Containing the 21 CFR 11 Problem: Purchase of Non-Compliant Systems

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The current emphasis of 21 CFR 11 is on the assessment of legacy systems and their remediation. However, a potential problem is the lack of measures to contain the problem. Organisations are still purchasing non-compliant equipment and systems; what are the steps to be taken to ensure that these new systems will also become compliant?

Introduction

Publication of the electronic records and electronic signatures final rule [Ref 1] in 1997 started a time bomb ticking for all organisations impacted by the regulation, as legacy systems were not excepted. The way the FDA will inspect firms has been laid out in the compliance policy guide (CPG 7153.17) published in July 1999 [Ref 2]. Administrative and procedural controls are expected to be in place, and action plans implemented with demonstrable progress towards technical controls for systems. Regulatory action is dependent on the compliance history, progress towards compliance and the seriousness of deviations; a warning letter has already been issued requesting the global plan for attainment of 21 CFR 11 compliance from at least one organisation [Ref 3].

Still Purchasing Non-Compliant Systems?

The emphasis since the publication of the Compliance Policy Guide has been on the assessment of legacy systems already installed and operating in organisations impacted by 21 CFR 11. However, as there are very few applications and systems that are currently compliant with the regulation, organisations are still purchasing non-compliant equipment and systems, thus perpetuating and compounding the non-compliance problem.

Discussions with attendees at training courses run over the past months have revealed that many organisations have no mechanism in place to prevent or mitigate purchase of non-compliant systems. This in the authors' view is exacerbating the problem.

Moreover, there is likely to be a relatively long wait until compliant versions of software are available. Quality software development takes time and should not be rushed, otherwise the resulting product may be worse than the current non-compliant one.

Parallels with Year 2000 Compliance

Recall if you will, the problems with Year 2000 compliance. One of the major challenges was containing the problem: purchasing departments had to be educated and involved, so that personnel did not order computerised systems and equipment without sufficient due diligence being performed. This would involve:

- Requesting a vendor's own evaluation of the Y2K compliance status of an item.
- Purchase order requiring the vendor to take back the item if not compliant.
- Updating the Y2K inventory when an item was received.
- Testing the item for compliance during installation.

21 CFR 11 Compliance—What has Changed?

Fast forward to today, substitute 21 CFR 11 for Year 2000 compliance, and ask yourself what has changed? Nothing - at least in the process that we should all be following.

However, we have differences in containing 21 CFR 11 compliance problems. We are not as well-organised, as there is not the fixed and immovable deadline of 31st December 1999 that was the situation with the Year 2000 problem. Talk to many involved in the assessment of systems for 21 CFR 11 compliance and ask them why there is nothing in place for containing the problem. Many will argue that work will suffer if they cannot purchase a new system regardless of the 21 CFR 11

compliance. If organisations can contain the Year 2000 problem why can't they contain the Part 11 problem?

Current Vendor Offerings

What are the current offerings from vendors of computerised systems and applications to the pharmaceutical industry? There is a great variation.

Some vendors have designed and produced products that they claim are 21 CFR 11 compliant (assuming that users implement appropriate controls and training to compliment the design). When examined for compliance by experienced personnel from an organisation this may be true, or it may be that the vendor has misunderstood what is required from 21 CFR 11.

For example, there are several applications, which the vendors claim to be 21 CFR11 compliant, which are non-compliant in the implementation of electronic signatures. For example:

- They do not display date, time or meaning of the signature whenever the signed record is displayed on screen.
- Linking electronic signature with the appropriate electronic record is achieved though the audit trail; the entry is therefore hidden until a specific sequence of commands is given to reveal it.

This raises the question of whether some vendors really understand the regulation. Apart from implementing an audit trail, compliance also requires that all versions of the original records be maintained and be retrievable for the record retention period. System security features must also be enforced. Whilst focusing on the audit trail, these other requirements have sometimes been overlooked. The reality is that a fundamental redesign of an application is often required to ensure 21 CFR 11 compliance.

Systems that are high up the corporate visibility scale, such as electronic document management systems (EDMS), enterprise resource management (ERP), electronic batch record (EBRS) and laboratory information management system (LIMS) are developed by vendors that will have implemented compliant software, or are in the process of doing so. Where systems are more local, such as supervisory control and data acquisition systems (SCADA), or laboratory systems and standalone equipment, the vendors have less push to produce compliant systems. Here, some vendors may not even be aware of 21 CFR 11, and have yet to undertake any planning to achieve compliance. Others are only just starting.

Where pharmaceutical industry is not the main commercial interest, some vendors may have no intention of providing a compliant product, as it is not commercially viable for them to do so. They may pay lip service to producing a compliant version of their product, but may not do so. These systems need to be identified, and plans drawn up to replace them with a compliant version.

Containing the Part 11 Problem

The way to proceed for containing the Part 11 problem is detailed below and shown as a process in Figure 1.

The first stage of effective containment is a policy or an SOP outlining what will be done to contain the 21 CFR 11 problem. For this containment policy to be effective, it is essential that it be linked with a centralised method of purchasing new equipment. The new Containment SOP needs to be communicated to all involved in the specification and purchase of computerised systems and equipment impacted by the Part 11.

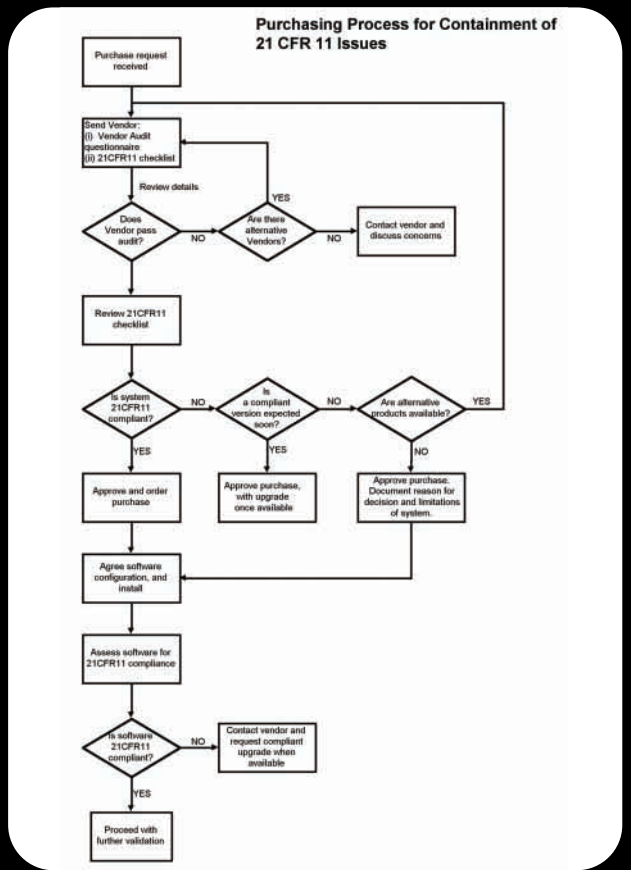
The communication and education process must include all the users who are involved with purchase, and they must be aware of why they need to purchase the most compliant product. From experience with Year 2000 compliance, the Policy may fail at this stage if users are not fully involved. Therefore there must be good communication between users, department's central purchasing team, and the 21 CFR 11 assessment team.

Any potential purchases must be evaluated for compliance with 21CFR 11 before the order is placed. This is most important, as the most compliant option should be purchased, following discussion between user and assessor/purchasing team, providing that it can undertake the work specified for it. Remember that a specific requirement of 21 CFR 11 [11.10a] is the formal validation of the system. Depending on the size of the system involved, either a user or system requirements specification or a specifically designed 21 CFR 11 checklist should be submitted to the vendor and the responses used to assess compliance of the system. This product evaluation prior to purchase must be adequate for the item, and forms a key part of the process of system definition and selection, and also validation. Each software revision requires its own product evaluation checklist.

There will be many instances where the required product is not compliant, and no other compliant alternatives exist. Here the reason for purchase must be justified under the 21 CFR 11 containment policy or SOP. If this is not done then you could be amplifying an already large problem. In cases such as this, the purchasing department must get a statement from the vendor that a compliant product will be available within, say, 12 months. Do not leave this as a simple statement; the purchase order should be linked to penalty clauses that if a compliant version of the system is not available then a percentage of the purchase price will be refunded by the vendor. This will indicate to any vendor that the organisation requires a compliant version of the system.

21 CFR 11 does not only set standards for software and maintenance of electronic records. It also includes many proceedural requirements, including documentation of experience and training of all who develop and use the system. Working in a GxP environment has always required that documented training records are maintained for users of the system. Now, in addition, it is necessary to obtain evidence from the vendor that their

Figure 1



staff, including software developers and maintenance staff, are also suitably experienced and trained. Such information must be provided in a vendor audit, which may either take the form of a full visit to the vendor site, or, full smaller systems, can be obtained by submission of a vendor assessment questionnaire.

Where several areas within the same organisation are reviewing compliance (for example across several sites or across research, development and production), a centralised database of vendor assessments and product evaluation checklists prevents unnecessary duplication of effort and requests for vendor information. All those involved in the purchase or assessment of systems must be able to access this information through the Organisation's central IT network. As the compliance requirements are essentially the same, irrespective of the functional area, it is recommended that a single assessment format is used throughout the organization.

Software upgrades are also covered by the containment procedure. Any system undergoing a software upgrade must be upgraded to the most compliant version. Again, good communication between the scientists in the lab and the 21 CFR 11 assessors is essential. It may be beneficial to hold back from upgrading old software to the current software version, if the 21 CFR 11 compliant version will be released in the near future. The containment process should ensure that these purchases are monitored and controlled. The practice of upgrading instrument software as part of a routine service contract must be prevented, as a compliant software package can easily be installed in a non-compliant manner unless the installation requirements are reviewed and agreed in advance.

Standard industry software packages still need to be assessed for compliance, even if validation is considered unnecessary. For example, a standard Oracle database does not itself require validation. However, where an application has been developed around such a database, then the whole application, including database use, must be assessed for compliance, and fully validated.

On a smaller scale, scanners may be used to record photographic data, or TLC plates. The software packages used are industry standards, and would not normally be subject to validation. However, if the scanned files are supportive of results in a submission to the FDA, then they are subject to 21 CFR 11. The software therefore requires assessment of its ability to maintain all records, provide an audit trail, etc. A further example is the CD-writer software, which may be used to backup the records to CD.

Formal assessment of compliance should be carried out once product is installed. This will be part of the formal validation of the system against the requirements detailed in the URS or a formal assessment using the organisation's 21 CFR 11 checklist.

Conclusion

Containment of 21 CFR 11 issues is essential to avoid prolonging the problem and increasing the expense of assessment and compliance. Parallels between containment of Part 11 and Year 2000 are striking and this will enable organizations to use past experience to good effect. ■

References

1. 21 CFR 11, Electronic Records, Electronic Signatures Final Rule, Federal Register 62 (1997) 13430 - 13466
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3. Baxter Healthcare warning letter, August 2000.

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