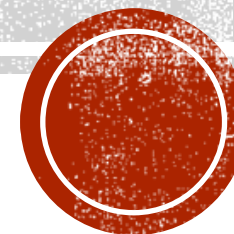


2021 PPAR PAT BENCHMARKING SURVEY*

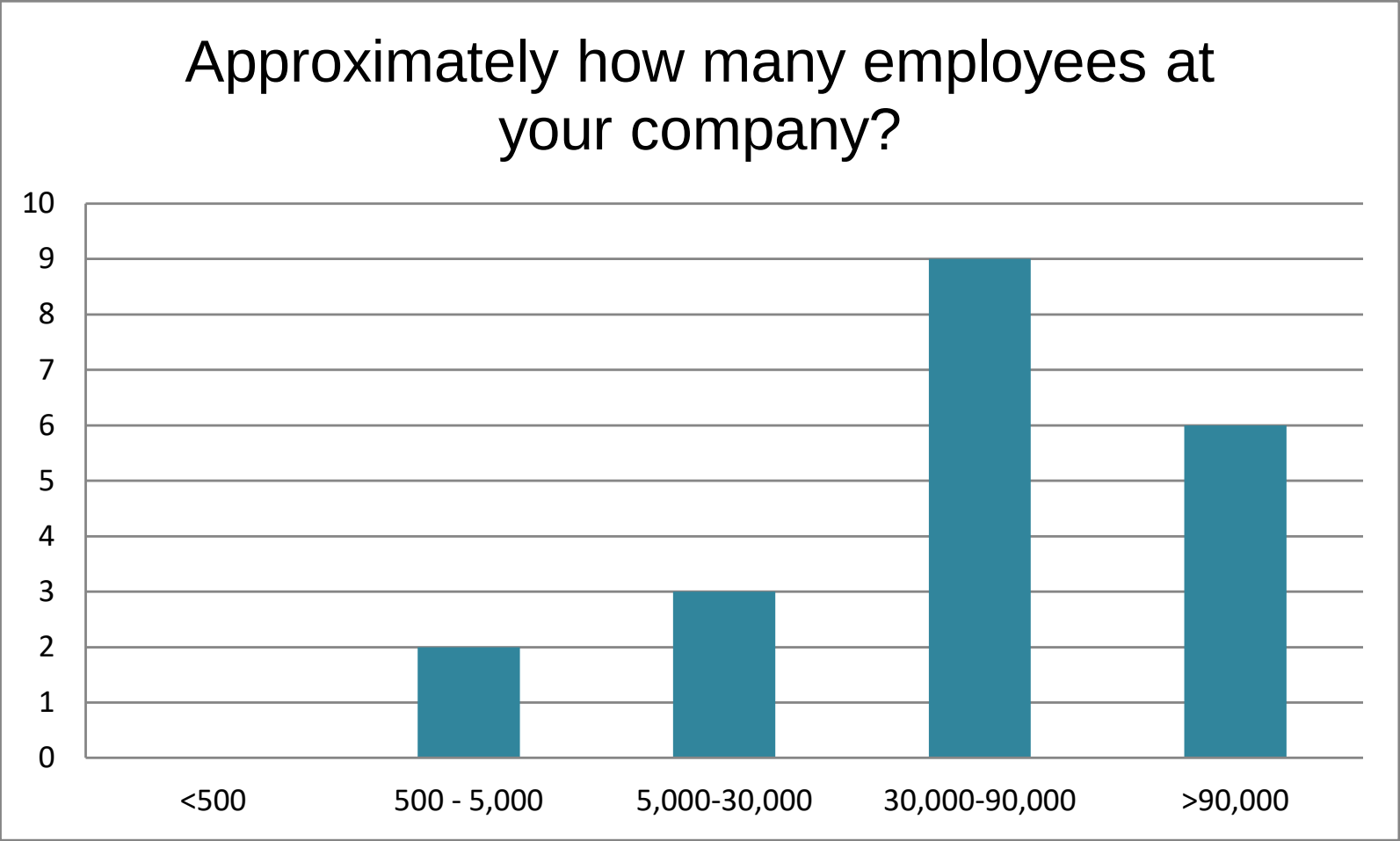


Assembled by:
Dan Hill – Biogen
Christian Airiau - Sanofi

**Content is generated and for the use by members of the PPAR Community during the Annual Meeting 9-10NOV, 2021.*

SURVEY DEMOGRAPHICS – N=19 + 2

Survey Respondents 2021 (22)
AbbVie
Amgen
AstraZeneca
Biogen
Bristol-Myers Squibb
Eli Lilly
GlaxoSmithKline
Hovione
Janssen Pharmaceuticals
Merck
Novo Nordisk
Pfizer
Roche (x2)
Sanofi
Takeda Pharmaceuticals
The Procter & Gamble Company
ThermoFisher Scientific
Vertex Pharmaceuticals Inc
Zoetis
CPAC - University of Washington
University of Massachusetts Lowell

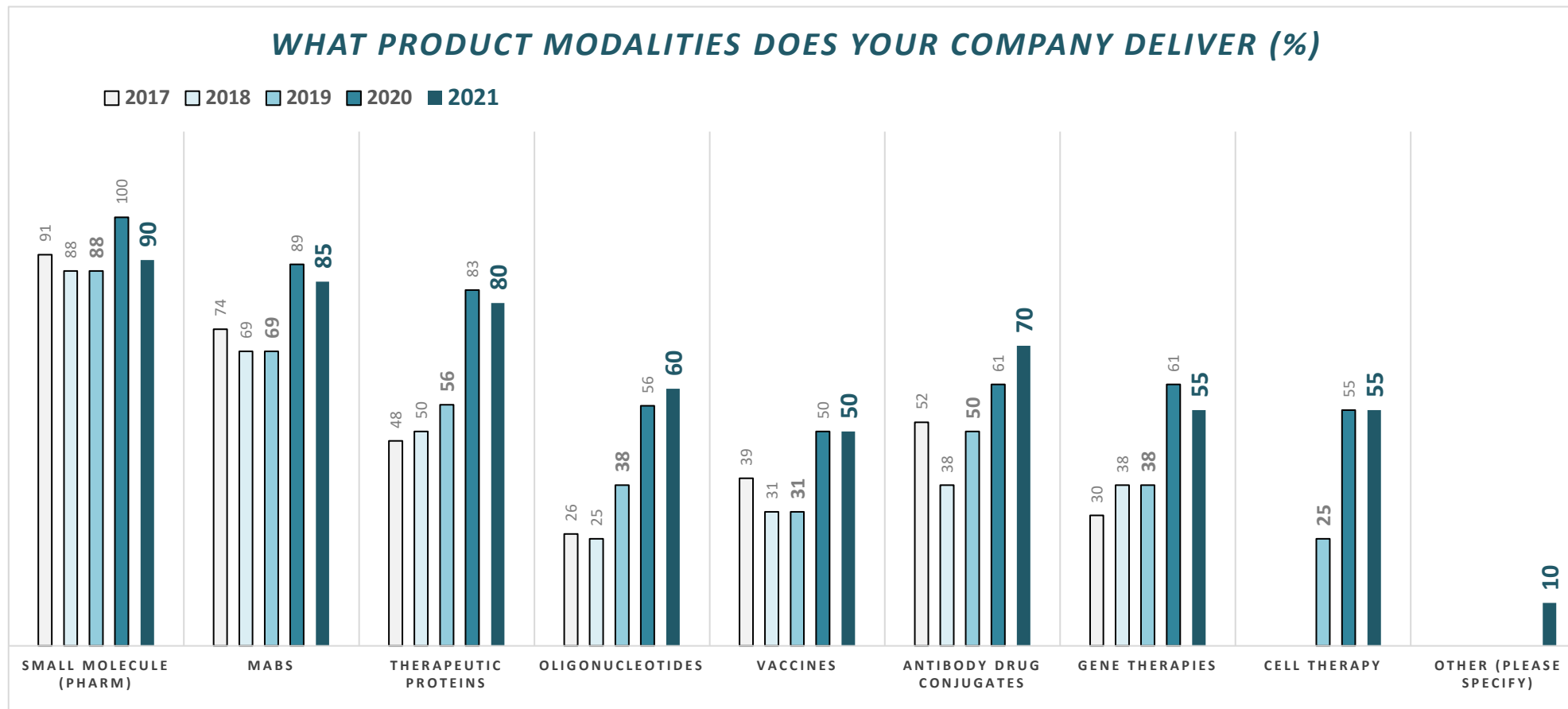


Note: 2 academic in this survey.



PRODUCT TYPES

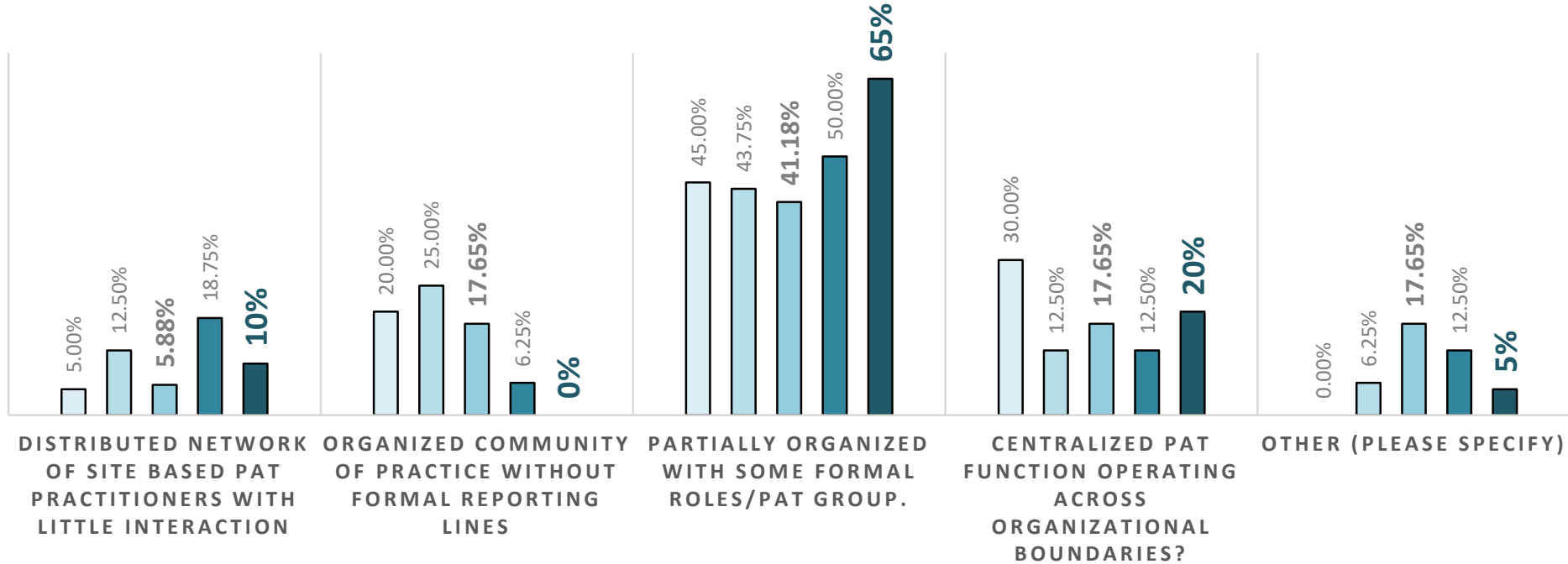
- Overall good consistency
- Main evolutions: ADC and Oligo continue to grow



TEAM ORGANIZATION

WHICH STATEMENT BEST REPRESENTS HOW YOUR PAT PEOPLE ARE ORGANIZED?

2017 2018 2019 2020 2021



- Consistent - mostly “Partially Organized with some formal roles/PAT groups”

- No CoP approach!

Other setup:

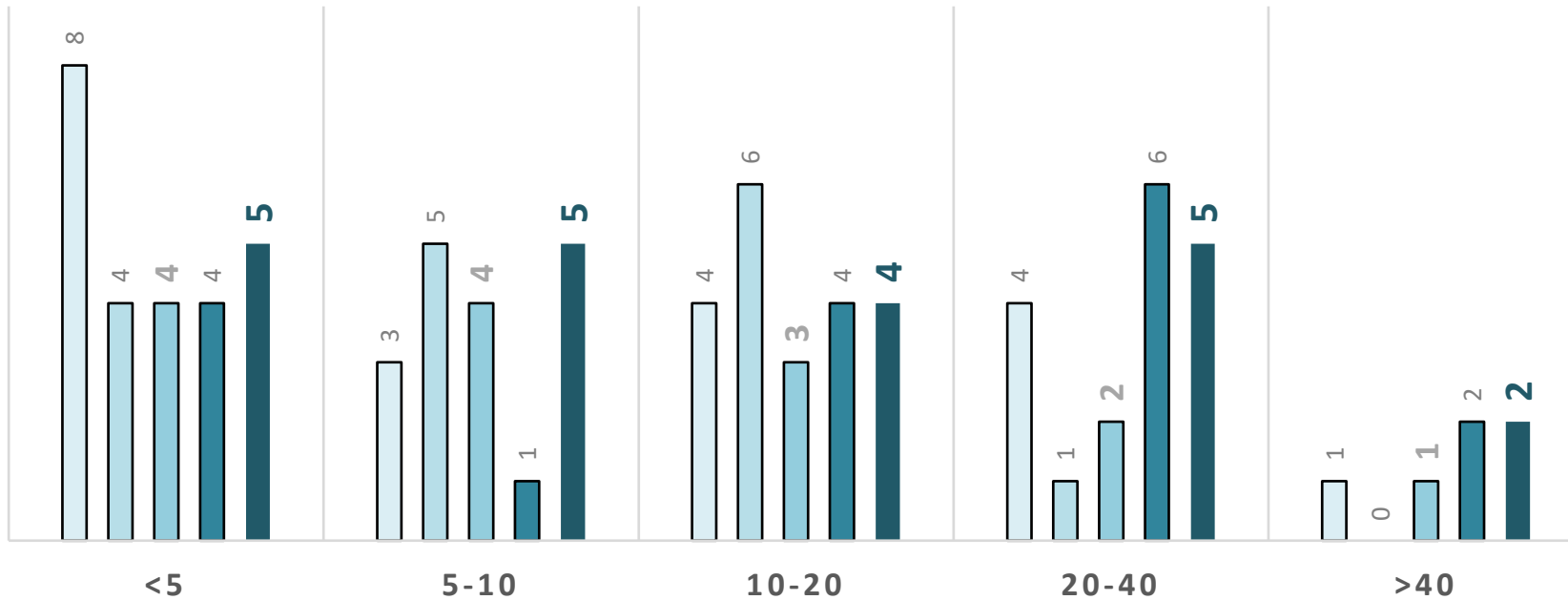
- Three separate centralized PAT functional groups operating across organizational boundaries



TEAM SIZE, FULL TIME

HOW MANY FULL TIME PAT PRACTITIONERS AT YOUR COMPANY?

2017 2018 2019 2020 2021



- 7 companies have >20 full time practitioners (8 last year)
- Larger number of companies with <10 (from 5 in 2020 to 10 this year)

Comments:

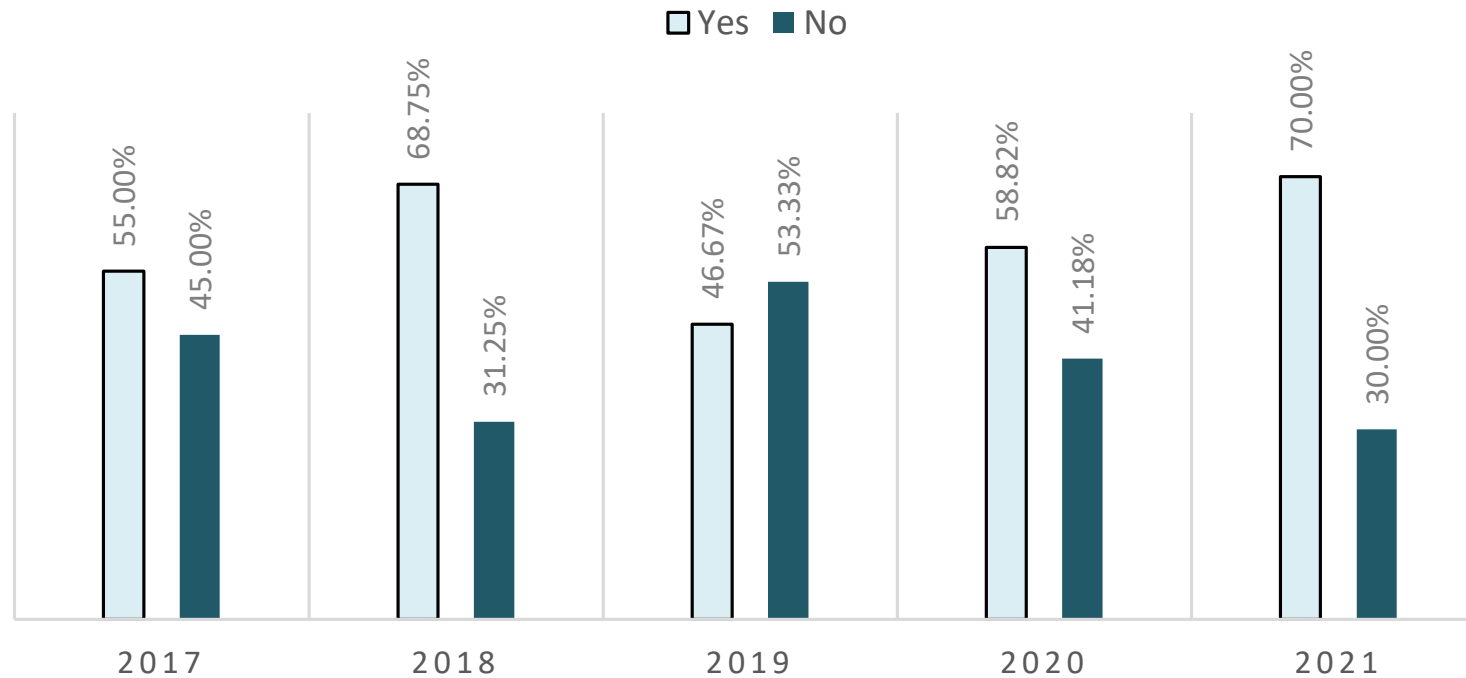
- Some are not full time
- 5 FTE and a collection of ad hoc members
- No one person is full time on PAT work for Bio-operations
- Professors and students



PAT STRATEGY

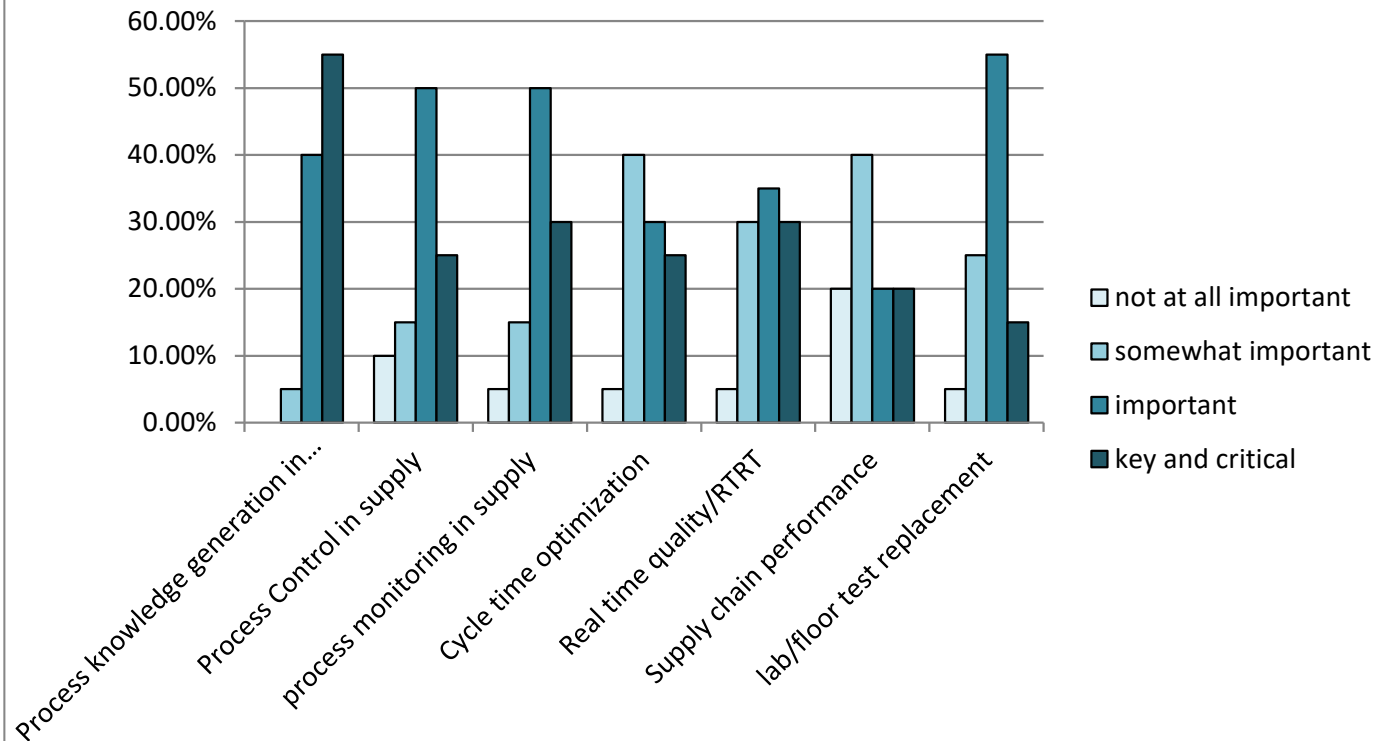
DOES YOUR COMPANY HAVE A FORMAL PAT APPROACH/STRATEGY?

- More companies with formal PAT strategy – 70/30 (60/40 in 2020)



PRIMARY DRIVERS

What are the primary drivers of value proposition for PAT at your company?



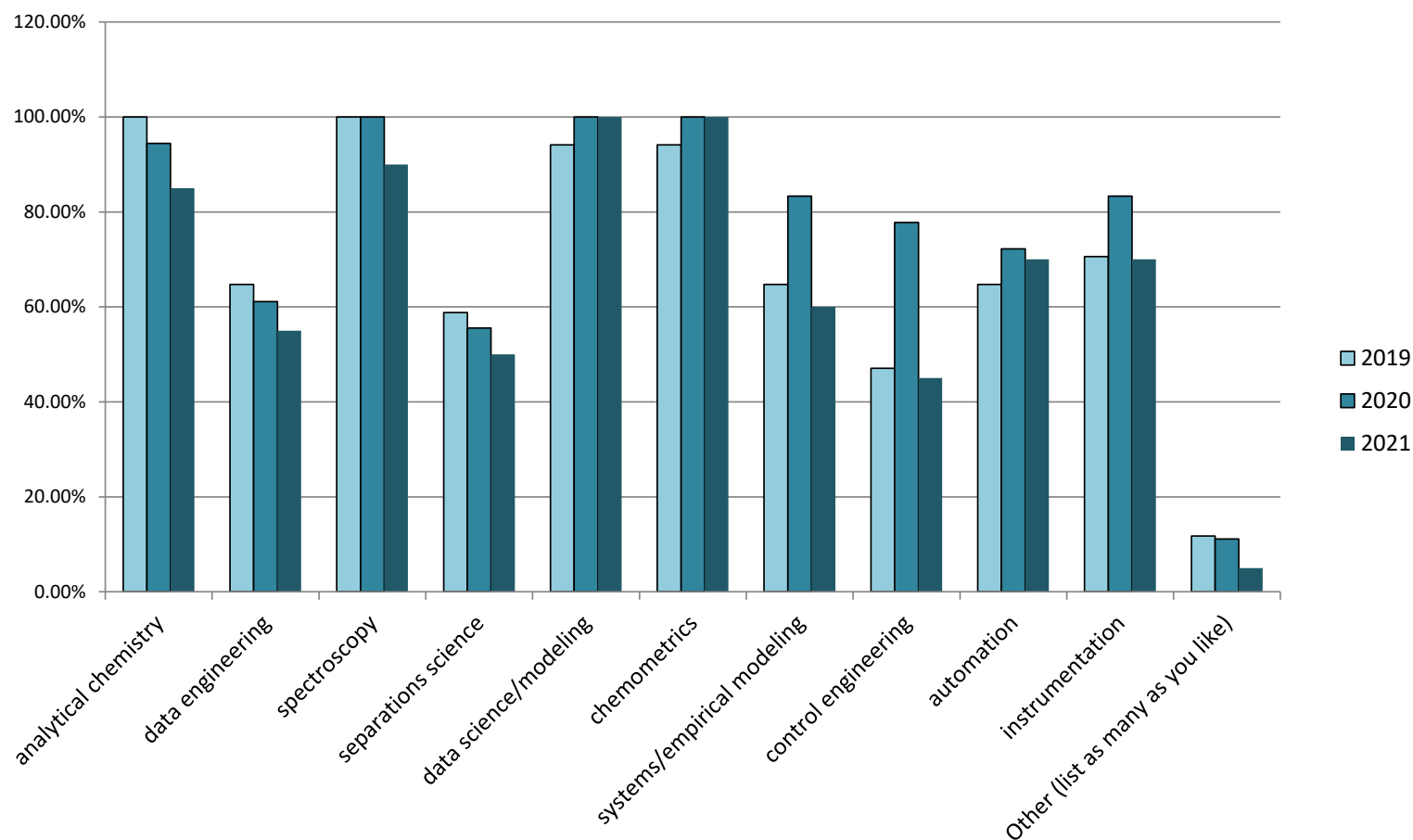
Main drivers remain:

- **Process Knowledge, Process Monitoring, Control**
- **Lab test replacement increasing**
- **Supply chain performance and cycle time optimization lesser focus**



CORE COMPETENCIES

What competencies/skills does your organization consider important for performing PAT work? (check all that apply)



Growing focus:

- Spectroscopy
- Data Sci. / chemometrics

Decreasing trend in:

- Analytical Chem.
- Data eng.
- Separation Sci.

Drop from 2020:

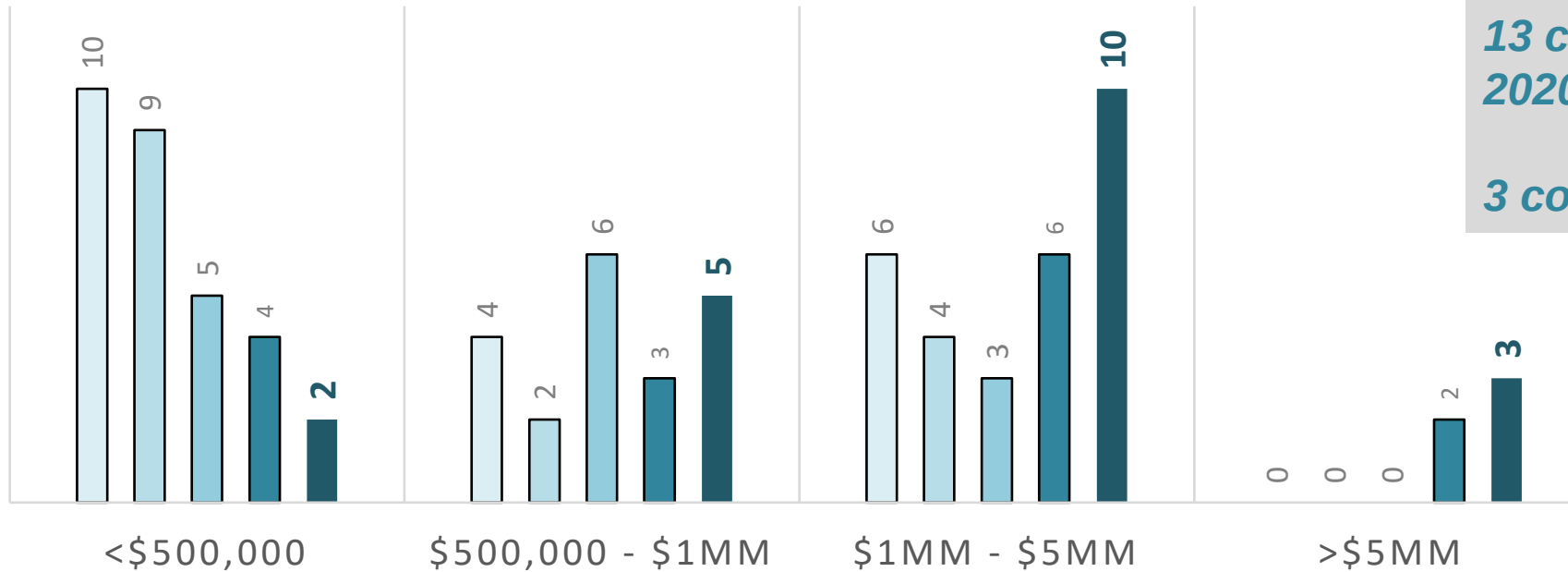
- Systems modeling / Ctrl/Eng.



ANNUAL INVESTMENT

WHAT IS YOUR LEVEL OF ANNUAL TECHNOLOGY INVESTMENT IN PAT?

2017 2018 2019 2020 2021



Investments continues to increase

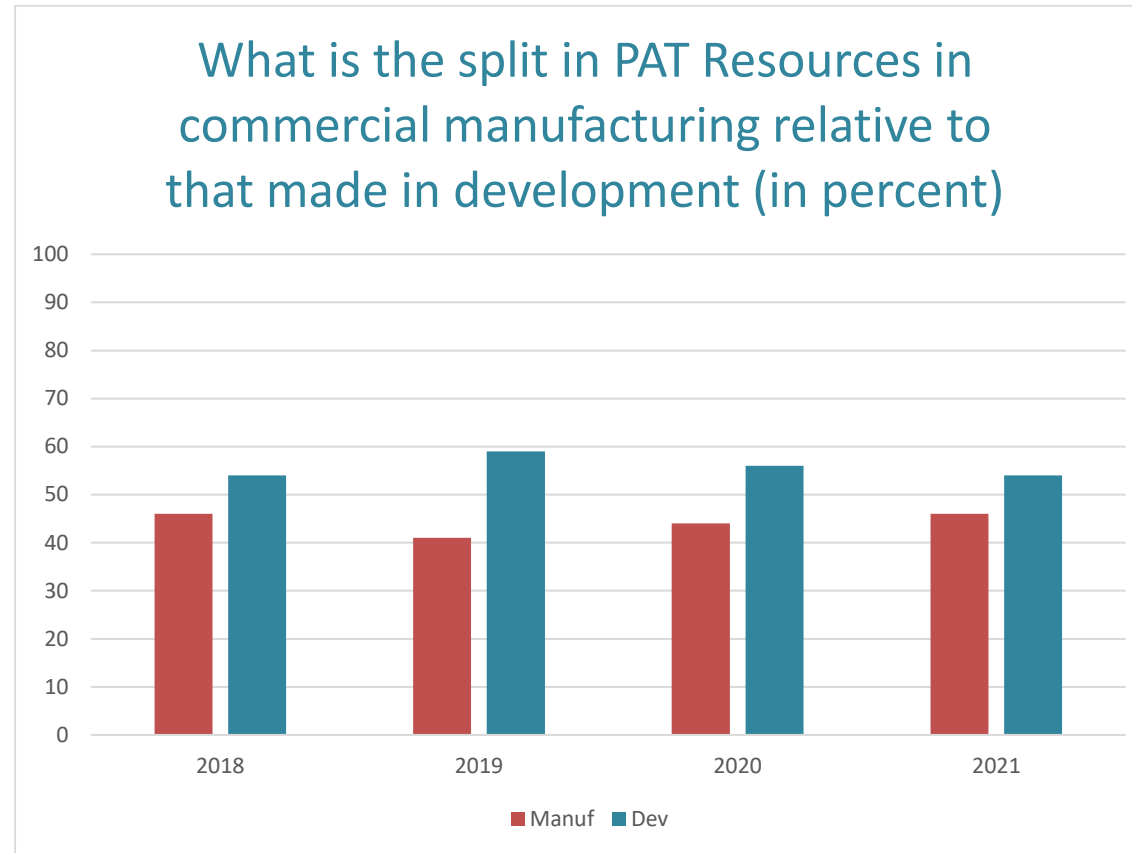
13 companies above \$1MM (8 in 2020)

3 companies above \$5MM



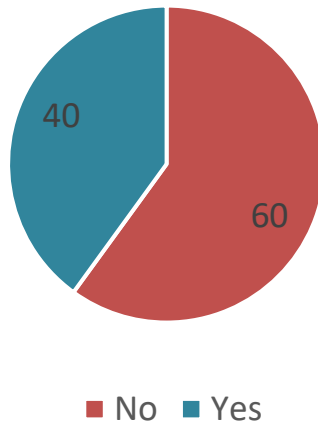
SPLIT BETWEEN MANUFACTURE VS DEVELOPMENT

Most deployment (54%) in Development
Not much change YOY



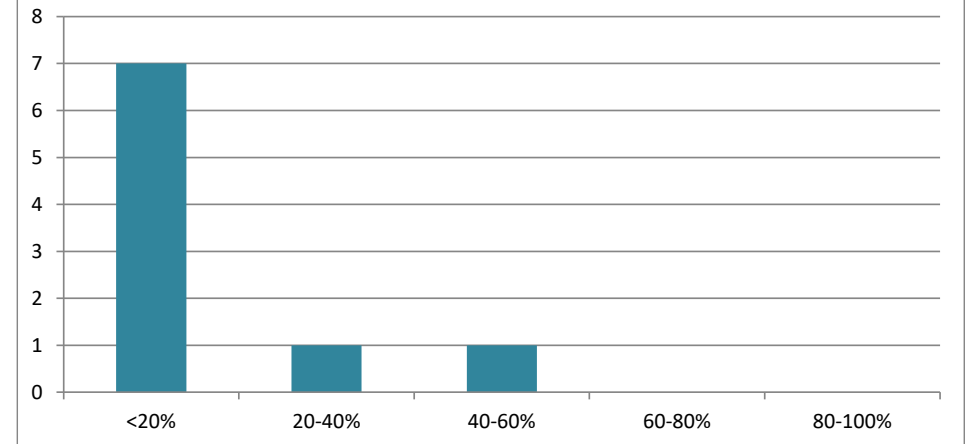
DO YOU OUTSOURCE ANY/PART OF YOUR PAT ACTIVITIES

Outsource PAT work?



Comparison YOY
2020: 35% outsourcing
2019: 43%
2018: 0% 2017: 25%

If yes - what percentage of PAT work is outsourced?



However, most companies outsource only <20% of their activities

50% of Companies request CRO/CMO to implement PAT as part of their core process work



LEADERSHIP COMMITMENT

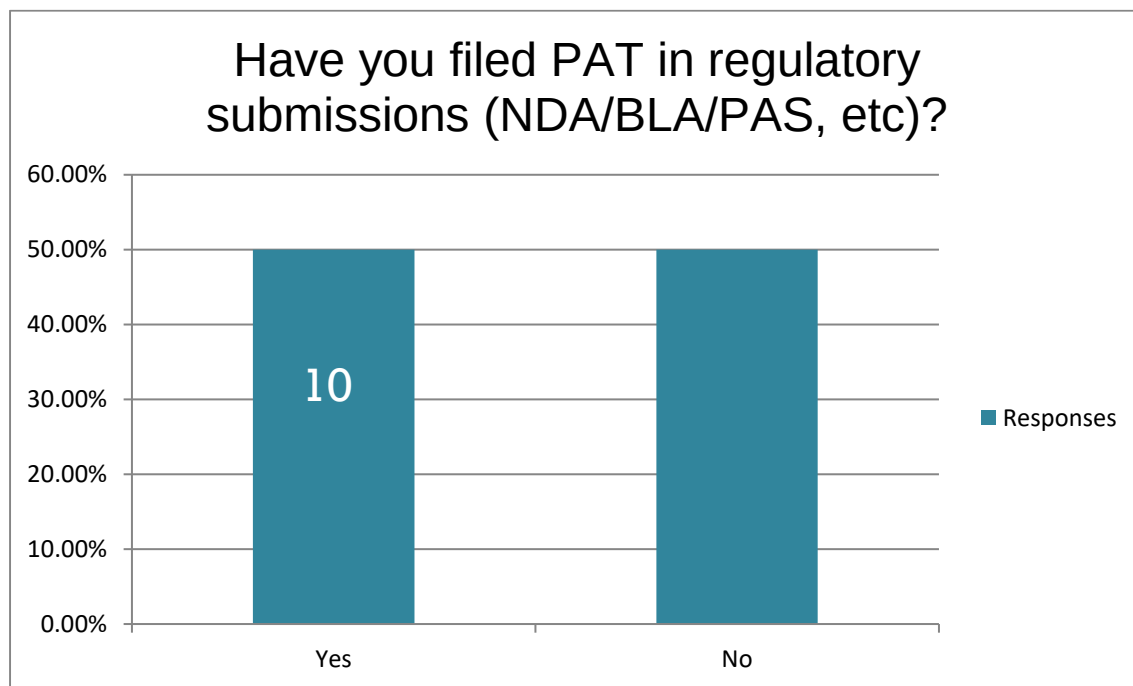


***55% of companies are either 4 or 5
“Good or Great support from most
leaders” – down from 65% in 2020***

Is the support at peak?



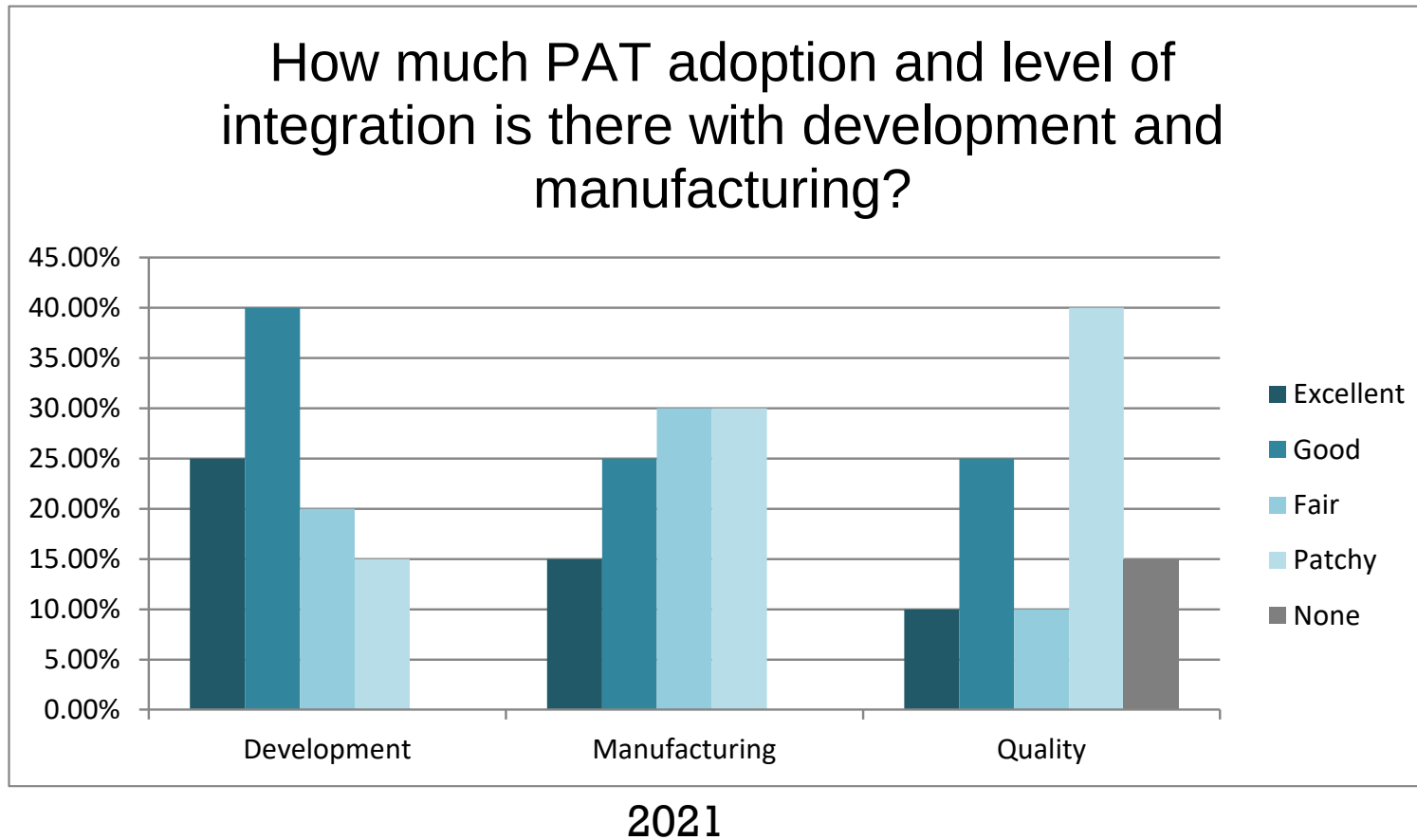
HAVE YOU FILED PAT METHODS IN REGULATORY SUBMISSIONS?



- 3 companies have between 1-3 dossiers with PAT
- 5 companies have 4-6 dossiers with PAT
- 1 company has >10 dossier with PAT



HOW MUCH PAT ADOPTION / INTEGRATION IN QUALITY, DEVELOPMENT, MANUFACTURING



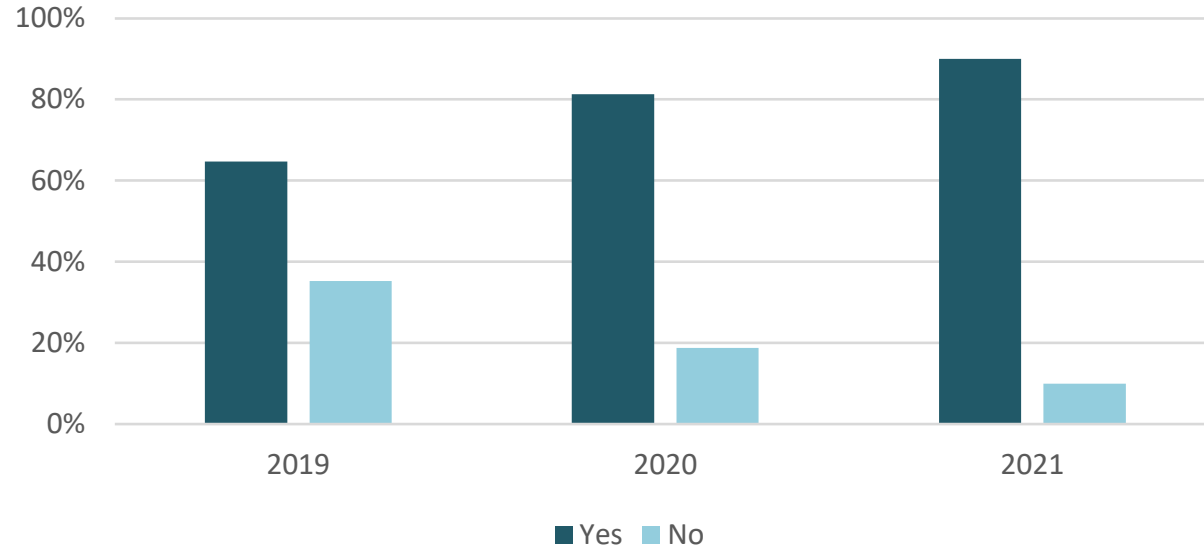
- Stronger adoption in Development
- Fair/patchy in Manufacture
- Quality is split:
 - 15% none
 - 34% good/excellent
 - Patchy most prevalent

Similar trend in 2020



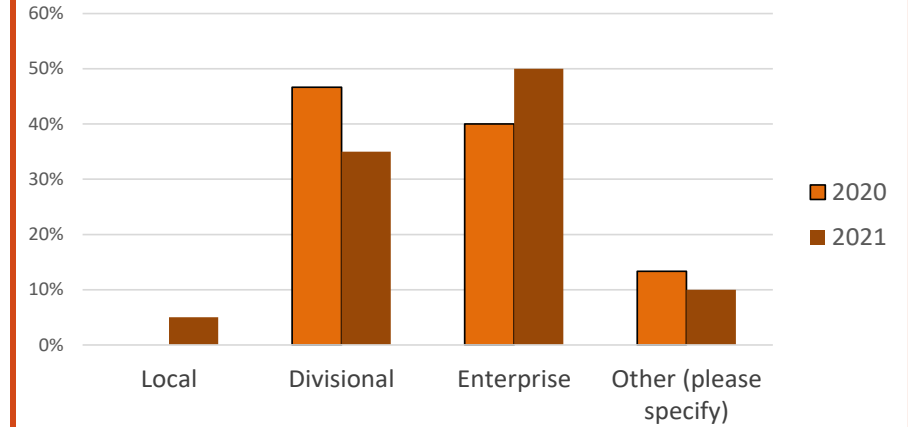
INDUSTRY 4.0

Does your company have a formal Industry 4.0/Digital Transformation initiative?



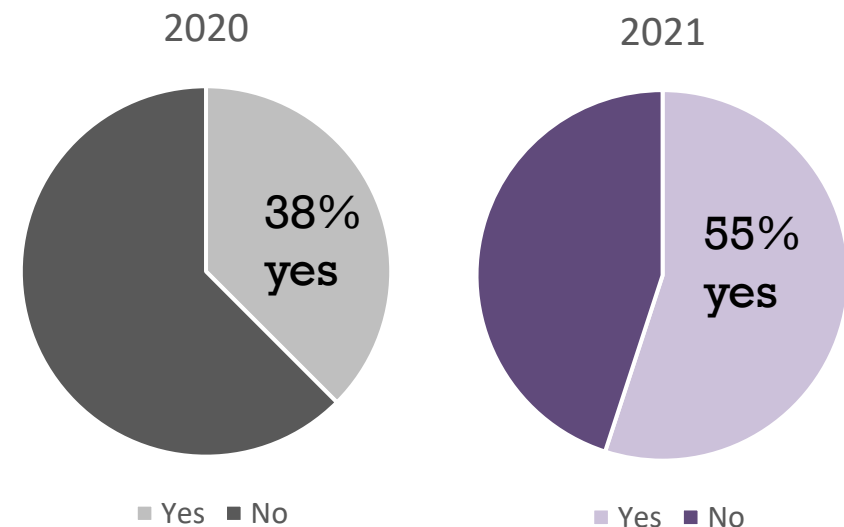
- Trend continues, 90% companies have a formal Digital Transformation program

If yes, is the strategy at a local, divisional, or enterprise level?



- Shifting from primarily Divisional (2020) to primarily Enterprise (2021)

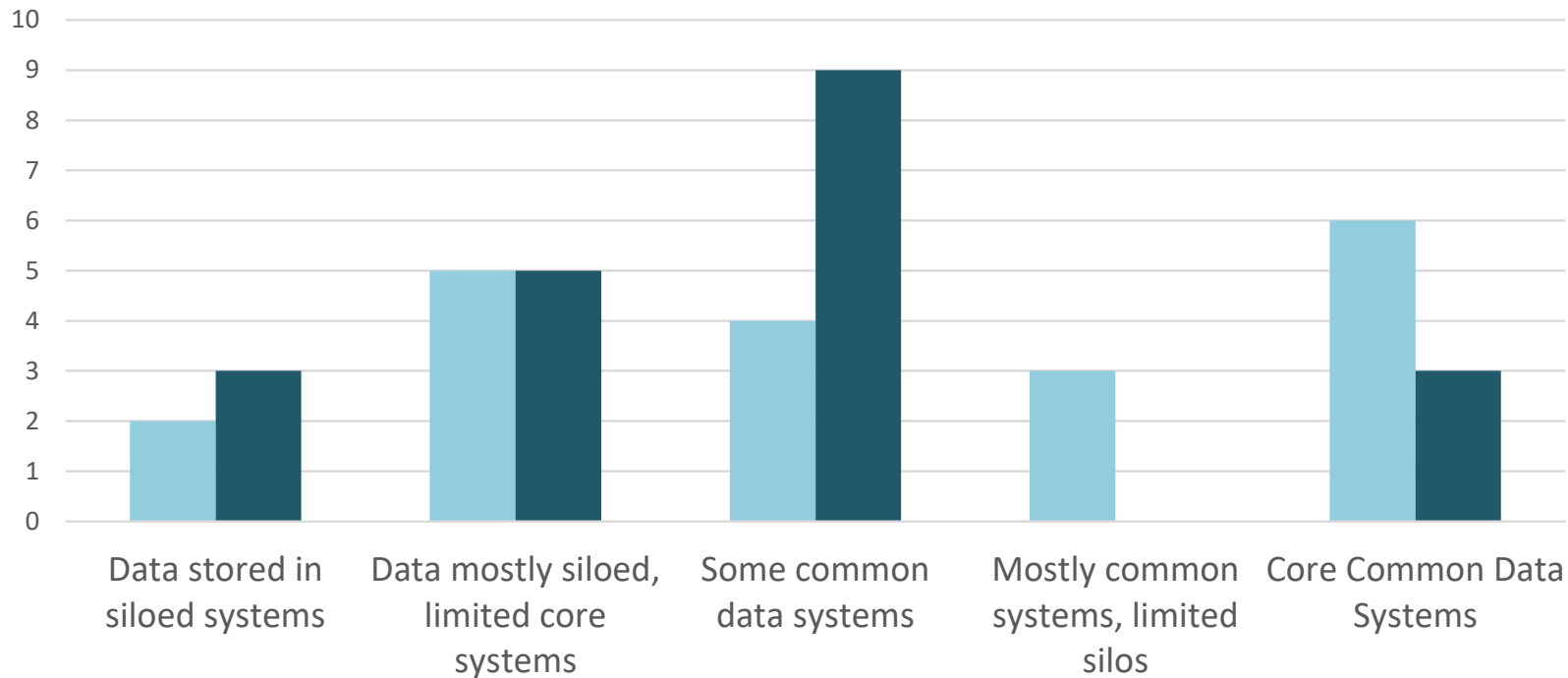
- PAT included in strategy for 55% of companies in 2021 Vs 37.5% in 2020



DATA MANAGEMENT — IN DEVELOPMENT & COMMERCIAL (NEW QUESTION 2021)

How do commercial and development data (including PAT) management compare?

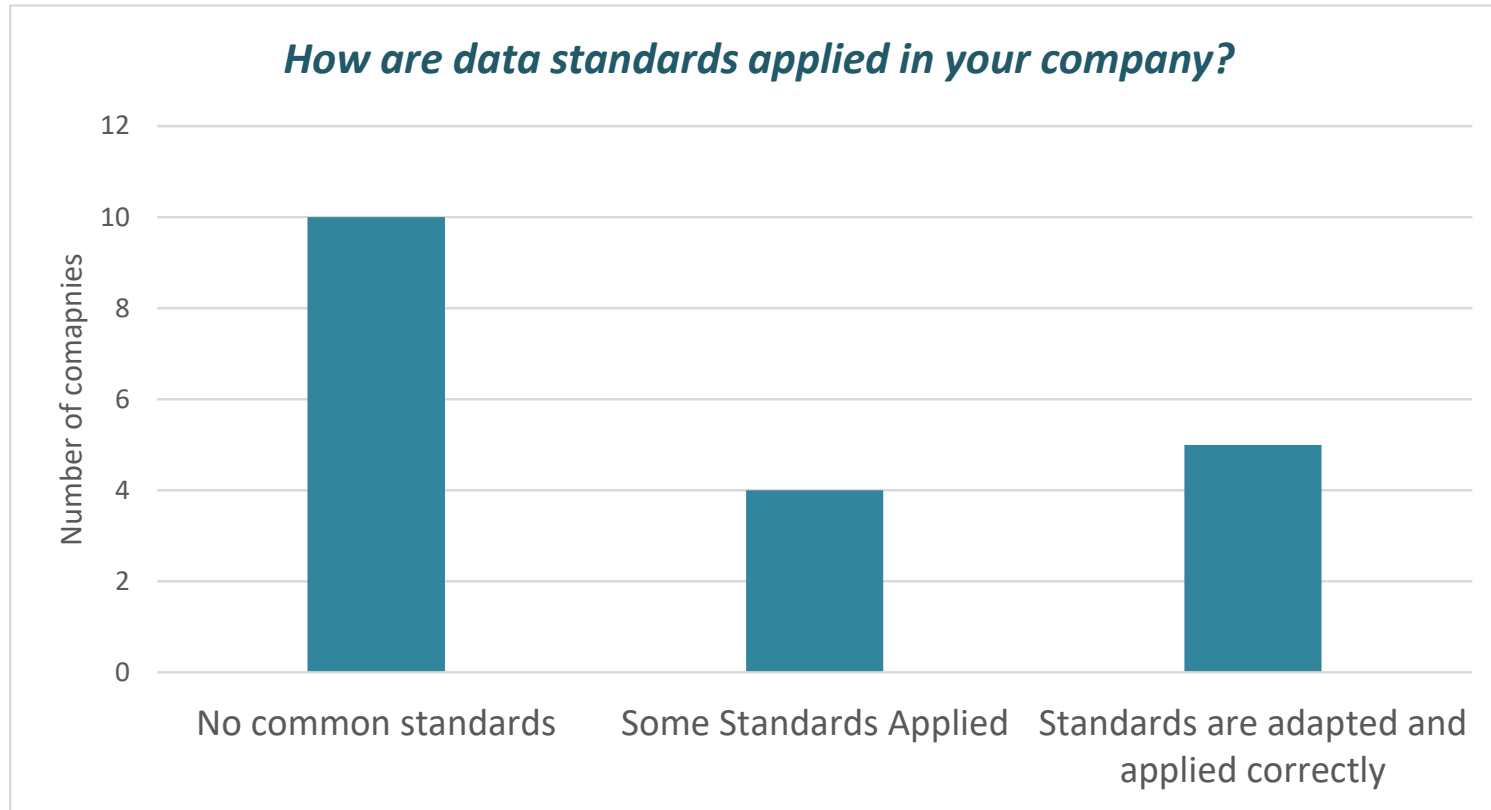
■ Commercial ■ Development



- In Development
 - 3 companies have common data systems in Development
 - Most (9) have only some common data systems
 - 8 companies have siloed / mostly siloed systems
- In Commercial – higher maturity
 - 9 companies have either Core or Mostly common systems



DATA STANDARDS – MATURITY (NEW QUESTION 2021)



- 10 companies have no common standards
- Relevant standards are used in 5 companies



CHALLENGES

- Lack of skillsets to support projects effectively
- Regulatory hurdles – adoption, framework
- Reliability of equipment

- Alignment between functions
- Model complexity – lifecycle
- Cost/benefits (for OTC products)
- Low dose challenges
- Integration to older Data/automation systems

2020

- Lack of available skills
- Budget constraints
- Data infrastructure, data access
- Vendor readiness, technology reliability
- Methods: Complexity of validation, not always sensitive enough,
- Regulatory challenges – global acceptance
- Lack of engagement between Development / Commercial:
- lack of strategy, lack of alignment
- Business case not well defined for commercial deployment
- Complexity to retrofit, need to integrate early during development
- Lack of capability from CRO/CMO
- Quality acceptance

Note:

- Complete list in Back-up



ENABLERS

- **Leadership engagement (x10)**
- **Dedicated resources / experts**
- **Budget & resource**
- Training
- Business relevance / demonstrated successes
- PAT embedded in quality systems
- Strategy alignment
- Common data ecosystem
- Adoption of new platforms e.g. continuous

2020

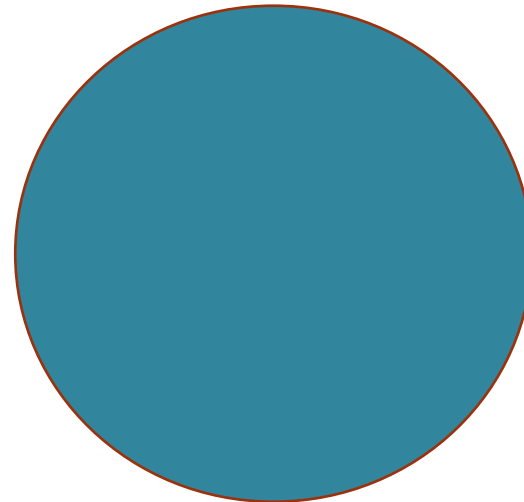
- Strong Strategy and vision, leadership, sponsorship from Executive level
- Deep expertise and collaboration
- Skill set (Training, hiring)
- Alignment with continual improvement and strategy
- Demonstrated successes, Business value
- Digital Transformation / Robust PAT infrastructure / data management
- Integration of PAT in the Control Strategy/manf systems
- Move to Continuous Manufacture

Note:

- Complete list in Back-up



WOULD YOU BE SUPPORTIVE OF SHARING THE BLINDED RESULTS OF THIS SURVEY WITH ORGANIZATIONS THAT ARE REPRESENTED AT PPAR?

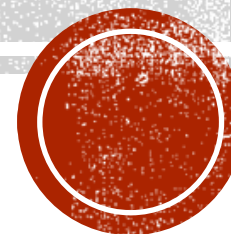


100% YES

Same as last year!!!!



BACK-UP



ENABLERS – COMPLETE LIST OF RESPONSES

Respondents	Responses
1	leadership engagement Agreed global roadmap
2	1 - Develop strategic roll-out plan that includes implementation plan to ensure application meets customers needs. 2 - Having data analysis/mining solutions that help organize/manage complex data streams; e.g. SynTQ, Sipat, PharmaMV, Lumetics etc. 3 - Enhance collaboration across SMEs with various skillsets; analytics, process engineers, statisticians etc.
3	good collaboration with stakeholders in key functions increasing pull from S&T analytical for rapid methods demonstrable success on POC, big organizational impact
4	1. Sponsorship from leadership 2. Technology maturity and availability 3. Criticality to key business outcomes
5	Digital Transformation programs, growing support by leadership for improved process and quality predictability, and improvements in data integration and RPA
6	a) Management support b) PAT ambassadors c) Resource allocation
7	Leadership endorsement Capital Investment Next-Gen Manufacturing (i.e. Continuous)
8	(1) Support and sponsorship from senior leaders across R&D and manufacturing (2) Technology "champions" that have the time and resources to dedicate to technology implementation
9	cross-functional collaboration, in-house expertise, senior leader support
10	1. working with vender to customize PAT tools to fit our purpose 2. working with process and analytical teams together
11	Flexibility Change in development strategy to include PAT method development Change Product Supply funding option from low cost to high capability measurement tools
12	support from management; sme
13	Scientists Commitment from management Funding
14	Communication across network Alignment for platform technologies.
15	- Support from the Top - QbD approach applied during development - PAT embedded in the Quality System
16	Matrix team of adhoc members, knowledge sharing across groups, different PAT strategies have been endorsement with project teams
17	Management sponsorship Talented PAT SMEs
18	necessity of continuous manufacturing/expectation for cycle time reductions/drive toward Industry 4.0
19	- Dedicated / ring fenced resources - Positive case studies - Resilience/PAT Leadership/Senior Management Belief/support



CHALLENGES — COMPLETE LIST OF RESPONSES

Respondents	Responses
1	Internal skills culture fundamental technical understanding
2	1 - PAT instrument suppliers are a concern for GMP compliant implementation with suitable support infrastructure 2 - Still challenging interacting with global Health Authorities for PAT marketing applications and implementation / audits. 3 - complexity of implementing chemometric models across a difficult analyzer landscape.
3	corporate support (staffing) across the enterprise strategic alignment between functions consistent definition of "success"
4	1.Investment cost 2.Perceived impact to project timelines - current capability of technology 3.Risk aversion - regulatory change
5	Analyzer reliability and plug-n-play capability, analyzer cost, lack of harmonization in agency support and expectations
6	1. Integration of PAT into existing manufacturing IT systems 2. Miss knowledge on health authorities expectations 3. Practical experience with developing PAT based control strategies in new manufacturing facilities
7	Regulatory Submissions PAT Talent Lifecycle Management
8	(1) Understanding the requirements for transitioning from monitoring to control in GMP manufacturing (particularly for PAT that requires chemometric models) (2) Developing compelling business cases (3) Defining strategy for model validation and life cycle management
9	regulatory hurdles
10	1. current technology is not good enough to implement in real-life practice. 2. dealing with multiple venders makes difficult to harmonize streamlined PAT workflow (eg. instrument-controller cross talk) 3. too expensive/ investment 4. Regulatory acceptance
11	No clear FDA guidance/investigator acceptance for PAT in OTC products Cost benefit for smaller margin OTC products
12	low dose; instrumentation
13	Instrument/mechanical robustness Complex process interface Low or complex dosage (measurement limitations) Legacy operating systems Supply chain complexity (robustness to second sources)
14	Too few PAT practioners for the needs
15	- Regulatory hurdles from multiple regions regarding model lifecycle management (post validation) - Clearer regulatory framework for model validation - Available talent available from recruiting pool
16	Resources with Expertise, lack of corporate endorsement and resources for full PAT team
17	Monitoring vs. Control and Regulatory huddles
18	staffing with appropriate skills/old architecture of digital systems/cost and sensor limitations
19	- Convincing Business Case - Technology (not off the shelf, difficult to implement) - Resources at site level for implementation

