ABSTRACT SUMMARY
A high potency mini-tablet is manufactured on a customized Korsch XL100 Pro. The single tip tooling ensures 100% force feedback and single tablet rejects. A vibratory feeder controlled by a Balluff level sensor is equipped with the press to maintain a stable powder level in the feed frame. The vibratory feeder on and off cycles are observed. Less than optimal on/off cycles are often associated with tablet rejects and press shut downs. However, the on/off cycle appears to be influenced by many material attributes and process parameters. The vibratory feeder on/off mechanism is thoroughly understood through this study. And the on/off times can be predictively set to the same optimal ratio to compensate for variations in material attributes for robust tablet manufacturing at the 405,405 tablet scale.

INTRODUCTION
A typical tablet press is equipped with either a force feeder or a gravity feed frame. Force feeders are more common on production presses to allow optimal press performance at high turret speeds with minimal weight variation. Gravity feed frames provide good performance for materials with good flow properties but are typically limited to slow turret speeds. On the other hand, gravity feed frames do not agitate the blend and impart no energy. Therefore, they offer advantages for blends where material segregation, overmixing, or grinding is of concern. For example, Multiple Unit Pellet System (MUPS) final blends should be compressed with a gravity feed frame to prevent abrasion or grinding of pellets.

A high potency 7.4mg 3mm round mini-tablet is manufactured on a customized Korsch XL100 Pro. Multi-tip tooling is not an option because each mini-tablet is a unit dose. 100% force feedback and single tablet rejects are preferred. 10 Stations with single tip B tooling configuration was selected for the 3kg or 405,405 tablet initial commercial launch scale.

Although the press is typically run at high speed, 60-70rpm, the powder consumption rate (theoretically 4.44-5.18g/min) is too low for a force feeder due to the small tablet weight, 7.4mg. Overmixing is likely with a paddle feeder. On the other hand, the final blend exhibits good flowability. It typically flows through a 4 to 6 mm orifice plate when tested on a Flodex. A gravity feed frame is feasible. However, the small tablet weight is very sensitive to feed frame powder level. By gravitational force alone, a stable powder level cannot be maintained in the feed frame to produce satisfactory mini-tabs.

The hopper-gravity feed frame configuration was modified to insert a vibrator controlled trough between the hopper and the feed frame (shown in Figure 1). And a Balluff level sensor is fitted in the feed frame, which switches the vibrator unit on and off to maintain a stable powder level in the feed frame. However, less than optimal on/off cycles are often associated with undesired tablet rejects and press shut downs. This study thoroughly investigates the vibratory feeder on/off mechanism to develop a robust process to consistently manufacture <1% weight variation mini-tabs at the 405,405 tablet scale.

EXPERIMENTAL METHODS
A 3kg placebo formulation consisting of mannitol, dicalcium phosphate anhydrous, hypromellose, croscarmellose sodium and pigment was wet granulated and subsequently lubricated with stearic acid and magnesium stearate.

The placebo final blend was compressed into 0.85mm thickness 7.4mg 3mm round mini-tablets on a 10 station Korsch XL100 Pro at 60rpm turret speed under force control (Target: ~1800N; M Set: ±150N; S Set: ±200N). The vibratory feeder intensity was set at 35%, 30%, 25%, 20%, 17% and 15%. The press ran for 15 min at each intensity. The feeder on/off times, level sensor amplifier voltage output, and press shut downs were recorded. 30 random tablets were tested for individual weight at each intensity.

In a separate study, the vibratory feeder was manually turned on, and the powder dropped from the vibrator controlled trough was collected for 1 min at each of the 35%, 30%, 25%, 20%, 17% and 15% intensities. The powder delivery rate (g/min) was calculated at each feeder intensity. The powder delivery rate for different granulation DOE lots and different lots of the same formulation was evaluated.

In separate studies, the design space for the fill cam, the level sensor position and sensitivity, the recirculation gate position, the vacuum pressure, the Kramer deduster and the Lock metal detector settings was established.

RESULTS AND DISCUSSION
The level sensor amplifier voltage output, the feeder on/off times, the individual tablet weight variation, and the press shut downs at 35-15% intensities were shown in Table 1. One “low mean force” press shut down was experienced at the 35% intensity. At the 15% intensity, the feed frame gradually ran out of powder, and the press shut down for “feeder empty” and “low mean force” constantly. Therefore, the 15 min compression could not be completed at the 15% feeder intensity.

The feeder on/off cycle appears to be influenced by many material attributes and process parameters. A mass
balance analysis unravels the determining factor behind the feeder on/off times, which is the powder delivery rate. 

**Powder consumption rate**

\[ \text{Powder consumption rate} = 0.0074g \times 10 \text{stations} \times 60 \text{rpm} \\
= 4.44g/min \]

**Powder delivery rate × Feeder on time**

\[ \text{Powder delivery rate} \times \text{Feeder on time} = 4.44g/min \times (\text{Feeder on time} + \text{Feeder off time}) \]

At steady state, the amount of powder delivered to the feed frame when the feeder is on equals the amount of powder consumed during one feeder on/off cycle. Thus, the powder delivery rate can be predicted by the observed feeder on/off times.

**Powder delivery rate**

\[ \text{Powder delivery rate} = \frac{4.44g/min \times \text{Feeder on time} + \text{Feeder off time}}{\text{Feeder on time}} \]

The predicted powder delivery rate by the above formula matched the actual powder delivery rate well as shown in Figure 2. At the 15% feeder intensity, the actual powder delivery rate (3.4g/min) is lower than the powder consumption rate (4.44g/min). Therefore, the feed frame gradually ran out at this condition.

It’s observed that final blends with varying flow properties have different powder delivery rate-feeder intensity profiles. It explains the varying feeder on/off cycles observed with different formulations or even different lots of the same formulation compressed at exactly the same process parameters.

The level sensor amplifier voltage decreases as the powder level increases. The voltage range corresponds to the powder level range in the feed frame. Table 1 shows a longer feeder on time yields a narrower voltage (powder level) range, and as a result, less tablet weight variation. The powder delivery rate can be reduced (lower feeder intensity) to achieve a longer feeder on time. However, if it’s too low and on the edge of failure, the feed frame may run out of powder and cause press shut downs as shown in Table 1, 15% feeder intensity.

Based on the tablet weight RSD results, a powder delivery rate approximately twice as much as the powder consumption rate is recommended to achieve minimal tablet variation. For example, the powder consumption rate at 60rpm on the customized Korsch XL100 Pro is 4.44g/min. ~8.88g/min powder delivery rate is recommended to achieve ~0.5% tablet weight RSD.

**CONCLUSION**

It’s expected that even different lots of the same formulation will have varying flow properties due to normal material and process variations. The same feeder intensity setting is likely to yield varying feeder on/off cycles. Therefore, it’s recommended to fine tune the feeder intensity to achieve approximately equal feeder on and off times, which corresponds to a powder delivery rate twice as much as the powder consumption rate based on the formula. On the customized Korsch XL100 Pro, robust mini-tab manufacturing can be achieved by compensating for variations in material attributes.

Three registration batches of a ~0.3% drug content mini-tab were successfully manufactured at the 3kg or 405,405 tablet scale on the Korsch XL100 Pro with <1% tablet weight RSD and <2% content uniformity RSD. The scale-up to the 26kg or 3,513,514 tablet full commercial scale on a Korsch XL200 WIP is yet to be evaluated.

**REFERENCES**

2. Allenspach, C. Recent Advances in Tablet Compaction Technology. NJPhAST; 2011 Apr 21

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**Table 1 Effect of Feeder Intensity on Feeder On/Off Times and Mini-Tab Weight Variation**

<table>
<thead>
<tr>
<th>Feeder Intensity (%)</th>
<th>Avg Low Voltage (V)</th>
<th>Avg High Voltage (V)</th>
<th>Avg ON Time (s)</th>
<th>Avg OFF Time (s)</th>
<th>Avg Cycle Time (s)</th>
<th>Predicted Powder Delivery Rate (g/min)</th>
<th>Actual Powder Delivery Rate (g/min)</th>
<th>Individual Tab Wt RSD</th>
<th>Stoppages</th>
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<td>5.508</td>
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<td>5.508</td>
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<td>3.4</td>
<td>Constant</td>
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**Figure 1 Vibratory Feeder on a Korsch XL100 Pro**

**Figure 2 Predicted and Actual Powder Delivery Rate**

**of a Vibratory Feeder**