



Fujirebio Obihiro Plant Site Tour

H.U. Group Holdings, Inc.
Sep. 22, 2023



Location



History



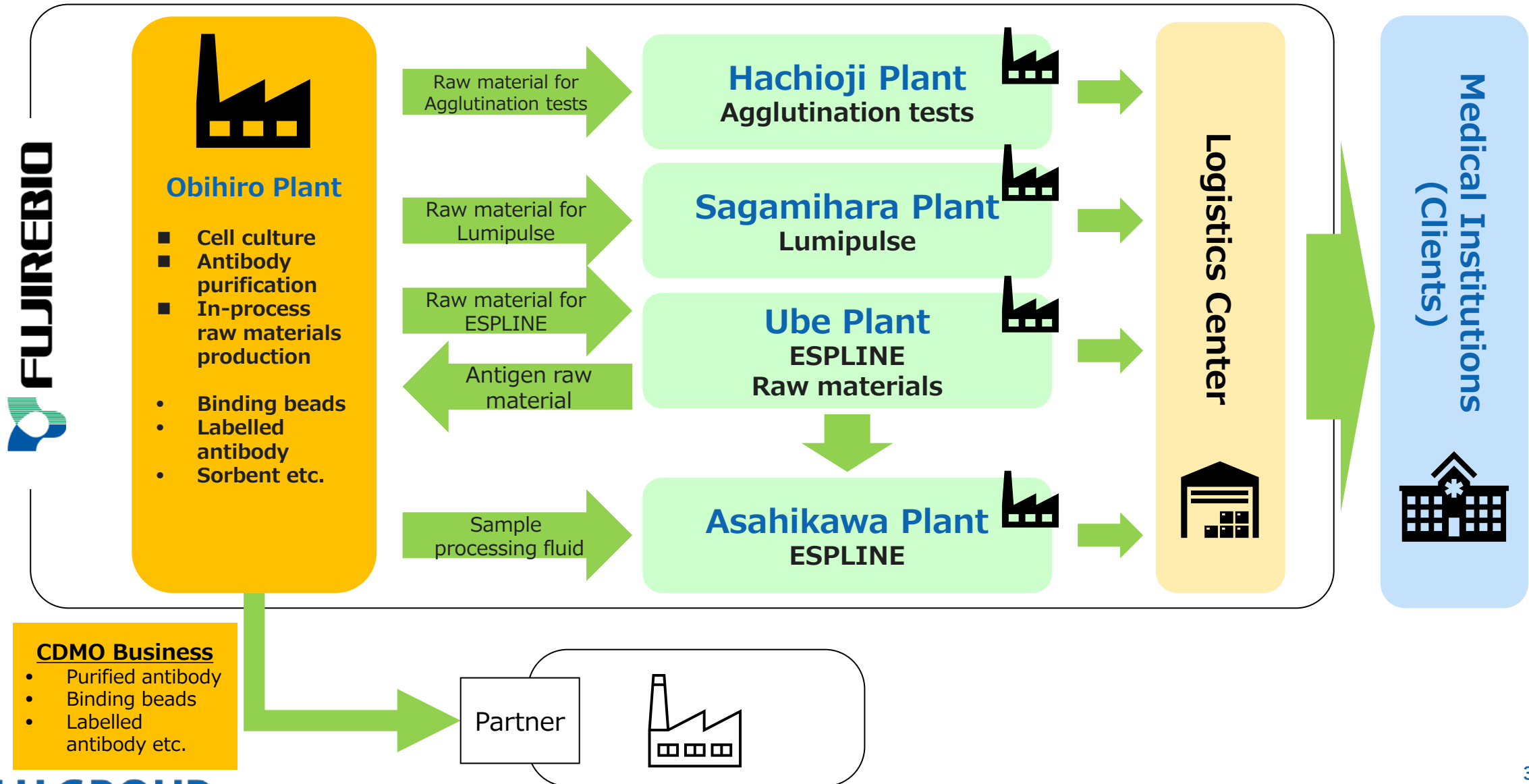
- 1973 Established Obihiro Research Center
- 1989 Established Manufacturing Division
- 2008 Research Group transferred
- 2009 Renamed as "Obihiro Office"

Obihiro University of Agriculture and Veterinary Medicine provides technical guidance on antibody purification from animals.

- 2011 May. Relocated to Otofuke IC Industrial Park
- 2011 Dec. Rearranged Research Group
- 2017 Apr. Relocated in-process raw materials for LUMIPULSE
- 2019 Apr. Research Group relocated to Hachioji
- 2020 Oct. Renamed as "Obihiro Plant"
- 2021 Mar. Constructed New prefab building
- 2021 Sep. Renovated and expanded prefab building
- 2022 Oct. First shipment as CDMO
- 2022 Dec. Registered as an IVD product manufacturer
- 2023 Jun. Registered with EU TRACES ¹

1. Required for exporting products containing animal-derived ingredients to the EU

Role of Obihiro Plant in the supply chain



Relationship between CDMO and Manufacturing of Lumipulse/ESPLINE

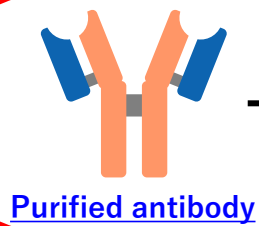
Sales image

Profitability image

Obihiro/Ube Plant

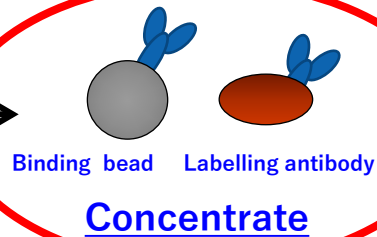
Culture/Purification

- Bioreactor
- Large-scale protein purification system



Purified antibody

Production/Labelling



Binding bead Labelling antibody

Concentrate

Sagamihara Plant

Filling/Packaging



Lumipulse Reagent

Asahikawa/Ube Plant

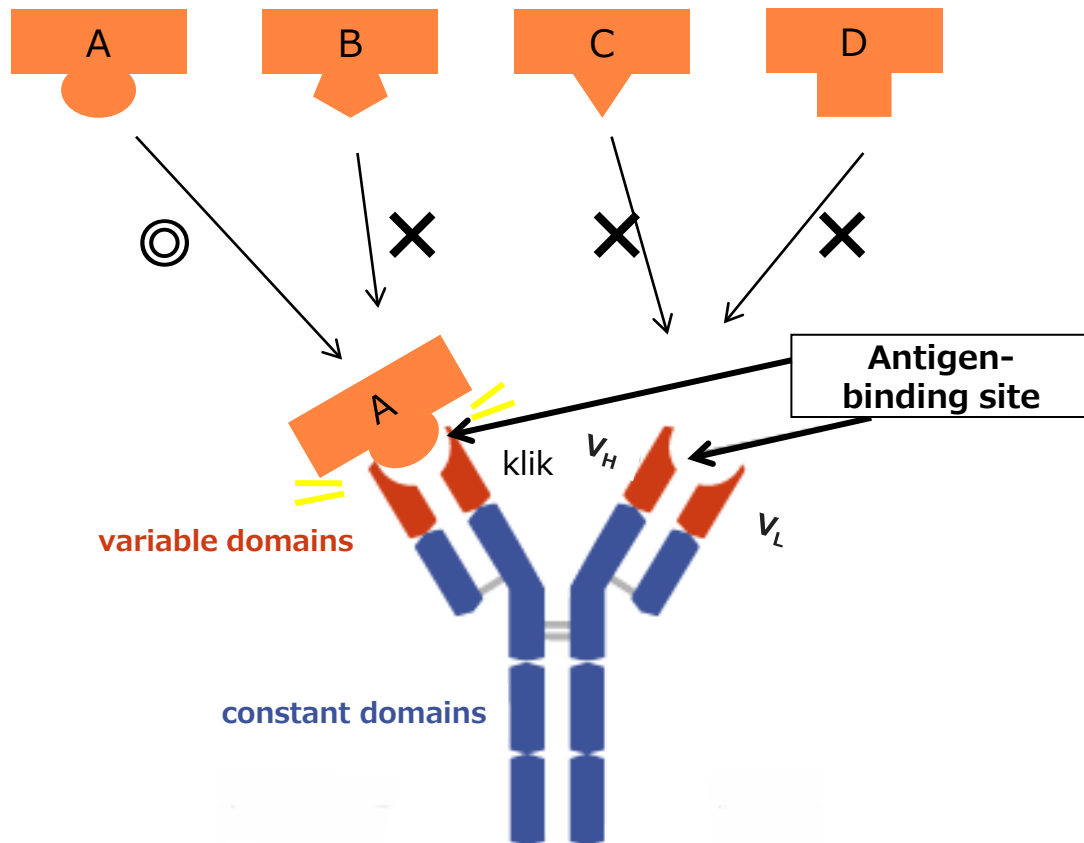
Filling/Packaging



ESPLINE

Supply to partner = CDMO Business

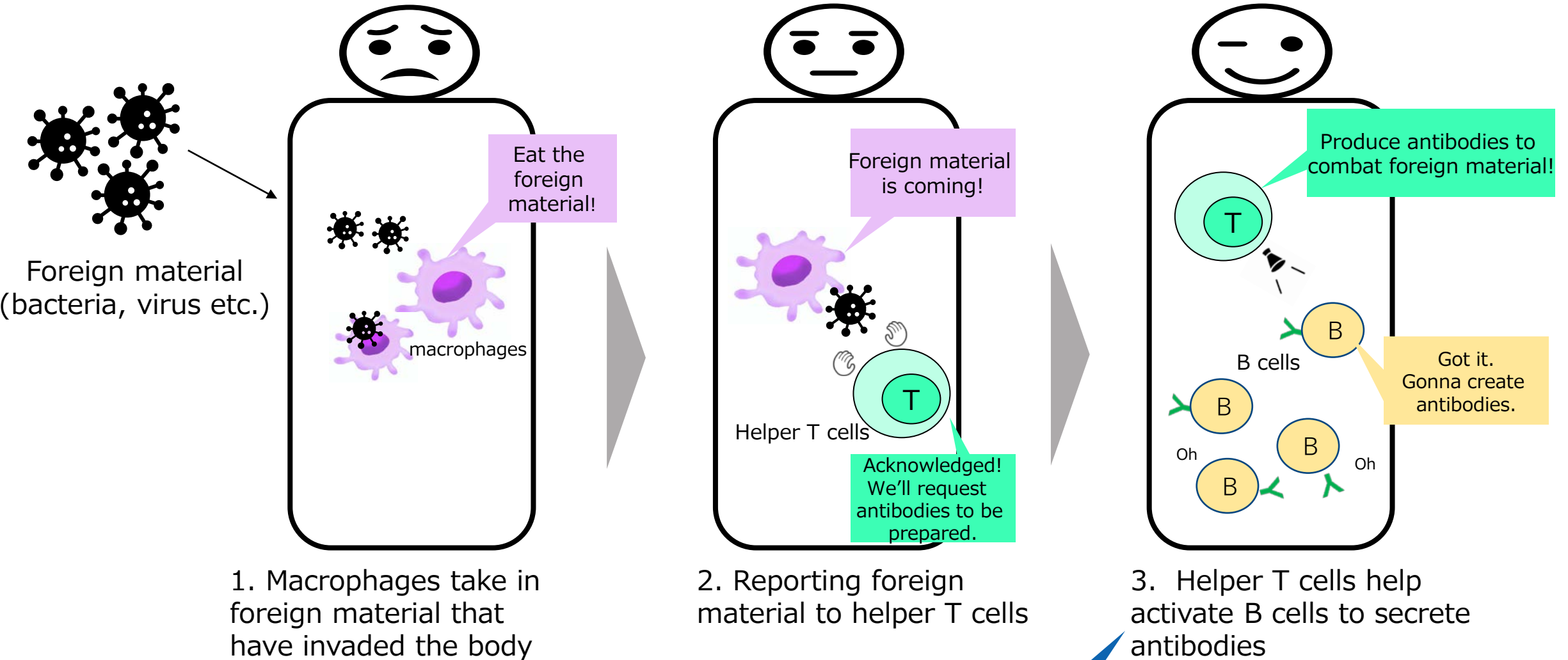
【Reference】 Properties of Antibodies



What is "Antibody"

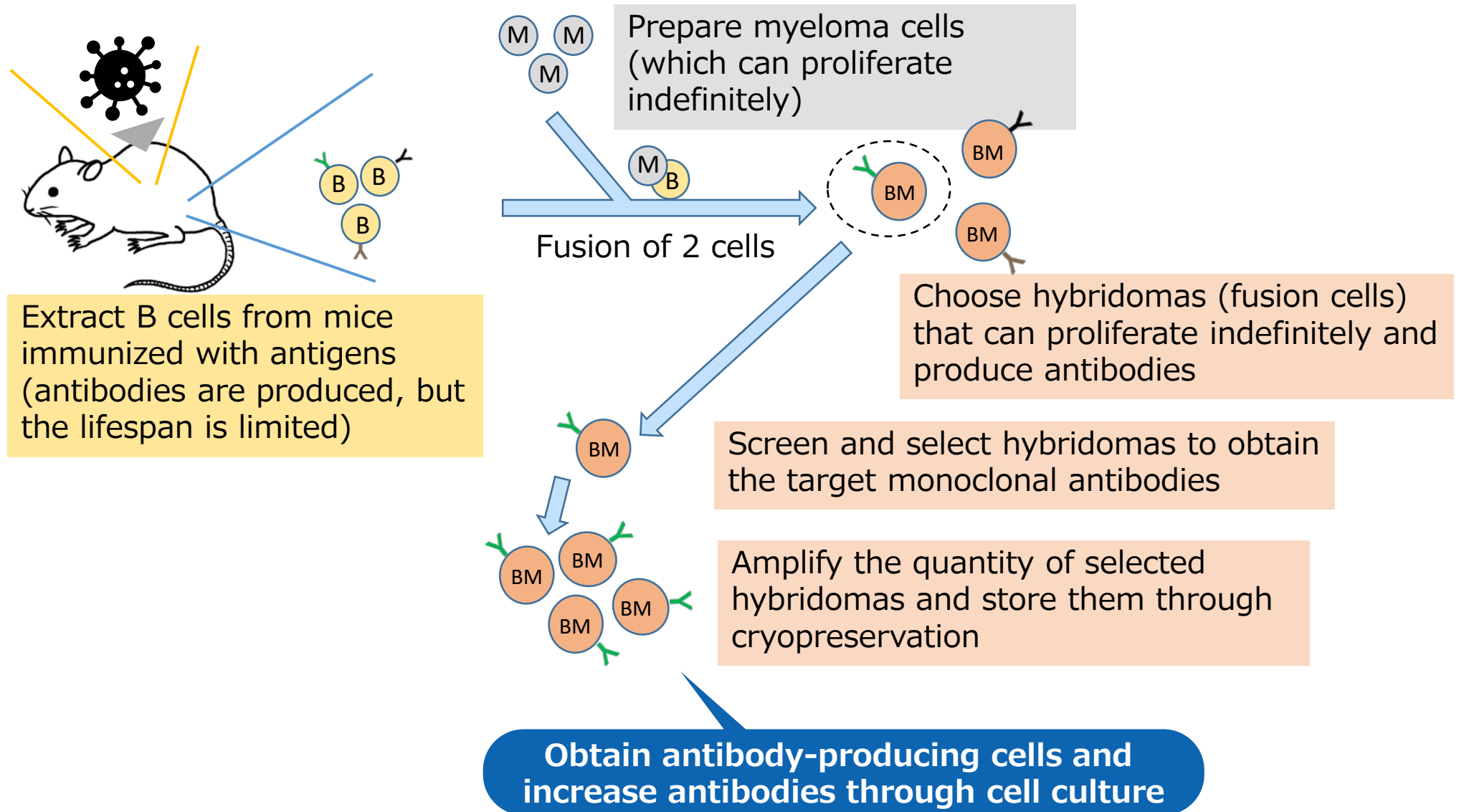
- A "Y-shaped" protein
- It is the "tip" of the Y that binds to the antigen
- **An antibody is characterized by its recognition of a specific antigen**
(In the image, it exclusively binds to antigen A)

【Reference】 Mechanism of Antibody Production "Inside" The Human Body



However, B cells have a limited lifespan and cannot continuously produce antibodies

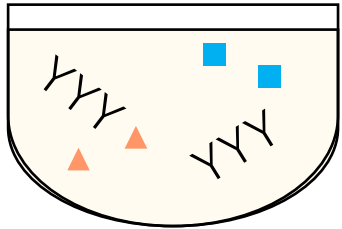
【Reference】 How to Produce Antibodies Outside of the Human Body



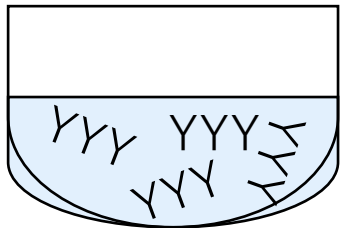
Manufacturing Process (conceptual overview)

**Determining which antibody to manufacture =
Specify the target reagent**
(Tumor marker? Infectious disease marker? Or Neuro ?)

Increase target antibodies
(Induce cells to produce antibodies)



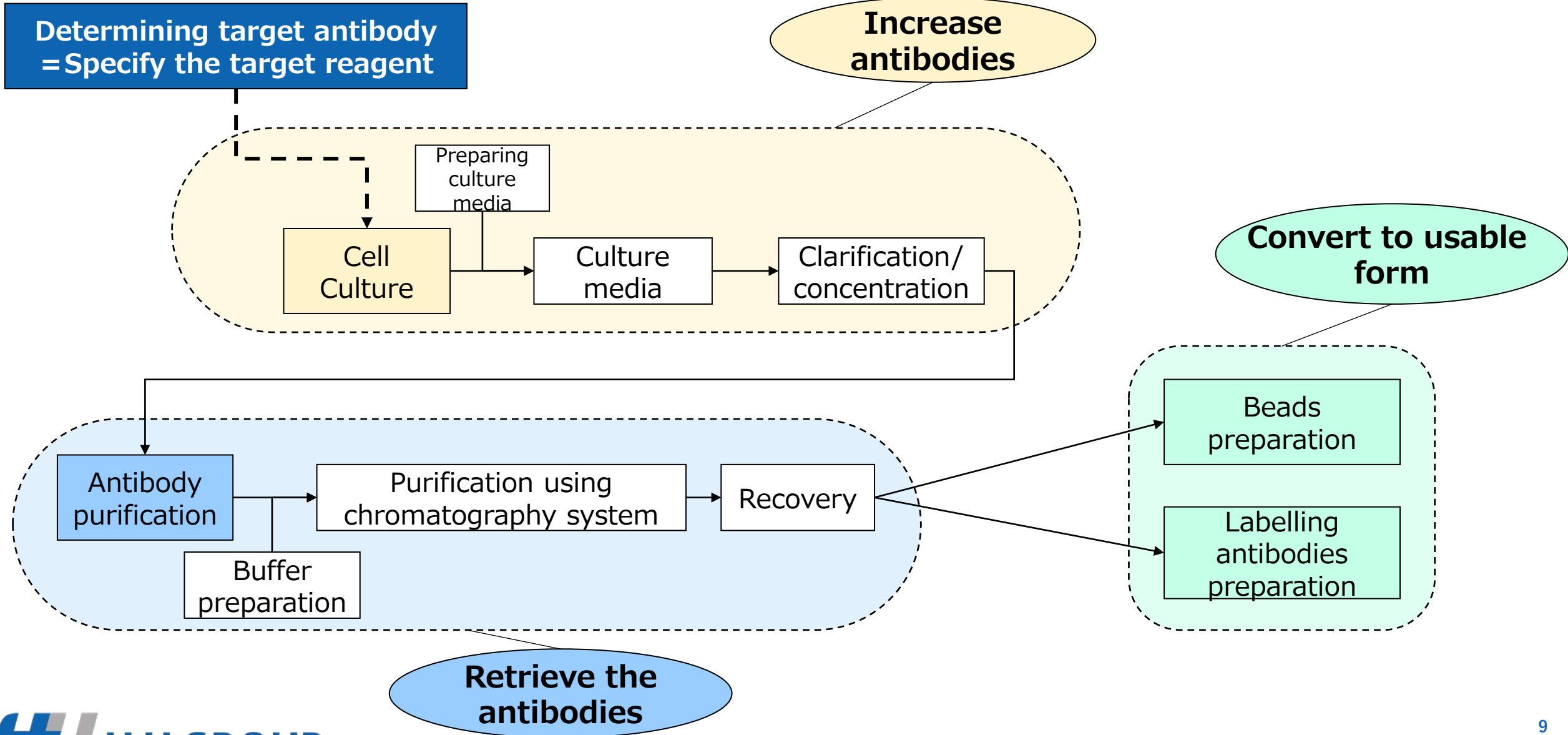
Purification of increased antibodies
(Remove the impurities and adjust concentration, etc.)



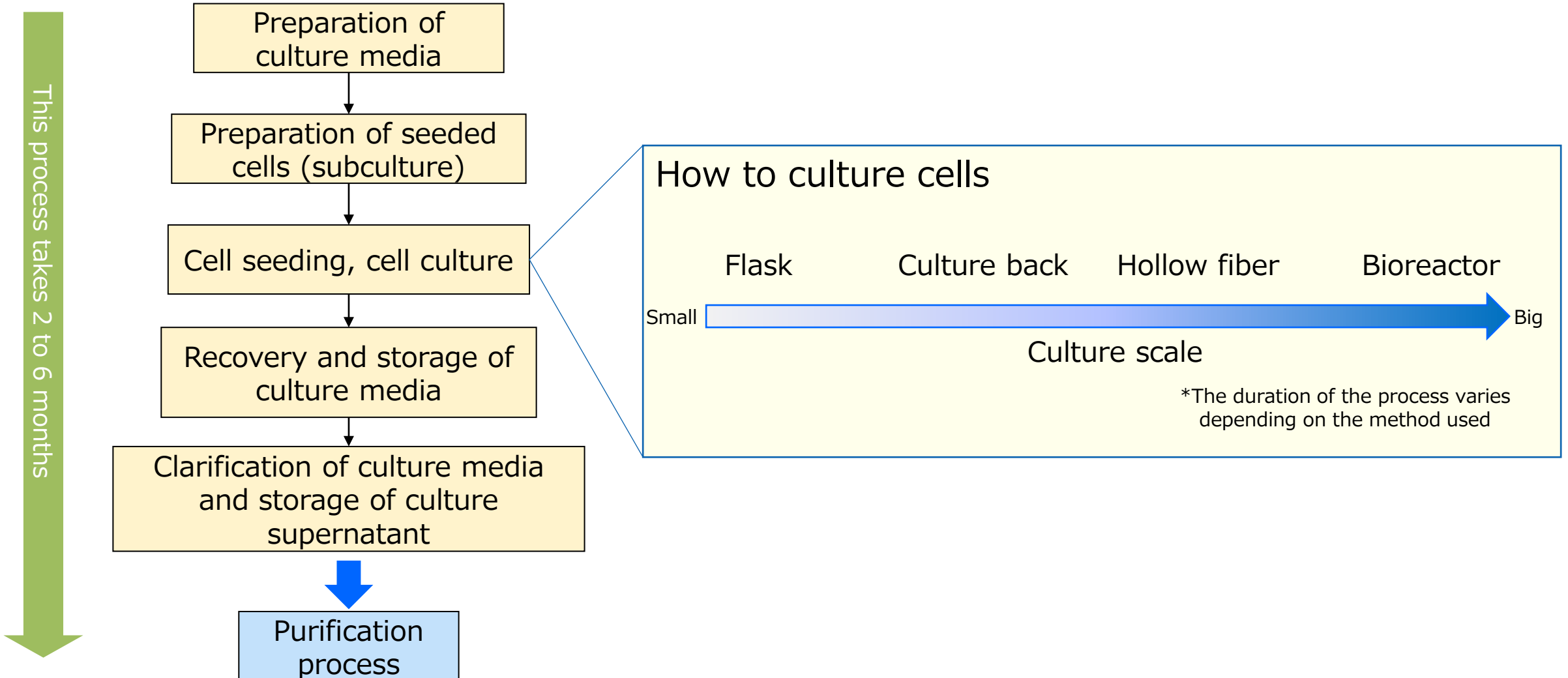
Create useable antibodies with automated analyzer
(bind antibodies to magnetic beads or enzymes)



Manufacturing Process



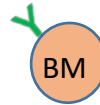
Cell Culture Process



Mechanism of Bioreactor

● : Antibody-producing cells (hybridomas in P7)

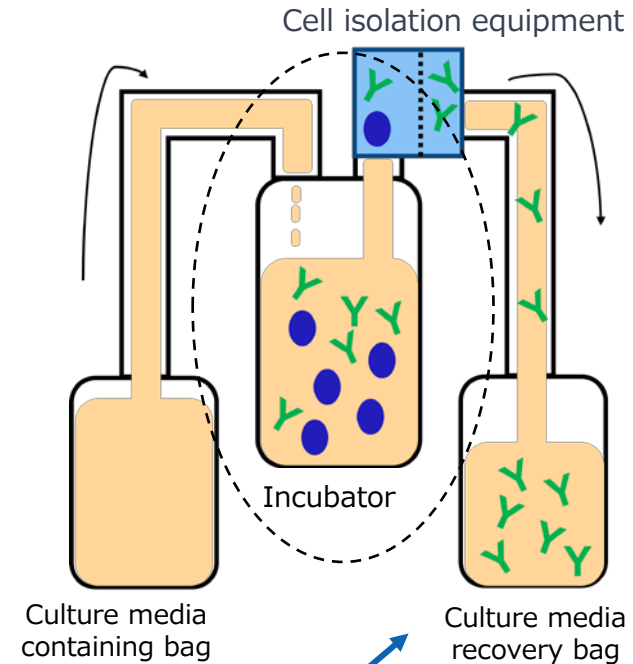
Y : Antibody



1. Supply the culture media to the incubator
2. Cultivate antibody-producing cells in an incubator to produce antibodies
3. Minimize cell leakage in cell isolation equipment
4. Recover culture media containing antibodies

Maintain a consistent rate for supplying and recovering culture media to ensure a constant volume of culture recovery

Schematic diagram of its operation

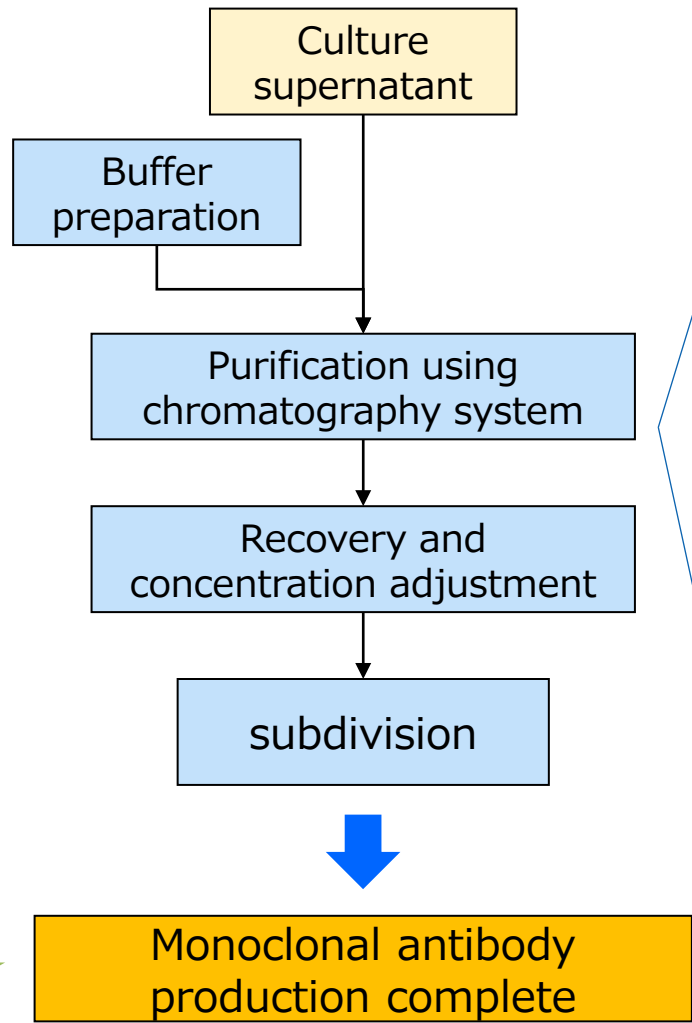


Cryogenic chamber side

Culture room side

Purification Process

This process takes 1 to 2 months



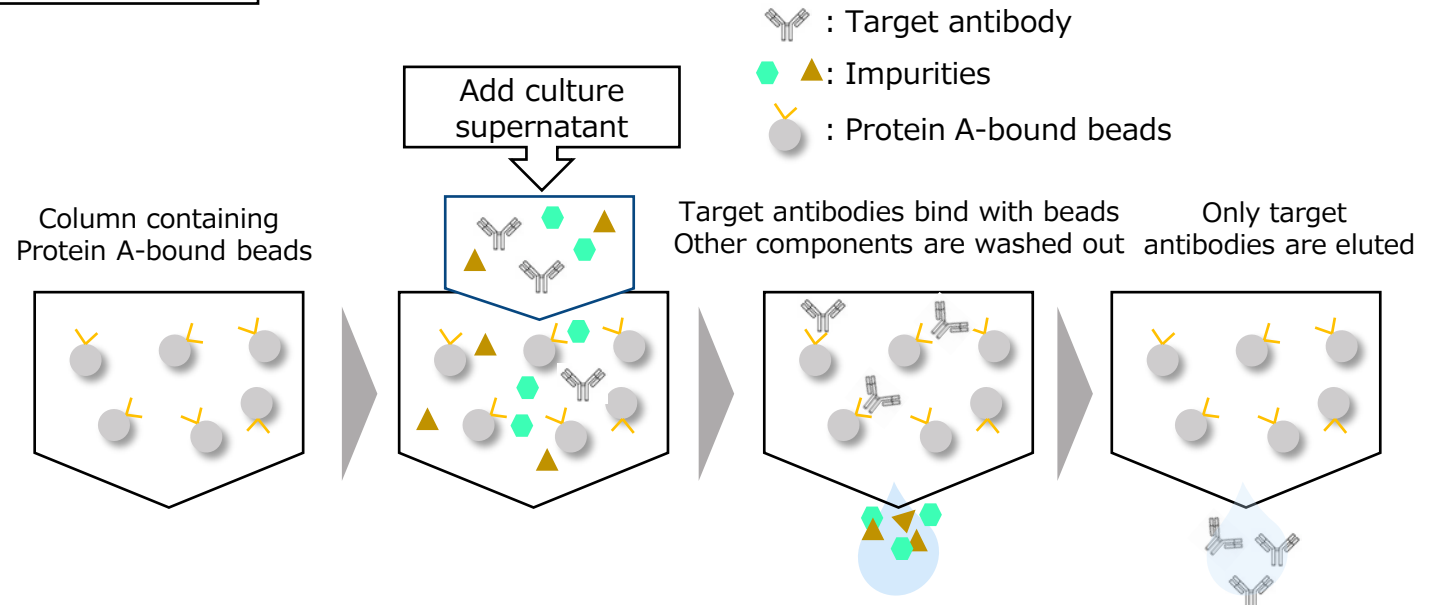
Method of purification

(Appropriate purification method is selected depending on the target item)

Gel Filtering

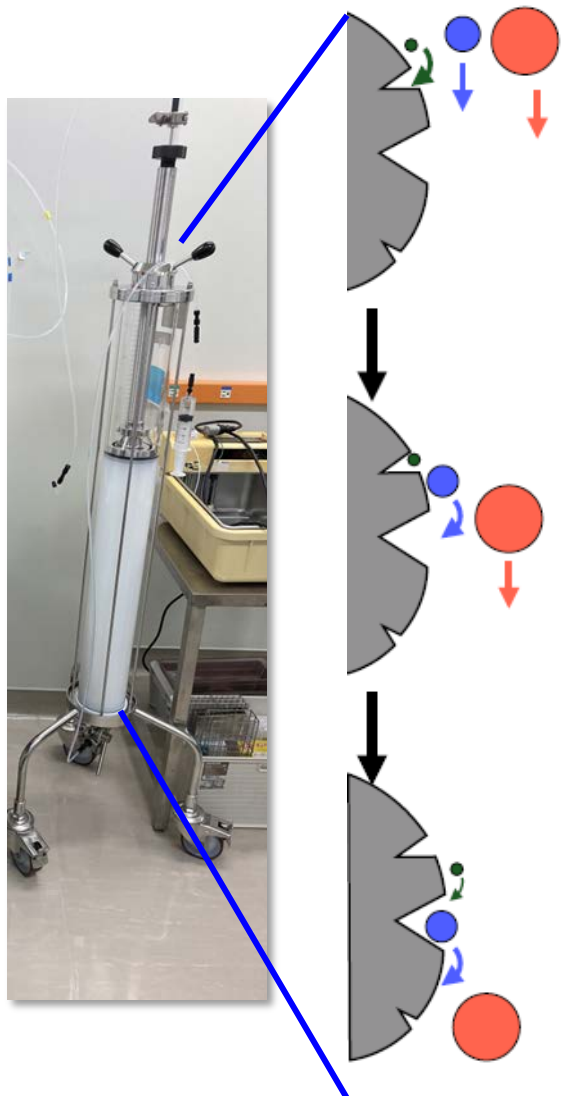
Smaller molecules pass through the pores, leading to a longer travel time within the column. This time difference is employed for molecule separation and purification. (Refer to page 13)

Protein A¹



1. Protein A is a cell wall protein found in *Staphylococcus aureus*. It is known for its specific binding to the Fc region of IgG antibodies from mammalian species.

Mechanism of Gel Filtration in Column Chromatography

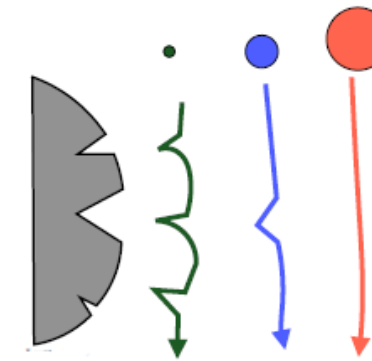
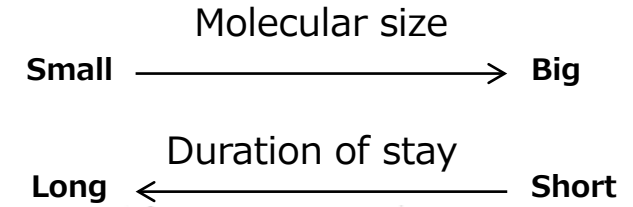
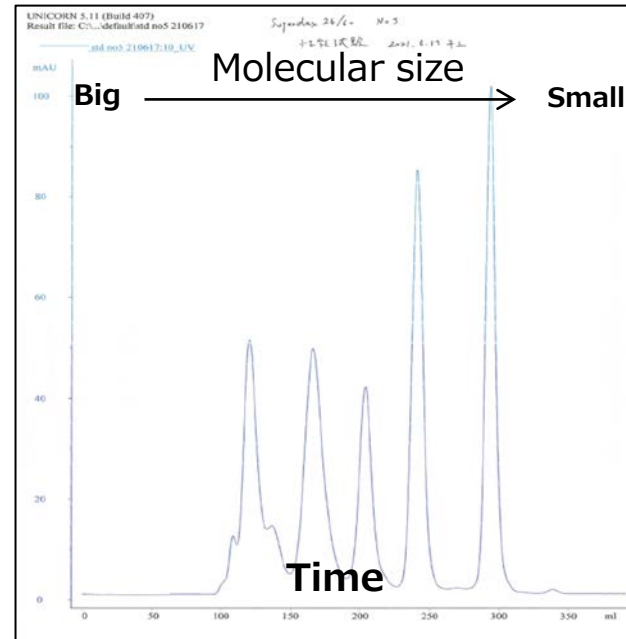


Schematic diagram of the mechanism of molecular sieving in gel filtration:

The gel filtration column's surface is made of porous material with many small holes.

As a protein moves through the column, it enters a pore if there is a big enough pore.

As a result, smaller proteins stay in the pores for a longer time.



The smaller the protein molecule, the longer the traveling path becomes **(which results in delayed elution)**



**Antibody-bound beads
(bound to antibodies)**



**Enzyme-labelled antibodies
(bound to ALP)**



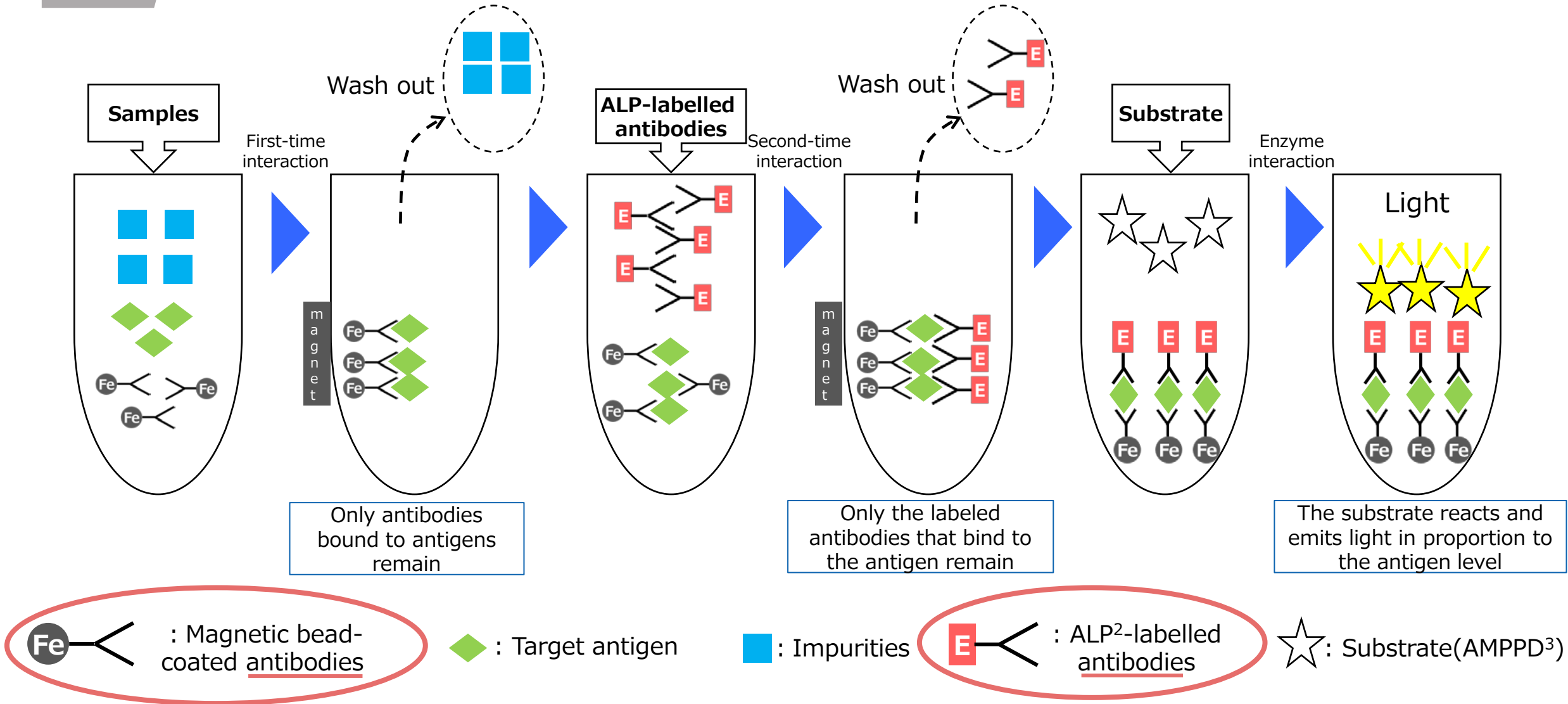
**Ship to other plants
(raw material of reagent)**

For Future Growth



- Acquired additional land to ensure manufacturing capacity for future CDMO business growth
- April 2022
- Area: 6,800m²

【Reference】 Detection Mechanism of CLEIA (Chemiluminescence Enzyme Immunoassay)



1. Prepared by the company as outlined in Handout1 from the Blood Business Subcommittee Steering Committee Meeting on Nov. 14, 2007.
2. Alkaline phosphatase: An enzyme that breaks down phosphate compounds in alkaline conditions.
3. Substances that produce light when broken down by ALP during the degradation process.

【Contact information】

IR/SR Department Email : ir@hugp.com

Disclaimer regarding forward-looking statement:

The performance forecast provided in this document is prepared by the management based on currently available information and various hypotheses and ideas including significant risks or uncertainties. Please be aware that the actual performance may turn out to be different from the forecast as a result of various contributing factors.

Factors affecting the performance include, among others, aggravation of the economic situation, fluctuation of the exchange rate, change of regulatory, statutory, and administrative requirements, delayed launch of new products, pressures from the product strategies of competitive companies, and decline of the sales potential of existing products.

Contents described in this document are simplified and some mechanism is omitted for better and easier understandings.