Integrated Plant Management System for Meeting Operational Changes in Drug-manufacturing Industry Due to Revision of Pharmaceutical Laws

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OVERVIEW: In recent years, international harmonization of regulations between the pharmaceutical industries of Japan, the USA, and the EU has been progressing steadily. Following this trend, Japan will enact a revision of the Pharmaceutical Affairs Law in April 2005. As for the revised Pharmaceutical Affairs Law, safety measures regarding medical equipment and products of biological origin have been reviewed. A point of note in this revised law is the revision to the system for approval and authorization of drug manufacturing. As a result of the revision to the system for approval and authorization, it has become possible to completely separate the manufacturing and sales of drugs. Changes in the drug-manufacturing business—such as spinning off of the production sector of the pharmaceutical industry—are being anticipated, and commissioned manufacturing is expected to expand even more in the future. Providing solutions for the increased number of commissioned manufacturers in the future, Hitachi has developed an integrated plant-management system based on Hitachi pharmaceutical plant management system. As a result of implementing this system, the system requirements of commissioned manufacturers can be integrated and satisfied by a single package.

INTRODUCTION

AIMED at preventing the spate of medical malpractice incidents and accommodating the international harmonization of drug regulations, revisions to the Pharmaceutical Affairs Law in Japan will be enacted in April 2005. An important point of this revised law is that the system for approval and authorization of drug manufacturing has been reconsidered. As for the system used up to now, companies interested in selling drugs were obliged to operate manufacturing facilities; in contrast, after the revision of the Pharmaceutical Affairs Law, it will be possible to consign all manufacturing processes to external contractors, thereby completely separating the manufacturing and sales of drugs. As a result, with new-drug development and cost reduction as targets, the pharmaceutical industry will be able to actively spin off production departments and commission manufacturing, thus increasing the scale of manufacturing trustee or commissioned companies (see Fig. 1).

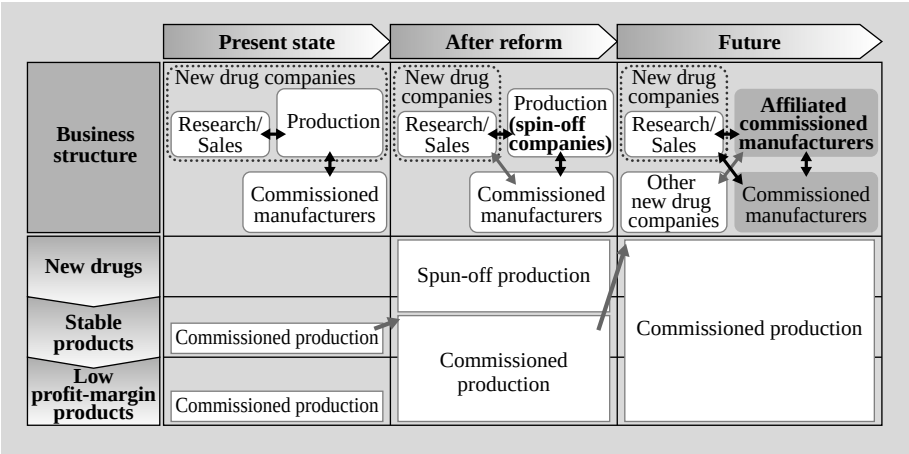

Fig. 1—Flow of the Regrouping of Drug Industry According to Revised Pharmaceutical Law. The spin-off of production branches of major drug companies is continuing, and manufacturing and sales are becoming separated. Increased production volume at specialized commissioned manufacturers is thus expected.

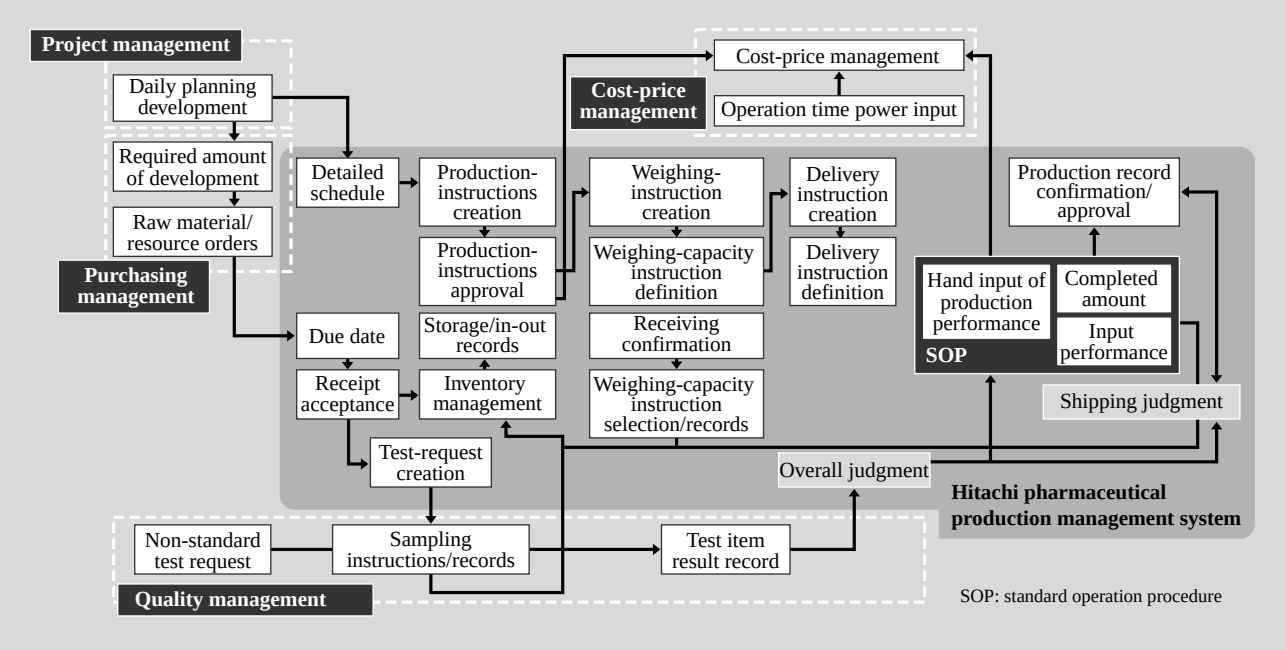

Fig. 2—Relations between Various Functions of Integrated Hitachi Pharmaceutical Plant Management System. As optional functions of Hitachi pharmaceutical plant management system, design management, purchasing management, cost management, and quality control are linked as shown in the figure. In line with the revised pharmaceutical law, solutions aimed at increasing commissioned manufacturers have been developed.

With these trends in mind, Hitachi has developed an integrated pharmaceutical-production management system—based on Hitachi pharmaceutical plant management system* (see Fig. 2)—as a solution meeting the requirements of commissioned drug manufacturers.

In the rest of this paper, the system requirements of commissioned manufacturers are explained, and the integrated drug-production management system is described.

CHANGES IN MANUFACTURING INDUSTRY DUE TO REVISED PHARMACEUTICAL LAW

Background and Key Features of Revised Pharmaceutical Law

Under traditional pharmaceutical laws, it was assumed that drug companies had manufacturing facilities, and manufacturing approval was given according the inspections of equipment and quality-control procedures in those factories. However, the system for assuring safety of manufactured drugs after sales was inadequate, and problems, such as not attaining compliance with the sales approval systems in the USA and Europe, were encountered.

In response to these problems, under the revised Pharmaceutical Affairs Law, new manufacturing and sales approval systems are being introduced, and the responsibility for quality of products on the market is defined as residing with individual manufacturers and suppliers. As a consequence of these revisions, from now onwards, complete outsourcing of manufacturing processes—and thus the potential to increase commissioned manufacturing—will be possible.

Needs of Manufacturers and Distributors (Commissioned Manufacturers)

In order that commissioned manufacturers can grab a share of the commissioned-manufacturing market, it is important to know how to respond to their needs.

To consign manufacturing to commissioned manufacturers securely, commissioned manufacturers must produce high-quality products under advanced production and quality-control procedures that satisfy GMP (good manufacturing practice) guidelines (i.e. standards for manufacturing and quality control of drugs). Moreover, correctly manufacturing and shipping products according to deadlines acts as a standard criterion on which a commissioned company is selected.

* 'Hitachi pharmaceutical plant management system' is called as "HITPHAMS" in Japan and the United States.

Response of Manufacturers (Commissioned Manufacturers)

As regards commissioning production of a large variety of products to a commissioned manufacturer, in response to the needs of the commissioned manufacturer under conditions of limited production of diversified products, high-efficiency production and stringent quality control are required.

These operational requirements are summarized as follows:

(1) optimized framing of production plans in response to limited production of diversified products;
(2) purchasing orders coupled with production plans;
(3) cost control linked with production results; and
(4) control of production and quality in line with GMP guidelines.

In the pharmaceutical industry, as tools for meeting these requirements, IT systems are being introduced without hesitation.

System Requirements of Commissioned Manufacturing Industry

Up until now, responding to the needs of the pharmaceutical manufacturing industry, Hitachi has been providing solutions centered on Hitachi pharmaceutical plant management system.

Introduced as a package developed to conform to the revised pharmaceutical laws in 1994, Hitachi pharmaceutical plant management system has been implemented in many plants and has been achieving good results up to the present. Utilizing operational engineering based on Hitachi's prolific implementation achievements and knowledge regarding regulations, the system enables customers to build a system that meets their requirements.

The results, in particular, important functions, of bringing together the systemization requirements of a commissioned manufacturer turned out to be production control, project management, purchasing control, cost control, and quality control.

Conventionally, as regards these functions, customer requirements have been met by combining several packages. However, in the case of combined packages, although a variety of functions are fulfilled, system management becomes troublingly complex. Accordingly, as an optional function of Hitachi pharmaceutical plant management system, an "integrated production management system"—bringing together required functions in a single package—was developed.

OVERVIEW OF INTEGRATED HITACHI PHARMACEUTICAL PLANT MANAGEMENT SYSTEM

As an IT system for supporting production carried out by commissioned manufacturers, the integrated production management system developed by Hitachi offers the functions outlined below.

Production Control

A core function of the integrated production management system is production-order control and production-record control according to a production plan. The system also performs production control regarding weighing, inventory, storage and dispatch, and input and output of materials.

Production-order and record management

Production orders are created and approved, SOPs (standard operation procedures) are displayed on terminals located around the factory, and records of completed production orders are collected in real time. Moreover, by means of connecting production equipment, recording operations are made more efficient (see Fig. 3).

Weighing management

While communicating with weighing machines, Hitachi pharmaceutical plant management system compiles weight records. And by keeping checks on values above or below the tolerance limits, operation errors can be prevented.

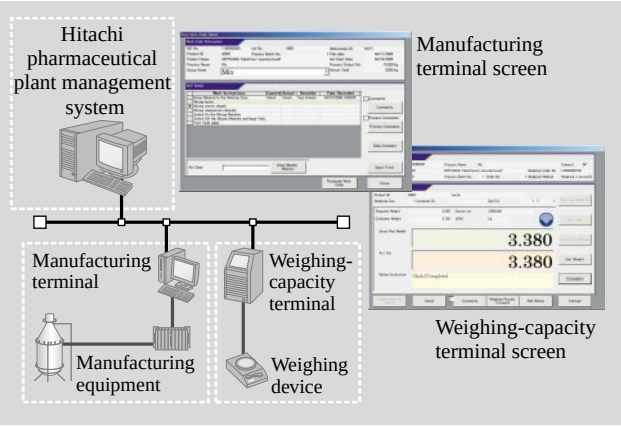

Fig. 3—Example of Operation Screen and Configuration of Hitachi Pharmaceutical Plant Management System.
Under the system configuration, a sever is located in a control room, and various operation terminals are located around each plant. Operations are carried out according to the instructions displayed on the terminals, production data is accumulated in the server, and thus production control is unified.

Inventory control, storage/retrieval control, and storage/materials in-out management

Inventory information on products stored in factories and warehouses is managed in a unified manner, materials provisions are processed according to instructions, and storage/retrieval instructions for the warehouse are created. And records of storage, taking in and out of materials, and audit trails are managed.

Planning Control

To develop plans from overall planning to every-day planning, Hitachi pharmaceutical plant management system takes into account each product and lot, delivery data and equipment, and manpower availability in framing a production plan and displaying Gantt charts, which express data in the form described as follows:

(1) Instruction display: Relations between each operation and each process are displayed, and instructions concerning delayed delivery times can be confirmed.

(2) Each resource display: Utilization ratios for each machine and personnel are displayed, and operation schedule and manpower deployment can be changed according to workloads.

As a result of drawing up optimum production schedules by using this planning function, lead times can be shortened and in-process inventory can be reduced, thereby allowing commissioned manufacturers to promptly respond to delivery dates.

Purchasing Control

The availability of the necessary raw materials and stock required by the production plan is estimated by MRP (material requirements planning).

An amount of buffer stock is secured for each item of goods, and in the case that the amount of required raw materials is less than the buffer-stock amount estimated according to the timing of MRP, a purchasing-order data is automatically generated. According to this data, a purchasing order is sent out for the necessary materials.

By means of this purchasing-control function, inventory control and production planning can be connected throughout the whole plant, thereby optimizing stock ordering.

Cost Control

Standard cost variation

Amount of materials due to arrive in each fiscal term, production plan of each department, amortization factors of indirect department costs, etc. are established, and an operation-time unit cost is estimated for each manufacturing department. Based on this unit cost and formulation information, a standard cost price is calculated.

Actual cost price

Data required for cost calculation are extracted from actual performance data (such as production records, storage, and receipts and disbursements), and actual costs for each item and process are accumulated.

Analysis of cost differences

Finally, the standard cost and the actual cost are compared, and a variation analysis on estimated cost, operational efficiency, quantity variation, etc. is performed.

By applying a cost-simulation function for efficiently estimating the standard costs when items are added to production lines, the relation between commissioned production volume and current-term profits can be ascertained and plans can be adjusted accordingly.

Quality Control

Hitachi pharmaceutical plant management system also has a function for managing testing operations concerning raw materials, semi-manufactured goods, and finished products. Quality-control operations of commissioned manufacturers are dependent on the quality-control standards of the manufacturing consigners. Consequently, it is necessary to accommodate a variety of test patterns. For example, according to the conditions at the arrival time of goods, it is necessary to select the test items to be examined (i.e. abbreviate the number of tests). As the number of patterns for these tests increases, it becomes difficult for a person to assess which of the test items to carry out. In contrast, with Hitachi pharmaceutical plant management system, according to the condition at the arrival time of goods, test items are automatically controlled (for example, additional tests on lots from the same manufacturer are omitted), and test instructions are created accordingly.

Integrated Master Control

In response to additions of production items and changes to operational procedures that transpire after a system becomes operational, so that the system can respond flexibly, it is necessary to unify management

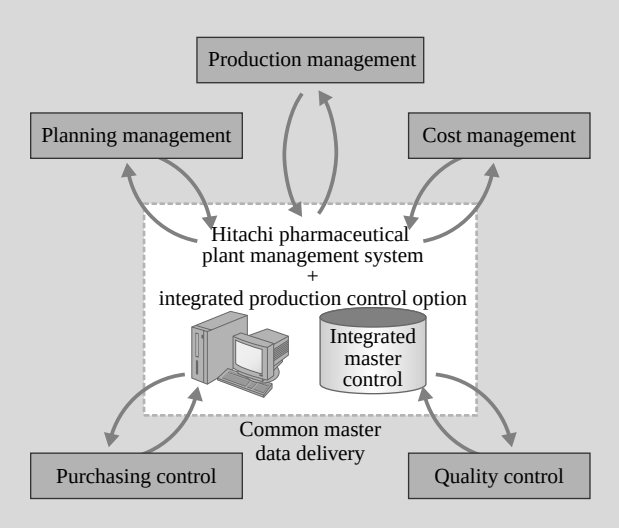

Fig. 4—Overview of Integrated Master Control.
By unifying the control of a common master (goods item master) being used with the various optional functions, system management becomes easier.

of master data in an integrated manner. Accordingly, in the developed system, unified management of a Hitachi pharmaceutical plant management system master and one of the integrated-production-management options previously mentioned (i.e., production planning, purchase planning, cost control, or quality control) is realized.

Common master data utilized with each option is controlled centrally and distributed to each function. As a result of realizing unified control of master data, duplex records are unnecessary, and system management (such as master maintenance after operation has started) becomes easier (see Fig.4).

CONCLUSIONS

In this paper, the system requirements of commissioned drugs manufacturers were explained, and Hitachi's integrated pharmaceutical-plant management system was described.

By consolidating functions such as production control and planning as a single package, this system lightens the operational load when a system is being established and after it is operational.

From now onwards, it is forecast that sharing of product quality-control data among manufacturers and manufacturers/distributors will be required. Accordingly, while further enriching the functions of this system, Hitachi will continue to offer solutions that realize such data sharing between manufacturers, distributors, and sellers.

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