Case Study – Sanico, Belgium

1. Introduction

Towards the end of 2008, Courtoy and Sanico started a close collaboration to evaluate and fine-tune Courtoy's latest compression technology, which is available on the PERFORMA™ P and the MODUL™ P, in real-life daily tablet production. To this end, a PERFORMA™ P was installed in Sanico's tablet production department, which produces ca. 5 billion tablets per year.

Sanico is a privately owned pharmaceutical third-party manufacturing company, employing approximately 250 people, situated in Turnhout, Belgium. Sanico offers the full range of non-sterile galenic forms for (non-) pharmaceutical products and clinical trials, taking care of all aspects of the production process: analysis, development, validation, stability testing etc. To read more about the company and the services it offers, we invite you to visit their website at www.sanico.eu.


Sanico, Turnhout

For tablet compression, Sanico uses a large number of rotary tablet presses, supplied by a well-known European manufacturer other than Courtoy. These machines are conventional tablet presses in the sense that tablet weight control is based on compression force measurement and the machines do not have extended dwell time capability. The MODUL™ P and the PERFORMA™ P, on the other hand, allow for both equal thickness (ETC) and equal force compression (EFC), and consequently offer the feature of extended and freely adjustable dwell time at pre-compression and main compression. We refer to Courtoy's publication "Ultimate Process Flexibility and Robustness" for a detailed technical description of these ground-breaking compression methods. The only way to extend the dwell time on a conventional machine is reducing the rotation speed of the turret, which will inevitably lead to a lower machine output.

The purpose of the collaboration between Sanico and Courtoy was mainly to investigate and qualify (and, whenever possible, to quantify) the advantages of Courtoy's innovative compression modes, in comparison with conventional tablet presses. The conventional type of tablet press described above is referred to as "Press Q" in the remainder of this article. The presses of this type used by Sanico are medium scale machines with 24 to 47 punch stations, depending on the exact configuration.

During a six-month period, over 20 different formulations were tested on the PERFORMA™ P and its performance in terms of machine speed and tablet quality was compared to that of the conventional presses. The results were quite sensational, as can be seen in the following overview.

2. Survey of production runs on the PERFORMA™ P

2.1 Difficult formulations on conventional presses

Ibuprofen - 400 mg

Formulation:	ibuprofen 80%; starch 10%
Process:	wet granulation with starch in fluid bed (top spray)
Press Q:	dry granulation step required prior to compression; maximum speed 50.000 tab/h.
PERFORMA™ P:	compression mode 3 – equal porosity tableting
	Compression possible without dry granulation; maximum speed 90.000 tab/h – nearly 2 x faster.

Paracetamol - 500 mg

Formulation:	paracetamol 77%; starch
Process:	wet granulation with starch in high shear mixer – drying in fluid bed
Press Q:	dry granulation step and addition of purified water in external phase required prior to compression; maximum speed 25.000 tab/h.
PERFORMA™ P:	compression mode 3 – equal porosity tableting
	Blend compressible without dry granulation or external water addition; maximum speed 110.000 tab/h – more than 4 x faster.

Formulation A - 5 mg and 10 mg

Formulation:	API 3%; lactose 80 75%; avicel 18%
Process:	dry blend
Press Q:	not faster than 100.000 tab/h due to risk of capping and sticking. Problems occur during packing. Maximum hardness 70 N, decreases significantly during stability testing.
PERFORMA™ P:	compression mode 3 – equal porosity tableting
	Problem free compression at 200.000 tab/h – 2 x faster. Hardness 100 N. No capping or sticking detected. Hardness does not decrease during stability testing.

Formulation B - 40 mg and 80 mg

Formulation:	API 20%; tablettose 80 40%; avicel 35%; starch
Process:	dry blend
Press Q:	problems (capping) occur during coating, due to inconsistent tablet compression quality.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Problem free compression at 150.000 tab/h. No problems detected at coating stage.

Formulation C

Formulation:	API 55%; lactose 200; starch
Process:	wet granulation with povidone in conical screw mixer
Press Q:	hardness too low; maximum speed achieved 45.000 tab/h.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Harder tablets produced at 175.000 tab/h – nearly 4 x faster.

Formulation D

Formulation:	disulfiram 71%; lactose 200; starch
Process:	wet granulation with starch in high shear mixer / drying in fluid bed
Press Q:	maximum speed limited to 50.000 tab/h to prevent capping.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Problem free compression at 150.000 tab/h – 3 x faster. Higher speed may be possible, but was not tested due to batch size.

Formulation E

Formulation:	API 70%; lactose 200; starch
Process:	wet granulation with starch in high shear mixer / drying in fluid bed
Press Q:	dry granulation step and addition of purified water in external phase required prior to compression; maximum speed 50.000 tab/h.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Blend can be compressed without dry granulation or external water addition; speed 120.000 tab/h – more than 2 x faster.

Formulation F - 1 mg and 2 mg

Formulation:	API 1%; lactose 200 81%; starch 13%
Process:	lactose is moistened with solution of active ingredient in chloroform
Press Q:	tablets are too soft; friability is too high. Dry granulation step required prior to compression.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Compression possible without dry granulation step.

2.2 Formulations not presenting compression problems on conventional presses

Formulation G - 2,5 mg

Formulation:	API 1%; lactose 200 88%; starch 1500 10%
Process:	lactose is coloured with aqueous solution and dried / active ingredient added dry
Press Q:	problem free. Slight sticking, but acceptable.
PERFORMA™ P:	compression mode 3 – equal porosity tableting
	Problem free, without sticking.

Formulation H - 1 mg

Formulation:	API 1%; lactose 80 44%; acivel 25%; starch 1500 20%
Process:	dry blend
Press Q:	problem free. Speed 120.000 tab/h.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time
	Problem free up to speed 150.000 tab/h – 25% faster.

Formulation I

Formulation:	API 20%; mannitol 70%
Process:	wet granulation with gelatin in high shear mixer / drying in tray dryer
Press Q:	problem free. Speed 85.000 tab/h.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time Problem free. Speed 140.000 tab/h – nearly 70% faster.

Ibuprofen - 400 mg

Formulation:	ibuprofen 67%; klucel 2,5%; avicel 11%
Process:	wet granulation with water in high shear mixer / drying in fluid bed
Press Q:	problem free. Occasionally, slight sticking is observed (acceptable).
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time Problem free.

Formulation J

Formulation:	dimenhydrinate 35%; lactose 200 42%; starch 15%
Process:	wet granulation with povidone in water in high shear mixer / drying in tray dryer
Press Q:	problem free.
PERFORMA™ P:	compression mode 1 – default Courtoy mode: compression with extended dwell time Problem free.

3. Conclusion

The main difference between any conventional type tablet press and the Courtoy PERFORMA™ P and MODUL™ P tablet presses is the extended dwell time at pre-compression and main compression, along with the ability to freely adjust this dwell time independently of machine speed.

Extensive comparative production runs with multiple formulations under real production conditions have turned up amazing results for quite a few formulations, known as “difficult” formulations for conventional tablet presses.

The results observed can be summarized as follows:

- The additional dry granulation step required to enable compression of several formulations on the conventional machines is no longer required to achieve the desired tablet quality (thanks to the extended dwell time).
- Machine speeds of two to four times the speed of conventional machines can be reached.
- In some cases, an important increase in tablet hardness is achieved. In many cases, the occurrence of capping is observed to decrease significantly or disappear completely.

The above process improvements enable substantial savings in production cost and a sizable reduction in product lead time.

For non-problematic formulations also, Courtoy’s innovative compression technology is able to make a considerable difference: speed increases from 25% to 70% have been achieved for these formulations.

The introduction of the PERFORMA™ P with Courtoy’s novel compression technology at Sanico has proved very successful, as it has enabled the company to increase their productivity and tablet quality significantly, as well as reducing product lead times.

Feel free to contact Sanico to inquire about the wide range of contract manufacturing & clinical trial services they are able to offer, or to learn more about their experience with the PERFORMA™ P.

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Please contact Courtoy to find out more about our unique compression technology or to perform product trials in our test facilities.

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