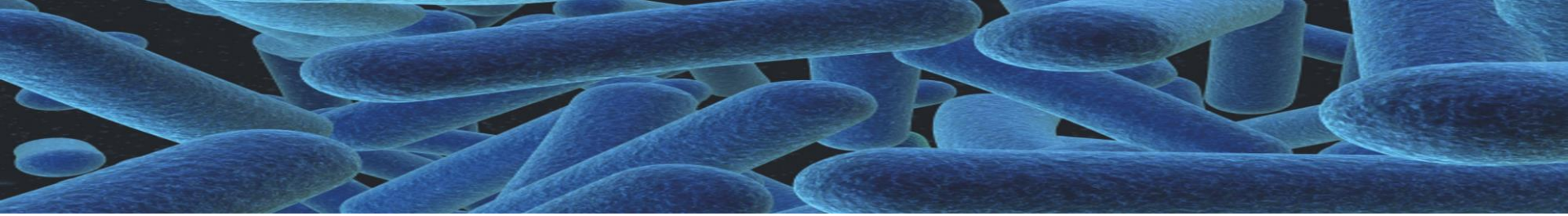
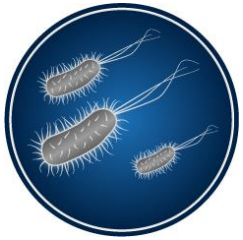


Evaluation, Validation and Implementation of Alternative and Rapid Microbiological Methods

Return on Investment

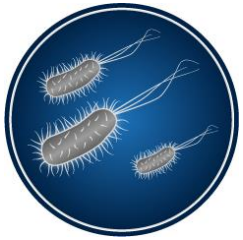
Michael J. Miller, Ph.D.

MICROBIOLOGY CONSULTANTS, LLC



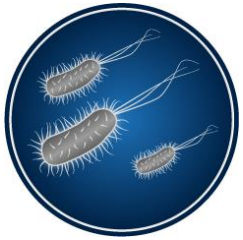
Develop a Business Case

- These are tough times for the introduction of new technologies, including RMMs
- Initial costs associated with feasibility studies, validation testing and installation activities can be significant
- It is unfair to only examine the up-front costs when evaluating a new project, as there can be substantial long-term cost savings or avoidances that may be realized
- Develop a comprehensive economic analysis to support the decision to purchase, validate and implement a RMM



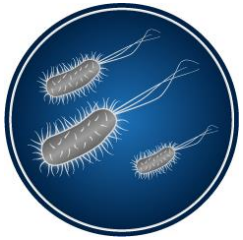
Develop a Business Case

- Compare the overall costs associated with the conventional method and the proposed RMM
  1. Direct and indirect costs for the conventional method
  2. Direct and indirect costs for the RMM
  3. Cost savings and/or cost avoidances associated with the RMM
- When all of the elements associated with the costs and savings for both the conventional method and the RMM have been collated, this information can then be used in financial models to calculate whether there is an economic advantage for implementing the RMM



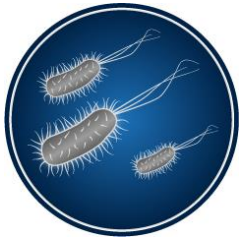
Costs Associated with the Conventional Method

- Cost per test (media, consumables, regents and supplies)
- Total sampling, transfer to lab, preparation, testing, data handling and documentation resource time per test (hours)
- Cost of labor including salary and benefits (local currency per hour)
- Cost to dispose of used media, reagents and consumables per test
- Laboratory equipment depreciation, calibration and qualification
- Overhead for laboratory and storage space
- Data management and record retention
- Preventive maintenance and service contracts for lab equipment



Costs Associated with the RMM

- Same as for conventional method plus:
- Capital costs for initial investment
- Training
- System qualification and method validation costs
- Software purchases and updates
- Regulatory filing costs, if applicable



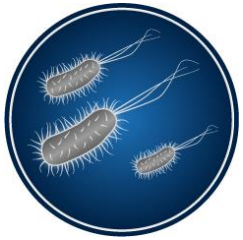
Cost Savings/Avoidances Associated with the RMM

- Reduced testing and finished product release cycle times
- Reduction or elimination of laboratory equipment and overhead
- Reduced headcount
- Reduced repeat testing and investigations, lot rejection, reprocessing and rework
- Reduction in plant downtime
- Increased yields
- Reduced raw material, in-process and finished goods inventory holdings

Financial Models

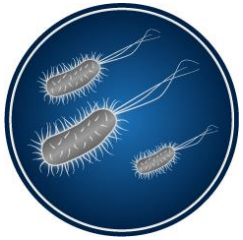
- Return on Investment (ROI)
- Payback Period (PP)
- Net Present Value (NPV)
- Your finance organization is a great resource for helping to develop an appropriate financial model

"Unfortunately, we were a little off-target again this quarter.



Return on Investment (ROI)

- ROI is the ratio of money gained or lost (realized or unrealized) on an investment relative to the amount of money invested
- Compare the cost of performing the conventional method with the cost (and savings) of using the new RMM
- The information is reported as a percentage (%) and usually represents an annual or annualized rate of return



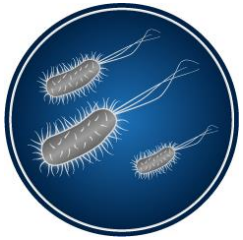
Return on Investment (ROI)

ROI = Annual Net Benefits / RMM Investment

$$ROI = \frac{([\sum \text{Costs}]_{CM} - [\sum \text{Costs} - \sum \text{Savings}]_{RMM})}{\text{RMM Investment}}$$

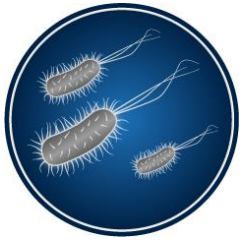
CM = current method

RMM = rapid microbiological method



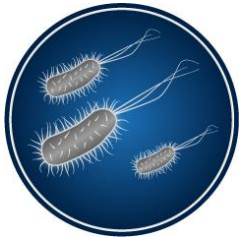
Return on Investment (ROI)

- The ROI can be calculated for the first year (where the initial capital investment will be made) and then every year thereafter once the RMM is routinely used
- The rate of return can take on any value greater than or equal to -100%
- A positive value corresponds to an investment gain, a negative value corresponds to a loss, and a value of 0% corresponds to no change
- The higher the ROI number is, the greater the return the firm will realize on the initial investment for the RMM



Payback Period (PP)

- The PP is the time required for the return on an investment to "repay" the sum of the original investment
- In the context of implementing a RMM, this would be the time (usually in years) required to realize enough cost savings/avoidances to pay for the initial investment of the RMM capital equipment, qualification and implementation activities



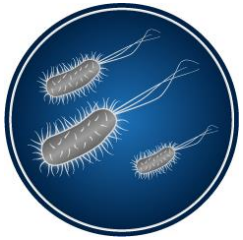
Payback Period (PP)

PP = RMM Investment / Annual Net Benefits

$$PP = \frac{\text{RMM Investment}}{([\sum \text{Costs}]_{CM} - [\sum \text{Costs} - \sum \text{Savings}]_{RMM})}$$

CM = current method

RMM = rapid microbiological method



Net Present Value (NPV)

- NPV is an indicator of how much value an investment or project adds to the company
- It is the total present value of a time series of cash flows, and is a standard method for using the time value of money to appraise long-term projects
- The NPV may provide information as to whether the investment in implementing a RMM would add value to, or subtract value from, the company over a period of time

Net Present Value (NPV)

NPV = Cash inflows generated by the RMM investment – RMM Investment (taking inflation and return into account)

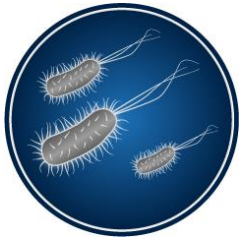
T: total period of time to consider

t: time of the cash flow

r; discount rate (e.g. company's investment yield rate)

Ct: cash amount at time t

$$NPV = \sum_{t=1}^{T} \frac{C_t}{(1+r)^t} - \text{Investment}$$



Net Present Value (NPV)

The period is usually 5 years for RMM investment, thus:

NPV = Year 1 cash inflow / $(1 + \text{discount rate})^1$

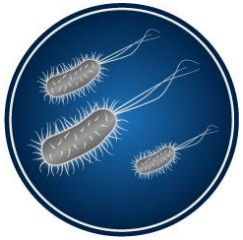
+ Year 2 cash inflow / $(1 + \text{discount rate})^2$

+ Year 3 cash inflow / $(1 + \text{discount rate})^3$

+ Year 4 cash inflow / $(1 + \text{discount rate})^4$

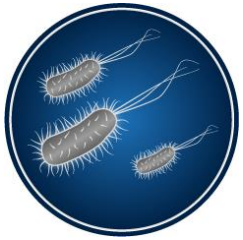
+ Year 5 cash inflow / $(1 + \text{discount rate})^5$

$$\text{NPV} = \frac{[\sum \text{Costs}]_{CM} - [\sum \text{Costs} - \sum \text{Savings}]_{RMM}\,[\text{year 1 to 5}]}{(1 + \text{discount rate})^{[1 \text{ to } 5]}} - \text{RMM initial investment}$$



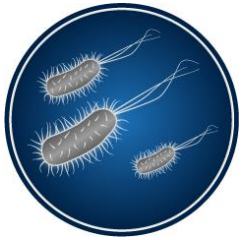
Net Present Value (NPV)

- When evaluating a new RMM, if the NPV is less than zero, the investment in the RMM would subtract value from the company and the project should not move forward
- If the NPV is greater than zero, then the investment in the RMM would add value to the company and the project would be accepted
- If the NPV is equal to zero, the RMM investment would neither gain nor lose value for the company and the decision to implement the RMM should be based on other criteria, such as technical, quality, regulatory and/or strategic factors not explicitly included in the calculation



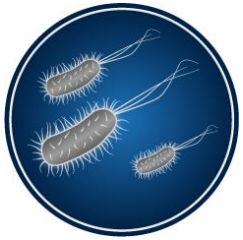
Develop a Business Case

- The results of the ROI, PP and/or NPV calculations can provide a company with a financial justification to purchase a RMM and initiate their validation plan
- Personalized financial analyses should be conducted for ***every*** RMM proposal to fully understand the savings potential
- This information should be used to complement the technical and business justifications for implementing a RMM for routine use



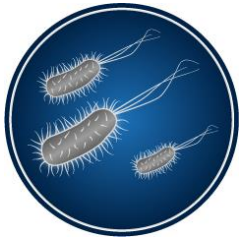
Develop a Business Case

- Some RMMs will provide a positive ROI (as compared with the current method) while others may not
- What attributes can contribute to a positive ROI?
  - Eliminate manual sampling and testing; automation
  - Reduced headcount
  - Higher sample throughput
  - Lower cost per test (consumables and supplies)
  - Time to result such that we can reduce product loss and downtime



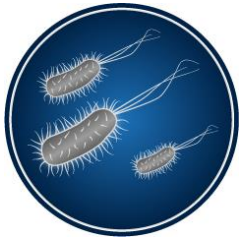
Case Study

- One company explored ways in which they can implement a RMM that will provide in-process monitoring capabilities while realizing significant cost savings
- After a review of their current microbiology program, the company identified active air sampling as their most expensive and time consuming activity, and performed a ROI calculation for for a real-time air monitoring RMM
- Published in:
  - *Miller, M.J., Rapid microbiological method and demonstrating a return on investment: It's easier than you think! American Pharmaceutical Review. 2009. 12 (5), 42-47*



The Scenario

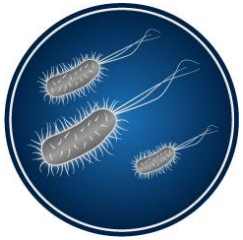
- A large fill-finish facility that processes 100,000 active air samples per year
- Manufacturing is performed in conventional cleanrooms
- The process is personnel intensive, resulting in environmental monitoring (EM) excursions on conventional media associated with three product batches each year
- Three product lots are rejected at a cost of $500K US per lot
- Three times each year, the affected line is shut down to conduct the EM investigations and no product is filled



Operating Costs

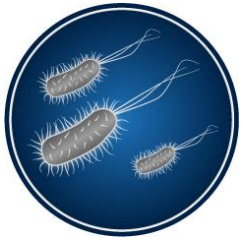
	Current Method	RMM Year 1	RMM Year 2+
Number of tests per year (1)	100,000.00	20,000.00	20,000.00
Cost per test (consumables, reagents, media)	1.00	0.00	0.00
Calculated annual cost per test	100,000.00	0.00	0.00
Total sampling, testing, data handling and documentation resource time per test (hours)	1.00	0.10	0.10
Cost of labor (local currency per hour)	50.00	50.00	50.00
Calculated annual labor	5,000,000.00	100,000.00	100,000.00
Cost to dispose of used media and reagents per test	0.50	0.00	0.00
Calculated annual disposal costs	50,000.00	0.00	0.00
Annual cost associated with lab equipment depreciation, calibration, qualification, space (2)	50,000.00	432,000.00	432,000.00
Annual maintenance and service contracts (3)	20,000.00	0.00	518,400.00
Total Annual Costs	5,220,000.00	532,000.00	1,050,400.00

(1) Because the RMM operates continuously, in this example we will assume that the actual number of tests performed can be reduced by a factor of 5 as compared with the CM.
(2) Depreciation for RMM equals 10% of capital cost (assumes 48 units at $90,000 USD each; pricing used is representative and is for calculation purposes only, as the supplier may vary the price based on configuration and quantities purchased).
(3) Annual maintenance and service contracts start in year 2 and are based on geographic region and services contracted. Pricing assumed equals 12% of capital cost (48 units at $90,000 USD each).



RMM Cost Savings

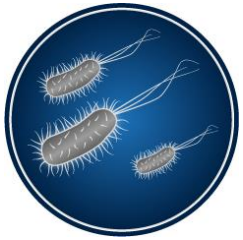
Reduction in lot rejection as a result of being able to segregate product during the detection of an actual EM excursion in real time (assumes the loss of three batches; each with a $500K USD value)	1,500,000.00
Reduction in the loss of additional product being made due to manufacturing down time during an EM investigation (assumes three batches not being made; each with a $500K USD value)	1,500,000.00
Reduction in investigation cycle time, lab resources, repeat testing and deviations during investigations of an EM excursion	350,000.00
Reduction in operator down time during investigations of an EM excursion	60,000.00
Total RMM Annual Savings	3,410,000.00



RMM Investment

	RMM Year 1	RMM Year 2+
Capital cost (1)	4,320,000.00	0.00
Qualification and regulatory costs	100,000.00	0.00
Training	10,000.00	5,000.00
Total RMM Investment	4,430,000.00	5,000.00

(1) Assumes the purchase of 48 instruments at $90,000 USD each.



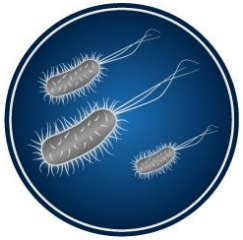
ROI Calculations

$$\text{ROI Year 1} = \frac{([5{,}220{,}000 - [532{,}000 - 3{,}410{,}000])}{4{,}430{,}000}$$

- The resulting ROI for the first year is equal to 1.828 or 182.8%, resulting in a first year savings equal to $3,668,000 USD

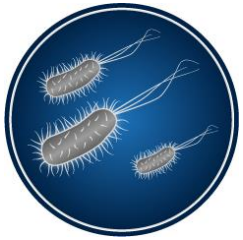
$$\text{ROI Year 2+} = \frac{([5{,}220{,}000 - [1{,}050{,}400 - 3{,}410{,}000])}{5000}$$

- The resulting ROI for the second and subsequent years is equal to 1,515.92 or 151,592%, resulting in second year and subsequent annual savings equal to $7,574,600 USD



ROI Calculations

- The five year ROI = 867.2%
- The five year cost savings = $33,966,400 USD



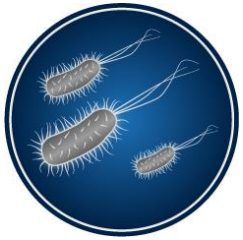
Payback Period Calculation

$$PP = \frac{4{,}430{,}000}{([5{,}220{,}000 - [532{,}000 - 3{,}410{,}000])}$$

- The **Payback Period = 0.55 years (6.6 months)**

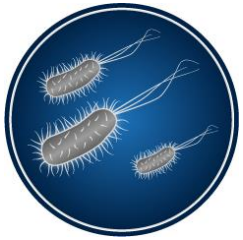
Summary

- This case study represents one example; your results may be significantly different
- Perform a ROI calculation for each RMM you want to implement
- Even if the ROI shows little or negative value, other factors may take precedence
  - Product quality
  - Process knowledge
  - Continuous improvement



What You Can Do

- This presentation provided one example of how a firm can use cost analysis models to support the business justification for implementing a RMM
- You can apply these models to any RMM
- Personalized financial analyses should be conducted for *every* RMM proposal to fully understand the savings potential
- This information should be used to complement the technical and quality justifications for qualifying and implementing a RMM for routine use



What You Can Do

- Some RMMs may not provide a positive ROI
  - Type of technology
  - Manual vs. automated systems
  - Applications
  - Products or processes
  - Facilities
  - Capital costs
  - Cost per test
  - Labor
- In these cases, some companies have placed a greater importance on the technical and quality attributes do implement the RMM

Summary and Discussion

- Senior management will require this type of information before making any financial commitments
- Work with your finance department
- Suppliers may have financial models you may use