

COURTOY MODUL™ Technology: setting the new standards for productivity, flexibility and safety in tableting operations.



Photo 1: the MODUL™ tablet press

Five years ago, Belgian tablet press manufacturer Courtoy nv, a company of the Niro Pharma Systems Division of the Germany-based GEA Group, introduced its revolutionary MODUL™ S tablet press concept to the market. In 2005, Courtoy continued its success story with a double-sided version of the machine, the MODUL™ D. With a new innovation - the MODUL™ P – having recently been introduced, the following overview of Courtoy's MODUL™ technology is perfectly timed.

The MODUL™ is based on the unique ECM concept (patented), whereby the isolated Exchangeable Compression Module is removed from the machine in a contained way in a matter of minutes.

The contaminated but fully contained ECM is then placed on a dedicated trolley and transferred to a separate washing area for OFF-LINE opening, cleaning and format change-over. As the machine itself does not require any cleaning after removal of the ECM, the MODUL™ tablet press can be changed over from one format to another in

as short a time as 30 minutes when using two ECMs. This leads to a significant reduction in the total product change-over time of the tableting line, resulting in an important increase in productivity.

PRODUCTIVITY

Since 2002, numerous existing and new Courtoy customers have installed MODUL™ machines in their tableting operations, attaining increased productivity and reduced cost per unit produced. To demonstrate the production gains, Courtoy has developed a simulation tool, which predicts to what extent the installation of one or more MODUL™ tablet presses will increase the productivity of an existing tableting operation. The simulation tool takes into account the customer's specific production pattern (number of products, batch size, campaign size, etc.), as well as the existing machinery.

For the calculation of the productivity increase to be accurate, a correct estimation of the change-over time of the entire tableting line is required. Therefore, it is of great importance to consider not only the tablet press itself, but also the upstream and downstream equipment.

With regard to the upstream powder feeding system to the MODUL™ tablet press, Courtoy's position is very clear. A closed powder feeding system is essential to avoid dust contamination of the top of the machine. Dust lying on the machine will eventually move inward, making it necessary to clean the inside, which should obviously be avoided. Such closed powder feeding systems are based on IBC technology, whereby the IBC is brought above the tablet press using a hoist (refer to photo 2) or the IBC is connected to the press inlet via a discharge station on the floor above (refer to diagram 1).



Photo 2: MODUL™ tablet press with powder IBC

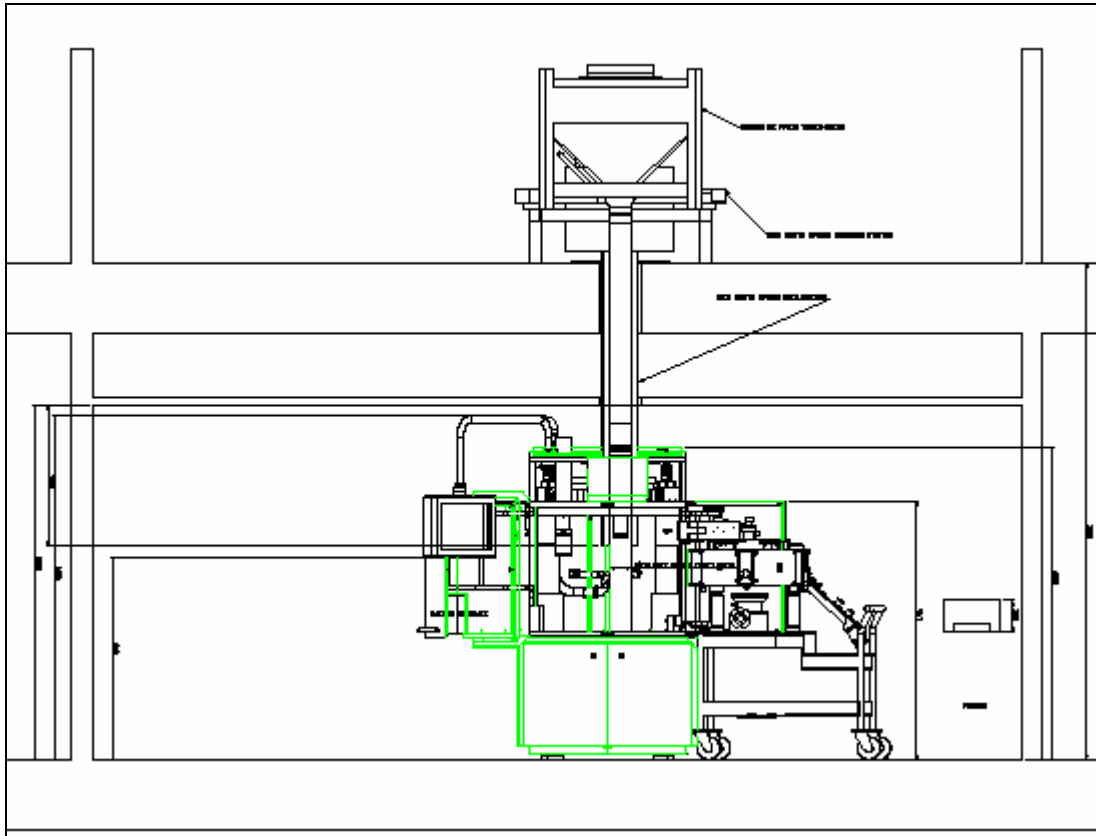


Diagram 1: MODUL fed from discharge station on floor above

In both cases a dust-tight connection to the press powder inlet is easily achieved with either lay-flat LDPE tubing or split butterfly valves. Niro Pharma Systems offers contained material handling systems through its company Buck Systems Ltd.

With regard to downstream equipment, Courtoy distinguishes between 3 possibilities:

1. Standard downstream tablet handling equipment with open interconnections.

In this case, standard-design tablet dedusters, metal detectors and/or tablet diverter systems are used in combination with open tablet recipients and the interconnections between the units are open. This will inevitably result in dust becoming airborne in the room, thus requiring the room to be cleaned at each product change-over. As a result, the product change-over time for the entire tablet production line is shorter than in case of a conventional tablet press, but still a large amount of time is spent on cleaning the tablet press room.

2. Standard equipment is used, but in a separate small clean room.



Photo 3: MODUL™ tablet press in contamination free room, with downstream equipment and tablet recipients in separate room

This “through the wall” (TTW) concept calls for separate clean rooms. These can be created easily by installing a thin separation wall in an existing clean room. The MODUL™ tablet press is installed in one room, while the downstream equipment and tablet recipient(s) are installed in another. The tablet chute of the tablet press goes through the separation wall into the peripheral equipment. Thanks to the ECM concept, the closed powder feeding and contained tablet transition to the other room, the room containing the MODUL™ does not need any cleaning, as no dust is released into this room. Room cleaning is now limited to the second, much smaller room, further reducing the change-over time of the tableting line.

3. Contained or “dust-tight” downstream equipment is used.

When all peripherals and their interconnections are dust-tight, no powder or dust can escape from the entire tablet production line. Such an installation eliminates the need to clean the GMP room and could in time even make the clean room redundant. The latter would mean a significant reduction in facility investment cost. The change-over time is further reduced compared to the TTW installation, increasing the productivity of the tablet production line. Ultimately, when the peripheral equipment is duplicated in the same way as the ECM of the MODUL™, ALL cleaning operations during product change-over are eliminated: the GMP room itself does not need any cleaning while all contaminated pieces of equipment are simply replaced by clean units, set up off-line. All removed equipment is cleaned off-line in a washing bay.



Photo 4: MODUL™ tablet press with contained peripherals

Of all proposed solutions, the last one demands the highest investment, but its unique benefit is a change-over time of less than 2 hours for the total production line, depending on local SOPs in use. No other tablet press concept available on the market today is up to this challenge and no other press has such extremely high productivity figures.

CONTAINMENT

Without doubt, the MODUL™ tablet press with its ECM concept will continue to impress tablet manufacturers with its extraordinary capacity to increase productivity. But the ECM concept also delivers enhanced operator and environment safety.

Newly developed APIs are ever more potent and pose a potential threat to the operators and maintenance technicians working on the tablet presses.

Several concepts have become available to tablet such potent drugs, such as the integration of isolators onto a standard tablet press and tablet presses with wash-in-place capability. Unfortunately, each of these concepts presents some major flaws.

The first concept, a tablet press with isolators, does indeed offer the highest possible level of isolation. Courtoy has supplied such a machine to one of its customers for development purposes. Measurements and analyses have indicated that the containment level is indeed extremely high. On the downside, cleaning, format change-over and maintenance are very difficult and time-consuming, due to the constraints of the isolators and glove port access.



Photo 5: Courtoy R190HC: high-containment tablet press based on traditional isolator technology

Therefore, there can be no doubt that such isolators or glove box concepts are only economically justifiable for formulation development purposes, where the toxicity level of the products to be handled in the very near future is unclear, or for mono-product production lines. The concept is not practical and cost-effective for production with regular product change-overs.

The second technique, the wash-in-place or clean-in-place approach, involves an automatic washing of the inside of the tablet press compression zone.

The obvious drawbacks of the WIP/CIP principle include (1) long downtimes, due to the complete washing and drying cycle taking place on the machine itself, and (2) the considerable risk of water mixed with product leaking into the electromechanical section of the machine, raising serious safety and decontamination concerns.

HC-ECM

To get around the above limitations of WIP/CIP machines, Courtoy developed the HC-ECM with WOL capability. The HC or 'High-Containment' ECM has been developed as a 'high-containment' alternative to the standard 'contained' C-ECM. The C-ECM containment level typically reaches down to 10 µg/m³, while the HC-ECM is designed to attain 1 µg/m³ and even 0,1 µg/m³ (exact containment level depends on product and process characteristics). The HC-ECM differs from the C-ECM mainly with regard to the sealing methods and a differential pressure sensor, which continuously monitors its containment level.



Photo 6: HC-ECM with WOL capability



Photo 7: WOL skid

The HC-ECM can be equipped with WOL or 'wash-off-line' capability, which means that special water-jet heads can be introduced into the HC-ECM (in a fully contained way) to allow for automatic washing of its inside. The actual washing cycle is performed in a separate washing area, where the HC-ECM – resting on its trolley – is connected to a purpose-designed WOL-water-prep-skid. During the automatic washing cycle, the turret of the ECM, including the tooling, is made to rotate and the paddle-wheels of the powder feeder are activated. This meticulously designed procedure ensures an optimal washing of the inside of the HC-ECM-WOL. The purpose of the WOL washing cycle is to:

- 1) knock down all airborne particles in the compression zone.
- 2) wash away as much product as possible, depending on solubility of the product.
- 3) wet all powder residues inside the ECM to eliminate any risk of particles becoming airborne.

After the automatic WOL-cycle is completed, the operator opens the ECM and performs final cleaning and drying manually with limited or even no personnel-protective equipment. This procedure is accepted for potent APIs below a certain OEL (Occupational Exposure Limit), as is the case for most containment applications today. The WOL ECM concept is practical, allows for a fast and flexible product change and offers just the right protection, without reverting to extremes. In case of concerns about cross-contamination, a product-dedicated ECM can be considered.

The obvious benefits of the OFF-LINE washing concept compared to wash or clean-in-place are the much shorter machine down-time when two ECMs are used and the elimination of machine contamination risk in case of leaking seals, as explained above.

THE MODUL™ D FOR BI-LAYER TABLETTING

With the introduction of the MODUL™ D in 2005, Courtoy extended the range of its unique MODUL™ technology. The MODUL™ D is the double-sided twin of the MODUL™ S and can be used for both single-layer/double-output and double-layer/single-output tableting. The change-over between single-layer and bi-layer mode takes less than 30 minutes.

The MODUL™ D is capable of producing both single-layer and double-layer tablets with the same ECM. Bi-layer tableting on the MODUL™ D requires only a limited optional set of specific parts (cam tracks, extraction nozzles and feeder base plate) and is based on the same weight control and compression technology as the well-known Courtoy R292F bi-layer tablet press. More details on Courtoy bi-layer tableting technology are available in a specific technical publication, downloadable from the library on our website (“Bi-Layer Tablets – Why Special Technology is Required”).



Photo 8: the Courtoy MODUL™ D

THE MODUL™ P FOR SMALL PRODUCTION VOLUMES

The MODUL™ P, the latest addition to the MODUL™ family, has been developed especially for formulation development, clinical trial production and small scale production. It will be available as of early 2007.

The MODUL™ P can be supplied with a "mixed" turret, which is combination of B and D tooling stations. This feature is particularly useful for formulation development purposes, as it saves the cost of having to buy two die tables. Another highly valuable option is the data acquisition and analysis system, which accurately records the various compression forces and punch movements for subsequent data processing, analysis and graphical representation.

Like the MODUL™ S and the MODUL™ D, the MODUL™ P can be supplied with a variety of ECMs: the standard C-ECM, the HC-ECM and the WOL-ECM.

A brand-new feature that will be available on the MODUL™ P is *Constant Density Tableting* (patent pending). Besides main compression to constant thickness, which is applied on all other tablet presses, the MODUL™ P will also have the ability to apply main compression to a constant compression force. This constant compression force is set up by the operator as a product recipe parameter and is exerted on the tablet using the unique Courtoy air compensator system. Compression to constant compression force has two advantages:

- 1) a constant final compression force results in a more constant tablet hardness and thus a more constant tablet dissolution time. This will in turn lead to a more constant bio-availability of the drug in the human body.
- 2) when the air compensator works at constant compression force, the compression time exerted by it on every tablet is much longer. This extended dwell time at final compression will allow the compression of formulations presenting very plastic behaviour (i.e. consolidation is very time dependent) at much higher machine speeds.



Photo 9: The Courtoy MODUL™ P

DUAL CONTROL FOR IMPROVED TABLET QUALITY

In addition to broadening the MODUL™ ECM range, Courtoy has developed and introduced an enhanced tablet production control algorithm, which is now available as an option on the Multi-Control 4 system for MODUL™ presses.

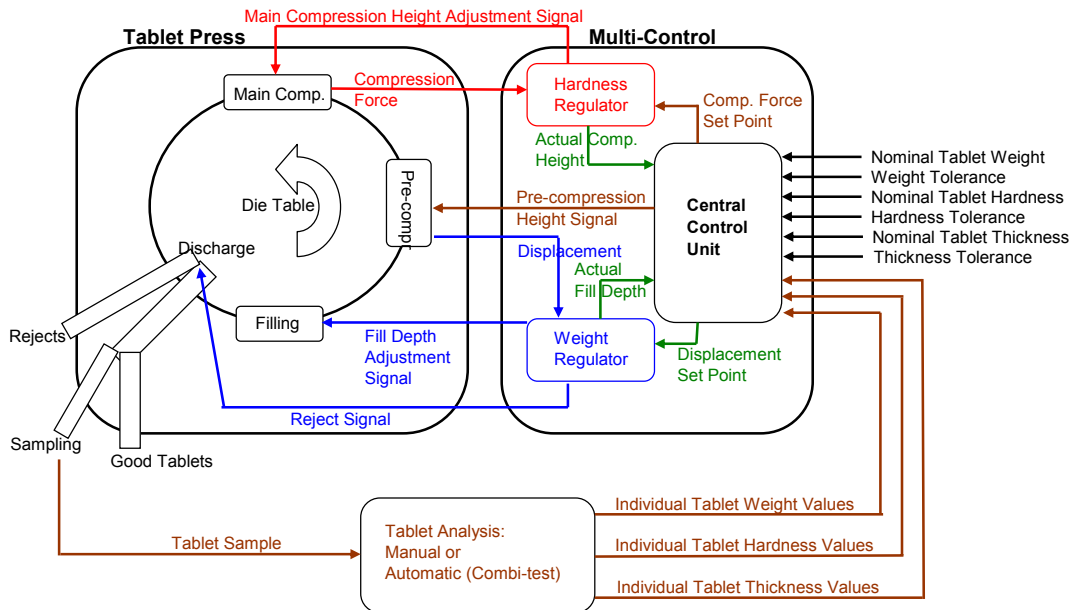


Diagram 2: dual weight/hardness control system

The Dual Control system is based on two simultaneous and continuous control loops, functioning totally independently from one another. The first loop monitors and controls tablet weight, while the second loop monitors and controls tablet hardness. Both control loops can be re-corrected on-line either manually by the operator or automatically when using an automatic tablet tester (only for weight control loop).

The Dual Control system fits perfectly in the current PAT (Process Analytical Technology) trend, aiming to better understand and control the process in order to improve and guarantee tablet quality. The combination of the extreme flexibility of the MODUL™ ECM concept and the Dual Control PAT, allowing for real time release of production batches, will make Just-in-Time production possible for the pharmaceutical industry in the near future.

More details on the Dual Control system are available in a specific technical publication, which can be downloaded from the library on our website (“Dual Weight and Hardness Control for Improved Tablet Quality”).

Courtoy – True Innovator in Tablet Compression Technology