Process ERP, an ideal software solution for Life Science industries

Update on FDA's current compliance requirements of GxP regulated computerized systems

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BATCHMASTER®
Process Manufacturing Software

Executive summary:

Complete control over business processes by integrated approach.

It is a challenge to be competitive as well as efficient and profitable. In the current industrial and economic context, pharmaceutical industries have to constantly and smoothly re-engineer themselves to respond to changing market demand, technological evolution, and simultaneously keep pace with the changing regulatory requirements. These regulatory requirements arise from aspects critical to patients and are associated with the development and implementation of new concepts to improve the way drug development and manufacturing is managed. Examples include a science-based risk management approach which focuses on product and process understanding, and the application of Quality by Design concepts. To meet these challenges pharmaceutical manufacturers have shifted their focus from isolated systems, which limit the overall efficiency and effectiveness of the organization, to a more integrated approach to have better control over their business processes.

ERP systems address both information and regulatory compliance needs.

In such an environment, it is unsurprising that Enterprise Resource Planning (ERP) systems have generated interest from large and medium-sized pharmaceutical companies. ERP is a planning system that responds to the market environment and optimizes company resources. An integrated plan helps the firm to better respond to customer demand and quickly identify supply gaps. This brings about higher sales, better customer service, lower inventories, and a lower cost of operation. Data that was once captured, replicated, maintained and reported on in many different systems can now reside in one system. ERP system providers have thrived on their ability to address a range of critical utility business processes including regulatory requirements in an integrated fashion. As a consequence more processes can be automated, and more users throughout the organization can access them, to work more efficiently and effectively. Because of the capacity of ERP systems to address both information needs as well as regulatory requirements of all departments and functions across a company, they have progressively become the reference solution for pharmaceutical companies. However, the challenge still remains in the selection of suitable software solutions that also offer the necessary modules to facilitate compliance, and which integrate in real time.

Introduction

GxP regulated computer systems keep information of GMP, GLP, GDP, etc.

The purpose of this white paper is to document and summarize the current status of the regulatory requirements set forth by different agencies like FDA (in US), ICH (in Europe), and that of Japan and China. In the first section of the paper we will provide the background information on the role of FDA, the regulatory agency in the USA, and the current state of cGMP “risk based approach” enforced by the FDA, which focuses on an integrated approach of good science and good engineering practices to bring about innovation in pharmaceutical industries. We will discuss collaboration between the FDA and different regulatory agencies of the world, especially in quality-related areas and the development of harmonized scientific standards for assessment of drug product quality. Cooperation of the FDA with the Pharmaceutical Inspection Scheme (PIC/S) has resulted in the “Guidance on Good Practices for Computerized system in regulated GxP environment”, where “GxP regulated Computerized systems” are defined as the systems that keep information related to Good Manufacturing Practice (GMP),Good Clinical Practice (GCP), Good Laboratory Practice (GLP), Good Distribution Practice (GDP), to ensure that computerized systems are fit for the intended use and compliant with applicable regulations. According to these guidelines a computer-related system is considered to be GxP if it impacts, or has the potential to impact, product quality (safety, quality, integrity, purity or potency). It is also a GxP system if it performs a function specifically governed by cGMP regulations. We will also briefly describe the GAMP-5 guidelines published in 2008, on how cGMP requirements can be addressed by computerized systems and about the typical layout of generic cGMP activities in pharmaceuticals and about the validation strategy. In the last section of the paper we will describe, using BatchMaster Software's 'BatchMaster® for Pharmaceuticals' as our example, how a typical GxP ERP system fulfills these cGMP requirements and can be validated in the regulated pharmaceuticals manufacturing industry. In the end we will describe non-cGMP features of BatchMaster for Pharmaceuticals like MPS, MRP, APS, finance, forecasting and business intelligence and their business benefits for making proactive and informed decisions about customers.

FDA : Food and Drug Administration (FDA) is a regulatory agency in the USA and is a part of the Department of Health and Human Services. Currently it regulates $1 trillion worth of products a year. It ensures the safety of all food except for meat, poultry and some egg products; ensures the safety and effectiveness of all drugs, biological products (including blood, vaccines and tissues for transplantation), medical devices, and animal drugs and feed; and makes sure that cosmetics and medical and consumer products that emit radiation do no harm.

FDA ensures that drugs are of high quality and safe.

Recently, in August 2009, tobacco products have also been included in the list of regulated products. FDA ensures that drug products in the USA are of high quality and safe for use. It does so by carefully monitoring drug manufacturers' compliance with its current good manufacturing practices (cGMP) regulations. The cGMP regulations for drugs contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product, and the strength it claims to have.

FDA monitors Manufacturers' compliance to cGMP.

In the past, as a result of the many uncertainties in drug manufacturing, the FDA exercised extensive control over virtually every aspect of the manufacturing process. Consequently, pharmaceutical companies have often been reluctant to change their manufacturing processes and equipment because of perceived, and sometimes real, regulatory hurdles. In August 2002, recognizing the need to eliminate the hesitancy to innovate, the Food and Drug Administration (FDA) launched a new initiative entitled "Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach." This initiative had several important goals. Listed in Table 1 are the main objectives of the 21st Century Risk Based approach. The goals were intended to ensure that pharmaceutical manufacturing continues to evolve with increased emphasis on science and engineering principles. This FDA initiative encouraged the use of an integrated systems approach, based on science and engineering principles, for assessing and mitigating risks related to poor product and process quality. Product quality and performance were ensured through the design of effective and efficient manufacturing processes. Product and process specifications were based on a mechanistic understanding of how formulation and process factors affect product performance, and through continuous real time quality assurance. In line with the risk-based approach, in 2004 and 2006 the FDA issued two initiatives clarifying their thinking on the implementation of a risk-based approach. In 2004 they issued "Guidance for Industry PAT A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance". The main philosophy behind it was "quality cannot be tested into products; it should be built-in or should be by design." In a PAT framework, validation can be demonstrated through continuous quality assurance where a process is continually monitored, evaluated, and adjusted using validated in-process measurements, tests, controls, and process end points. Risk-based approaches are suggested for validating PAT software systems. In 2006 the FDA issued "Guidance for Industry Quality Systems Approach to Pharmaceutical CGMP Regulations" which describes a comprehensive quality systems model based on continuous improvement and risk management, and how manufacturers implementing such a comprehensive quality system can ensure that they comply fully with the CGMP regulations (21 CFR parts 210 and 211).

Table 1 : Main Objectives of 21st century Risk Based Approach

- **The most up-to-date concepts of risk management and quality systems approaches are incorporated into the manufacture of pharmaceuticals while maintaining product quality**
- **Manufacturers are encouraged to use the latest scientific advances in pharmaceutical manufacturing and technology**
- **The Agency's submission review and inspection programs operate in a coordinated and synergistic manner**
- **Regulations and manufacturing standards are applied consistently by the Agency and the manufacturer**
- **Management of the Agency's Risk-Based Approach encourages innovation in the pharmaceutical manufacturing sector**
- **Agency resources are used effectively and efficiently to address the most significant health risks**

Current FDA policies support innovation of manufacturing processes and plants.

PAT framework: "Quality cannot be tested into products; it should be built in".

FDA 21 CFR Part 11 Background and current state:

In March of 1997, the FDA issued final part 11 regulations that provide criteria for acceptance by the FDA, under certain circumstances, of electronic records, electronic signatures, and handwritten signatures executed to electronic records, as equivalent to paper records and handwritten signatures executed on paper. These regulations, which apply to all FDA program areas, were intended to permit the widest possible use of electronic technology, compatible with FDA's responsibility to protect the public health.
After part 11 became effective in August 1997, significant discussions ensued among industry, contractors, and the Agency concerning the interpretation and implementation of the regulations. Concerns were raised that some interpretations of the part 11 requirements (1) unnecessarily restricted the use of electronic technology in a manner that was inconsistent with the FDA's stated intent in issuing the rule, (2) significantly increased the costs of compliance to

an extent that was not contemplated at the time the rule was drafted, and (3) discouraged innovation and technological advances without providing a significant public health benefit. These concerns were raised particularly in the areas of part 11 requirements for validation, audit trails, record retention, record copying, and legacy systems. As a result in 2003, the FDA issued a new guideline, “Guidance for Industry Part 11, Electronic Records; Electronic Signatures Scope and Application”. In this guidance they specified that the FDA is re-examining part 11. While the re-examination of part 11 is under way, the FDA intends to exercise enforcement discretion with respect to certain part 11 requirements. It does not intend to take enforcement action to enforce compliance with the validation, audit trail, record retention, and record copying requirements of part 11; while the things which remain unchanged are requirements regarding controls for closed systems, controls for open systems and electronic signatures. In the mean time “Hybrid systems” a combination of electronic and paper records will be acceptable to the FDA for maintaining the records required as per cGMP regulation requirements.

CFR Part 11: Electronic records & signatures equivalent to handwritten records and signatures.

FDA and International Collaboration

It is crucial that pharmaceutical quality standards or requirements be harmonized internationally to the fullest extent possible. The development of a global economy during the last few decades has had a profound effect on product development. To achieve its public health goals and leverage its resources, the FDA has increased its collaboration with international health and regulatory partners. Working together, international regulatory authorities have continued to harmonize their activities, especially in quality-related areas, and increased the sharing of regulatory information. The FDA actively collaborates with other regulatory authorities in multilateral, international forums, such as the International Conference on Harmonization of the Technical Requirements for Registration of Pharmaceuticals (ICH) regulatory agency of Europe, which follow guidelines outlined in ICH documents such as Q8 Pharmaceutical Development, Q9 Quality risk management and recently, in 2009, new guidelines Q10 Pharmaceutical Quality System has been issued. This international cooperation between the FDA and ICH has resulted in the common harmonized regulatory requirements; In addition, the FDA has extended this kind of co-operation with the regulatory agencies of non-European countries like Japan and China. The FDA is a member of the “Pharmaceutical Inspection Cooperation Scheme (PIC/S)” and has been instrumental in the development of “Guidance on Good Practices for Computerized Systems in Regulated 'GxP' Environments”. In order to develop standards to support the introduction of innovative tools and technologies under the PAT framework, the FDA teamed up with ASTM International and issued a consensus standards guideline for various pharmaceutical supporting industries “ ASTM E2500 Standard Guide for Specification, Design and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment.”
In summary, the FDA's international efforts have yielded common harmonized regulatory policies and alignment of consensus standards. It will strengthen the FDA's oversight of non-USA drug manufacturing sites that produce FDA-approved pharmaceuticals for Americans, and at the same time help their regulatory counterparts to manufacture drugs of high quality.

FDA's international collaboration has resulted in common regulatory policies and standards.

GAMP5 Guidelines for GxP Computerized Systems:

The Pharmaceutical Industry Systems Validation Forum in the UK developed the “Good Automated Manufacturing Practice (GAMP) Supplier Guide” to assist software suppliers in implementing an appropriate quality management system. The GAMP Guide (and appendices) has evolved largely to define best practices in specifying, designing, building, testing, qualifying and documenting these systems to a rigorous validation management scheme, largely for the controlling system. The GAMP Forum is now sponsored by ISPE and has international membership and participation, including 'GAMP Americas'. The latest version of GAMP, GAMP5 published in 2008 entitled “A Risk-Based Approach to Compliant GxP Computerized Systems”, defines critical requirements expected of GxP computerized systems to comply with current regulatory and industry development requirements. It focuses on aspects critical to the patients like i) avoiding duplication of activities (e.g. by fully integrating engineering and computer system activities so that they are performed only once), ii) leveraging supplier activities to the maximum possible extent, while still ensuring fitness for intended use, iii) scaling all life-cycle activities and associated documents according to risk, complexity and novelty. GAMP guidance aims to achieve computerized systems that are fit for intended use and meet current regulatory requirements, by building upon existing industry good practice in an efficient and effective manner. Examples of GxP regulated computerized systems include systems used in manufacturing, resource planning, manufacturing execution, warehousing and distribution, adverse event reporting and document management. These computerized systems should meet all applicable pharmaceutical and associated life science regulatory requirements.

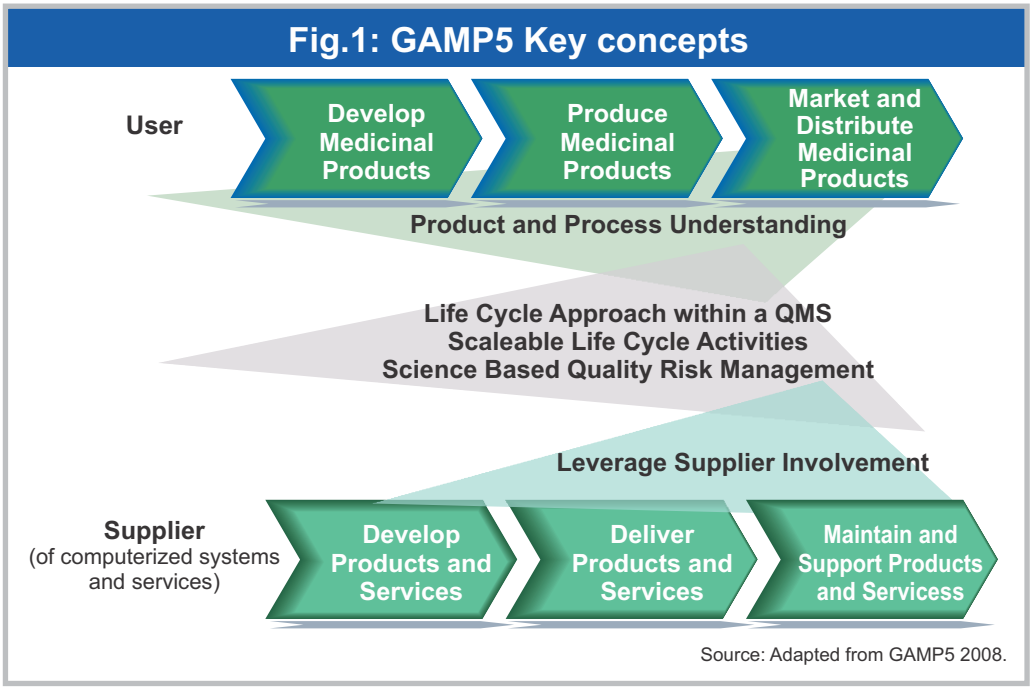
GAMP5 “A risk-based approach to compliant GxP computerized Systems”.

GAMP5 Guidelines have identified five key concepts (Fig.1), which are currently used by innovative pharmaceuticals. These include

1. Product and process understanding
2. Life cycle approach within a QMS
3. Scalable life cycle activities
4. Science based quality risk management
5. Leveraging supplier involvement

GAMP focuses on aspects critical to patients.

Fig.1: GAMP5 Key concepts



Source: Adapted from GAMP5 2008.

Software solution requirements are dictated by Product and Process Understanding.

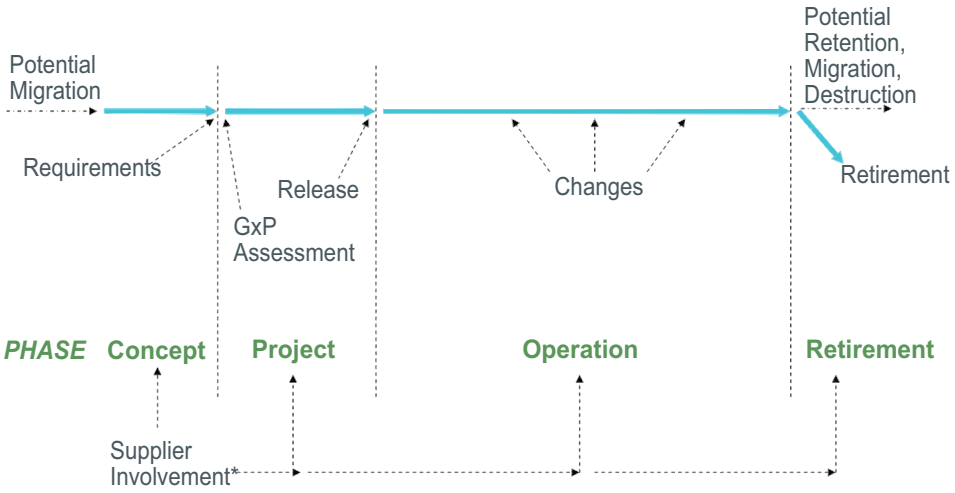
1. Product and process understanding is fundamental to determine system requirements. It focuses on the aspects that are critical to patient safety, product quality, and data integrity, and forms the basis for making science and risk based decisions to ensure that the system is fit for intended use. Incomplete process understanding hinders effective and efficient compliance and the achievement of business benefit.

2. Life cycle approach within a QMS enables the assurance of quality and fitness for intended use. The life cycle approach is structured into four phases which define activities in a systematic way from system conception to retirement. Shown in Fig.2 is the graphical representation of life cycle and associated activities. Typical activities i) in the **concept phase** include development of initial requirements and consideration of potential solutions, ii) Main activities during the **Project Phase** include Planning, Supplier assessment and selection, various levels of specification, configuration (or coding for custom application), verification leading to acceptance also termed as Validation, and release for operation. During the project phase Risk Management is applied in all the above activities to identify the risk and / or remove or reduce them to an acceptable level, iii) **Operation Phase** in the life cycle approach is the longest Phase. It is managed by use of the defined, up to date, operational procedures by trained personnel to ensure fitness for intended use and compliance. Management of changes of different impact, scope and complexity is an important activity during this phase, iv) For the **Retirement Phase**, decisions about data retention, migration or destruction are planned.

QMS based on life cycle approach ensures high quality product.

Life Cycle approach includes four phases: Concept Phase, Project Phase, Operation Phase, Retirement Phase.

Fig.2: Life Cycle Phases



Source: Adapted from GAMP5 2008.

Software used in Pharmaceuticals belong to GAMP Category 4.

3. Scaleable Life Cycle Activities: Life cycle activities are scaled according to system impact on patient safety, product quality and data integrity (Risk assessment), system complexity and novelty (architecture and categorization of system components) and outcome of the supplier assessment. Typically, software most commonly used in pharmaceuticals e.g. LIMS, ERP, MRP and CRM are Category 4 configured software which provide standard interfaces and functions that enable configuration of user specific business processes without altering software code with predefined modules. Risk associated with the software is dependent on how well the system is configured to meet the user's business processes.
It demonstrates that the supplier has an adequate QMS, Risk-based approach to demonstrate the application works as designed in a test environment, and business process. Procedures are in place for maintaining compliance and fitness for intended use and managing data.

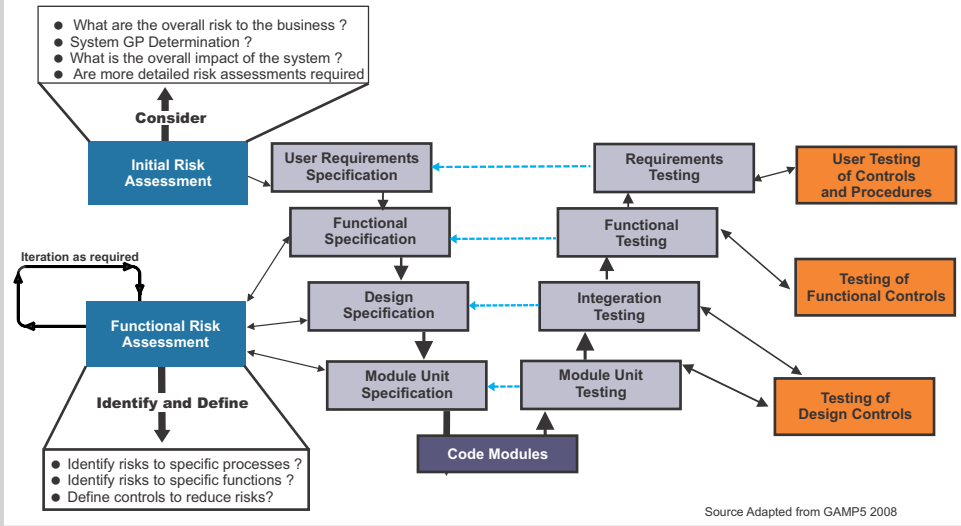
4. Science Based Quality Risk Management: is a systematic process for the **assessment, control, and review** of risks. Quality Risk Management is based on clear process understanding and potential impact on patient safety, product quality and data integrity. It is an iterative process used throughout the entire computerized system life cycle from concept to retirement. Quality **risk assessment** is performed by assessing the impact of the computerized system on patient safety, product quality and data integrity; regulatory requirements, user requirements, system architecture and supplier capability. Quality **risk control** involves elimination by design, reduction to an acceptable level and verification to demonstrate that risks are managed to an acceptable level.

Quality Risk Assessment determines impact of computerized system on patient safety and data integrity.

Quality risk management process: Shown in figure 3 are the different steps followed for category 4 configured software to assess and mitigate the risk of business process:
Step 1: Perform initial risk assessment and determine system impact.
Step 2: Identify functions with impact on patient safety and data integrity.
Step 3: Perform Functional Risk assessment and Identify Control.
Step 4: Implement and verify appropriate controls.
Step 5: Review Risks and monitor controls.

Leveraging supplier involvement: As shown in Fig. 1 and 2, pharmaceutical companies seek to maximize supplier involvement throughout the system life cycle in order to leverage knowledge, experience and documentation to avoid wasted efforts and duplication. Justification of the use of supplier documentation is provided based on supplier assessment outcome. If another regulated company has already assessed the supplier for the same reason, an additional assessment may not be necessary. The justification for not assessing a specific supplier should be formally documented. The Supplier may assist with the requirements gathering, risk assessments, the creation of functional and other specifications, system configuration, testing, support and maintenance.

Fig.3: Quality Risk Management Process



Generic cGMP Activities of a Typical Pharmaceutical Company:

Shown in Tables 2 and 3 are generic cGMP related activities of a typical Pharmaceutical company. To ensure that cGMP information related to patient safety, integrity of critical records, data and decisions is not compromised by the computerized system, its validation is performed.

Software should permit purchase of cGMP material from approved vendors only.

Software should control and track movement of purchased material.

Software should provide tight control over formula modifications.

Table 2: Generic cGMP Material/batch Handling requirements of FDA

Supply Chain
- Supply chain enters the list of the cGMP approved suppliers/ and warehouse storage location where purchased material will be stored
- QA Reviews I confirms that the entered information is matching with the material specification

Purchase
- System shows list of approved cGMP suppliers only entered in the Item Master.
- System permits to create PO only to these suppliers.

Material Management
- System should permits storage of the received material in the Quarantine storage location only.

Quality Control
- QC upon testing assigns the status P (Pass) or F (Fail)
- In the System.

Quality Assurance
- Based on QC results, QA reject or Release the received material.

- Move the released containers to the Release warehouse storage location .
- Move the rejected containers to a Reject warehouse storage location.

Table 3: Generic cGMP Material/batch Handling requirements of FDA

Manufacturing	Quality Assurance/ Control	Material Management
● Create Intermediate Formula ● Create Intermediate BOM ● Create Intermediate Batch ● Allocate Batch	● QA Verify the Formula	
● Intermediate/finished batches	● QC Receive & analyze sample ● QC assigns a P (Pass) or F (Fail) in the system	● Receives a batch of filled or finished product . ● Dispenses the approved material.
● Reconcile Batch. Account for inspection, rejects & samples ● Close batch	● QA prints Passed or rejected batch labels.	● Selects Release or reject warehouse storage location, sticks the appropriate labels and move to hose locations.

Validation of computerized systems:

Validation ensures that GxP-regulated systems are compliant and fit for intended use.

The nature of the pharmaceutical and other life sciences industries requires that systems are developed, documented and tested following good engineering practices. To assure that the GxP regulated systems are compliant and fit for intended use, regulated pharmaceutical companies define their policies in a Validation Master Plan (VMP). A VMP focuses on the validation of functionalities that impact the safety, quality, integrity, purity and potency of a product for human use (referred to as a cGMP product). A VMP describes the areas of the company where validation is required and provides an overview of the validation approach, references policies and procedures. It also specifies scope, resources, deliverables, roles and responsibilities. Computerized system validation is often a subset or chapter of a VMP covering all of an organization's validation activities. It describes in detail how the validation is to be performed for specific systems. Software functionality not impacting cGMP activities is not required to adhere to this master plan. A VMP is prepared and executed by the regulated pharmaceutical company during the 'Project phase' of the life cycle model. The VMP, along with the associated reports, may be one of the first documents offered during an audit to demonstrate regulatory compliance. It is therefore written at a level suitable to be understood by a wide readership, with efforts made to avoid technical details.

Validation master plan describes master plan, policies and procedures.

The deliverables and specifications requirements for new systems are determined by their GAMP software categories. Tables 2 and 3 identify the GAMP categories and the deliverables required for a computer related system. In the GAMP5 guidance published in 2008 there is a change in category definitions as compared to GAMP4. There are only four software categories, 1,3, 4, and 5 (table. 2). The previous Category1 Operating Systems is expanded to include infrastructure software, and now also includes layered software components such as database managers, middleware and ladder logic interpreters. Category 2 Firmware is no longer a separate category, since modern firmware can be so sophisticated that there is no longer any justification for differentiation. The previous Category 3 Standard Software has been renamed as Non-Configured Product and includes many examples of firmware. The remaining categories (4 and 5) are essentially unchanged from previous usage.

Table 4: Software categories and typical examples:

Category	Description	Typical Examples
1. Infrastructure Software	- Layered software - Software used to manage the operating environment	- Operating systems - Database Engines - Middleware - Programming languages - Scheduling tools - Version Controls
3. Non-Configured	- Run time parameters may be Entered and stored, but the software cannot be configured	- Firmware-based applications. - COTS software - Instruments
4. Configured	- Very complex Software, - Configured to meet user's specific needs and Business Process. - Software code is not altered.	- LIMS - ERP - Data acquisition systems - MRPII - Clinical trial monitoring - CRM - SCADA - CDS
5. Custom	- Software custom designed - Coded to suit the business Process	- Internally and externally developed IT applications - Internally and externally developed process control applications. - Custom ladder logic. - Custom firmware.

Category 4 software meets user's specific requirements without code alteration.

As outlined in table, 2, ERP software used commonly by pharmaceuticals to manage their business processes belong to GAMP Category 4. ERP software provides standard interfaces & functions that enable configuration of user specific business processes by predefined software modules. ERP software is used to create and change the master data for cGMP products. These are also used to manage production planning, purchasing, warehouse inventory, product status change (i.e.: Quarantine at the time of receipt, Sample, Pass, Fail, Release and Reject) and order tracking. Deliverables required for Validation of such software is listed in Table 3.

ERP software configures user-specific business processes by pre-defined software modules.

Table 5: Deliverable requirements of different GAMP software

	System Software GAMP Category				
	1	2	3	4	5
1. Life cycle Model			*	*	*
2. Risk Assessment (RA)			*	*	*
3. Supplier Assessment			*	*	*
4. User Requirements Specifications (URS)			*	*	*
5. Functional Requirements Specifications (FRS)				*	*
6. Design Specification				*	*
7. Installation Qualification (IQ)				*	*
8. Operational Qualification (OQ)			*	*	*
9. Performance Qualification (PQ)			*	*	*
10. Requirements Traceability Matrix (RTM)				*	*
11. Validation Summary Report			*	*	*
12. Change Control, Procedures in place for maintaining compliance and fitness for intended use, Procedures in place for managing data.			*	*	*

Supplier's QMS based on software validation life-cycle (SVLC) provides assurance of high quality product.

Deliverable requirements of GAMP4 softwares:

1. Life cycle model: A suitable life cycle, properly applied as intrinsic part of the company's QMS enables the assurance of quality and fitness for intended use. The Software Validation Life Cycle (SVLC) applies to all cGMP computer-related systems. The SVLC enables management control and consistent approach across systems covers activities from conception through retirement of a computer-related system (fig.2). A well managed and understood life cycle facilitates quality by design approach.

Risk management of cGMP computerized systems focuses on critical aspects which impact cGMP products.

2. Risk assessment: Appropriate risk management process is followed throughout the life cycle in order to manage identified risks and to determine the rigor and extent of the activities required at each phase of the life cycle. Application of risk management enables efforts to be focused on critical aspects of computerized systems in a controlled and justified manner. It is based on clear process understanding and potential impact on cGMP products. Both qualitative and quantitative techniques are used to identify and manage risks. Controls are developed and

monitored to ensure ongoing effectiveness. An **Initial Risk Assessment** is performed during planning to determine whether the system is GxP regulated. Depending on the system and software category further assessments and specifications are developed. The assessment is based on an understanding of business processes and business risk assessments, user requirements, regulatory requirements and known functional areas. It also include risk introduced by computerization of business process (e.g. electronic record integrity). Focus of the risk assessment should be to GxP risks, rather than detailed functions and technical aspects. **Functional Risk Assessment** identifies and manages risks to patient safety, product quality and data integrity that arise from the failure of the function. Results of functional risk assessment in turn influence the extent and rigor of verification activities. Testing is focused on the high risk functionalities and with fewer efforts on low risk areas. **Operation Risk Assessment** identifies the risk associated with different operation activities like system availability, frequency of backup and recovery, disaster planning, system security, change control. **System Retirement Risk Assessment** identifies risk associated with data, record, retention, migration and verification in the planning of system retirement.

Pharmaceutical companies perform risk-based assessment of the supplier prior to contract placement.

3. Supplier Assessment: Although the responsibility for compliance lies with the regulated company, the supplier has a considerable involvement in the process. Based on the criticality of the system/services being provided, the regulated pharmaceutical company performs a risk-based assessment of the supplier. They verify, prior to contract placement, that the supplier has adequate expertise and resources to support user requirements and expectations.

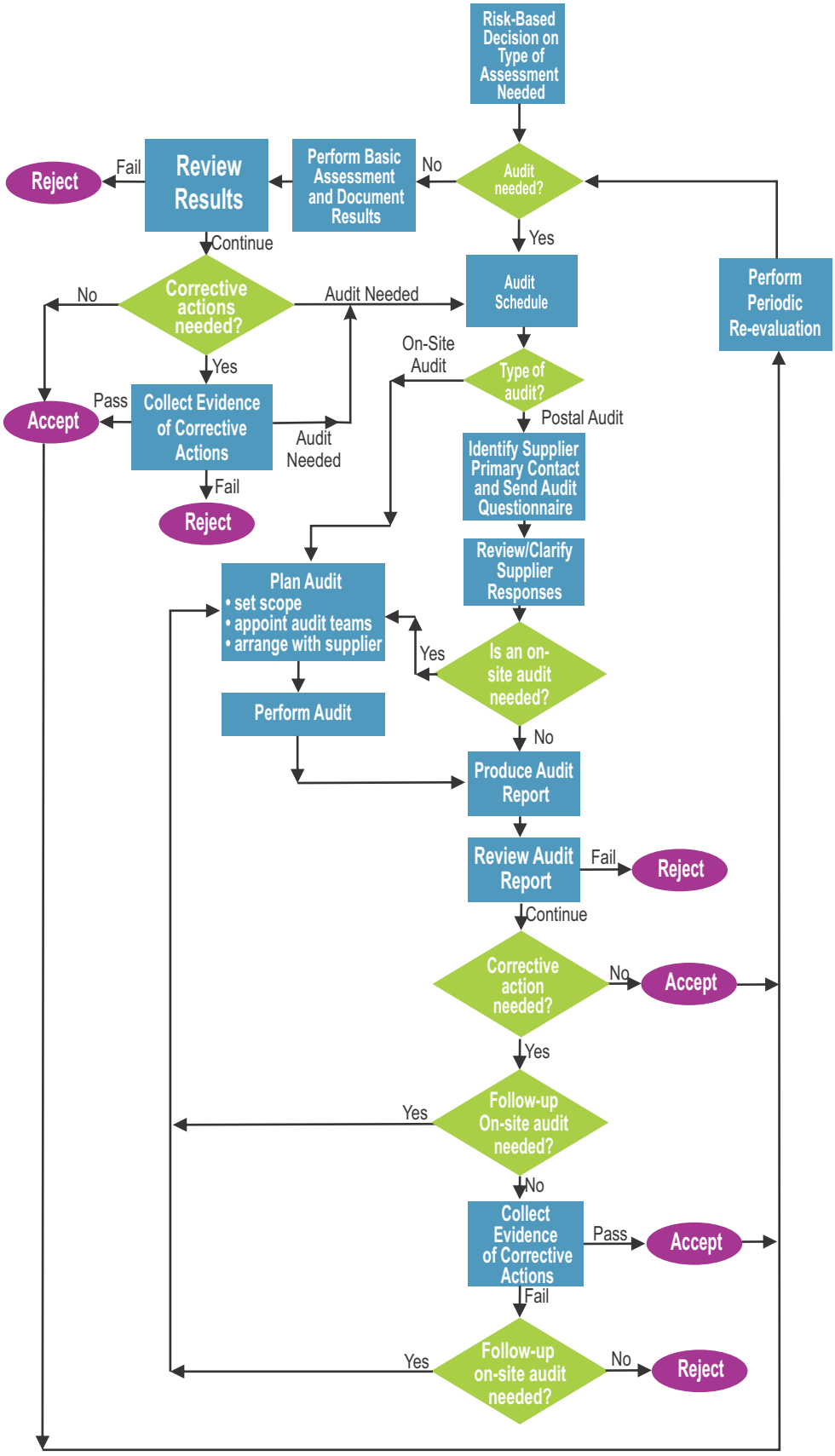
Since the supplier may provide deliverables or directly support these activities, planning provides the opportunity to decide how best to leverage supplier activities and documentation to avoid unnecessary duplication. It is done to get a high level of confidence that computerized systems will meet their technical, commercial and regulatory requirements. If another regulated company has already assessed the supplier for the same reason, an additional assessment may not be necessary.

Supplier assessment is performed : basic assessment, postal audit, on site audit.

The justification for not assessing a specific supplier should be formally documented. Typically, supplier assessment is performed by one or all of the three methods described below, and in the assessment process in Fig.4.

1. Basic assessment based on validation information. (For components which are considered as commodities e.g. common desktop applications, a documented decision not to perform any assessment may be appropriate)
2. Postal audit, using a questionnaire.
3. On-site audit, by relevant specialist, auditor or audit team.

Need for Audit



Systems developed following defined methodology, e.g. GAMP5, needs reduced testing by the user.

To meet the expectations of regulated companies, suppliers are encouraged to develop systems following defined methodologies such as those described in GAMP guidance's, the most recent of which is GAMP5 (2008). Appropriate testing conducted by the supplier is likely to allow reduced testing by the user to avoid unnecessary duplication. It is expected of a Supplier to play a support role in achieving and maintaining system compliance and fitness for intended use. Specific activities of the supplier include: Provision of existing documentation - support role in preparation and review of documentation like URS, FRS, OQ, PQ and SOP; Acting as SME, for technical aspects such as: configuration and design options, performing and supporting testing, change and configuration management; Last, but not least, maintaining system compliance by providing software patches and second tier support for problem resolution processes.

Supplier plays a support role in preparation of URS, FRS, OQ, PQ, and SOP.

4. User Requirements Specifications (URS): URS define clearly and precisely what the regulated company requires the system to do. It is driven by the business needs of the user, describing those requirements which need to be tested during the validation of the system. The URS is the responsibility of the regulated company, which may take the help of subject matter experts, including those from third parties or suppliers, to understand the operational needs and to document appropriate requirements. The URS is written independently of a specific solution, and describes the functionality the users need in the system to manage risk to patient safety, product quality and data integrity. It also lists any constraints, regulatory and documentation requirements. The URS is typically the basis for PQ testing, as well as the Functional Specification.

5. Functional Requirements Specification (FRS): An outline document that demonstrates compliance of the functional design with the URS. This document describes the standard and/or configurable functions required of the selected software solution. The FRS identifies the standard functions included in the application system, and also identifies any customization/configuration to the standard off-the-shelf package and/or any custom modules that may need to be developed for additional functionality. The FRS also identifies the functions that are needed to satisfy GMP predicate rules and 21 CFR Part 11 requirements. The FRS forms the basis for Design Specifications (Solution Document), as well as Operational Qualification (OQ) testing.

URS describes the functionality users need in the software to manage patient safety, product quality and data integrity.

6. Design and Configuration Specification (aka: Solution Document (SD)): Based upon the type of system (e.g., configurable or custom), design specifications provide a detailed, technical expansion of the FRS. It defines how the software will implement the requirements in the URS and FRS. Its purpose is to ensure that the system will satisfy the requirements and specifications in the FRS and URS. This information provides the basis for subsequent configuration management that typically describes the system or component structure, algorithms, control logic, data structures, data set [file]

use information, input/output formats, interface descriptions, etc. Typically ERP systems used by pharmaceuticals are based on Commercial Off-the-Shelf (COTS) Programs and end users use information derived from a vendor-supplied User Manual. COTS programs provide convenience to end users to use the application with little or no adaptation by “filling in the blanks”, without altering the basic program. The Design and Configuration Specification is proprietary of the supplier.

IQ verifies that the software is installed according to pre-approved specifications.

7. Installation Qualification (IQ): An Installation Qualification is generated to verify that the system is installed according to written and pre-approved specifications. Checking, testing, or other verification demonstrates correct installation and configuration of software and hardware. The scope of hardware components include computer hardware components and connections, hardware manuals, operating procedures, and other documentation pertaining to the system's hardware (unique equipment ID, connections, and components), whereas the scope of the IQ Software components includes the required software (e.g., application software and layered software such as the operating system) and configurations. Software manuals, operating procedures, software listing (e.g., software name, manufacturer, version and location of master copy) and other documentation pertaining to the software are addressed in this document. At the time of IQ, system documentation inventoried and it's storage location are captured in individual IQ packages. The following is an example of what a computer related system documentation listing may include:

- Manuals for Hardware Components
- Manuals for Software Components
- Equipment/Vendor Documentation
- Standard Operating Procedures
- Preventative Maintenance Procedures

8. Operational Qualification (OQ): OQ is a documented verification that a system operates according to written and pre-approved specifications throughout specified operating ranges. OQ involves testing or other verification of the system against specifications to demonstrate correct operation of functionality that supports the specific business process throughout all specified ranges. An Operational Qualification test script is generated and executed to perform functional testing. The URS is the source document for the FRS, whereas the FRS serves as the source document for the Solution Documents. Confirmation of usability and effectiveness of the SD is done by parent (or normal) OQ test scripts. OQ test scripts serve as the basis for PQ and SOP. The Test Scripts executed in the OQ can be categorized as Normal, Limit, Stress, and Security tests. The Risk Assessment identifies the OQ Test Scripts for each category.

PQ demonstrates that the software meets the performance requirements outlined in the URS.

9. Performance Qualification (PQ): PQ is developed to demonstrate the system meets the performance requirements, typically detailed in the user requirements specification (URS) document. The PQ tests the system as an integrated system and is typically executed with product and/or product components. The PQ will include the execution of all cGMP functionality by trained and proficient system users during normal operations. If successful, OQ and PQ test scripts are used for preparing Standard Operating Procedures (SOP's) or Work Instruction (WI) documents. Once the system passes this level of testing, it is deemed ready for release to the operation phase.

10. Requirements Traceability Matrix (RTM): Traceability is focused on aspects critical to patient safety, product quality and data integrity. It ensures that requirements are addressed and traceable to the appropriate functional and design elements in the specifications. It also permits requirements to be traced up to the appropriate verification. The Requirements Traceability Matrix (RTM) is the mechanism used to verify that all requirements and specifications have been met and tested. It maps the system's requirements and specifications (URS, FS, and SD, if applicable) to the test cases / steps in the Protocols (IQ, OQ and/or PQ) where they are verified.

Traceability matrix maps the software's requirements (URS, FRS, SD) and their verification (IQ, OQ, PQ).

11. Validation Summary Report: The Validation Summary Report summarizes the activities performed, any deviation from the validation plan, any outstanding corrective actions, and fitness for intended use of the system.

Fig. 5: Example Format for a Validation Certificate

Project Name:		Project Number:
Controlling Specification Reference:		

FINAL SYSTEM VALIDATION APPROVAL

The signatories below have reviewed the validation documentation for the [name of company and name of system] Computerized System. This review included assessment of the phase reports listed below, including details of the execution of approved test scripts, the Recommended Actions, Conclusions and an assessment of Project Status derived from the outcome of each phase:

[List documents required by Validation Plan in section below]

Test Report / Document Title [those listed are for example only]	Report / Document Reference	Functional Specification Reference
Project Environment Detail Design Document	PE/5P961/250	FS/4F1956/001
Project Environment System Architecture	PE/5P961/251	FS/4F1956/001
Installation Tests – Peripherals	TR/4F1956/573	RS/4F1956/045
Installation Tests – Project Environment	TR/4F1956/213	FS/4F1956/047
Test Plan	SP/4F1956/128	Not Applicable
Test Report – Purchasing Modules	TR/4F1956/173	FS/4F1956/014
Test Report – Sales Modules	TR/4F1956/174	FS/4F1956/015
Test Report – Financials Modules	TR/4F1956/175	FS/4F1956/016
Test Report – Quality & Production Support Modules	TR/4F1956/176	FS/4F1956/069
Test Report – Custom Interfaces	TR/4F1956/178	FS/4F1956/012
Test Report – Security	TR/4F1956/181	FS/4F1956/092

STATUS

As a result it is determined that the [name of system] Project has been validated to date in accordance with the requirements of [Validation Plan reference] and can be used in the operational environment by suitably trained and authorized business personnel.

It is recognized that continued performance monitoring of the system will proceed after Go-Live in order to maintain the full validation requirements for this system.

APPROVAL DATE
[Must be prior to "go-live" date]

By signing below, each individual approves the validation status of the [name of system] Project:

Name	Job Title	Signature	Date
[Project Leader]			
[Project Manager – IT]			
[Validation]			
[Quality Assurance]			

Validation summary report summarizes all the validation activities, deviations, and outstanding corrective actions.

The level of detail in the report reflects the risk, and the complexity of the system. The structure of the report mirrors the structure of the corresponding plan. Contents of the computerized system validation report normally include: a.) Introduction and scope. b.) Scope changes. c.) Supplier assessment. d.) Summary of activities. e.) Summary of deliverables. f.) Summary of deviations and corrective action. g.) Statement of fitness for intended use h.) Glossary. i) Appendices. The report is approved as a minimum by the process owner and the quality unit. In many situations system owners and users are also involved. It is common to produce one final report. Shown in Fig. 5 is an example of such a validation report template. Validation documentation is maintained by the Document Control Unit (DCU). Validation data is usually stored in electronic or paper form, or a combination of both. Validation documentation is retained for the specified periods in accordance with cGMP requirements.

12. Maintenance of compliance and fitness for intended use throughout the life cycle: As part of the preparation for final acceptance and formal handover to live operation, the regulated company ensures that documents for operational processes, procedures, and plans to maintain compliance and fitness for intended use throughout its operational life, have been prepared, checked, and are supported by appropriate training. These procedures often involve the supplier in support and maintenance activities. The operational phase of a system may last many years, and may include changes to software, hardware, the business process, and regulatory

requirements. Despite this, regulatory requirements demand that the integrity of the system and its data is maintained at all times and verified as part of periodic review. Supporting documents prepared for maintenance of compliance and fitness for intended use during operation phase include **a) Change management, b) Continuity management, c) Security and system administration,** record management. Supporting documents for the Retirement Phase include **withdrawal, decommissioning, disposal and data migration.**

Change management ensures computer system remains in a validated status during the operational phase.

a) Change Management: The process of assuring that a computer system maintains a validated status following a change to the software, hardware, or any associated documents during the operational phase. All the changes that are proposed during the operational phase of a computerized system, whether related to software (including middleware), hardware, infrastructure, or use of the system, is subject to a formal change control process. A plan of the change control process should be very clearly laid out, and documented during validation. It should include assessment of the impact of the change and ensures that changes are suitably evaluated, authorized, documented, tested, and approved before implementation. The change request is normally pre-approved prior to the change (with the exception of an emergency change). The impact to the system validation is addressed by revisions to the applicable system's documentation (e.g., URS, FRS, SOP's, drawings) to reflect the change and the creation of a protocol or test plan to qualify the change. The test plan may include regression testing to demonstrate that existing requirements impacted by the change are still being met. The change request, affected documents, and protocol/test plan will then be completed and post-approved.

Important components of continuity management include: system backup and restoration, disaster recovery, security and system administration.

b) Continuity Management: Continuity management involves planning for system backup and restoration, business continuity planning and disaster recovery. **System Backup and Restoration:** A system backup and restoration document is prepared to describe how the computer system software and data will be securely backed up. The document will also describe how the work process and the computer system will be restored. The recovery actions are based on the type of disruption and the time the system is unavailable. **Business continuity planning:** A business continuity plan defines how the business may continue to function and handle data following failure. It identifies the critical business processes, and the systems supporting these processes and activities, to be performed to ensure the timely and effective resumption of these official business processes and systems, and how data generated during the disruption should be managed. **Disaster Recovery:** A predetermined plan that allows for computers, manufacturing areas, and facilities to be reinstated to operating conditions in the event an accident, fire or other natural and/or man-made catastrophe occurs. A Disaster Recovery plan is created to describe how the computer system software and data will be secured against damage or loss (e.g. use of Uninterruptible Power Supplies (UPS), and the processes to follow at the organization and/or department level, to continue to conduct business in the event that the system becomes temporarily disabled. If it is not possible to perform the work process without the computer system, the plan must state this.

c) Security and System Administration: The computerized system and data should be adequately protected against willful or accidental loss, damage or unauthorized change. Security management describes the procedures for managing secure access, including adding or removing privileges for authorized users, virus management, password management and physical security measures. Once a system is in operation, the users of the system will require support. The System Administration Plan provides administrative support for systems, including the performance of standard administration tasks. The extent of this process varies greatly depending on the nature of the system.

'Retirement of the System' describes policies regarding withdrawal, decommissioning and data migration.

Record Management: Policies for retention of regulated records are established, based on a clear understanding of regulatory requirements and existing corporate policies, standards, and guidelines. **Archive and retrieval:** Archiving is the process of taking records and data off-line by moving them to a different location or system, often protecting them from further changes. Procedures for archiving and retrieval of records are established based on a clear understanding of regulatory requirements.

Retirement: Includes policies regarding **withdrawal, decommissioning, disposal** and **data migration. Withdrawal:** Includes policies related to removal of the system from active operation i.e. users are deactivated, interfaces are disabled and no data is added to the system from this point forward. Special access is retained for data reporting, result analysis and support. **Decommissioning:** Is the controlled shutdown of a retired system. **Disposal:** Identifies polices regarding destruction of documentation, software or hardware. Due to the volume of data and records involved, retirement is a major task, for IT systems in particular. Policies also define documentary evidence to be retained of actions taken during retirement of the system, GxP records to be maintained, their required retention periods, the need to migrate records to a new system or archive, methods of verifying and documenting this process, and the ability to retrieve

migrated records on the new system. **Data Migration:** Data migration may be required when an existing system is replaced by a new system, when an operational system experiences a significant change, or when the scope of use of a system changes. The migration process should be accurate, complete and verified.

Plan Review Period: The Review period of the Master Validation Plan should be clearly stated. The plan must also be reviewed when practices of validation within the company require revision or modernization. If the review process identifies changes are necessary, the plan must be revised and approved by the appropriate positions/roles.

BatchMaster for Pharmaceuticals and regulatory compliance

BMP is a vertical Solution developed by BatchMaster, a leader in Process ERP, to cater to the needs of Life Science i ndustries.

BatchMaster® for Pharmaceuticals (BMP) is a preconfigured, windows-based, GAMP category-4, process ERP software specifically developed for process manufacturers who make their products using a formula or a recipe. It serves as an excellent platform for life sciences and pharmaceutical industries involved in the manufacture of tablets, syrups, creams, biopharmaceuticals and bulk drugs, which make their products using a formula, and in batches. The key driver behind the design of BMP has been to equip their customers to safeguard patient safety, product quality and data integrity, while also delivering enormous non-cGMP business benefits. BMP rests on the solid foundation of BatchMaster ERP, a leader in process ERP, with a track record of 30 plus years and with more than 1500 customers around the globe (Table 6). The Customer profile of BatchMaster includes both regulated and non regulated process industries like pharmaceuticals, bio-pharmaceuticals, nutraceuticals, food and beverage, cosmeceuticals, and coatings and chemicals. A long successful track record of performance of the software, accompanied by a competent BatchMaster team which includes experts from diverse areas like information technology, life sciences, engineering and finance to carry out the support activities and fulfill the responsibilities expected of the supplier as per GAMP guidelines, makes BMP software an attractive proposition in the life science sector.

BMP is manufactured as per GAMP guidelines with QMS based on the life-cycle model.

The fact that BMP has been designed and manufactured according to GAMP guidelines, and with a QMS based on the life cycle model, helps its smooth implementation following the same guiding GAMP principles. Implementation of BMP is based on a complete life cycle approach as part of a Quality Management System (QMS), from concept to retirement, and with a scalable approach to achieve and maintain GxP compliance.

Table 6: BatchMaster Software - Profile

- 30+ years Process ERP Experience
- Globe Customer Base of 2000+
- 200+ software Professionals with 24x6 Support
  - Domain expertise from many fields
  - Understand your specific business requirements
- Vertical solutions for different Industries.
- Proven GAMP Implementation Methodology
- Constant up gradation of the products with new technology
- Develops Flexible Software
  - Scalable
  - Customizable

BMP software contains three modules: Administration, Distribution and Manufacturing (Fig. 6).

Modules are the functional areas which use information from both Master Data and Transactions.

In addition, BMP provides an open platform and can be very easily integrated to analysis software like accounting, forecasting and business intelligence for enhanced functionality. These software applications are not part of core BMP, but they utilize all the information of BatchMaster to perform their various analyses.

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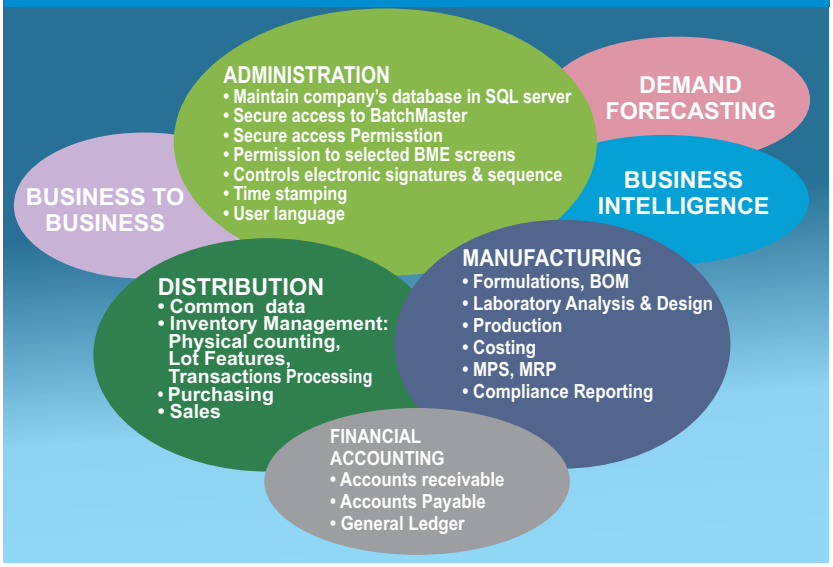
Fig. 6: Batch Master for Phramaceuticals: an Overview



BatchMaster comprises three modules: Administration, Distribution, Manufacturing.

In BatchMaster Pharmaceutical, an Administrator who has the authority to access and make changes in the Administration module also has rights to provide permission to users to the various BatchMaster Pharmaceutical screens they are authorized to view. Shown in Table 7 are some of the key features of BatchMaster's Administration Module. It allows administrators to create the company's database, and define user groups and users belonging to those groups. Administrators also maintain passwords, provide access rights to users to various system screens based on their role, and give permission to modify the screens only to authorized personnel. Administrators also define approver groups for formulation changes, and purchase and sales requisitions if required. Shown in Table 8 are the password functionalities used by BMP which are as per CFR part 11 requirements.
Distribution module users maintain the common data and master data that under-pins all the transactional processes. The different functional areas which can be performed through the

Password functionality of the Administration module fulfils all the CFR Part 11 requirements.

Table 7: Administration Module

- Create Manufacturing company Database
- Server where database will be stored
- Define User groups (Role Based)
- Maintain Passwords of the Users
- Provide users the access rights to screens
- Permission to modify the screens to authorized people only
- Define Approver group for PR and SR
- Default ledger setup

Table 8: BMP ADMIN: Password Functionality

- Password reuse (Admin)
- Failure Log in attempts
- Maximum allowed inactivity period
- Alpha Numeric Password
- Temporary Auto Password by Admin
- Edit/ write permission to restricted people
- Last log on and Log off display

BMP controls GxP related activities through the Distribution and Manufacturing modules.

Distribution module include: inventory management, sales, purchase and accounting (Table 9). In the Manufacturing module users maintain all the information of Formulas, Bills of Material and Production (Table 10). Functional areas which can be performed through the Manufacturing module include production and master production scheduling, material resource planning and Advanced Planning and Scheduling.

BMP has robust unit conversion capabilities - user can purchase, stock and sell cGMP products in different units.

Table 9: BMP Distribution Module

- Common Data, Master Data
- Manage Inventory: Item Master, Item Location, Bin Master, Physical count, warehouse transfers, Transactions, maintain lots
- Sales
- Purchase
- Finance

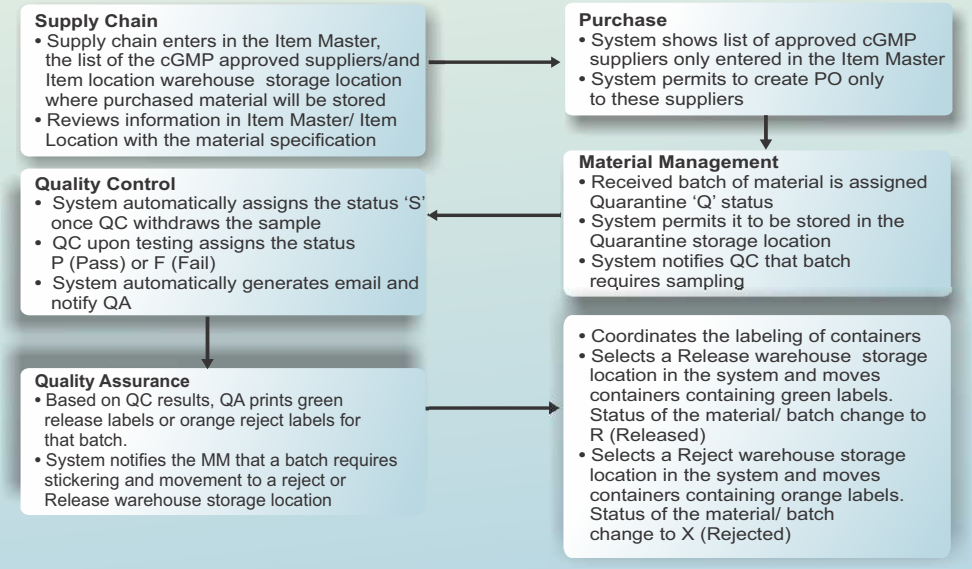
Table 10: BMP Manufacture Module

- Permits user to initiate full or partial closing of batch tickets for urgent shipments
- Batch sizing wizard to support batch sizing by weight, volume, physical property, available materials or expected yield
- Flexibility in inventory handling. It permits both hard and soft allocation
- Number of management reports including critical materials to flag shortages, Expiration dates to assure that materials are viable, Material where used to show where specific

GxP related activities of BMP are controlled mainly through the Distribution and Manufacturing modules. Shown in Table 11 and Table 12 are details of generic GxP related activities of a typical Pharmaceutical company and the manner in which BMP software address them.

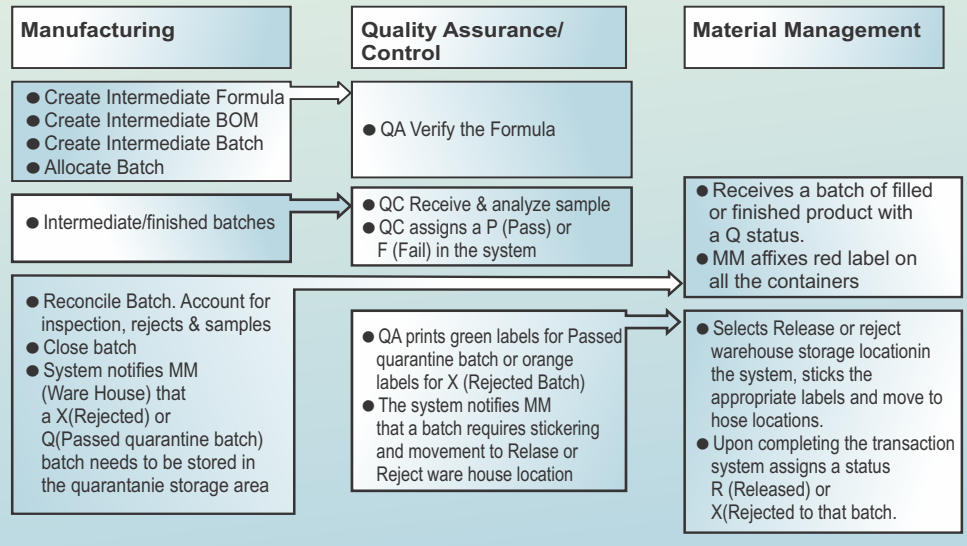
In case of product recall BMP provides complete structure of cGMP product, its raw materials and recipient customers.

Table 11: cGMP Material/batch Handling by BMP are in compliance with FDA Requirements



BMP permits customers to create formulas based on active ingredients or biologic activities.

Table 12: cGMP Material/batch Handling by BMP is in compliance with FDA Requirements



Some of the advanced features of BMP which help pharmaceuticals to perform their tasks with great ease include: powerful **Unit conversion** capability; **Lot strength feature; Formula** module; **Laboratory** module. In BMP, a user can define a unit conversion globally in US and UK systems of measurement, or define a unit conversion even at the item level, including density / specific gravity. The Unit Conversion utility is one of the very strong features of BatchMaster. In addition, it permits a user to purchase in one unit, maintain stock in another unit, and sell the product in a third unit. A 'Toggle Unit' facility is available in sales, purchase and inventory screens to switch between different units.

BMP has robust **Lot Feature** functionality (Table 13). In case of a Product Recall, Lot Explosion capabilities provide complete the structure of a product and provide complete information about the sources of raw materials used in the product, production details and customers to whom this product has been sold, even when quantities of the same Lot have been used in multiple batches.

BMP provides tight control over the changes to formulas and maintains records and reasons for revisions by authorized persons with date/time stamping.

One of the more advanced features of Batch Master Lot Feature is “Lot Strength” which permits R&D to create a formula based on biological activities of the ingredients.

For Formulators, BMP's **Formula module** provides the flexibility of resizing a formula based on different constraints (Table 14). Complete records of all versions of a formula are maintained, along with the records of persons who revised them and the reason for revision. BatchMaster also determines the theoretical costs of producing a formula including materials, labor and overhead.

BMP also provides a facility of re-sizing production batches of a formula based on active ingredients which may vary from lot-to-lot during purchase.

Another unique feature of BMP is the **Laboratory module**, in which formulators can make changes in the physical properties and analyze their impact on the quality of the product with a very strong quality control module. The combination of these two (laboratory physical property analysis and strong quality control) permits the pharmaceutical developer to have complete control over the process and perform the necessary risk assessment. It results in high quality product which improves with every batch. This functionality can be very useful in a transition from traditional to PAT compliance, and for contract manufacturers who normally make small batches.

Implementation of BMP in Pharmaceuticals is performed in accordance with GAMP guidelines.

Table 13: BMP : Lot features

- Robust Lot Strength feature which allows to create formula based on biological activities of the ingredients.
- Product Recall and Lot Explosion Capabilities: Provides complete structure of a product. Enables to track the source.
- Helps in lot picking based on Expiration Date.
- Lot Quarantine Support.

Table 14: BMP Formula Functionalities

- Formula can be defined on the basis of active ingredient using “Lot Strength” feature
- Unlimited Inventory materials, Intermediates
- Unlimited manufacturing instructions
- Formula Revision history (CFR Part 11 compliant)
- “Where used” capability by material, formula or QC control
- Sizes formulas

Validation Strategy of BMP

Implementation of BMP in pharmaceuticals is performed in accordance with GAMP guidelines. Its implementation involves all the activities mentioned in Table 3. During Validation of computerized systems, the BatchMaster team supports and performs all the activities expected from the supplier. The Validation Plan and testing documents of BMP software remain as part of the Master Validation Plan of the regulated pharmaceutical company. The BatchMaster team plays a support role in the development of URS. Based on the URS, the BM team creates the FRS and design or solutions documents. OQ and PQ is performed jointly by BatchMaster and the regulated company to ensure that all the URS have been met, and the system as a whole is fulfilling all the business needs and regulatory requirements.

Successful validation reference of BMP in USA, along with document support, greatly reduces the documentation load of BatchMaster's customers For validation.

In GAMP5 guidelines there is an increased emphasis on avoidance of duplication of activities, increased involvement of the supplier and wherever possible leverage of supplier documentation after risk assessment. The fact that BMP ERP is in current use by pharmaceutical customers in US, after its validation as per FDA cGMP requirements, suggests its suitability in other countries like Europe, China and Japan as well, which have similar regulatory requirements to the FDA.

Reference of validation performed in one pharmaceutical enterprise provides an assurance about the quality of the software and supplier, and is used in subsequent validations. It tremendously reduces the documentation load to fulfill the regulated company's obligatory compliance requirements. Shown in Tables 15-17 and Fig.7 and 8 are examples of generic templates prepared by BatchMaster of URS, FRS, SD SOP and traceability matrix prepared for the Purchase of cGMP product, as an example. Generic templates prepared and available with BMP also become part of the regulatory compliance document preparation of BatchMaster's pharmaceutical customers.

During validation of BMP, FRS demonstrates compliance of functional design with URS.

Table 15: Generic Template of BMP URS

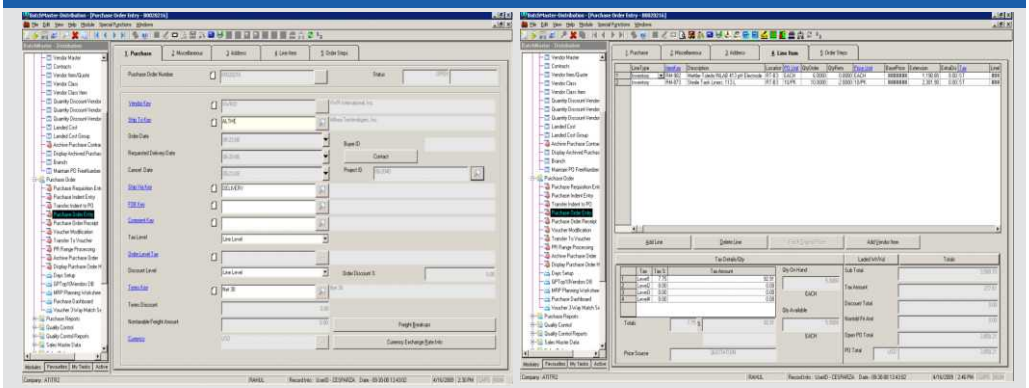
User Requirement Specification Number	Detail
URS-PM-001	The system should allow purchase of cGMP materials from active approved suppliers only.

Table 16: Generic Template of BMP FRS

	Corresponding URS number	Statement
URS-PM-001	**URS-PM-001**	The system restricts purchasing from unapproved vendors by design. System permits creation of purchase orders from 'Active' status approved vendors only.

During validation of BMP, SD ensures that software satisfies URS and FRS requirements and specifications.

Fig. 7: Generic Template of BMP Solution Document of Purchase Order Entry process

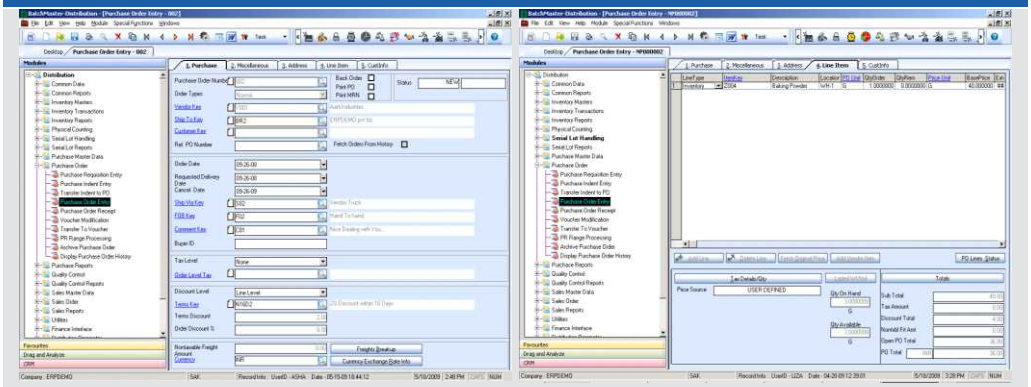


1. The system will allow a single character prefix to the order number.
2. The system will record the date by which the material is required at <Regulated Company> facility for each ordered item.
3. The system will record the Project ID to indicate the project for which the purchase order has been created.
4. The system will default the tax rate from the value maintained in the vendor master. It may be modified on a case basis.
5. The system will default information from the vendor master into the Purchase Order Entry screen. Example: Ship via key, FOB key, Terms, etc.
6. The system will allow recording the vendor contact associated with this purchase order from the list of contacts defined for the vendor.
7. The system will allow entering as many item lines as required.
8. The location at which the ordered items will be received will be defaulted to the default location maintained in the vendor master.
9. The system will allow entering the ordered quantity in any unit of measure besides the unit defined as the default 'Purchase Unit of Measure' in the item master.
10. The system will record the date by which the vendor has promised delivery for each ordered item.
11. The system will allow printing the Purchase Order to be sent out to the vendor.
12. The system will allow copying an existing order with a new number for repeat orders.

BMP's dashboard interface, designed for managers, provides dynamic, real-time information for each department.

Robust MPS and MRP modules of BMP help managers maximize production capacity and reduce holding cost of inventory.

Fig. 8: Generic Template of BMP Standard Operating Procedure/ Work Instructions Document of Purchase Order Entry process



1. Click on the Insert button on the toolbar to prepare the screen for data entry.
2. Click on the magnifying glass available next to the PO Number field and select a Series.
3. Click on the arrow available next to the Order Types field to select the order type as Normal.
4. Click on the magnifying glass available next to the 'Vendor Key' field and select a Vendor. Upon selecting the vendor, it's associated Ship TO, Taxes, Discounts, Vendor Clas, Vendor Address and Ship To Address, SHIP Via, FOB comments should default to their respective fields.
6. Change any of the defaulted values, if required.
7. Switch to Tab 4: Line Items tab.
8. Click on the Add Line button to insert a new line in the grid
9. Click on the arrow available at the Line Type field and select the line type as Inventory.
10. Click on the right of the Item Key field to pop up the Item Location lookup and select the desired Item.
11. Click on the right of the Location field to pop up the Location lookup and select a location.
12. Enter the quantity to be ordered at the 'QtyOrder' field.
13. Repeat steps 7 to 10 to add more lines.
14. Click Save to save the order.

Table 17: Example Format for Traceability Matrix

	FRS Number	Solution Document Number	Testing or operational Qualification Number	Standard Operating Procedure (SOP) Number	Comments
URS-PM-001	FRS-PM-001	SD-PM-001	OQ-PM-001	SOP-PM-001	

Non cGMP business benefits of BMP:

Three tier support of BMP (Table 18): BatchMaster is user- friendly software which provides secure access to all users, irrespective of their position in an organization, to perform their work smoothly and efficiently.

Integration of BMP with business intelligence helps top management to respond quickly to changes in the marketplace, and in out-pacing the competition.

Table 18: BMP : Three Tier Support

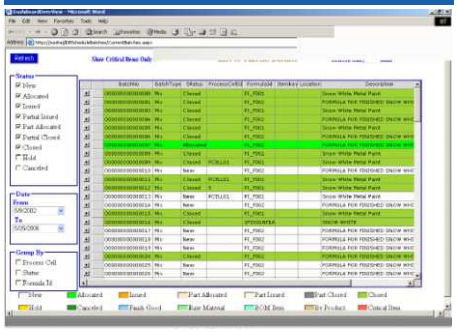
Higher Management
1. Variety of strategic reporting tools for quick response to changes in the market place;
2. Analysis of Key Performance Indicators
3. What-if analysis in decision making about the direction enterprise should be heading.

Middle Management
Dash Board Interface to view the complete real time information (with user defined refresh rate) of purchase, sales and inventory.
Very efficient MPS and MRP functionality for production scheduling based on Forecast and Demand.

Lower Management
It provides secure access to perform routine tasks.
It permits the user to keep shortcut of routinely performed jobs in favorite menu for faster access.
Easy switching between the modules and open multiple screens at one time to perform tasks more efficiently.
F1 help for access to BME library and F4 help to open look up for specific field with auto complete feature.

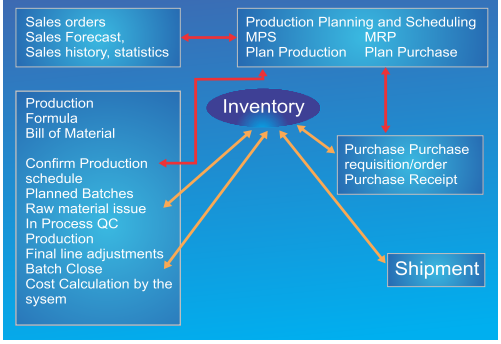
It permits lower management employees to maintain shortcuts to routinely performed tasks. It permits them to open multiple screens at one time and switch easily between the modules.
To the new user it provides F1 help for access to the BME library and guidance about the particular screen.
To middle management managers, BMP provides dashboard interfaces where they can view dynamic, real-time information of the state of affairs in their Departments with user defined data refreshes (Fig.9).

Fig. 9: BMP Dashboard - Production



Dashboards also provide critical information about the issues which need attention from upper management.

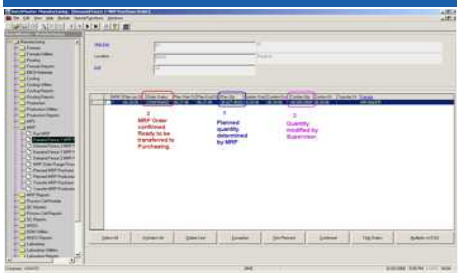
Table 19: General Business Flow



Shown in Table 19 is the generic general business flow. Confirmed sales orders and forecasts generate demand. Demand triggers production, planning and scheduling. First the Master Production Schedule is run and production is planned and confirmed. It is followed by Material Resource Planning, in which an algorithm based on scheduled batches and the lead time of procuring raw materials automatically generates Purchase Requisitions/ Purchase Orders for different time intervals. Once materials are received and tested, they are maintained as inventory and issued to production. Again finished products thus produced are checked for quality control and released. QC checked finished products are kept as inventory till shipped.

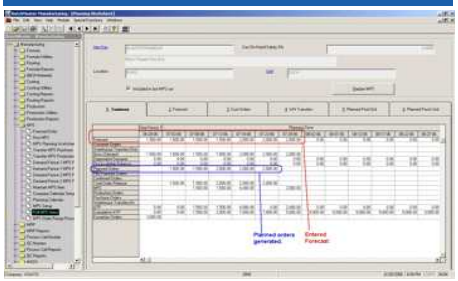
New FDA directives have been developed which consider the current scenario of a global economy for Pharmaceuticals, having multiple units all over the globe.

Fig 10: MRP (Material Requirement Planning)



BMP has very powerful MPS and MRP scheduling modules. MRP (Material Resource Planning) helps Middle Management to reduce the holding cost of inventory with no risk of shortages (Fig.10).

Fig 11: MPS (Master Production Scheduling)



MPS (Master Production Scheduling) helps managers to schedule production in order to maximize capacity and to fulfill shipping promises (Fig.11). Advanced Planning and Scheduling (APS), often an elective module of the BMP ERP software solution, enables managers to gain a real time picture of current shop floor activities. This capability allows the manger to invoke last minute production adjustments to make allowances for absentee workers, machine down times and bottlenecks, as well as to accommodate rush orders.

Integration of Business Intelligence with BMP (Fig.12) provides top Management a variety of strategic reporting tools to monitor metrics and trends in an easy to use display. This information can be used for quick response to changes in the market place and outpacing the competition. Graphical displays of Key Performance Indicators which evaluate business health are helpful in focusing on immediate potential issue areas. In addition, "what-if" analysis of financial information is useful in decision making and deciding the direction the enterprise should be heading.

Fig.12: Business Intelligence Dashboard

Conclusion:

There is an increased realization that Process ERP may provide the ideal software solution for Life Science industries.

The last decade has witnessed a big shift in the FDA's thinking and expectations. To ensure that high quality pharmaceutical products are available to American consumers, new concepts have been developed to improve the way drug development and manufacturing is managed. To bring innovation to pharmaceutical industries, new FDA directives focus on the use of an integrated approach and process understanding involving good science and good engineering practices. New challenges arising as a result of development of a global economy with pharmaceuticals, having multiple units all over the globe, have also been addressed in the new polices. The FDA has increased its collaboration with international health and regulatory partners. Working together, international regulatory authorities have continued to harmonize their activities, especially in quality-related areas, and increased the sharing of regulatory information. These international efforts have yielded common harmonized regulatory policies and alignment of consensus standards. It is hoped that it will strengthen the FDA's oversight of non-U.S. drug manufacturing sites that produce FDA-approved pharmaceuticals for Americans and at the same time help their regulatory counterparts to manufacture drugs of high quality. In this kind of environment, there is an increased realization amongst pharmaceutical manufacturers that process ERP maybe the ideal solution software for them because their products are made using a formula and are manufactured in batches. Process ERP not only helps them to comply with their obligatory regulatory requirements but also provide them enormous non-cGMP business benefits. In this paper, using a process ERP solution (BatchMaster Pharmaceutical) as an example, we have shown how cGMP requirements can be complied with using this software, and how its non cGMP functionalities provide complete control over all business processes.

About the Author:

Dr. Ravi Jotwani has been a Senior Research Scientist at the University of Louisville, Louisville, Kentucky.

Dr. Jotwani has a Ph.D. in Medical Microbiology from the All India Institute of Medical Sciences (New Delhi). He started his post-doctoral career at a managerial level in research for the Microbiology & Immunology Unit of Ranbaxy Diagnostics, New Delhi, India. He subsequently undertook a Post-doctoral fellowship at the Institute of Anaerobic Bacteriology, Gifu, Japan, where he received the Best Paper of the Year (1992) by JARMAM, Japan at the 6th Annual Meeting of the Assn. for Rapid Methods and Automation in Microbiology at Yokohama, Japan. On his return to India he worked as a Senior Research Associate, National Institute of Immunology in New Delhi.

Since 1997, he has held various positions at USA universities, including Assistant and Associate Professor Research at State University of New York, Stony Brook, NY. During this period he has published 30 original research articles, contributed to a textbook, and has guided many Master and PhD students.

Three years ago, he realized that there is an increasing demand for professionals having joint expertise in biotechnology and information technology, and has dedicated much of his time to research in this area.

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