When It’s Documented, It Happened
A New Approach to Tracking Generic Drug Development

Rigour amongst health and medicine agencies worldwide has significantly increased over the past decade, and their scrutiny when inspecting one’s system-based approach and documentation is not a “new thing” any more. “What has not been properly documented, did not happen.”

We know that public health benefits from generic drugs and agency diligence. However, can generic drug manufacturers benefit as well from the new “normal”? Yes, indeed.

Drivers
While it is somewhat challenging to control an R&D project over a typical timespan of 30 months, it is quite feasible to control key deliverables - DOCUMENTS. What hasn’t been documented did not happen, remember? There are many drivers that make us take a close look at every stage of that process.

New Chemical entities (NCE) Development

They must demonstrate clinical bioequivalence to the innovator drug and
they must be the first to file their dossier for review and approval.

A generic pharma company will have months, not years, to reverse-engineer the performance of a brand product and demonstrate its bioequivalence.

In-depth knowledge of IP, monitoring data exclusivity and demonstrating superior formulation and the overall development process is not enough. Project management becomes a key ingredient.

Some Documents Are Gatekeepers
The process is long, but it also produces thousands, if not hundreds of thousands of documents. These documents are either archived or used for different purposes (development reports, quality control, registration dossier, purchasing and production).

It is therefore of paramount importance that the right versions of these documents are readily available to authorised persons, that all of the changes are immediately propagated, and that the person in charge of the development process can track the life-cycle of each of the relevant documents.

But there is more to it: Some of these documents are milestone marks; they represent the end of a particular development process phase. A stability report or bioequivalence study clearly marks the end of the corresponding phases. Every phase, standard or customised for a particular method/product/company has such a document.

By tracking these outputs, we can easily monitor the whole process against set deadlines.

These requirements can only be achieved by use of modern electronic document management system (EDMS) and reporting tools, and it is therefore strange that there are so few dedicated development solutions in the market.

In this article, we will discuss the important features of such a solution using the example of one commercially available solution. Although the solution is also applicable for the development of innovative drug products, we will concentrate on development of generic drug products.

R&D Project Management Support
The development of a generic drug product usually starts with a strategic marketing decision on the desired product’s characteristics International Nonproprietary Name (INN), form, dose, markets, referent product, targeted launch date...). In most companies, the development process is project-oriented, so the next step is choosing a project manager and project team. The project manager then puts together the project plan (usually with MS Project or a similar tool), in which all project-related information is available (start and finish date of each activity, milestones, usage of resources...). The result of each project activity is usually a document, so in order to complete the project, the project manager has to gather all of the relevant documents and compose them into the project report.

But the real problems begin with the actual start of the project, since in most cases real life does not follow the plans. Dates shift; people are not available any more; new reminders have to be sent out for commencement of activities. Information on all executed actions has to be entered in the project management application. This puts a tremendous strain on the project
The manager and his limited timeframe, and it often fails to perform these duties in timely manner. In addition, the project management tool makes only one piece of information available on the project deliverables, namely if the document in question is finished or not. For all of the other information (if the work on the document has commenced or not, which life-cycle stage the document is on, if there is a new version of the document in preparation...) the project manager has to consult other applications (most frequently a large Excel spreadsheet), which again is only as good as it is diligently updated.

These problems can only be solved by combining the project-oriented approach with document management. The project plan is put together in the usual way (using MS Project), but after the approval, it is transferred to the document management solution. The project is represented as a virtual document, and each of the project activities automatically creates a binder, in which the relevant project information (start date, finish date) are represented as document attributes (metadata) (Fig. 1).

1. At the predetermined start date, the project manager gets a reminder from the system to start the task. The project manager determines the roles on the document (author, reviewer, approver) and starts the task.
2. The author gets the task in his inbox, writes the document, and finishes the task by sending the document to the reviewer.
3. The reviewer performs the review and finishes the task by sending the document to the approver.
4. After approval, the document becomes effective, and the project manager gets the information in his inbox that the document is available. This information can be e-mailed as a follow-up action, but also a colour-coded scheme to visualise the progress on each dossier (Fig. 2.)

Fig. 2.

It is worth mentioning that the document is automatically stored in a predetermined place in the database (based on the document attributes), and it is linked to the appropriate binder in the virtual document structure. In this way, there is always only one valid document in the system, it is transparent where this document is used, and if the new version of the document is available, all users of the old version are able to see it.

Fig. 3.

During the whole document creation process, the project manager is able to check where the document is, who is in charge, whether the process is on time, and even the content of the document. When the due date of any activity is approached, the task performer will get a reminder, and if the activity is not finished by the due date, the reminder goes to the project manager. In this way the project manager can see the status of all project activities at a glance, and get information on all overdue activities - all from one solution, without manually entering all the status changes. A consolidated view of several projects by management is also possible, even on the level of activity or group of activities comparison. This can than help in increasing the overall process performance (Fig. 4.).

When all of the project activities are finished, all of the documents can be merged into a single PDF file by a simple command, and published with a table of contents (ToC) and hyperlinks, forming the so-called Development Dossier. The final document (in PDF, or both PDF and virtual document form) is then made available to all of the relevant departments, to be perused in whole or in parts.

If an individual document is to be used for other purposes (for example, the specification in purchasing,
quality control and registration dossier), and other solutions are available, the document is not copied, but again linked in the appropriate virtual document (registration dossier, analytical procedure...).

Fig. 4.
As described above, there are a lot of advantages in utilising document management solutions in managing the drug development process. The process is transparent, the project manager and the management are able to monitor all of the activities, documents are stored only once in the system and are reusable and, last but not least, the whole process is well documented in compliance with 21 CFR 11 and EU GMP Chapter 4 and Annex 11 requirements. All of this together guarantees a smooth and efficient development process, improved time-to-market and fewer worries about regulatory compliance.

It is also a very powerful infrastructure to build on, either for management reporting, process improvement or interfacing other systems using business intelligence reporting tools.

Here are is one example
a) Tracking multiple projects using an slice & dice tool
b) Drill-down: delayed projects