Cost-cutting exercise

Specification software for the pharmaceutical industry

Benjamin Bryant

The use of the eSpec electronic specification system can save time in deploying the complete specification required to plan, source, manufacture and deliver a new pharmaceutical product – which in the case of a blockbuster drug can mean savings of over a million pounds a day.

It takes substantial investments of time and resources to bring a new drug to market. The average time from original idea to product launch was 15 years in the mid-1990s. All the major players worked on ways to reduce the time from development to market, and by the end of the 90s this was down to 9 to 10 years. These reductions saved the industry billions of dollars and further cuts would obviously save billions more.

One improvement needed was the prompt, accurate sharing of dose form and package specifications across internal functions. The trend to distribute risk and manage resources has resulted in many firms depending on outsourced or external teams. Thus, the total number of people in the team that have to participate in the accurate expedition of new drug development has greatly expanded beyond what previous practices can deal with.

As the total time to develop and launch new drugs has been compressed, pharmaceutical companies increasingly encounter missed handoffs and constraint surprises that caused late launch dates for 25% of new products in some companies. Many of these delays are coming from the Chemical and Manufacturing Control (CMC) requirements for filing rather than from the clinical side of the operation. These extra requirements are proliferating just as pharmaceutical companies are gearing up to double the number of products they develop and launch each year.

Product life cycle management

What clearly emerged was the overwhelming need for an electronic product life cycle management system that can manage the development and deployment of the complete specification required to plan, source, manufacture and deliver a product. This would include all specifications of intermediate and finished products, raw materials, resources (assets), and processes (recipes).

To work towards a solution to the above challenges, it is helpful to study the process and needs in current practice today. The development of a drug encompasses nearly 1,000 discrete steps stretched across continents, years and thousands of professionals. When a drug is first approved to enter man, there is already a lot of knowledge accumulated about the molecule: its tendency to be absorbed by animal models, broken down and excreted. Soon, data on its side effects, the toxicological patterns of the molecule and its metabolites also become known. In addition, the typical impurity levels of the raw drug, as well as its tendency to break down on storage with heat, moisture, etc., are measured. And this is years before the ultimate dose form that will be registered is defined.

If the dose form is a tablet, there will be data on those degradents, including their FDA-allowable limits. 90% of the tablet will most likely be made of inactive binders, fillers, coatings and colorants. Each of these in turn will have set proportions defined to the active, as well as defined, degradation "children" (not to mention the results of component interactions!).

By the time Phase III trials are beginning, the final dose form will not only have been chosen and made to be tested in those trials, but its shape, imprint, hardness, etc. – all kinds of characteristics – are defined by data and set in bounds called specifications. All possible packages will have been roughly defined and the products will have been already put up on tests to see if the package protects or interacts with the materials it holds under different conditions. All of these final summary statistics are evaluated, reported on and submitted to regulatory authorities. But it does not end there.

Data on the cost and process of making the active molecule as well as the tablet is captured and controlled according to set processes and specifications. Economic estimates and the accurate cost of materials are linked to the actives as well as to the inactive materials and packaging components.

Packaging problems

Packaging creates one of the greatest volumes of data on a pharmaceutical product, as every component's content and appearance must be controlled and pre-approved. Some countries require transparent blister packs, some childproof packaging. All require an unambiguous label that cites the product name, corporate logo, address, brand, ingredients and so much other data that a ten or twelve page insert must accompany (it cannot fit on even a large-size bottle.) And each country may have unique, specific language and registration formats or codes on the label and/or insert.

While it is reasonable on a generic basis to describe all of this data as being specifications, it is not treated as such in a uniform basis through the entire 10 to 15-year process. Information is passed on in stages and in some firms it is kept in an evolving "pro-

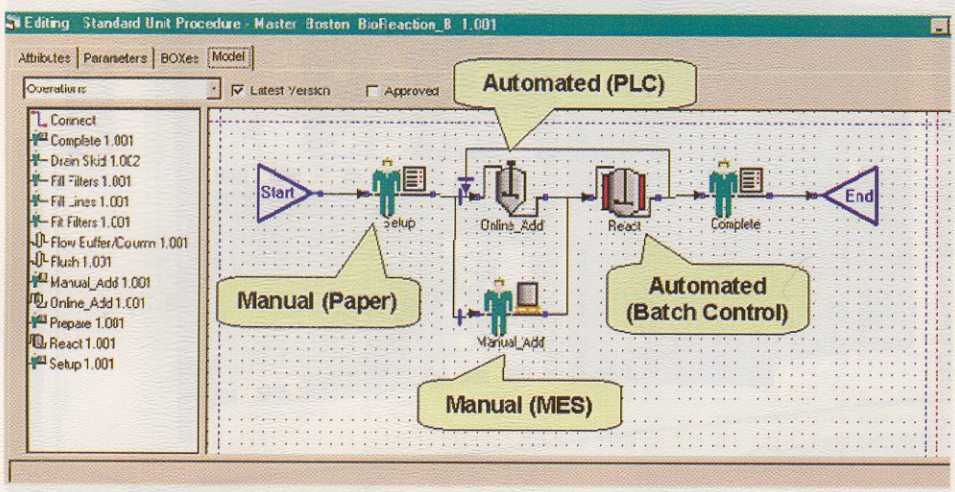
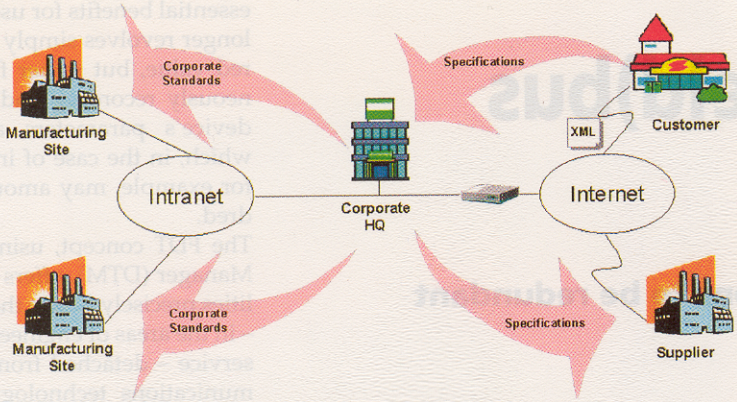


Fig. 1 From concept to integrated manufacturing execution

Fig. 2 Open architecture to support the extended enterprise



duct definition file". This begins as a description of what the ideal product character is hoped to be, and actual data is compared to that ideal as information comes in. Ultimately, the medical data is garnered from the clinical trials and distilled into a strong framework required for the regulatory filing. The non-clinical data is also distilled into the complementary CMC section, as "ownership" of it passes on from clinical and development groups to Regulatory (a department within the company.) Other groups that "own" data include the analytical group, the toxicology group, finance, marketing and sales. Packaging is a subset within manufacturing that files considerable amounts of unique data as well as the manufacturing operations themselves, including the quality control group.

In a jam

In 2000, a collaborative process between the Honeywell POMS Corporation, a business unit of Honeywell's Hi-Spec Solutions, and the J. M. Smucker company purchased a comprehensive manufacturing solution for the myriad challenges affecting the pharmaceutical industry. One unique circumstance surrounds the genesis of this breakthrough solution – the J.M. Smuckers Company makes jam, preserves and a host of other packaged foodstuffs, not pharmaceuticals. The company selected the POMS products because it wanted to manufacture to pharmaceutical-grade quality standards.

As Smuckers found operations becoming more diverse and complex, the company saw the need for a complete specification management system to define their products. Smuckers engaged Honeywell POMS in the co-development of what became POMS eSpec. The extensive experience of the Honeywell-POMS organization in the pharmaceutical industry and with manufacturing standards was used to develop POMS eSpec into a solution that particularly fits this industry.

The eSpec electronic specification system

POMS eSpec offers practical solutions for the pharmaceutical, biotech, nutraceutical and healthcare markets to operate in a more flexible and innovative manner. It is ideal for companies that use flexible manufacturing facilities to develop many new products in many different dosage forms.

For example, a product development department needs a highly flexible development sandbox where a number of alternatives can be evaluated. After the development process is completed, a global standardisation department creates a specification that can be applied constantly throughout the enterprise. The manufacturing site may need to make an adaptation for local legislation, language and unit measure. The manufacturing plants require a level of detail that is sufficient to support manual, computerised and automated execution of the procedure. POMS eSpec provides the capability to define dedicated environments for these development stages tailored to specific requirements. A very special feature of the system is that it combines the capabilities of product data management applications, batch recipe management applications and formulation development applications into one comprehensive solution to support product AND process development in a collaborative environment.

The eSpec system supports the full product life cycle, from product development to enterprise standardisation and consistent multi-site manufacturing execution, bridging the gap between product development and manufacturing and streamlining the product transfer process. The application also supports the entire extended supply chain by enabling cooperative development and exchange of specifications with customers and internal or external suppliers through the Internet. It is an object-oriented, web-based application, conforming to industry standards and designed to adapt to changing business requirements, fully incorporating S88 manufacturing standards. The manufacturers believe the software to be a flexible and open solution to solving specification problems with real capability to reduce time-to-market, saving a lot of money for the pharmaceutical manufacturer, while increasing product consistency and enterprise agility.

www.honeywell.com

▶ **cpp 235**
www.honeywell.com

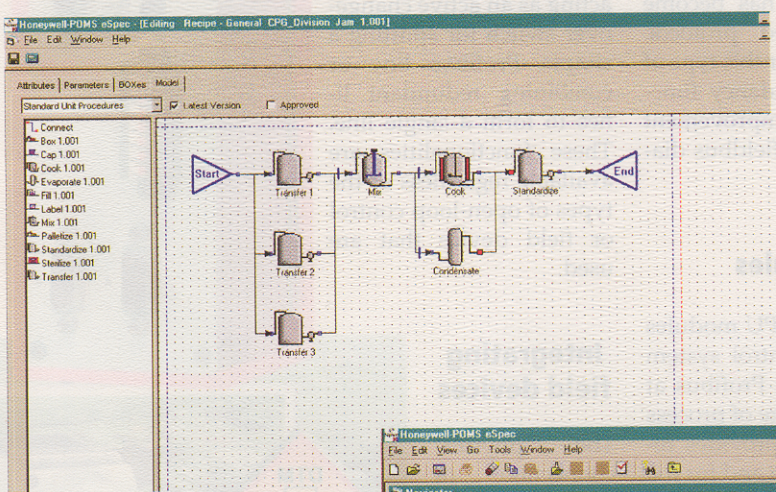


Fig. 4 Standard unit procedure

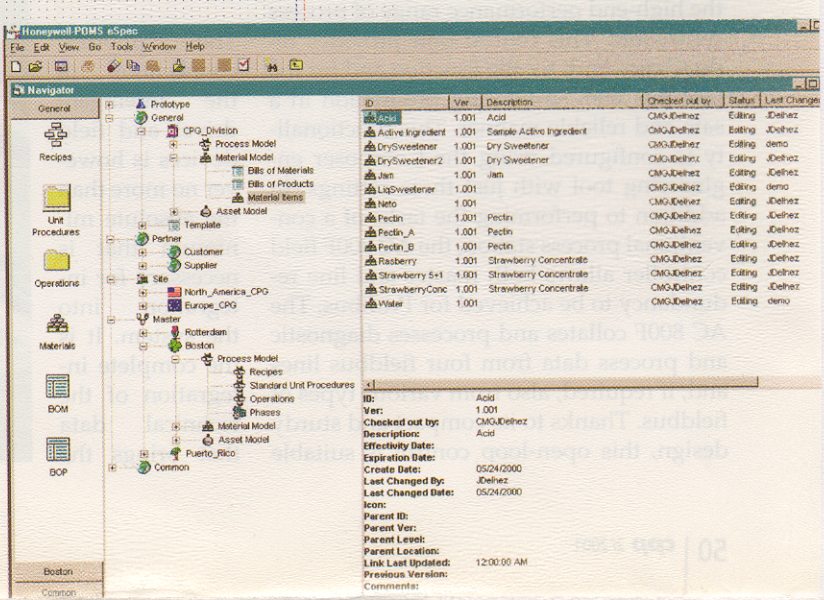


Fig. 3 The eSpec Navigator