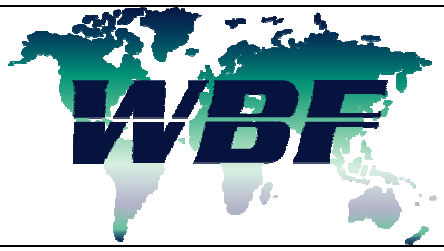
Presented at the
WBF
North American Conference
Atlanta, GA
March 5-8, 2006



195 Wekiva Springs Road, Suite 200
Longwood, FL 32779-2552
+1.407.774.5764
Fax: +1.407.774.6751
E-mail: info@wbf.org
www.wbf.org

MANAGING COMPLEX EQUIPMENT STATUS IN A GMP ENVIRONMENT

Mark Albano
Senior Marketing Specialist
Honeywell
2500 W. Union Hills Drive
Phoenix, AZ 85027
USA
602-313-4518
mark.albano@honeywell.com

Tom Farenholtz
Principal Consultant
Honeywell
13655 Dulles Technology Drive
Herndon, VA 20171
USA
703-793-4449
tom.farenholtz@honeywell.com

Steve Zarichniak
Applications Consultant
Honeywell
1100 Virginia Drive
Fort Washington, PA 19034
USA
215-641-3244
steve.zarichniak@honeywell.com

KEY WORDS

Batch Equipment Status, GMP, Batch Automation Systems

ABSTRACT

MANAGING COMPLEX EQUIPMENT STATUS IN A GMP ENVIRONMENT

Batch manufacturing systems must maintain the status of equipment, including which are available, dirty, out of service, etc. In industries that enforce Good Manufacturing Practices (GMPs), additional status types and values for process equipment must be maintained. Rules associated with the equipment status can be complex and involve the equipment class, current equipment state and time in the current state. This paper will cover the operator interface used to review the equipment status and the interlocking requirements between the recipe and batch phases based on multiple status types. Coordination, timing and reporting of the equipment status transitions both internal and external to the batch system are discussed. Sample system architectures illustrating how GMP status can be applied to current batch implementations will be presented.

MANAGING COMPLEX EQUIPMENT STATUS IN A GMP ENVIRONMENT

Introduction

For manufacturers subject to regulations enforced by the FDA in the United States and other agencies worldwide, it is critical that processes and systems are validated.

By definition, equipment, units and devices are not compliant by themselves. The combination of the equipment, process definition, operating practices and maintenance policies are all subject to the validation criterion established by a manufacturer.

This document provides an overview of equipment status in a regulated environment and explains its application in a complex batch environment.

Validation

Validation requires the establishment of documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.[1]

The purpose of validating automation systems is to prove with a high degree of assurance that the system will work correctly and consistently. For 21 CFR Part 11 compliance, validation should also prove the accuracy and reliability of the data collection and management system.

Equipment Status Management Issues

Methods for managing equipment status vary from paper-based Standard Operating Procedures (SOPs) to computer-based Manufacturing Execution Systems (MES), Enterprise Asset Management (EAM) systems and Process Automation Systems.

These methods have evolved over time and tend to be specific to each manufacturer. Mergers and acquisitions of companies have led to multiple systems and methods across their corporate enterprises.

Maintaining and harmonizing computer-based systems that meet GMP regulations and internal corporate standards is an expensive proposition.

Internally developed systems promise maximum functionality and flexibility but the reality is that these systems rarely get completed with all of the expected features. When a new operating system platform emerges, support for older versions is dropped. Compliant systems must be on a supported platform so eventually the bespoke system must be migrated to a new platform. The revalidation cost is often as much as the original system implementation.

Commercial off-the-shelf (COTS) applications, such as maintenance management systems, provide affordable solutions, but are generally standalone and are not integrated with batch or process control systems.

Before defining a solution, a discussion of some equipment management requirements is in order.

[1] FDA Guidelines on General Principles of Process Validation, May 1987.

Equipment Definitions

S88 defines:

> **Unit**: "A collection of associated control modules and/or equipment modules and other process equipment in which one or more major processing activities can be conducted."
>
> **Equipment Module:** "A functional group of equipment that can carry out a finite number of specific minor processing activities."

Presently multiple batch automation systems may be needed to manage units, equipment modules and other resources. The primary management function conducted by the batch automation systems are availability (ownership) and process capabilities (class parameters). An additional requirement for GMP processes is the management of equipment unit status.

This paper defines a common equipment status management scheme for all equipment including units, equipment modules and other process equipment. Process capability is not considered part of equipment status. It is important to manage all of these equipment types, not just the units, the same way in a GMP plant.

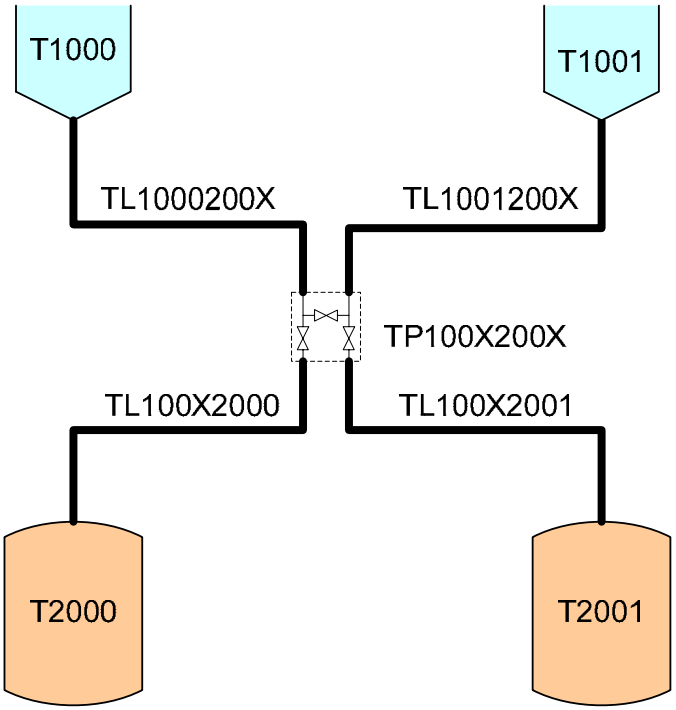


Figure 1 – Equipment Model

Figure 1 contains four units (T1000, T1001, T2000 and T2001), one control module TP100X200X and four other pieces of process equipment (TL1000200X, TL1001200X, TL100X2000 and TL100X2001).

Equipment Status Data Management

In addition to managing ownership and capacity, additional status types need to be defined for the equipment in a GMP plant. Status types are class based. Looking at Figure 1, the following status types could be defined:

Equipment Class	Members	Status Type	Status Values
Prep Tank	T1000, T1001	AVAILABILITY	AVAILABLE, IN-USE, OUT-OF-SERVICE
		CLEANLINESS	DIRTY, CLEAN
Mix Tank	T2000,T2001	AVAILABILITY	AVAILABLE, IN-USE, OUT-OF-SERVICE
		CLEANING	DIRTY, CLEAN, STERILE
		PROCESS	EMPTY, MIXING, MIXED
Transfer Line	TL1000200X, TL1001200X, TL100X2000, TL100X2001	AVAILABILITY	AVAILABLE, IN-USE, OUT-OF-SERVICE
		CLEANING	DIRTY, CLEAN
Transfer Panel	TP100X200X	AVAILABILITY	AVAILABLE, IN-USE, OUT-OF-SERVICE
		CLEANING	DIRTY, CLEAN

Table 1 – Class-Based Status Types and Values

Table 1 shows how different classes of equipment have their own requirements for the management of several different types of status values. Batch automation systems usually have a single status type for equipment. If a single status type is all that is available then there are a great number of unique status values to cover all possible combinations. In Table 1 there would need to be six (3 x 2) values for the prep tank, transfer line, and transfer panel and 27 (3 * 3 * 3) values for the mix tank. Transition logic would use enumerations of these combinations. Adding status values or types multiplies the number of combinations. These large enumeration sets for each unit class are difficult to maintain and makes it difficult to configure control strategies based on status.

A better approach is to allow equipment to have multiple status types defined and to enable the control strategies to set and check them in any combination.

Batch Independence & Genealogy

GMP equipment status is persistent across batches and exists even if no batch is active on a unit. Batch systems are designed to process batches and do not carry status from batch to batch. Historically, the process control system has been the usual place to maintain persistent data for the process. GMP requires the maintenance of an equipment log showing historical status change events and genealogy of the equipment and batches. The process control system maintains current status and relies on a data historian or process logs for any type of event data based on time but not by batch. Batch association is important for genealogy (association of equipment with a batch).

Persistence of the equipment status must also be maintained if the batch automation system fails or undergoes a warm or cold restart. Storing status value(s) in process control registers requires careful design and analysis of failure modes.

Unit Class Status for Process State

Looking at Table 1, a process status type ("PROCESS") has been defined for the mix tank. This is a very useful status type that can be used to assist in coordination of processes. For example, consider a mix tank that holds an intermediate product for use in the next process step. Once the mixing is done and the batch is complete, the mixer availability status is set to available so it can be acquired by a process that needs to transfer material out of the mixer. What is to prevent a cleaning procedure from being run on the unit? Without maintaining a process status, the unit is available and can be acquired by a cleaning batch. This could unintentionally ruin the intermediate material in the mixer.

Currently this problem is solved by the use of either an expensive finite scheduling system or by communicating the current status of a unit to operators on a white board mounted on the unit.

Manual log sheets for the equipment are used to verify that the equipment has followed the correct sequence of events. SOPs require the operator to check the logs and white boards before starting a batch and then sign the batch record that the check was performed. As part of the batch release process, manual verification of equipment logs is required. This process is manual and as such is prone to human error.

Association of Other Non-Class Based Equipment

Management of other process equipment is left up to the control system vendor or process engineer to determine how to add it into the overall strategy for a project. It falls somewhere between a batch and process control system. Referring to Figure 1, the transfer lines and transfer panels are shared between different units at different times. Batch systems allow these types of equipment to be managed as resources. One of the drawbacks to batch systems is a built-in feature that automatically releases resources at the end of some process steps. The ability to associate other process equipment with a unit and have the association persist across operations, unit procedures and batches would remove unnecessary logic from control modules and phases.

An example using the model in Figure 1 would be a cleaning procedure that used a reusable operation to clean two lines and a transfer panel. A Clean in Place (CIP) skid would be required to support each cleaning cycle. If the CIP skid was released between CIP cycles, this would prevent the orderly completion of all cleaning cycles.

Equipment Status Rules

The discussion to this point has assumed that the status values are static and only change when commanded by a process request or event. There has been no restriction on legal transitions from one status value to another. Also, several of the status values may require an expiration to be associated with them.

Equipment Class	Members	Status Type	Status Values	Timeout and Next Value	Allowed Transitions
Mix Tank	T2000,T2001	CLEANING	DIRTY	No Timeout	CLEAN
			CLEAN	14 days → CLEAN_EXPIRED	DIRTY, STERILE
			CLEAN_EXPIRED	No Timeout	CLEAN, DIRTY
			STERILE	10 hours → CLEAN	CLEAN, DIRTY

Table 2 – Status Value Rules

Table 2 illustrates the addition of transition and timing rules for the cleaning status type for the mix tank. One additional status value, “CLEAN_EXPIRED”, was added to the list of status values. This value is set if the “CLEAN” value expires after the timeout period.

An independent process to monitor equipment rules and change the status when a timeout occurs needs to be part of the equipment management solution. In order for this to work, a timestamp needs to be associated with each status change.

Equipment Status Solution

A solution for equipment status management in a GMP environment requires significant additions to the standard capabilities of batch and process control systems. Status management also involves and impacts other plant systems including MES, EAM, ERP, Finite Scheduling and the Data Historian. Automatic timeout monitoring requires a component that is not currently present in any plant system.

Given the global impact of equipment status management, there is sufficient functionality, commonality and complexity to define a new class of system.

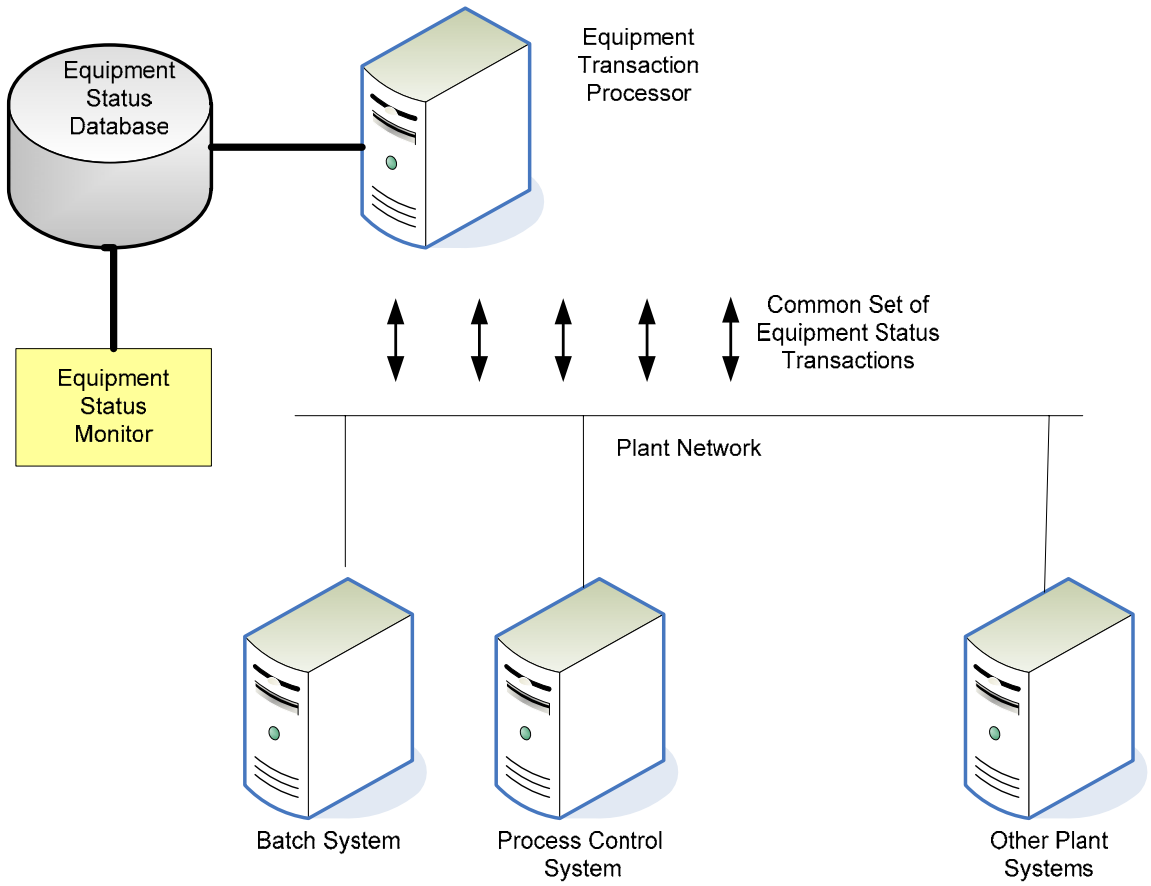


Figure 2 – Equipment Status Architecture

- Equipment Status Database – Relational database to support the equipment status model. Includes a configuration utility to manage the model and status rules.
- Equipment Transaction Processor – Standard to High-performance (depending on the plant size), scalable, real-time transaction processor.
- Common set of Transactions – Well-defined and documented set of transactions to support equipment status change requirements.
- Equipment Status Monitor – Processes automatic status changes based on rules.

Characteristics of Equipment Status Management

Important characteristics of status management include:

- Real-time – needs to support process control systems
- Highly Available – must be as reliable and as available as the process control system

- Secure – the data must be on a secure server that is configured with data redundancy and backup capabilities
- Scalable – must be able to expand to accommodate growing plant needs
- Configurable – must be able to be configured online without a system restart for changes to take effect

Conclusions

- Today's systems are too simplistic for complex equipment status management
- Complexity results in the tendency to go back to paper, which has many disadvantages:
    - Limits production yield
    - Operating in a non real-time environment
    - After-the-fact checking
- Solutions
    - Status management application component
    - Need to develop industry standards

Definitions

- **Non-Unit Based Equipment –** equipment that requires status management where processing activities do not occur.
- **Auxiliary Equipment –** equipment that is not a unit and can be used in the execution of a batch
- **Status repository** - the repository with all current and historical equipment statuses in the enterprise
- **Equipment Status Type**: An attribute of equipment relating to its status. Status types are assigned a unique status value from a list of allowable status values and their associated rules.
- **Equipment Status Value**: State assigned to a Status type for a piece of equipment such as clean or dirty.
- **Class Based**: Equipment that whose attributes, properties and status types are defined in an equipment class but whose values are maintained for individual equipment in the class.
- **Equipment Genealogy**: Record of all activities that occur in a batch pertaining to equipment. The genealogy records are constructed in a manner that allows for tracing both forward and backwards through subsequent and prior batches.
- **Electronic Record**: Any combination of text, graphics, data, audio, pictorial, or other information in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system.
- **Electronic Signature**: Computer data compilation of any symbol or series of symbols executed, adopted or authorized by an individual to be the legally binding equivalent of that individual's handwritten signature.

References

- 21 CFR Part 11
- 21 CFR Part 210, 211
- FDA Guidelines on General Principles of Process Validation, May 1987
- Guide to Validation of Automated Systems in Pharmaceutical Manufacturing, April, 1998
- ANSI/ISA-S88.01-1995