

IPFA 4th Asia Workshop

Practical Considerations for fractionation and/or Toll Manufacturing

7 MAR 2019

M. Tsuda

Introduction of JB

Establishment of JB

Japanese Red
Cross Society (JRC)

Japanese Red Cross
Plasma Fractionation
Center, Chitose

Mitsubishi Tanabe
Pharma Corporation
(MTPC)

Benesis

Japan Blood Products Organization
non-profit organization

JB has started its operation from OCT 1, 2012

Philosophy

➤ Philosophy:

Bridging Good Faith and Healthcare

Through blood products derived from voluntary non-remunerated blood donations, we contribute to people's health with the highest sense of ethics and responsibility.

➤ Vision:

- ✓ We contribute to **achieve secure supply and self-sufficiency** of blood products, giving the highest priority to their safety and security.
- ✓ We strive to be the best partner for patients and healthcare professionals.
- ✓ We strive to be a leader of plasma fractionation operations in Japan and around the world.
- ✓ Bear in mind the limitation of blood resources, we strive to explore new possibilities of blood products through everlasting challenge to innovate.
- ✓ We foster the corporate culture which respects pride and satisfaction of every employee.

JB Profile

Name : Japan Blood Products Organization

Head Office: Hamamatsu-cho, Minato-Ku, Tokyo

Start-up: October 1, 2012

Representative : Takahide Ishikawa / President

Number of staff: approx. 1,200

Business sites

Headquarter: Tokyo

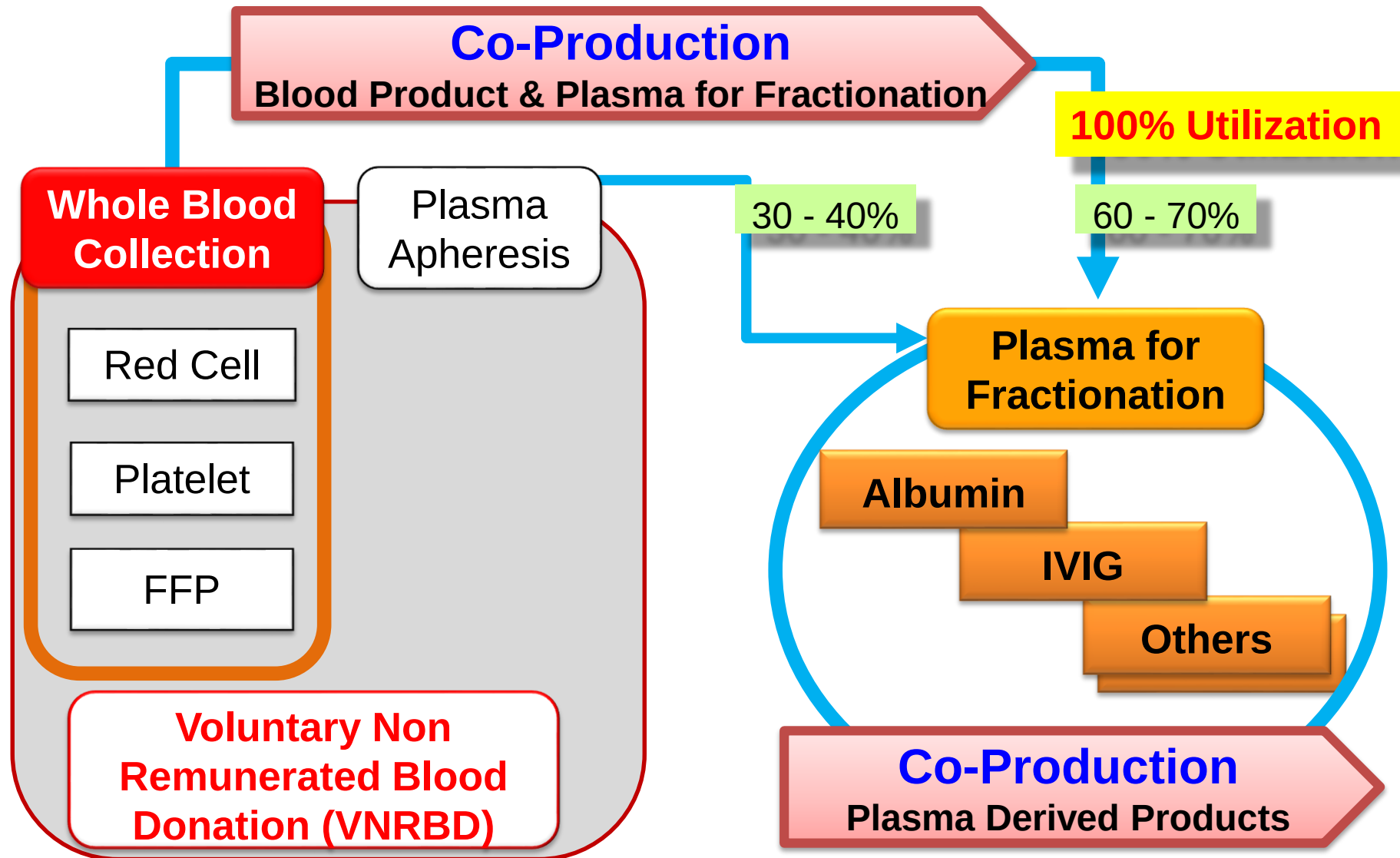
Lab. : Port Island, Kobe

Plants: Chitose Plant (former JRC)
Kyoto Plant (former BC)

Sales network: 8 branches

Plasma Fractionation Business in Japan

Blood & Plasma for Fractionation in Japan



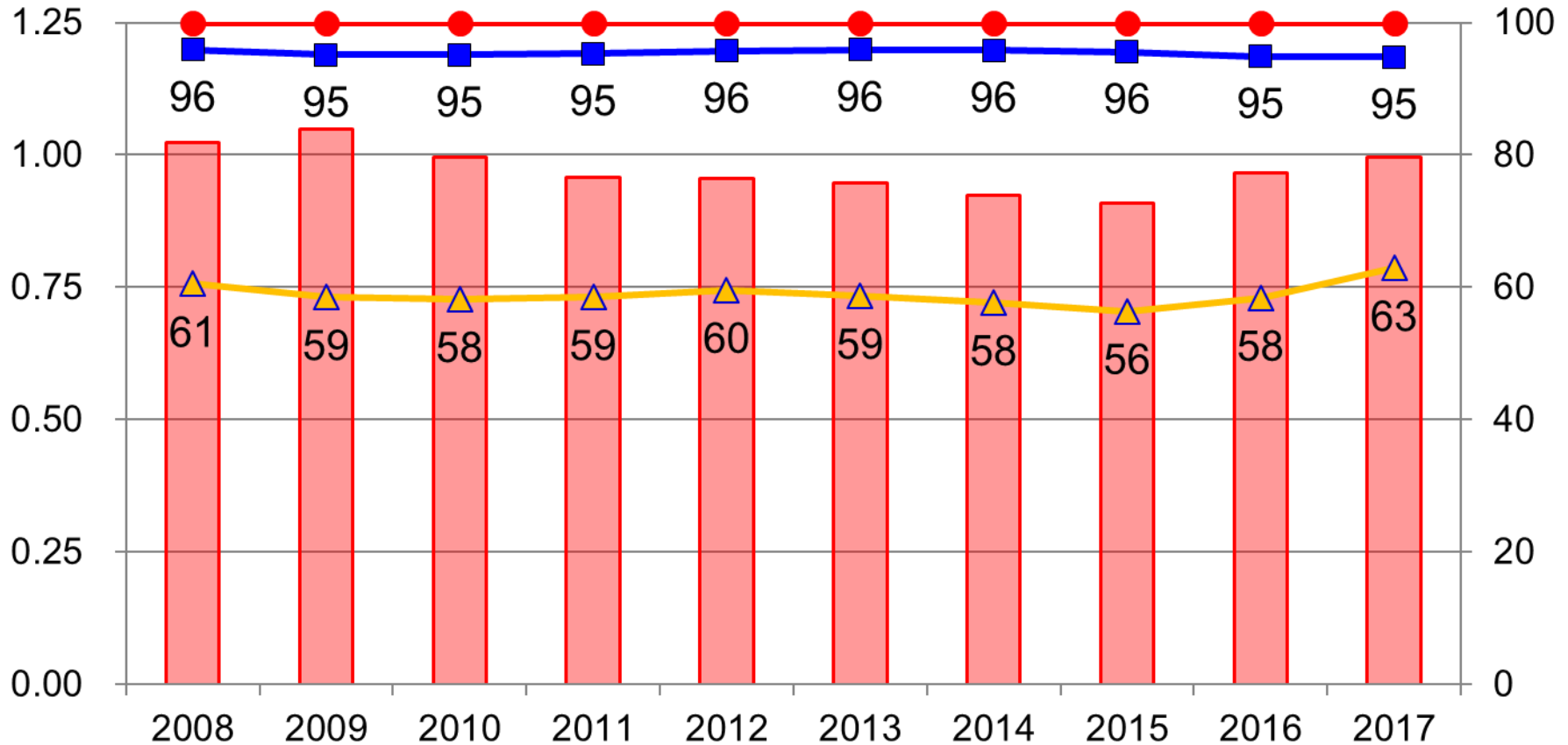
Japanese Fractionators



Self-Sufficiency in Japan (2008-2017)

Liter (Million)

Self-Sufficiency (%)



Domestic Plasma IVIG Albumin Factor VIII (without rFVIII)

(Source: Council Committee on Blood Products, MHLW)

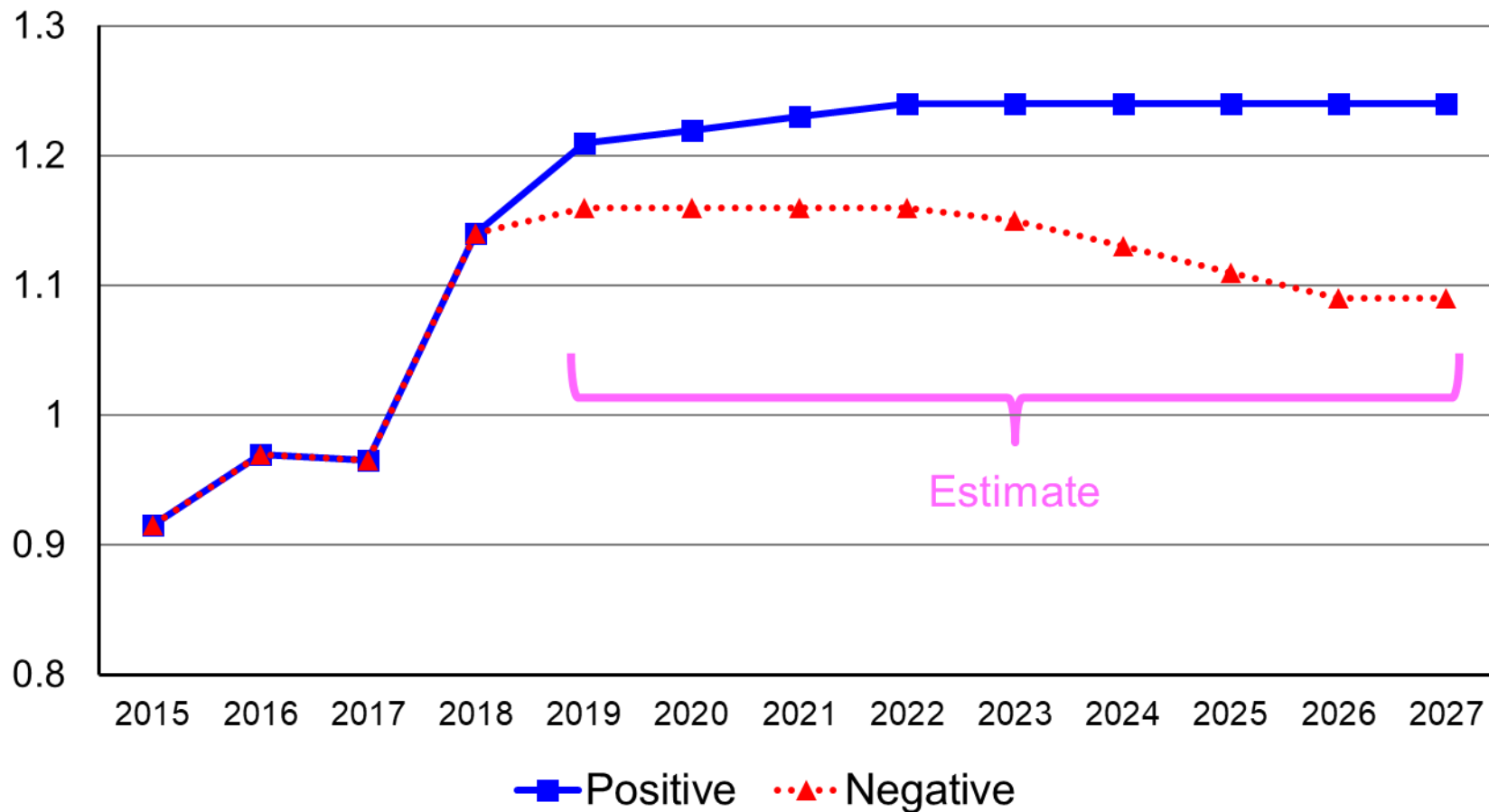
Indications of IVIG in Japan

Fractionator	JB	Nihon Pharmaceuticals	KM Biologics
PID / SID	X	X	X
Severe Infectious Disease such as sepsis	X	X	X
ITP	X	X	X
Kawasaki Disease (KD)	X	X	X
CIDP / MMN	X	X	
Guillain-Barre Syndrome (GBS)	X	X	X
Pemphigus	X	X	
Churg-Strauss Syndrome Allergic Granulomatosis Angitis			X
Polymyositis / Dermatomyositis	X		
Myasthenia Gravis	X		
Toxic Epidermal Necrolysis (TEN) Stevens-Johnson Syndrome (SJS)		X	
IgG2 Deficiency	X		
Bullous Pemphigus	X	X	

Necessary Volume of Plasma for Fractionation

Necessary volume of plasma for fractionation will be increased.

Liter (Million)



(Source: Council Committee on Blood Products, MHLW)

Clinical Studies for New Indications of IVIG

Fractionator	JB	Nihon Pharmaceuticals	KM Biologics
Microscopic PolyAntitis (MPA)			Phase III
Optic Neuritis			Filed
Kidney Transplantation	Filed		
Infertility	Phase III		
Optica Spectrum Disorder		Phase II	

Japanese fractionators continue to perform clinical studies to save Japanese patients.

Challenge

◆ Plasma Collection:

Japanese Red Cross Society has no experience of collecting over one million liters of plasma for fractionation for the last 10 years.

◆ Yield Improvement of IVIG:

Every Japanese fractionator has to improve yield of IVIG to save plasma collection volume.

Setting up a Fractionation Plant

Necessary Conditions for Fractionation Plant

1. Plasma-derived products market

- ✓ Enough market size: 300,000L ?
- ✓ Well-balanced consumption of each product

2. Initial plant investment

- ✓ 100 – 200 million USD ?

3. Running cost for plant investment

- ✓ Maintenance of facilities (several million USD / year ?)
- ✓ Correspondence to GMP Upgrade
- ✓ Replacement of plant (every 20 - 30 years?)

4. R & D activity

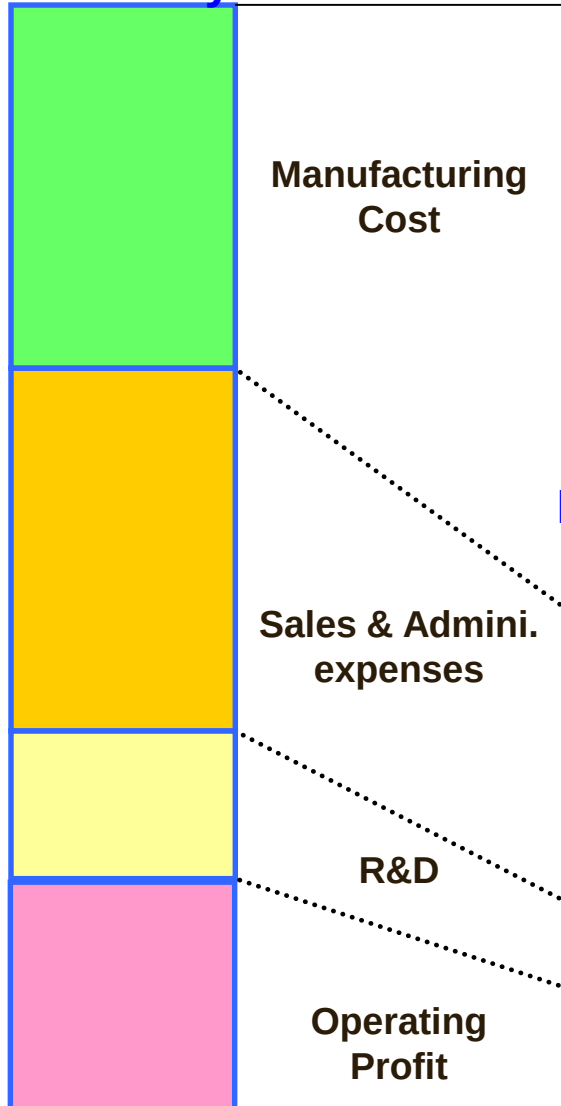
- ✓ Continual Technology Update (need R&D investment)

5. Secure safe & enough volume of plasma for fractionation

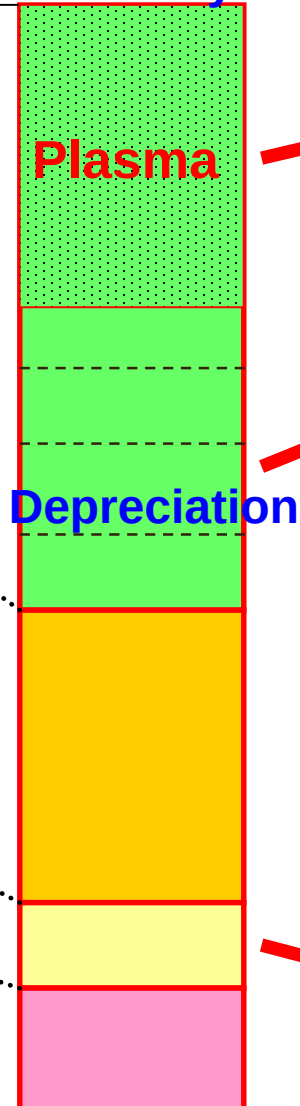
- ✓ GMP regulations

Cost Structure Comparison (Image)

Pharmaceutical Industry



Plasma Industry



➤ High manufacturing cost

✓ Large burden of plasma cost

- Enough market size
- Well-balanced products

✓ Large plant investment

- Initial plant investment
- Maintenance of facilities
- Correspondence to GMP
- Replacement building

➤ Small R&D Investment

Current Situation in Southeast Asia

Market in Southeast Asia

➤ **Small Market:**

- ✓ Difficulty to use plasma-derived products due to economical background or small population.

➤ **Unprofitable Production:**

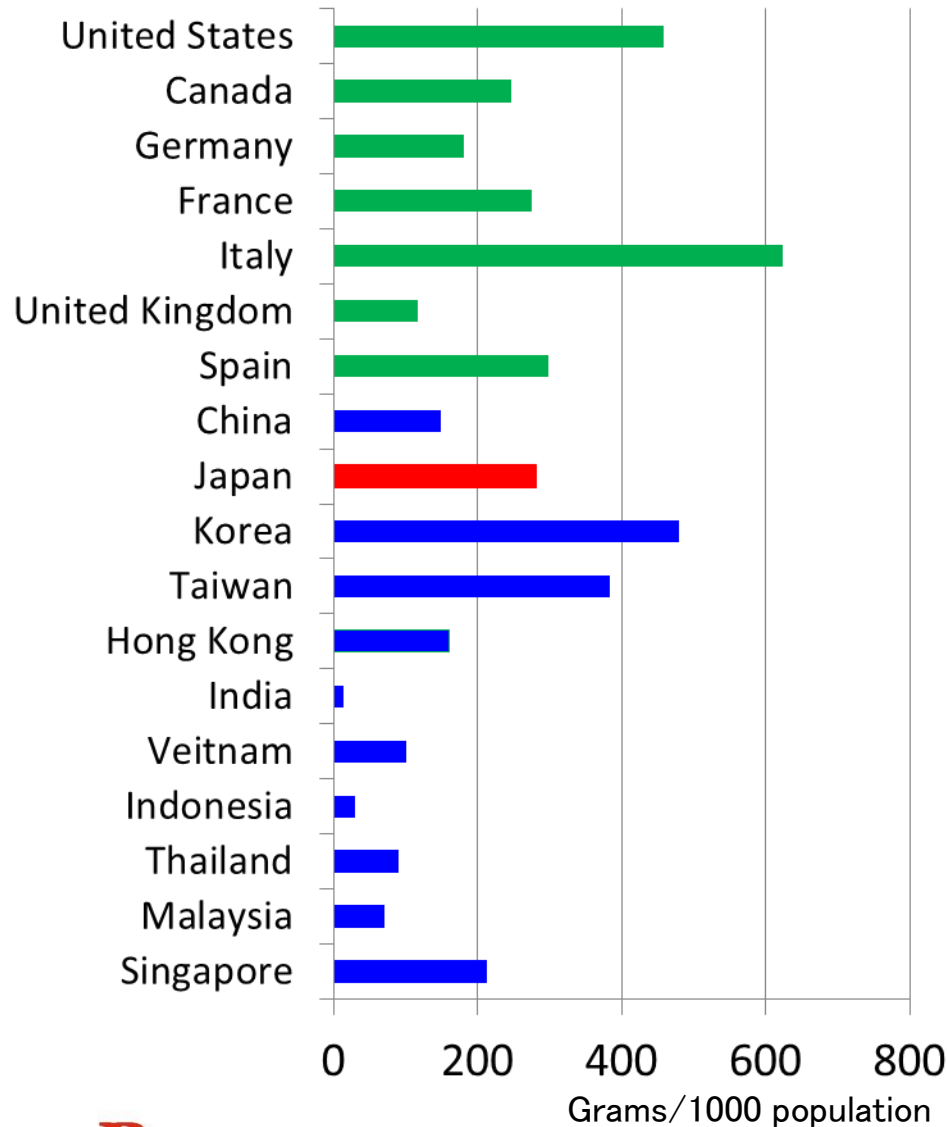
- ✓ Unbalanced consumption of Albumin and IVIG.



**Unfavourable business environment
for setting up of a local plant at this point.**

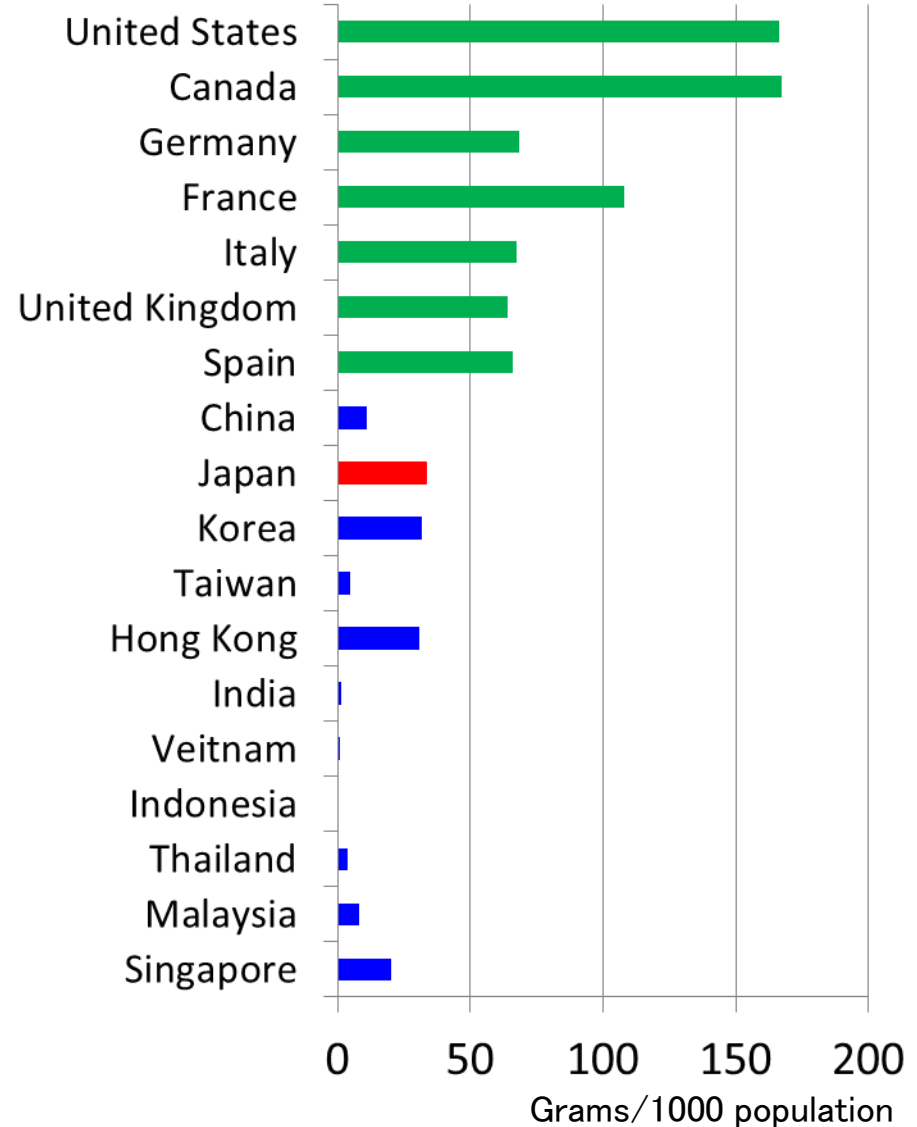
Consumption of Albumin & IVIG

Albumin

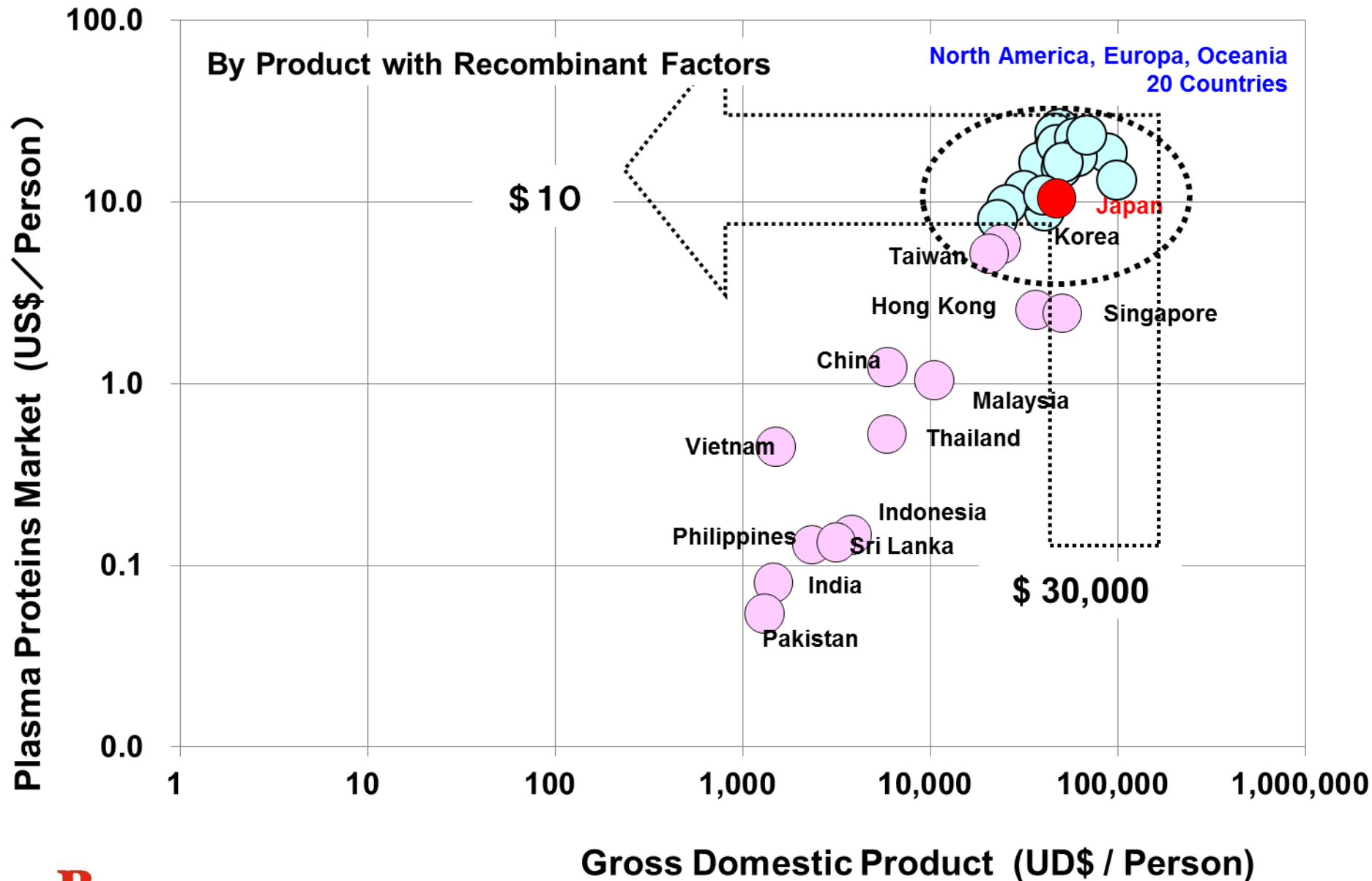


IVIG

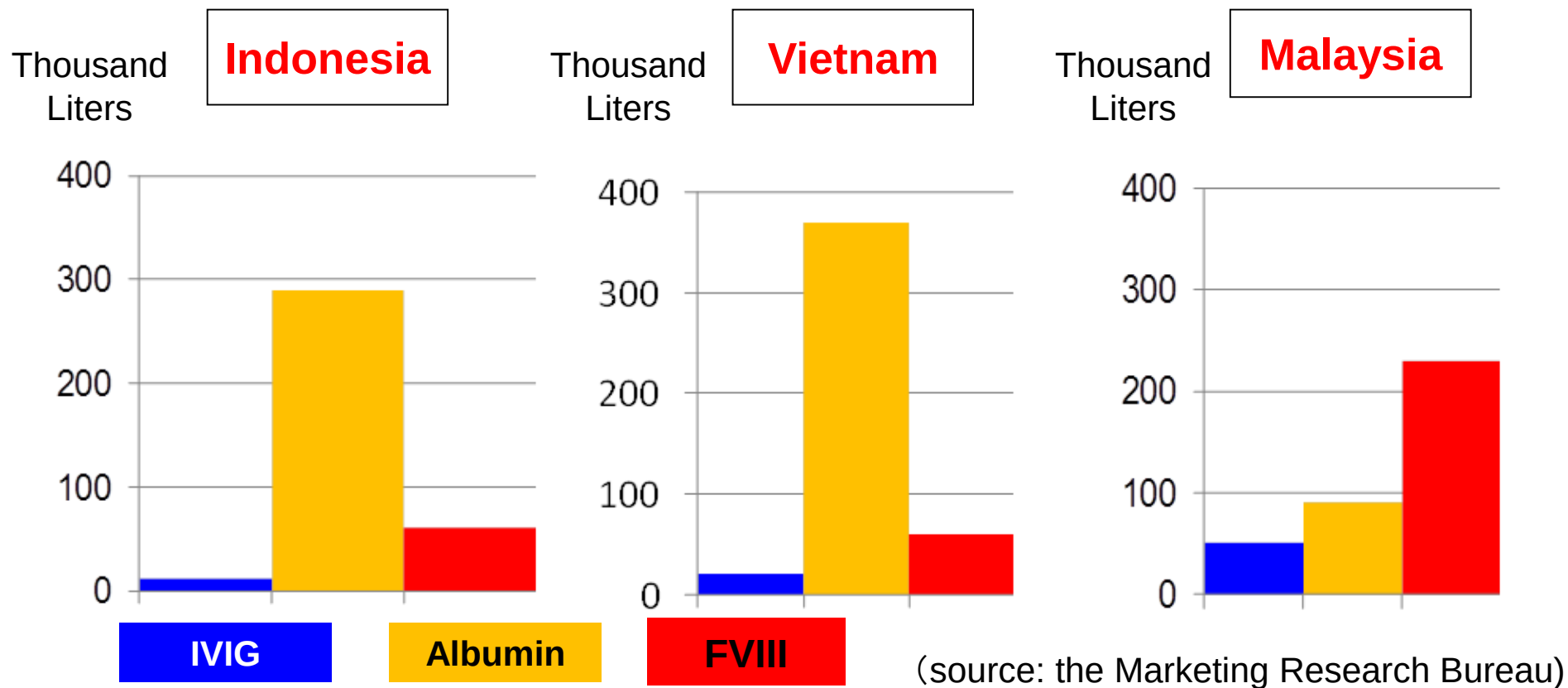
(source: the Marketing Research Bureau)



GDP vs Market Size



Plasma Balance in SE Asia



Unbalanced consumption results unprofitable production.

US / EU

Southeast Asia

Revenue from Plasma \$ 400 – 700 / L Plasma

\$ 127 / L Plasma

Plant Investment & Technology for SE Asia

Plant Investment

Large initial investment

- ✓ Equipment for plasma fractionation are dedicated.
- ✓ Equipment is expensive as US/EU level.

High running cost

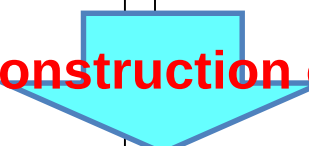
- ✓ Maintenance of facilities
- ✓ Correspondence to GMP upgrade
- ✓ Replacement of facilities

Technology / Technical Transfer

Initial technical transfer

- ✓ No knowledge and experience for plasma-derived products.
- ✓ Need technical transfer from third party.

(After construction of plant)



Continuous technical improvement

- ✓ No goal even if initial technical transfer is done. Need to introduce new technology by oneself.
- ✓ If no own technology, need another technical transfer from third party (= need technical transfer fee).

Unprofitable Production in Southeast Asia

Unprofitable Production in Southeast Asia:

- ✓ Small market of plasma-derived products
- ✓ Unbalanced consumption result in unprofitable production (Albumin vs IVIG)



Even if construction of plant is done...

➤ Difficulty of continuous operation:

- ✓ Difficulty of investment recovery
 - Can keep to invest in maintenance of facilities?
- ✓ Less technical capability
 - Can invest in R&D activity to have own technology?

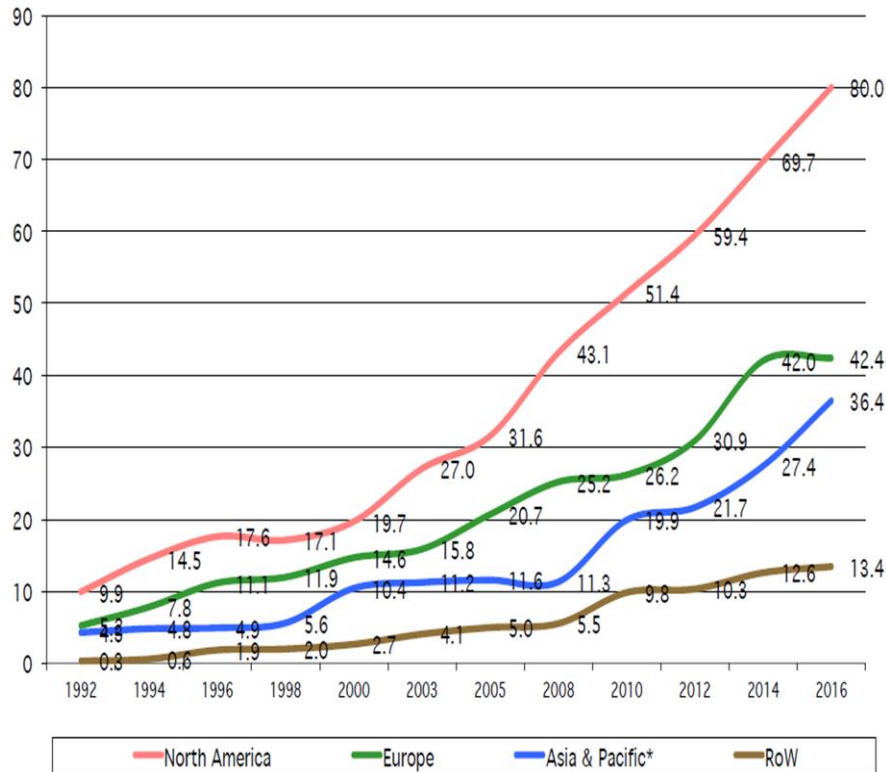
Toll Manufacturing is better

Plasma for Fractionation

Global Plasma Derived Products Market

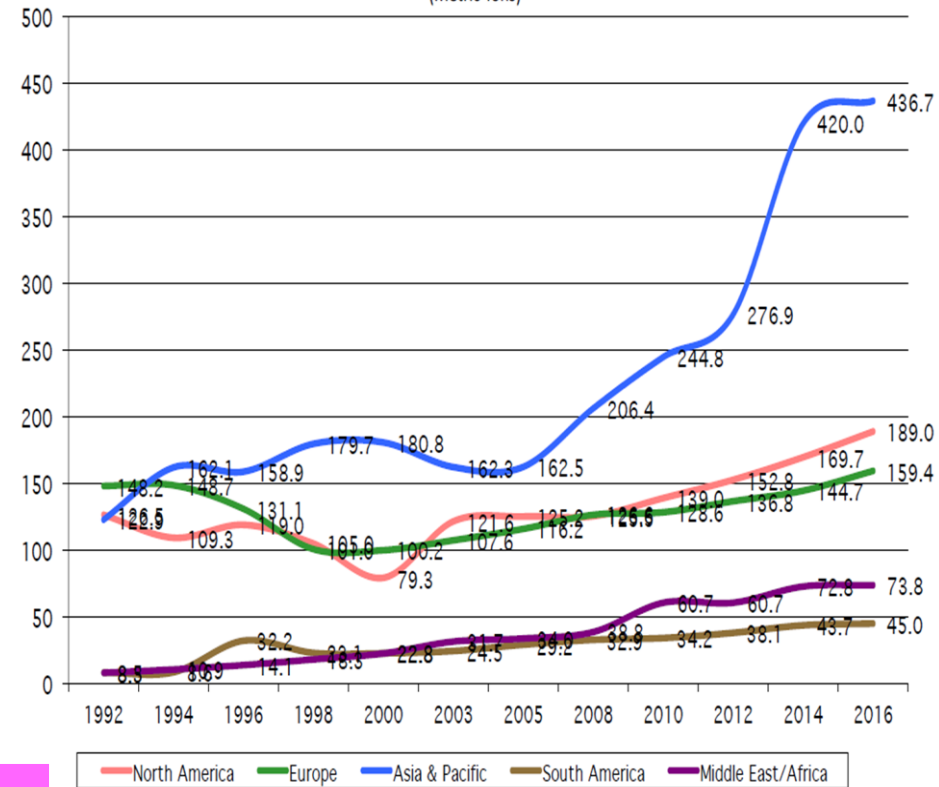
Market size of plasma-derived products are increasing.

WORLDWIDE POLYVALENT IMMUNE GLOBULIN (IVIG/SCIG) SALES BY REGION
FROM 1992 TO 2016
(Metric Tons)



The Marketing Research Bureau, Inc.

WORLDWIDE ALBUMIN SALES BY REGION
FROM 1992 TO 2016
(Metric Tons)



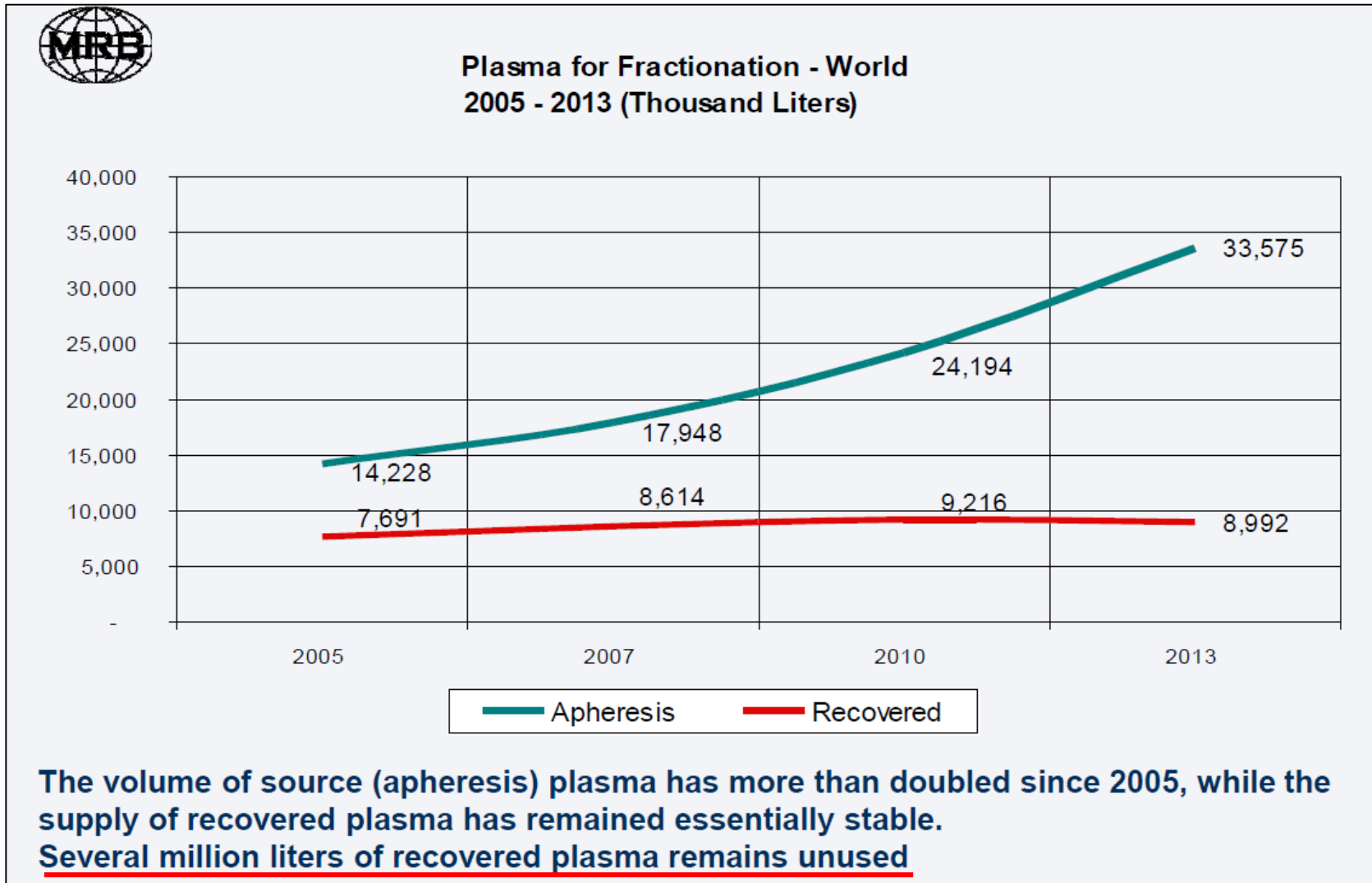
Marketing Research Bureau, Inc.

Necessary volume of plasma for fractionation are increasing.

(source: the Marketing Research Bureau)

Global Plasma Collection

Several million liters of recovered plasma remains unused

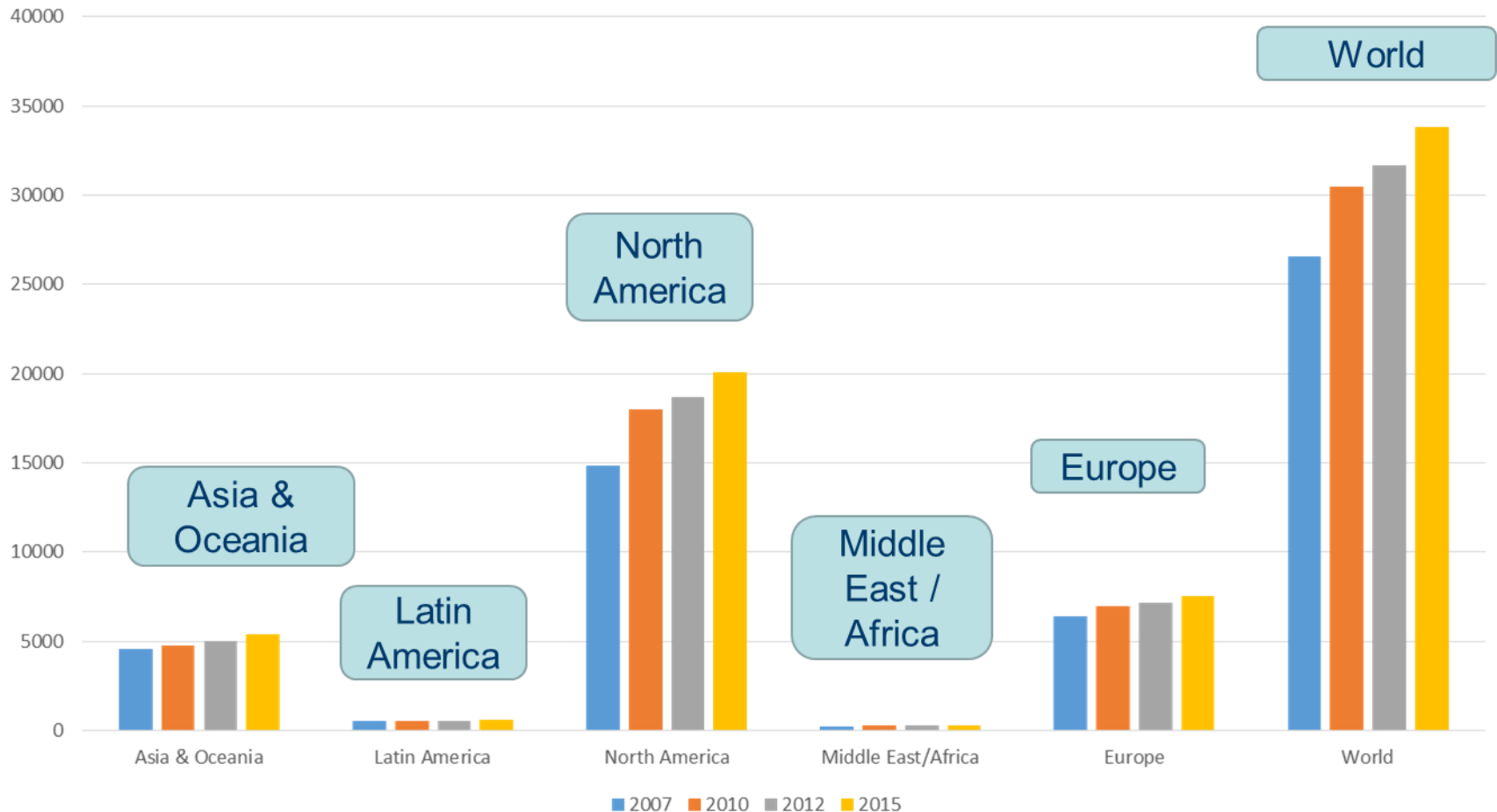


Global Plasma Collection



**Global plasma supply is out of balance
Depend too much on the US**

Global Plasma Collection Volume



Necessity for Self-Sufficiency

➤ Depend too much on the US

→ Risk

- ✓ Difficulty in collection of enough volume of plasma for fractionation around the world
- ✓ Difficulty in supply of plasma-derived products to low price market



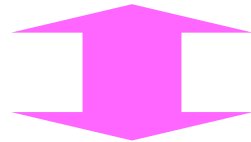
➤ Risk hedge

Need to secure plasma for fractionation in own country
= Self-sufficiency

How to Collect Plasma for Fractionation

- Huge volume of plasma is discarded in Southeast Asia

Country	Population (000)	Donations (000)	Plasma Wastage
Vietnam	96,491	1,171	80%
Indonesia	266,795	2,488	80%
Philippines	106,512	853	80%



- Plasma for fractionation is ready from VNRBD in Southeast Asia.
- Plasma for fractionation is not needed to collect from paid donors.
 - ✓ If plasma for fractionation is collected from paid donors, it is difficult to collect enough volume of blood for transfusion.

(Source: Marketing Research Bureau)

Plasma for Fractionation

Before utilizing plasma to manufacture plasma-derived products...

➤ **Secure plasma for fractionation**

Is GMP regulations for blood / plasma collection ready in your country?



➤ **If not,**

- ✓ **Need to establish GMP regulations first**

Summary

➤ Construction of plasma fractionation plant

It is not economical to have a fractionation plant as mentioned above in Southeast Asia.

- ✓ Small market
- ✓ High cost of initial plant investment & technical transfer
- ✓ High running cost for plant investment & R&D activity

➤ Toll Manufacturing

Toll manufacturing is better until the time that the local fractionation becomes economically feasible.

- ✓ Effective use of own country's plasma from VNRBD
- ✓ Achievement of self-sufficiency

➤ Secure plasma for fractionation

- ✓ If no GMP regulations for collection of blood / plasma, need to establish GMP regulations first

Thank you

