Ensuring Supply Chain Security and Continuity in Global Vaccine Manufacturing

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CONTENTS

Vaccines Overview

- Vaccines are the most powerful way to protect billions of people worldwide and have transformed public health. The WHO estimates that 2–3 million lives are saved each year by current immunization programs.
- A vaccine is a biological product that can be used to safely induce an immune response that confers protection against infection and/or disease on subsequent exposure to a pathogen.
- Vaccines can be classified as live-attenuated vaccines, or non-live vaccines, also, whole-organism vaccines, subunit vaccines, and nucleic acid vaccines.
- The global vaccines market is projected to grow from $61.04 billion in 2021 to $125.49 billion in 2028 at a CAGR of 10.8%.
- North America is the dominant in the global vaccine market, while Asia-pacific is the fastest growing region.

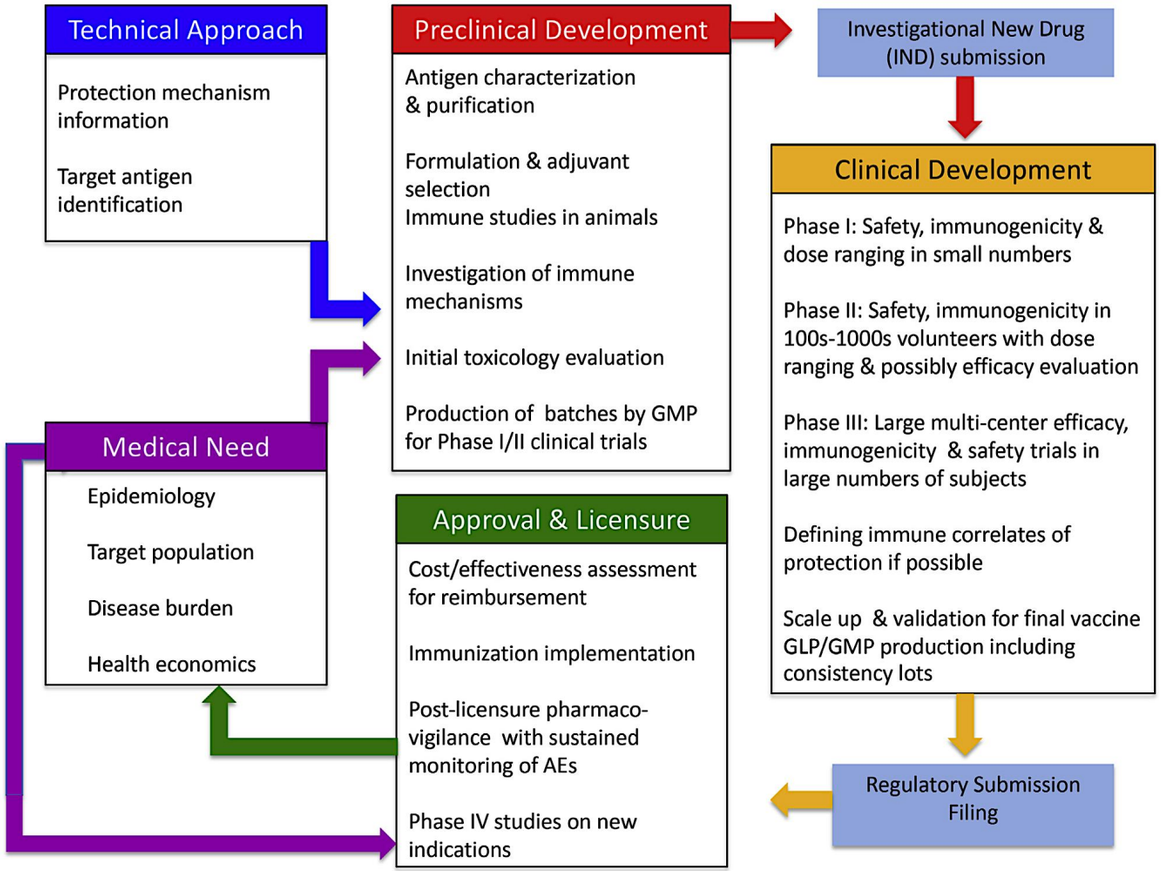
- A guide to vaccinology: from basic principle to new developments. Nature reviews, Imunology, Vol 21, Feb2021, 83-98
- Vaccine manufacturing: challenges and solutions. Nature Biotechnology, 24, 1377-1383 (2006)
- Fortunebusinessinsight.com
- WHO global vaccine market report, 2022, a shared understanding for equitable access to vaccine

Type of vaccine	Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)	Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism	Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid	Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)	Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle	Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle	Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate	*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored	Ebola	2019 (Ebola)
Nucleic acid vaccine	SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored	Experimental	–
Antigen-presenting cell	Experimental	–

Vaccine Development

A typical process that FDA expects vaccine developers to follow:

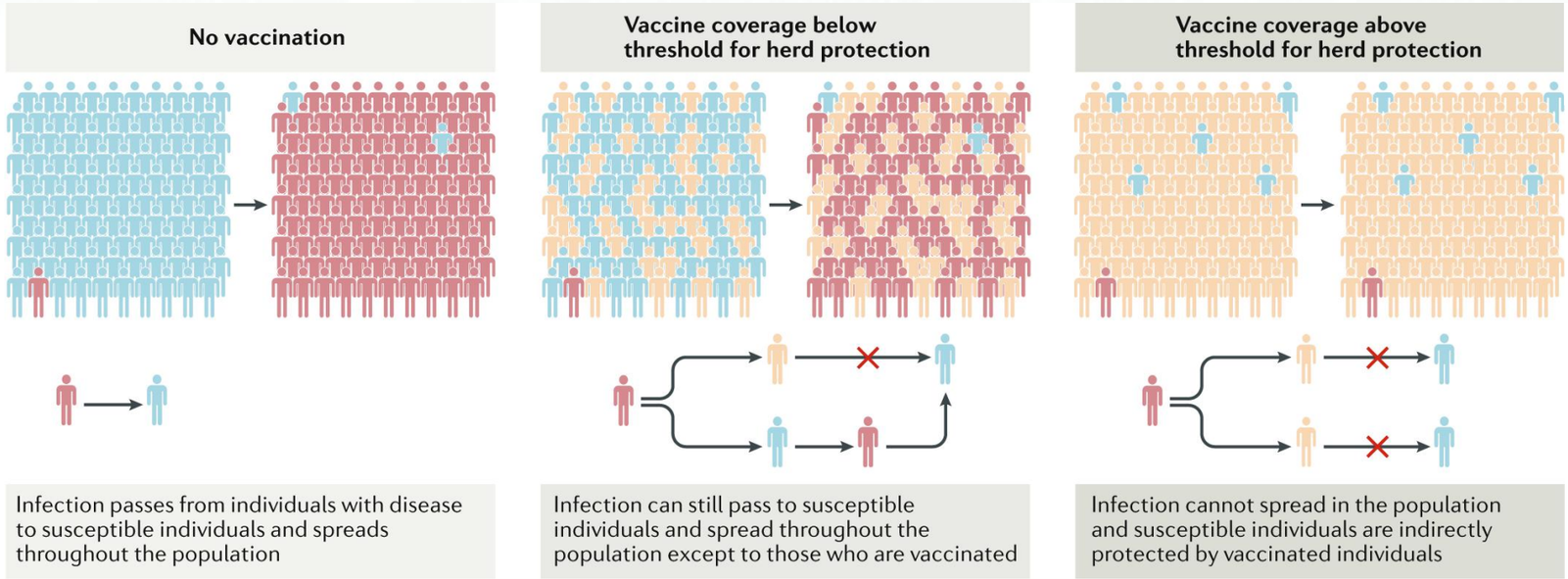
R&D → Pre-clinical → Phase I → Phase II → Phase III → BLA Submission → Phase IV



- Traditionally, the preclinical, clinical and post-licensure phases can take a long time (10-30 years).
- New type of vaccines and technologies can speed up the development and improve safety, tolerability, and potency.
- Covid-19 vaccine proved that when stakeholders make a concerted efforts, "a vaccine development process that takes an average of 10 years and has never taken less than 4 years was compressed to 11 months" .
- Vaccination is only one component of disease prevention, it also requires the medical infrastructure, public education, for successful implementation.
- The challenge is coordinating the diverse agendas

- Vaccine development, FDA website.
- Key steps in vaccine development, Ann Allergy Asthma Immunol, 2020, Jul, 125(1), 17-27
- WHO global vaccine market report, 2022, a shared understanding for equitable access to vaccine

Herd Immunity

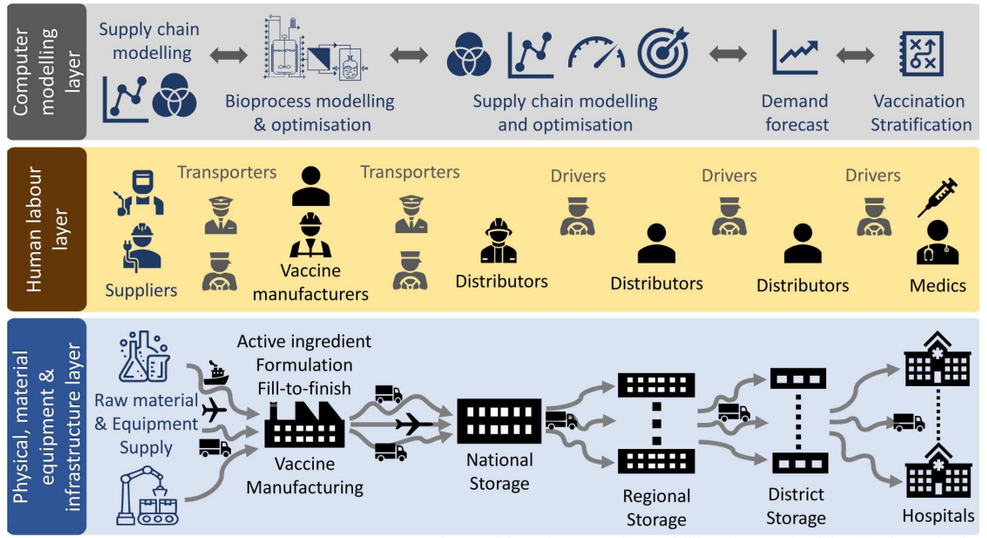


"Herd immunity" or "herd protection"

If enough individuals are vaccinated, and if vaccination prevents not only the development of disease but also infection itself, transmission of the pathogen can be interrupted and the incidence of disease can fall further than would be expected, as a result of the indirect protection of individual who would otherwise be susceptible.

A guide to vaccinology: from basic principle to new developments. Nature reviews, Imunology, Vol 21, Feb2021, 83-98

- To reach the population-scale effects, a key goal is to provide protection as widely as possible to have sufficient coverage in all countries at risk, this can only be achieved by global cooperation.
- Mass production of vaccine can be a daunting task, it requires the vaccine manufacturers to achieve large-scale production at rapid pace. Scale-up and supply chain strategies have to be established from earlier phases.
- To accelerate vaccine production, it is essential to collaborate with multiple supply partners and testing



Is the world ready to produce a billion doses of a COVID-19 vaccine?

Manufacturing and Materials

21CFR 210 & 211:
Component of the quality System

- Vaccines have to be manufactured according to the relevant cGMP guidelines.
- Scaling up and expanding manufacturing capacity by adding sites all need to have secure access to enough GMP materials.
- Typically, more than 200 individual materials are required for production of a vaccine. Many of the materials are often produced in different counties and need global

Materials → Process → Product

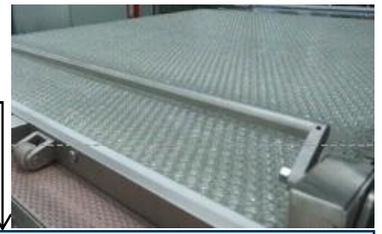
- Once the materials are chosen and defined in BOM, it cannot be easily changed – change control and QRM.
- Large amount of supporting data is provided by different suppliers - supplier selection and qualification are critical.
- Materials are also important for manufacturing cost and timeline planning – Tech. Transfer.

Vaccines must be manufactured at huge scale to make inroads into global populations

- Manufacturing, safety, and quality control of vaccines. WHO vaccines explained series.
- Vaccine production, navigating scale-up challenges, biopharma technology networks, 2021.

Incoming Materials

Incoming Materials



Raw Materials

- Solid, liquid, gas
- Active ingredients
- Inactive ingredients
- Excipients
- Processing aids

Consumable Materials

- Product contact
- Non-Product contac
- Plastics
- Metals, Chemicals
- Single-use vs. Multiple use

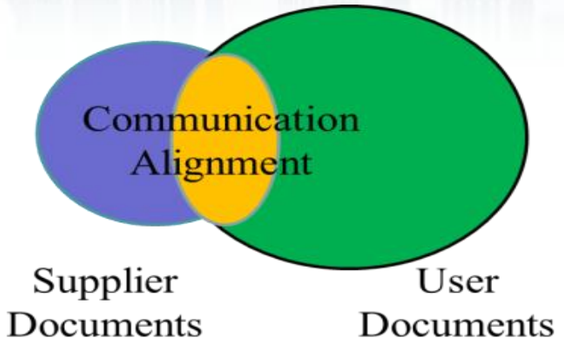
Packaging Materials

- Vials and seals
- Syringes
- Ampules, Cartridges
- Auto-injectors
- 2nd Packaging and Outer

- Incoming materials are critical components of all vaccine manufacturing processes.
- Quality of incoming materials need to be tightly controlled and monitored to ensure drug product quality, efficacy and safety. Insufficient material control can lead to inconsistent performance, interruption/delay to production, and loss of expensive vaccine products.
- "even one component falls short, the production of vaccine can be delayed". Materials need to be delivered on time, with full compliance and consistency:

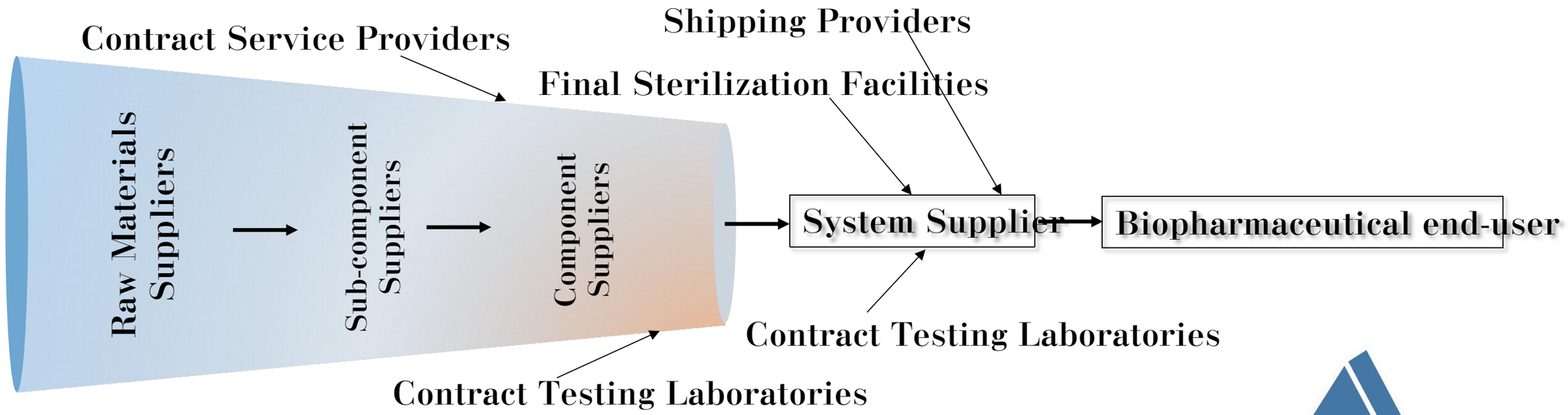
Materials Selection

- A thorough understanding of material properties and manufacturing requirements is the key to making confident and successful material choices.
- It is also critical for vaccine producer end-users to work closely with suppliers to align the requirements and share responsibilities.
- Build the materials database from start, share data and experience.

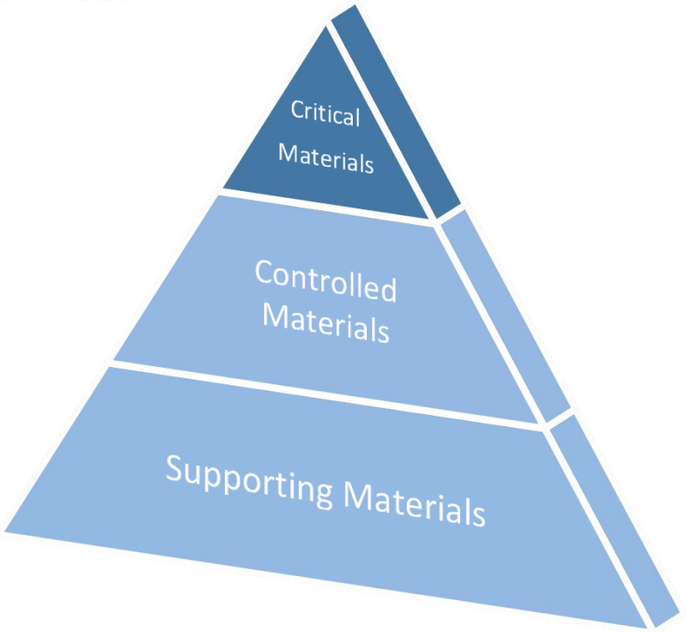


Physicochemical Properties	Safety and Quality	Application Considerations
• Physical properties (e.g. solubility, viscosity) • Chemical Compatibility • Mechanical Properties • Thermal Properties • Surface Characteristics (e.g., fluid interaction) • Barrier Properties • Optical Properties	• Biocompatibility • Bioburden • Endotoxin • Particulates • ADCF or TSE/BSE Risk Analysis • Extractables and Leachables • Lot-to-lot consistency • Certificates (COC, COA, COP, etc.)	• Design Complexity • Available Packaging Size, Scalability • Facility and Machine Compatibility • Cost, Lead Time • User Experience • Customer Service • Supplier Data Package • Validation Studies

Supply Chain Security



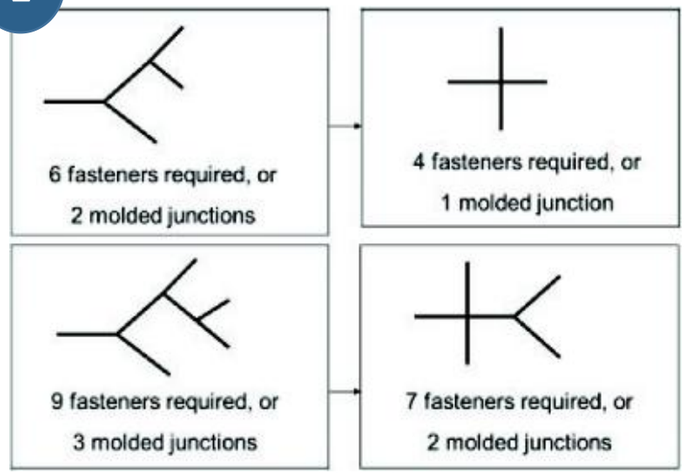
- Vaccine manufacturers needs to ensure supply security to guarantee production continuity and avoid vaccine shortage.
- Suppliers also have complex supply chains.
- Any time the end-users add on products or components can increase the supply chain complexity, also increase the risks of supplier initiated changes.
- Effective supply chain management include supply chain simplification and maximize the data sharing and leverage among different products and facilities.



Standardization Consideration

- **Simplify supply chain**: build and maintain database, avoid duplications, and reduce risks.
- Build and maintain a collection of parts and assemblies that can be used in different products and processes. "Design once, but use many times" – Standardization.

1 Design consideration



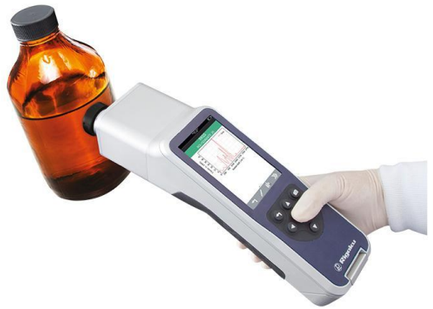
Source: Design and Deployment Strategy for SUS

2 Component selection

Sterile Connectors

New technologies

3



FDA guidance for industry: PAT – a framework for innovative pharmaceutical development, manufacturing and quality assurance

4

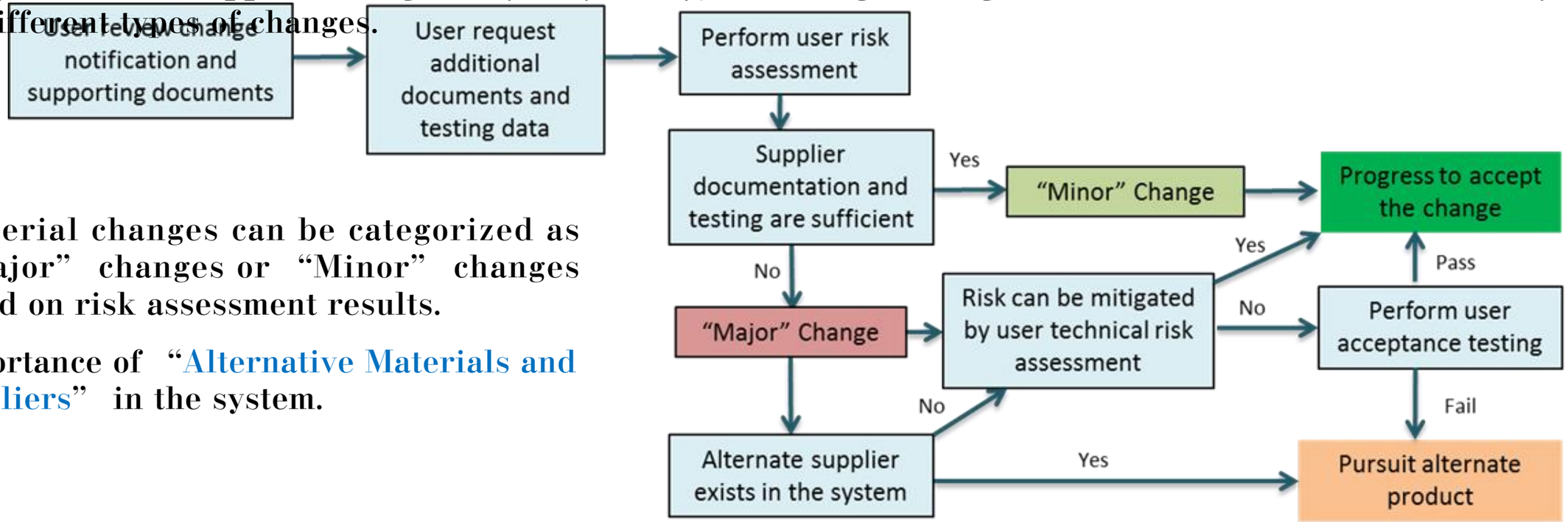
Process, Equipment and twin facilities

- Standardization on designs, materials, technologies, systems, and facilities to leverage data and save time

- Benefits of single-use standardization: adopting a standard design approach. BPI, May 2021

Supplier Initiated Changes

- Many biopharmaceutical end-users have experienced large amount of change notifications. Especially from "Localization" efforts.
- BPOG / BPSA has generated "An Industry Proposal for Change Notification Practices for Single-Use Biomanufacturing Systems" and "Best Practices for Raw Material Supplier Change Notifications" to guide the topic.
- It is typically difficult to deal with supplier changes, especially with multiple companies and multiple groups involved. Supplier changes may vary vastly, and change management should be handled differently for different types of changes.



- Material changes can be categorized as "Major" changes or "Minor" changes based on risk assessment results.
- Importance of "Alternative Materials and Suppliers" in the system.

Data Management

- Data Integrity Challenges: Many sources of data and large amount of data
- Ensure supplier data integrity: supplier qualification and audit

External Data

Sub-supplier Data

Contract Testing Lab Data

Material/Equipment Supplier Data

Published Research Data

Data Collection, Processing, Analysis

Data Reports

Quality and Regulatory Decisions

Direct Manufacturing Operation and/or Continuous Improvement

Internal Data

R&D Lab Data

PD Lab Data

MS&T Lab Data

Manufacturing

In- or/and at-line Data

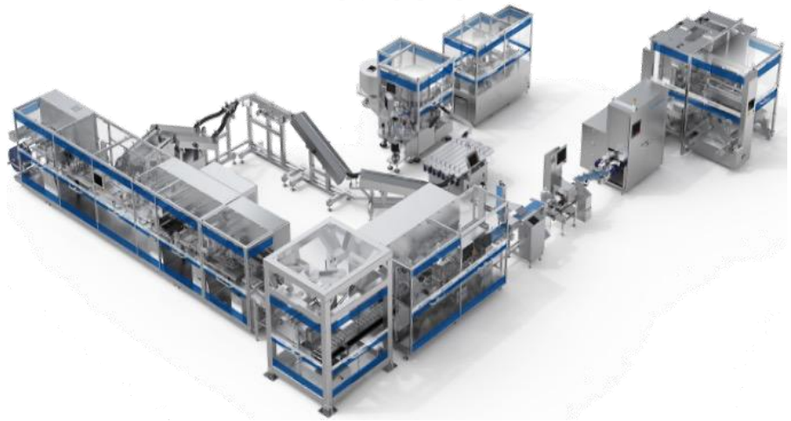
On-Line Data

QC Lab

Off-Line Data

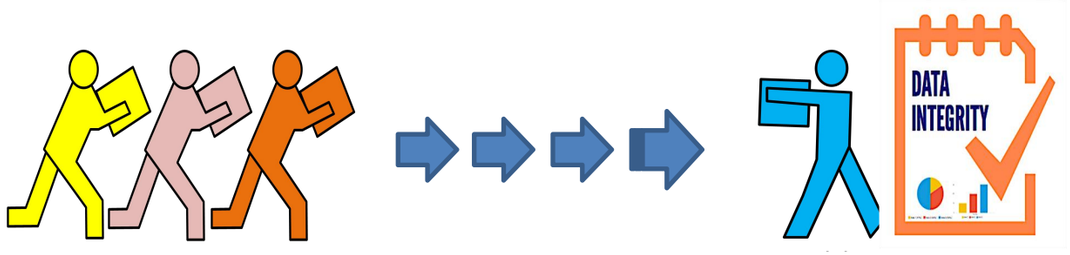
LIMS Data

Contract Testing Laboratories / Service Providers



Supplier Management

- Biopharmaceutical end-users and suppliers relationship is extremely important, it needs to be a long-term formal partnership, not stopping at purchase orders.
- Suppliers can be classified into different groups based on strategic importance, performance evaluation, and supplier qualification results. Supplier classification is the basis for the company's supplier portfolio development and QRM.



Manufacturing needed Equipment, Instrument, Materials

Supporting Data Packages

Post-sale Maintenance and Services

Troubleshooting and Investigation Support

Industrial Information and Experience Sharing

New Technologies for Continuous Improving

Supplier Life-Cycle Management (SLM)

1. Identification
2. Qualification & Selection
3. On-boarding
4. Performance Monitoring
5. Risks, Changes, & Relationship Management

- SLM is based on value, risk, and performance. Choosing the best suppliers and then managing them in a joined-up, integrated and consistent manner.

- Supplier lifecycle management: reduce risk, improve performance, and drive supplier value.

Truking Integrated Bio-engineering BU

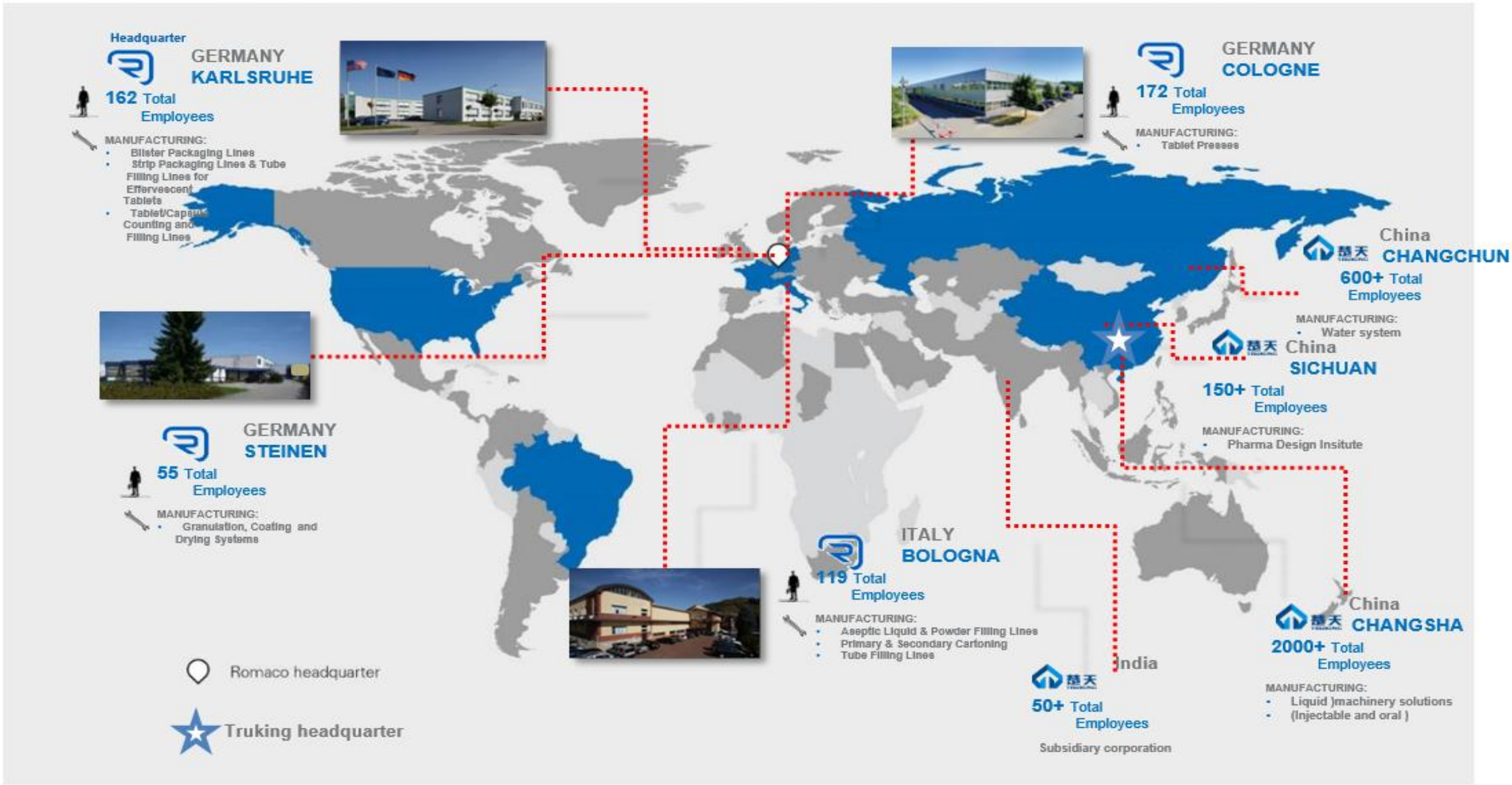
THE R&D

- The central R&D is in Changsha with1700 engineers & scientists,
- Europe, Italy Product Development center & R&D with 300 engineers & scientists,
- Suzhou R&D with 300 engineers & scientists
- As of August 31, 2022, a total of 4342 Chinese patent applications (1028 invention patent applications, 2876 utility model patents, 438 design patents) have been filed,
- There are 2684 valid patents (468 invention patents, 1983 utility model patents, and 233 design patents)
- Another 40 PCT international patent applications were filed and 20 patent authorizations were obtained in the United States, Russia, India, South Korea, Germany, Indonesia, Europe, and other countries.





Global Factories & PD UNITS



Integrated Solutions & Equipment System List

TRUKING


Automatic Inline Conditioning Chromatography System

Slurry Tank

Truking Media


Bioreactor


Wave


Depth filtration System


Tangential Flow

Single - use bag


Automatic Chromatography Column

Buffer Preparation

Column Packing

Cell Culture/Fermentation

Clarification

Capture


Prodution Chromatography System

pH adjustment virus inactivation

Polish

VF

UF/DF


Prodution Ultrafiltration System


Virus filtration

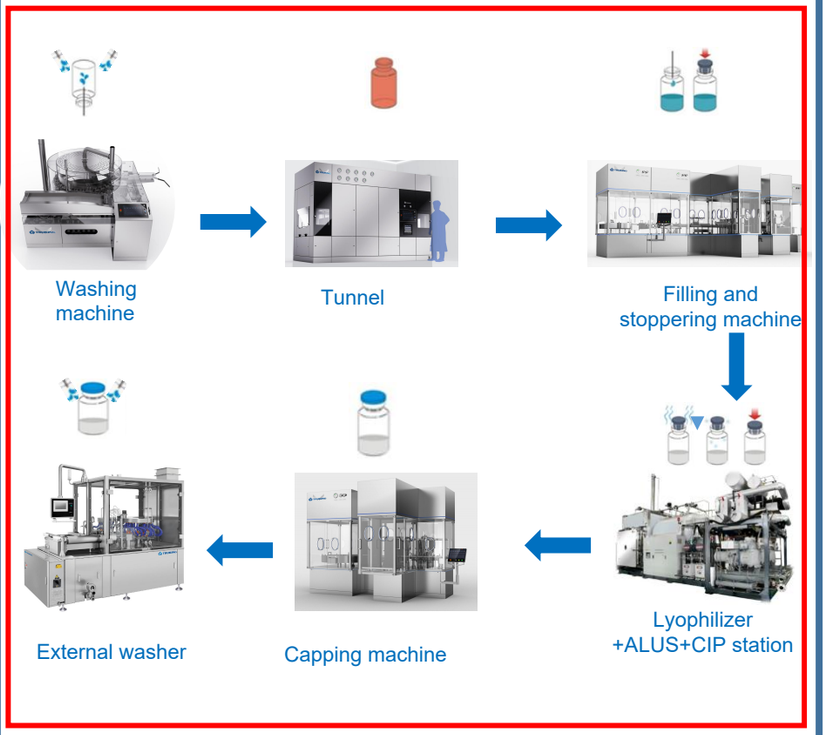

Easy Chromatography Column

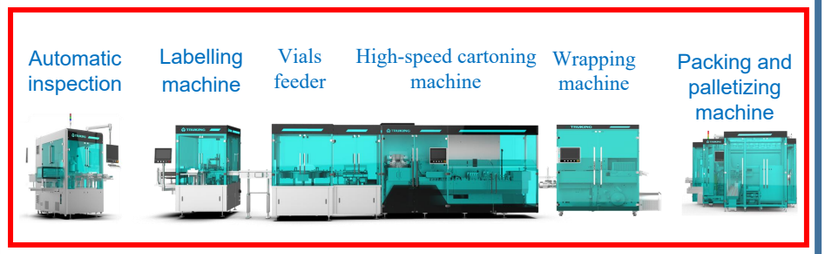

Prodution Chromatography System


Reservoirtank


Magnetic stirring

Drug Substance





Drug Product

Solution Key Part: USP

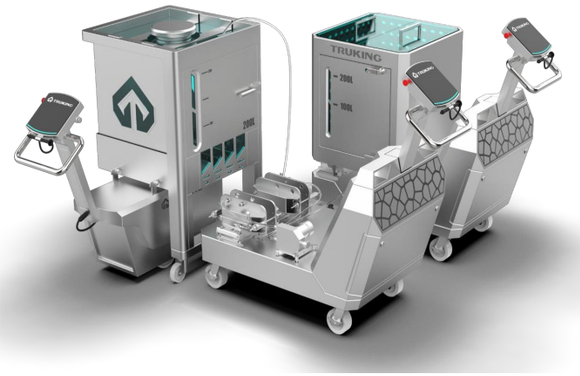
SU Wave Bioreactor

- Wave bioreactor with adaptive bag provisions
- Adaptive top tray for two-bag installation with full operational control

SS Bioreactor

- **SS best in class design and fully customizable as per process needs**
- **Software user-friendly with a common interface for hazel-free operations**

DF Clarification

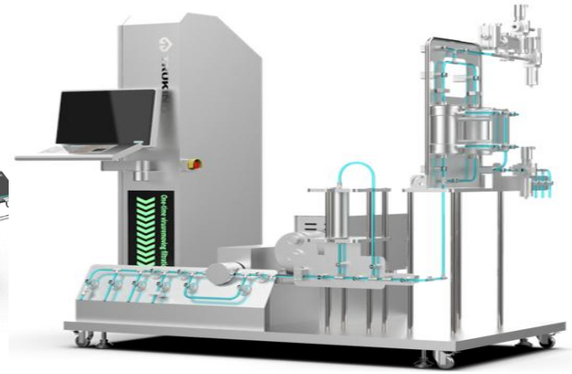


- Process automation with all available DF consumables
- CIP automation and SS-SU integrated products as per process demands

SU Bioreactor

- SU bioreactor with adaptive bag provisions and can retrofit to customers' present SU setup Cylindrical or Square designs

Solution Key Part: DSP



SS & SU Chromatography System / Columns

- Patented combined hybrid technology of Pack-in-place
- Axial compression packing for any resin
  Four points attachment with two-pillar top adapter movement is more reliable
  Lowest maintenance time and space requirements with NO-SWING OUT mechanisms

Multi-column continuous chromatography system

- Adaptive and dynamic control of titer concentration in perfusion-fed batch Mab platform technology
- Effective utilization of Protein A resin dynamic binding capacity without fear of losing molecules

Ultrafiltration & Diafiltration SU and SS

- Multi-cassette compatible holder
- Single Use cassette operational compatibility
- Most compact designs to avoid facility revalidation

Virus removal filtration system

- Match with different virus removal filters and filtration systems
- Single-use flow path
- Single-use sensors (all market leaders)
- Automatic operation, data management, computerization

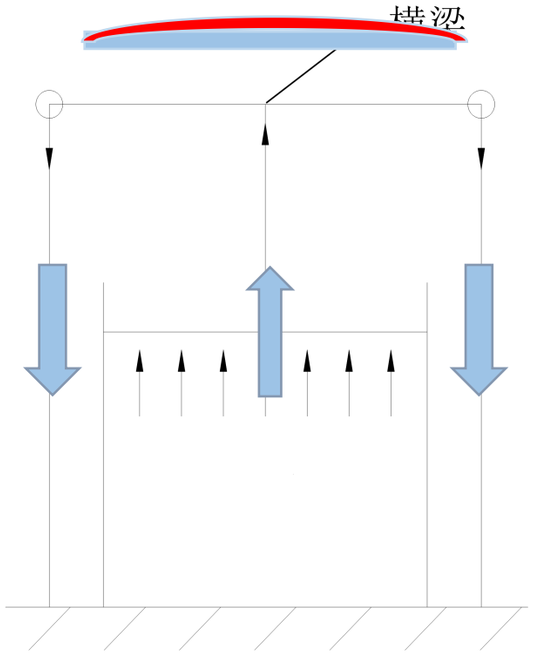
Patented mechanical structure design

Truking Structure

- Truking Ingenuity **Fully-Automatic** Chromatography Column

The triangular mechanical structure strengthens the overall strength of the equipment and makes the equipment simple, lightweight, and safer.

Traditional Structure



Patented Column Disassembly Structure

Truking

Truking's Patented Column Disassembly Structure Adopts the hoisting method, which occupies a small area, saves space, and is convenient for transportation. It only takes 15 minutes to disassemble.

The hook design is cumbersome to operate. The entire operation is time-consuming

Others

Auto Packing Station System

- Adaptive to column sizes from 300mm to 2000mm
- Automatic guided operation mode: instructions for column packing, unpacking, cleaning, and disassembly.
- Integrated with two Tapflo flow pumps without damaging resins slurry

Product model	APS050	APS100	APS200
Maximum flow (L/min)	50	100	200
Main piping size	DN20(3/4")	DN25(1")	DN40(1.5")
Protection class	IP54		
Wetted material	316L、PP、EPDM		
Operating Temperature Range	2~40°C		
Operating pressure max.	6 bar		
Adaptive Column	300/400/450/600	450/600/800/1000/1200	1200/1400/1600/1800/2000
Dimensions (L× W × H)	650×560×1130 mm	650×560×1130 mm	1100×740×1130 mm
Weight (kg)	145	185	265

Truking SUT Plants

Plant in Changsha

- Changsha plant: 6000 m^2, including a C+A production environment specially designed for highly clean applications, sate of art facility will further expand in the National Science and Technology Industrial Park
- Quality management system meets multi-national regulations including cGMP, ICH, USP, EMA, ISO, etc. Comprehensive validation packages according to industrial guidance and best practices, including PDA, BPOG, BPSA, etc.

Global Quality Standards






- Final products meet ISO， USP，E.P. requirements, industry guidelines and best practices (e.g., BPOG， BPSA， PDA，etc.)
- Materials management and manufacturing follow cGMP requirements. For example, biocompatibilities testing includes：
  - Gamma sterilization validation
  - Extractables/leachable studies
  - Particulate control
- Strictly testing and controlling materials to meet bioprocess application requirements, including physical, mechanical, and surface properties, chemical compatibility, barrier properties, optical properties, shelf life, etc.
- High-quality management system to ensure batch-to-batch consistency of raw materials and final products

Truking Supports

1 Technical Support

- Automation systems, hardware manufacturing, product design, simulation modeling, and analytical techniques. turnkey project, Tech transfer assessments

2 Financial Support

- Investment from cooperate to enable SUT development, from daily routine operation to facility expansion.

3 Manufacturing Capabilities

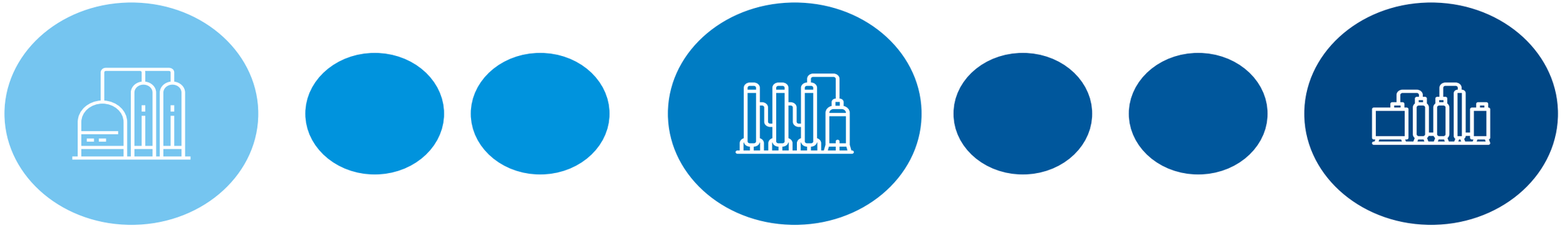
- Strong equipment manufacturing capabilities with large MFG capacities, can help SUT with stainless vessels and molds for various applications.
- Customized solution as per client requirement

4 Development Platforms

- TK AI, automation and marketing platforms can help develop unique world-leading automatic and semi-automated solutions for single-use & Multi-Use products.

Extended Support

TRUKING



Customer-centered, highly flexible manufacturing to ensure internal and external supply and demand balance

High-quality products based on user requirements, ensure data integrity and traceability throughout the entire production process

Assist users to assess the risks of single-use products, provide complete technical and application data packages

Provide customize, Affordable, High-Quality SU & SS Products for Biopharmaceutical Users

Plants are designed to meet FDA, EMA and NMPA standards, products range from DS to DP manufacturing

The facilities will undergo regular, comprehensive annual audits to meet the appropriate cGMP and ISO quality standards

Management team has extensive experience in both multi-national biopharma and SUS companies.

TRUKING

TRUKING

THANK YOU!

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