

# MERCK

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Deutschland

Food and Drug Administration  
Dockets Management  
Branch (HFA-305)  
5630 Fishers Lane,  
Room 1061  
Rockville MD 20852.

**Comment on Draft Guidance for Industry - 21CFR11; Validation,  
Docket Number 00D-1538.**

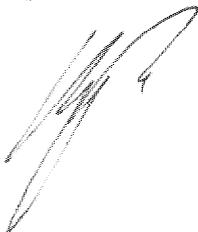
Dear madams, dear Sirs,

please find enclosed our comments on the Draft Guidance for Industry – 21CFR11, Validation,  
Docket Number 00D-1538. Please note that Merck KGaA Darmstadt is not linked to  
Merck&Co.

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We wish you a merry Christmas and a happy new year

Regards



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00D-1538

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**Comment on Draft Guidance for Industry - 21CFR11; Validation,  
Docket Number 00D-1538.**

Dear Madams, dear Sirs,

We appreciate the thinking of the FDA that some guidance may be needed on some topics of 21CFR11. The published compliance policy guide 160.850 is quite a good example on what the agency expects the industry to do to achieve compliance with 21CFR11.

One of the essentials of 21CFR11 is the requirement to validate the system handling electronic records and signatures. It is our understanding that the topic of validation of computer systems is an established process in the industry and is well guided by several guidelines like the PDA TR. 18 and GAMP which are published in 1995 and 1998. These guidelines are also listed in the appendix A of this draft guidance document. There is no need for additional guidance on how to validate computerized systems. In our opinion there should be no distinction between computer validation in general (as a requirement according to 21CFR211.68) and computer validation due to 21CFR11. 21CFR11 requires some specific functionalities to the computerized system which have to be tested during the validation process. Therefore we think that this guidance document will result in more confusion with respect to the process of achieving compliance with Part11 in the industry.

In the following we give detailed reasons why this document is not needed.

## **5.2 Key principles**

In the recent years the pharmaceutical and API producing industry has developed a common understanding of the general principles of computer validation. This common understanding is based on several guidelines issued by either agencies (e.g. FDA) or industrial interest groups (e.g. GAMP). Each firm has defined in company specific procedures how to deal with these requirements. These company procedures adress the specific needs of each of the companies. For example in our understanding the quantitative results of validation tests are part of the corresponding test plan (DQ/IQ/OQ/PQ), the report gives a qualitative summary of all tests performed.

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So we think by describing the procedure like in this chapter there will be confusion to an already established system of computer validation.

In **5.3 Equipment Installation** standard operating procedures are mentioned. It is not explained what kind of SOPs. In general the handling of documents needed for an IQ (installation Qualification) described is in all companies computer validation guidelines and SOPs.

## 5.4 and 5.6

The described test considerations and extends should not be a general requirement for all parts of the system /software.

The extend of validation and key testing considerations are described in detail in a risk analysis of the system. There the single risks to the quality of the product and data or risk to the patient and consumer are considered. Only in those cases where a certain risk is detected, the extend of testing as described in chapter "test conditions ff." may be performed as appropriate.

This also applies to 5.4.2, "structural testing". Only in the case of own developed software a code review may be necessary if there is a potential risk discovered in the risk analysis.

In general we think that the instrument of "white box testing" is outdated because modern software consists of several thousand up to million lines of code of which all should then be read and tested without any additional security. In the case of commercial, or off-the-shelf software there is usually no access to the source code.

## 5.5 Static verification

The check of system development is done in the course of a system vendor audit. This is standard in the industry by now.

## 5.6 Extend of validation

As mentioned above, performing a risk analysis is usually one of the first steps in computer validation by now. The check of data confidentiality is in our understanding not a GMP requirement but a security issue of every company.

## 5.8 Change control

It is our understanding that the term "revalidation" means the re-testing of the complete computer system (performing all validation tests). Every company has a

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change control system in place, this chapter may create confusion on what the agency expects.  
Also the term "regression analysis" is not understood. The actions described in this chapter are covered by a risk analysis.

## 6.1. Commercial, Off-the-shelf software

6.1.1 The requirement specifications relative to 21CFR11 are added functionalities which have to be implemented and validated during the course of validation. There is no need for an extra document.

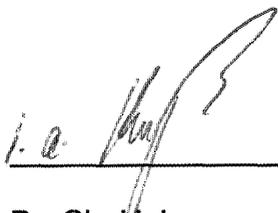
6.1.2 Because almost all of the installed software in industry is commercial software, the structural integrity is tested by the means described here as appropriate. It is not always possible to do "all of the following".

6.1.3 Functional testing is a well established practice in computer validation. The extend of testing required is determined by a risk analysis mentioned above.

## Summary and conclusion

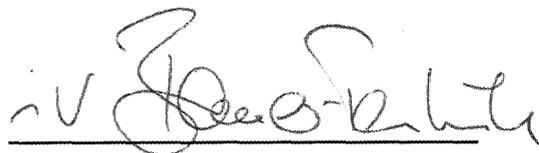
How to perform a computer validation is an established process well guided by company-own SOPs and several guidelines like GAMP. The requirements of 21 CFR 11 are also well described and known. In our understanding of validation it is naturally that these additional functionalities have to be proper validated and tested like every other critical software function. Therefore there should be no distinction between computer validation for 21CFR11 and "regular" computer validation.

We therefore suggest not to implement this document. It may create confusion in the industry and will slow down the process of achieving compliance with 21CFR11.



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