Old Becomes New: Retrofits of Lyophiliser Control Systems

While lyophilisers can remain operational for many years, lyophiliser control technology has moved on – and it is this that can render a system out of date. As a way of controlling costs, one option is to retrofit the control system alone – producing a lyophiliser that will provide many more years of reliable service, without the expense of buying new equipment.

Stainless steel is everlasting – which is one reason why lyophilisers can still be in operation after 15, 20, and sometimes over 30 years without a discernible drop in performance (vacuum, heating and cooling). In this respect, such lyophilisers are often comparable with new equipment – but to keep up with the latest technology, it is the control systems that need to be updated. Together with documentation and validation requirements, it is the lyophiliser control system that has moved on, while the basic technology has remained unchanged. The development of reliable computers – with benefits in terms of usability, security (for example, 21 CFR Part 11), visualisation and documentation – has led to a significantly different approach regarding equipment operation.

As a way of controlling costs, especially during the recent downturn, pharmaceutical companies have looked to replacement of the control system – just one part of the overall equipment – as a cost-effective option. However, retrofitting a lyophiliser control system is not without risks. There are several critical items to consider and the work must be carried out by experienced technicians. At GEA Lyophil, we have performed more than 30 control system retrofits for our own-brand lyophilisers and also for other models.

A strategy and shared experience for a successful retrofit project is described below (see Figure 1).

RISK ASSESSMENT

A risk assessment is mandatory to identify, benchmark and mitigate the existing risks; this is required for the documentation, hardware (mechanical and electrical), control system and functionality.

The first step of a retrofit process is a critical assessment of the current status of the equipment. The general conditions have to be verified in terms of mechanical and electrical hardware to define areas to be modified that are close to the control system retrofit itself.

The control system for a lyophiliser consists of a programmable logic controller (PLC) and a human machine interface (HMI)/supervisory control and data acquisition (SCADA) system, and the related hardware. Even if in most cases the desired new functionality is limited to a new SCADA application, the entire control system must be carefully evaluated. This evaluation will determine, via a risk assessment, all the critical parts that should be replaced during a retrofit.

For example, it may be difficult to get spare parts for hardware components (for example, former operating systems for the HMI), or the new PC operating system might be incompatible with the current HMI/SCADA application.

Also, legal requirements have to be evaluated and brought into the project; for example, it might be necessary for the pressure vessels to be inspected by the authorities. If this inspection is required in the near future – for example in one or two years’ time – then it should be done as part of the retrofit process to avoid further stoppages later. With respect to documentation and mechanical
hardware, the risk assessment may define areas and reasons why the current status should remain unchanged – even if it does not represent the most up-to-date practice. It might be sufficient to ‘grandfather’ these aspects if the equipment has proven capable of manufacturing to the required product quality.

LIMITATIONS & ITEMS TO CONSIDER

In order to reduce associated risks, the existing functionality must remain as validated. This applies, for example, to interfaces to the existing PLC if these do not require replacement, or if the process control is to be done in the same way as before (for example, the pressure regulation must be done with the same components).

The whole refit will need to be performed in accordance with the tight schedule of a planned shutdown period. Planning must include necessary aspects such as replacement, commissioning and qualification.

GOALS & BENEFITS

There are several advantages to installing a new control system. The main goals to aim for are:

- Implementation of 21 CFR Part 11 compliance: a new SCADA system may include audit trail, user-log and user security functions that fulfil 21 CFR Part 11 requirements
- State-of-the-art equipment: current hardware components are more efficient and also more reliable, and the availability of support and spare parts is guaranteed
- Usability: the opportunities offered by the new control system provide better usability in terms of parameter handling, visualisation and help functionality. Networks can provide system access at various places, and the readability of results and reports can be improved
- Safety: product safety may be increased due to reliability and redundancy, for example, redundant array independent disks (RAID) technology. Also, better data storage and back-up functionality can be implemented

FURTHER POSSIBILITIES

If a decision is made in favour of an upgrade of existing equipment, then it is probably worth thinking differently. It makes sense to combine all near-future upgrades into one single change as, after implementation of a new software application, comprehensive testing will be required. Several modifications are possible without having a major impact on the mechanical hardware:

- Replacement of refrigerant: for legal reasons, and in view of economic and ecological factors, consideration should be given to replacing the refrigerant from the compressors. This will probably also lead to better performance of the cooling system
- Electronic expansion valves: the replacement of these valves, which control the direct expansion of refrigerant into the condenser pipes, will lead to much better performance and regulation. This also reduces energy consumption
- Silicone oil leak detection: adding a device to identify traces of silicone oil in the system (for example, a Lyoplus® device) might be considered
- Optimisation of auxiliary processes such as clean in place (CIP) or sterilise in place (SIP) to reduce lead time, and usage of steam and WFI in recent years, the cost of supply media has increased rapidly. The reduction of operating costs and shortening of turn-around time – as well as other factors – are now a focus of the manufacturing process, whereas previously quality was the only concern. Software adaptations and process optimisation can be done to reduce process times and the use of utilities
- H2O2 gas sterilisation: for an old lyophiliser that has not been designed as a pressure vessel, it may be advisable to install an H2O2 unit for gas sterilisation of the system. This can be added to any lyophiliser on the market and is accepted by the authorities
- Process analytical technology (PAT): tools for analysing and controlling manufacturing during processing can, in most cases, be added to existing equipment. This not only applies to integral monitoring methods that evaluate a specific value within the entire system – such as pressure or moisture content – but also for single container-based (vial or tray) monitoring devices that measure a value within a specific container (such as Lyosense™ Impedance Measuring)
It has to be considered, of course, that implementation of a new control system will take some time. Generally, it should be possible to finalise the related hardware modification during regular shutdown periods, such as maintenance activities. Such modification is limited to electrical cabinets and control rooms, and so access to the clean areas is not necessary.

Extension to customer site network: it should be possible to extend a new SCADA system to the customer site network for, for example, data export to a central archive server or connection to a higher-level system, such as manufacturing execution systems (MES).

CHALLENGES TO A SUCCESSFUL PROJECT

The implementation of a new process control application will have a major impact on the system. This is independent of other modifications performed concurrently (for example, a PLC application or mechanical modifications).

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Our experience has shown that these retrofits should follow the same life-cycle approach as a completely new lyophiliser project. This requires very detailed planning and project management; user requirement specifications are needed, detailed quality planning must be done and design specifications (like functional, hardware and software design specifications, FDS, HDS and SDS) must be developed and approved prior to software coding and hardware configuration. Also, the verification must be performed in terms of providing documented evidence that the new system is ready for its intended use.

It is also advisable to perform a file allocation table (FAT) data recovery software programme at the supplier’s site. This serves as an initial testing of the new SCADA software, identifies areas to be improved and may also be used as part of the qualification activities. The installation of the computer should be verified, while the related documentation and most of the functionality can be demonstrated in simulation. To reduce the shutdown time of the lyophiliser, tests do not need to be repeated if there are no changes or it doesn’t matter where the test is performed — for example, testing the password functionality, screen layout and documentation. The number of tests required — and those that need to be repeated — has to be defined as part of the risk assessment.

CONCLUSION

We have recently undertaken several successful projects that have been completed according to the approach described above. It is very important to pay the same attention and put the same competence into a relatively small project as would be given to a complete lyophiliser project. An ultimately successful outcome will show that it is worth the effort.

A project must be correctly prepared and accompanied by dedicated risk assessments and the prescribed GAMP approach. This reduces the time that the equipment is out of operation and helps to guarantee a successful outcome.

When correctly planned and performed by experienced technicians, a retrofit project will produce a lyophiliser that will provide reliable service for 10 years or more, without the expense of buying new equipment. Isn’t it worth considering?