

Regulatory Perspective on Quality Aspects for Microbiome Medicines in Japan

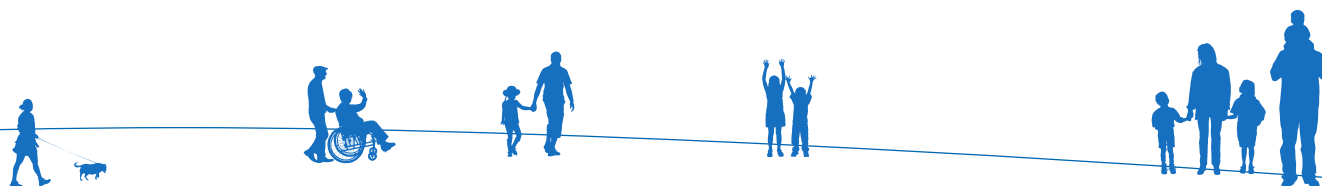
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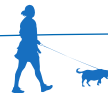
Pharmaceuticals and Medical Devices Agency (PMDA), Japan

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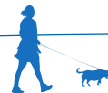
Agenda

- Science Board Activity for Live Biotherapeutic Product (LBP)
- Future Activity of Regulatory Science for Fecal Microbiota Transplantation (FMT)



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Points to Consider for Gut Bacterial Products Based on Microbiome Research

– Considerations for the Development and Evaluation of **Live Biotherapeutic Products** –

February 25, 2022

Subcommittee on Microbiome of the Science Board

<https://www.pmda.go.jp/files/000249812.pdf>



Points to Consider for Gut Bacterial Products Based on Microbiome Research

Introduction

1. Current Status for the development of LBPs for infectious immunologic, and nonimmunologic diseases

1.1 Major disease areas for which LBPs are being developed are as follows

1.2 FMT

1.3 Challenges in LBP Development

2. New technologies for evaluation of LBPs

2.1 Recent trends in classification and identification techniques

2.2 Trends in methodologies for characterization of microbial consortia

2.3 In silico safety evaluation

2.4 In vitro evaluation

3. Non-clinical studies

3.1 Pharmacological Studies (including Efficacy Support Studies)

3.2 Pharmacokinetic Studies

3.3 Non-clinical safety studies

4. Manufacturing (bank establishment) and quality control of LBPs

4.1 Approaches to drug substance manufacturing and cell banking

4.2 Characterization of LBPs

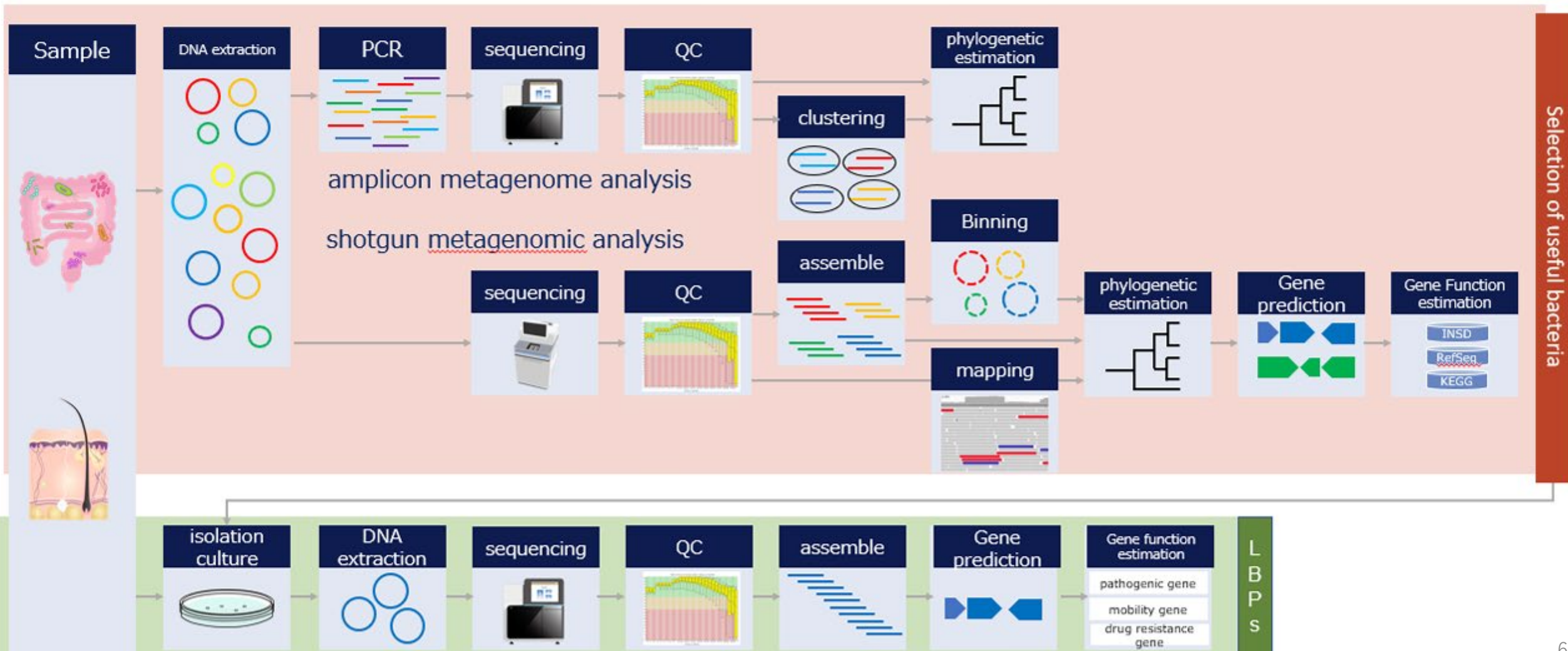
4.3 Specification test and acceptance criteria of LBPs

4.4 Formulation Process Development

5. Considerations for clinical trials



Flowchart of Genome and Metagenome Analysis



Quality Aspects for LBP

- ✓ In silico safety evaluation

Toxin-related genes, Antibiotic resistance genes, Mobile genes such as transposons

- ✓ Analyze and Characterization of MCB/WCB
Genotype and Phenotype

- ✓ Donor information

Obtaining information on the infectious agents present in the donor and their medical history is desirable

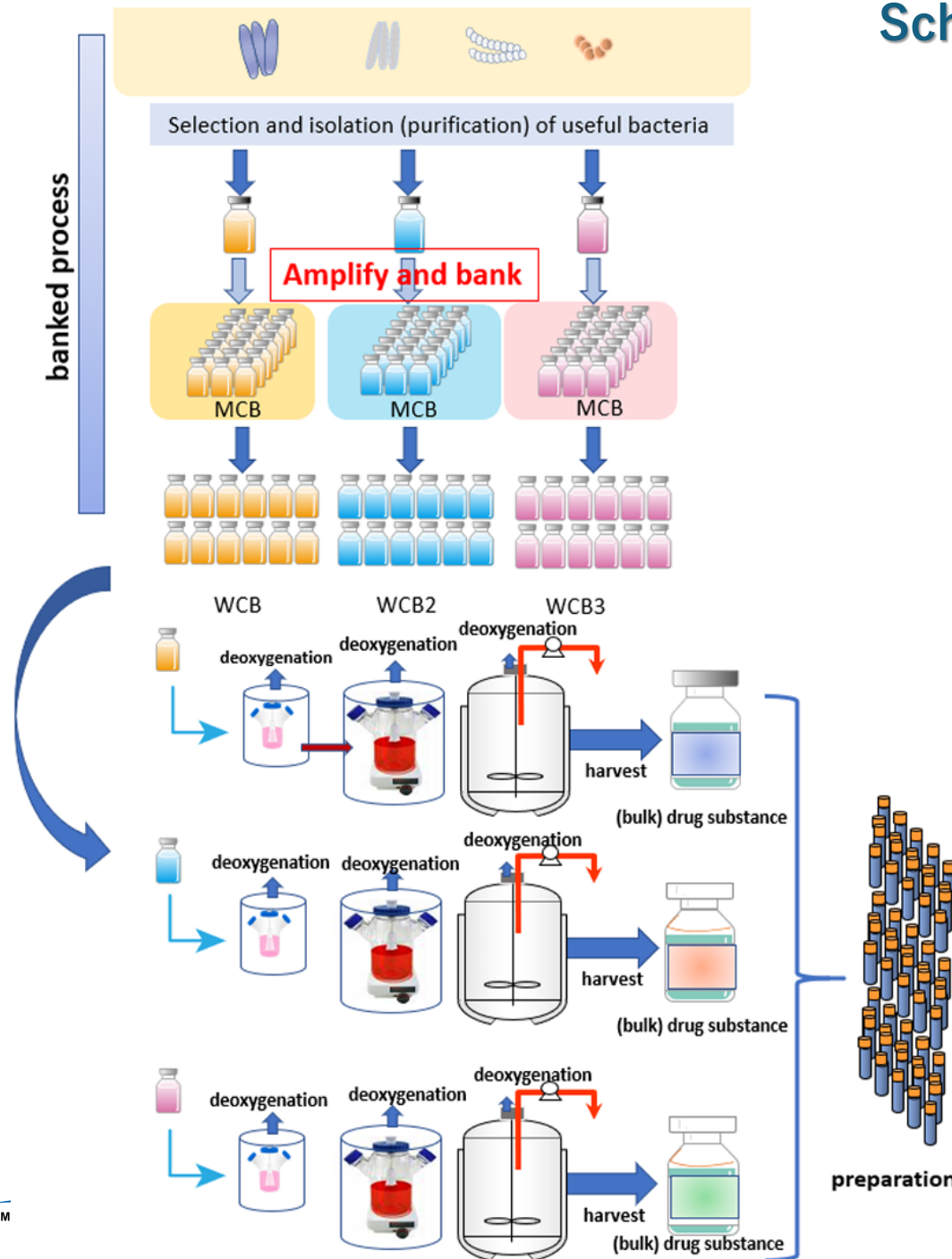


Examples of Tests to be performed at MCB/WCB

Characteristic Items		Considerations for conducting the test
Genot type	16S rRNA gene sequence	16S rRNA gene sequence unique to the strain: purity and identity of the target strain
	Whole Nucleotide Sequence Analysis	
Pheno type	Protein Expression Profiles	MALDI-TOF MS analysis: purity and identity of target strains (may vary depending on culture conditions)
	Morphology	Observation under the microscope, colony morphology
	Gram stainability	
	Ability to produce useful substances	Indicators related to drug efficacy and biological activity
	Proliferative properties	Depends on culture conditions
	Drug resistance	
Purity test		Heterologous microorganism denial test



Schematic flow-diagram for the manufacturing of LBPs



- The bacteria are isolated and banked by species.
- Each useful bacteria should be cultured and expanded under optimal conditions.
- Each harvested bacteria should be purified and tested for quality as a drug substance.
- For LBP products consisting of multiple bacteria, these bacteria are mixed in a predetermined mixing ratio and formulated.

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Future Activity of Regulatory Science for FMT

FMT is a treatment in which intestinal bacteria prepared from stool derived from a healthy donor are transplanted into the patient.

Japan is considering to create the Points to Consider on **Quality focused on the Safety of FMT for Early developments** from FY 2025!

- ✓ Donor screening
- ✓ Standards for Biological Raw Materials
- ✓ Documents of other regulatory agencies (e.g., Health Canada, EDQM, U.S. FDA)





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Thank you for your attention!

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