Advances in Vaccine Manufacturing by Tofflon

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Tofflon Science and Technology Group Co., Ltd.
Business Scope
Learn From Medical Science; Contribute to Medical Equipment

Machine

**Tofflon Pharma**

<table>
<thead>
<tr>
<th>DS</th>
<th>DP</th>
<th>API</th>
<th>OSD</th>
<th>DPP</th>
</tr>
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<tbody>
<tr>
<td>Bio/CGT</td>
<td>Injection</td>
<td>API</td>
<td>OSD</td>
<td>Packaging</td>
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<tr>
<td>CES/SUB/SSB</td>
<td></td>
<td>Synthesis</td>
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<td>Weighing</td>
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<tr>
<td>Purification &amp; Filtration</td>
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<td>Drying Syst.</td>
<td>Granulating</td>
<td>Inspection</td>
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<tr>
<td>Bio-solution Prep.</td>
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<td>Fermentation</td>
<td>Drying</td>
<td>Labeling</td>
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<td>Freeze &amp; Thaw</td>
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<td>Herbal</td>
<td>Mixing</td>
<td>Cartoning</td>
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<td>Inactivation</td>
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<td>Palletizing</td>
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<tr>
<td>Cell Processing Station</td>
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<tr>
<td>Cryopreservation Syst.</td>
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**Engineering**

- MNGT.
- Clean Room

- Service
- Eng.

- CD, BD, DD
- Project MNGT.
- Validation MNGT.
- HVAC
- Water Sys.
- Automation
- Clean Room Constr.

**Consumables**

- Consumables
- Packaging

- SU Bags
- Culture Media
- Resins
- Filters & Membrane
- COC/COP Vial

**Smart Factory**
(Tech. + Auto. + Data)

**Drug Manufacturing Science**

- API
- Synthesis
- Drying Syst.
- Fermentation
- Herbal
- Solution Prep.
- Filling Syst.
- (Vial/Ampoule/BFS/PFS)
- Freeze Drying
- Barrier Syst.
- Freeze & Thaw
- Inactivation
- Cell Processing Station
- Cryopreservation Syst.
- CES/SUB/SSB
- Purification & Filtration
- Bio-solution Prep.
- Drying Syst.
- Fermentation
- Herbal
- Solution Prep.
- Filling Syst.
- (Vial/Ampoule/BFS/PFS)
- Freeze Drying
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- Freeze & Thaw
- Inactivation
- Cell Processing Station
- Cryopreservation Syst.
Experts in Biopharmaceutical Company

- **30 Years Expertise**
- **USD 600 Million** Revenue (FY 2021)
- **50 Countries & Regions Installations**
- **Since 1993**
- **600+**
- **6000 Employees**
- **2,800+**
- **50 Countries & Regions Installations**
- **Serving over 2800 pharmaceutical companies worldwide**
- **6 Global JV and Tech Partners**
  - Kyowac (Japan)
  - Top (Japan)
  - Airex (Japan)
  - Omca (Italy)
  - Itema (Italy)
  - Praxair (USA)

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DS-Hybrid

Cell vial → Incubation → seed → Production → Depth Filtration → Chrome → Inactivation → UF/DF → Bulk Freeze

Cell bank, CO2 incubators, Wave Bioreactor, SUB, Depth Filtration skid, Column: Manual & Autopack & Chrome skid, SU Mixer system, TFF system, Freeze & Thaw system & Quick freezers
DS-SS

- Cell vial
- Incubation
- Seed
- Production
- Depth Filtration
- Chrome
- Inactivation
- UF/DF
- Bulk Freeze

Cell bank
CO2 incubators
Glass Bioreactor
SS Bioreactor / Fermenter
Depth Filtration skid
Column: Manual & Autopack & chrome Skid
Vessel system
TFF system
Freeze & Thaw system & Quick freezers
Advanced Injectables

Compounding  Filling  Lyophilization  Inspection & Detection  Secondary Packaging
1. Steel frame transformed to Module Manufacturing Workshop for pre-assembly, floor & part of the wall installed simultaneously
2. Main duct, firewater piping installation.
3. Piping, cable tray installation
4. Roof installation (onsite installation space to be reserved)
5. HVAC room (2nd floor) installation (in sync with 1st floor)
6. Before Factory Acceptance Test, key equipment will be pre-assembled, pre-engineered, pre-qualified in the modules.
7. Each module will be shipped by trucks after disassembling
Single use Fixed bed Bioreactor

Application
- Vaccine production MRC5 cell lines,
- Cell & Gene therapy
- Adeno-associated virus (AAV)
- Lentivirus (LV)
- Adenovirus (Adeno),
- Oncolytic virus (oncolytic)
Large scale integrated SS project

Industry Challenges:
- Complicated process with many docking units and control strategy
- Higher Utility costing
- Integrated complex piping
- Flexibility
Large Scale Vaccine Manufacturing

Industry Challenges:
- Complicated process with many docking units and control strategy
- Higher Utility costing
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- Flexibility
Approach 1 – Optimized TCU system

Contributes significantly reduction in operation cost
## Approach 1 – Optimized TCU system

<table>
<thead>
<tr>
<th>Jacket type</th>
<th>Total jacket water volume</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Dimple</td>
<td>1,706L</td>
<td>Totally 43 sets of process vessels from 300L to 7,000L</td>
</tr>
<tr>
<td>Half coil</td>
<td>4,265L</td>
<td></td>
</tr>
<tr>
<td>Guide plate</td>
<td>8,530L</td>
<td></td>
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Centralize TCU system ensures minimal water waste

- Volume calculation
- Temperature range
- Loop pressure and flow rate
Approach 2 – Optimization of Clean Room

Black area: CNC room  C Grade

Reduce clean room area more than 30%
Approach 2 – Optimization of Clean Room

Reduce clean room area more than 30%
Approach 3 – Modular Design and Installation

Modular Design → Modular Manufacturing → Modular Installation
Approach 3 – Modular Design and Installation

Moveable vessel
- Jacketed vessel with insulation
- Vent filter
- Magnetic agitator
- Flush bottom valve
- Load cell
- TT/PT/CT/PH
- Sampling valve

Function skid
- Temperature control through jacket
- Sterilization for vessel
- Utilities docking
- Drain line connection
- Control cabinet

CIP skid
- Circulation pump
- Air filter
- Alkali/Acid dosing
- Conductivity meter
- Sampling
- Control box

Filtration skid
- Filtration for liquid
- CIP/SIP is available (need to connect with CIP skid and vessel)
- Control box
Thank You For Your Kind Attention