The Digital Thread - ROIC of automation with a digital plant maturity model (DPMM) for life sciences

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Vision

Our vision is a world in which access to life-changing therapies transforms human health.

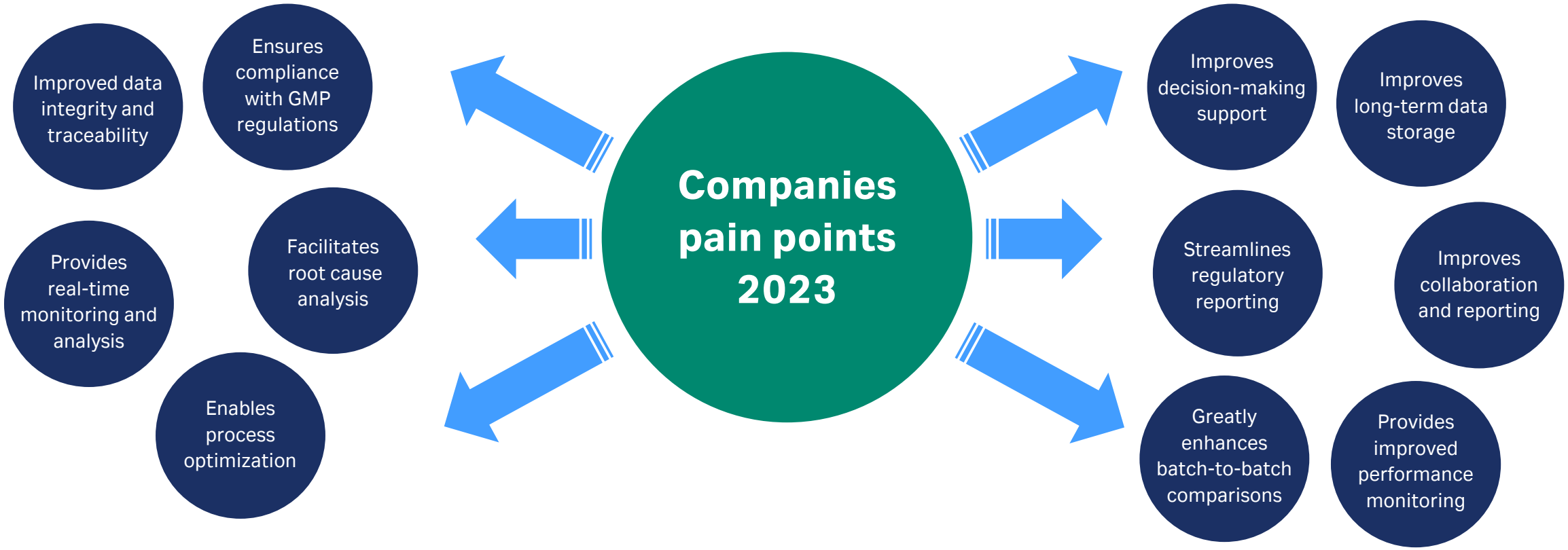
Mission

Our mission is to advance and accelerate therapeutics.

1

What is happening in industry

Greater then 30% of companies were planning to evaluate and/or test bioprocessing control, monitoring in 2023[1]

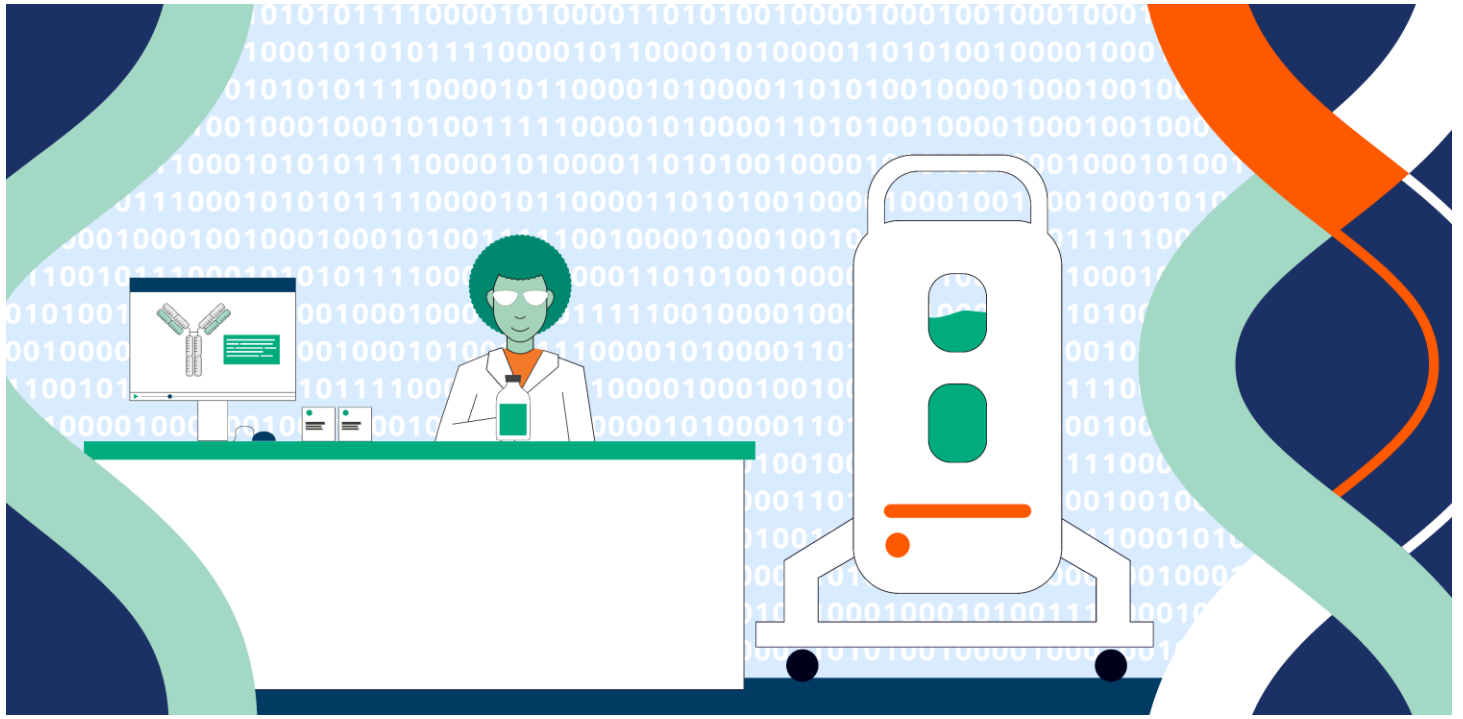


[1]Report and survey of Biopharmaceutical Manufacturing Capacity and Production, BioPlan Associates, April 2023, page 86

Data enablement is a fundamental building block for increased digital maturity

"Data is the DNA of digital transformation."

- Data enablement is the automatic electronic capture of process, raw material, and machine data for conversion into knowledge
- Addresses deficiencies including:
  - Data access and visualization
  - Data context
  - Data retrieval
  - Data quality/accuracy
  - Data formats
  - Data analysis



BioPhorum Operations Group. Digital technologies roadmap. July 2022. https://www.biophorum.com/download/digital-technologies/

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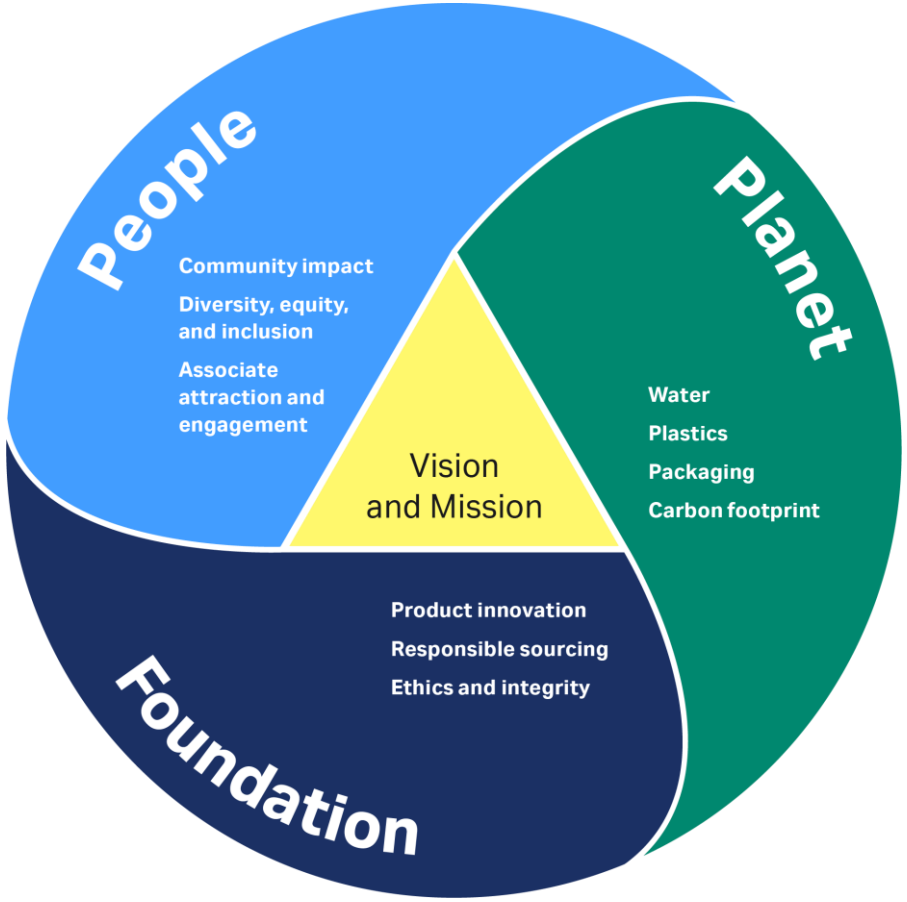
Where digital and sustainability intersect

Deploying digital solutions supports sustainability

Digital solutions can help manufacturers reduce waste, manufacturing time, and energy consumption.

- Fewer visits to clean rooms reduces gowning consumables
- Fewer deviations can prevent rework or lost batches that reduce manufacturing run time
- Modeling software can reduce development and manufacturing operations, decreasing carbon footprint, manufacturing consumables, packaging, and gowning consumables
- Predictive maintenance programs can reduce carbon footprint and manufacturing run time



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What is return on invested capital (ROIC), and why does it matter?

What is ROIC (return on invested capital)

Return on invested capital (ROIC)

A calculation used to assess a company's efficiency at allocating the capital under its control. [1]

$$\frac{\text{ROIC}}{\text{Cost of capital}} > 1 = \text{healthy growing company}^{1}$$

$$\frac{\text{ROIC}}{\text{Cost of capital}} < 1 = \text{unsustainable business model}^{1}$$

Weighted average cost of capital (WACC)

A firm's average cost of capital, weighted to reflect that different sources of capital, like common stocks and bonds, carry different return expectations. [1]

Company health ratio or (%) = ROIC / WACC

Note: Anything over 10% is considered strong

$$\text{ROIC} = \frac{\text{Net operating profit after taxes}}{\text{Invested capital}^{1}}$$

1 Investopedia https://www.investopedia.com/terms/r/returnoninvestmentcapital.asp Accessed Sept 2023

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An industry definition of digital and plant maturity from BPOG/BPIT

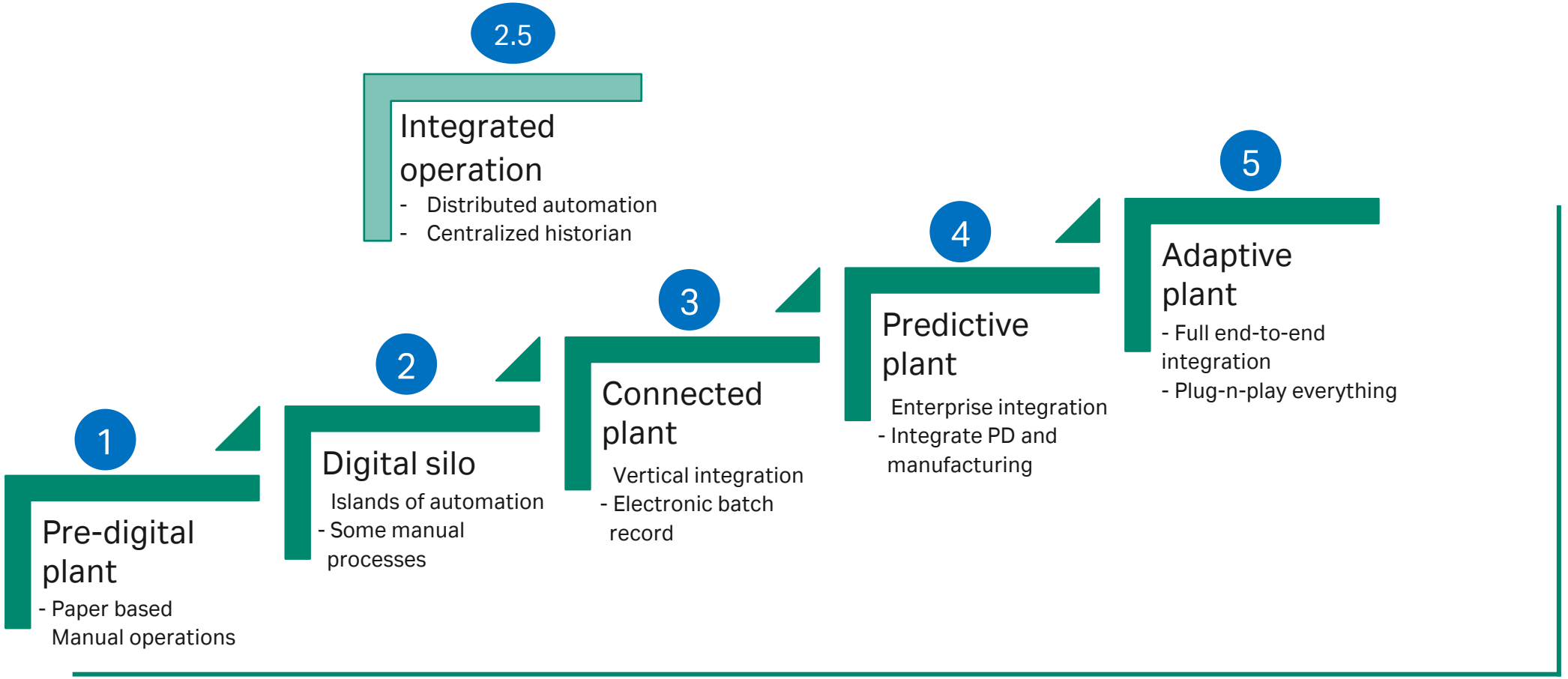
BioPhorum

- Founded in 2008 – brings leaders and SMEs together to collaborate
- 7,500 active subject-matter experts
- Ten technical forums transforming the industry through over 110 initiatives

"Our mission is to create an environment where the global biopharmaceutical and device industry can collaborate and accelerate rate of progress – for the benefit of all."[1]

1 BioPhorum. https://www.biophorum.com/about/. Accessed October, 2023

DPMM maturity level definition



Many biomanufacturers are at DPMM Level 2 and may not realize or be able to quantify the benefits of increasing digital maturity

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Who is BIOPHARMA SERVICES LIMITED (BPS)?

Companies struggle to justify the initial capital costs associated with enabling higher digital plant maturity

Problem statement

- Biotech companies have an intuitive understanding that increased digital maturity is beneficial
- Biotech companies have difficulty quantifying the benefits of increased digital maturity
- Biotech companies struggle to justify the investment in digital technologies

Solution

- BIOPHARM SERVICES LIMITED's Biosolve™ software models the costs and associated benefits of increasing digital maturity for mAb processes
- The modeling makes the value of increased digital maturity more tangible by highlighting benefits that may include:
  - Increased throughput
  - Increased yield
  - Reduced labor requirements
  - Reduced total cost of ownership
  - Increased speed-to-market
  - Reduced risk

mAb – monoclonal antibody

BIOPHARM SERVICES LIMITED's Biosolve™ software evaluates total cost of ownership required to achieve a higher digital plant maturity

Cost contributors	Assumptions to adapt model for higher DPMM
Capital costs	Increased to reflect incremental automation costs
Labor[1]	• Engineering and general/logistics labor reduced for DPMM level 2.5[2] and 3.0[3] as some manual tasks and inefficiencies are eliminated • Second person verification eliminated at DPMM 3.0 due to introduction of MES and ERP • QA labor reduced from 2 to 1 resource for DPMM level 3.0 due to use of full eBR • De-skill resources - error-proof procedures require lower skilled/more junior resources with less training time
Facility utilization	Increased from 70% to 80% to 90% from level 2.0 to 2.5 to 3.0 as fewer manual operations improve facility management (operational tasks and time management), which enable optimal resource utilization while facility assets are better utilized with increased productivity

[1] Note the model does not include labor costs associated with increased automation staffing, if any
Note: All above data are assumptions and are inputs into the DPMM model. Other(s) data and assumptions might be similar or different depending on other(s) circumstances and experiences.
[2] DPMM level 2.5 represents addition of a Distributed Control System (DCS) and in-line sensors
[3] DPMM Level 3.0 represents level 2.5 plus addition of MES system, and integration with ERP to provide electronic batch records
Definitions: MES – Manufacturing Execution System, DPPM – Digital Plant Maturity Model, ERP – Enterprise Resource Planning, eBR – Electronic Batch Record, QA – Quality Assurance

BIOPHARM SERVICES LIMITED's Biosolve™ software evaluates total cost of ownership required to achieve a higher digital plant maturity

Cost contributors	Assumptions to adapt model for higher DPMM
Batch failure rate	Fewer operator errors and failures to meet spec[1] results in: • Reduced rate from 1.2% (level 2.0) to 0.25% (levels 2.5 and 3.0 for commercial manufacturing) • Reduced rate from 1.2% to 0.19% (levels 2.5 and 3.0 for clinical manufacturing)
QA batch release time	• Reduced by 50% from level 2.0 to 2.5 and 50% from level 2.5 to 3.0 due to easier access to more accurate electronic data from a single source • Reduced by addressing quality events in real time versus at the end of the batch
Deviations	• Deviations per batch were reduced from 1.5 to 1.0 to 0.5 for DPMM level 2.0. 2.5 and 3.0, respectively • Personnel required to investigate deviations was reduced from 2 for DPMM level 2.0 and 2.5 to 1 for level 3.0 due to fully electronic batch records

1. Bioplan Associates, "17th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production," April 2020: https://bioplanassociates
2. DPMM – Digital Plant Maturity Model
3. Note: All above data are assumptions and are inputs into the DPMM model. Other(s) data and assumptions might be similar or different depending on other(s) circumstances and experiences.

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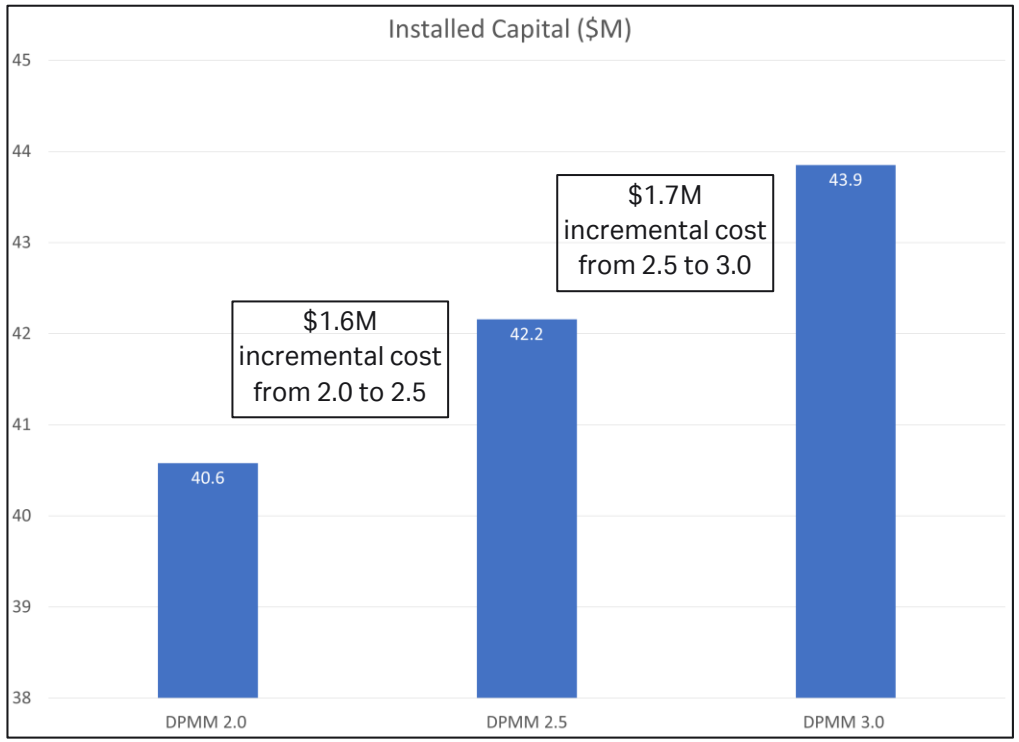
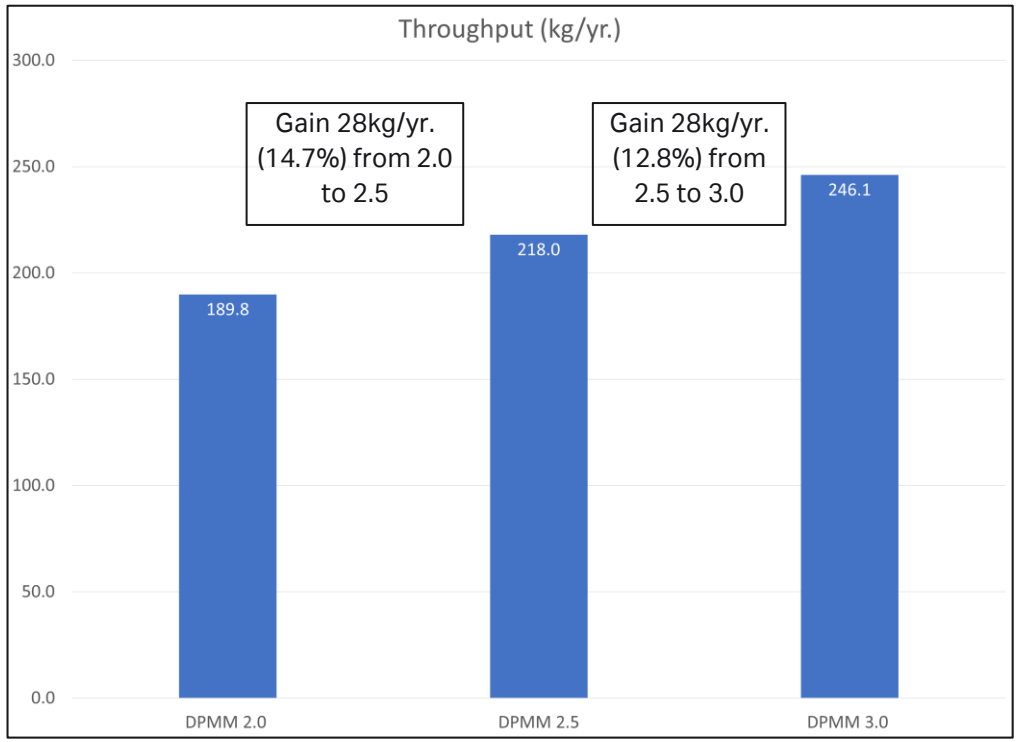
Analysis of the COGS and ROIC for a manufacturing plant's digital maturity

Increasing digital maturity requires higher automation costs but results in additional annual throughput

Increased digital maturity leads to increased number of batches and higher production



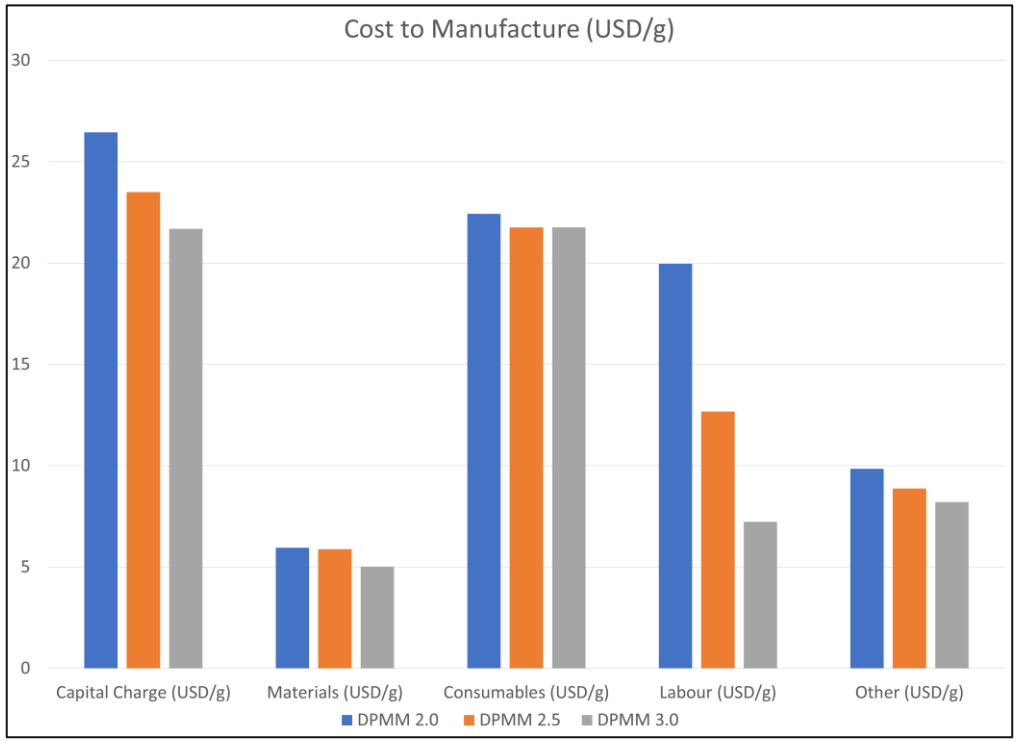


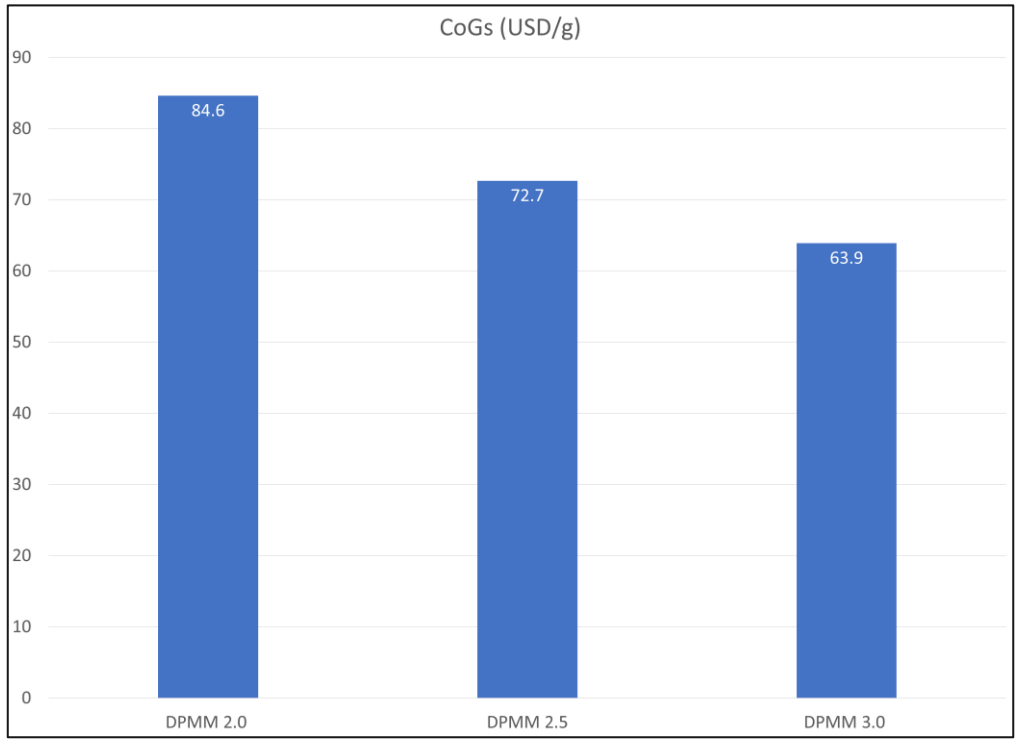
Note: Output reflects commercial manufacturing (2 x 2000L, 5g/L), 25 – 27 – 31 batches

Note: The above data was generated using BIOPHARM SERVICES LIMITED's Biosolve™ software and having it configured for our DPMM simulation / model. The above results are for modelling purposes only. Other(s) assumptions or input(s) can change the result of the model.

Additional throughput drives down manufacturing costs with labor reduction being primary driver

Increased digital maturity results in significantly lower cost of goods sold





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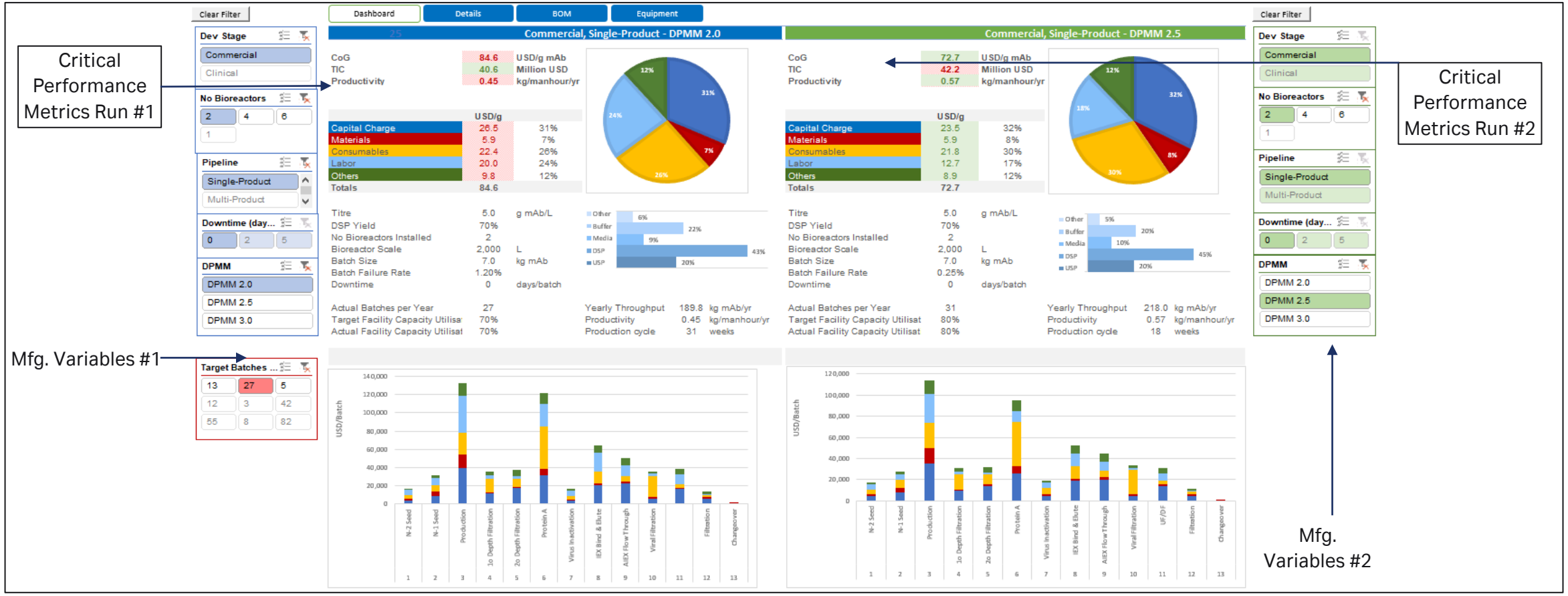
Side-by-side manufacturing comparison highlights difference in critical performance metrics



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Calculated ROIC

	DPMM 2.0	DPMM 2.5	DPMM 3.0
Capital	$40.6M	$42.2M	$43.9M
Quantity of drug product	189.8KG	218KG	246.1KG
Selling price per gram	$100	$100	$100
COGS $/gram	$85	$73	$64
COGS	$16.1M	$15.8M	$15.7M
Revenue	$18.9M	$21.8M	$24.6M
Net Operating Profit	$2.9M	$5.9M	$8.8M
ROIC	**7%**	**14%**	**20%**

Note: The above did not account for taxes in the calculation
Note: Definitions of terms used: DPMM – Digital Plant Maturity Model, COGS – Cost of Gods Sold, ROIC – Return On Invested Capital
Note: The above table was created by C. Sandusky 2023

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Summary of benefits of digital maturity and considerations

Increased digital plant maturity can justify incremental automation costs

The introduction of advanced automation capabilities into a mAb process results in several advantages

Parameter	Unit of measure	Percent improvement DPMM level 2.0 to 2.5
COGS	(USD/gm)	Reduced up to 25%
Throughput	(kg/yr.)	Increased up to 25%
Productivity	(kg/man-hour/yr.)	Increased up to 50%

These advantages provide several benefits:

- Reduced scrap
- Reduced labor
- Reduced deviations
- Reduced batch review time
- Increased facility utilization

Additional advantages not factored into model include:

- Improved regulatory compliance & audit results
- Greatly simplified and less costly manufacturing transfers
- Faster and less costly regulatory filings
- Amortize automation costs by using in future clinical and commercial campaigns

Cytiva's digital ambition: deliver *fast, flexible, and reliable* process development and manufacturing

- … with **integrated digital process technologies**
- that harness product and process data for **predictive operations**
- and **address the regulatory barriers** that prevent rapid operational improvements

Cytiva's digital toolbox for CMC acceleration

1 Data access

Data Bridge
- Raw material characterization data

OptiRun Connect
- Remote Asset Performance Management

Figurate™
- Industrial BioProcess Automation
- Rockwell Pharma Suite

2 Data management

Chronicle™
- GMP manufacturing solution for cell therapy (eSOP, etc)

FlexFactory™ Historian
- Enterprise level Data Historian

3 Process modelling

Cytiva Bioreactor Scaler
- Scaling and tech transfer support

GoSilico
- Downstream Mech modelling

Analytics services
- Custom data science projects (yield, etc.)

...Solutions to build Digital Plant Maturity

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