White paper:

12 common GMP challenges facing maintenance departments in pharmaceutical plants

This white paper lists the GMP compliance problems often seen within the maintenance departments of pharmaceutical operations. These are the problems that will cause you grief when an auditor arrives.

It is recommended that you identify, investigate, and fix them before the auditor's next visit!

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Challenge 1

A risk-based approach to maintenance is not used

It's common to treat every piece of equipment within a pharmaceutical plant equally when it comes to maintenance. A better way is to use a risk-based approach that classifies each piece of equipment in terms of its impact on product quality and we recommend a simple four-category system:

Direct impact (product critical equipment)

- Any equipment whose failure may directly impact or affect product quality
- For example a mixing vessel

Indirect impact (process/system critical equipment)

- Equipment whose failure may indirectly affect the process or system performance, thus affecting final product quality or safety
- For example the temperature monitor in an autoclave

No impact equipment

- Equipment whose failure will not impact final product quality, safety or the environment
- For example the security boom gate at the site entrance

Safety/environmental impact system

- Equipment whose failure may directly affect the safety or the environment.
- For example a boiler

This categorisation system is detailed in the *ISPE Baseline Guideline on Qualification and Commissioning, Volume 5, Impact Assessment*. The Direct, Indirect, No Impact and Safety categories are sometimes referred to as the DINS system.

Using a risk-based approach such as DINS can dramatically impact the amount of work facing a maintenance department. For example, your maintenance schedule may require all temperature transmitters to be calibrated annually which means the same frequency for an autoclave and the ambient air temperature measurement in a warehouse.

Which one is more likely to impact product quality?

Using the risk-based categorization approach, the temperature transmitter in the autoclave may need calibration every three months, but the warehouse temperature transmitter may only need calibration once every two years.

Challenge 2

Computerized Maintenance Management Systems (CMMS) are not utilised, are underutilised or are not validated

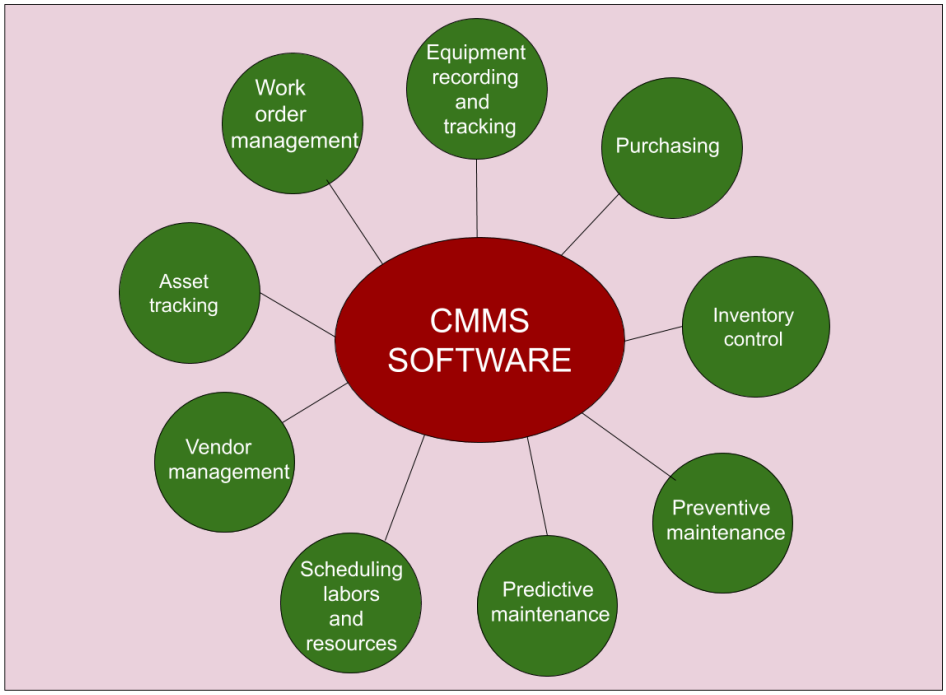
A CMMS typically performs five GMP-critical tasks:

- allocating a Unique Identifying Number (UINs) to each piece of equipment
- describing the validated plant configuration
- being the repository of maintenance plans
- holding records of maintenance activities
- scheduling maintenance activities.

As consultants to the industry, we often see hybrid management systems within maintenance departments. These hybrid systems may keep the UIN list in a spreadsheet, store the plans and records as paper files and schedule maintenance activities with a computer system. More often than not, records that are maintained in a spreadsheet or manually on paper are neither updated to the current listing nor signed (approved), either periodically or when major changes occur.

Whenever a hybrid system exists, the computer system gets preference, paper systems are neglected, and maintenance job sheets get lost. An auditor will target this area because it's often difficult for companies to get right.

Our advice? Use a validated CMMS system. When using a risk-based approach to validation, you need to validate only the functions that you will be using, e.g., the five GMP-critical tasks listed above – not the whole system.



Challenge 3

Maintenance plans are not updated as part of new equipment introduction

Buying a new piece of hi-tech machinery is very exciting. All the engineers scramble to be the first one to stroke its gleaming steel, however, amongst all that excitement, the maintenance plan is often neglected.

Updating the maintenance plan should be included as an activity in the procedure covering new equipment installation (e.g.., in the change request). If the equipment has a direct impact, where validation is necessary before use, it is recommended to include the verification that the equipment is listed in the maintenance database as part of the validation exercise.

Challenge 4

Maintenance staff and contractors are not trained properly

Do your maintenance workers and contractors know the impact of changing a setting on a piece of the production equipment?

Do they understand the concept of a validated state?

Do they know when to involve QA?

Let's face it – maintenance staff would rather watch 15 hours of snail racing than complete paperwork, yet simple maintenance activities such as changing filters or adding lubricant can dramatically impact product quality.

The GMP regulations require all contractors to be trained appropriately before they enter GMP areas. Developing tight, long-term relationships with your contracting suppliers is critical. Their HR systems should trigger GMP training for every new hire.

You could request that small contracting companies use a simple checklist when a new hire commences work. "GMP training" could be on that checklist. A service-level agreement (SLA) could also be in place to mandate the contracting companies to train service engineers on GMP before sending them to your premises for servicing.

Another challenge for contractors providing maintenance documentation is to get them to adhere to the company's good documentation practices and it is a challenge to chase them to correct the documentation after the service is performed.

Challenge 5

The GMP impact of lubricants is not considered

When we ask the question, "What effect do your lubricants have on product quality?", we frequently get a puzzled look and a shrug.

Lubricants are often ignored in terms of their GMP impact, yet they can have direct contact with the product and, as such, are considered GMP-critical. Make sure that lubricants are on your criticality assessment list. The assessment and impact of lubricants on product quality should be documented. The introduction of new lubricants should be assessed and documented. Bottom-mounted or indirect drive systems used in plant design are strongly recommended.

Companies sometimes are confronted to maintain numerous types of lubricants due to an array of equipment used. Consolidating the lubricants to a few would require the assessment of their suitability to substitute the current. However, the substitution of a food-grade lubricant has often been overlooked during this exercise. Another pain of a possible error could be prevented.

A plant lost a batch worth half a million dollars after an uncontrolled filter change. Maintenance replaced the filter during scheduled maintenance. Due to poorly documented maintenance plans, it was not checked. Product was filtered and packed, and only later was it found that the filter's pore size was 2 µm, not 0.2 µm. the error was found before release and distribution. The batch was disposed of. A simple error, but easy to prevent.

Challenge 6

Maintenance of utilities and supplies falls between departmental cracks

The not-so-glamorous end of the maintenance activity list includes:

- chemicals
- power supplies
- fire protection systems
- security systems
- HVAC
- water and gas supplies.

Make sure it's clear who manages all this non-production equipment. Too often these items fall into the cracks between departments. The finger-pointing starts when things go wrong, and the cracks are revealed.

We recommend that "who is responsible for what" be documented in the quality system.

Challenge 7

Maintenance activities are undocumented

Policies, procedures and work instructions should exist for all maintenance activities. These documents form an essential training resource for maintenance staff and contractors. This documentation will also be requested by auditors, who know that maintenance is a GMP risk. They will ask to see the documentation that describes what, when and how of maintenance. Make sure that you have it and that it's followed. It's worthwhile to get a professional technical writer to produce this documentation; this will ensure that the documents are useful and understandable.

Use a risk-based approach to prioritise the documentation needed. The highest risk occurs during times of change, including projects and annual shutdowns. Start by documenting how these are handled.

The documentation system **must** be kept simple. Say what you are going to do and do what you said. The auditors will ask staff to "show me," so if the documentation says that you do it, they will ask to see proof of it. They have a trained eye to detect impractical systems and drill down.

Auditors have a trained eye to detect impractical systems and drill down. You do not want to be at the bottom of the drilling.

Challenge 8

Modern maintenance management techniques are not used

It's easy to keep doing things the way you've always done them – particularly with daily pressures to manage. With a few exceptions, we've seen little adoption by pharmaceutical plants in Australia and New Zealand of maintenance best-practice techniques.

Total Preventative Maintenance (TPM) is one we recommend, as well as Condition Based Monitoring (CBM) and Lean Maintenance. With both GMP and your company's expectation that you are continuously improving your processes, we recommend that you get some training in these techniques or call in a consultant to help.

Challenge 9

Equipment documentation is not readily accessible

The ideal is for all the documentation for a piece of equipment to be in the hands of the maintenance technician before he starts work. This documentation includes:

- the manufacturer's operation manual
- the manufacturer's installation manual
- the manufacturer's service manual
- details of the validated state of the equipment, e.g., settings used
- any maintenance records
- any work instructions or procedures covering the use of the equipment
- engineering drawings
- process and instrument diagrams.

The ultimate system would be to have controlled electronic copies of all these documents that the technician calls up from a wireless tablet PC. Realistically, you are more likely to have paper-based documentation stations within the plant.

We recommend that you assign someone to keep manufacturers' documentation up to date (often a simple web search and download). This person can also make photocopies of documentation (never let maintenance staff walk off with the originals) and issue uncontrolled copies of quality documents as needed.

Bookmark the support section of each manufacturer's website on the PC in the document station. This makes it easy for technicians to find the information they need to solve a problem with a piece of equipment.

Challenge 10

Maintenance is not considered during equipment purchases

The maintenance department is often at the bottom of the heap when it comes to selecting new equipment. The production engineers and product development scientists base their selection on criteria such as throughput and ease of cleaning. The ease and impact of maintenance also need to be on the list.

Let's say you have a choice between two products for a cleanroom. They are pretty well equal on most selection criteria, but one is installed completely inside the cleanroom. The other has its maintainable "bits" outside the cleanroom, and only its product-contact components are inside the controlled area. Which one are you going to buy? The second one, because any maintenance tasks performed on it are unlikely to threaten the validated state of the cleanroom. The tasks will also be much quicker and easier to complete than if they had to be performed inside the cleanroom, making the cost of owning that equipment less than the other choice.

Challenge 11

Spare parts listing or inventory not managed.

Having spare parts on hand is a crucial aspect of maintenance, as every manufacturing facility needs to carry a certain level of spares to be able to recover in the event of a failure. It is not just feasible to keep one of everything kept in their stores, especially if the business wants to reduce inventories to a minimum.

Keeping spares signifies capital expenditure on products that has no tangible contribution to returns. A large number of spare parts also require additional valuable space to store. So, by reducing spares, you're reducing space waste and holding costs.

A risk-based approach on which spares to keep is recommended. A good list of approved standard parts stops the wrong parts from being ordered. A warehouse with meaningful and minimal parts is more likely to be orderly, meaning there's less chance of something being misplaced and ordered by accident, or not being reordered once it's been used.

Challenge 12

Original engineering documentation not updated.

Manufacturing facilities are provided with as-built engineering documentation (process flow diagrams (PFD), piping and instrumentation diagrams (P&ID), isometrics, ladder diagrams, logic, engineering specifications etc....) at the end of the installation and commissioning. These are significant pieces of information in performing maintenance and investigations. The proper maintenance of equipment is tantamount to a smooth operation and ascertain processes to keep its validated state.

Through time, process enhancement and initiatives are inevitable. However, the engineering documentations are not updated leaving the maintenance department in wonder during an investigation or troubleshooting.

It is a good practice to include the assessment of updating engineering documentation when initiating changes in the process. Up-to-date engineering documentation ensures that employees have the correct versions of the documents they need. The availability, accessibility and clarity of information should also be part of the aspects covered by the document control procedure.

Sources

Links used within this document are prone to change. Please refer to the appropriate source for the most recent information. We endeavour to keep an up-to-date record of information at www.pharmout.net

21 CFRs, Parts 210 and 211

The Draft ISPE BASELINE® GUIDE, Volume 8, MAINTENANCE

FDA, Guidance for Industry Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice, August 2003

FDA Guidance for Industry, Quality Systems Approach to Pharmaceutical cGMP Regulations, September 2006

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