Flexibility in a Biotech Manufacturing Facility: An Options Analysis for Monoclonal Antibody Production

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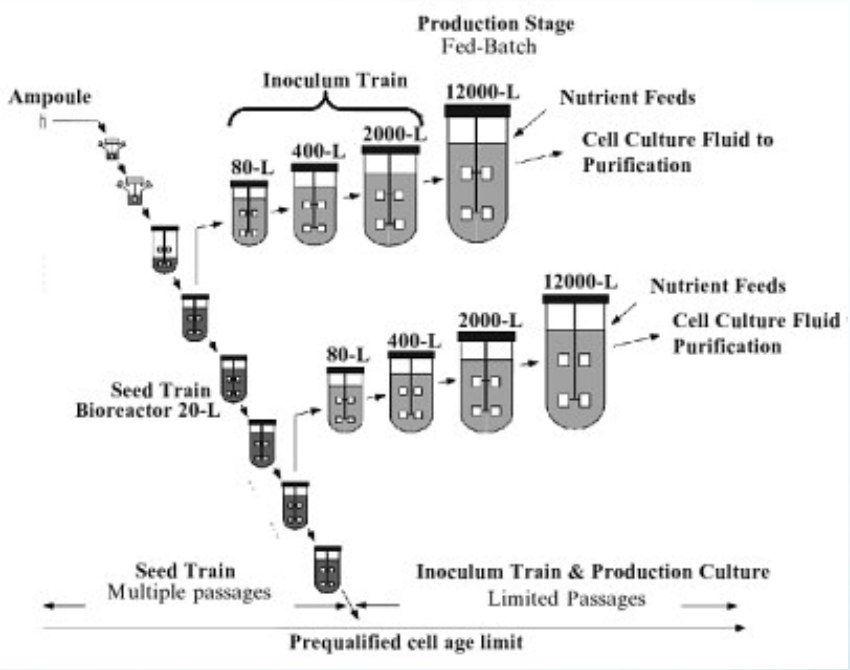
Agenda

- Overview of Biotech Manufacturing
- Demand Uncertainty
- System Designs Analyzed
- Simulation Setup & Results
- Sensitivity Analysis
- Discussion

(1)

Biotech Manufacturing

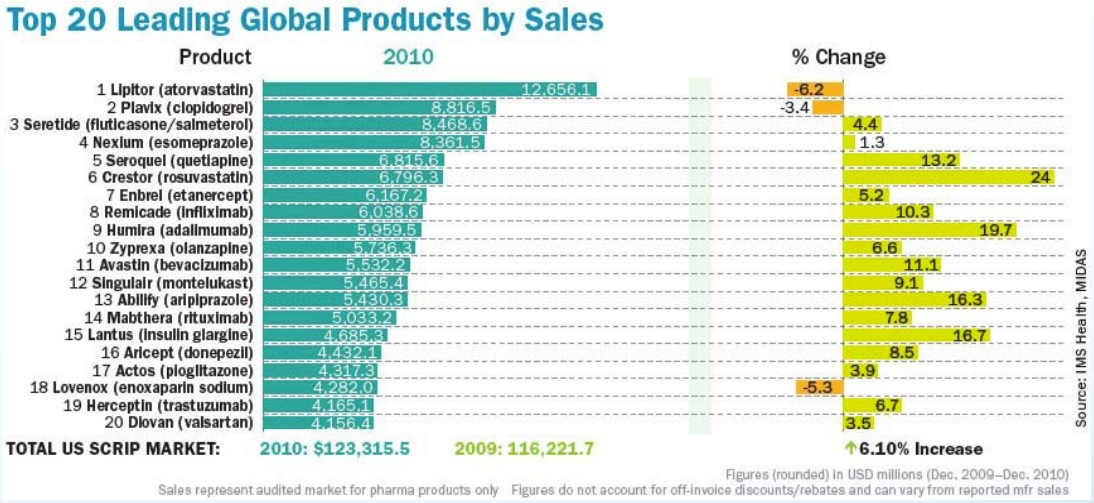
- Industry started in mid-1970s ("buckets and hoses")
- Vast improvements with maturity
  - Higher Yields
  - More Automation
- Upstream Versus Downstream Unit Operations
  - Design Lever: additional bioreactor trains



(2)

Product Demand Uncertainty

- "Nishumab" – based on Avastin (Genentech)
- Factors affecting sales
  - Competition
  - Regulation
  - Patent Protection
- First 10 years
  - Mean = 6.5%
  - S.D. = 5%
- Last 10 years
  - Mean = 2%
  - S.D. = 2%



(3)

Designs Applied

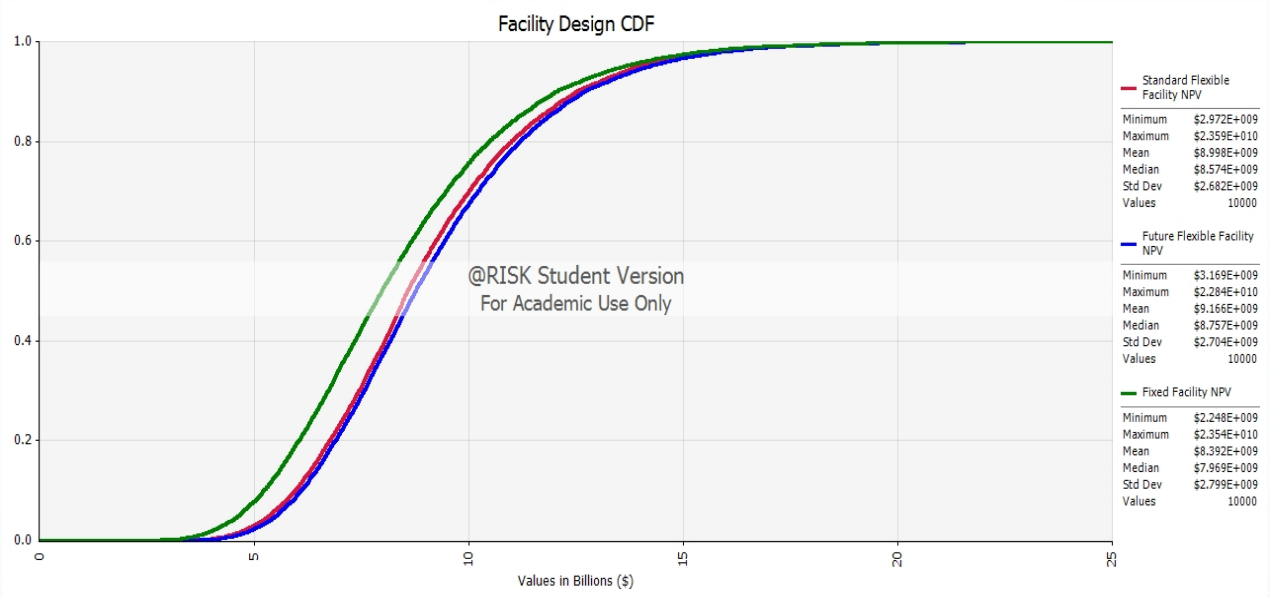
1. Fixed Design
   - 6 stainless-steel bioreactor trains, 15,000L final size (90,000L total capacity)
2. Standard Flexible Design
   - 2 stainless-steel bioreactor trains initially built, 15,000L final size (30,000L total capacity)
   - Expand by 1 bioreactor (15,000L)
3. Future Flexible Design
   - 15 single-use disposable bioreactor trains, 2,000L final size (30,000L total capacity)
   - Expand by 5 additional trains (2,000L x 5 = 10,000L total capacity)

Simulation Setup

- Monte Carlo Simulations using @Risk
- Cost Models for All Three Designs
- Decision Rule for Simulation Analysis
  - Decision Factor = 80%
- Sensitivity Analysis
  - Decision Factor Range: 50% - 150%

		Fixed Facility	Standard Flexible Facility	Future Flexible Facility
Time Horizon	years	20	20	20
Discount Rate	%	10%	10%	10%
Initial Demand	g	1,000,000	1,000,000	1,000,000
Revenue	$/g	2,000	2,000	2,000
Capital Investment				
Initial	$	500,000,000	300,000,000	200,000,000
Additional	$/train	-	75,000,000	5,000,000
Operating Costs				
Depreciation (initial)	$	25,000,000	15,000,000	10,000,000
Raw Materials	$/g	10	10	20
Labor	$/person	150,000	150,000	150,000
Maintenance & Projects	$	5,000,000	7,500,000	300,000
Formulation/Fill/Finish/ Packaging & Distribution	$/g	80.00	80.00	80.00
Inventory	$/g	100.00	100.00	100.00
SG&A Expenses	% revenue	30%	30%	30%
R&D Expenses	% revenue	20%	20%	20%
Capacity				
Initial # of trains		6	2	15
Final Bioreactor Size		15,000	15,000	2,000
Batches Per Train	1 year	20	20	20
Titer	g/L	5	5	5
Yield	%	75%	75%	75%
Maximum number of trains		6	6	45
Additional trains added		0	1	5
Employment				
Initial # of employees		300	120	120
Additional employees	per train	0	45	6
Inflation (applied after first year)	%	3%	3%	3%
Decision Rule (when to add trains)	%	80%	80%	80%

Simulation Results

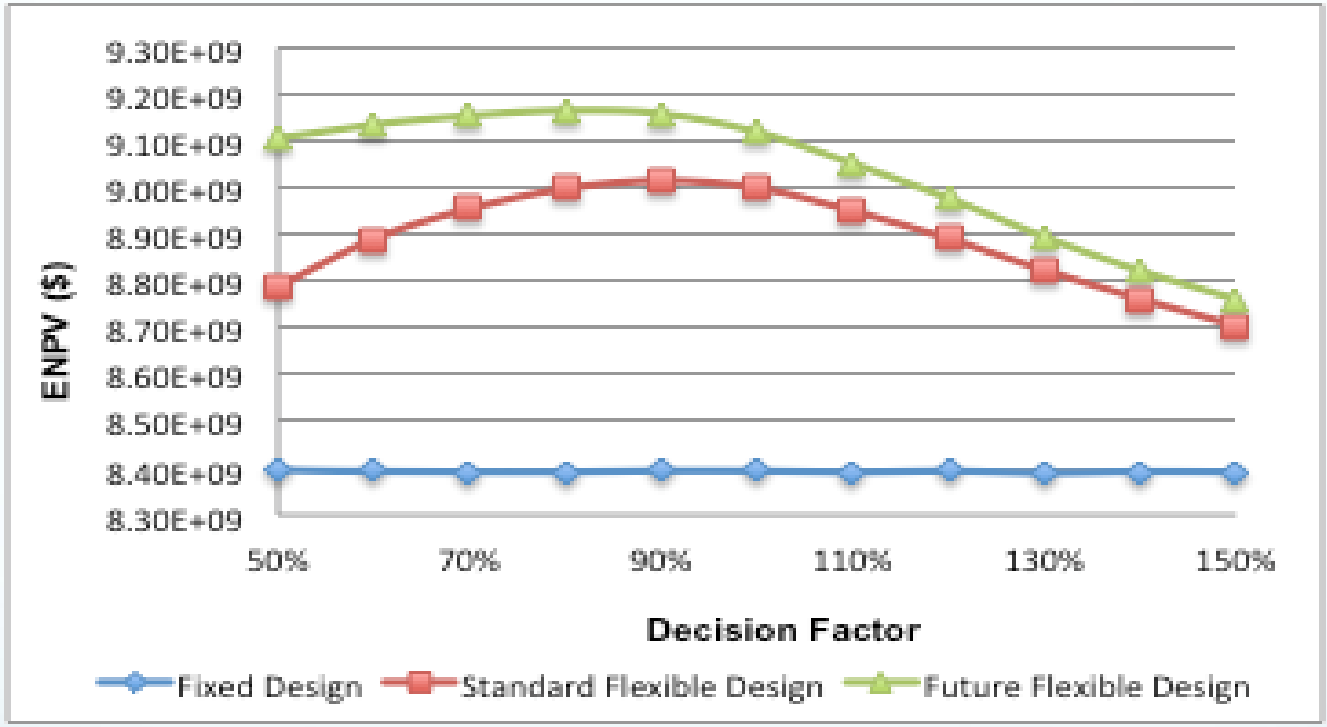


	Fixed Design	Standard Flexible Design	Future Flexible Design
Mean ENPV	$8,391,950,000.00	$8,998,303,000.00	$9,165,863,000.00
Standard Deviation	$2,798,677,000.00	$2,681,876,000.00	$2,704,029,000.00
Minimum	$2,248,373,000.00	$2,972,429,000.00	$3,168,993,000.00
Maximum	$23,541,420,000.00	$23,588,710,000.00	$22,842,500,000.00
P_5	$4,631,118,000.00	$5,355,173,000.00	$5,509,338,000.00
P_{95}	$13,619,440,000.00	$13,971,700,000.00	$14,208,500,000.00

Simulation Results

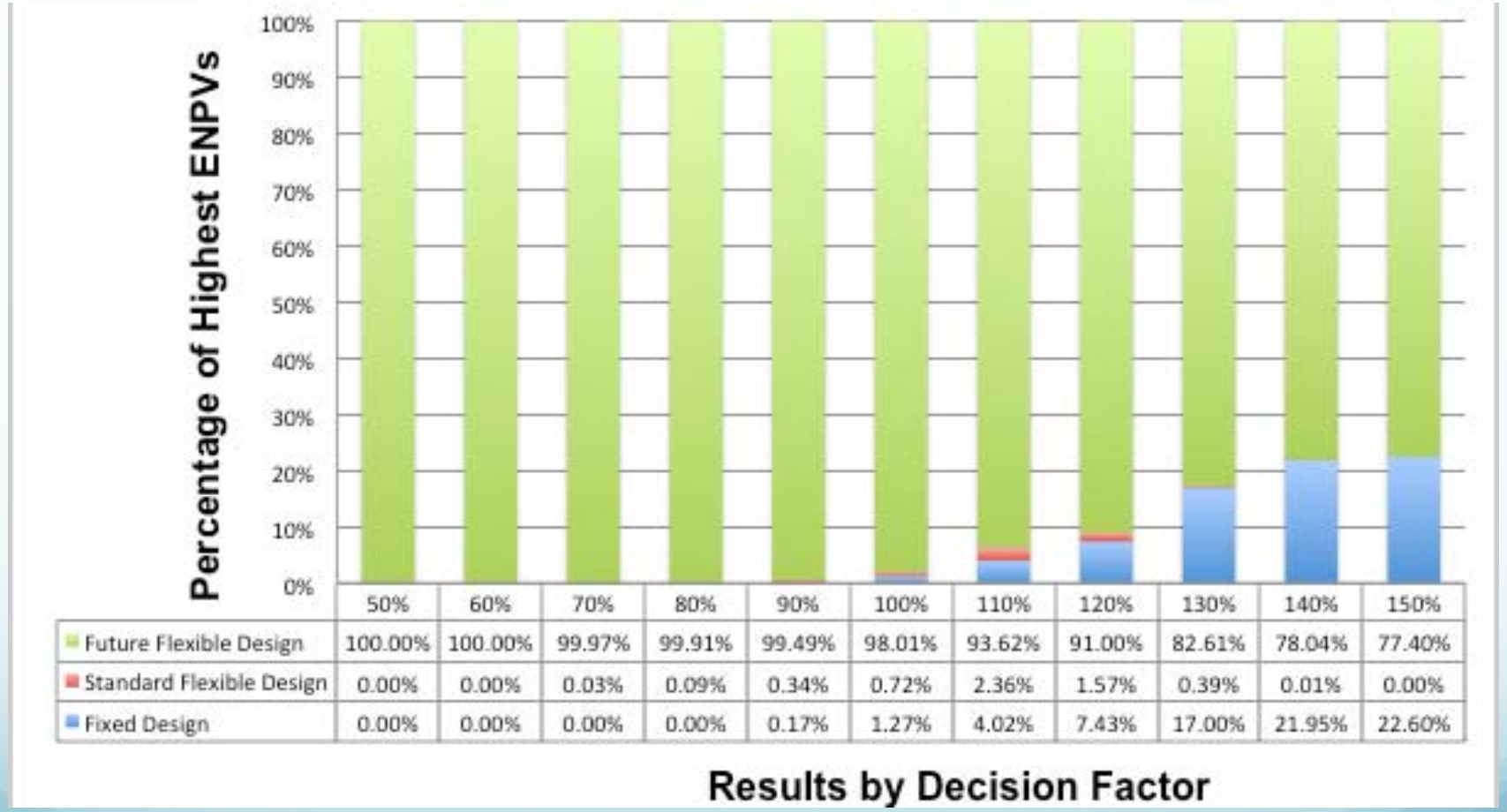
- Flexible Designs outperformed Fixed Design (mean ENPV)
  - Cost of maintaining 6 bioreactor trains
- Future Flexible Design had the highest mean ENPV of all the designs
- However, Future Flexible Design had the lowest max ENPV
  - Raw material costs
  - Expansion amounts (10,000L Versus 15,000L)

Sensitivity Analysis



*Decision Factor = 80% - 90% (“Sweet Spot”)

Sensitivity Analysis



	50%	60%	70%	80%	90%	100%	110%	120%	130%	140%	150%
Future Flexible Design	100.00%	100.00%	99.97%	99.91%	99.49%	98.01%	93.62%	91.00%	82.61%	78.04%	77.40%
Standard Flexible Design	0.00%	0.00%	0.03%	0.09%	0.34%	0.72%	2.36%	1.57%	0.39%	0.01%	0.00%
Fixed Design	0.00%	0.00%	0.00%	0.00%	0.17%	1.27%	4.02%	7.43%	17.00%	21.95%	22.60%

Discussion

- Flexible Designs outperformed Fixed Design in almost every category
  - Future Flexible Design would be chosen among the three
- However, certain cases exist where the Fixed Designs are more valuable
- Expansion “sweet spot” is 80% - 90% based on the cost model used
- What I Learned:
  - Biomanufacturing Cost Analysis
  - NPV Analysis & Simulation

References

1. Plants for the Pharmaceutical Biotechnology (Linde Group). Online: <http://www.linde-kca.de/international/web/le/kca/likelekcacom.nsf/docbyalias/biotech_pharma>

2. Eibl, Roger and Dieter Eibl. *Disposable Bioreactors* (Heidelberg, Germany: Springer-Verlag, 2009), 191.

3. Cacciotti, Jerry and Patrick Clinton. “12 Annual Pharm Exec 50.” Pharmaceutical Executive. Online: <http://pharmexec.findpharma.com/pharmexec/Global+Report/12th-Annual-Pharm-Exec-50/ArticleStandard/Article/detail/719596>.

*full Works Cited included in the report