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Precision Medicine: Legal and Ethical Challenges
The University of Hong Kong

Genomic Medicine in Japan: Recent Changes in the Government Policy, and New Ethical and Legal Challenges

Kazuto Kato, PhD
Professor, Department of Biomedical Ethics and Public Policy,
Division of Social Medicine,
Graduate School of Medicine, Osaka University

Member of the Expert Panel on Bioethics of the Council for Science, Technology and Innovation Policy (CSTI), Cabinet Office, Japan.
Steering Committee member of the Global Alliance for Genomics and Health.

Today's topics

1. Recent changes in the government policy for medical research and genomic medicine in Japan

2. Return of results of genomic analysis

3. Revision of Personal information protection legislation and its influence to genomic medicine

1. Recent Changes in the Government Policy

History of AMED
(Japan Agency for Medical Research and Development)

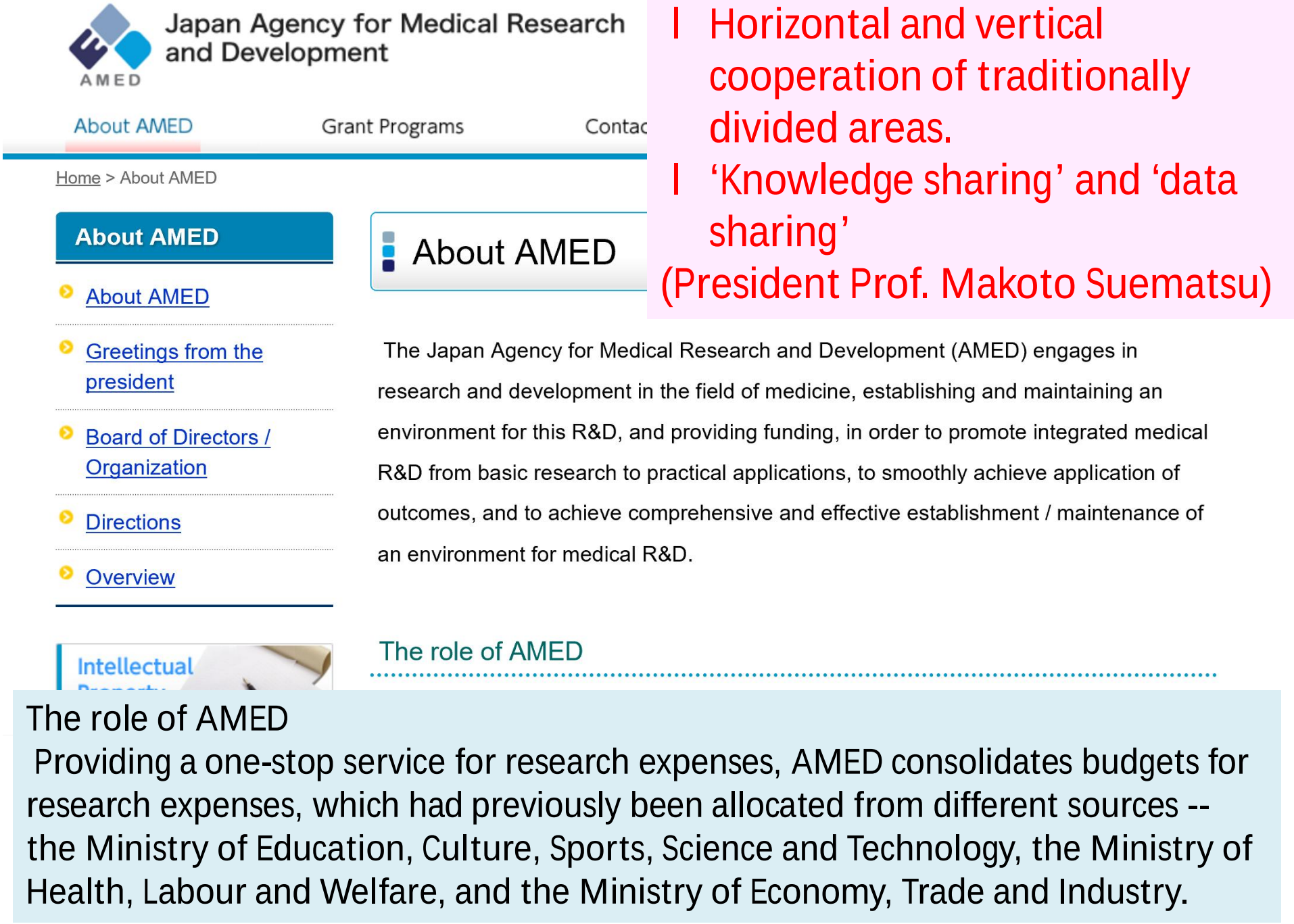
Feb 2013 Office of Healthcare Policy established in the Cabinet Office.

Jun 2013 Cabinet approves establishment of 'control tower' function for medical R&D. in line with "Japan Revitalization Strategy -- Japan is Back" policy strategy.

Feb 2014 Cabinet approves bills for Act on Promotion of Healthcare Policy and Act on the Independent Administrative Agency of Japan Agency for Medical Research and Development.

May 2014 Act on Promotion of Healthcare Policy and Act on the Independent Administrative Agency of Japan Agency for Medical Research and Development pass.

April 2015
Japan Agency for Medical Research and Development (AMED) established.



- Horizontal and vertical cooperation of traditionally divided areas.
- 'Knowledge sharing' and 'data sharing'

(President Prof. Makoto Suematsu)

The role of AMED

Providing a one-stop service for research expenses, AMED consolidates budgets for research expenses, which had previously been allocated from different sources -- the Ministry of Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare, and the Ministry of Economy, Trade and Industry.

5. 疾病克服に向けたゲノム医療実現化プロジェクト

日本医療研究開発機構対象経費 平成28年度予算額 89億円

インハウス研究機関経費 平成28年度予算額 24億円

Genomic Medicine projects

FY2016

疾患及び健常者バイオバ［…］タ解析を実施し、［…］の同定・検証並びに日本人の標準ゲノム配列の特定を進める。また、共同研究等による難治性・希少性疾患等の原因遺伝子の探索や、ゲノム情報をいかした診断治療ガイドラインの策定に資する研究やゲノム医療実現に向けた研究基盤の整備及び試行的・実証的な臨床研究を一体的に推進する。

フェーズ：基礎研究 ／ 応用研究 ／ 非臨床 ／ 臨床研究・治験 ／ 実用化

■文科省、■厚労省

研究開発

平成28年度予算額 19.3億円

●ゲノム医療実現推進プラットフォーム事業

ゲノム医療実現を目指し、既存のバイオバンク等を研究基盤・連携のハブとして再構築するとともに、その研究基盤を利活用した目標設定型の先端ゲノム研究開発を一体的に推進

MEXT

導出

還元

●臨床ゲノム情報統合データベース整備事業 平成28年度予算額 25.9億円

オールジャパンのネットワークを形成・整備し、全ゲノム情報等を集積・解析した情報を医療機関に提供することで個別化医療を推進

●ゲノム医療実用化推進研究事業 平成28年度予算額 3.7億円

適切なゲノム医療実施体制に係る試行的・実証的な臨床研究、これに関わる医療従事者の教育プログラムを確立

●ゲノム診断支援システム整備事業 インハウス研究機関経費 平成28年度予算額 10.0億円

NCに［…］所で活用するための診療基盤」を整備し、［…］

●N［…］事業 インハウス研究機関経費 平成28年度予算額 3.5億円

高［…］NCを活用した臨床研究・治験を推進

MHLW

目標設定型の研究の推進
研究基盤の利活用促進と連携強化

目標設定型の研究の推進
研究基盤の利活用促進と連携強化

研究基盤

●オーダーメイド医［…］ 平成28年度予算額 14.0億円

血液等からのDN［…］並びにゲノム解析の研究基盤をいかし、疾患の発症原因や薬の治療反応性及び副作用の予測診断に資す［…］

BBJ

●ナショナルセンターバイオバンクネットワー［…］ インハウス研究機関経費 平成28年度予算額 10.7億円

NCを受診した患者の手術切除検体等と臨床［…］ホート研究や特定の疾患へのゲノム情報を用いた臨床応用を推進

NBN

●東北メディカル・メガバンク計画 平成28年度予算額 26.5億円

被災地を中心とした健常人15万人規模のゲノムコホート研究を実施し、地［…］もに、次世代医療体制の構築を図る。さらに、バイオバンク構築や収集した試料等の分譲等の実施に［…］けた基盤整備を推進

ToMMo

連携（データ共有等）

実用化（市販・［…］

Implementing Genomic Medicine

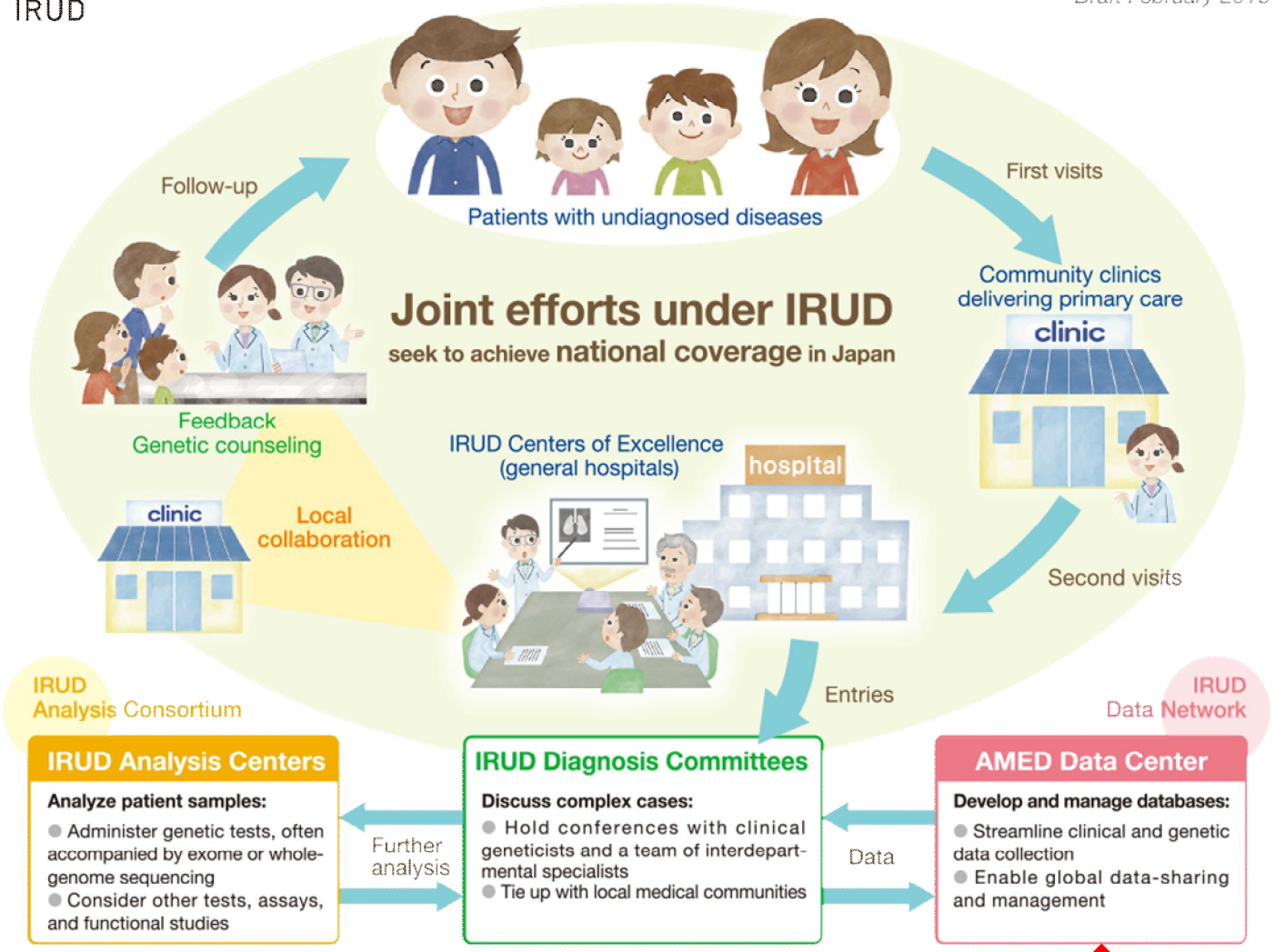
【2015年度までの達成目標】
- ○バイオバンクジャパン、ナショナルセンターバイオバンクネットワーク、東北メディカル・メガバンク等の連携の構築
- ○疾患に関する全ゲノム・多様性データベースの構築
- ○日本人の標準的なゲノム配列の特定、疾患予後遺伝子の同定
- ○抗てんかん薬の副作用の予測診断の確立

【2020-30年頃までの達成目標】
- ○生活習慣病（糖尿病や脳卒中、心筋梗塞など）の劇的な改善
- ○発がん予測診断、抗がん剤等の治療反応性や副作用の予測診断の確立
- ○認知症等のゲノム医療に係る臨床研究の開始
- ○神経・筋難病等の革新的な診断・治療法の開発

Initiative on Rare and Undiagnosed Diseases (IRUD): Integrating Knowledge for Diagnoses

IRUD

Draft February 2016



Single IRB
Return of results
Genetic counseling

Data sharing with 1) UDN of US and other countries
2) Matchmaker Exchange

Challenges

- Funding:
  - For connecting clinicians, researchers and patients across the nation
  - Wider use of genetic testing
- Training and Capacity building of professionals
  - Clinicians, bioinformaticians, ELSI specialists, etc.
- Regulations
  - ethics review, informed consent, data protection, etc.

2. Return of results of genomic analysis

Recommendation of American College of Medical Genetics and Genomics (ACMG)：（Green et al. *Genetics in Medicine*, July 2013）

It was recommended that: laboratories performing clinical sequencing (whole genome/exome sequencing) seek and report mutations of the specified classes or types in the genes listed in the document.

The list includes 56 genes for 24 diseases. Many of the diseases are cancer (16) and others are cardiac ones (7). All the mutations show high penetrance and are clinically actionable.

The first version was criticized since it made reporting obligatory and also recommended that results are returned to children.

The ACMG revised the recommendation in 2014 so that receiving results is opt-in option. It also decided to use the term “secondary findings” in stead of “incidental findings.”

Government policy for RoR in genetics in Japan

Minari et al, *SCRIPTed,* 2014

1. Japan has worked actively on ethics of human genome/genetic research since the end of the 1990s.

2. In 2000, the Government adopted ***Fundamental Principles of Research on the Human Genome*** as a basic policy for the country. It clearly states (as one of the principles) that **research participants has both right to know and right not to know their genetic information.**

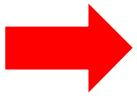
3. More practical guidelines: ***Ethical Guidelines for Human Genome/Gene Analysis Research*** was published in 2001, and their revision in 2004 set **the policy of "disclosure in principle"** However, **there were also exemptions and researchers did not have to return the results** when they are not accurate and useful.

Recent trend which may lead to more disclosures of research results

1. Revision of the Government Guidelines in 2013.
   Researchers have to establish their own policy for RoR.
   “Incidental finding” is also mentioned for the first time.

2. New policies for some biobanks.
   A new biobank, **the Tohoku Medical Megabank**, has set a policy of disclosing “some results that are useful for health obtained by genetic analysis”

However, these policies are in the research setting.



How about discussions and policy in the clinical setting?

Projects that perform large scale genomic sequencing in Japan

- Clinical sequencing projects in university groups
- Tohoku Medical Megabank
- Projects in National Center (for medical research)

  NCC, NCNP, NCCHD, NCVC, NCGM, NCGG
- Prefectural Cancer centers
- AMED IRUD project
- Biobank Japan
- Clinical Genetics Department network of Japan

"AMED Project of implementation of genomic medicine" 2014-2017

- Survey current status of handling of 'incidental findings" (IFs)
- Formulate a guidance that can be used nationwide in Japan.

Summary of 2014-2015

1. Many organizations are working on the issue of IFs (struggling to decide what to do) in the context of clinical sequencing.

2. The most advanced activities are found in cancer area and some organizations are returning the results of IFs to patients.

3. Some organizations have prepared the procedures including method of consent, decision making and counseling. They may serve as guiding examples to others in Japan.

Summary of 2014-2015

4. Most of the organizations consider the ACMG recommendations and list of genes/mutations useful. (However, there is a need to analyze other major initiatives such as genomics England.)

5. There are other issues such as disclosure to family members, lack of databases for interpretation, who has responsible for the decision making, etc.

Challenge now is to make guidelines which can be applicable to many hospitals across the country. (2016-2017)

3. Changing landscape for personal information protection

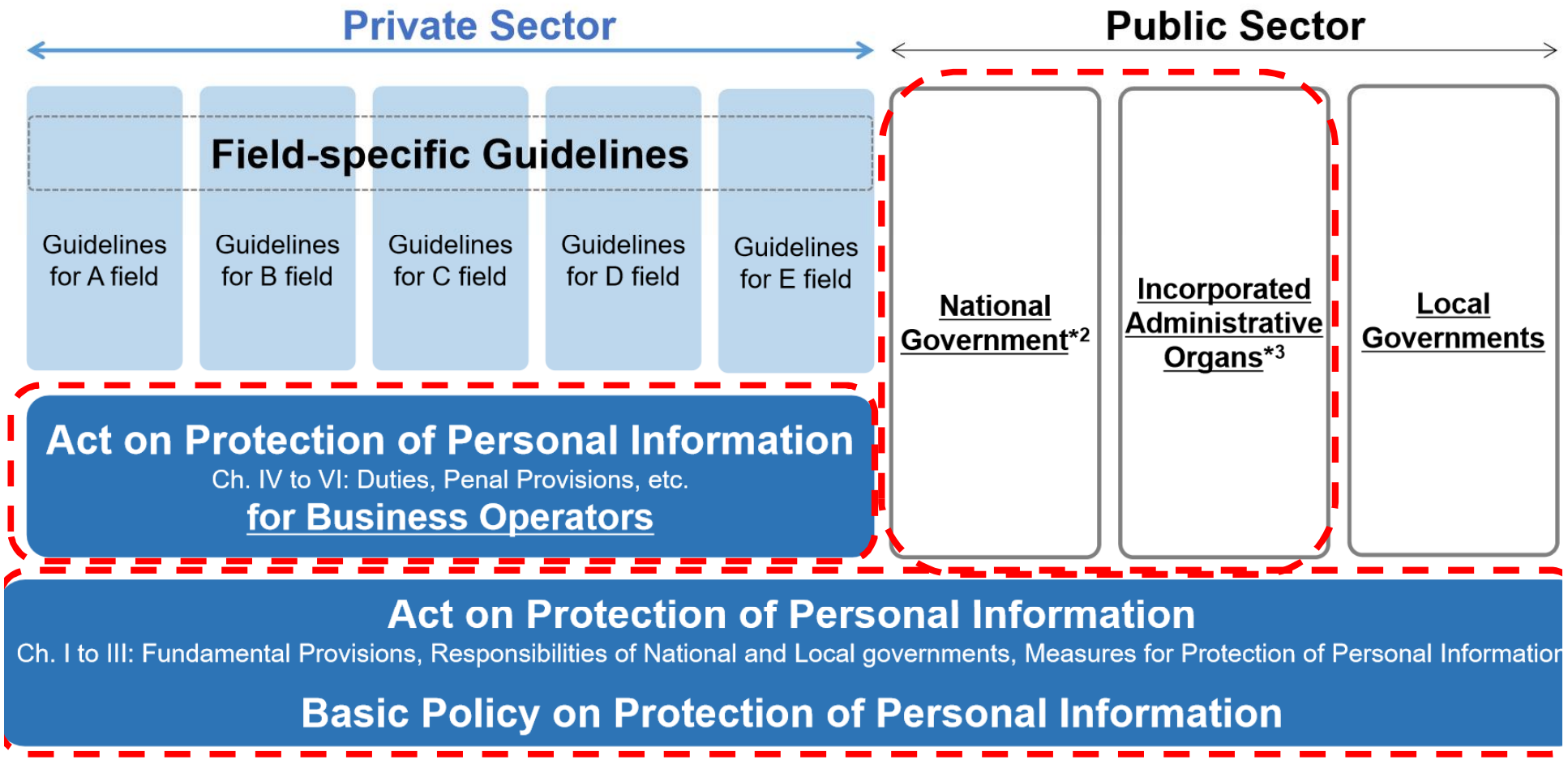
EU: The new Regulation (which would replace Data Protection Directive) is being prepared.

The Regulation will be legally binding with influences to genomic research.

(and some other features: e.g. Right to be forgotten)

Japan: The government is also working for revision of personal information protection legislation. It has passed some of the main laws. But, how the entire legal system will handle genomic information is not clear yet.

Current Legal Framework of the Protection of Personal Information*1



*1 This framework is implemented until the amended Act on the Protection of Personal Information comes into force, which is within 2 years from the promulgation, September 9, 2015.
*2 Act on the Protection of Personal Information Held by Administrative Organs
*3 Act on the Protection of Personal Information Held by Incorporated Administrative Agencies, etc.

Genomic data in personal information protection legislation in Japan (Current status of discussions)

- In principle, genomic data is personal information even when it is anonymized.
- Details will be determined under the Cabinet Order, which is now being prepared and finalized this year in the government.

Genomic data in personal information protection legislation in Japan (Current status of discussions)

- Two definitions of data will be relevant to genomic research.

1. “Personal Identification code”

>> genomic data

(sequence data without interpretation)

What kind of genomic data?

Not clear yet. >> Cabinet order

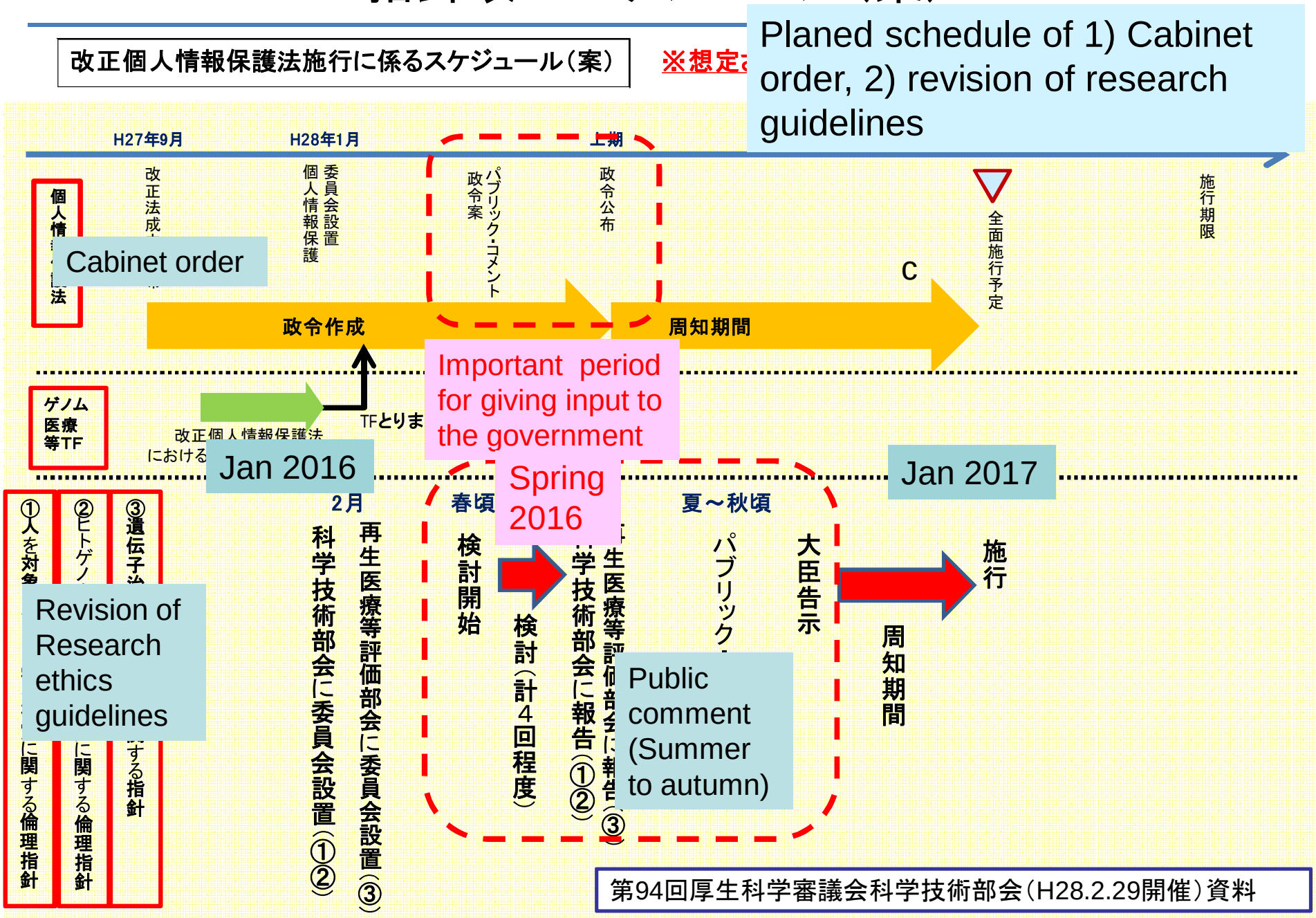
2. “Sensitive personal information”

race, religion, medical history, personal information which has potential to bring about unjustifiable discrimination or prejudice

>> genetic information

>> What kind of information? Not clear either.

指針改正スケジュール（案）

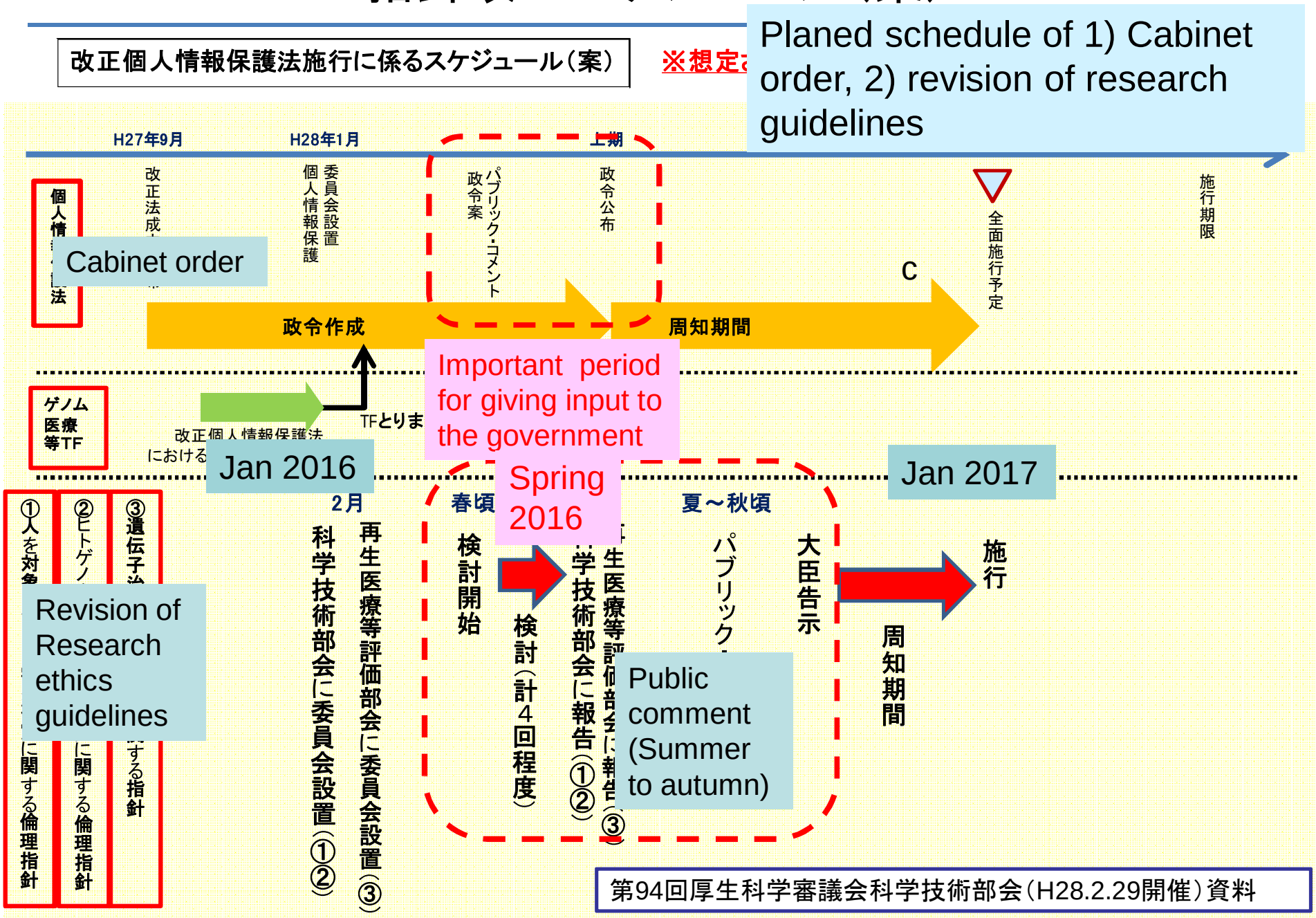


Genomic data in personal information protection legislation in Japan (Current status of discussions)

- In addition to the Cabinet order under the Act on Personal Information Protection, the revision of research ethics guidelines will start this month (April 2016). How they define the actual procedures of handling of genomic data is also quite important for genomics research.

- There are other concerns such as whether existing samples (old samples) without detailed consent can be used or not. (for the third party use, for example)

指針改正スケジュール（案）



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Year End party, 2015

Thank you for your attention!