# Development of HITPHAMS Version 2.0: Powerful New Manufacturing Execution System for the Pharmaceutical Industry

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*OVERVIEW: The pharmaceutical industry is moving aggressively to adopt MESs to streamline and tighten their manufacturing operations in order to implement stricter manufacturing and quality controls. Hitachi, Ltd. has supported this movement with the development of HITPHAMS (Hitachi Pharmaceutical Plant Management System), a powerful MES package specifically designed for the pharmaceutical industry. MES packages were widely adopted in the latter half of the 1990s, but now hardware maintenance contracts are expiring and systems are being replaced one after another. Based on a survey of pharmaceutical companies that have already introduced MES packages, we found a strong demand for a system that is not dependent on Windows versions, supports record entry using a handheld PDA, and permits access from a Web browser. Responding to this feedback, Hitachi redesigned its MES package and come out with a new and more powerful Version 2.0 of HITPHAMS.*

## INTRODUCTION

GMP (good manufacturing practice) guidelines have been established in the pharmaceutical industry to ensure the highest quality drugs and other pharmaceutical products are produced. To streamline and tighten their manufacturing operations, drug manufacturers have moved quickly to adopt MESs (manufacturing execution systems) as a way of implementing more exacting manufacturing and quality control procedures based on the GMP guidelines. Hitachi has supported these efforts with the development of an MES package called the HITPHAMS (Hitachi Pharmaceutical Plant Management System) that was specifically designed with the pharmaceutical industry in mind, and the system has been widely adopted since it was made

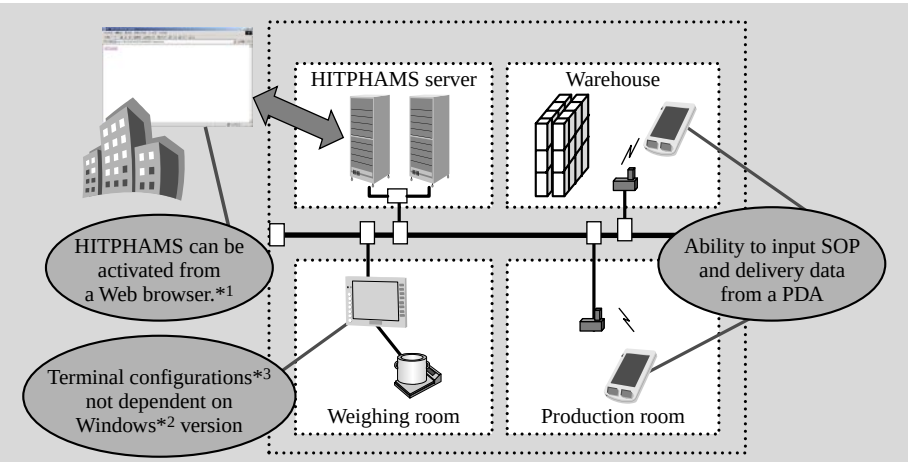


*Fig. 1—New Functions and Features of Manufacturing Execution System HITPHAMS Version 2.0.*
*The new version HITPHAMS can be accessed from a Web browser, is no longer dependent on Windows OS (operating system) version, supports SOP entry from PDAs, and permits entry of delivery control data.*

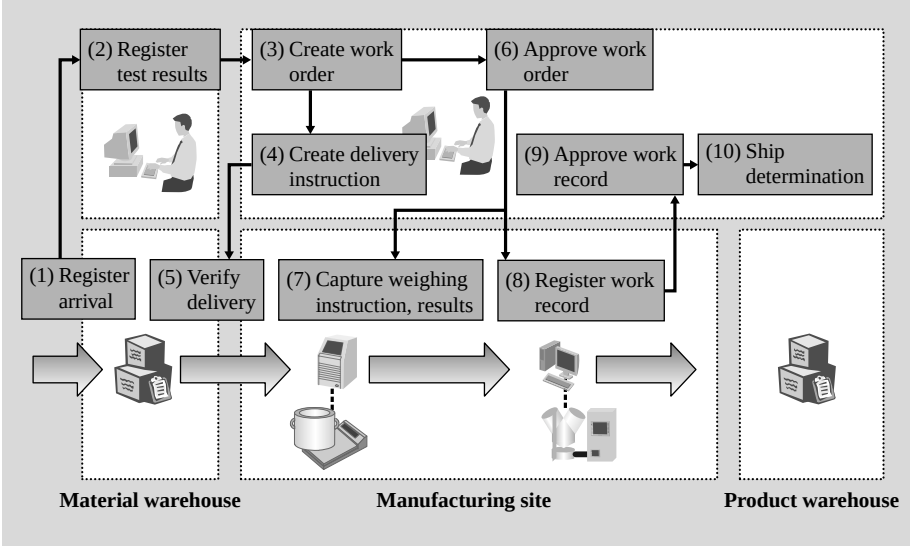


*Fig. 2—HITPHAMS Functions. Tighter and more streamlined drug manufacturing operations with enhanced functions: arrival management, work order control, inventory control, quality control, test results control, and ship determination.*

available in 1995. Now, based on ten years of feedback from the drug manufacturers, we have come out with an improved version of HITPHAMS that incorporates new features and capabilities that the drug makers have been asking for: greater system and hardware flexibility that is not dependent on Windows versions, the ability to input manufacturing related data from handheld PDAs (personal digital assistants), and the ability to access production information from Web browsers. This paper provides a detailed look at the functions and features of the new Version 2.0 HITPHAMS (see Fig. 1).

## MES DEVELOPMENTS IN THE PHARMACEUTICAL INDUSTRY

The widespread adoption of MES by the pharmaceutical industry in the latter 1990s is closely linked to the 1994 revision of Japan's Pharmaceutical Affairs Law. With this revision, the former GMP compliance rules became much stricter approval and authorization requirements, and this accounts for the rush to implement MESs that were largely spearheaded by the major pharmaceutical companies.

The more recent revision to the Pharmaceutical Affairs Law in 2005 has generated a new surge of interest in the MES market. One key aspect of the revised law involves the system of approval and licensing for manufacturing drugs and other medical products. The earlier law required all pharmaceutical distributors to have their own manufacturing plants and manufacture their own products, but the revised Pharmaceutical Affairs Law permits all manufacturing to be consigned or outsourced to another company. As a result, the major drug manufactures have moved aggressively to outsource at least some of their production to cut their own in-house manufacturing costs, the outsourced manufacturing market has greatly expanded, and the secondary tier of consignment manufacturers that never considered MES before are now suddenly very interested in deploying these systems.

## HITPHAMS FUNCTIONS

### HITPHAMS Overview

Hitachi's MES package HITPHAMS was originally developed with the 1994 revision of the Pharmaceutical Affairs Law specifically in mind. By installing the package, drug manufacturers are able to streamline their GMP management and compliance, and also improve the consistency and reliability of product quality.

Fig. 2 shows a schematic overview of the functions supported by HITPHAMS. The most basic functions are work order control and maintenance of records. This allows work order data to be displayed on terminals at the production plant, and records can be updated interactively as work progresses (see Fig. 3). The ability to input performance and other manufacturing related data in the terminal right at the work site makes the recordkeeping work more efficient and also helps detect and eliminate manufacturing mistakes.

### Legacy HITPHAMS System Configuration

The legacy HITPHAMS system was configured as a fat-client system, and the client part of the application

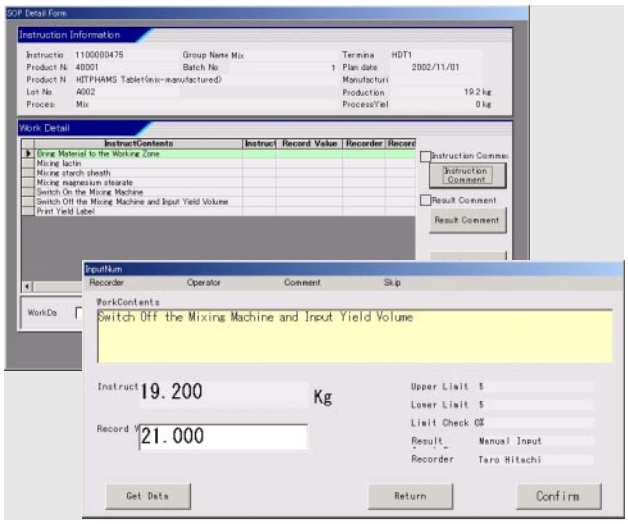


*Fig. 3—HITPHAMS Work Record Input Screens.*
*Efficiency is improved and errors are reduced by performing work tasks based on orders displayed on screen at the manufacturing site.*

was implemented using Microsoft Office Access*. Both server and client parts of the application ran on Windows. A fat-client system refers to a conventional client-server system in which much of the program processing is executed on the client PCs (personal computers).

### New Version Eliminates Drawbacks of the Old System

The legacy HITPHAMS application was developed using Microsoft Access and ran on Windows, and therefore was affected by Windows operating system and Access version changes. Specifications had to be changed every time the version of Windows or Access was upgraded, and this sometimes involved considerable maintenance work.

Furthermore, the life of a typical server is about six years, but when replacing hardware, it is almost impossible to get new equipment that runs the version of Windows that was on the old equipment, so clients are generally forced to upgrade to the latest version of Windows. Essentially, this meant that customers were faced with the financial burden of HITPHAMS maintenance work every time they replaced their hardware, and this was a fundamental reason that we decided to develop a new version of HITPHAMS. The new version was also motivated by: (1) the need for work record entry from a handheld PDA for greater convenience, digitization of recordkeeping, and cost cutting, and (2) the need to verify manufacturing progresses at the plant from the central office in real time.

Hitachi thus undertook development of HITPHAMS Version 2.0 as an MES package that would fully address all of these needs.

## FEATURES OF HITPHAMS VERSION 2.0

### Ability to Flexibly Accommodate System Changes

In conventional client-server system configurations, the scope of maintenance work generally tends to increase when upgrading Windows or other operating system for a number of reasons: (1) the application software itself is typically dependent on the version of Windows or other operating system software, and (2) the communication between server and client is typically dependent on the version of the database software or other basic software.

To address these problems in the new version of HITPHAMS, we completely reworked the platform on which programs run and the communication scheme between server and clients in a way that flexibly and easily accommodates Windows or other basic software version upgrades. In reworking the program platform, we adopted .NET Framework, a software platform from Microsoft. This enabled us to continue offering the same advanced user interface as in the earlier version, while solving the problem of Windows operating system dependence for any OS (operating system) that is compatible with .NET Framework 2.0. For the server-client communication, we implemented a communication scheme that works without being dependent on any particular version of software. This means that it is no longer necessary (as it was in the previous HITPHAMS) to maintain compatibility with the server-client communication software version, and users now have the option when replacing server and client hardware of separately upgrading the version of Windows on just the servers or on just the clients.

Building a system this way, we can deploy a configuration of terminals that is not dependent on the operating system. This arrangement enables lower cost and more flexible transitions when replacing hardware, a situation that was fraught with problems in the past as we described earlier. Even in situations where new terminals are added to the network and only terminals with a new version of the operating system are available, old and new operating systems comfortably

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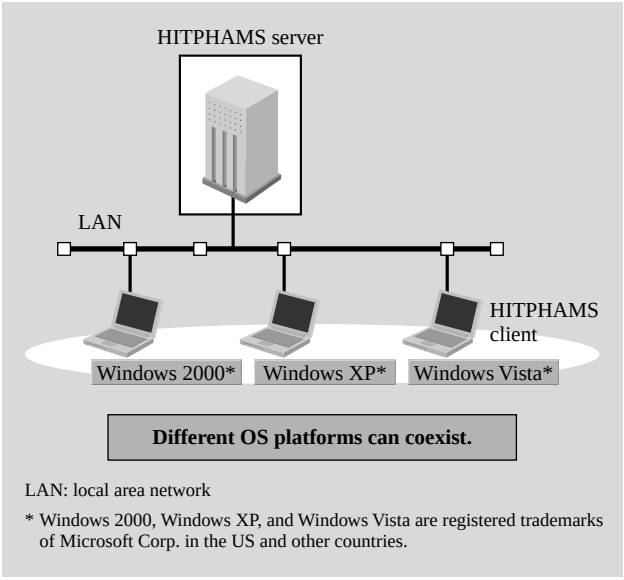


*Fig. 4—More Flexible System Configurations That Are Not Dependent on Windows Version.*
*Client terminals with different operating systems can be connected to the same system, and more terminals can be readily added in the future.*

coexist for long-lived system stability (see Fig. 4).

### More Efficient Record Entry Using Handheld PDAs

MES terminals in the past have generally been desktop computers, notebook PCs, or other fixed terminal installations. The problem with fixed terminals is that the actual work is usually done at some distance from the terminals, so one has to get back to where the terminals are located to enter the manufacture related data, and this of course reduces efficiency. In addition, the information to be recorded is first handwritten in a notebook, and this raises the possibility of transcriptions errors when the information is entered into the system.

As illustrated in Fig. 5, we came up with a simple solution in the new version of HITPHAMS in the form of a handheld PDA that can be carried around and taken right to the location where the actual work is being done. The work record entry screens display detailed work procedures, so onsite work records can be recorded accurately and efficiently. And when delivering materials from warehouses to the manufacturing site, the HITPHAMS delivery control function ensures accurate and efficient picking at warehouses scattered around the region.

### Web Browser Access to HITPHAMS

Because the previous version of HITPHAMS was a fat-client system, the HITPHAMS application had to be installed on client terminals, and data could not be entered or accessed from any terminal that did not have the application installed on it. In the new version, HITPHAMS can be started up from a Web browser even on terminals that do not have the HITPHAMS application installed (note that some functions accessed from a Web browser are limited). This enables users to access progress, performance, and other pertinent data recorded at actual manufacturing sites using computers that do not have the HITPHAMS application installed.

## CONCLUSIONS

This paper presented an overview and highlighted the key features of HITPHAMS Version 2.0, a new version of Hitachi's powerful Management Execution System designed for the pharmaceutical industry. By adopting Microsoft's .NET Framework as the system platform, we successfully built a system that is not dependent on the Windows operating system version. Our commitment at Hitachi Group is to listen carefully

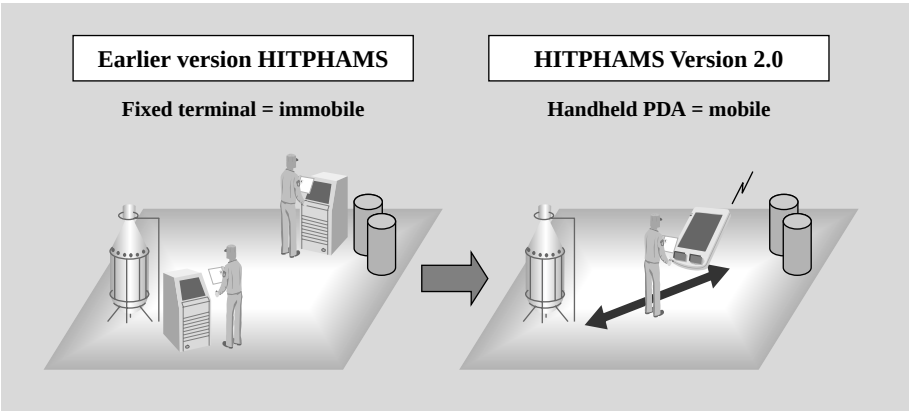


*Fig. 5—Onsite Work More Efficient Using a Handheld PDA.*
*Onsite work is more streamlined and efficient using a portable handheld PDA. And one plant can share a PDA if different parties do not need the device at the same time.*

to our customers so that we can provide MES solutions for the pharmaceutical industry as quickly as possible that are based on the needs and feedback from our clients.

## REFERENCES

(1) Ministry of Health, Labour and Welfare, "Standards for Manufacturing Control and Quality Control of Drugs and Quasi-drugs," MHLW Ministerial Ordinance No. 179, Revised as of December 24, 2004

(2) S. Serizawa et al., "Integrated Plant Management Systems Meeting Operational Changes in the Drug Manufacturing Industry due to Drug Laws Revision," *Hitachi Hyoron*, Vol. **86**, No. 10, pp. 695-698 (Oct. 2004)

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