Korea FDA's Past, Present and Future on Regulation of Biopharmaceuticals & A Consideration of Microbiome Related Metabolomics

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Hallym University & Cochair for Global Export Supporting committee (Dynamic Bio of KFDA)
GREETINGS FROM KOREA
Disclaimer

The views expressed in this talk represent the views of the speaker and do not necessarily represent the views of Korea FDA (MFDS: Ministry of Food & Drug Safety).
Experiences

- Reviewer for Biopharmaceuticals: Vaccine, Blood Products, Advanced Biopharmaceuticals, In vitro Diagnostics as Director for responsible Division
- Involved in Test Method Validation with WHO & OECD
- Teaching Test Method Validation for Specification for Biopharmaceuticals including CE, MS, Virus clearance test methods & many others
- Director General for Center for Analysis of Korea Food & Drug Agency: Instruments including MS/MS, MS/TOF etc.
Biopharmaceuticals Analytical Test Methods For Recombinant Protein Therapeutics, Cell Therapeutics & Gene Therapeutics:
Specification: Identification, Purity & Potency

Division of Advanced Biotherapeutics
Suenie Park
1. Definition
2. Specification & Test Methods Item
3. Products Classification
4. Identity, Purity, Potency
5. Capillary Electrophoresis
6. High Performance Liquid Chromatography
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1) Introduction of MFDS(KFDA) in general

2) Korea FDA’s Special Programs: DynamicBio, Biopharmaceutical Industry Strategies Developing Committee, GBC & Bio IT-Platform

3) Global Export Supporting Division

4) A Consideration on Microbiota Related Metabolomics, Test Methods including CE &/or CE/MS etc
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Korea FDA is named as MFDS (Ministry of Food & Drug Safety) http://www.mfds.go.kr/index.do

MFDS’s Declaration that We are with People for Ensuring the Safety of Food & Drug
Bio & Cosmetics

- Approval Process
- Regulations
- Manufactures
- International Events
- Biosimilar
- Related Organization
A Cyber Investigation Team was created to combat the illegal sales of food and medicine online.

The Ministry of Food and Drug Safety introduced the National Petition Safety Inspection System under the catch phrase of “If the people want, the Ministry of Food and Drug Safety will perform an inspection”.
MFDS White Paper: Contents

1. Outline
2. Food
3. Medical Products
4. Risk Prevention
5. Research and Development for Food and Drug Safety
6. Appendix
Vision: Objective

1. Vision·Objective·Core Strategies

“Safe Food and Drug, Healthy People, Happy Society”

Customized Promotion

Experiential Marketing

Participatory Promotion
# Vision: Core Strategies

## Implement a Government-guaranteed food safety system

| 01 | Proactive safety management for agricultural, livestock and fishery products |
| 02 | Enhance management of changes in food trends |
| 03 | Improve food safety management system |

## Prevent anxiety factors in daily life

| 01 | Establish management system for hazardous substances and products |
| 02 | Strengthen safety management of food and medicine for the vulnerable |
| 03 | Expand the public participation and communication |

## Improve the publicity of medicine, etc.

| 01 | Improve the publicity through user-centered safety management |
| 02 | Strengthen safety management for from ingredients to side-effects |
| 03 | Improve the safety management system for drugs and medical devices |

## Lead innovative growth with customized regulations

| 01 | Create an innovative regulation ecosystem for the 4th industrial revolution era |
| 02 | Provide strategic support for global market entry |
History

2013.03 **Establishment of the Ministry of Food and Drug Safety (MFDS)**
- Headquarter : 1 Planning and Coordination Office, 5 Bureaus (1 office and 4 Departments), 53 Divisions
- Institute : 3 Departments, 28 Divisions
- 6 Regional Administrations (8 Imported Food Inspection Centers)
- Established Emergency Planning Office under the Planning & Coordination Bureau.
- Abolished GMP and Quality Research Team under the National Institute of Food and Drug Safety Evaluation.
- Established Biopharmaceutical Quality Management Division under Biopharmaceuticals & Herbal Medicine Bureau.
- Established Cell & Gene Therapy Division under Biopharmaceuticals and Herbal Medicine Evaluation Department.
- Changed Advanced Therapy Products Division to Recombinant Protein Products Division.
- Reorganized the Medical Devices Evaluation Bureau based on the different clinical fields. Diagnostic Medical Devices Division, Therapeutic Medical Devices Division and Medical Materials and Supplies Division changed to Cardiovascular Devices Division, Orthopedic & Restorative Devices Division, and Dental & Gastroenterology Devices Division.
- Established High-Tech Medical Devices Division.

2011. • Abolished GMP and Quality Research Team under the National Institute of Food and Drug Safety Evaluation.

1998.02 **Establishment of KFDA (Korea Food & Drug Administration)**
- The Food and Drug Safety Administration was newly established and there were affiliated agencies such as national toxicology laboratory and six regional food and drug safety administrations.

1996.04 Establishment of the Korea Food and Drug Administration Headquarters and six Regional Offices under the Ministry of Health and Welfare.
Location: 2010. 11, Osong Period Started

- Korea Food & Drug Administration moved from Seoul, capital city, into the Osong Health Technology Administration Park
- Complex located in Cheongwon, Chungbuk Province
Organization

2017. 03, The 15th Amendment

- Headquarter: 1 Planning and Coordination Office, 7 Bureaus (+2 offices), 53 Divisions
- Institute: 6 Departments, 35 Divisions
- 6 Regional Administrations (8 Imported Food Inspection Centers)
Biopharmaceuticals and Herbal Medicine Bureau

- Biopharmaceutical Policy Division
- Biopharmaceutical Quality Management Division
- Herbal Medicine Policy
- Cosmetics Policy Division
- Quasi-drug Policy Division
Main Tasks Biological Products

Biopharmaceutical Policy Division

• Establish and coordinate policies related to biological products, gene recombination medicine, gene medicine, cell medicine, tissue engineering medicine, and human tissue and plasma safety

• Supports exports & involves in international cooperation
Main Tasks  Biological Products

Biopharmaceutical Quality Management Division

• Establish manufacturing and quality management standards for biopharmaceuticals, manage and operate change, establish and coordinate plan for monitoring of human tissue transplants (PMS, GMP inspection)

• Coordinates all compliance actions: product recalls and regulatory letters
Organization
NIFDS  National Institute of Food and Drug Safety Evaluation

Director General

General Affairs Division

Research Planning & Management Division

Vaccine Division

Blood Products Division

Food Safety Evaluation Department

Drug Evaluation Department

Biopharmaceuticals and Herbal Medicine Evaluation Department

Medical Device Evaluation Department

Pharmaceutical and Medical Device Research Department

Toxicological Evaluation and Research Department
Biopharmaceuticals and Herbal Medicine Evaluation Department

- Biologics Division
- Recombinant Protein Products Division
- Cell and Gene Therapy Products Division
- Herbal Medicines Products Division
- Cosmetics Evaluation Division
Main Tasks

- Coordinates administrative work: Marketing authorization for biopharmaceutical products
- Evaluates CMC section
- Evaluates pharmacology, toxicology and clinical data section
- Support GMP, GLP, GCP compliance
- Conducts research of biopharmaceutical products effectiveness
- Collaborative activities with WHO, ICH etc
Biological Products Approval Process

Sponsors have submitted application as electronic documents through KiFDA online system since Oct. 2nd, 2006.
IND (Investigational New Drug Application) Review Process

IND submission to Clinical Trials Management Division
- CMC
- Stability
- Pharm/Tox
- Clinical data
- IRB

Review by Biologics Division

Clinical hold
- objection
- within 1 month

Review Complete and Acceptable?
- Yes
- No, Additional Info Requested

Clinical Trials Management Division
- Notify

Applicant

- Study Ongoing
- Study completion
- Inspection
Dossier for NDA (BLA)

Biological Products

- **Origin or backgrounds leading up to discovery and development**
  - **Structure • physical, chemical and biological nature**
    - A. Drug Substance
    - B. Drug Product

- **Clinical data**
  - A. Clinical data package
  - B. Bridging Data

Comparison with domestic copies & special features of the drug concerned

- **Uses in other countries**

**Stability**
- Stability test data
  - A. Drug Substance
  - B. Drug Product
  - Long-term, accelerated, stressed

**Toxicity**
- A. Single dose toxicity
- B. Repeated dose toxicity
- C. Genetic toxicity
- D. Carcinogenicity
- E. Reproductive and developmental toxicity
- F. Others: antigenicity, immunotoxicity, local toxicity, dependency, etc

**Pharmacologic effects**
- A. Efficacy studies data
- B. Safety or general pharmacology studies data
- C. ADME
- D. Other pharmacologic effects
Number of Staff: 1,858 as of March 30, 2018

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Annual Important Programs for Biopharmaceuticals

1. Announcement for Annual Important Policies on Biopharmaceuticals
2. Dynamic Bio Program
3. GBC2018 (June 26~28) Global BioConference
4. Bio IT Platform

2018 Feb. 21
KoBIA (Korea Biomedicine Industry Association)
http://www.kobia.kr
The Korea Biopharmaceutical Industry Association posts regulatory reports published and released by relevant public organizations. You can find useful regulation of biological products licensing and policy of drug pricing in Korea at a glance. Kobia hopes you find valuable information on biopharmaceutical policies and regulation of Korea through our website.

- Biopharmaceutical Policy & Regulation
- Pricing System Overview
- Biopharmaceutical Regulation
- Policy Reports
Dynamic BIO is a consortium composed of experts from industry, government, and academia.
It plays a role of control tower for biopharmaceutical industry development.
Established by the Korea Food and Drug Safety in Sep. 2010.
Run by the Korea Biomedicine Industry Association since Jan. 2012 with MFDS
GBC: Global BIO Conference
GBC role, Aim and History

- GBC is an international conference about the latest development trends and regulatory harmonization in the biopharmaceutical fields.

- The GBC is aimed at facilitating regulatory harmonization and establishing a close network among expert through sharing the latest development trends of biopharmaceuticals and relevant global issues.

- Each year, the conference attracts many of the world’s most influential people in the biopharmaceutical area to explore and collaborate in shaping our healthcare trends and future.

- Started as GBF2013 and continued as GBC2015

- Since 2015, the Ministry of Food & Drug Safety (MFDS) has annually held the conference.
For More Information, Please visit websites below;

- MFDS  http://www.mfds.go.kr/eng/index.do
- KoBIA  http://www.kobia.kr/e_main.php
- Dynamic BIO  http://www.kobia.kr/e_sub01/sub04.php
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Dynamic BIO

Business Development

Structure of Dynamic BIO

**Head**
Director of Biopharmaceuticals and Herbal Medicine Bureau, Ministry of Food and Drug Safety

- General Planning Division
- Global Market Entry Support Division
- Vaccine/Blood Products Division
- Cell and Gene Therapy Product Division
- Recombinant Protein Products Division
- GMP Division
Dynamic BIO

Global Export Supporting Division
Nomination & Awards from MFDS
Bio IT Platform

- Regulatory Information: Korea and Other Countries
- Industry Information
- Consulting Program
Agenda for Global Export Supporting Division

Identifications of Export related Problems

- Hard to find Reliable Local Collaborater abroad
- Low Effectiveness of Mutual Recognition of MFDS with Other Country’s Regulators

01 Case Study for Export Success & Failure

2 Identification of Service for BioDrug Export from KOTRA (Korea Trade Association)

3 Community Operation among Members for Network Strengthening

4 Questionnaire for Success/Failure Cases related to MOU
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Microbiome: Genomes of Commensal Microorganisms

- Bacteria
- Fungi
- Viruses
- Protists
WEF (World Economic Forum): Top 10 Emerging Technologies 2014

Top 10 Emerging Technologies 2014

Human Microbiome Therapeutics

The human body is perhaps more properly described as an ecosystem than as a single organism: microbial cells typically outnumber human cells by 10 to one. This human microbiome has been the subject of intensifying research in the past few years, with the Human Microbiome Project in 2012 reporting results generated from 80 collaborating scientific institutions. They found that more than 10,000 microbial species occupy the human ecosystem, comprising trillions of cells and making up 1%-3% of the body’s mass.

Rising Interests in the Microbiome

Obtained from SK Choi

http://www.medpace.com
Compositional differences in the microbiome by anatomical site.

Figure 1 | Compositional differences in the microbiome by anatomical site. High-throughput sequencing has revealed substantial intra-individual microbiome variation at different anatomical sites, and inter-individual variation at the same anatomical sites. However, higher-level (for example, at the level of phyla) taxonomic features display temporal (longitudinal) stability in individuals at specific anatomical sites. Such site-specific differences and the observed conservation between human hosts provide an important framework to determine the biological and pathological significance of a particular microbiome composition. The figure indicates the relative proportion of sequences determined at the taxonomic phylum level at eight anatomical sites. Certain features, such as the presence (+) or absence (–) of Helicobacter pylori, can lead to permanent and marked perturbations in community composition.

The human microbiome: at the interface of health and disease. Ilseung Cho1,2 and Martin J. Blaser1, 260-270 | APRIL 2012 | VOLUME 13 www.nature.com/reviews/genetics
The human gut harbors hundreds of species of microorganisms, thought to play a role in metabolism and disease. Interactions between species are likely to influence the functional properties of the microbiome, but the complexity involved resulted in difficulties to identify the underlying mechanism (de Souza N., Nature Methods.2018 Aug;15(8):572)
Startups Targeting the Microbiome

Startups in Korea targeting the microbiome

출처 : https://www.cbinsights.com/
Role of gut microbiota metabolites on health & disease

SCFA (short chain fatty acids), Butyrate, Propionate etc.

Detection Methods

• gaschromatography (GC),
• liquidchromatography (LC),
• highpressureLC (HPLC),
• ultra pressureLC (UPLC),
• Fouriertransforminfraredspectroscopy (FTIR),
• ioncyclotroneresonance-FT (ICR-FT),
• capillary electrophoresis (CE) coupled to massspectrometry (MS),
• nuclear and proton nuclear magnetic resonance spectroscopy (NMR-1H-NMR)
Recent Activities on Microbiome
Cochair for Global Export Supporting Division for MFDS
RFP Prepared for Establishing Guideline & Safety & Quality Control Test Methods for Products Based on Microbiome Studies etc. 2018.08.16.
Development of Test Methods

- Seeking for Collaborators
- A Consideration on Microbiota Related Omics including Metabolomics,
- Test Methods including CE &/or CE/MS etc?

-> If any organization is interested in collaboration, let me be informed~~
Collaboration → Success

Thank you for Listening~~

(경청해주셔서 ! 감사드립니다^*)