

## Compliance Newsletter

Issue September 2008

Page 1/1

### General Comments

Despite media messages to the contrary, there are no recent Warning Letters addressing Part 11 issues. Actually, the summer has been very quiet in terms of WLs, which allows space to devote to other issues.

Validation documentation has evolved in the industry to be separately managed and maintained from project information, and GAMP5 has done little to reduce this organizational empire-building. Efficiency demands integration of validation within engineering projects, and in the last issue, I gave examples of how to use the computer system for creating configuration documentation when configured (category 4) computer systems are involved. In this issue, I would like to remind you to use existing software development tools for creating software specifications.

For those new to the newsletter, it is built from hyperlinks. You can view the linked documents when you are on-line.

### Development (Design) Specifications

Development (synonym Design) specifications are needed whenever programming is required. These specifications represent the deepest level of specifications and are intended to define the programming effort. For a complete bespoke system, or for an extensively modified SAP system, the management of development specifications can be an even larger problem than the maintenance of Customizing Documentation discussed in the last newsletter. This is why CASE (Computer-aided Software Engineering) tools are so important.

Most programming is now object-oriented, and you can read more about my views on this subject in the May 2004 issue of the [Journal of Validation Technology](#). It suffices here to say that the CASE tool should be used for controlling, approving and documenting the design.

## Compliance Newsletter

Issue September 2008

Page 2/2

Documenting for validation purposes, implies Development Specifications can take the form of extracted information from the tool. For efficiency, the organization of these specifications should reflect the organization of objects within the project maintained by the tool. For the IT Crowd, extracting such specifications fits well with a prototyping approach to software development. GAMP5 also acknowledges this approach:

“... specification activities may be distinct from, or tightly coupled with, configuration and coding activities depending on the software development method being adopted.”

With SAP, the CASE tools are included as ABAP Workbench Tools, and include the Object Navigator and the Workbench Organizer. Our SAP validation template did not anticipate using the ABAP workbench directly for development specifications because it was oriented upon a category 4 (configurable software) solution with SAP. However, the process-oriented document tracing included with this template becomes impractical when managing an SAP project that includes many modifications, enhancements, etc. per tracing number. If SAP's Solution Manager is not being used to support traceability, traceability may need to also be requirement-oriented.

Sometimes a project will put heavy reliance upon requirements management, (e.g. relying upon requirement management tools). While good for the higher levels of specifications, requirements are still far away from programming, which is why prototyping is so popular. For rapidly changing systems, requirements management can divert valuable resources from the actual programming effort, by forcing the separate maintenance of detailed textual requirements (by the thousands) for development specifications. Hardly any project can afford to do this; rely upon the CASE tool.

### FDA Revisions to the GMPs with Regards to Automation

The FDA has just finalized a new interpretation of the current GMPs in the [Federal Register](#). The one of particular interest to our work concerns verifications by a 2<sup>nd</sup> person for certain critical processing steps when automation is involved. If you are working with MES or process control systems, you have to consider these verifications for:

- Dispensing components (21CFR211.101(c));
- Adding pre-dispensed components to a batch (21CFR211.101(d));
- Making yield calculations for a batch (21CFR211.103);
- Cleaning and maintenance of major equipment (21CFR211.182);
- Steps in batch production and control records (21CFR211.188(b)(11)).

## Compliance Newsletter

Issue September 2008

Page 3/3

Some of these operations may also be supported by higher level ERP systems, as well. Because the interpretation of these verifications by a second person was unclear, implementations have sometimes involved implementation of frequent electronic signatures, and even manual checking of the results calculated by the computer.

The FDA has attempted to clarify the interpretation when automation is involved. Of course, a precondition is that the computerized system has been validated for the activity. The changes have not yet been edited into the code and posted, so they have to be extracted from the Federal Register at the moment. The first major statement is:

“..automated equipment used to perform operations addressed in §§ 211.101(c) or (d), 211.103, 211.182, or 211.188(b)(11) can satisfy the requirements in those sections for the performance of an operation by one person and checking by another person if the equipment is used in conformity with § 211.68 and one person checks that the operations are properly performed.”

Unfortunately, this checking can be misinterpreted to mean that the remaining person must check every action and calculation of the automation. That is not the intent, as stated in the Federal Register:

“We stated in the preamble of the direct final rule that these revisions would clarify our longstanding policy that verification by a second individual may not be necessary when automatic equipment is used under § 211.68.”

Further, it is stated,

“For suitably validated automated systems, even with real time alarms, it is still necessary for a human to verify that the systems are operating as planned and to monitor for abnormalities. We agree that the level, nature, and frequency of such human verification will vary depending on the level of automation used as well as the nature of the system and controls, and the manufacturer has the flexibility and responsibility to determine what is suitable and necessary.”

I would interpret these statements to mean that operations can be designed with minimal human verification activities. Review of the operating log, attention to alarms, and a single approval step for a series of operations could suffice. This is especially interesting in dispensing and batch addition operations, where routine electronic signatures could be reduced. (They are driving the operators crazy anyways.)

## Compliance Newsletter

Issue September 2008

Page 4/4

Before you start re-engineering, stay informed about the next revision of the Annex 11 of the EU GMP guidelines (see April issue). In the draft under discussion, checking on the computer control for a critical process is still required, but within the context of a risk assessment of the criticality.

### GMP Refresher

The Warning Letter to [NeoChild LLC](#) points to the minimum what you need for GMPs as a manufacturer of a high risk device and to what you apparently can get away with (at least for a while). From NeoChild's responses, "get away with murder" comes to mind. However, the FDA found one area adequate, Medical Device Reporting. NeoChild now has a procedure and apparently there have been no injuries or malfunctions to report.

Contributing Author:  
Dr. Paul Thomas Noble  
Mobile: +49 172 6868 591  
Email: [PaulThomas.Noble@ids-scheer.com](mailto:PaulThomas.Noble@ids-scheer.com)  
[www.ids-scheer.com/pharma](http://www.ids-scheer.com/pharma)

If you have any further questions or comments, please don't hesitate to contact me directly via phone or email!