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Automation Solutions

QUALITY WITHOUT THE PAIN

Peter Woods, programme manager at GB Innomech describes new automated approaches in pharmaceutical manufacturing

Pharmaceutical and medical device manufacturers are constantly focused on guaranteeing product quality and patient safety. The highly regulated environments in which such products are manufactured forces suppliers of automation in this market to themselves meet demanding levels of quality assurance, often associated with a significant overhead of documentation.

In the current business climate where decisions to invest in capital equipment are being deferred if not cancelled, suppliers of automation, as in many other sectors, are under pressure to compete on price and to provide solutions that are within the affordability of limited client budgets.

In such a business environment, it is natural to feel that effort should be directed at progressing the project as efficiently as possible, whilst avoiding procedures that go beyond the strict requirements of the quality system to ask 'what-if' questions.

This article argues there are benefits from investing in the rigorous risk assessments that lie at the heart of quality systems such as GAMP 5, and that these benefits could be lost if the process is reduced to the minimally acceptable level of producing only the required documentation. These benefits have been obtained largely within this regulated domain but the approach we are recommending can be applied to any custom engineering project, and are worthwhile no matter what the economic climate.

The V Model

Automated assembly and on-line test machines are often designed for purpose, and are specific to a product or process. As a result, each system is unique and by its nature complex. This combination carries with it significant scope for the delivered system to fail to work in the way its users believed was specified, or to have unforeseen side effects in operation.

Consequently, engineering a new process or converting a previously manual one to an automated one requires careful capturing of required function and an understanding of what may go wrong in converting a user's aspirations into a piece of machinery.

User interfaces for automated manufacturing and testing systems need to be designed to minimise the need for operator training but also to ensure operators cannot inadvertently alter key system parameters

In the pharmaceutical and medical device arena, there are well-established methodologies and validation approaches designed to address key technical risks applying to automated systems, such as ASTM 2500 and GAMP 5.

At the heart of these quality systems is the "V" model. First developed as a model for software development, it came to symbolise the approach defined in the GAMP guidelines. The prime motivation for the V model and its associated documentation is the control of risk, our main area of concern in this article.

The V model is illustrated in figure 1 [overleaf]. The left hand arm of the diagram represents the succession of specification documents that start with the user requirement specification (the URS) against which a functional requirement specification (FRS) can be generated and, in turn, a set of implementation specifications can be defined to embody the way a specific solution will be engineered.

In this model, the risk of an unintended outcome is managed primarily by rigorously tracing each individual user requirement through to a machine function, and ultimately testing that the implemented machine performs as specified in order to meet all of the original requirements.

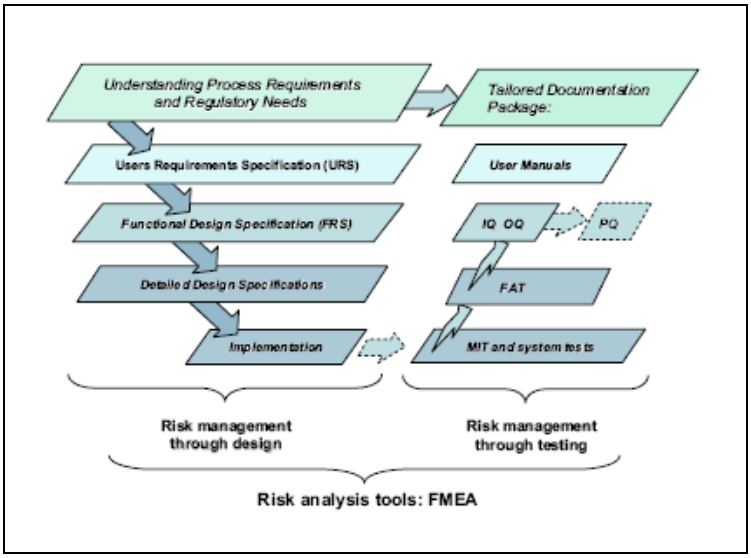


Figure 1
The V model – first introduced for software development – is at the heart of current Good Automated Manufacturing Practice when developing systems for pharmaceutical and medical device manufacturing.

The left hand arm defines system requirements and specification documents; the right side the testing methodologies.

However, this model does have some drawbacks. User requirements are intentionally made to be independent of a specific implementation, so cannot easily anticipate which features of the implementation are important for practical use.

For example, even a simple operator user interface could be designed in many different ways to fulfil the same functional requirement. A user interface that on paper meets the stated needs completely, might in reality still be highly non-intuitive. As a result, even when judged successful, an automated production system might require its operators to be carefully trained not to press the wrong button at the wrong time. Similarly, it is common to hear stories of installations where the system may work well when nursed by its supplier but problems return as soon as the maintenance engineer has gone home.

Issues such as these may be painfully evident, but do not fundamentally affect the capability of a machine to perform as specified. However, a similar lack of visibility of factors within the process, where a human cannot accommodate the shortfall could have far more serious consequences. In these cases, there may be no choice other than to re-implement some aspect of the machine design, often at a late stage which could add significant delay and involve substantial cost.

These types of issues arise despite appropriate processes being in place to meet the GAMP requirements, and arguably could be more likely to arise because of these provisions. Focussing on efficiently documenting and cross-referencing requirements to tested functions could, in reality, divert attention from spotting opportunities to improve the production process being automated and identifying all the critical success and risk factors.

What is needed is a means to make visible and to control all of these factors. There are methodologies for this, and certain variations have been adopted in different industries. An example would be the SAE J1739 standard used in automotive manufacture. Although these methodologies differ in detail, they share a common process of:

1) Identifying a risk factor
2) Assessing its impact
3) Applying mitigation if required
4) Iterating if necessary

In engineering domains this general methodology is called Failure Modes and Effects Analysis (FMEA). However a similar process is used more widely in assessing health and safety risks, as well as in insurance assessments.

The question is not whether such a process is appropriate, or which variant is preferred, it is all to do with how and when it is applied.

Earlier is Better

The number of potential failure modes in a complex new system can often be considerable, particularly when integrating new materials, technologies and functions whilst also attempting to meet demanding user expectations of performance.

Consequently, the proving of a piece of automation largely pivots on a formal acceptance test that demonstrates its correct operation, with the test schedule covering tests of the various defined functions of the machine.

It is not untypical to find much of the test and compliance effort being addressed late in the project, with the FMEA process being applied to a finalised design to confirm important failure modes are identified. Such a retrospective analysis can miss the intended purpose of minimising risk

through design, because even if valuable improvements are identified it is too late in the process to incorporate them into what is delivered.

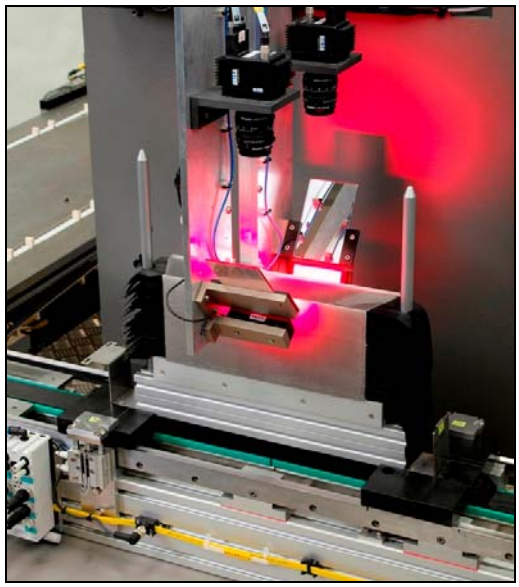
Worse still, by focussing narrowly on confirming tight statements of functionality, the risk analysis and testing strategy does not encourage a consideration of how a system might fail in practice, which might have usefully informed the original design process.

For example, one test specified for an end-of-line automated test platform for a medical device was intended to ensure that two similar mechanical components in the device had not been exchanged in error, since in this case an assembled device would appear normal but would fail to operate effectively. Although the test was feasible and the tester worked reliably, a better solution, if recognised earlier through an examination of risk, would have allowed a design modification to one of the components to make it impossible for them to be confused during assembly.

Multi-dose injector pens and other innovative medical devices are designed to ensure every component within the device is unique and cannot be switched or assembled wrongly to produce a product that looks right but fails to operate effectively.

A more effective use of the FMEA approach can be illustrated by another example, this time concerning the assembly of optical tiles for large area video displays as used for outdoor displays mounted, say, on the wall of a building. Here, the display is composed of an array of tiles which can be linked in rows and columns without any visible gaps or joins.

Each tile consists of a luminescent display unit about the same area size as a laptop computer display, coupled to a block composed of thousands of individual lightguide elements. In order for the composite display to work, the lightguide elements within each tile must be registered extremely accurately to the underlying display unit. This registration is complicated by the fact that each line of lightguides in the tile is a different shape to the ones either side of it.



The FMEA approach to risk analysis was used extensively when developing this optical tile assembly machine. This visual inspection station scans and validates the integrity of all pixels in a newly added row before the part-assembled tile can move on to have the next row added.

Consequently, the tile assembly machine must thermoform individual components from stock mouldings, then assemble these row by row to form the tile, using specially developed adhesive. Registration accuracy can be affected by the thickness of glue dispensed and the precision of the thermoforming process, as well as the repeatability of placement of the parts relative to each other. It was always obvious these processes would need to be controlled to achieve the target precision.

However, only in a more detailed analysis of possible exceptions did it become clear that critical elements of the part handling mechanics would need to be repeatable to a few microns, many times more stringent than expected, in order to ensure the necessary consistency of registration in the assembled product.

This challenging requirement was accommodated in the engineering specification for the part-handling systems, which added cost, but allowed the quality of product to meet end-user requirements, giving excellent process yields. Without this attention to detail in the early-stage design, the precision requirement may have only come to light once the machine had been assembled and commissioned, and testing had revealed a poor process yield. Should that have occurred, the cost of rectification may have been untenable.

If a similar problem arises in a machine for a medical or pharmaceutical application, in addition to the cost and delay of the engineering rectification, a further huge inertia would need to be overcome in updating design documents, revisiting testing specifications, and deciding what retrospective retesting might be involved after

implementation of the change. At best, the change adds cost and potential delays to the supply of the automated system. At worst, the end-user's product could be impacted in terms of performance or time-to-market.

Evolution of Risks

As a project to develop and supply a piece of automation evolves, it should be expected that previously identified risk factors are monitored, addressed and are eventually resolved. However, focussing only on the factors identified during a one-time exercise can be another reductive exercise whereby the items in the risk register are ticked off one-by-one, typically by identifying a test condition to be incorporated into one or other test specification. It is important to realise that in the lifetime of a project, new risk factors might emerge at any time, and that the nature of previously identified risks might change.

As an example, in developing an automated end-of-line test system for a medical device, an analysis of failure modes of the initial system design highlighted that the test procedures specified by the user could not be guaranteed to correctly identify the defects of manufacture they were intended to reveal. Consequently it was possible to agree modified test protocols that were not affected by the exceptions that had been identified. The machine design was revised accordingly.

It was realised in a subsequent review that during the original design that an earlier sound decision to effect a movement pneumatically could now potentially lead to error in the measurement system because the test functions had been revised. The actuator was subsequently replaced with a servo motor to eliminate the risk of that error. If this potential effect had not been spotted in the review, proceeding with the original design may have led to incorrect results from the testing process that might not have been recognised before the system went into production.

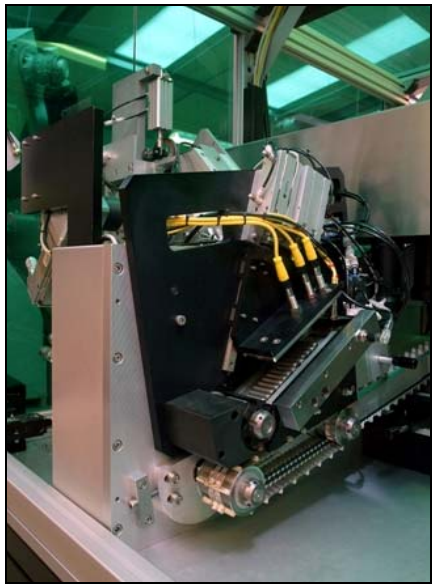
Further Benefits

Sometimes risk analysis can throw up unexpected benefits. In designing an inspection system to examine both upper and lower surfaces of an assembly, handling the part to invert it was identified as a key risk, due to the nature of the assembly and difficulty in gripping it in a way that allowed it to be inverted and precisely positioned within the confined space of the inspection cell.

Having highlighted the problem we were able to eliminate it completely by restating the requirements for the inspection cell so that only one of the two surfaces is inspected at a time. A single point of inversion could then be easily implemented elsewhere in the machine where the space constraints do not apply. The assemblies perform two orbits through the system instead of one so that both surfaces are inspected.

This not only resolved the initial risk associated with handling but produced a system design that was intrinsically simpler and cheaper than the original concept but with the same performance.

Without focussing on the particular risk factor, this significant improvement to the overall architecture might never have been conceived at all.



Efficient medical device manufacturing relies to a large extent on the unique design of components and sub-assemblies. The system above checks the orientation and multiple body features of the components before allowing them to pass into the next stage of the assembly process.

Summary

It is important to adopt an enlightened approach to the analysis and mitigation of risk in the supply of custom engineering, especially for applications in pharmaceutical or medical device production and testing. In summary, we offer the following advice:

When selecting an automation provider, check their understanding of the customer's regulatory environment – because a supplier with the right experience and accreditation will make life easier for the organisation on the receiving end.

Remember that the both the customer and the automation provider should be using risk analysis as a tool to manage the project through its life, as well as simply a means of demonstrating that necessary quality and regulatory standards have been met. We recommend the FMEA formalism for this purpose.

Trying to minimise effort on a project by generating only the documents demanded by the quality regime, without a more lateral analysis, can be counterproductive.