Evaluation of a High Productivity Coating Formulation in Continuous Coating Processes

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Continuous Coating Processes - Outline

- **Introduction**
  - Batch coating vs. Continuous processes (advantages and disadvantages)
  - Opadry® QX
- **Case study 1. Thomas Engineering Flex ® Continuous Tablet Coater (CTC).**
  - Evaluation of coated tablet uniformity at varying throughput rates.
  - Evaluation of tablet transit times and uniformity of tablet progression
- **Case study 2. GEA ConsiGma™ semi-continuous coater**
  - Process DOE and Raman Spectroscopy
- **Case study 3. Driam DRIACONTI-T® semi-continuous coater.**
  - Evaluation of coated tablet uniformity at varying coating solids concentrations

Coating uniformity dynamics

- 60” scale batch process
  - Weight gain: 1%
  - Solids conc.: 13%
  - Pan load: 350kg
  - Coating time =

$$\frac{350\ kg\ X\ 1\%\ WG}{13\%\ solids\ X\ 0.8kg/min} = 34\ min.$$

  - Add 20 minutes for loading, heating, cooling and unloading for total coating time of <u>54 minutes for 350kg of tablets</u>.

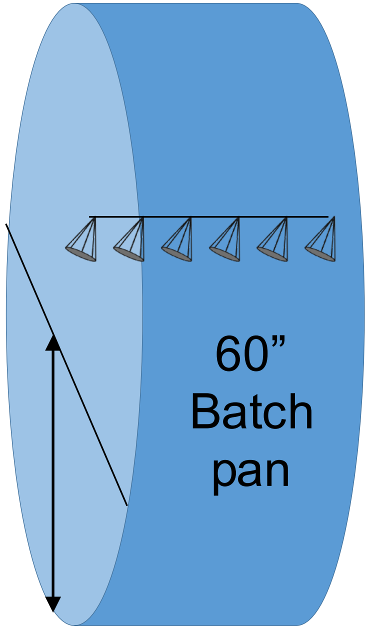
- 24” continuous process
  - Weight gain: 1%
  - Solids conc.: 13%
  - Pan load: 100kg
  - Throughput =

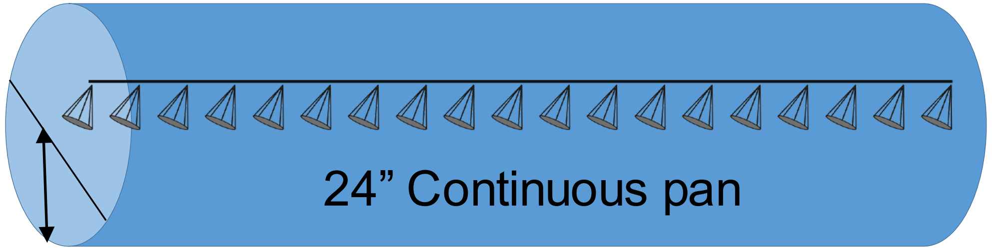
$$\frac{0.8kg/\min\ X\ 13\%\ solids}{1\%\ WG} = 10.4\ kg/min.$$

<u>*= 624 kg hour throughput*</u>

- Loading and unloading process time must still be taken into account but is minimal if coater allowed to run for significant periods.

Coating Uniformity Factors	60" Diameter Batch Pan	24" Diameter Continuous
Spray zone (width X depth)	36” X 3”	100” X 3”
Pan speed (rpm)	5	12
Linear speed of tablets (in/min)	942	905
Number of tablets in spray zone at any given time	1,080	3,000
Number of tablets exposed to spray zone per minute	340,000	905,000
Pan charge (kg)(number of tablets)	350 (875,000)	100 (250,000)
Time between passes (min)	**2.57**	**0.28**
Total number of passes	**13.2**	**35.3**
Solids applied per pass (mg)	0.30	0.11





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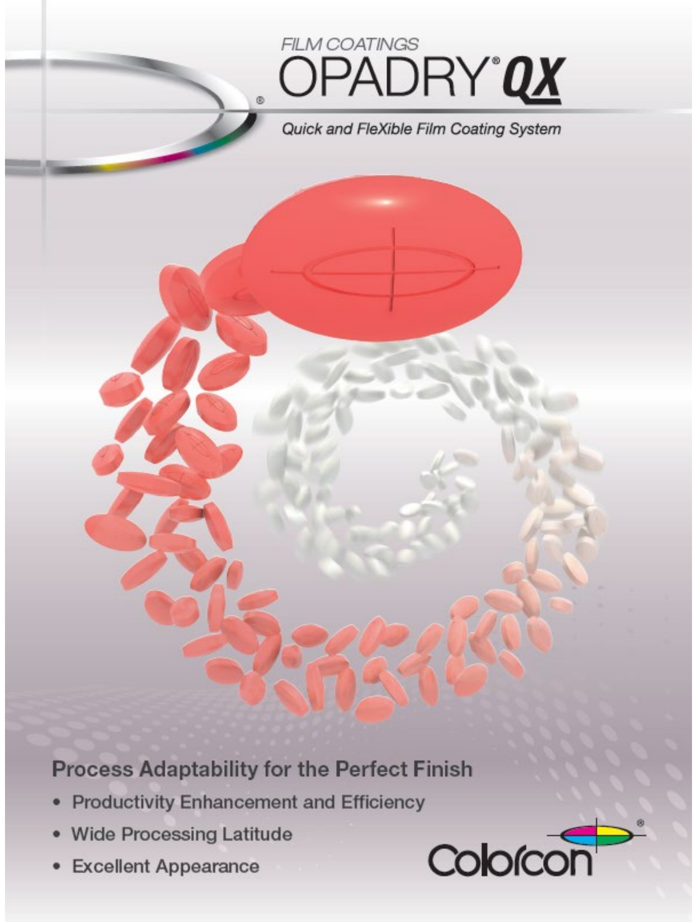
All data from: Mancoff WO, (1998) Film coating compressed tablets in a continuous process. Pharmaceutical Technology 22 (Oct): 12-18

Opadry QX Coating System

Composition based on:	Function
Polymer (mainly PVA-PEG graft co-polymer)	Film former
Pigment	Colorant
Includes talc	Detackifier system



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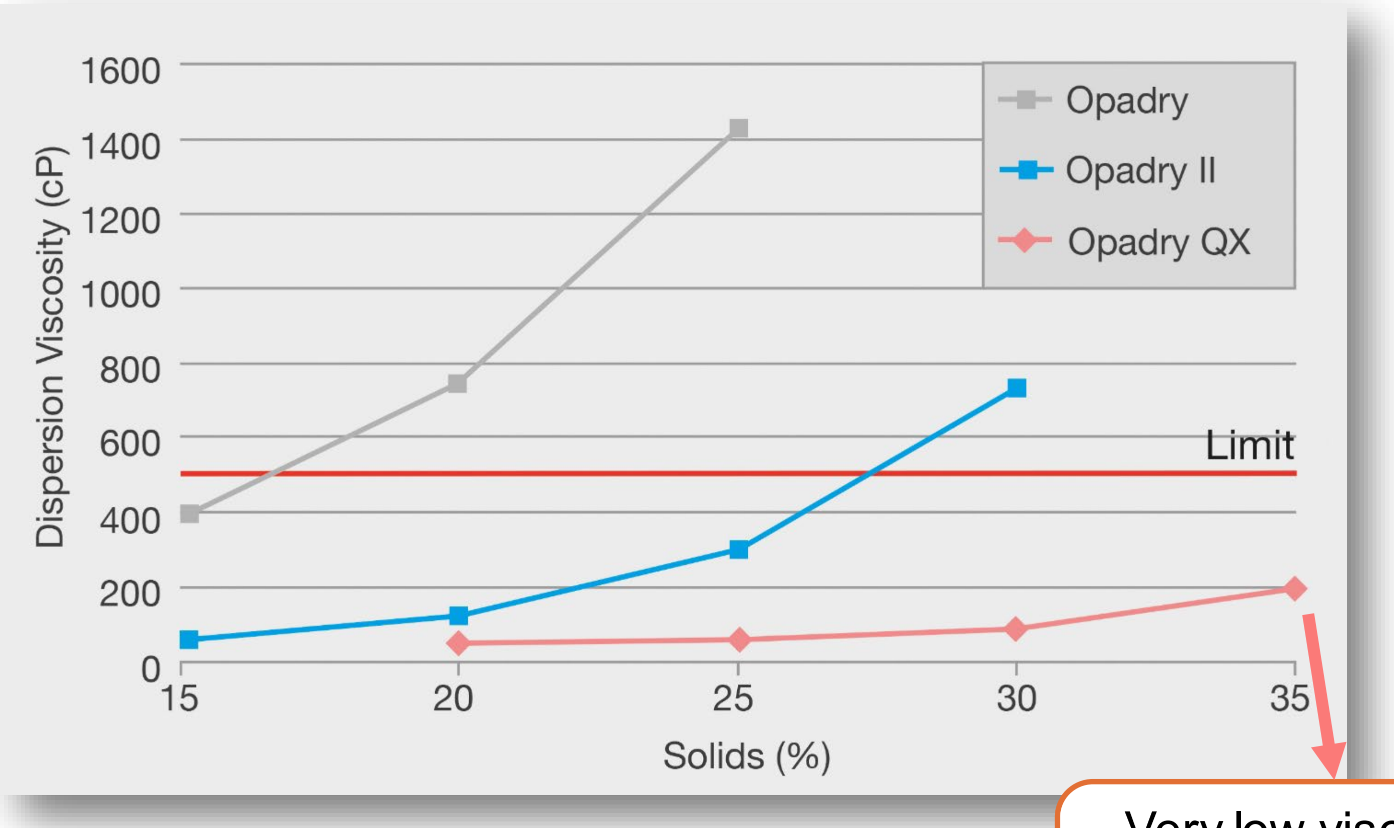
Low Viscosity and High Solids for Process Efficiency



Very low viscosity – even at 35% solids concentration

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Coating uniformity study

Thomas Engineering CTC

Equipment

- Thomas Engineering CTC (Continuous Tablet Coater)
  - 18 individually controlled spray guns on two independent manifolds
  - Pan Dimensions - 24" dia. x 13.3’

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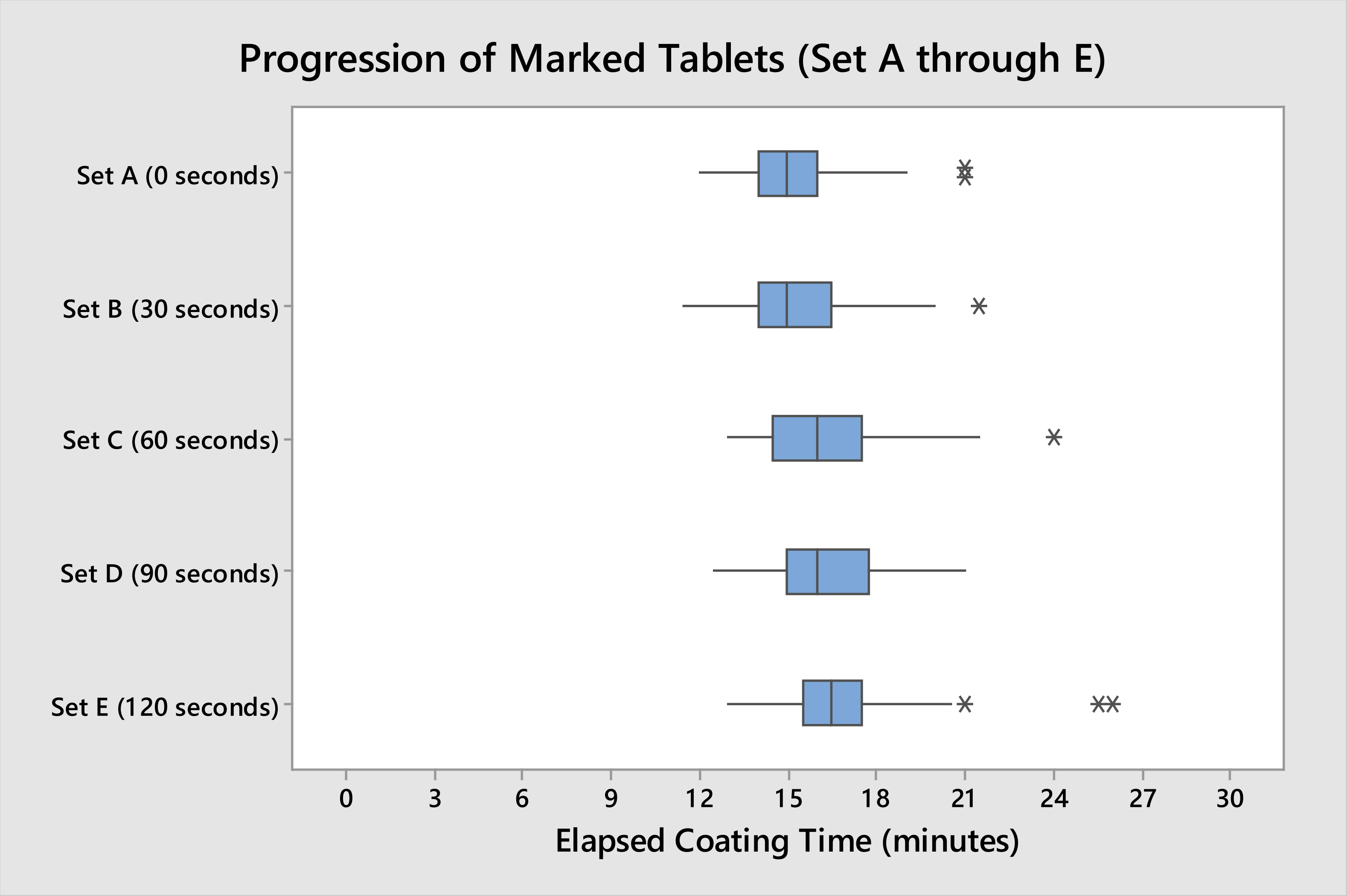
Trial process parameters

- Trials (and sampling) conducted in fully continuous mode of operation.

Parameter	Trial 1	Trial 2
Inlet air temperature	75°C	72°C
Inlet air flow rate	6700 cfm	6600 cfm
Target exhaust temperature	47°C	47°C
Target bed temperature	45°C	45°C
Opadry QX Solids concentration (%)	20	25
Solution spray rate	1700 g/ min	1700 g/ min
Water spray rate	1360 g/ min	1275 g/ min
Atomizing air pressure	35 psi	35 psi
Pattern air pressure	30 psi	30psi
Drum speed	12 rpm	12 rpm
Resultant EEF*	3.26	3.25
Tablet feed rate	680 kg/ hr	850 kg/ hr
Coating weight gain (%)	3	3

Tablet progression – Trial 1

680 kg/hour



IQ range

2.0

2.5

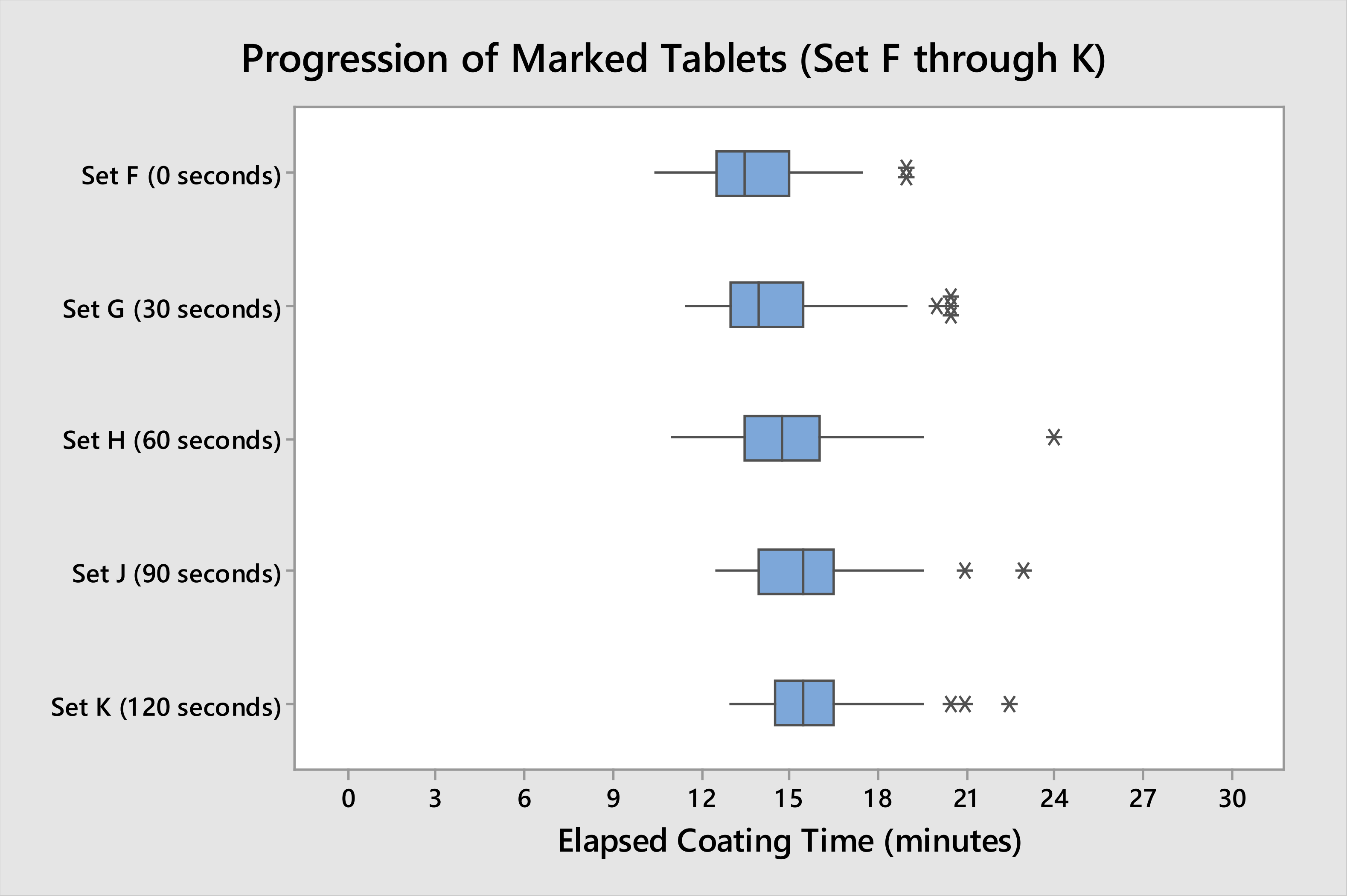
3.0

2.8

2.0

Tablet progression – Trial 2

850 kg/hour



IQ range

2.5

2.5

2.5

2.5

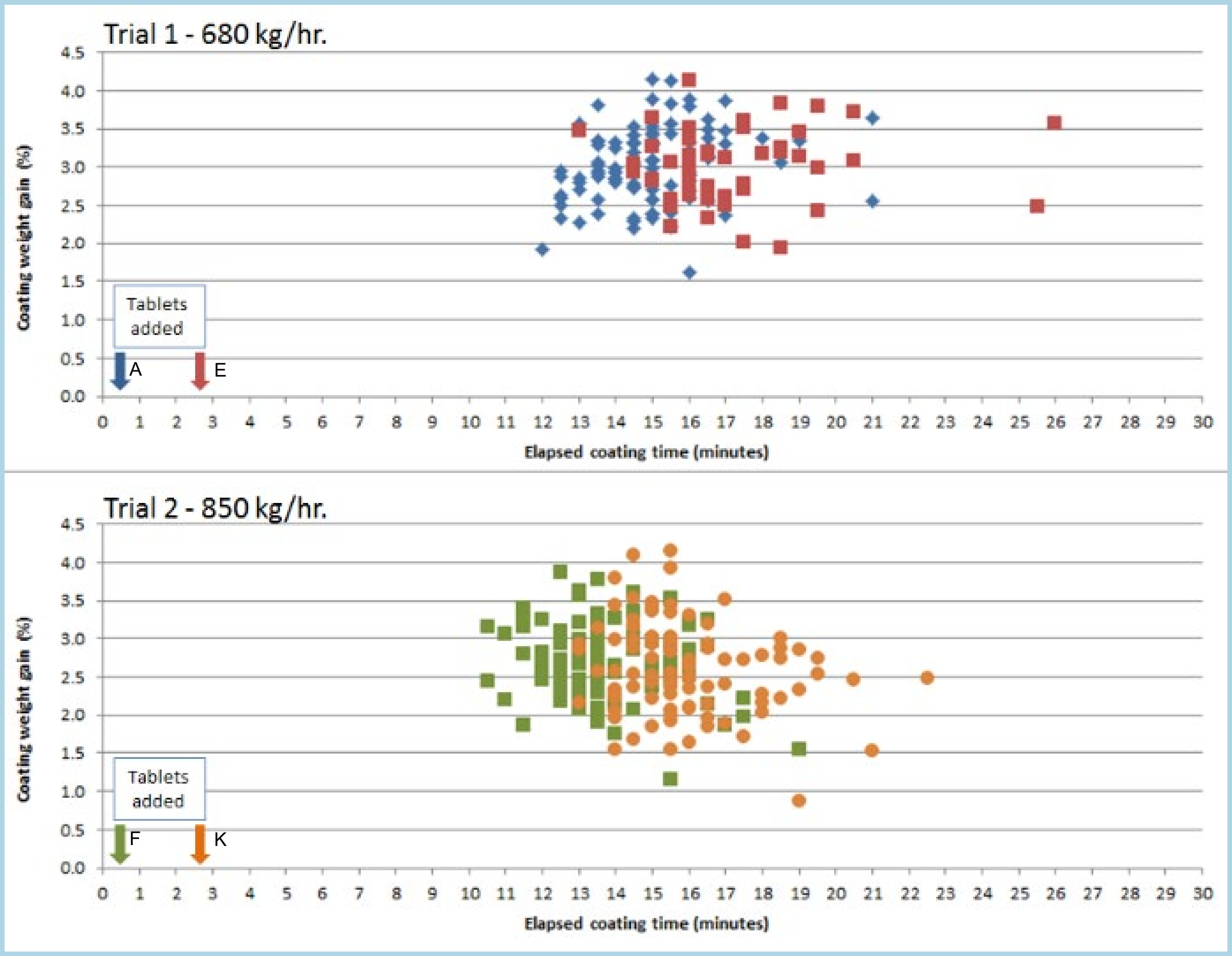
2.0

Progression discussion

- Discussion
  - During the continuous coating process, the 500 marked tablets were entrained in ~343,000 of placebo tablets (120kg pan load).
  - The discharge rate was as high as ~41,000 tablets / minute.
  - Overall, tablet distribution seemed fairly narrow.

  - Does the span of distribution affect weight gain??

Residence time vs. weight gain



Surprisingly, weight gain is independent of residence time.

Distribution is fairly narrow with respect to total throughput rate.

Summary and perspective

Parameters	24" CTC	48" Batch	24" CTC	48" Batch
Solids conc. (%)	20		25	
Spray rate (g/min)	1700	400	1700	400
Pan speed (rpm)	12	6	12	6
Pan load (kg)	120	130	120	130
EEF	3.25	3.23	3.26	3.22
Total coating time (min.)	15 (average residence time)	49	14 (average residence time)	39
% RSD (by actual mg gain)	15.90	18.74	21.10	23.90

- Demonstrated tight distribution of tablet movement through process.
- Coating weight gain not directly correlated to time in the pan (within the span of progression).
- Uniformity (%RSD) comparable or better than production scale pan at conditions studied.

Application of a New, High Productivity Film Coating in the GEA ConsiGma™ Coater

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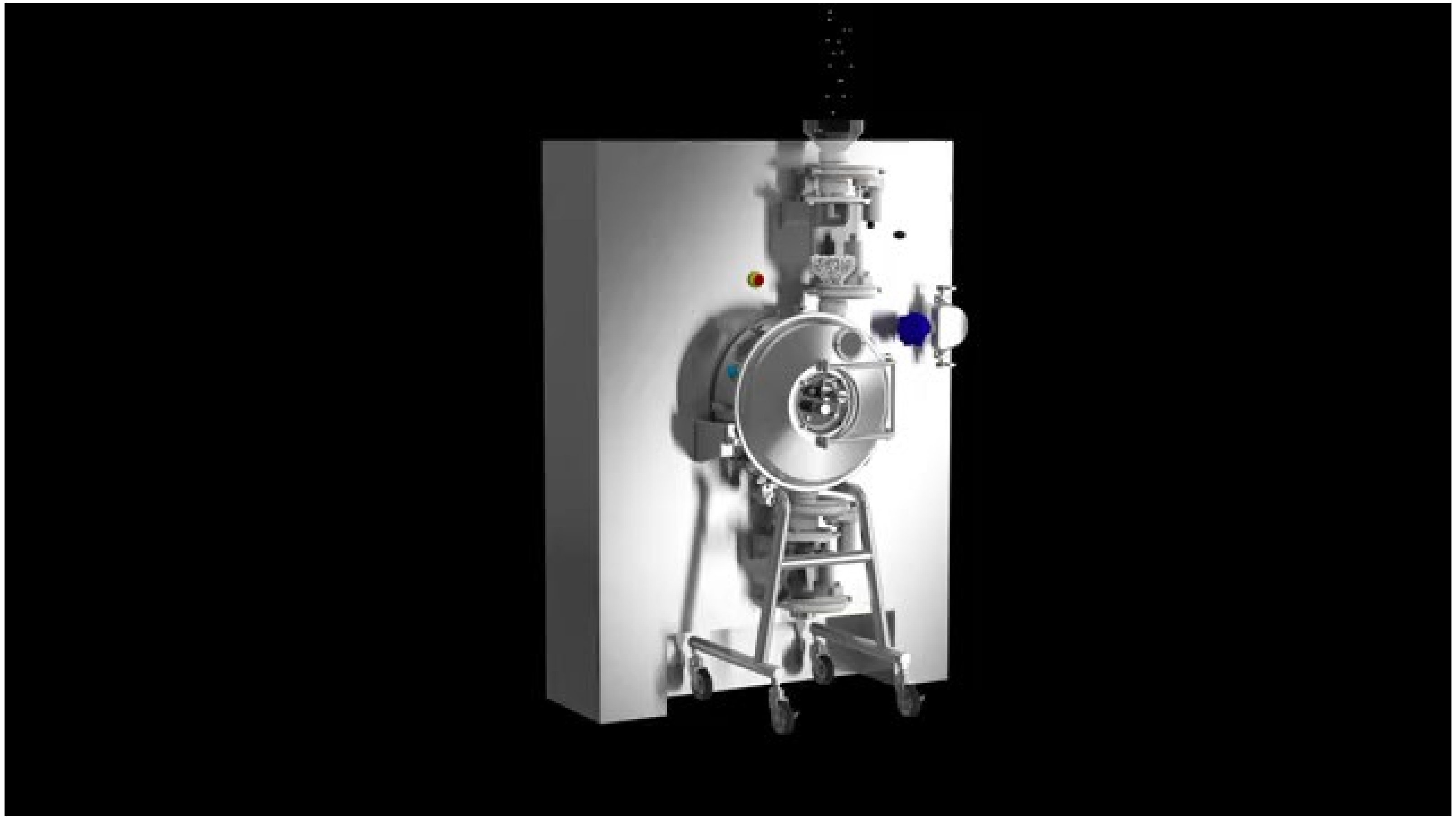
Video



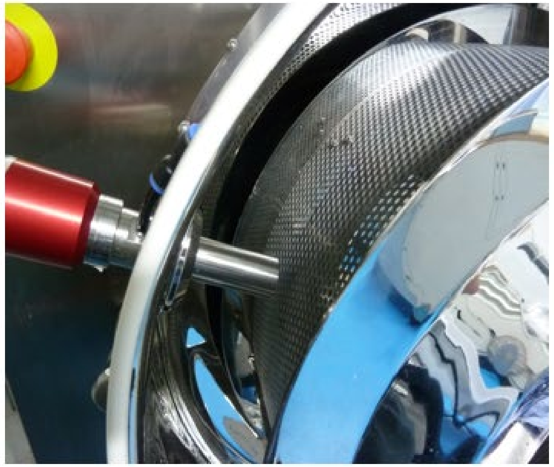
Methods – 3.0kg batch size

- A Design of Experiment (DOE) strategy was used to vary inlet temperature, spray rate and coating solids concentrations over a wide range.

Trial no.	Solids concentration (w/w %)	Inlet temp (°C)	Spray rate (g/min)	Total spray time (min)
1	27.5	90	60	5.5
2	27.5	75	80	4.1
3	35.0	90	80	3.2
4	20.0	60	80	5.6
5	20.0	75	60	7.5
6	35.0	60	40	6.4
7	27.5	75	40	8.2
8	27.5	60	60	5.5
9	20.0	90	80	5.6
10	27.5	75	60	5.5
11	27.5	75	60	5.5
12	27.5	75	60	5.5
13	35.0	60	80	3.2
14	20.0	90	40	11.3
15	35.0	75	60	4.3
16	35.0	90	40	6.4
17	20.0	60	40	11.3
18	30.0	75	60	5.0
19	30.0	90	80	3.8

Methods

- Tablets were sampled from the process at 1%, 2% and 3% theoretical weight gain (WG) and assessed instrumentally for color development and uniformity, surface roughness, gloss and coating weight variation.
- A large volumetric focal volume Raman (PhAT) probe (Kaiser Optical Systems Inc.) was focused inside the coater (Figure 3) to non-destructively measure % WG during each coating cycle and then correlated to an off-line primary gravimetric method.

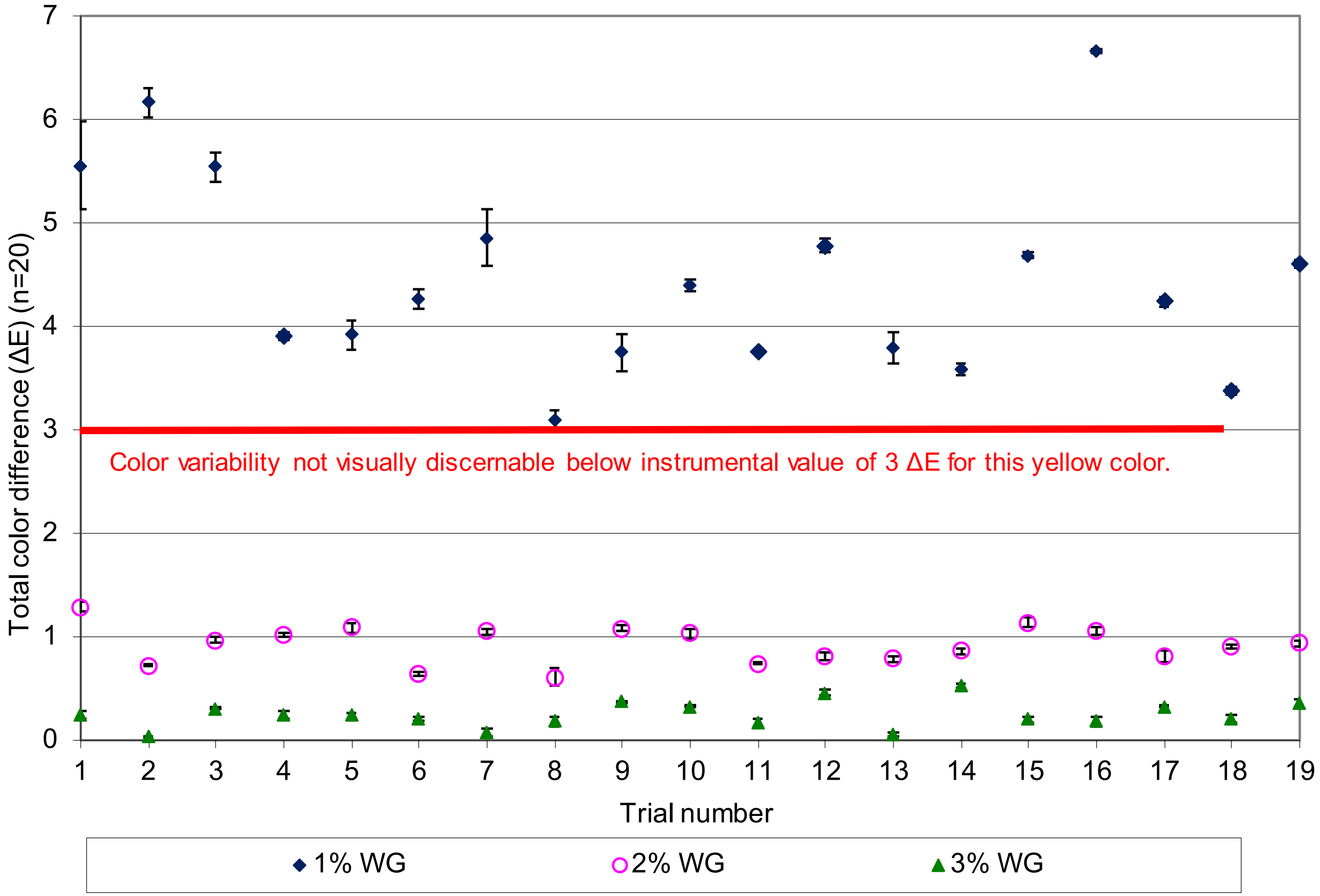


Coater Open with PhAT probe inserted into the Omega Coater (looking into cascade)

PhAT probe port view. Coater mesh is observed

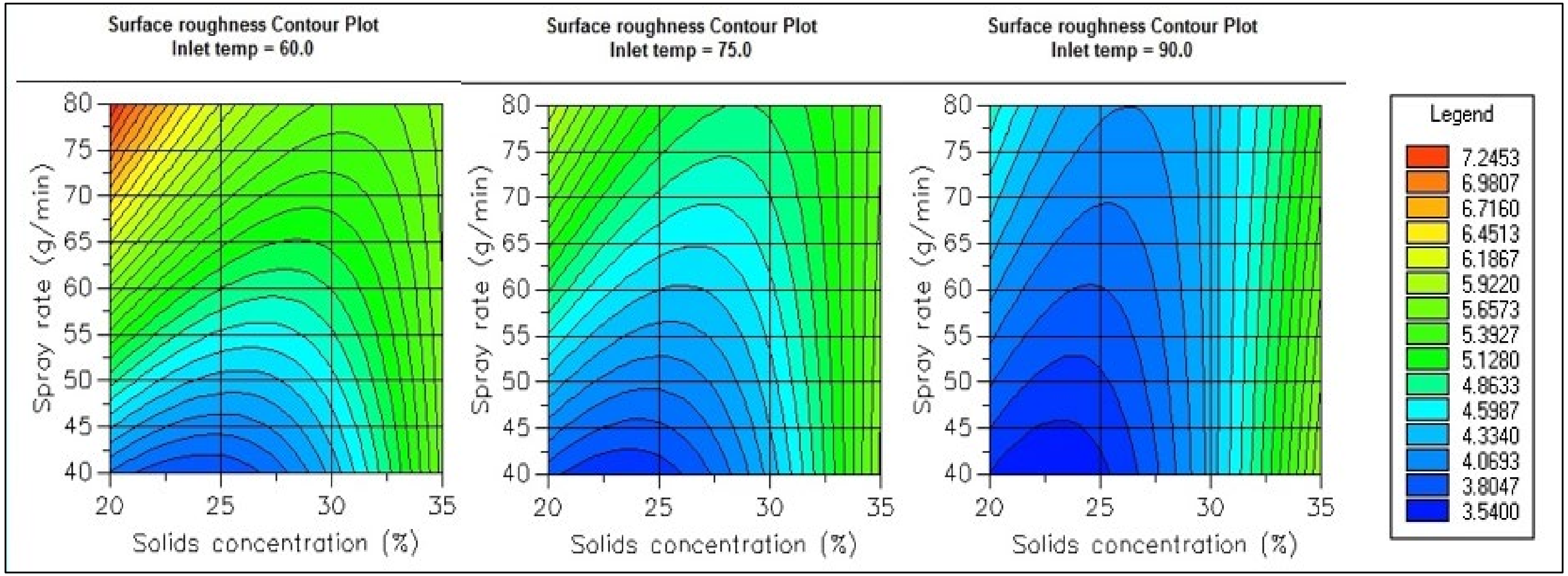
Coater Closed with PhAT probe in place looking into cascade

Results – Color Uniformity



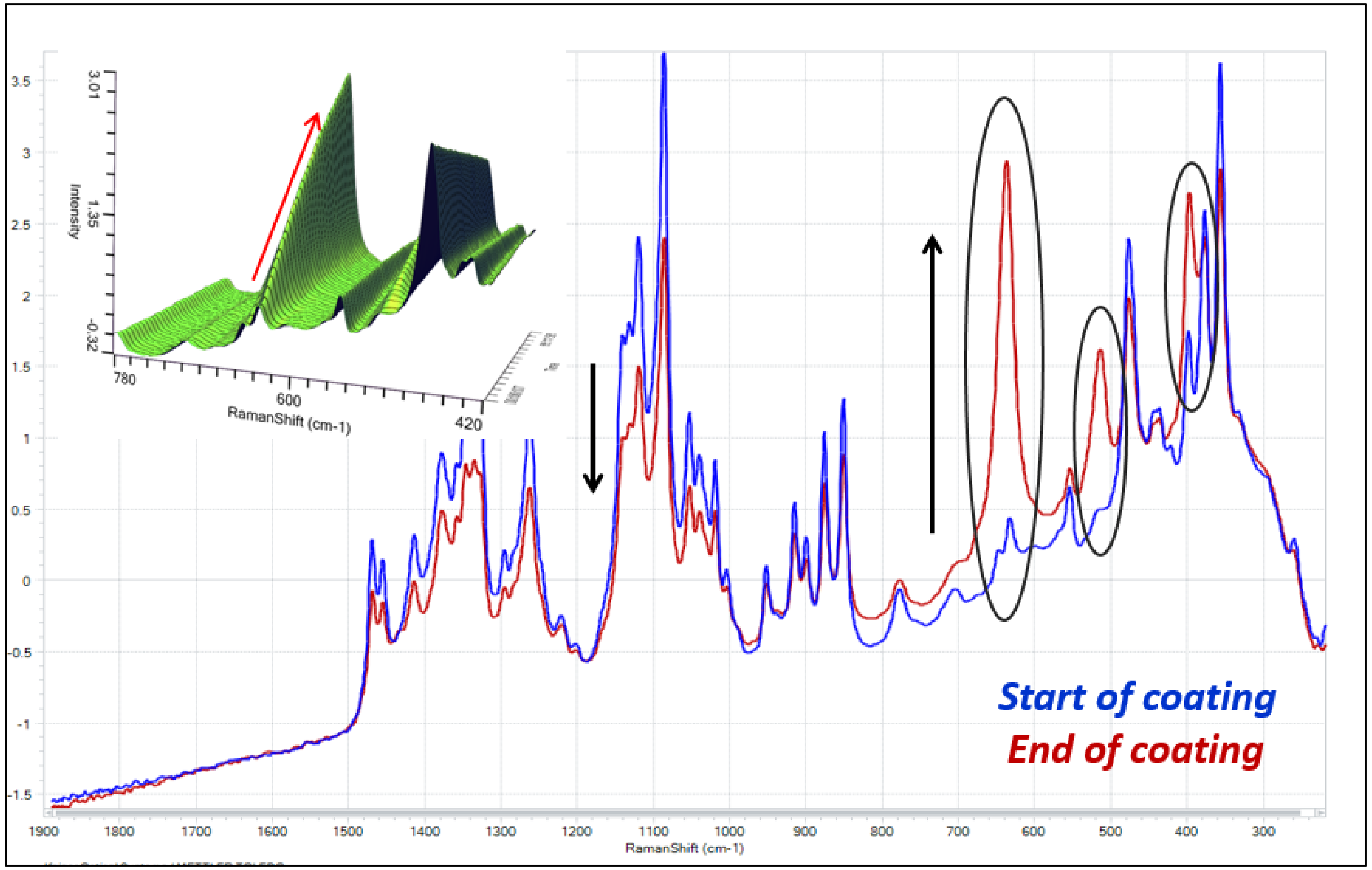
Results – Gloss and roughness

- Coatings were visually smooth and glossy, with instrumental surface roughness averaging < 5.5 Sa and gloss between 70 and 85 GU, for all but the wettest conditions (trials at the lowest solids and fastest application rates), where some increase in roughness was seen (up to 7.0 Sa).



Results – Raman

- A correlation between Raman signal change over time and % WG was made via a Partial Least Squares (PLS) multivariate modeling approach.



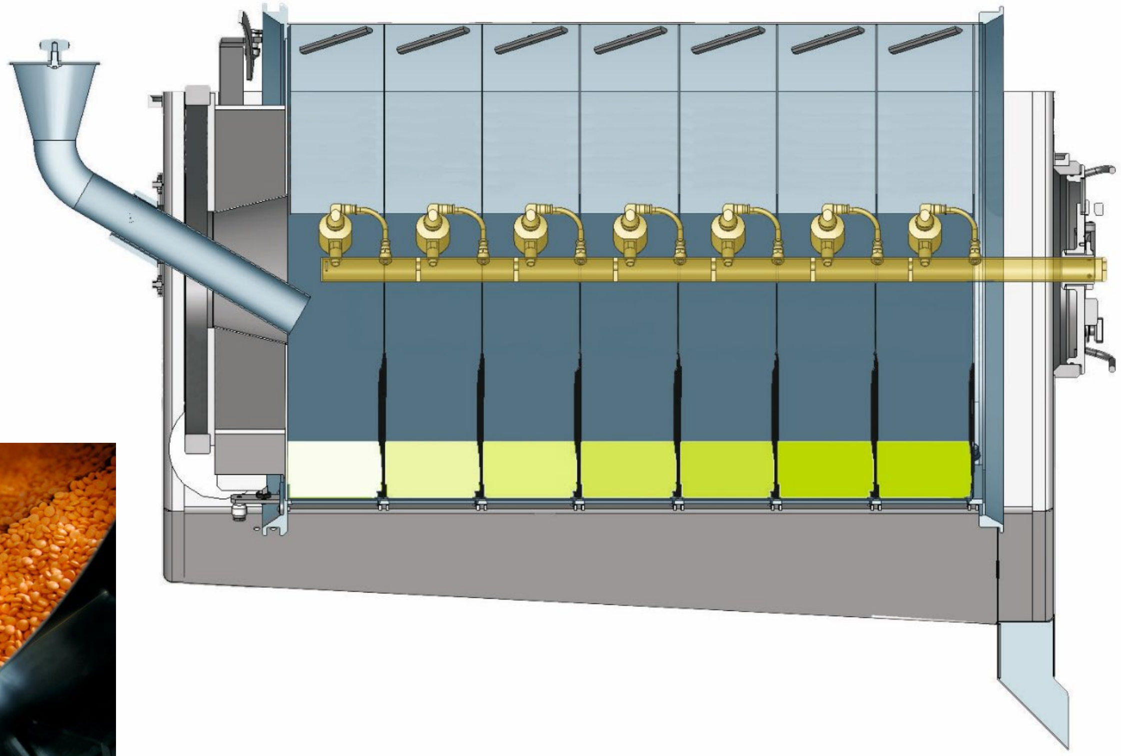
Conclusions

- The flexibility of the coating to be applied over a wide range of solids concentrations (up to 35%), along with fast attainment of coating uniformity in the coating process, allows wide adaptability to meet continuous tableting line throughput requirements.
- Due to the novel design of the process and speed of coating, the entire 19 trial DOE was completed in one day, in effect at production scale.
- On-line Raman spectroscopy successfully allowed for real-time monitoring of coating build rates and was used to quickly identify any process deviations.

Evaluation of a Continuous Cycled Film Coating Process with Opadry QX

Methods - equipment

- The coating evaluations were conducted in a DRIACONTI-T® continuous cycled coating machine (Driam GmbH, Eriskirch, Germany).



Methods – trial parameters

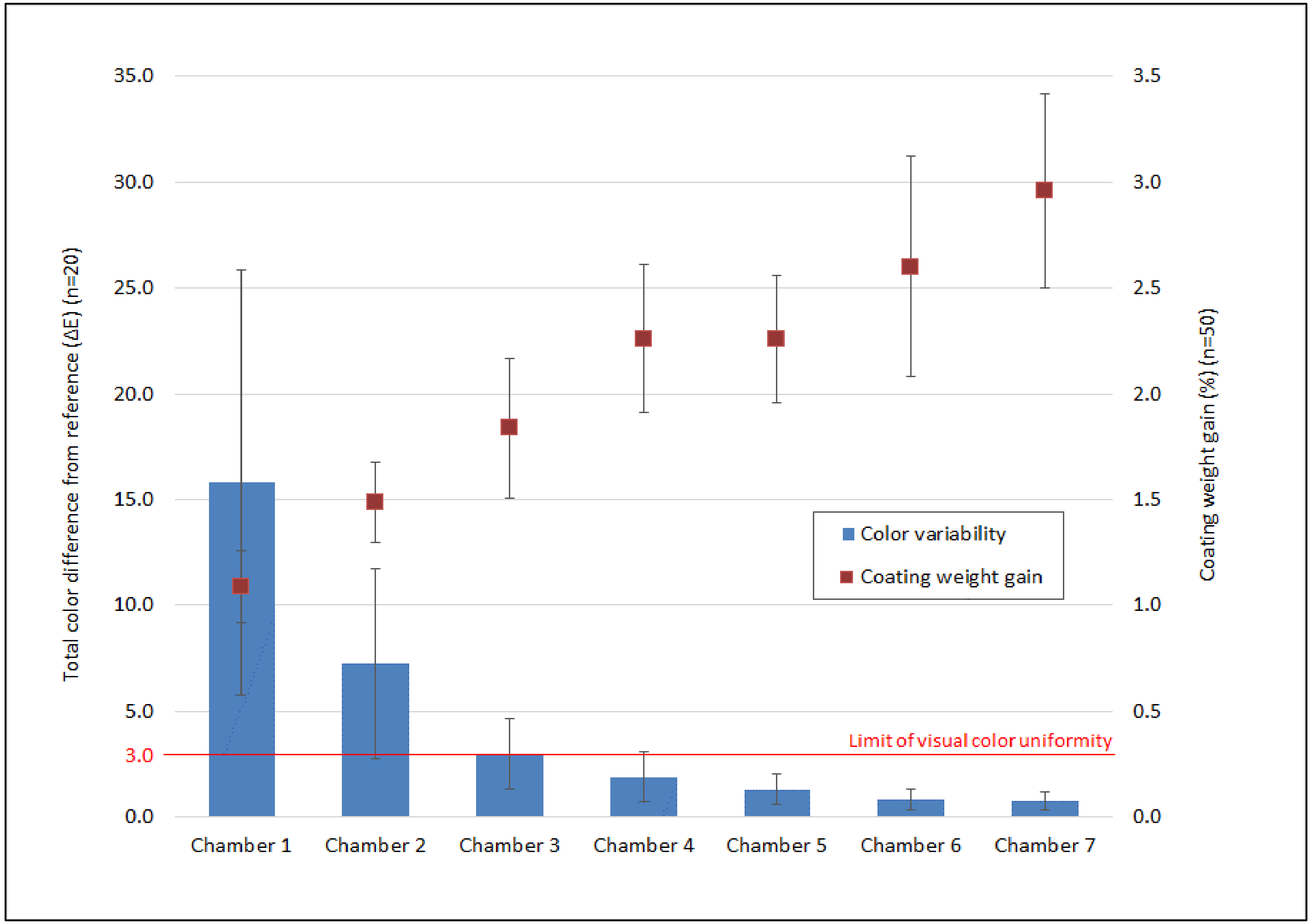
- Four trials were conducted to assess the impact of increasing coating solids concentration on production throughput rates, coating uniformity and tablet surface properties.
- Placebo tablets (300 mg, 10 mm, round with debossed Colorcon logos) were used as the substrate for the coating trials.
- The target coating weight gain (WG) was 3.0%.
- As the solids concentration of the coating formulation for each trial increased, the tablet throughput rate was increased proportionally to maintain the target 3.0% WG.
- All other coating parameters were held constant.

Methods – trial parameters

Process Parameters	Trial 1	Trial 2	Trial 3	Trial 4
Coating solids concentration (%)	20.0	25.0	30.0	35.0
Resident pan load (kg)	126			
Load per chamber (kg)	18			
Process air volume (m^3/h)	3500			
Inlet temperature (°C)	68-73			
Exhaust temperature (°C)	48-50			
Product temperature (°C)	42-46			
Spray rate (g/min)	44			
Atomizing air pressure (bar)	1.1			
Pattern air pressure (bar)	0.5			
Pan speed – coating (rpm)	8.0			
Pan speed – product transfer (rpm)	2.0			
Coating time per cycle (min)	8.8	7.0	5.8	5.0
Product transfer time per cycle (min)	0.9	0.9	0.9	0.9
Total tablet throughput rate (kg/hr)	110.2	135.0	158.8	180.0

Results – color and weight uniformity

- 30% solids concentration, 159 kg/hr throughput rate



Results – coated tablet appearance

- Coated tablets from all trials were smooth and free of defects.
- Visually, the effect of increasing solids concentration was virtually indistinguishable between the coated tablet samples from each trial.
- Logo definition was excellent even for the tablets coated at 35% solids concentration.

Trial 4
35% solids
concentration

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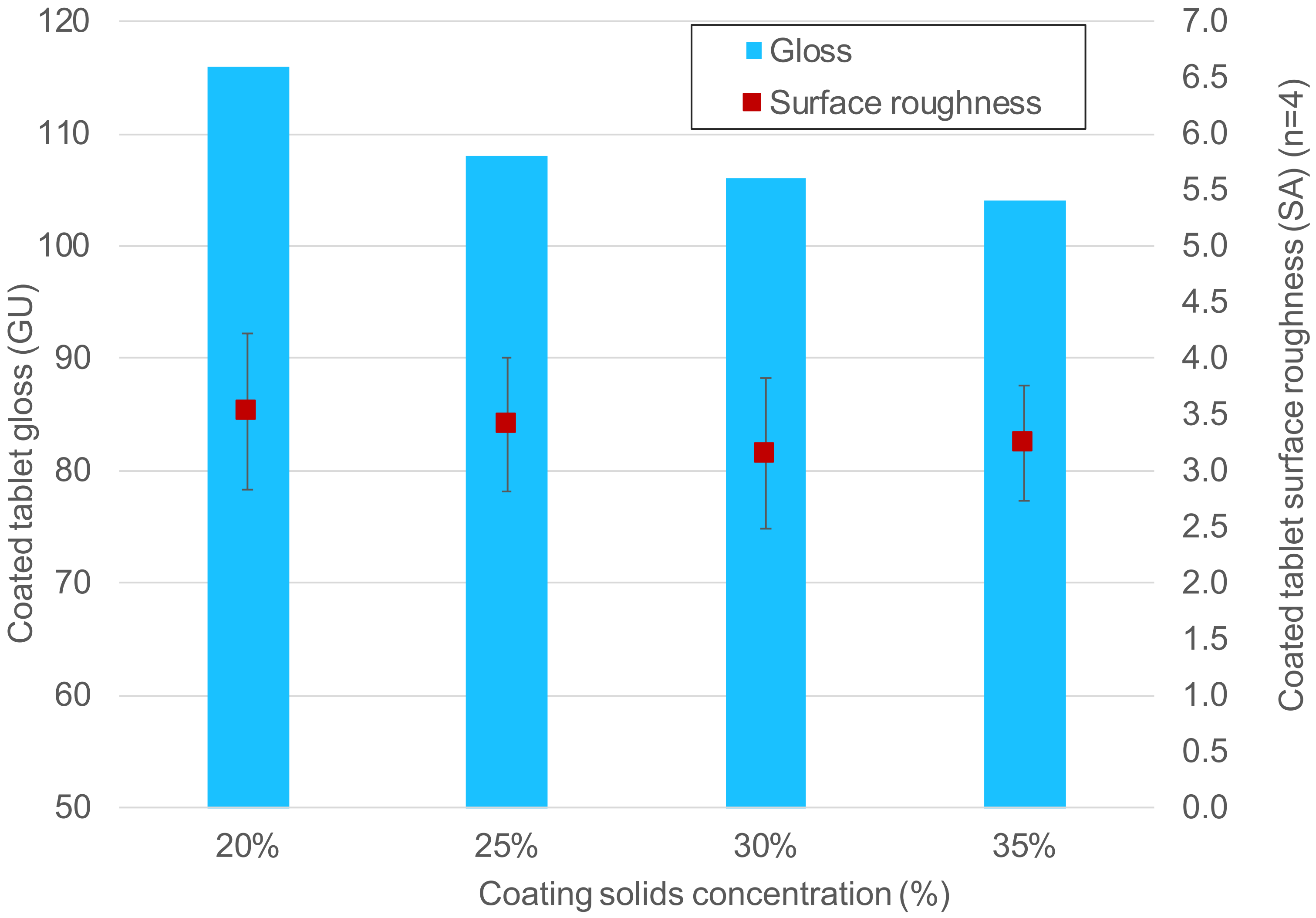
Results – coated tablet gloss and surface roughness



Conclusions

- The flexibility of Opadry QX to be applied over a wide range of solids concentrations (up to 35%), along with fast attainment of coating uniformity in the coating process, allows wide adaptability to meet any continuous coating requirements.
- There is a wide variety of continuous coating equipment available to meet a broad range of Continuous throughput targets.