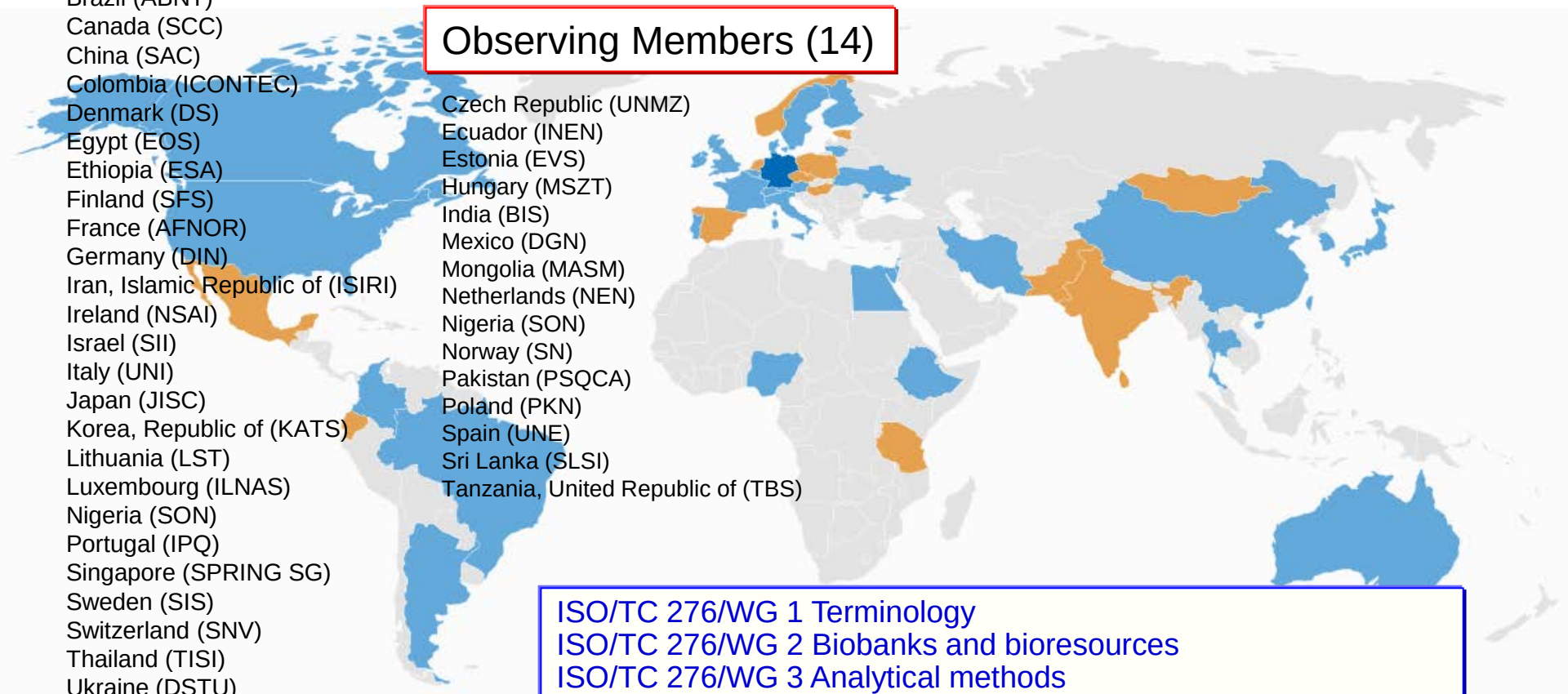
Participating Members (31)

Argentina (IRAM)
Australia (SA)
Austria (ASI)
Belgium (NBN)
Brazil (ABNT)
Canada (SCC)
China (SAC)
Colombia (ICONTEC)
Denmark (DS)
Egypt (EOS)
Ethiopia (ESA)
Finland (SFS)
France (AFNOR)
Germany (DIN)
Iran, Islamic Republic of (ISIRI)
Ireland (NSAI)
Israel (SII)
Italy (UNI)
Japan (JISC)
Korea, Republic of (KATS)
Lithuania (LST)
Luxembourg (ILNAS)
Nigeria (SON)
Portugal (IPQ)
Singapore (SPRING SG)
Sweden (SIS)
Switzerland (SNV)
Thailand (TISI)
Ukraine (DSTU)
United Kingdom (BSI)
United States (ANSI)

Secretariat: DIN (Germany)
Secretary: Ms. Petra Bischoff (Germany)
Chairperson: Mr. Ricardo Gent (Germany)
Vice Chairperson): Mr. Xun Xu (China)
Creation date: Feb. 2013

Observing Members (14)

Czech Republic (UNMZ)
Ecuador (INEN)
Estonia (EVS)
Hungary (MSZT)
India (BIS)
Mexico (DGN)
Mongolia (MASM)
Netherlands (NEN)
Nigeria (SON)
Norway (SN)
Pakistan (PSQCA)
Poland (PKN)
Spain (UNE)
Sri Lanka (SLSI)
Tanzania, United Republic of (TBS)



ISO/TC 276/WG 1 Terminology
ISO/TC 276/WG 2 Biobanks and bioresources
ISO/TC 276/WG 3 Analytical methods
ISO/TC 276/WG 4 Bioprocessing
ISO/TC 276/WG 5 Data processing and integration

As of 2019-01-21

(https://www.iso.org/committee/4514241.html?view=participation)

ISO/TC 276 (Biotechnology) Scope

- 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.
- ISO/TC 276 Biotechnology will work closely with related committees in order to identify standardization needs and gaps, and collaborate with other organisations to avoid duplications and overlapping standardization activities.
- The committee will not pursue subjects within the scope of other TCs including but not limited to ISO/TC 212 and ISO/TC 34/SC 16.

(https://www.iso.org/committee/4514241.html)

WG 1 Terminology

- Terminology: Working Group 1 will work on identification of currently used national and international standards, guidelines and other relevant documents, as well as terms and definitions, related to ISO/TC 276 Biotechnology. The work of this working group focuses initially on harmonization (where possible) rather than on standardization.

(https://livelink.din.de/livelink/livelink?func=ll&objid=20855499&objaction=browse&sort=name)

Projects of WG 1 origin

- ISO/DTR 20386 *Inventory of biotechnology-related terms*

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

WG 2 Biobanks and bioresources

- The ISO/TC 276/WG 2 will elaborate a package of International Standards in the Biobanking field including human, animal, plant and microorganism resources for Research & Development, but excluding therapeutic products.

(https://livelink.din.de/livelink/livelink?func=ll&objId=20855719&objAction=browse&viewType=1)

Projects of WG 2 origin (1/2)

- **ISO 20387:2018 *Biotechnology -- Biobanking -- General requirements for biobanking*（2018年発行）**
- ISO/AWI TR 22758 *Biotechnology -- Biobanking -- Implementation guide for ISO 20387*
- ISO/DIS 21899 *Biotechnology -- Biobanking -- General requirements for the validation and verification of processing methods for biological material in biobanks*

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

Projects of WG 2 origin (2/2)

- ISO/AWI 21709 *Biotechnology -- Biobanking -- Process and quality requirements for establishment, maintenance and characterization of mammalian cell lines*
- ISO/AWI TS 22859-1 *Biotechnology -- General guidelines for biobanking human MSCs -- Part 1: Derived from umbilical cord*
- ISO/AWI TS 20388 *Biotechnology -- Biobanking -- The Collection, processing, storage and transportation criteria for animal genetic resources*
- ISO/AWI TS 23105 *Biotechnology -- Biobanking -- The collection, processing, storage and transportation technology criteria for plant genetic resources*

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

WG 3 Analytical methods

- The Analytical Methods Working Group aims to develop standards for accurate, reproducible and robust measurement and analysis in support of biotechnologies. WG 3 will develop a package of International standards for biologically relevant molecules and entities, including nucleic acids, proteins, and cells. This WG will develop horizontal standards and, when applicable, vertical / particular standards for industry sectors. The WG will also coordinate with relevant technical committees and standardization initiatives.

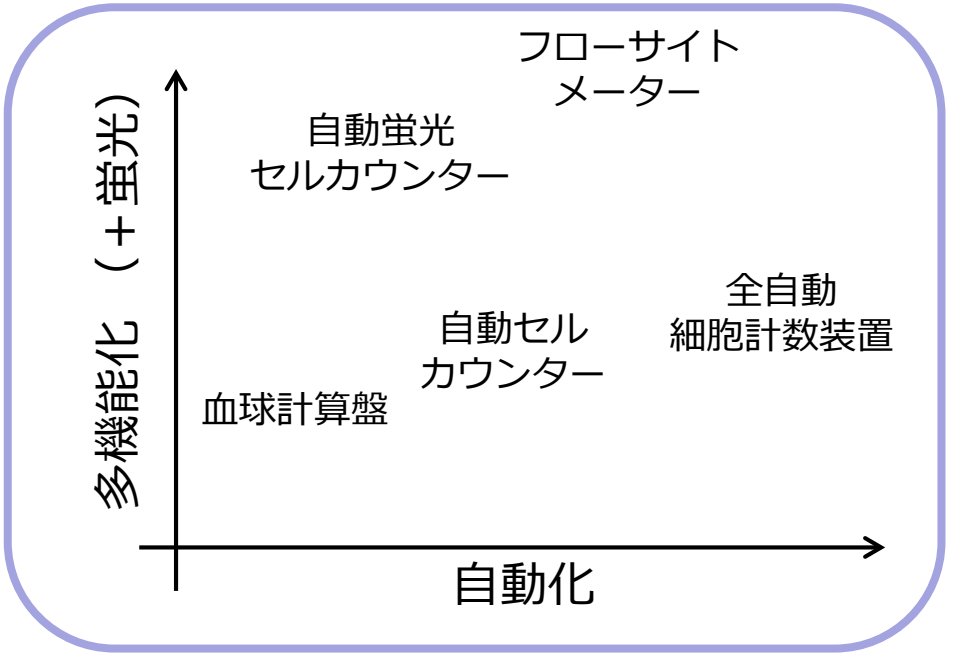
Projects of WG 3 origin (1/2)

- **ISO 20391-1:2018 *Biotechnology -- Cell counting -- Part 1: General guidance on cell counting methods*（2018年発行）**
- ISO/DIS 20391-2 *Biotechnology -- Cell Counting -- Part 2: Experimental design and statistical analysis to quantify counting method performance*
- ISO/CD 23033 *Biotechnology -- Cell Characterization -- General guide for characterization of human cells for therapeutic applications*
- Preliminary Work Items
  - Cell line authentication

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

Cell Counting standards

- How can evaluate reliability of data when there are on standard reference sample nor standard measurement methods?
- How can we verify the selected measurement method?



Projects of WG 3 origin (2/2)

- ISO/DIS 20395-1 *Biotechnology -- Requirements for evaluating the performance of quantification methods for nucleic acid target sequences -- Part 1: qPCR and dPCR*
- ISO/DIS 20688-1 *Biotechnology -- Nucleic acid synthesis -- Part 1: General definitions and requirements for the production and quality control of synthesized oligonucleotides*
- ISO/WD 20397-2 *Biotechnology -- General requirements for massive parallel sequencing -- Part 2: Methods to evaluate the quality of sequencing data*
- Preliminary Work Items
  - next-gen (massive parallel)sequencing

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

WG 4 Bioprocessing

- WG 4 aims to develop ISO deliverables for ensuring consistent, controlled and tracked processes to give confidence to suppliers and users of products. WG 4 will develop a package of ISO deliverables for four major technology spaces: 1) component materials control; 2) upstream processes (e.g., cell cultivation, fermentation, and bioconversion); 3) downstream processes (e.g. collection, separation, purification and formulation); and 4) handling, transportation and storage, where standardization needs and gaps are identified. The WG will also coordinate with relevant technical committees and standardization initiatives.

(http://isotc.iso.org/livelink/livelink?func=ll&objId=16444279&objAction=browse&viewType=1)

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

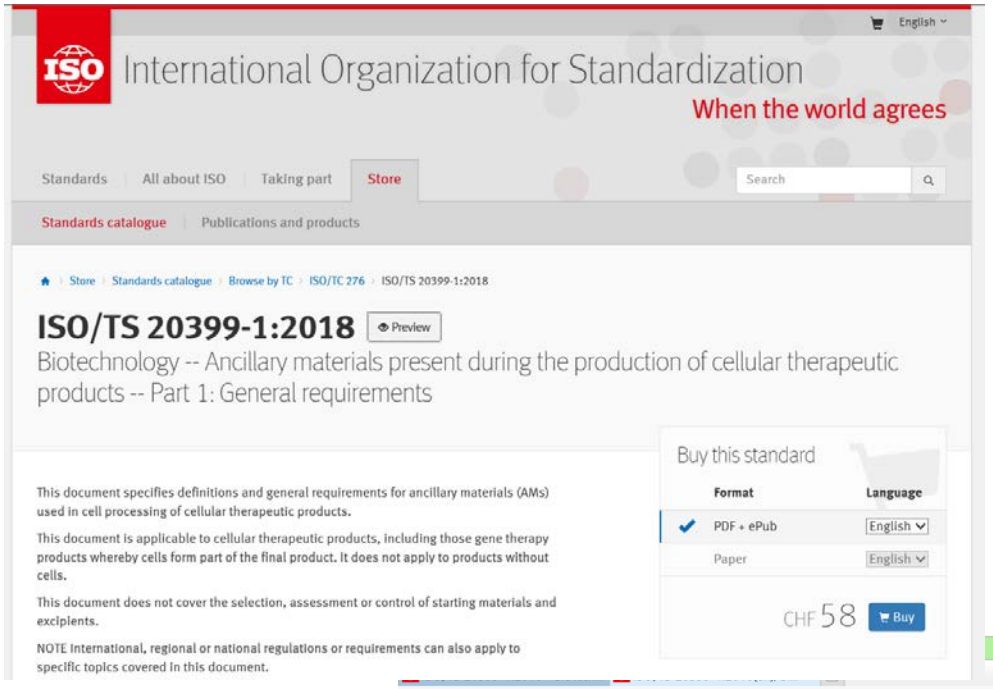
Projects of WG 4 origin (1/2)

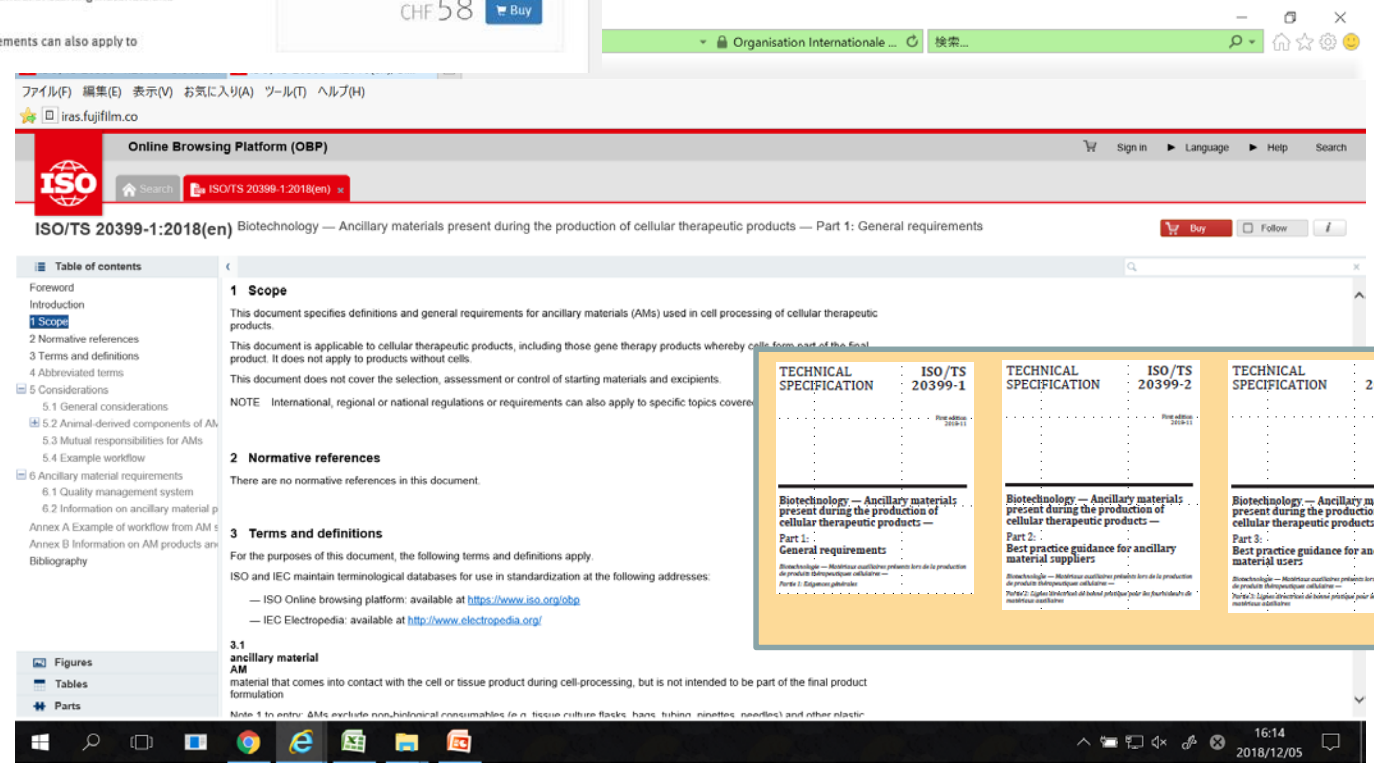
- **ISO/TS 20399-1:2018 *Biotechnology -- Ancillary materials present during the production of cellular therapeutic products -- Part 1: General requirements*（2018年発行）**
  - **Terms, definitions and general requirements**
- **ISO/TS 20399-2:2018 *Biotechnology -- Ancillary materials present during the production of cellular therapeutic products -- Part 2: Best practice guidance for ancillary material suppliers*（2018年発行）**
  - **To maintain a high level of lot-to-lot consistency**
- **ISO/TS 20399-3:2018 *Biotechnology -- Ancillary materials present during the production of cellular therapeutic products -- Part 3: Best practice guidance for ancillary material users*（2018年発行）**
  - **AM users' key questions for risk management**

Ancillary materials standards

Now, available in ISO web site

https://www.iso.org/standard/67897.html?browse=tc





Projects of WG 4 origin (2/2)

- ISO/AWI 21973 *Biotechnology -- General requirements for transportation of cells for therapeutic use*
- ISO/AWI TS 23565 *Biotechnology -- Bioprocessing -- General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products*

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

WG 5 Data processing and integration

- ISO/TC 276/WG 5 “Data processing and integration” aims to develop ISO deliverables for traceable, searchable, and interoperable data together with integrated data processing for biotechnology/life sciences.
- The main foci are:
  - definition of data and model formats and their interfaces;
  - definition of metadata and relations of data and models;
  - quality management of processed data and models.
- WG 5 will build on existing community standards and develop ISO deliverables where needs and gaps are identified.
- WG 5 will coordinate its work with relevant technical committees and standardization initiatives. This includes coordination with all working groups of ISO/TC 276.

(http://isotc.iso.org/livelink/livelink?func=ll&objId=16444279&objAction=browse&viewType=1)

Projects of WG 5 origin

- ISO/WD 20691 *Biotechnology -- Requirements for data formatting and description in the life sciences for downstream data processing and integration workflows*
- ISO/CD 21710 *Biotechnology -- Data management and publication in microbial biological resource centers*

(https://www.iso.org/committee/4514241/x/catalogue/p/1/u/1/w/0/d/0)

Table of contents

4. 今後の展望

- 課題
  - 参加国の増加（p-メンバー：10カ国→31カ国）
  - 参加者の増加（エキスパート100名超のWGも出現）
  - プロジェクト数の増加（PWI含め23のプロジェクトを同時に開発）
  - WG間のinteraction増加（単一WGに帰属困難なプロジェクトの発生）
  - 会議の負荷の増加（WG会議5日（+Plenary会議1日）を終日実施）
    - 既に年2回開催しているため頻度を上げることは困難、
    - 複数WGに属するエキスパートが多く会議の細分化も困難
- 成長期→成熟期への移行期
- 対策
  - 効率化・高質化の追求
    - メンバー
    - プロジェクト
    - 開発プロセス

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

ISO/TC 276 The 7th plenary meeting
Tokyo, Japan, June 10th-15th, 2019

New ideas will start here