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Tablet Press Automation: A Modular Approach to Fully Integrated Production

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ABSTRACT

Fully automated tablet production is an exciting and emerging trend in the pharmaceutical industry. Improved tablet quality, manufacturing efficiency, and process validation are major reasons for the increasing emphasis on automated technology. This paper outlines the vast options and possibilities associated with tablet press automation and presents a specific modular approach in which the extent and time frame for the automation transition is dictated by the tablet manufacturer. This modular approach uses the tablet press control system as the central building block on which a variety of control modules are constructed to facilitate automated material flow, data collection, and remote process monitoring. The emphasis is placed on design flexibility due to the fact that each company will construct a unique definition of automation, which may be subject to change as various phases of automation are implemented and evaluated.

The single most important attribute of an automated compression system is design flexibility in both the tablet press, and more importantly, the control system. The specific methods for material handling, process control, and quality control are as diverse as the products themselves. There is no automated compression system that is appropriate for every production situation. Each production area has a preexisting system in place and it is the task of the vendor to provide an automated design that emulates this system in an automated fashion. For these reasons, it is critical that an automated tablet press be equipped with a control system that can be modified and customized to support the specific requirements of a particular production situation. Further, an automated compression system must have the inherent flexibility to be changed and improved over time as production procedures are modified to accommodate new products or an additional level of automation in the compression process, or in those processes that precede or follow tablet compression.

The tablet press control system must provide the central building block of an automated design. It should serve as the central processing unit that monitors and regulates each module of the automated compression system. The control system must be formatted in such a way that it can readily communicate with a central plant computer to facilitate remote monitoring, collection, and control of all critical process parameters.

TABLET PRESS CONTROL

It is critical that an automated compression system be constructed around a machine that has an extremely well-designed control system. Even the most elaborate automated support equipment cannot guarantee consistent, superior quality tablet production. The control theory and feedback loop algorithms must be carefully scrutinized to determine if they are appropriate to support long-term unattended operation. There are several key aspects of the tablet press control system that must be examined:

1. In-process tablet weight control
2. Long-term control of weight, thickness, and hardness
3. On-line quality control: single-tablet rejection

In-Process Tablet Weight Control

In general, it is the mechanical design of the tablet press, and the specific flow and compression characteristics of the product, that will determine the performance of the in-process tablet weight control. Even the most sophisticated control system cannot correct for tablet weight variations caused by mechanical problems with the machine. Poor tool tolerances, and improper tool travel through the filling cam or dosing cam, can result in tablet weight variation that cannot be offset with electronic controls. To a very large extent, the process capability of the machine, that is, the tablet weight variation at any given time, is a function of the mechanical design, and will not be greatly impacted by the specific algorithm or quality of the control system. It is the function of the control system to keep the process centered, to ensure that the process capability limits remain within acceptable specification limits for the product.

The most important control algorithm in the automated compression system is that of in-process tablet weight control. Because it is not practical to measure the weight of each tablet, a secondary parameter, usually pressing force, is used as the principal control parameter. The press force control system is based on the general theory that with a constant tablet thickness, the pressing force for each tablet will be indicative of the tablet weight. This theory also assumes that the tool tolerances are consistent, that the mechanical speeds of the press and feeder are constant, and that the material quality is completely consistent from tablet to tablet. These assumptions are, of course, not 100% valid, but in general, press force control is an effective means of monitoring and controlling tablet weight.

In a force control algorithm, the compression force of each individual tablet is monitored continuously and the average force is periodically compared with a preset band or a specific force control setpoint. Based on the average compression force over a number of die table revolutions, a slight correction (usually in 0.01 mm increments) is made to the dosing cam to control the level of die fill. There are two basic press force control algorithms: the comparator control system and PID control system.

In a comparator press force control system, the average press force is allowed to vary within preset upper and lower limits. When a deviation from this "good" band is detected, a correction is made (via the dosing cam) to bring the average force back within acceptable limits. The comparator control system utilizes correction steps of a constant magnitude and calculates the number of steps required to return to the acceptable control band. This type of system is the most widely used press force control system, but there are several limitations. The range of press force between the upper and lower adjust limits translates to an acceptable force variation—without dosing cam correction. If this band of acceptable variation is reduced in an effort to minimize the variation, it is possible that the constant step-size correction will exceed the range of the band and result in a control algorithm that is not stable. A general overview of the comparator press force control system is shown in Figure 1.

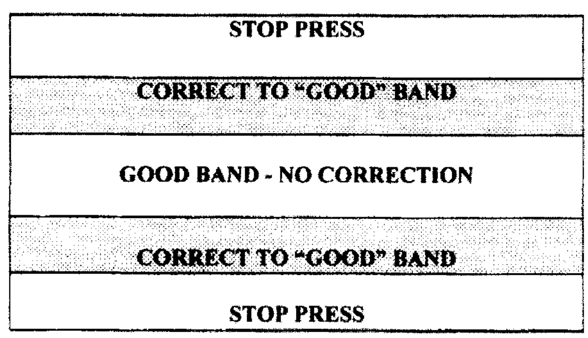

Figure 1. Comparator press force control system.

In a PID (proportional-integral-derivative) press force control system, a press force setpoint is established that corresponds to a specific tablet weight. The average press force (for each die table revolution) is calculated and compared to the average press force setpoint. Based on the magnitude of the error, the PID algorithm computes the size of each step and the number of steps to return the press force to the desired setpoint. The PID algorithm eliminates the variation inherent to a two-point comparator control system. A properly tuned PID loop should result in tighter press force control. The limitation to a PID control system is the complexity associated with the calculation, and hence, the algorithm requires extremely high-speed electronic processing and response, which is not typically available in standard controllers and microprocessors. A general overview of the PID press force control system is illustrated in Figure 2.

A key factor in real-time tablet weight control is that of effective and consistent die fill. The mechanical design of the feeder is very important, and the control algorithm for feeder speed must be designed to permit the feed rate to be synchronized with the speed of the die table. In some cases, the standard deviation of the individual press force peaks can be evaluated as a measurement of fill consistency and the feeder may be adjusted to reach a minimal value of press force deviation. This minimum deviation in punch force translates to optimal die fill and a minimum deviation in individual tablet weights.

On-Line Quality Control: Single-Tablet Rejection

It is critical for any on-line tablet weight control system to have the capability to reject individual tablets determined to be out of specification. In some cases, tablet presses are interfaced directly with packaging equipment and there is no intermediate step for off-line

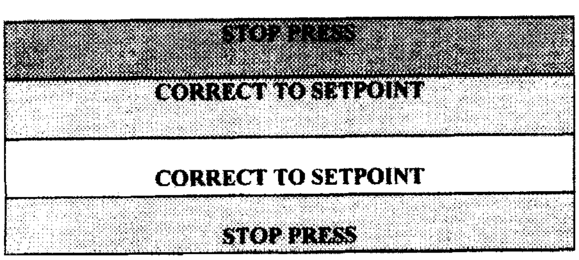

Figure 2. PID press force control system

quality control inspection. This application requires a tablet press that can reliably detect and reject individual tablets that are out of specification. In this case, it is the individual press force that indicates whether there is excessive or insufficient filling of the die, thus resulting in a press force value that is out of present limits. There are several commonly employed methods to reject an individual tablet, as explained below.

Mechanical "Fast Gate"

With a mechanical "fast gate," the tablet stream is interrupted by a mechanical gate that deflects tablets into a bad channel in the discharge chute. A timer is utilized that triggers the fast gate after the high or low punch force is detected at the main compression station. In most cases, the fast-gate technology will reject more than one tablet, due to the mechanical reaction time of the rejection device. This is especially the case at higher press speeds. These systems can usually provide some indication of the punch number that caused the rejection, but the identity of the rejected tablet is not maintained after rejection. In some cases, the fast-gate technology requires that the system be recalibrated each time there is a significant adjustment of press speed.

High-Pressure Air

With a pneumatic system, high-pressure (90 psi) air is used to deflect tablets from the good stream to the bad channel in the discharge chute. Typically, a very high-speed solenoid is utilized to ensure that the "blowing time" can be reduced to the point that only one tablet is rejected at a time. In this system, the mechanical displacement between the compression station and the blow-off point is precisely calibrated, and a dedicated control circuit is utilized to calculate the specific delay time after the bad tablet has been produced. Since the system is calibrated to a fixed displacement, the calculation of the blow time is adjusted automatically to compensate for speed changes in the machine. In this way, the system need only be calibrated one time. The pneumatic system can ensure that one—and only one—tablet is rejected at even the highest pressing speeds, thus maintaining the identity of the tablet after rejection. This system can document the specific punch station that produced the bad tablet and will indicate the specific pressing force that triggered the rejection. This type of single-tablet rejection system has been validated successfully at 8,000–10,000 tablets per minute.

These types of systems can also be useful to diagnose problems related to tool tolerances or tool face conditions. Press stations that consistently cause rejected tablets may be identified and inspected to ensure a proper working length and suitable face condition. In some cases, picking and sticking may be detected with an increased compression force, which can be corrected.

Long-Term Control of Weight, Thickness, and Hardness

When a press force control system is utilized, there is an assumption made that the correlation between press force and tablet weight is essentially constant over time. In many applications, this is not the case. Changes over time in the granulation (i.e., bulk density) require that the press force setpoint be periodically adjusted to maintain the desired tablet weight. In essence, the system must periodically verify the press force–tablet weight correlation and make the appropriate correction to ensure that the process remains centered around the desired tablet weight setpoint. In most tablet production operations, a manual measurement of average tablet weight is made periodically by the operator and the press force setpoint is adjusted if the measured value exceeds preset limits. An automated weight verification system will sample random tablets, calculate the average tablet weight, and correct the force control setpoint to maintain the desired tablet weight. In an automated weight verification system, the control algorithm should be flexible to accommodate the specific requirements of the production operation.

It is very important to note that the various control algorithms may require variations in the tablet sampling capability. Sample format (single tablets vs. ten-weights), sample size, and sampling interval should be flexible to permit the use of specific control algorithms. In addition, the tablet sampling system should be capable of random sampling to ensure statistical relevance and "intelligent" sampling, in which individual tablets are sampled from specified punches to support correlation of force-weight data, and to identify tooling problems (i.e., tolerances, surface defects) at specific punch stations.

Similar feedback control algorithms are possible for the parameters of tablet thickness and hardness. In most cases, however, very tight weight control maintained at a constant tablet thickness will result in minimal variations in tablet hardness. It is critical, in any case, that tablet thickness and hardness be monitored periodically to detect variations in granulation quality and to assure compliance with the specified product parameters.

TABLET PRESS DIAGNOSTIC MONITORING SYSTEM

An automated tablet press control system must be equipped with an extensive internal fault monitoring and indication system to ensure the reliability of unattended operation. All subsystems of the press and related peripheral equipment must be considered for potential faults, and in a fully unattended operation, more fault diagnostics must be added to monitor conditions that would otherwise be readily observed by the operator. A general list of associated diagnostic points is provided in Table 1.

Though not intended as a complete list, these items highlight the diverse requirements for internal fault recognition. In addition to sensing the fault, it is desirable for the system to provide diagnostic information that recommends appropriate corrective action. It is possible to integrate the fault detection system with an expert system that will recognize the fault and provide on-line diagnostic support. The expert system prompts the user through a series of questions to ascertain the symptoms or circumstances associated with a particular problem. Based on the user's answers to these questions, the system engages a method of rational, deductive reasoning to decide which course of action should be initiated to arrive at a specific diagnosis or remedy.

The fault detection system should be equipped with the capability to store and retrieve fault history. This information is extremely valuable as efforts are made to evaluate production efficiency or uptime. Historical data from the fault indication system can be used to identify the major cause of lost production time and can serve as the basis for projects aimed toward productivity improvement.

MODULAR COMPONENTS OF THE AUTOMATED SYSTEM

The tablet press control system must be able to support a variety of modular components to permit fully integrated and automated production. These modules each provide some additional information or an additional level of automation to the basic control system. It is essential that the control system be designed with flexibility to accept each module so that the system can

Table 1

Automated Tablet Press: Fault Diagnostics

Lack of compressed air	Tablet weight out of range
Press window or panel open	Tablet thickness out of range
Lower material level warning	Tablet hardness out of range
Low material level stop	Tablet sampling system fault
Flow problem in hopper	Blockage in tablet discharge chute
Feeder blocked	Output container indexing fault
Tablet sticking to upper punch	Deduster unit fault
Punch breakage	Stop by metal detector
Lower punch tight	Stop by tablet counter
Upper punch tight	Main press motor overload
Dosing cam limit	Lubrication pump fault
Precompression force overload	Lubrication pump low level
Main compression force overload	Compression zone temperature
Average press force out of range	Compression zone humidity
Excessive single-tablet rejection	Lack of dust extraction pressure
Fuse blown	Intentional/manual stop

evolve as the transition toward complete automation is implemented. A fully automated and integrated compression system may be equipped with the following control modules:

1. Automatic product setup
2. Automated quality control sampling
3. Material handling interface
4. Monitoring of compression environment
5. Packaging equipment interface

Automatic Product Setup

An automated tablet press should be equipped with an automatic product setup capability. This system minimizes the time required for product setup and serves as permanent documentation of press control and product-specific parameters. If possible, direct access to the setup parameters should be limited via password protection to those authorized to modify production standards. An effective product parameter database will specify equipment control setpoints, initial force control parameters, sampling parameters, and product specifications.

Automated Quality Control Sampling

In addition to the sampling necessary for tablet weight verification and control, tablets must be periodically sampled for the purpose of in-process quality control. A quality control sampling system should permit flexibility of the following parameters:

1. Sample size (number of tablets per sample)
2. Sample interval (number of samples per batch)
3. Source of sample (by punch number or at random)

The ability to select the punch number of sampled tablets provides an important troubleshooting tool for the detection of tolerance problems associated with specific punches. If a punch repeatedly produces a tablet that is rejected, the system should be capable of identifying the suspect punch (normally from a report generated from the single-tablet sorting system). Once the suspect punch is identified, the quality control sampling system can be programmed to isolate that station and provide a statistical assessment of the tablets produced by that punch. This system provides an efficient method of identifying problem punches, verifying the problem through direct tablet measurement, and removing a bad punch from the press. Even in the instance where tablets are sampled on a random basis, the knowledge of the punch station and the press force that produces the specific tablet can be very valuable as correlations are established between the pressing force and the parameters of the tablet weight, thickness, and hardness.

The quality control sampling system must have the ability to perform a statistical analysis of the data and must provide an appropriate report. Data can also be transferred via the in-house network directly to the quality control laboratory for documentation and correlation with the other results from friability and disintegration testing. If tablet samples are to be collected, an indexing collection system should permit samples to be stored so that they may be analyzed after batch production is complete. In more elaborate systems, it may be desirable to transport sampled tablets from the compression room for in-process quality control analysis.

Material Handling Interface

A fully automated compression system must interface with material handling equipment for both the incoming granulation and the outgoing tablets. Due to the fact that many different systems are possible, it is critical that the press control system have the flexibility to communicate with, and in some cases control, the flow of material to and from the press.

Overhead Feeding Systems

It is possible to equip an overhead feed system with level sensors or load cells that indicate the quantity of material awaiting compression. Low-level sensors on the material hopper can initiate a manual or automatic process to load the next overhead feed container. It is also possible to detect when a batch is in transition, that is, when a new batch is entering the system. When a batch transition takes place, the control system will trigger a tuning phase in which the sample frequency is increased and the control parameters for the new batch are established. With the increased sample frequency, variations in the upcoming batch are detected sooner, and the appropriate adjustments are made to maintain specified product parameters. After a preset transition cycle during which the new batch has achieved a steady state, the sampling interval is reset and the normal control algorithm is invoked. It is also possible to install a bar code reader on the overhead tote that could be integrated to the press start permissive string to ensure that the correct product has been loaded before the press can be released for production.

Tablet Collection Systems

It is possible to set the output container size, in number of tablets (specific to each product as part of the automatic product setup), in order to control the transfer of tablets from the press to the output containers. Circular carousels or straight-through conveyor systems can be controlled to permit continuous tablet production. The tablet press control system should be flexible enough to interface with the indexing collection system selected by the customer. In addition to the output that will trigger the collection system to index, the press control system should be integrated to receive feedback that the collection system is powered on and no fault exists with the system, and a positive confirmation that an indexing cycle has been completed and the next tote is ready to accept the tablets.

Monitoring of Compression Environment

In those production operations in which environmental control is important, the automated system must be equipped to monitor critical parameters and to stop tablet production if the environmental conditions exceed preset limits. It is possible to install sensors in the compression zone of the press to monitor temperature, humidity, and dust extraction pressure. The temperature and humidity can simply be monitored, or can be used as control parameters with feedback directly to the control unit, or indirectly through the distributed control system. The dust extraction pressure (differential pressure of sensors mounted within the press zone and outside the press) can be monitored and used as a control parameter for a closed-loop system in which a damper in the dust extraction duct is adjusted to maintain a constant extraction pressure. This ensures that fluctuations in the main extraction pressure (which depends on the number of machines operating and the required CFM of each machine) do not impact the steady-state operation of the automated press. Isolating the press and maintaining a constant, optimal (for each product) dust extraction pressure will prevent excessive dust buildup associated with insufficient extraction and costly material loss associated with excessive extraction pressure.

To supplement long-term record keeping, it may be advisable to integrate these environmental parameters to a central data acquisition system in order to document the conditions for each production batch. These data can be archived with the batch record file (weight, thickness, hardness, etc.) for future retrieval if the particular batch is brought into question at any time after the product is distributed.

Packaging Equipment Interface

In some production situations, it is advantageous to integrate the tablet press directly to the packaging equipment to permit a continuous, flow-through process. This type of system, again, highlights the importance of the flexibility of the tablet press control system. It is unlikely that the press vendor will dictate the type of packaging equipment to be used. In most cases, a system module must be designed that is customized to communicate with existing packaging equipment. The packaging control module should be configured such that the tablet press drives the packaging system as a function of the press output. The press control system must be made aware of all faults in the packaging line and a proper algorithm must be designed to slow the press speed (while maintaining tablet specifications) or stop the press depending on the nature of the fault. The packaging line fault can then be integrated into the overall downtime reporting system of the production control analysis module for a realistic assessment of the operational efficiency of the integrated process. When a fault is cleared, a proper algorithm must be designed to restart the press or increase the press speed to resume normal production. Similarly, the packaging control module must be designed to control the response of the packaging line. In essence, a custom interface must be developed to link the two systems such that they operate as a single integrated machine.

SUPERVISORY CONTROL AND DATA ACQUISITION

The most critical aspect of tablet press automation is centralizing and acquiring information through a distributed control system or central plant computer. The flexibility of the control system must permit the development of a communication protocol that links the tablet press control system with the existing, or specified, central control system. The result can be a central, remote station in which all tablet production is monitored and controlled, from which all required resources to support tablet production are deployed, when and where they are needed. The basic components of an integrated system are as follows:

1. Central monitoring and control
2. Data acquisition
3. Batch reporting and file management

Central Monitoring and Control

It is critical that the tablet press vendor provide a system that can interface to the central plant computer, and even more important, provide a protocol of communication that can be understood and fully supported in-house by the user. A "black box" interface protocol is unacceptable for a number of reasons, primarily from the perspective of troubleshooting and validation. Most manufacturers of distributed control systems have developed a standard protocol intended for communications with external equipment. It is the responsibility of the tablet press manufacturer to understand the protocol and to configure an interface module that readily communicates with the central control system.

In addition to the link between the tablet press and the centralized control system, it is certainly advisable to integrate the off-line quality control laboratory to permit data entry of off-line QC analysis. Tablet dissolution, tablet friability, and tablet assay analysis are several examples of data that should be included in the final batch report.

Data Acquisition: Process Parameters

In order to generate a comprehensive batch report, the following process parameters should be collected over the course of production:

1. Tablet parameters
   - Tablet weight
   - Tablet thickness
   - Tablet hardness
   - Tablet dissolution (off-line from QC lab)
   - Tablet friability (off-line from QC lab)
   - Tablet assay analysis (off-line from QC lab)
2. Machine parameters
   - Precompression force
   - Main compression force
   - Press speed
   - Feeder speed
3. Other process parameters
   - Temperature
   - Humidity
   - Dust extraction rate

For a more detailed characterization of the compression process, it may be advisable to instrument a production press to permit periodic evaluation of the following press parameters:

1. Main compression force
2. Precompression force
3. Tablet ejection force
4. Tablet scrape-off force

Once these parameters are established for each product, limits can be established that will detect if the product is deviating from any expected process parameters.

The extent of this deviation may be used to evaluate the batch-to-batch variation inherent in the granulation. Collection of these data over time can be used to assist in the evaluation of steps that are taken to reduce this variation.

Data Acquisition: Production Efficiency Analysis

A completely automated compression system should have the capability of monitoring and reporting on the production efficiency or uptime, and the causes for machine downtime. The internal fault indication system can be integrated with a real time clock that tracks production uptime (and calculates average output rates) and records the downtime associated with each fault as it occurs. The production control module can be programmed to require a coded entry that denotes the reason for the press stoppage prior to permitting the press to begin or continue production. Code numbers for product setup, changeover, and maintenance can be entered by appropriate personnel who will track the downtime associated with the service of the machine. It is possible to track the daily performance of the press, and then integrate the data to generate monthly or quarterly reports. In this way, improvement projects can be monitored and the actual impact on production downtime assessed. A report for the production efficiency can then be easily generated (Figure 3).

It is also possible to use the information from the press internal fault indication system to evaluate the major cause of press stoppage, and to take appropriate action, based on this information, to correct the problem. For instance, the Pareto diagram in Figure 4 shows excessive press stoppage due to upper punch tightness. A potential solution to this problem is less important than the fact that the problem was brought to light by correlating the historical data on what is causing the press to stop. Without this system, someone would have to keep a manual record of the number of press stops due to each point of internal fault monitoring.

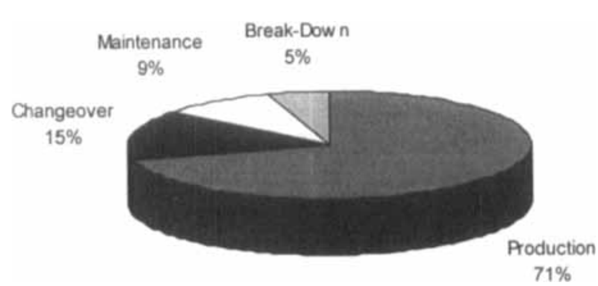

Figure 3. Production efficiency analysis.

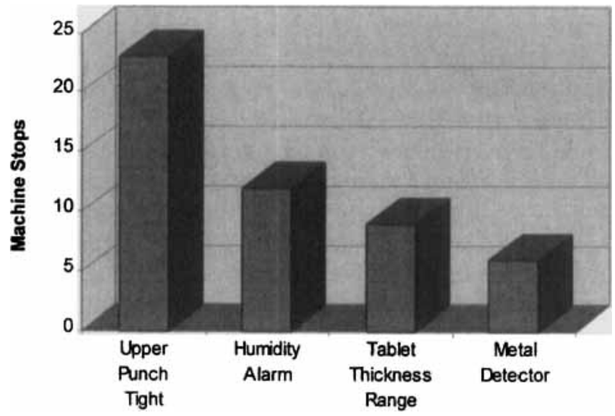

Figure 4. Press stop frequency analysis.

Batch Reporting and File Management

A centralized plant computer system provides the opportunity for extensive data collection of production batch data. For each production batch, it is possible to store all critical parameters, from batch start through batch completion, in a file that can be catalogued and stored appropriately. Each file should contain the complete history of each batch, including tablet parameters, applicable machine parameters, and other process parameters that are deemed to be important (i.e., humidity—for an effervescent tablet production).

These records are extremely valuable for two primary uses. First, a detailed production history can be acquired and maintained for each batch until this product is distributed and consumed. This provides a level of security in which any questions of quality can be met with an exact record of the specific production batch.

Second, these files can be used in-house, to derive a detailed understanding of the production parameters for each product. In this way, standard parameters can be generated to permit earlier detection and measurement of production variability. These records can also be correlated to establish standard efficiencies (uptimes) and to isolate specific problems that are major contributors to production downtime.

CONCLUSION

It is apparent that tablet press automation is being considered more seriously now than ever before. The modular approach provides a flexible automation design that permits the tablet manufacturer to dictate the extent and the time frame in which the automation is implemented. The modular design permits gradual integration of automated techniques that provide time to adapt, understand, and derive confidence in the automation, after each phase is implemented. For those companies that prefer a more rapid transition to fully automated "lights out" production, the modular approach also provides the opportunity to modify a specific module as production methods are improved or altered—without impacting the other modules, or the functions of the system as a whole.

It is important to understand that automation is not so much a new technology, but a combination of existing technologies. Automated production techniques are utilized extensively in other industries. The automation of tablet production equipment and the integration of tablet production information to a centralized control system is a natural, if not overdue, progression in the pharmaceutical industry.