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Regulatory Perspective on Quality Aspects for Microbiome Medicines in Japan

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The views expressed in this presentation are those of the author and do not necessarily reflect the official views of Pharmaceuticals and Medical Devices Agency.

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－

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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

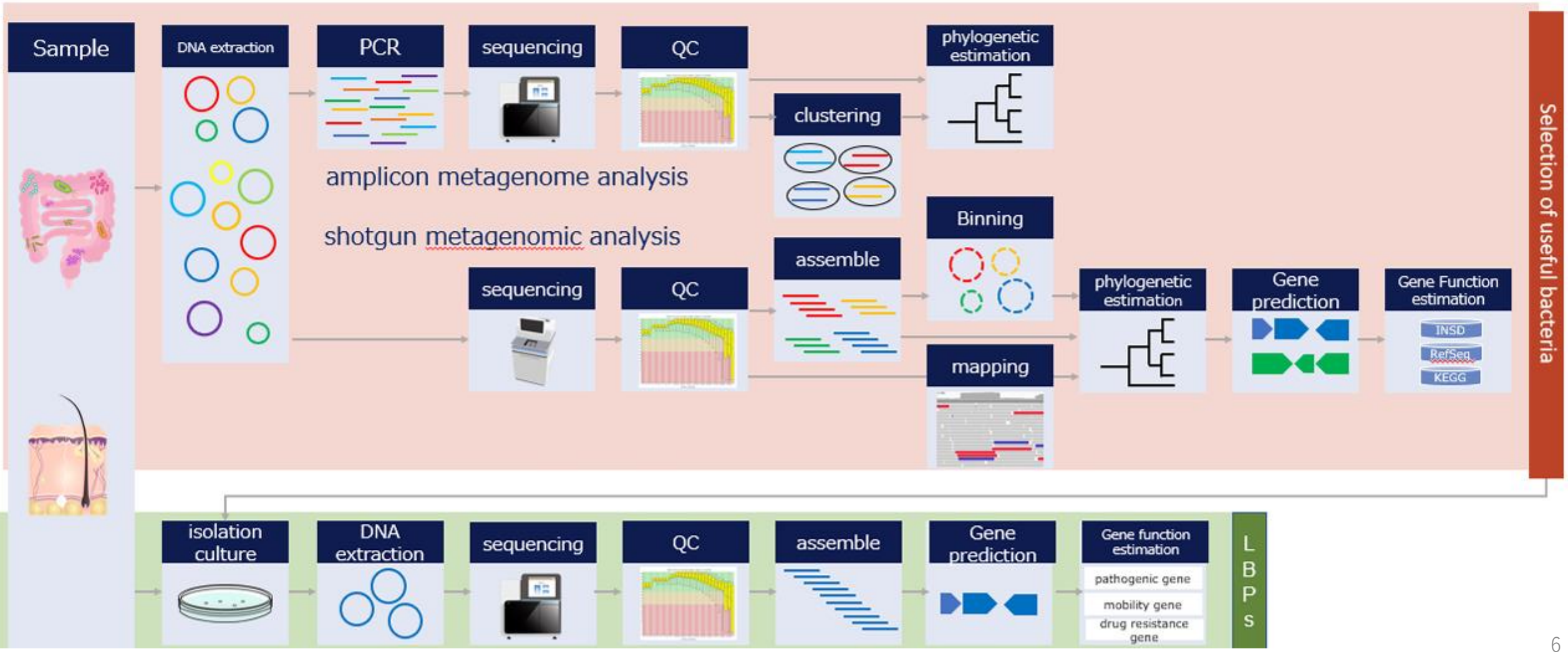
4.2 Characterization of LBPs

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



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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

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Examples of Tests to be performed at MCB/WCB

Characteristic Items		Considerations for conducting the test
Genotype	16S rRNA gene sequence	16S rRNA gene sequence unique to the strain: purity and identity of the target strain
	Whole Nucleotide Sequence Analysis	
Phenotype	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

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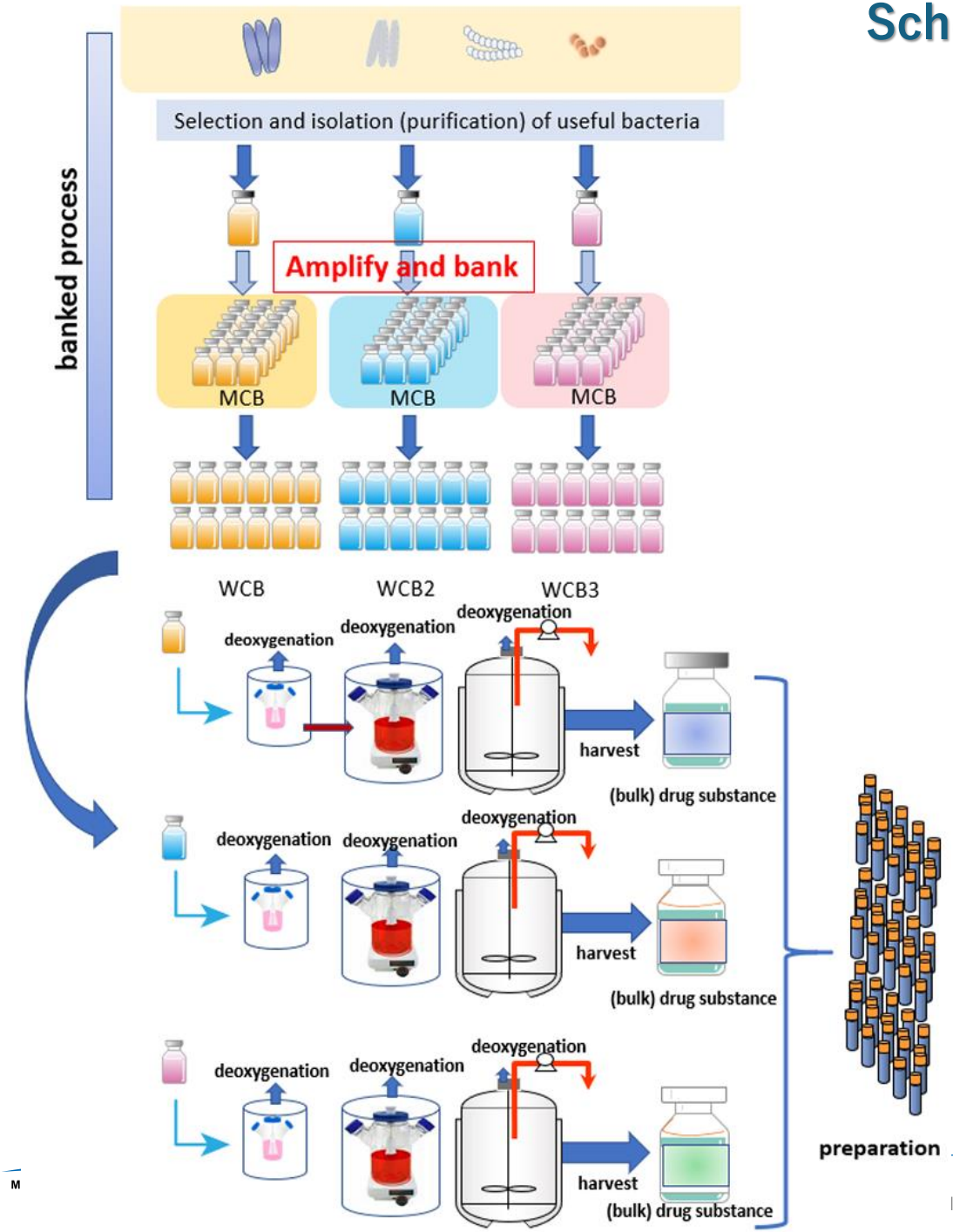
Schematic flow-diagram for the manufacturing of LBPs



- 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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Thank you for your attention!

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