Evaluating the Scalability of Coating Process Parameters for Opadry® 200

Jason Teckoe, Laura Scattergood, Jeffrey Gimbel and Ali Rajabi-Siahboomi

Poster Reprint
AAPS 2013

Purpose

In a previous pilot scale QbD study[1], optimized process parameters and an acceptable operating space were identified for film coating with Opadry® 200, optimized performance coatings. In this work, three sets of coating process parameters identified as being acceptable from the pilot scale work in a 24" diameter coating pan were scaled up to production scale in a 48" diameter coating pan to confirm suitability.

Methods

Three distinct coating conditions determined to be within the acceptable operating space of the previous pilot scale study were used to identify if coating scale had any impact on the critical quality attributes. The relative location of the trials in the acceptable operating space of the pilot scale study are shown as an X in Figure 1 and include an optimized process condition (X^1), a low bed temperature condition (X^2) and a low airflow condition (X^3).

A thermodynamic modeling program (TAAC, Thomas Engineering, IL, USA) was used to identify environmental efficiency factors (EEF) for each coating at pilot scale (Figure 2).

Figure 1. Pilot Scale Acceptable Operating Space

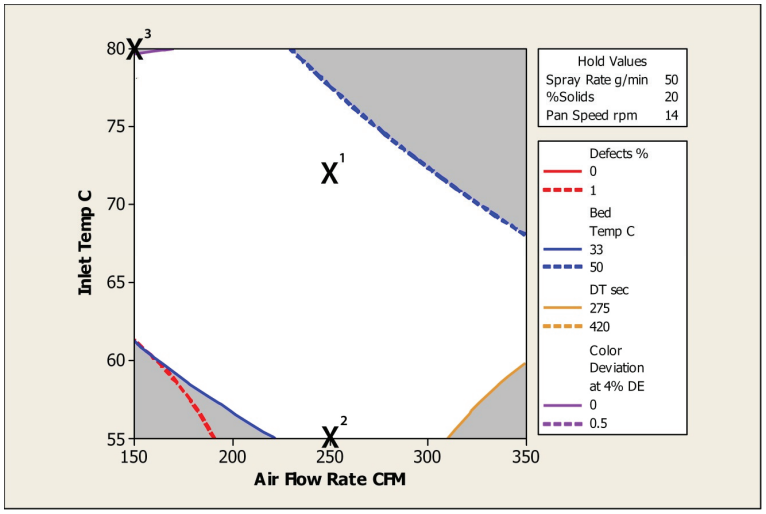
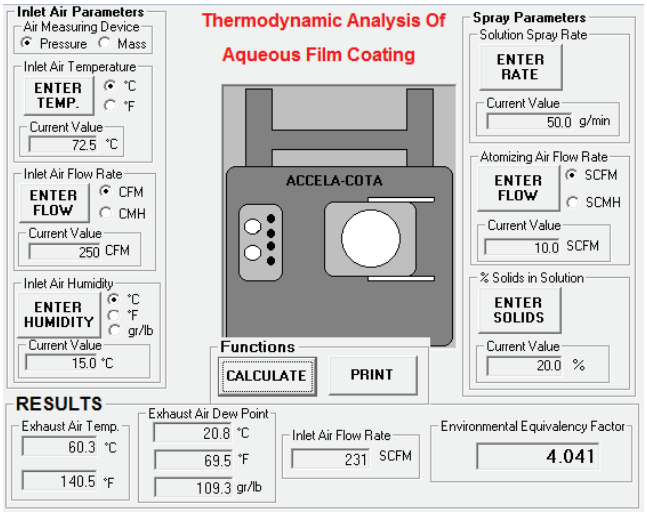


Figure 2. TAAC Program Interface



The EEF is a relative measure of the rate at which water evaporates from the surface of the tablet bed (higher values indicate drier conditions), and is determined based on convective heat and mass transfer calculations.[2] Maintaining a similar EEF value enables equivalent drying conditions to be achieved across multiple pans and coating scales. Tables 1 and 2 indicate the process parameters and the EEF values used for the coating trials at pilot and production scale respectively.

Table 1. Pilot Scale Coating Process Parameters

Trial No.	Spray Rate (g/minute)	Inlet Temp (°C)	Airflow Rate (CFM) / (m^3/hr)	%Solids (%)	Pan Speed (rpm)	Atomizing Airflow rate (SCFM)	Dew point (°C)	Bed Temperature (°C)	EEF
Optimal	50.0	72.5	250 / 425	20	14	10	15	46.5	4.04
Low bed	50.0	55.0	250 / 425	20	14	10	15	34.0	2.73
Low airflow	50.0	80.0	150 / 255	20	14	10	15	43.4	2.82

Table 2. Production Scale Coating Process Parameters

Trial No.	Spray Rate (g/minute)	Inlet Temp (°C)	Airflow Rate (CFM) / (m^3/hr)	%Solids (%)	Pan Speed (rpm)	Atomizing Airflow rate (SCFM)	Dew point (°C)	Bed Temperature (°C)	EEF
Optimal	330	68.0	1750 / 2937	20	7	20	15	45.8	3.80
Low bed	310	51.0	1800 / 3058	20	7	20	15	35.6	2.76
Low airflow	325	76.0	1100 / 1869	20	7	20	15	44.5	2.83

Coating Process

All pilot scale coating trials were conducted in a 24" fully perforated O'Hara Labcoat II coating pan. In each trial, 15 kg of biconvex placebo tablets (10 mm diameter) were coated to a 4% weight gain (WG) with the same lot of a blue Opadry 200 formulation.

All production scale coating trials were conducted in a 48" fully perforated O'Hara Fastcoat coating pan. In each trial, 130 kg of biconvex placebo tablets (10 mm diameter) were coated to a 4% weight gain (WG) with the same lot of a blue Opadry 200 formulation.

The critical quality attributes (CQAs) previously identified in the pilot scale study were coating defects, tablet gloss, color difference, and disintegration time (DT) in purified water. Coated tablets from each production scale trial were visually evaluated and compared to the CQA results from the pilot scale study. Defects, gloss, color difference and disintegration times (DT) in purified water were determined using the following methods.

Defects

At the end of each coating trial, samples were collected and assessed for the percentage of tablets having defects. For the purposes of this evaluation, a defect was defined as any instance where the coating was not contiguous and the tablet core was exposed. The number of defects in a batch was determined by visual observation of 100 tablets and repeated 4 times per trial.

Disintegration Time

Disintegration time was tested following the standard USP method in deionized water at 37°C and the average result determined from 6 tablets per trial. To enable comparison between pilot and production trials, the results have been adjusted to account for differences in the disintegration times of uncoated tablets from different batches.

Color Development and Uniformity

Film coated tablets were sampled during each trial at theoretical 1, 2, 3, and 4% weight gains and tested for color development and uniformity using a reflectance spectrophotometer (Datacolor, NJ, USA).

Tablets with 4% coating weight gain were regarded as the target reference color for each trial, and all other weight gain samples were measured against this to calculate color difference (DE). Twenty tablets were tested from each batch at each theoretical weight gain to determine the color development versus the standard and also color uniformity within the sample.

Gloss

Thirty-nine film coated tablets with a 4% weight gain of Opadry 200 from each trial were analyzed for gloss using a gloss meter (Tricor, IL, USA). Results were reported in gloss units (GU).

Results

Defects

The results for tablet defects observed at both pilot and production scale are shown in Table 3. These trials indicate that even when a wide range of coating parameters and coating scales were employed, the number of defects observed with the Opadry 200 film coating were less than 1%.

Table 3. Coating Defects Observed per Trial

Trial Number	Coating Defects at Pilot Scale (Defects per 400 Tablets)	Coating Defects at Production Scale (Defects per 400 Tablets)
Optimal	0	1
Low Bed Temperature	1	2
Low Air Volume	0	0

Disintegration Time

Tablet disintegration times for the uncoated and coated tablets from each coating trial are shown in Table 4. The disintegration times for tablets coated at different scales and conditions are very consistent after adjustment for the different batches of uncoated placebo tablets.

Table 4. Coated and Uncoated Tablet Disintegration Times per Trial

Disintegration Time	Optimal	Low Bed Temperature	Low Air Volume
Pilot Scale			
Uncoated placebo tablets (seconds)	200		
Disintegration Time (seconds)	288	282	288
Adjusted Disintegration time (seconds)	88	82	88
Production Scale			
Uncoated Placebo Tablets (seconds)	58		
Disintegration Time (seconds)	149	143	138
Adjusted Disintegration time (seconds)	91	85	80

Color Development and Uniformity

Color development and color consistency throughout the batch provide a visible indication of quality and uniformity of the applied coating. At 4% weight gain, all coating trials gave excellent color uniformity. Figures 3 and 4 show the tablet color development data for the pilot and production scale coating trials, represented as color difference (DE) versus the reference at 4% weight gain and color uniformity between tablets in each sample set.

Figure 3. Pilot Scale Color Difference

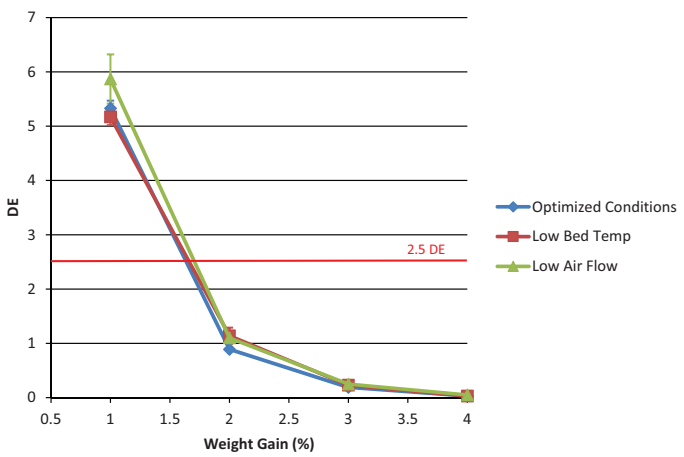
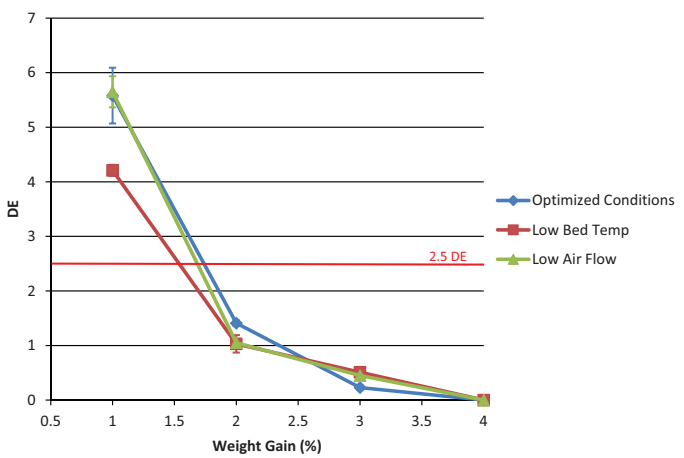


Figure 3. Production Scale Color Difference

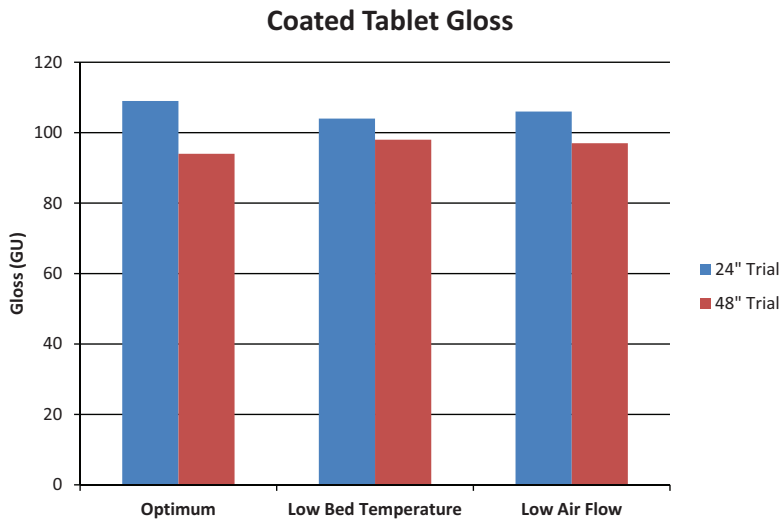


At both pilot and production scale, all samples had a color difference of less than 2.5 DE at a theoretical 2% weight gain, which is not visually discernible. The color uniformity for each sample is indicated by the error bars which show that after 1% weight gain, there is minimal variability in tablet color. At weight gains > 2.5%, the variability was so low that the error bars are hidden by the data markers. The 1% weight gain result for the low bed temperature condition at both pilot and production scale have lower DE values than the other coating conditions and relatively small values for color uniformity. This result may be a consequence of the relatively slow drying conditions employed and the ability for droplets to spread prior to drying, allowing the coating material to transfer between tablets during the coating process.

Gloss

The gloss results (Figure 5) indicate that all coating trials produced tablets with high gloss values. The results are very consistent at each coating scale, but the pilot scale trials led to tablets with slightly higher gloss than those from the production scale trials. Increased gloss levels can typically be achieved with reduced % solids, reduced spray rates, as well as with increased pan speed (increased movement of the tablets). In this case, as the coating formulation and drying conditions are equivalent, it is likely that the small difference in gloss observed can be associated with differences in tablet movement at pilot and production scales.

Figure 5. Tablet Gloss versus Coating Scale



Conclusions

Coating of Opadry 200 has been successfully scaled up through the use of previously identified pilot scale process parameters and a thermodynamic model to determine process parameters that offer equivalent drying conditions at production scale. Coating productivity, color uniformity and very low defect levels were obtained with Opadry 200 even when using a broad range of coating process conditions and coating scales.

References

1. Teckoe J., Mascaro T., Farrell T.P., and Rajabi-Siahboomi A. Process Optimization of a Novel Immediate Release Film Coating System Using QbD Principles, *AAPS PharmSciTech*; Vol. 14 Number 2, Jun 2013.
2. Ebey G.C., A Thermodynamic Model for Aqueous Film Coating. *Pharm Tech*. Vol.4, 1987.

North America **+1-215-699-7733**

Europe/Middle East/Africa **+44-(0)-1322-293000**

Asia Pacific **+65-6438-0318**

Latin America **+54-1-5556-7700**