



RAPID MICRO METHODS

PPAR 2013



Alternative /Rapid Microbial
Methods Team

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Rapid micro-biologic testing

- Success stories: in-line TOC, etc..

Value, gaps, and roadblocks

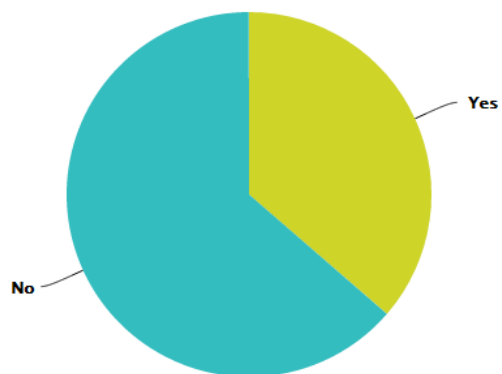
- RMM testing and continuous mfg

- ***Rapid Micro Methods are ~ 5 years behind PAT systems.*** J Weber
 - Opportunity to take lessons learned and apply to RMM arena.
 - Unfortunately consultants are reaping the benefits (\$)
 - Lack of guidance and understanding

“It should be noted that **microbiology** is a scientifically based discipline that deals with biological principles substantially different from those of analytical chemistry and engineering disciplines. Many times it is difficult for individuals without specific microbiological training to make the transition.”

Does your company use Rapid Micro Methods?

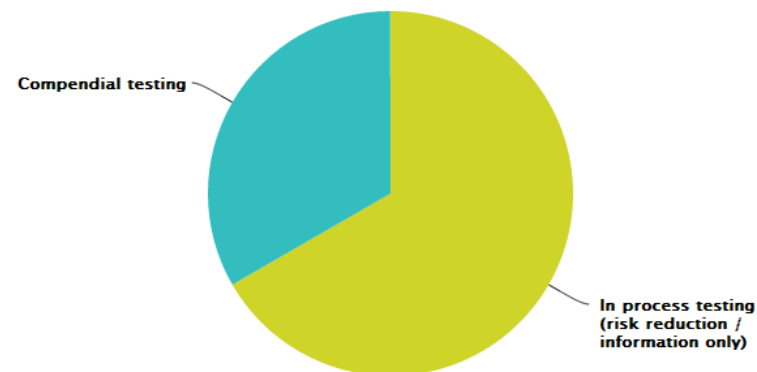
Answered: 11 Skipped: 0



Answer Choices	Responses
Yes	36.36% 4
No	63.64% 7

How are RMMs used at your company?

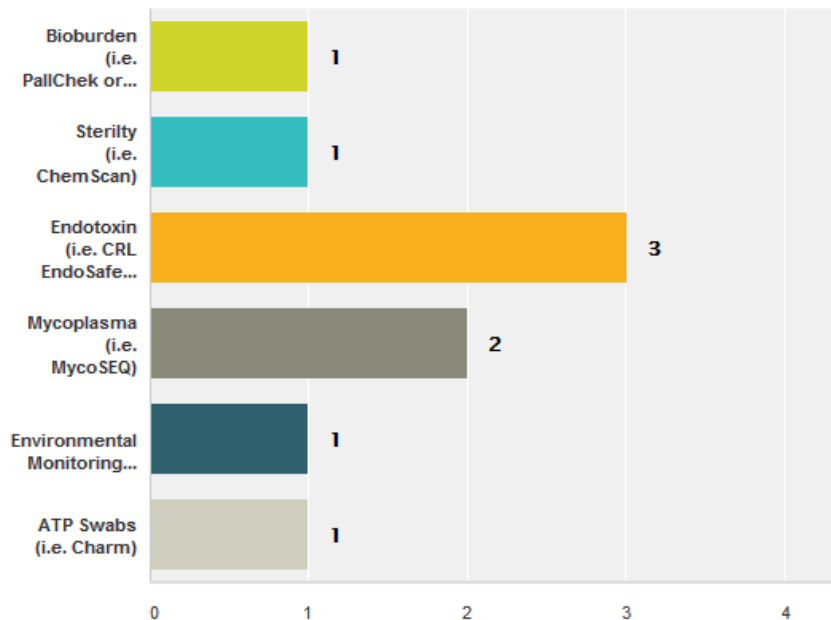
Answered: 3 Skipped: 8



Answer Choices	Responses
In process testing (risk reduction / information only)	66.67% 2
Compendial testing	33.33% 1
Total	3

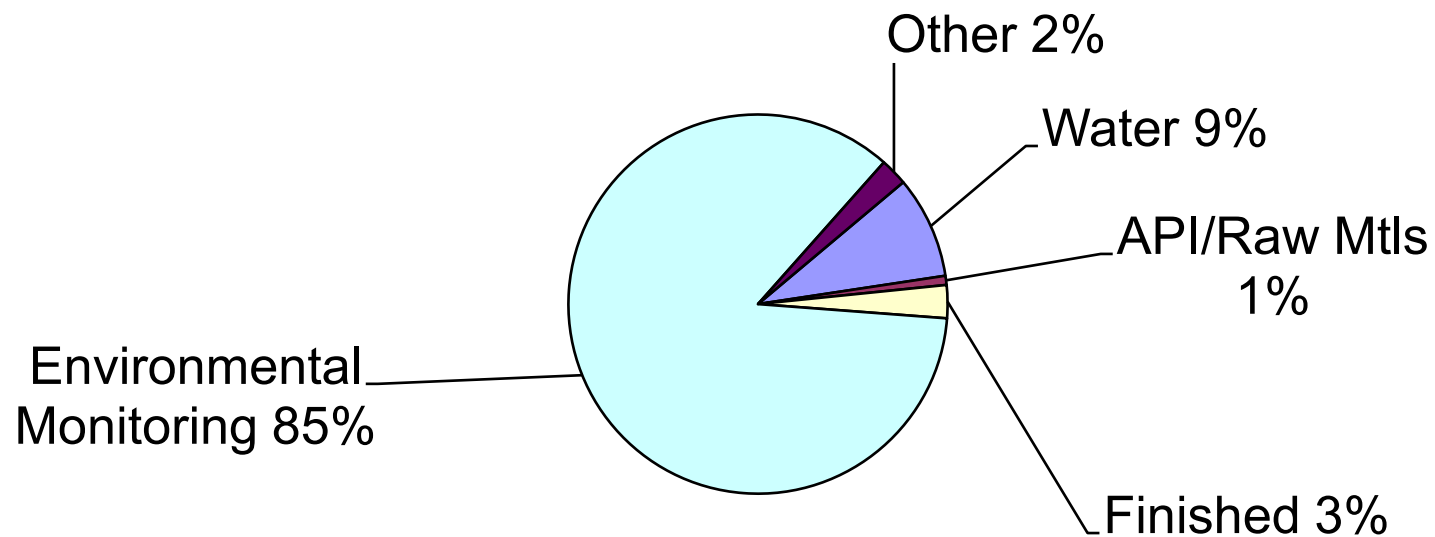
The RMM systems our company has implemented are ____

Answered: 3 Skipped: 8



what is the biggest gap for RMM systems?

- Staffing
- Environmental Monitoring





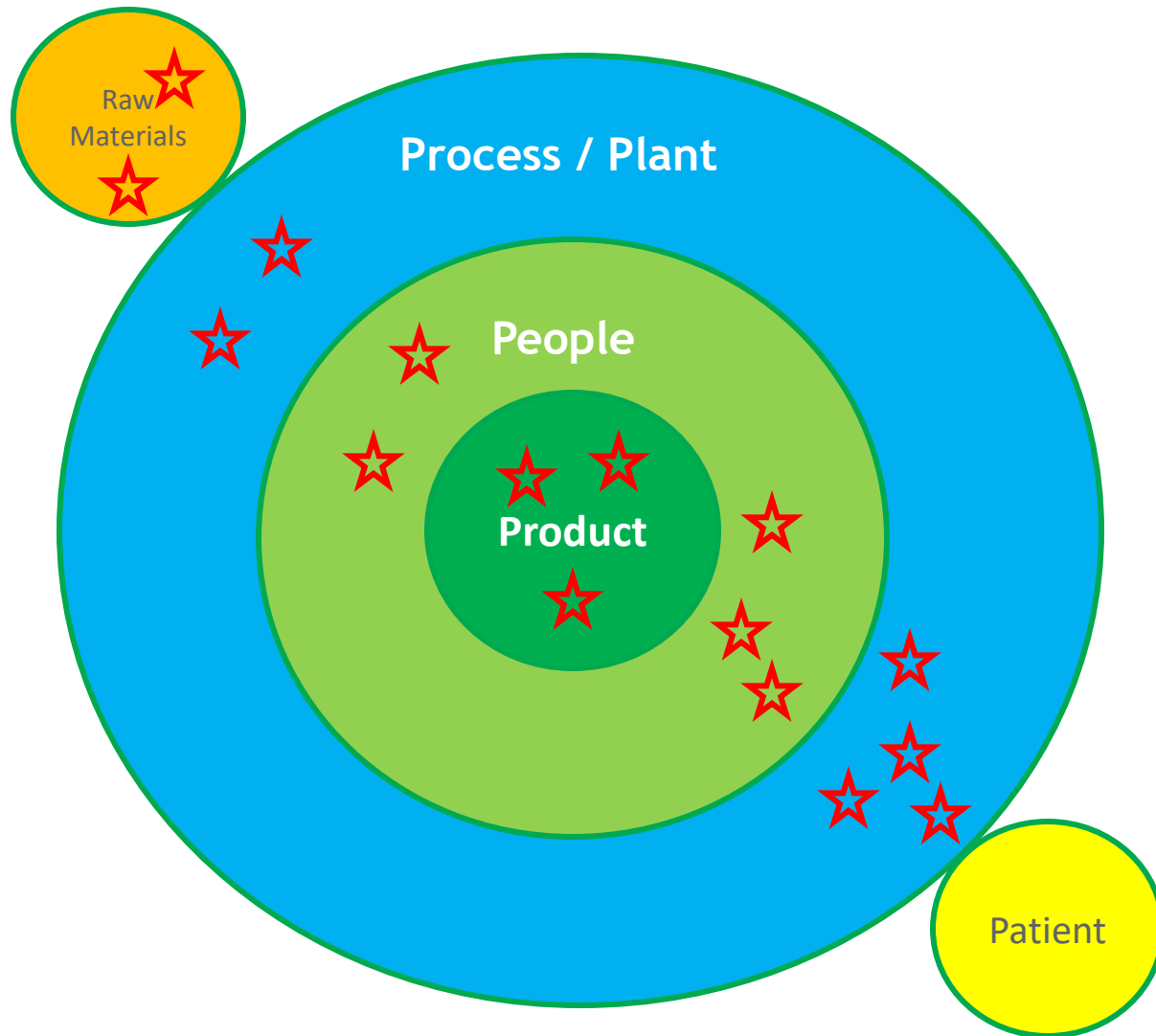
Manufacturing (PAT)

- In-plant testing
- Raw materials screening
- Process decisions
- EMA / EP support

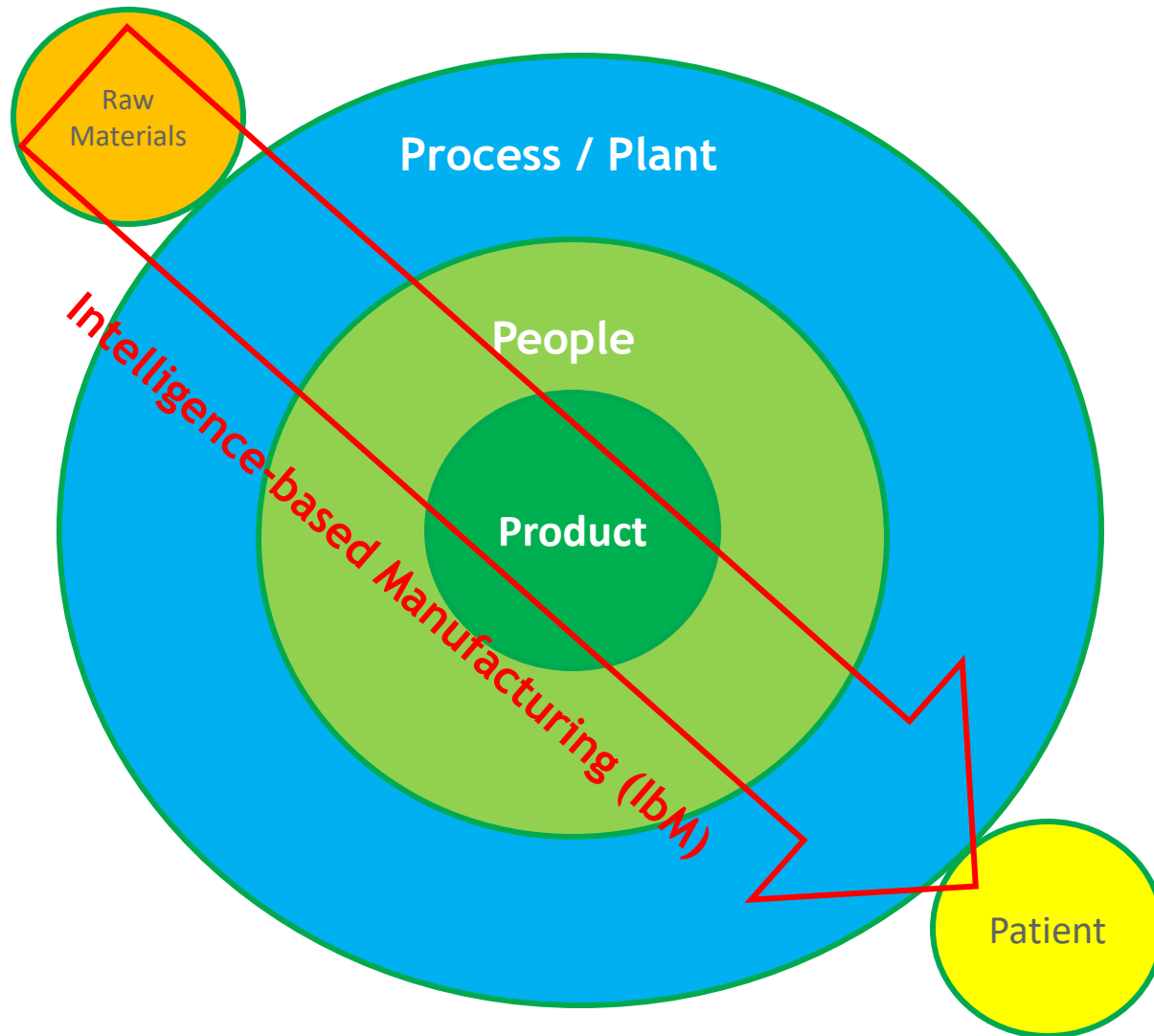
QC (Micro Labs)

- Lean labs
- More automation
- Less “micro” training
- USP / FDA aligned

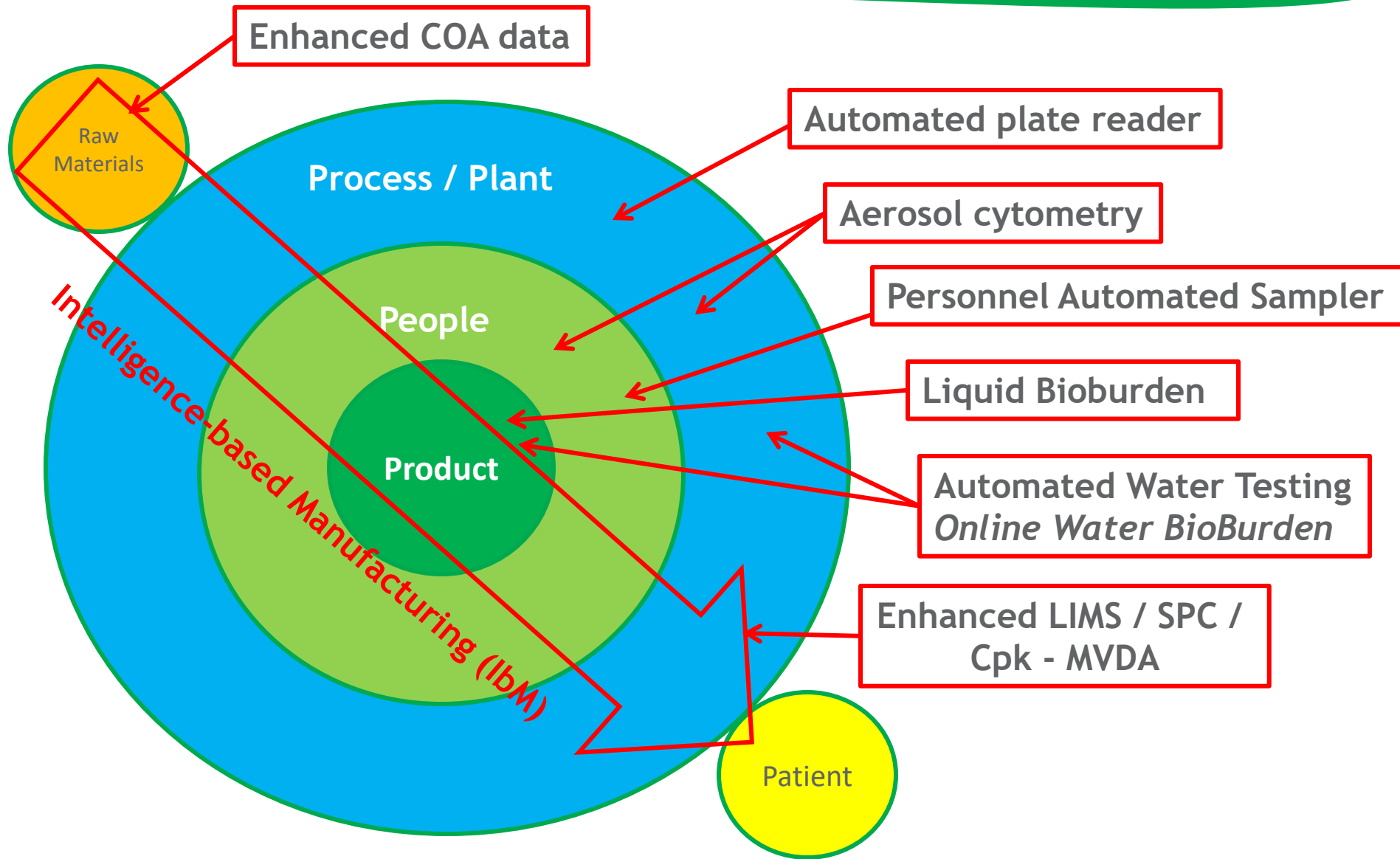
Is this an opportunity to align micro with PAT and engineering?



- Discrete point sampling
 - EM
 - Raw Materials
 - Personnel
 - Sterility testing
- Limited temporal information
- Retrospective
 - “all or nothing”
 - Silos



- Continuous monitoring
 - Holistic control
 - Raw material characterization is part of process
- Extreme temporal information
 - Infinite sublots
- Real Time Release Testing (parametric release)



- **Online Total Organic Carbon for Water**
 - Minimal regulatory impact to online testing
 - Improved process control over grab samples
- **No guidance from USP, EP or JP initially for use of online testing**
 - ASTM guidance E2656-10
- **Companies have moved to RTRt water release**
 - Business benefit

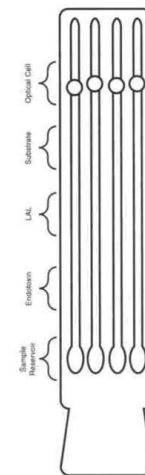
Technology: Chromogenic Limulus amoebocyte lysate, or LAL assay. USP <85> and EP 2.6.14 Method D. A simplified and rapid endotoxin testing method.

Recommended Applications

- Compendial endotoxin testing
- Development studies
- In-process testing

System Roles

- Water testing (routine and post-maintenance)
- Buffer hold times
- Cleaning verification
- Endotoxin removal efficiency
- Final Product testing



- **RMM systems are orthogonal to compendial testing**
- **Different units**
 - CFU versus BioCounts
- **How to react to new information?**
 - Regulatory requirement (i.e. heavy metals)
 - Product Quality
- **Interaction with Regulatory Agencies**

- **Pfizer would like to see the development**
 - Online Water Testing
 - At-line bioburden
 - BioBurden Testing
 - Simplified testing
 - Online Endotoxin
 - Environmental Monitoring



PROBLEM SOLVING

When the obvious eludes you.

Classic culture assay is less than perfect!

