WHITE PAPER

A Path to Prescriptive Maintenance in Biomanufacturing Operations

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01 Introduction

This paper presents various accepted maintenance models and provides practical guidance to enable more efficient equipment with the help of advanced process instrumentation.

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Proper maintenance of equipment in a production environment is essential to product quality, worker safety and return on investment. Although industries may vary by product types, regulatory compliance, and manufacturing methods, the maintenance organization is an essential business function. Maintenance Operations must be agile enough to adapt to changes in the business environment and technological advancements.

This paper presents various accepted maintenance models and provides practical guidance to enable more efficient equipment with the help of advanced process instrumentation. Intelligent equipment makes for a more intelligent maintenance model program. The result: decreased operating costs, improvements in maintenance team morale and engagement, increased productivity, and a more thorough integration with automation and enterprise resource planning (ERP) systems.

A company’s maintenance organization is likely to be employing some form of one of the well-established maintenance model types listed on the next page. Broadly speaking, a maintenance model encompasses how resources are applied and how data is used in the production environment.

Maintenance Models

Understanding maintenance models is key to optimizing operations and preventing costly, time-consuming breakdowns.

	Reactive Maintenance	Preventative Maintenance	Condition-Based Maintenance	Predictive Maintenance	Prescriptive Maintenance
How it Works	Action based on failure or event.	Action based on fixed schedule.	Action based on system feedback or alarm state.	Monitors multiple data streams over time to predict event(s).	Pred + instructions on how and what to replace during event(s).
Pros / Cons	Pro: Minimize upfront effort Con: System downtime long during event	Pro: Scheduled equipment downtime Con: Cost and inventory of spare parts	Pro: Improves OEE based on alarms or thresholds Con: Sensors and fault correlation analysis	Pro: Efficient scheduling of resources to handle for equipment engineer	Pro: Same as predictive with right time, right part, right technician Con: Development time
OEE Score	2/5	2.5/5	4/5	4.5/5	5/5
Actions to Achieve Next Model Type	Review system failure modes and recommended manufacturer maintenance schedule	Implement a digital control system that alerts during out-tolerance process conditions	Multiple data streams over time versus multiple process conditions to predict key components' interval period	Review more data to link repair activity with failure mode	Sustaining continuous improvement
Relative Effort to Next Step	Low	Medium	Medium	High	N/A

Terms to Know

Overall Equipment Efficiency (OEE): Associates how well a company makes use of facilities, material and time.

Choosing a Maintenance Model

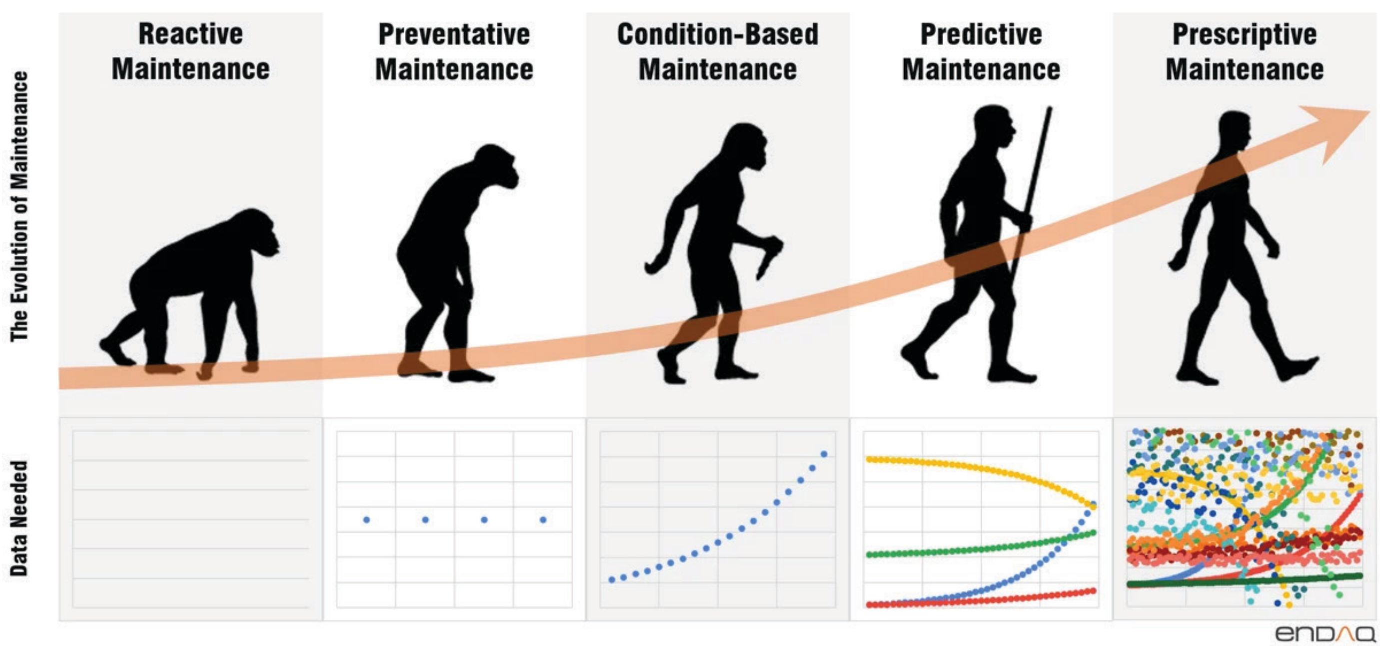
The chosen model type and the extent to which it is being applied depends on numerous factors, including business maturity, cost-benefit impact, equipment and process sophistication, equipment age, facility infrastructure, and regulatory support, among others. The maintenance organization's state – defined by its capacity, skills, tools, objectives, and performance – must align with the model and its application within production.

Focusing on maintenance operations as the part of the organization that will contribute to an overall improvement in the business by applying data more thoroughly within the maintenance model, we will again make use of our model biopharmaceutical industry and bioreactor as the bioprocess equipment, from the previous articles. However, the reader should be able to identify similarities and apply the discussion to their own industry and product.

Key Takeaway

As you read this paper, consider which maintenance model you operate with today and if it adequately supports your current business and assets. And, perhaps even more critically, consider if there are business or equipment changes driving the need to reconsider where you are with the current model or if a new model would better suit these changes.

We presuppose that continuous improvement, or kaizen is a driver in all business functions, Maintenance Operations included. Improvement in this area of the business may be defined as improvements within a given model or a transition to another, higher-level model type. Looking at the evolution of maintenance models depicted in the graphic below, evolution is driven by data need, availability, and utility. Availability and utility can facilitate Maintenance Operations' kaizen effort. Improving OEE: greater equipment availability, less wasted material, and more efficient troubleshooting could be the focus of such an effort.



Graphic courtesy of Endaq

02 Mapping Your Journey

Different Starting Points, Different Destinations
If a prescriptive maintenance model is the ideal destination, or future state, representing the pinnacle of evolutionary improvement, is there a single path to this destination? Probably not, depending on your starting point, or current state. Your current state will be defined by one or more of the factors mentioned previously, such as equipment age or facility infrastructure. Also, your starting point is partly established by the state of Maintenance Operations, in particular, capacity, skills, and tools.

We will briefly outline three starting point scenarios. Since we contend that with more, and richer data available from IIoT devices, more effective and efficient maintenance programs are achievable. Each scenario incorporates these intelligent devices.

1. **Retrofitting a device into at least one piece of equipment:**
   An opportunity becomes available as the result of an MFC failure due to system contamination from a backstreaming incident. The bioreactor's design, at the time it was built, included analog MFCs. This failure offers the possibility to introduce digital MFCs along with their available data. Such a change would be a small but useful step along a path to improve the use and maintenance of this bioreactor.

2. **Replacing a piece of equipment, or unit operation in a production line:**
   In this scenario the opportunity could arise because the bioreactor reached the end of its service life. Alternatively, the business could be adding a new product to a current production line, and the existing bioreactor is not adequate to produce it. In this situation, the bioreactor needs to be replaced while the other production equipment can remain. This is a bigger step along the path but exists as only an improvement to a single unit operation.

3. **Production capacity needs to increase:**
   The business is growing, and a new production line needs to be purchased. The capacity expansion could be associated with a business introducing its first product or a well-established business increasing production to meet greater market demand. The former case offers the opportunity to start from day one with bioreactors designed and built with intelligent, data-rich devices, including MFCs. The latter case could be more complicated. The well-established business already has a production line. The existing production line could have been delivered with analog or digital devices, among them, MFCs in the bioreactor. If analog, the choice could be to move to digital, thereby making a significant step along the path to a new destination. Remaining on either an analog or digital platform is not about journey since the respective start and destination are the same.

Hopefully, as these scenarios were able to demonstrate, starting points can vary. Consequently, the destination and the path taken can vary, too. Before charting your course, it is essential to get your bearings. In other words, know where you are starting from – the current state; what destination, or future state can be reached; and determine what is needed to get there. The journey and ultimate destination will have an important impact on the overall business. Therefore, this is a cross-functional activity and should involve all relevant stakeholders.

Integral to this activity, will be answers to an innumerable number of questions, some general, some more specific. Questions may include, but are not limited to, these categories:

- **General:**
  - Are there already other changes driving the reconsideration of how some or all the business functions operate?
  - How would a change from analog to digital technology affect:
    - facility and information technology infrastructure,
    - staff skill development and training,
    - or maintenance tools (e.g., software, signal analyzers)?
  - Will an improvement effort have sufficient value to the business?

- **Maintenance Operations:**
  - Which maintenance model best characterizes your current operations?
  - Does it make good use of facilities, equipment, and process data?
  - Does it adequately support current business needs?
  - Can the current maintenance model adapt to changes in the business, including changes in facilities, equipment, or process?

- **Project:**
  - Will your given scenario fit into a capital project or some form of maintenance project?
  - Which stakeholders should be involved?

The graphic in the next section represents eight focus areas, to aid you in getting your bearings. Additionally, these eight areas can serve as sign posts along the path to your final destination.

03 Application to Real-World Examples

Effective Use of Equipment Data
It may be more likely than not that you have process data, items like pH, RPM, gas flow rate, temperature; but machine data (bioreactor machine) may be lacking. The lack of machine data may be a consequence of its design. More specifically, the lack of intelligent (IIoT) devices capable of reporting pedigree, performance, or health parameters. These parameters, when associated with process specific data, may facilitate significant progress along the maintenance model path thereby achieving better value from Maintenance Operations.

Effectively using equipment data for maintenance involves several best practices to ensure data quality, actionable insights, and optimization of maintenance processes.

Guideposts Along Your Journey

- **Data Collection & Integration**
- **Data Quality Management**
- **Collaboration & Communication**
- **Training & Skill Development**
- **Continuous Improvement & Feedback Mechanisms**
- **Scalability & Flexibility**
- **Regulatory Compliance**
- **Leveraging External Expertise**

Applying the Eight Focus Areas

The side-by-side comparison below is intended to provide real examples of the eight focus areas. The four real-world examples following that are meant to show some practical comparisons on the impact of data and the realization of specific maintenance models. In our first paper in this series, we introduced gas mass flow controllers (MFCs) as critical components of the bioreactor. Now, we will apply these eight focus areas to two MFC platforms from Brooks Instrument – one analog and one digital.

The 5850e MFC is an analog device launched in 1983 and continues to be an industry standard. Launched in 2020, the SLA5850 MFC with the Biotech options package is a complete digital offering with the EtherNET/IP interface capable of delivering pedigree, performance and device health data. Many users are content with a 40+ year old platform or simply may not be aware of the system advantages unlocked via the latest platform. The examples listed below are from the context of the utility of a bioprocess controller, utilizing one of these two MFC platforms.

5850e MFC Analog	SLA5850 MFC Advanced Digital
Data Collection and Integration	
A fully analog unit capable of closed-loop control via a 0-5 Vdc signal. No pedigree, reliability, or instrument health data available from the device itself. Available data is limited to the analog setpoint and gas flow output signal.	A fully digital unit capable of bi-directional communication over EtherNet/IP, including control and cyclic messages. 500+ attributes are available for pedigree, reliability, or instrument health data monitoring and maintenance model application.
Data Quality Management	
Routine analysis of historical flow output data to ensure reproducible results and lack of system-dependent noise.	Configuration management via the embedded web server. Configuration and alarm harmonization can be integrated with various DCS, PLC and data management systems. Data is traceable and attributable.
Collaboration and Communication	
Maintenance cycles are typically conducted on a preventative method. Historical data, physical documentation make work between stakeholders more of a manual process.	Maintenance cycles can be scheduled via the respective methodology utilizing one or more available attributes e.g., total gas hours and Performance FingerPrint. Available attributes can satisfy the data of multiple business stakeholders.
Training and Skill Development	
5850 requires manual adjustment of potentiometers for calibration. Multimeters and other electronic tools needed to own and maintain these instruments.	SLA5850 EtherNet/IP offers calibration checks, historians and configuration verification via the BEST software or web server tools.

5850e MFC Analog	SLA5850 MFC Advanced Digital
Continuous Improvement and Feedback Mechanisms	
Limited device data requires reliance on other record-keeping processes. No inherent pedigree, performance, health attributes prevents more detailed, higher level data integration. More difficult to achieve benefits of data-dependent maintenance model programs.	Analysis of system performance attributes and warnings could lead to intelligent adjustment of the SLA5850 thresholds based on the recipe sensitivity and vessel volume. For example, in heavy use area, include the backstreaming alarm to ensure no valve sequencing errors occur.
Scalability and Flexibility	
Limited in-device flow scalability and gas flexibility with an analog-only device. Monitor process faults versus flow and other critical utility conditions. Facilities that share the same gas feed and utilize a single pressure regulator to multiple reactors can experience inlet pressure fluctuations. Pressure droop from the regulator every time the high flow MFC on the higher volume reactor turns on. Should we isolate each reactor with its own regulator to avoid an initial flow fault -especially as the process scales up.	High turndown ratio for flow scalability. Multiple gas pages for gas flexibility. More or fewer attributes may be chosen for incorporation to support process, equipment, or business needs. Selection takes greater upfront work to identify which parameters may complement non-MFC data for better effectiveness in the maintenance program/ facility operation. Automation and ERP integration of attribute data requires thoughtful planning. The zero historian of the SLA could be adjusted to a very sensitive Cell & Gene Therapy process where flow accuracy is critical.
Regulatory Compliance	
Compliance solely dependent on metrology records and automation historian data. On-going calibration certification is external to device and depends on other standard work processes or 3rd party involvement. Material and pedigree certifications are as shipped.	Three levels of metrology/maintenance permissions and user access are built into the SLA 5850 via the webserver. Security ensures configuration and data integrity. A BEST software license is available to produce traceable on-going calibration certificates. Customers can easily access the pedigree of unit (including 3.1 material certs and NIST traceability) via the product QR code.
Leveraging External Expertise	
Continue to work with Industry best practices (ISPE/BPE/BPOG/Emerson Exchange, etc.) and leverage out of the older analog systems and components. Work on a risk-reduction/upgrade program when CAPEX investment is appropriate.	Continue to work with Industry best practices (ISPE/BPE/BPOG/Emerson Exchange, etc.) and leverage more utility out of the digital systems. Collaborate with the key OEM/Integrator and process instrument suppliers for best practices and emerging trends.

A Practical Comparison of Maintenance Models

Four Real-World Examples

Pump Leak

Includes Pressure & Temperature Sensors

Reactive Maintenance: Replace pump seal when no liquid source alarm noted.

Preventative Maintenance: Calendar-based replacement of seals.

Condition-Based Maintenance: Replace seals with pump rpm at zero exceeds high warning.

Predictive Maintenance: Ultrasonic flow data, pump temperature and rpm, pressure and temperature sensors from pump housing.

Prescriptive Maintenance: Pred + health function + instructions on how to repair and clean pump seal and tip to maximize performance.

Leaking Fitting

Reactive Maintenance: Fix quick connect fittings after a system leak discovered.

Preventative Maintenance: Calendar-based replacement of quick-connect fittings.

Condition-Based Maintenance: Replace fitting after pressure gauge drop noted below 3 psi.

Predictive Maintenance: MFC 1-6 zero historian, pressure gauge drop, system leak checks, Facility utilization rates for total monthly gas consumption.

Prescriptive Maintenance: Pred + flow totalizer + MFC fingerprint + System + leak repair instructions.

Noisy Dissolved Oxygen (dO_2) Signal)

Reactive Maintenance: Replace dO_2 sensor after system shut-down because of instability and inability to control.

Preventative Maintenance: Change sensor electrolyte routinely, discard sensor after defined number of in-service hours.

Condition-Based Maintenance: Change electrolyte more often, discard after fewer hours of service.

Predictive Maintenance: Use O_2 Flow totalizer, + MFC stability parameter, + dO calibration and process historian data.

Prescriptive Maintenance: Pred + Foam detection data + MFC fingerprint +instructions.

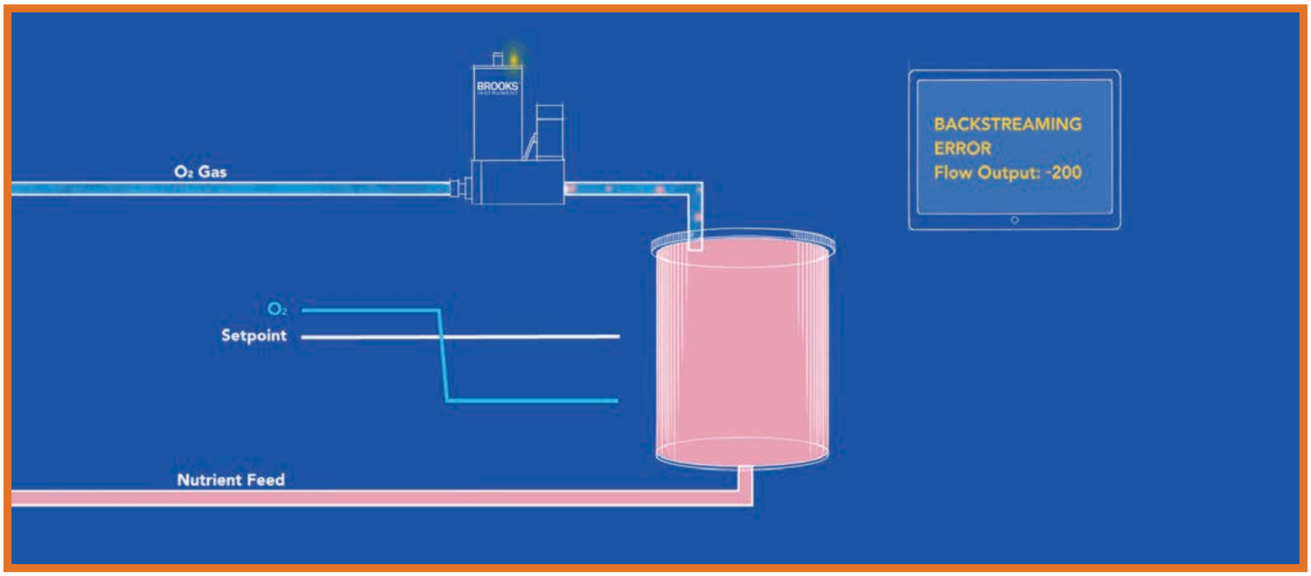
Backstreaming
Liquid Backflow from the Process

The scenario of backflow through the MFCs occurs more often than equipment and process engineers would like to admit. Liquid flowing through an MFC will cause immediate inaccuracy and requires system maintenance. This can occur by an inadequate dry-down after a SIP/CIP cycle, user override of the valves sequencing of the MFCs and a mechanical failure of the check-valve/filter. A gas MFC that has been exposed to a liquid can report a maximum negative flow as the thermal sensor outgasses. Let's walk through the five maintenance model maintenance actions for the backflow error.

Reactive Maintenance
Purge MFC when liquid enters for a check valve failure – MFC reports -erratic flow and -200 SLPM during the backflow condition.

The most costly method that involves waiting to replace the MFC, check-valve and dry-out the system when a back-flow event occurs. The bioreactor will alarm when the MFC is reporting a -200 SLPM of flow instead of the required 50 SLPM. If the End User does not have the critical spares of the check-valves and MFCs – the system can be down for several weeks.

Backflow Alarm from the MFC



Enabled by digital MFCs and Ethernet-based network protocols, the backflow alarm alerts the operator to stop the process due to bioprocess liquid being pushed backward through the flow path to the MFC.

Preventative Maintenance
Calendar-based replacement of check valves.

Replace the filters and check-valves on a yearly basis regardless of usage or potential issue. This approach allows some of the known failed components to be stocked and replaced before a backflow event occurs. This will require coordination from the maintenance team and the spare parts buyer.

Condition-Based Maintenance
Replace valves after a 3-5 psi change noted at pressure transducer upstream of bioreactor filter.

Monitor the pressure downstream of the check valve or filter. Scheduling a maintenance event based on a pressure variance/threshold could reduce unnecessary downtime and reduce spare inventory costs.

Predictive Maintenance
MFC zero historian, pressure gauge drop, close response from valve bank, filter housing temperature, bag pressure, inlet liquid flow rates.

This model should include continuously monitoring multiple data streams. The MFC (eg. Brooks Instrument SLA Series) can report if the sensors report a backflow condition with a full scale flow threshold and time limit. The data streams recommended would be pressure downstream of the filter, zero historian of the MFC, valve states, and SLA backstream alarm state. The multi-variable analysis is key to fine tune the correct sensitivity when the bio-controller proactively schedules a maintenance event.

Prescriptive Maintenance
Attributes of predictive maintenance model + liquid flow historian + auto procedure to idle the process, switch to another active MFC and purge cycle the impacted MFC to a divert.

Could be utilizing the predictive data collection along with several service techniques. The biocontroller software could pinpoint which isolation valve needs to be replaced and directions on how to replace and dry-down the system. A more advanced approach could be automatically switching to another MFC in the gas panel if a sensitivity level is triggered. This gas subcontroller could be cycled to purge out any potential moisture to a divert set-up. This would allow the system to continue operating and “fix itself” from a backflow condition. This will require the highest amount of upfront software development and intelligence which needs to be weighed against the realized savings.

TALK TO OUR FLOW EXPERTS

Contact our flow experts for a powerful demonstration of how intelligent IIoT devices can boost your team’s productivity.

04 Summary

Maintenance operations is an essential business function, affecting quality, safety, and productivity. Within the biopharmaceutical manufacturing environment there is a variety of equipment used in making a monoclonal antibody, for example. Different pieces of equipment perform the various functions in the drug-making process. Equipment may differ in size or quantity. They may also differ in age. Age, in years, certainly has maintenance-related implications. However, age, as it relates to the technology available when the equipment was designed and built, influences maintainability as well as the extent to which process improvements can be made.

Data drives today's business in ways that were almost inconceivable only a few short years ago. We presented five well-known maintenance models which can be characterized by their dependency on and use of data. The simplest model (reactive) is the least reliant on data and does not achieve the level of effectiveness as the prescriptive model, which relies on vast amounts of data. Equipment data availability is dependent on the design, with newer equipment having the advantage over older equipment. The ability to improve within any given maintenance model will be affected by data availability, however, the ability to progress to a higher level model is more significantly driven by the utility of the data.

When upgrading or replacing existing equipment, consideration should be given to the integration of data-rich devices when- and where-ever possible. Although this may result in a patchwork of data pools, the additional data would make, at least some, maintenance processes more efficient and would better facilitate continuous improvements. For new production lines, the integration of intelligent, data-rich devices would offer the greatest opportunities for maintenance effectiveness and business process improvements.

Perhaps one of the most significant results from an improvement in any maintenance model is codifying data- and component-related requirements into the user and equipment requirements. Partnering with the business's sourcing function, these requirements will become a permanent, persistent way of evaluating potential equipment suppliers. Including external collaborators, like equipment and device suppliers, to supplement your internal stakeholders can have a significant beneficial effect.

No matter which maintenance model you currently fall under, there is likely to be some improvement to be made. This may result from the internal continuous improvement ethos, may be triggered by a new technology, a device failure, a new product to produce, or something else. The path will be influenced by the where you start and destination you intend to reach. We hope the representative questions we posed and the eight sign posts serve to get your started and can act as aids along your journey.