The Key Elements for self-sufficiency of plasma-derived products

MAR 3, 2017
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: Yuji Akiyama / Chairman of the Board
Takahide Ishikawa / President
Number of staff: approx. 1,100

Business sites
  Headquarter: Tokyo
  Lab.: Port Island, Kobe
  Plants: Chitose Plant (former JRC)
         Kyoto Plant (former BC)
Sales network: 11 branches
Self-Sufficiency in Japan
Self-Sufficiency in Japan

Self Sufficiency vs Plasma Balance
- Issue: Self-sufficiency of Albumin
- Approach: - Appropriate usage
  - Expand IGIV market

(source: Blood Products Research Organization)
Growth of IGIV Market in Japan

Liters (Million)

(source: Blood Products Research Organization)

IGIV market is growing with new indications
## Approved Indications of IGIV in Japan

<table>
<thead>
<tr>
<th>Approved year</th>
<th>Indication</th>
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<tbody>
<tr>
<td>1980</td>
<td>Primary Immunodeficiency / Secondary Immunodeficiency</td>
</tr>
<tr>
<td></td>
<td>Severe Infectious Disease such as sepsis</td>
</tr>
<tr>
<td></td>
<td>Idiopathic Thrombocytopenic Purpura (ITP)</td>
</tr>
<tr>
<td>1990</td>
<td>Kawasaki Disease (KD)</td>
</tr>
<tr>
<td>1996</td>
<td>Chronic inflammatory Demyelinating Polyneuropathy (CIDP) / Multifocal Motor Motor Neuropathy (MMN)</td>
</tr>
<tr>
<td>2000</td>
<td>Guillain-Barre syndrome (GBS)</td>
</tr>
<tr>
<td>2008</td>
<td>Pemphigus</td>
</tr>
<tr>
<td>2010</td>
<td>Churg-Strauss Syndrome / Allergic Granulomatosis angiitis</td>
</tr>
<tr>
<td></td>
<td>Polymyositis / Dermatomyositis</td>
</tr>
<tr>
<td>2011</td>
<td>Myasthenia Gravis</td>
</tr>
<tr>
<td>2014</td>
<td>Toxic Epidermal Necrolysis (TEN) / Stevens–Johnson Syndrome (SJS)</td>
</tr>
<tr>
<td>2015</td>
<td>IgG2 Deficiency</td>
</tr>
<tr>
<td></td>
<td>Bullous Pemphigoid</td>
</tr>
</tbody>
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Approach to Self-sufficiency of Albumin

Japanese fractionators are performing clinical trials for new indications of IGIV.

(Even if we have the height numbers of indications of IGIV)

<table>
<thead>
<tr>
<th>Development Phase</th>
<th>Investigational Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>P III</td>
<td>Microscopic PolyAngiitis (MPA)</td>
</tr>
<tr>
<td>P III</td>
<td>Optic Neuritis</td>
</tr>
<tr>
<td>P III</td>
<td>Infertility</td>
</tr>
<tr>
<td>P III</td>
<td>Kidney Transplantation</td>
</tr>
<tr>
<td>P II</td>
<td>Optica Spectrum Disorder</td>
</tr>
</tbody>
</table>

Our Approach:
- Expand IGIV market with new indications.
- Increase plasma throughput for IGIV.
- Achieve self-sufficiency of Albumin by increasing plasma throughput.
Structure of Plasma Fractionation Business
Common Success Elements in Plasma Business

- **Raw Material:**
  - Source Plasma (volume & quality)

- **Revenue from Plasma:**
  - Market Size
  - Well-balanced consumption of each product

- **Investment:**
  - Plant Investment
  - Continual Technology Update

- **Others**
  - GMP regulations
  - Safety (e.g. Virus)
  - …..
Cost Structure Comparison (Image)

- High cost of Plasma
  → Revenue from Plasma
    ✓ Market Size
      Certain Scale of Market (Revenue)
    ✓ Well-balanced products
      (Plasma balance: Profitability)

- Large Plant Investment

- Small R&D Investment

<table>
<thead>
<tr>
<th>Pharmaceutical Industry</th>
<th>Plasma Industry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturing Cost</td>
<td></td>
</tr>
<tr>
<td>Sales &amp; Admin. expenses</td>
<td></td>
</tr>
<tr>
<td>R&amp;D</td>
<td></td>
</tr>
<tr>
<td>Operating Profit</td>
<td></td>
</tr>
</tbody>
</table>
Large Plant Investment:
- Long manufacturing processes for plasma-derived products require large space and a lot of equipment

Updating a Technology (R&D Investment):
- External environment, cost structure and progress of science require to update a technology.
  - Product / manufacturing process / Yield
  - Virus safety

Plasma business requires large investment.
Current Situation in Southeast Asia
Market in Southeast Asia

- **Small Market:**
  - Difficulty to use plasma-derived products due to economical background.

- **Low Profitability:**
  - Unbalanced consumption of Albumin and IGIV.

- Difficulty to get enough revenue
- Difficulty to continue business operation
Consumption of Albumin & IGIV

Albunin

United States  | Canada  | Germany | France | Italy |
United Kingdom | Spain   | China   | Japan  | Korea |
Taiwan        | Hong Kong| India   | Vietnam| Indonesia|
Thailand      | Malaysia| Singapore|

IGIV (source: the Marketing Research Bureau)

United States  | Canada  | Germany | France | Italy |
United Kingdom | Spain   | China   | Japan  | Korea |
Taiwan        | Hong Kong| India   | Vietnam| Indonesia|
Thailand      | Malaysia| Singapore|
Plasma Balance in SE Asia

Unbalanced consumption results unprofitability.

<table>
<thead>
<tr>
<th>Country</th>
<th>IGIV (Thousand Liters)</th>
<th>Albumin (Thousand Liters)</th>
<th>FVIII (Thousand Liters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indonesia</td>
<td>300</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Vietnam</td>
<td>400</td>
<td>0</td>
<td>300</td>
</tr>
<tr>
<td>Malaysia</td>
<td>100</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Revenue from Plasma:

- **US / EU**: $400 – 700 / L Plasma
- **Southeast Asia**: $127 / L Plasma

(source: the Marketing Research Bureau)
Large Plant Investment:
- Equipment is expensive as US / EU level.
  - Equipment for plasma fractionation are dedicated

Update a Technology:
- No goal even if technical transfer is finished from third party.
- Need to introduce new technology by oneself.
  - Product / manufacturing process / yield
  - Virus safety
- Cannot survive if don’t have technology by oneself
Profitability in Southeast Asia

- Revenue from Plasma:
  - Small market of plasma-derived products (due to economical background)
  - Unbalanced consumption result unprofitability (Albumin vs IGIV)

- Investment:
  - Large plant investment (long processes and economical background)
  - Less technical capability and investment potential
Summary

- Plasma fractionation business is difficult.
- Business environment is not ready in Southeast Asia.
- Toll manufacturing is better until business environment is ready.
- Long term of technical guidance as well as initial technical transfer are important to construct plasma fractionation plant.
Thank you