Science-based Initiatives of PMDA

Dr. Tetsuo Nagano

Executive Director,
Pharmaceuticals and Medical Devices Agency
(PMDA)

pmda
Pharmaceuticals and Medical Devices Agency

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Today's Presentation

1. Introduction: Products from Japan
2. Current Status of Pharmaceutical Affairs Consultation on R&D Strategy
3. Updates of Science Board
4. Advanced Review/Consultation System

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Innovative Medicinal seeds from Academia in Japan

POTELIGEO® Injection (Mogamulizumab (r-INN))

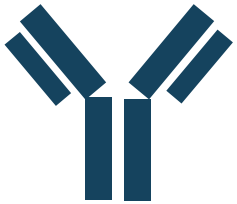
Approved in JAPAN; March 2012
(First marketing authorization)

- Target Identification / Target Validation

Professor Ryuzo Ueda (Nagoya City University, Japan) discovered CCR4 as the pathogenic factor of Adult T-cell leukemia (ATL) (Clinical Cancer Res 2003; Sep 1; 9(10 Pt 1):3625-34)

- Extensive research & Development

POTELIGEO® (Mogamulizumab) is a humanized monoclonal antibody targeting CCR4 developed by Kyowa-kirin Co., Ltd . It is considered to bind with CCR4, suppressing tumor growth by antibody-dependent cellular cytotoxicity (ADCC).



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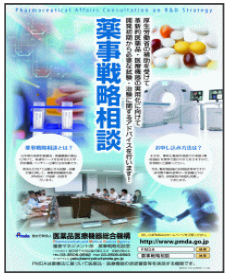
Pharmaceutical Affairs Consultation on R&D Strategy

Valley of Death

-Shortage of funds, Knowledge on Regulation and developmental strategy



Pmda Strategic Consultation

Basic Research

Pharmaceuticals and Medical Devices candidates

Quality Study

Non-Clinical Study

Clinical Trial (Up to POC studies)

Practical Use

Innovative Products

* Further studies are handled by the Regular Consultation

Consultation on quality and battery of pre-clinical, including examining tumorigenicity, biological ingredient safety

Consultation on endpoints or sample size of early clinical trial

Flow of Strategy Consultation

Introductory Consultation (775)

Pre-Consultation (937)

Face-to-Face Consultation (236)

(7/1/2011 – 10/31/2014)

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Case of Face to Face consultation

Consulter	Product under development	Intended performance, Intended use, Indications
National Institute of Neuroscience, NCNP Department of Molecular Therapy Shin'ich Takeda	Morpholino oligos (Antisense)	Remedy for Duchenne muscular dystrophy (DMD)
Molecular Medicine and Therapy, Medicine (ART), Tohoku University School of Medicine, Toshio Miyata	PAI-1 Inhibitor (TM5509)	Hematogenic recovery of cord blood transplantation
Center for iPS Cell Research and Application (CiRA), Kyoto University, Shinya Yamanaka	iPS Cell (Allo)	Starting Materials for cellular & tissue based products derived from iPS Cells
Sapporo Medical University, Osamu Honmou	Mesenchymal Stem Cell (Auto)	Improvement of neurological sign, activities of daily living disorders in daily activities, and dysfunction associated with Stroke
CYBERDYNE INC.	ROBOT SUIT HAL (Hybrid Assistive Limb®) and partial Equipment for the subset of function of HAL used for movement training	Devices for assistive movement with in patients. Planed to introduce models which differ in intended use or indications.

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For PMDA To Be More Science-Based

Basic Research

Seeds of new drug / medical devices

Quality Tests → Non-clinical tests → Clinical Trial → Review → Approve → Post Marketing

Pharmaceutical consultation on R&D Strategy

Clinical Trial Consultation

Review

Post Marketing Safety Measure

Offices of Review (Drugs & Medical Devices), Office of Safety

Office of Review Innovation

Practical use

Innovative medical products

Establishment of the Science Board

The Science Board was established in May 2012 to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage such as basic research, development support, product review, and post market safety measures.

Board members

Academia

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Working policy of discussion on Subcommittees (1st Stage: Jul. 2012-Mar. 2014)

Pharmaceuticals Bio-based Products

Aiming at summary of " Recommendation for the review policy of the pharmaceuticals regarding personalized medicine" and discuss needed items in order of priority.

Cellular & Tissue-based Products

Discussing how to ensure the safety of cellular and tissue-based products and aiming at revealing the predictable risks in the products as possible.

Medical Devices

Starting from discussion about the common issues as many kind of medical devices as possible because of big differences among product attributes of the medical devices.

Outcomes of the Science Board (1st Stage)

Cellular & Tissue-based Products

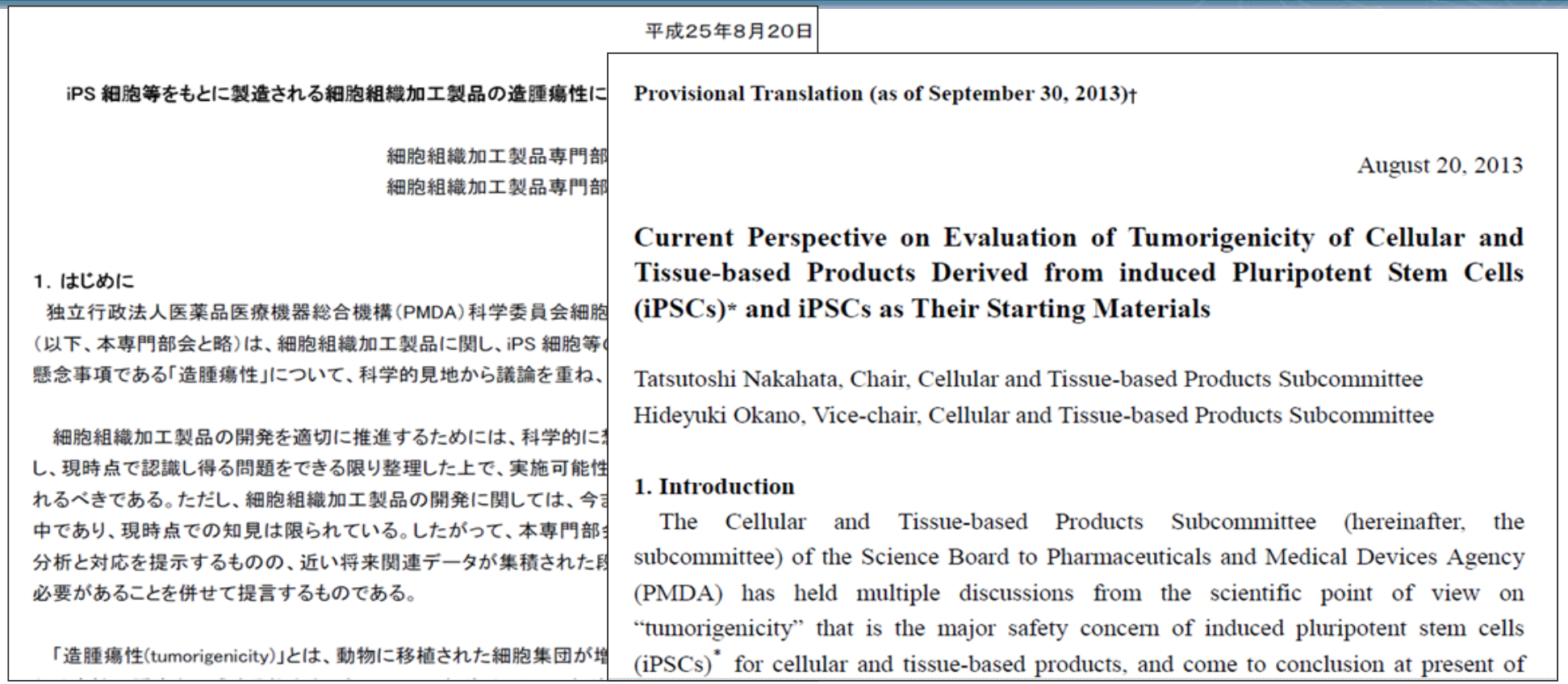
- Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from iPSCs and iPSCs as Their Starting Materials (Aug. 21, 2013)

Pharmaceuticals, Bio-based Products

- Summary of Discussion on Non-clinical Pharmacology Studies of Anticancer Drugs (Dec. 10, 2013)

- Summary of the discussion on assessment of the current status of personalized medicine related to development and review (Mar. 11, 2014)

Outcomes of the Science Board (1st Stage)



平成25年8月20日

iPS 細胞等をもとに製造される細胞組織加工製品の造腫瘍性に

細胞組織加工製品専門部
細胞組織加工製品専門部

1. はじめに

独立行政法人医薬品医療機器総合機構（PMDA）科学委員会細胞
（以下、本専門部会と略）は、細胞組織加工製品に関し、iPS 細胞等
懸念事項である「造腫瘍性」について、科学的見地から議論を重ね、

細胞組織加工製品の開発を適切に推進するためには、科学的に
し、現時点で認識し得る問題をできる限り整理した上で、実施可能性
れるべきである。ただし、細胞組織加工製品の開発に関しては、今
中であり、現時点での知見は限られている。したがって、本専門部
分析と対応を提示するものの、近い将来関連データが集積された
必要があることを併せて提言するものである。

「造腫瘍性(tumorigenicity)」とは、動物に移植された細胞集団が

Provisional Translation (as of September 30, 2013)†

August 20, 2013

Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from induced Pluripotent Stem Cells (iPSCs)* and iPSCs as Their Starting Materials

Tatsutoshi Nakahata, Chair, Cellular and Tissue-based Products Subcommittee
Hideyuki Okano, Vice-chair, Cellular and Tissue-based Products Subcommittee

1. Introduction

The Cellular and Tissue-based Products Subcommittee (hereinafter, the subcommittee) of the Science Board to Pharmaceuticals and Medical Devices Agency (PMDA) has held multiple discussions from the scientific point of view on "tumorigenicity" that is the major safety concern of induced pluripotent stem cells (iPSCs)* for cellular and tissue-based products, and come to conclusion at present of

Japanese　　English（Provisional Translation）

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Subcommittees on 2nd Stage (Apr. 2014 -) and Their Activities

Category of Drugs

a. Subcommittee on Placebo-controlled Trials (held 2 times till end of Feb. 2015)
b. Subcommittee on Non-clinical Studies (held 3 times till end of Feb. 2015)

Category of Medical Devices

c. Subcommittee on Application of Numerical Analysis to Non-clinical Evaluation (held 3 times till end of Feb. 2015)
d. Subcommittee on Evaluation of Medical Devices for Pediatric Use (held 2 times till end of Feb. 2015)

Category of Cellular & Tissue-based Products

e. Subcommittee on CPC (Cell Processing Center) (held 4 times till end of Feb. 2015)

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Advanced Review/Consultation System

Analysis by PMDA

Giving additional scientific value to submitted data

Cooperation with Academia

Regulatory Science

A rational & effective evaluation process for regulatory decision

Practical use of Innovative Medical Products

MAA etc.

e-Submission of study data

Accumulation data

Database

Sophisticated NDA review

- Each reviewer utilizes innovative assessment techniques

Cross-Products Analysis

- Innovative evaluation methods
- Active utilization of Modeling & Simulation
  - Disease model
  - Objective B/R assessment
  - Identifying AE-related factors etc.

Sophisticated Consultation

- More evidence-based consultation

Effective and High Quality Review

- More predictable efficacy/safety after approval
- Reduction of applicant's work load
- More scientific regulatory decision

Effective and Successful Development

- Epoch-making proposal leading the world
- Proactive publication of guideline

Utilization of study data and expected outcomes

Clinical: evaluation of data from Japanese subjects, comparison with those from non-Japanese subjects, etc.

Subject	Outcome
Prediction of drug interaction using a model	•Increase of study success rate •Avoidance of unnecessary studies •Confirmation of model appropriateness in the review process, decrease of regulatory inquiries
Development of a dose-response model and prediction of optimal dose	
Development of a new evaluation indicator for disorders with no appropriate indicator	
Identification of factors affecting efficacy or safety	
Evaluation of class effect in rare adverse events	•Enhanced safety prediction, etc.
Prediction of QT prolongation based on simulated blood concentration-QT relationship	

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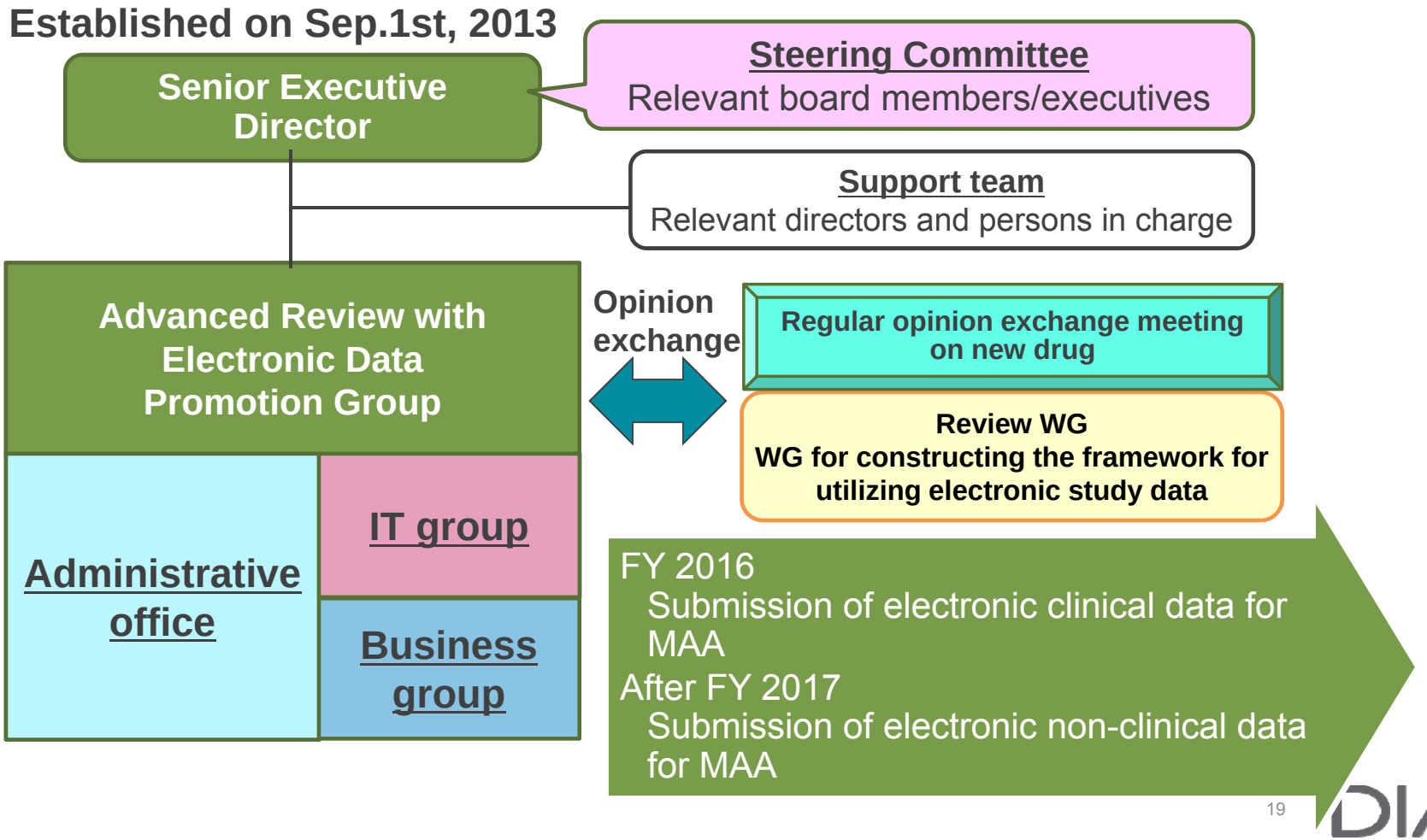
Task Force for Advanced Review / Consultation



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Summary

- *Pharmaceutical Affairs Consultation on R&D Strategy* is offering consultation for innovative products developed by academia/venture businesses.
- *Science board* was established for review/consultation in PMDA to become more science based.

Thank you for your attention !

http://www.pmda.go.jp/

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Ask