Building a world class vaccine manufacturing plant in Bangladesh: Challenges and Opportunities

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Research experience on –
1. Anti-tumor antibiotic, University of Dhaka & IPGMR (BSMMU)
2. Dosage Form Design, Long Island University, USA
3. Special research interest on Aerosol, Nanotechnology, Sustain release drug, Lyophilyzation, Design of Pharmaceutical Factory
What is a pharmaceutical product?

Pharmaceutical products are usually small chemical compounds which have been developed into a dosage form according to route of administration intended for use in -

- Diagnosis,
- Treatment, or
- Prevention of disease
Incepta Pharmaceutical Ltd
Dhaka, Bangladesh

A private limited company having about 5,000 employees which produces such pharmaceutical products.
GMP approval from various Authorities

UK MHRA GMP certificate
European GMP certificate
Turkey GMP certificate
Kenya GMP certificate
Ethiopia GMP certificate
Uganda GMP certificate
D R Congo GMP certificate
Yemen GMP certificate
Sudan GMP certificate
Fact Sheet: Incepta Pharmaceuticals Ltd

- Year of Establishment: 1999
- Year of Business Operation: 2000
- Turnover: ~120 million USD
- Exporting to: 47 countries
What is a Vaccine?

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains -

- Weakened or killed forms of the disease-causing microorganism,
- Its toxins or
- One of its surface proteins
- Others
## Difference between Vaccine & Pharma products in technology

<table>
<thead>
<tr>
<th>Pharmaceutical products</th>
<th>vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small chemical molecules</td>
<td>Large protein molecules</td>
</tr>
<tr>
<td>Heat stable (more or less)</td>
<td>Heat labile</td>
</tr>
<tr>
<td>Can be processed by terminal sterilization</td>
<td>Can not be processed by terminal sterilization</td>
</tr>
</tbody>
</table>
Similarities between Vaccine & Pharma products in technology

• There are some similarity in manufacturing process with pharmaceutical injectable products

• Injectable products which are produced in aseptic filling process requires similar stringent environmental control, i.e class A

• Also, gowning requirement, microbiological testing etc. are somewhat similar
Incepta Vaccine Ltd
Incepta Vaccine Ltd

• For catering global need and that of Bangladesh, Human vaccine division “INCEPTA VACCINE LIMITED” emerged.

• It will provide vaccine to vast majority of population at an affordable cost.

• It has state of art facility fully compliant with WHO-GMP & International Standard

• It is a self sufficient unit with its own dedicated technical manpower, utilities and Animal house.
Incepta Vaccine Ltd has state of the art facility with following areas:

- Research and Development Block
- Antigen Production Block
- Fill Finish Block
- Microbiology Lab
- Chemistry Lab
- Animal House
- Day Store
- Dispensing Area

- Clean Utility Area
- Packing and Storage Area
- Ancillary Utilities Area
- Laundry
- Stability Area & Retained Sample Area
- Central Warehouse and Central Power Plant
Vaccine Production Requires

- Lab for viral & bacterial vaccine development
- Pilot scale GMP facility
- Antigen manufacturing
- Fill Finish
Research and Development Block
Lab & Pilot scale GMP Facility

• Fully equipped with production and QC
• Cell Culture for Viral Vaccine
• Fermentors for Recombinant & Bacterial vaccines
Lay out of R & D Area
Vaccine R&D
Inverted Microscope
Incepta Vaccine Ltd has already launched 3 vaccines:
Viral Particle analyzer (q-viro-X)
Mammalian Cell Culture bioreactor
Gel Doc XR+
(Gel Electrophoresis)
Bacteria Handling Lab
Fermentation
Centrifuge & Purification
Spectrophotometer

Tangential Forward Flow (TFF) system for Filtration of Protein
Antigen Production Block
Antigen Production

• Bacterial Line with 1500 L Fermentor
• Bacterial Line with 750 L Fermentor
• Viral Line with 450 L Bio-reactor
• Each Line is equipped with individual down-stream process
Challenges

• Lack of Trained Manpower
• Highly Expensive
• Long development process
• Cumbersome approval process
• Cumbersome public purchase process
Lay-out of Antigen (Bacterial)
Lay-out of Antigen (Viral)
Fermentor for Antigen production (for Bacterial line)

Under construction
Fill Finish Block
• Incepta Vaccine Ltd can produce any dose size from 0.1ml to 15 ml, with 4 different products simultaneously and has capacity to fill more than 2,40,000 ampoules and 3,60,000 vials per day.
The yearly capacity is **180 million** vials and ampoules.

<table>
<thead>
<tr>
<th></th>
<th>Capacity / Hour</th>
<th>Capacity / Day</th>
<th>Capacity / Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vials</strong></td>
<td>18,000</td>
<td>360,000</td>
<td>108,000,000</td>
</tr>
<tr>
<td><strong>Ampoules</strong></td>
<td>12,000</td>
<td>240,000</td>
<td>72,000,000</td>
</tr>
<tr>
<td><strong>Total capacity per year</strong></td>
<td></td>
<td></td>
<td><strong>180,000,000</strong></td>
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Fill & Finish

For fill & finish Incepta vaccine Ltd has 4 manufacturing lines which contains -

- Washing line
- Lyophilization line
- Filling line
- Packaging line
Incepta Vaccine Ltd – Filling Lines

• Four German filling lines have been provided, independent of each other so that four different products can be manufactured simultaneously.

• Each area has been provided with dedicated HVAC system to prevent cross contamination.

• All the filling area rooms are provided with terminal HEPA filters, with required air changes so as to create Class A, B, C & D environment, as the requirement of GMP.
Incepta Vaccine Ltd – Filling Lines

• Each filling line is provided with a sterilizing autoclave and decontamination autoclave.

• Each line is connected to independent visual inspection and labeling machine so as to prevent the chances of cross contamination.
Incepta Vaccine Ltd – Process

• The antigens are processed aseptically to produce the final liquid bulk which is then filled into individual vials or ampoules.

• The filling is done as required and vials are stoppered and sealed automatically and passed to visual inspection and labeling Area.

• Once the QC and QA have released the batch, the material is sent to central depot for further distribution.
Incepta Vaccine Ltd – Packing Area

• Big packing area, covering around 9,000 square feet.

• Material air lock. Provided with Access control.

• Day cold room with 5°C to 3°C temperature is provided so as to maintain cold chain during Packing.
Incepta Vaccine Ltd – Storage

• Two -20°C cold rooms are provided to store finished products and Bulk separately.

• Three 5 3°C cold rooms are provided. One for storage of bulk and two for finished product.

• All the cold rooms have 5 temperature sensors and two sensors for Data loggers, so as to monitor Cold chain every minute through wireless receivers.

• Total Capacity to store 500 million doses at 2°C - 8°C is available.
Incepta Vaccine Ltd – Quality Control

Quality control is done in 3 steps:

- Microbiology
- Chemical Lab, and
- Animal Tests
Incepta Vaccine Ltd – Microbiology

• Divided in Infectious and Non-Infectious Area

• This Microbiology area is dedicated for Sterility testing, Endotoxin testing, Bio-burden testing, cell culture testing and all other microbiological testing.
Lay-out of Fill
Finish
Production Area
Lay-out of Packaging Area
Lay out of Micro-biology area
Production area
Ampoule washing machine, Germany
Vial washing machine, Germany
Vial washing machine, Germany
Rabies filling machine, Germany
Rabies lyophilizer machine
Vial filling machine, Germany
Vial sealing machine, Germany
Ampoule filling machine, Germany
Dry heat sterilizer, Italy
Roll label machine
Fill Finish Facility, Challenges

- Requires processing of Heat Labile substances
- Aseptic Procedure
- Does not allow long room temperature exposure
- Some products require Lyophilization
Fill Finish Facility, Challenges (Cont.)

• Small Fill volume requires Precision filling 0.01 ml level

• Huge quantity of WFI

• Class 100, 10,000, Clean Room

• Highly Expensive
Animal House

- Largest lab animal house in Bangladesh covering around 24,000 square feet area.
Animal House

Rabbit

Guinea pig
Incepta Vaccine Ltd – Animal House

• The Animals are provided with 12 hour day light and 12 hour dark cycle and are maintained at comfortable temperature at 23 ± 2 C and Relative Humidity at 50%.

• All area are supplied with dedicated HVAC system to prevent cross contamination.

• Bio safety level 3 standard lab for testing various vaccines which involve challenge with infectious organisms.

• Can hold 6 various species of lab animals without any cross contamination.
Incepta Vaccine Ltd has already launched 4 vaccines:

- Vaxphoid®: Typhoid polysaccharide vaccine BP
- Vaxitet®: Adsorbed Tetanus vaccine BP
- Rabix-vc®: Rabies vaccine (human) BP
- Hepa-B®: Hepatitis B vaccine (rDNA) BP
A number of exciting vaccines are in pipeline:

1. Tetanus immunoglobulin
2. Haemophilus influenzae b (HIB)
3. Meningococcal
4. Measles & Rubella
5. Polio
6. Pentavalent (DPT,HIB,HB)

DPT: Diphtheria, Pertussis, Tetanus
HIB: Haemophilus influenzae b
HB: Hepatitis B
Incepta Vaccine Ltd can become a global supplier of high quality vaccine.
Every year Bangladesh Government has to purchase more than 90 million doses of different vaccines for Expanded Program on Immunization (EPI) for children of 0-1 year. In private sector other than EPI, every year more than 30 million doses are required. Incepta Vaccine Ltd is poised to supply world class vaccine at affordable price.
Thank You