

PHARMACEUTICAL ENGINEERING

How to Tackle the Cartridges

Bayer HealthCare is offering the first-ever oral contraceptive for a flexible control of menstruation. The experts at Bayer Technology Services charged with developing the production concept for the complex packaging of this product had to be flexible as well.

Never before have I had to enter so much uncharted territory.” And Jürgen Evers is by no means a newcomer in his profession. He has already worked at Bayer Technology Services for more than 15 years. During this time the project manager has been involved in the construction of several production facilities. However, this project, focusing on the new application of an oral contraceptive, was definitely something special – and not only because it was “unchartered territory”. “Never before have so many specifications been changed during the course of a project,” Evers added.

Project Management & Engineering, Healthcare is the title on his business card. This basically means the German engineer designs and builds facilities in which pharmaceutical products are manufactured in compliance with the strict regulations of Good Manufacturing Practice (GMP). And this is exactly the field he studied. “Pharmaceutical

The 120-tablet regimen allotted per cycle is packaged in cartridges containing 30 pills each. The users place the individual cartridges in a digital dispenser called a Clyk, which “smartly” assists her with the usage. The Clyk sounds a daily alarm to remind the user to take the pill. Should the user nevertheless forget the tablet, the dispenser will inform her what to do. And if the woman decides she wants to have a period, all she has to do is stop taking the tablets.

The principle may sound simple, but the challenge was to develop a complex packaging line for the many processing steps and components. The dispensing cartridges, in particular, caused some headaches. Due to the sensitive active ingredients and the other contents, the tablets – and therefore also the cartridges – must be protected against oxygen and humidity. Only a hermetically sealed pack can ensure the efficacy and shelf-life of the product in all climate zones.

Blister packs were found to be perfectly suitable, and of course they are not unusual in pharmaceutical applications. And yet there was nevertheless a problem. At the lower end,



“In terms of time plan, costs and quality on target or better – that is rare.”

Dr. Hans-Joachim Raubach, Site Management Berlin, Bayer HealthCare

Technology” was the name of his special course of studies at the Albstadt-Sigmaringen University of Applied Sciences in Southwestern Germany.

Consequently, Evers already knows a lot about production facilities in which, for example, tablets with sensitive ingredients have to be packaged. However, this case did not simply involve tablets. The element Evers most closely associates with this particular project is a special cartridge, which is namely the core aspect of the entire process when it comes to the packaging concept.

The springboard was an innovative administration regimen that Bayer HealthCare planned for one of its well-established oral contraceptives. The new version of this product carries the added description “Flex”, because it gives women the flexibility to go up to 120 days without getting their period, if they choose not to do so.

where a special mechanism allows the dispensing of each individual tablet, the packs are just under two centimeters thick. “Until now there hasn’t been a single product with these proportions that is blistered for pharmaceutical requirements,” explains Evers. A drawing depth of two centimeters had always been considered too much.

At first the team favored a pouch system, by which the cartridges are packed in sealed bags. However, a risk evaluation showed that the absolutely essential air tightness of the bags could not be sufficiently guaranteed at the high production speeds required for series manufacturing. As a result, the team decided instead to seek the advice of leading manufacturers of blister machines. Within three months a plausible and functioning packaging concept was developed with two producers. Eventually, an agreement was reached with one of them, and the work began.



Soon to be found in many handbags? The Clyk dispenser (left) for flexible periods.

The solution is a double-chamber blister. “Each of two foils is extended over half of the required depth,” says Evers. A cavity of just under two centimeters is formed after bonding the two halves together. The cartridge fits perfectly into this space, and the blister can be sealed. It is a real innovation!

However, this development only resolved one of the many challenges. Changes in the product details also kept Project Manager Evers busy. Plans for the packaging line were in full swing, when, for example, the dimensions of the cartridge were modified once again. For Evers’s team it was roughly as if they were supposed to plan a house, although the designated living space was changed on a daily basis.

“The cartridges had to be placed onto a conveyor belt mechanically, filled with the tablets, weighed, placed in collapsible boxes and then finally packed in cartons,” says Evers, listing only some of the processing steps that had to be adjusted to the new dimensions of the cartridge. So, each and every modification had consequences for the respective function in the packaging line.

Another challenge was printing on the cartridges, which was also new territory because of the curved surface. Here too adjustments were necessary up to the final stages of the project because major label elements were only specified by the authorities as part of the registration process.

By completion, Evers and his project team had developed and implemented a packaging line some 250 meters in length, which involves assembling the various individual components of the Clyk and the cartridges, handling, filling and blistering as well as packing the final product in cartons and palletizing them. This kind of packaging line is absolutely unique worldwide. “It is designed to manage 250 blisters per minute,” Evers adds. This means 7,500 tablets are processed every minute.

Bayer HealthCare divided the various production steps between two sites. The cartridges and the Clyk dispensers roll off the production line of a subcontractor, whereas the actual filling and packaging take place at Bayer HealthCare’s Supply Center Berlin. Dr. Hans-Joachim Raubach, Site Management Berlin, is clearly impressed by the results: “In terms of the time schedule, costs and quality, you have been on target or even better. That happens only rarely, especially considering the many technical innovations and constant modifications – literally up to the last minute.”

The project was a fulltime job for Jürgen Evers for three years. He has long since moved on to the next construction project, but he did feel proud when women in Australia obtained the very first product packaged at the Supply Center Berlin in late 2012. During 2013 the product will become available in pharmacies of some EU countries as well. ■