

This article presents a number of examples of software tools which provide an integrated approach to qualification and the validation lifecycle.

# Using AIMS Tools to Automate the Qualification and Validation Lifecycle

by Fursey Duggan and Nick Giuffrida

## Introduction

There is currently a great effort within the regulated life science industries to re-evaluate and improve the efficiency of the compliance processes by which they are obliged to conduct their business. The drive for more efficient compliance is being encouraged by the regulators to the industry, as best exemplified by the US FDA's risk based approach initiative.<sup>1</sup> There has never been a better time for the industry to examine its traditional approaches to compliance and explore more innovative options.

In the past few years, a number of software tools and solutions supporting part of the validation and compliance process have emerged within the industry. These solutions are generally referred to as Automated Information Management System (AIMS) Tools. This article describes a number of examples of the application of these new tools, which offer a complete and integrated approach. This has significant advantages for the efficiency of the processes involved, especially qualification and

validation. This article also examines the wider issue of information management in the compliance process with Web-based AIMS tools.

## Automated Information Management Systems

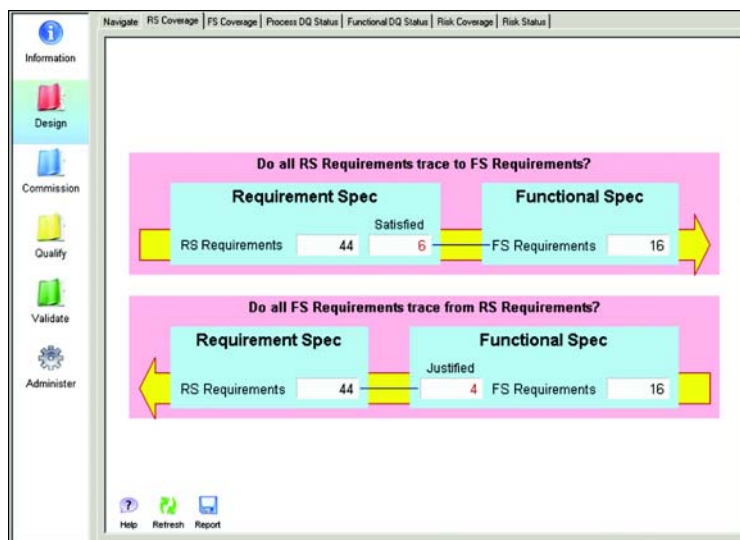
Perhaps the most powerful feature of AIMS tools is their ability to establish *dynamic* links between statements within a single document or even across multiple documents of different types. This linking is achieved not just at the document level, but also between the actual statements themselves.

AIMS tool statement linking is dynamic in nature allowing the user to quickly navigate between two or more linked statements (effectively jumping from a section in one document to a linked section in the other document) or to manipulate the documents so that linked statements can be readily shown in useful views of the source documents. This linkage can be performed upon documents that are created within the AIMS application itself; this is typically the same as creating a document in a word

processor environment, or documents that are imported into the AIMS application from external programs such as Microsoft Word and Excel, likewise, documents and document views generated within the AIMS environment can be readily exported to such external applications.

An obvious advantage of linking functionality is the ability to establish links between any statements, e.g., of requirements held in one document to a statement of how that requirement is

Figure 1. AIMS Tool coverage statistics.



to be met in one or more other documents. Other typical life science examples of where such linkage could be applied would be between a clause in a regulation and the section of a standard operating procedure that has been written to comply with that clause or a clause in a regulatory standard and the section of a specification document that specifies the necessary compliance.

In a further example, links can be readily established between the statements contained in a supplier's proposal and the relevant requirement statements contained in the original tender or Request For Proposal (RFP) document. The ability to make links between statements within multiple documents is the key to the functionality features of AIMS solutions that hold particular compliance benefits for life science industry users. These features are further explored below:

## Coverage Analysis - The Basic AIMS Compliance Tool

Once links have been established between documents, coverage analysis is an *immediately available* AIMS output. Coverage analysis can be used, for example, to ensure that every compliance statement in the source document is matched by

one or more compliance statements in one or more other documents. Typically, an AIMS tools coverage analysis will report coverage statistics that show the proportion of requirements that have been addressed, as well as allowing the user to open a view of the source document that shows only those requirements that have not been addressed - *Figure 1*.

This type of coverage analysis could be applied, for example, to ensure that every clause in a regulation or standard has been addressed by the company's procedural documents. In a design context, it can be used to ensure that every clause in a regulatory standard has been captured in the design requirements documentation or to ensure that every requirement in a tender document has been addressed in the supplier's proposal. While such coverage analysis can be achieved by manual means, it is typically time consuming and gets proportionately more difficult with the size and complexity of the source and responding documents. With AIMS tools, coverage analysis can be performed instantaneously and is a by-product of linkage requiring little extra effort in itself.

Coverage analysis should be considered the initial step of compliance verification. Every compliance professional knows it is not enough to merely have specification statements

URS	FRS	Verified?	Comment
<b>3 GMP/QUALITY REQUIREMENTS</b>			
<b>3.1 Operation and Control</b>			
The new Control System must stop the feeder process automatically when the desired amount of raw material has been transferred to the Collette Bowl.	FRS-47 The transfer process routine is cut off when a signal from the loss in weight hopper device indicates that the specified limit has been met.	No	Hoppers are loss in weight design. Cot of signal should be received from Hopper not Collette bowl.
This value should be within 100 grams of the set point.	FRS-48 The communication speed between the load cell signal being sent and the transfer routine being shut off will be such that less than 100 grams more than the set point limit.	No	See FRS-47 cuff off signal should be sent from loss in weight Hopper not Collette bowl.
<b>3.2 Materials of Construction</b>		Yes	
<b>3.3 Cross Contamination</b>		Yes	
<b>3.4 Electronic Records; Electronic Signatures</b>		Yes	
<b>4 OTHER OPERATIONAL REQUIREMENTS</b>			
<b>4.1 Environment</b>			
4.1.1 Operating Environment			
4.1.2 External Environment			
<b>4.2 Human Factors</b>			
4.2.1 Training			
4.2.2 Health and Safety			
4.3 Facilities			

Figure 2. AIMS tool Design Qualification view generated from specification documents.

ID	Hazard	Cause	Severity	Probability	Risk	Controls	Actions
RA-3	Contamination of Powder	Bowl and bag seals not properly sealed	High	Low	Moderate		
RA-4	Contamination of Powder	Contamination from contact parts	High	Low	Moderate		
RA-5	Sub-potency Products	Less than the required amount of the key ingredient is weighted out	Medium	Low	Minor		

Figure 3. An AIMS risk analysis module with linkage to design specification documents. Colored arrows are active dynamic links to these other documents.

matched by compliance statements but true compliance can only be achieved when the compliance statement fully captures the intent and meaning of the requirement. The verification of compliance can be greatly assisted by using AIMS tools, which like coverage analysis is another by-product of the dynamic linking discussed above.

Once documents have been linked, the AIMS tool can quickly generate views that place the linked statements side by side. For example, this means that a clause in a regulation or standard can be quickly viewed *right next* to the very section or sections of the document or documents that were written to implement its compliance. This makes compliance verification so much easier than working at the document level in the traditional way, where such compliance verification would involve searching through multiple documents to find the compliance statements and then having to compare them back to the relevant clause, while flipping between two or more documents.

### Using AIMS Tools for Risk Management and Design Qualification

An area where the viewing functionality of AIMS tools has huge potential benefit is Design Qualification (DQ). DQ entails the verification that the design of a facility, system, or equipment is suitable for its intended purpose.<sup>2</sup> By using AIMS tools to establish links between the design requirement documents (e.g., Requirement Specification) and the design specification documents (Functional Specification, design specification documents, specification drawings, etc.), design qualification views can be generated that match each of the individual requirement statements with their corresponding design specification, thereby facilitating the verification that the design intention is appropriately captured - *Figure 2*. This not only facilitates compliance, but also ensures that the implementation of the design is controlled from the start to meet the design requirements, the key to successful design.

There are associated benefits of these generated DQ views for the design review process, whereby the design stage documentation is reviewed to ensure that the design inten-

tion is being met. The fact that all parties participating in the design review can be given access to the DQ view (as discussed later some AIMS tools are Web based) means that the reviewers have early access to the pertinent sections of the design documentation that specify how the relevant design requirements are to be fulfilled. This would allow the design review process to be performed in a continuous proactive manner, allowing the reviewer's feedback to be incorporated into the design specification documentation as it develops. This is much more efficient than the typical end of stage one off design review meeting, which invariably leads to much duplication of effort as the reviewed documents go through multiple revisions to satisfy the various review comments.

It also is worth noting that currently available AIMS tools feature automated risk analysis modules. These tools can be readily adapted to analyze the hazards associated with life-science design activities - *Figure 3*. The AIMS tool can automatically calculate the risk of the safety hazards associated with a particular design feature based upon their severity and probability of occurrence and then dynamically link the identified risk mitigation controls to the specification document that specifies their implementation.

### Using AIMS Tools to Track the Validation Life Cycle (Traceability)

The use of AIMS tools is not just restricted to one-stage activities that involve establishing compliance between statements contained in one or more documents as in the previous examples. The power of AIMS tools could be applied with great effect to the more complex multi-stage projects that are performed by the life science industries.

The validation life cycle involved in the design, commissioning and qualification, and validation of facilities, equipment, and systems is an example of such a project and an area where both regulators and the industry<sup>3</sup> are focusing on for potential compliance efficiencies. It has already been discussed in this article how AIMS tools can be applied to the design process, but what is their potential use in the remaining steps of the validation life cycle? Once links have been

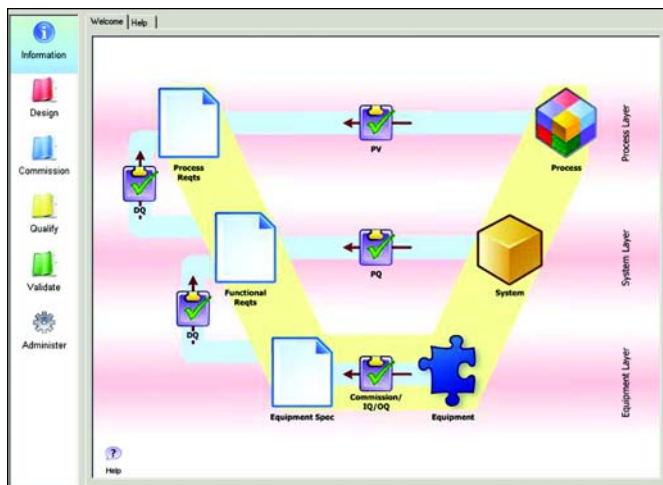


Figure 4. Use of an AIMS Tool to track the overall Process Validation Life Cycle.

established between the design requirements, risk analysis, and the design specification documents, the AIMS tools can link these in turn to the test documentation that is generated to plan and report both commissioning and qualification activities - *Figures 4 and 5*.

The ability to link statements within documents that occupy different levels of a multi-document hierarchy generated at different stages of a project provide AIMS tools with perhaps their most powerful compliance feature - traceability. Traceability can be used, for example, to track a design specification that has been defined as critical by risk analysis through its implementation in the relevant equipment specifications through to the very sections of the commissioning and qualification document that verifies it has been appropriately implemented.

Once such traceability has been established, the coverage analysis and verification viewing functionality of AIMS tools can then be used to analyze and view the implementation and testing of the feature at any stage of the project. This means that its criticality is recognized at all stages of the project, thereby ensuring it is not neglected during the project and that its implementation throughout the project can be quickly traced by any interested party, including those responsible for Quality Assurance.

This ability to verify the implementation of critical features at any stage of the project should then give the Quality unit the confidence to entrust more of the testing activities to the engineering disciplines, allowing them to focus on the true purpose of the Quality role, the verification of compliance. For example, the verification of a critical installation feature, such as material of construction of product contact parts, can be planned as part of the commissioning performed by the engineering disciplines. The AIMS tool would be used to link the test planning documentation for this verification to the risk assessment documentation that determined that material of construction of product contact parts is a critical feature. The Quality unit can then use the AIMS tool's traceability to identify and see all instances where this and other critical features are planned for verification in the

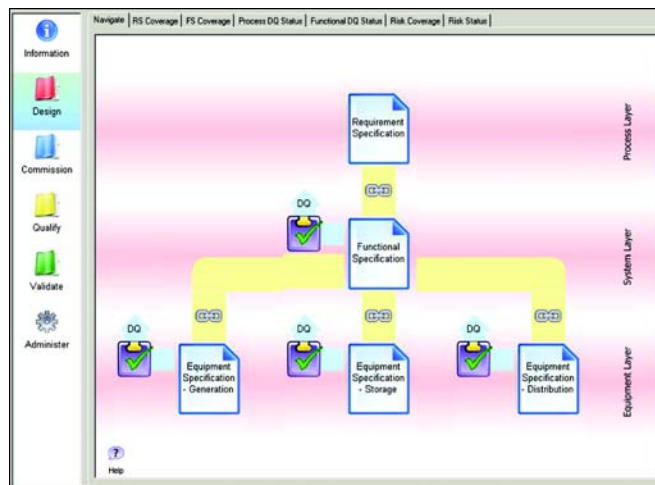


Figure 5. Use of an AIMS Tool to drill into the Process Validation Life Cycle.

commissioning test planning documentation. This allows them to ensure that the test planning documentation is set up to appropriately document the verification. Once commissioning has been completed, the documented results of the testing of the critical features can then be quickly located in the commissioning documentation to assure it has been appropriately tested and documented. The Quality unit does not now have to repeat the testing during qualification, but instead can use Installation Qualification (IQ) and Operational Qualification (OQ) as an audit activity that verifies the outcome of the commissioning. This means that commissioning and qualification can be considered two parts of the one activity rather than two separate activities with consequent savings in terms of the time and costs that are avoided by not having to replicate commission testing during qualification.

## Additional Features of AIMS Tools

In addition, AIMS tools allow the user to add additional attributes to any piece of data. So for example, it is possible to add the attribute "Critical" to a specification statement within the equipment specification which is automatically inherited in the commissioning and qualification test documentation, which means that the user will be instantly alerted to its importance no matter what stage of the validation life cycle it is encountered. In fact, there is no limit to the attributes that can be added to a piece of data using an AIMS tool. For example, a component specification could be supplemented with useful maintenance and regulatory compliance attributes such as cost, supplier, quantity on hand, calibration due dates, applicable regulations, etc.

AIMS tools can mark individual specifications no matter how numerous and ensure that they are addressed at the predefined project stage. The advantage of using Web-based AIMS tools for this type of test planning is that it can be agreed at early stages in the project in a collaborative environment that can involve all interested stake-holders, including those not working at the actual site undergoing commissioning and qualification. The latest generation of AIMS tools are now available in a hosted Web-based environment that

particularly facilitates this kind of multi-site collaboration in a secure and cost effective manner.

A hosted service means that the data entry, viewing, and other functionality of the AIMS tool takes place on the provider's server not on the users own network. This means that all stakeholders can quickly be provided access to the project data without the large infrastructure efforts and at very much reduced cost than is usually associated with similar multi-site software based applications.

## Test Planning

The test planning benefits of Web-based collaboration made possible with AIMS tools goes beyond merely deciding when an attribute is to be tested. Web based collaboration makes it possible to present the individual test cases next to the specification that they are designed to test in verification views that are accessible to all project stake-holders.

As these attributes, target values, and test cases are the most meaningful parts of the test planning (protocol) documents that are used to plan and document the execution of commissioning and qualification exercises, the collaborative use of the AIMS tool means that the individual test cases can be agreed in advance of the commissioning or qualification document being prepared. This advance agreement would significantly reduce document review and approval cycles, which is frequently one of the biggest causes of delays in validation projects. As discussed earlier, the verification views can be directly exported into external applications such as Microsoft Word or Excel meaning that the commissioning and qualification worksheets can be generated directly from the AIMS tool itself. Therefore, AIMS tools have the potential to not only reduce the commissioning and qualification documentation review cycle, but also the time taken to generate the vast number of documents that are typically required.

In addition to the reduced project time advantage of on-line collaborative review, there also are significant compliance advantages to capturing the commissioning and qualification attributes and test cases within an AIMS tool. By dynamically linking these test cases to the specifications that

they are devised to verify, it can be assured that all specifications have been covered by appropriate test cases. This includes the facility, equipment, and system attributes assessed as critical that must be verified during qualification.

The primary source of regulatory body dissatisfaction with the qualification process is where the qualification protocol either does not test all of the critical specifications of the item being qualified or the test cases it defines are considered inadequate for their verification. The risk of this type of non-conformance increases with the complexity of the item being qualified. The coverage analysis and verification viewing functionality of AIMS tools discussed previously can greatly reduce the risk of inadequate protocols. Coverage analysis ensures that each specification is covered by a test case. Verification viewing means that each test case can be compared side by side with the specification that they are there to verify enabling the reviewer to ensure that the specification is appropriately verified by the test case. In other words, the use of AIMS tools would significantly reduce the risk of inadequate qualification protocols and consequent adverse observations from regulatory reviewers.

The tracking of criticality through the project documentation also should provide Quality Assurance with the confidence to entrust more of the test activities to the engineering disciplines knowing that the AIMS tool is tracking compliance upon their behalf.

Once verification views of the commissioning and qualification stages of the project have been established, it is then a relatively easy task to populate them with the results of each of the individual test cases - *Figure 6*. If this is performed as the project progresses, the Web-based accessibility of these views means that all project stakeholders can keep track of the project's progress. For example, coverage analysis can quickly show the proportion of qualification activities that have been completed with the potential for providing project metrics, filtered verification views that can quickly focus on items that have not yet been completed or have failed particular qualification tests. The ability to highlight test failures (deviations) is of particular note.

ID	Test Item	Item Type	Target Value	Test Method	Com Actual Value	Com Verified	IQ Actual Value	IQ Verified	Comments
Gen ET-1	<b>1 PW Generation</b>	n/a				No		No	
Gen ET-2	PW Generation System	Description				No		No	Nothing to comment here
Gen ET-3	Commissioning Protocol	Attribute	Available	Check documentation	25	Yes	100	Yes	This is a comment
Gen ET-4	Commissioning Report	Attribute	Approved	Check documentation	30	Yes	110	Yes	Another comment
Gen ET-	IQ Protocol	Attribute	Approved	Check documentation		No		No	Works fine

Figure 6. IQ data captured using an AIMS Tool.

The populated verification view also would be of tremendous benefit during regulatory and other third party inspections. The populated view would in effect provide a traceability matrix showing the traceability between the specifications, test cases, and implementation documentation with dynamic linking to the design specifications and risk analysis documentation. For example, in a regulatory inspection scenario, the AIMS tool would quickly locate the objective evidence that a specification marked critical by risk analysis has been tested and implemented, thereby ensuring expeditious delivery of this evidence to the inspector.

## Impact Analysis and Change Control

Another significant benefit of a populated verification view held in an AIMS tool is in terms of impact analysis and change control. The verification view and other traceability features of an AIMS tool mean that the impact of changes can be quickly analyzed across the whole project, using the information already documented. For example, a proposed change to a piping specification can be quickly analyzed in terms of the test cases that would have to be re-verified in the related commissioning and qualification documentation.

In fact, there is no reason why the use of the verification view for impact analysis has to end with the project in which it was generated. Because the verification view holds the individual specifications in the same location as the compliance documentation, it would provide an effective compliance register of the completed facility or system at the end of the project. Therefore, the populated verification view could be used in conjunction with routine change control to quickly analyze the validation impact of any proposed change.

## Using AIMS Tools for Secure Readily Retrievable Data Storage

It also should be noted that some commercial AIMS tools are linked to secure data storage environments. In this context, the populated verification view can be considered a portal to these secure environments from which the data can be readily retrieved in the same structure that it was entered. By providing access to a secure, easily retrievable data storage environment, AIMS tools also have the potential to solve the electronic data compliance challenges that face the life science industries.

## Summary

AIMS tools have tremendous potential to improve the efficiency of activities associated with demonstrating compliance in the life science industries. This arises from their ability to link statements across multiple documents that are generated at different project stages. These links mean that it can be quickly verified that all specification requirements, risk information, and even the details of test plans or scripts

have been addressed and verified and to trace their implementation throughout the project. These advantages are further leveraged when subsequent changes are made to validated processes, equipment, and systems. Web-based AIMS tools provide a cost-effective collaborative environment that facilitates project planning to better leverage good engineering practices in qualification activities. AIMS tools also provide an opportunity to exploit secure, readily retrievable storage environments for compliance data.

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## About the Authors



**Furse Duggan** is a regulatory compliance consultant to the life sciences industries. He has worked for almost 15 years within these industries and has supported pharmaceutical, biotechnology, and medical device companies through all stages of the regulatory approval cycle. Duggan graduated from Dublin City University (DCU) in 1990 with an honors degree in biotechnology and worked in various quality assurance roles within the regulated life science industries before becoming founder of First Solutions Ltd. where he has worked as Managing Director and Senior Consultant since 1998. He can be contacted by telephone at: +353-1-8859339 or by e-mail at: [fursey@firstsolutions.ie](mailto:fursey@firstsolutions.ie).

First Solutions Ltd., 17 Hollystown Park, Hollystown, Dublin 15, Ireland.



**Nick Giuffrida** is one of the founders of Comply-Serve UK Ltd. Comply-Serve provides companies with an easy and efficient way of navigating and managing the regulatory and standards compliance world, through an internet-based managed service. Over the years, Giuffrida has moved from a senior technical role to a more strategic and commercial role.

Giuffrida was previously Sector Manager responsible for the Life Sciences Industry for Telelogic, a Swedish software company. He can be contacted by telephone at: +44-7824486177 or by e-mail at: [nick.giuffrida@complyserve.com](mailto:nick.giuffrida@complyserve.com).

Comply-Serve Limited, Townsend House, 79 Station Road, Leicester, LE9 6PU, United Kingdom. 