Much discussion has been focused on the costs and effort required by the pharmaceutical industry to become compliant with the requirements of 21 CFR Part 11 (Electronic Records and Electronic Signatures) regulation. The preamble to the final rule estimated that industrial implementation of the requirements of 21 CFR Part 11 would be “broadly cost neutral”, in marked contrast to the projections of two companies that estimated the cost for compliance to be in the US $130–150 million range. Most emphasis has been placed on the assessment of current (legacy) systems and becoming compliant.

However, the purpose of this column is to draw attention to the benefits that can be exploited from implementing a compliant CDS for both electronic records and electronic signatures. It develops the theme of an earlier article, which proposed that when implementing a compliant system you should consider redesigning your existing processes to exploit the benefits that are possible under the scope of 21 CFR Part 11.

Benefits Possible in any Chromatography Laboratory

Whilst I may be focusing on the pharmaceutical industry, the requirements for electronic signatures and electronic records actually benefit all chromatography laboratories regardless of industry sector. For example, chromatography laboratories operating under ISO 17025, the quality system for testing and calibration laboratories, would benefit from using the approach in this column.

Fear of Change

While many computerized systems fall under the electronic record section of Part 11, many organizations are wary of implementing electronic signatures even when compliant solutions are available. Reasons for this are many and include the following:

- fear of change in working practices
- electronic signatures are unknown or should be avoided
- comfort with using existing paper records and systems.

In fact, implementation of electronic signatures is relatively simple provided there is a compliant solution available. This is in contrast to the problems faced with managing electronic records over the entire record retention period. This might include changes in file format, different archive media used over time, plus potential data migrations and being able to replay the data.

Benefits from a Regulation?

You may think that I’ve gone insane when I suggest that you can have benefits from a regulation but this is exactly what I am suggesting. Streamlining your current process and working electronically will allow substantial business benefits, providing your CDS is compliant. However, don’t just take the vendor’s word for it — you must check this out yourself.

To illustrate the benefits possible under 21 CFR Part 11, we will look in an analytical laboratory, specifically at the process for analysing samples using a CDS. This scenario is based upon several laboratories.

When upgrading to a compliant system, take advantage of the significant business opportunity this presents, benefit from 21 CFR Part 11 and work electronically. Some of the aims should be to

- reduce process bottlenecks
- design efficient handoffs and transfers between groups and systems
- eliminate paper
- reduce the number of systems and hence the overall validation burden
- eliminate multiple manual entries into systems and paper
- rationalize the electronic signature and electronic identification requirements to ensure compliance
- save time and personnel effect through the new process
- design the process for consistency.

After all, as the pharmaceutical industry asked for a regulation on electronic signatures in the first place, let all chromatography laboratories exploit the regulation and obtain the benefits.

Map the Existing Process

To exploit 21 CFR Part 11 benefits, the existing process is unlikely to be particularly...
efficient; many processes in your laboratory have evolved over time and these were not usually designed. Only when a process is mapped will the users and process owner appreciate how inefficient and ineffective the process actually is. Therefore, before implementing a 21 CFR Part 11 compliant system and exploiting the benefits of the regulation, the process needs to be mapped and understood, the bottlenecks identified, where are signatures (as opposed to identification) required and the process metrics measured (sample turnaround time, number of samples etc.).

Automation in a Sea of Paper
We’ll look at a chromatography laboratory that has the following computerized systems that accompany a paper-based process:
• LIMS that is used for sample tracking and reporting results
• CDS for analysing data and measuring peak area
• Excel used for calculating results from the CDS, such as system suitability tests criteria and analyte amounts.

The process is essentially manual: entries into all systems are typed in. This scenario is typical in many organizations and as we walk through the process redesign you’ll be able to see the benefits that can be obtained from 21 CFR Part 11.

The existing analytical process is shown in Figure 1; analysis of this process shows that there are five process steps with the following features:
• mainly manual work with multiple data entries and transfers into the three applications (LIMS, CDS and Excel)
• a paper-based approach to records management with handwritten signing
• three potential rework loops because of transcription errors following the manual entry of data into the three systems
• four printouts to manage plus any associated laboratory notebook entries
• three individual system validations are required for the three applications
• three hybrid systems with the associated problems of managing and synchronizing the electronic records and associated signed paper records
• bottlenecks in the process that cause delays in the process.

21 CFR Part 11 compliant CDS and LIMS can be implemented either on the process outlined in Figure 1 or on a redesigned process. Excel can be made compliant with the use of add-ins such as DaCS (Wimmer Systems). However, given the high level of manual involvement in the process it is unlikely that significant business benefit will be obtained if the existing process is updated with Part 11 compliant software applications, as there is the inherent inefficiency of the current process. Therefore, the process should be examined to see where improvements could be made to take advantage of 21 CFR Part 11. We will explore some of the process redesign options to see which changes can be made.

Simplify and Redesign the Process (1): Discard Excel
As a starting point for reviewing the process, assess if the calculations performed by Excel can be undertaken by the CDS. For example, the system suitability calculations that are performed in the spreadsheet can usually be performed in the CDS as these calculations are an integral part of the chromatographic process. Calculation of analyte amount or concentration is part of the usual functions of the CDS, so why do analysts use spreadsheets?

Custom and practice is a normal response: “we have always done it this way”. The reason is that the spreadsheet is relatively easy to use and users can develop their own calculations and this can be easier than learning to use the CDS functions. However, eliminating the spreadsheet and performing the calculations in the CDS will eliminate
• one application (Excel)
• one hybrid system
• one rework loop
• one paper printout
• manual transfer into Excel.

The process is now redesigned as shown in Figure 2.

One advantage is now apparent from...
Questions of Quality

Process redesign is an essential tool in exploiting 21 CFR Part 11 as working electronically allows an organization to obtain significant business benefits.

elimination of the spreadsheet; as the results are now all contained within a single system you can now use electronic signatures to sign-off and approve the final results. Here mapping the process will be very useful as you can highlight where in the current process the approvals and identification on existing paper records are to be found. Again there is the issue of custom and practice; there is a tendency to sign virtually all records that are on paper. Review these and compare them against the signing requirements in the predicate rule to ascertain if all are required? Ensure that the CDS can identify the individual making any changes to the electronic records and check that the electronic signatures in the new process are in the correct place and cover all appropriate records.

At the end of this phase of the process redesign, the CDS will be compliant with the 21 CFR Part 11 with electronically signed records. However, the system is only standalone and to transfer results to the LIMS the results must be printed out and then entered manually into the LIMS. To improve the process further and obtain further business benefits, we need to consider interfacing the CDS with the LIMS.

Simplify and Redesign the Process (2): Interface CDS and LIMS
As outlined above, the next stage is to look at interfacing the CDS with the LIMS. This will be covered in two parts: first, the unidirectional interface and second, bi-directional interfacing.

To speed up and improve the process, interface the two systems to transfer approved and electronically signed results from the CDS to LIMS automatically. Once this process is completed and validated, you can eliminate
• one manual transfer and replace with a validated automated one
• transcription error checking the manual entry
• two printouts (one from the CDS and one from the LIMS).

This redesign step will provide a rapid payback of the investment in the design and validation of this interface as manual input should be eliminated from the process. This process is shown in Figure 3. The final stage of this process redesign is to complete the LIMS to CDS interfacing and allow the download of a work list from the LIMS to the CDS. This allows the CDS to import the file and incorporate it in the sequence file. This will save manual input of the order of the sample analysis and eliminate the final paper printout. The final process redesign is shown in Figure 4.

Cost-Benefits of the Process Redesign
Process redesign is an essential tool in exploiting 21 CFR Part 11 as working electronically allows an organization to obtain significant business benefits. Significant cost and time savings can be obtained if you stand back to map and review your process. Some of the savings that can be realized are based upon the following activities:
• reduce number of applications to validate
• eliminate manual involvement in the process (e.g., tasks such as typing data into systems followed by manual transcription error system)
• eliminate tasks from the process to save overall time for process execution.

References

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Figure 3: Redesigned process after connecting the CDS to the LIMS for unidirectional results transfer.

Figure 4: Paperless process utilizing bidirectional data transfer between the LIMS and CDS.

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