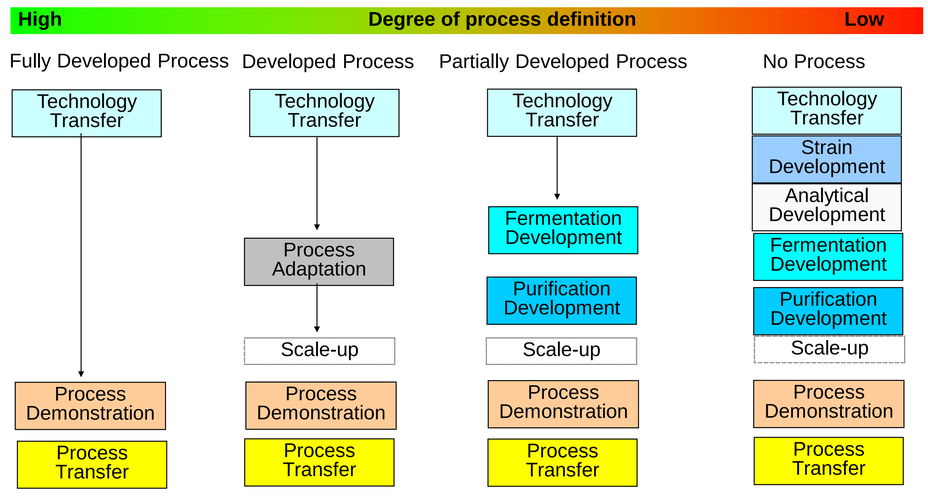
Ultra-Large-Scale Biomanufacturing Empowered by Efficient Technology Transfer and PanFlex® System

Chi-Ming Yu, W. Roy Lin, Peng Jiao
Boston Institute of Biotechnology LLC, 225 Turnpike Rd, Southborough, MA 01772

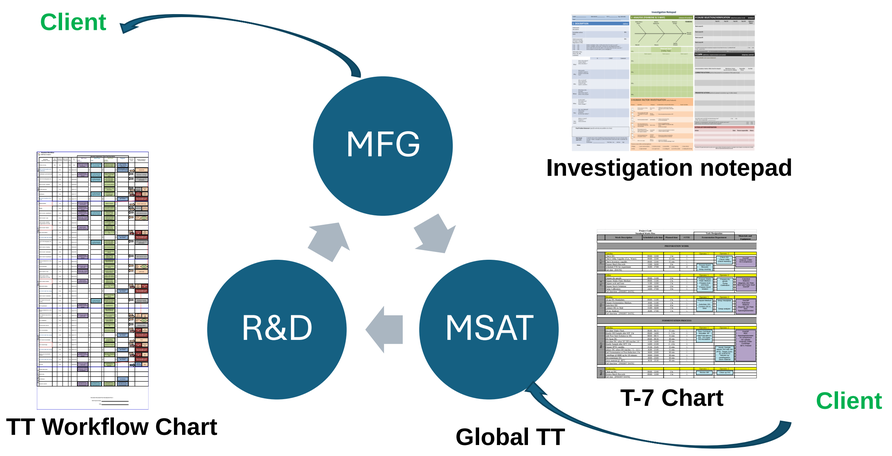
Abstract

Challenges on time and cost effective biologic manufacturing persist within biomanufacturing despite collaborative efforts by industry, academia, and government. Driven by biologics technological innovation and socio-economic development, Biologics manufacturing has undergone three waves of evolvement since the 1980's, which differentiate themselves by their technology platform, facility capacity scale, and mode of production. With increasing global market and demand for protein-based drugs, the capacity shortages in biologics manufacturing have become prominent, and large-scale commercial production through external CDMOs is progressively becoming an industry trend (aka the 4th wave of biologics manufacturing). BIB, a global CDMO featuring 30,000-liter ultra-large bioreactor production platform, is uniquely prepared to transform the biologics manufacturing market. Empowered by its unique flexible integrated PanFlex® system including facility/equipment design and technology transfer, we are currently building the next generation Mega-factory with a total planned capacity of over 1.2 million liters at half-time and half-cost. Leading the 4th wave of ultra-large 30,000L scale biomanufacturing, BIB will shape the future of biologics manufacturing for the benefit of patients worldwide.

Technology Transfer (TT) Strategies



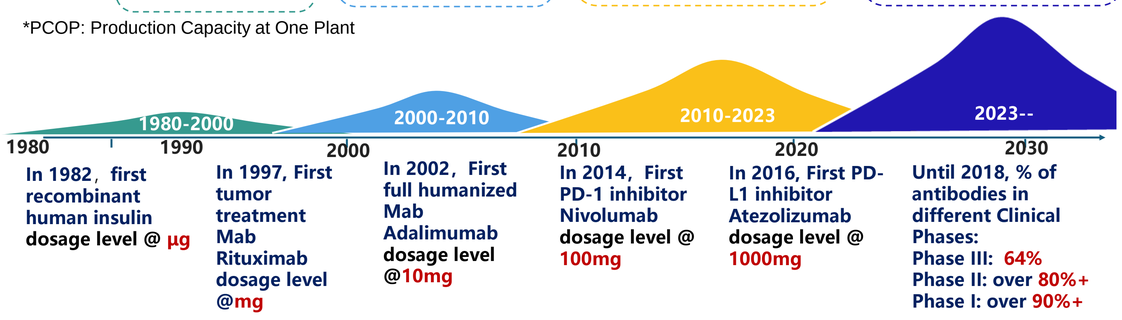
An Integrated TT System



The Revolutionary 4th Wave of Biologics Manufacturing is Coming

	1st wave (1980-2000)	2nd wave (2000-2010)	3rd wave (2010-2023)	4th wave (2023-)
Production Scale	Hundred Liter production line	Kiloliter scale production line	Large-scale (15KL) production line	Ultra-large Scale (30KL) production line
PCOP* Scale	Fragmented market, PCOP scale <10kL	Emergence of PCOP scale of 100kL+	PCOP starts to concentrate up to 500KL	PCOP scale is over 1 million Liters: Mega factory
Operations	Biopharma dominates	CDMO>10%	CDMO>20%	CDMO as the operation model
Products & Technology	Cytokine-based drugs, demand of target products below kg level	Antibody drugs emerge, demand of target products @ 100 kg level	Antibody drugs soar, demand of target products @ tons level	Antibody drugs prevail, demand of target products @ larger tons level

*PCOP: Production Capacity at One Plant



Accelerated TT and MFG Support

- ❑ Synergy between R&D and MFG with harmonized planning and operating practices
  - ➢ Common OE and PM tools
  - ➢ Harmonized R&D protocols and MFG batch records
- ❑ Scale-up/down approaches:
  - ➢ Comparable k_La (oxygen transfer capability) or P/V (power input per volume) at different scales
  - ➢ Client specified (e.g., similar OUR profile)
- ❑ Tech Transfer - R&D to Manufacture
  - ➢ R&D bench and pilot-scale demo, followed by MFG Engineering / GMP run
- ❑ Manufacture Troubleshooting
  - ➢ Scale-down model (SDM)

Ultra-Large GMP Capabilities is The Trend

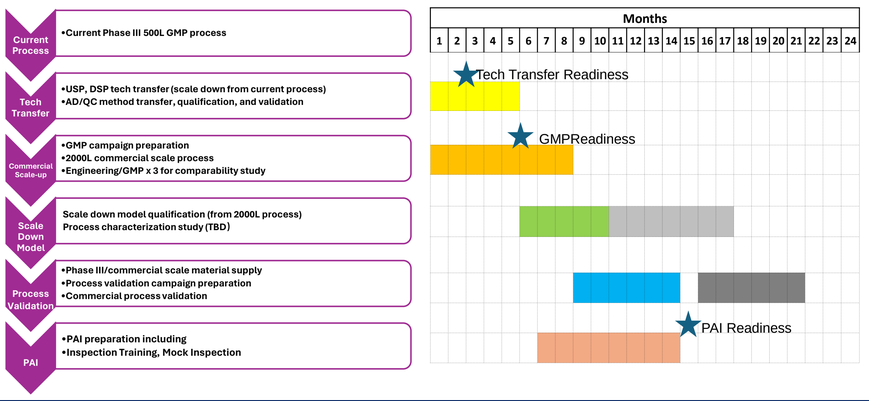
BIB's GMP drug substance capacities:

Application	50L	200L	500L	2,000L	10,000L	30,000L
Microbial	●	●	●	●	●	●
Mammalian		●	●	●	●	●
Gene Therapy		●	●	●		
pDNA	●	●	●	●		

BIB's GMP drug product capacities:

Application	Capacity
Lyophilized Products	30 m^2
Liquid Vials	24,000 per hour
Pre-Filled Syringes	10,000 per hour

Accelerated Timeline



Conclusion

- ❑ The revolutionary 4th wave of ultra-large-scale manufacturing is coming
- ❑ The ultra-large 30,000L scale biologics manufacturing is the trend
- ❑ Effective technology transfer (TT) from client to CDMO is crucial to ensure successful ultra-large-scale production
  - ➢ Flexible TT strategies
  - ➢ Integrated TT system
  - ➢ Accelerated TT and manufacturing support
  - ➢ Accelerated timeline
- ❑ This strategy has been successfully applied to several client projects

PEGS Boston, 13-17 May 2024