CASE STUDY

Working the Problem - How to Resolve Sticking Issues in Tablet Production

In this case study, a prediction model is used in conjunction with an examination of a tablet profile to resolve sticking issues.

Novartis, is a company providing innovative healthcare solutions that address the evolving needs of patients and societies. Head-quartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines, over-the-counter and animal health products.

The Problem

The Italian division of Novartis approached I Holland and local agent Vis Viva with a sticking issue on an anti-epileptic drug in the form of a coated tablet.

FIGURE 1: Sticking & picking halted production

Novartis reported a strong sticking/picking problem causing the press to be stopped several times during manufacture for cleaning and maintenance of the punches, which resulted in production downtime.

These two problems can be caused by various factors related to the physiochemical properties of the formulation components, the surface characteristics of punch face, as well as factors related to the machinery and the environment, for example. Compression force and speed, temperature and humidity.

Tablet sticking is one of the most common problems in tablet manufacture. This build-up of granule on the punch tip face causes tablet press downtime and reduced tablet output. It has a negative effect on tablet appearance and often results in the removal of tablet tooling from production for regular cleaning and maintenance, as experienced by Novartis.

Picking was another problem encountered by the company - this is when compressed granule that has adhered to the detail on the punch face, results in 'picking out' of parts from the tablet face.

Understanding problems that can occur during manufacture will ultimately result in higher yields, less waste and money saving implications. To achieve this, it is important to understand the product being made and how it interacts with the tooling used during the production process.

The Trial

Novartis had previously looked at the coating being used on the tooling to overcome the sticking/picking problem. Pro-actively seeking a solution, the company tried several different coatings including HC (Hard Chromium), CrN (Chromium Nitride) and TN (Titanium Nitride). With unsatisfactory results from these initial trials, Novartis Italy contacted I Holland for expert advice and analysis of the problem with the support of local agents Vis Viva.

Sample tools were examined, with the tablet design and tool material selection and coating studied. I Holland used its TSAR≈Predict (Tabletting Science Anti Stick Research) model. With sticking and picking being such a universally significant problem in the pharmaceutical industry, I Holland invested in a two-year research programme to develop a predictive model that could be used to reduce downtime and ultimately costs. The model comprises data on a range of parameters including surface chemistry, temperature, humidity, size of the granule, and whether it is elastic or plastic for example, to provide fast guidance to the tablet producer. This reduces the need to carry out expensive in the-field testing which is time consuming and requires the tablet manufacturer to take time out of tablet production to run trials with coated punches.

As well as using the predictive model, the tablet profile was examined. The type of profile required is influenced by several factors; the granule, embossing requirements, coating process, packaging and the company's branding. If the design is to be heavily embossed with a lot of characters it is important to avoid tablet profiles with a deep cup, such as the ball or pill. Deep cup profiles can cause a softer core in the tablet which can in turn lead to sticking. It will also reduce the available space for the embossing itself; the use of a profile that is shallower, with a reduced cup depth, will allow for a larger embossing area.

The Solution

The tablet design, including the embossing, was examined and new and improved designs were created which included anti-picking features. Together with results from the TSAR≈Predict model, which selected the use of I Holland's PharmaCote CN+ (Chromium Nitride Plus) surface engineered anti-stick coating, new upper and lower punches were provided and implemented in production.

The selected anti-stick coating was used on the punches and applied to the tooling by using an electron beam process. This is one of the smoothest and most defect free methods of applying a PVD coating as it does not create droplets during the atomisation process. The atomic particles

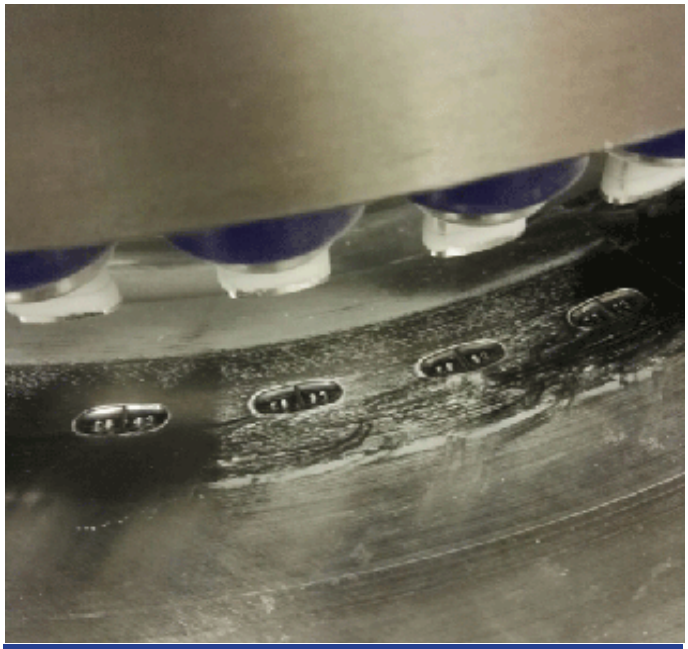

FIGURE 2: The removal of the tablet tooling from production for regular cleaning & maintenance was required due to the problem of sticking.

are attracted to the tooling leaving an even surface which is far less susceptible to breakaway defects.

From the first trial of the new design and tooling using PharmaCote CN+, improvements were seen and all sticking/picking issues were instantly resolved resulting in a 25% increase in production. This was achieved over a five-day working week, with reduced hours, resulting in a full day's production time saved.

Before the implementation of the new tablet design and tool coating, four batches of the tablet were produced during a 6-day working week. This included the extra time required for cleaning and maintenance due to the original sticking/picking problem. Once I Holland's improvements were adopted, a further batch was produced in the same time-period with a total of five batches manufactured without the need to stop production.

As a result of this outcome, Novartis is now looking at further products to be analysed to improve production and reduce downtime.

The Conclusion

I Holland's understanding of years of tabletting science has proven that when coatings are developed correctly, and their beneficial characteristics are matched to those of the formulation, they can help to prevent sticky formulations adhering to the punch tip faces. I Holland has deployed many advanced techniques to help improve the performance of its coatings. As a result, it has a proven range of anti-stick solutions based on that research. TSAR≈Predict gives a predicted particle adhesion force against each of the PharmaCote anti-stick coatings in I Holland's range.

To improve tablet production efficiency, it is imperative to implement an effective tooling specification. To find the correct design for the product being produced, consultation with an expert tablet designer should take place in the early stages of the process. The design should not only be unique and visually appealing, but also robust and producible in a rigorous tablet manufacturing environment. By making just a few simple changes to a design it can stop future problems.

By adopting new science-based innovations, like those from I Holland, and investing in research and development, Novartis is pro-actively bringing important treatments to patients globally.