Aquarius™ Genesis – an ultra-high speed, high gloss film coating system in continuous and batch processes

PharmSci 2019

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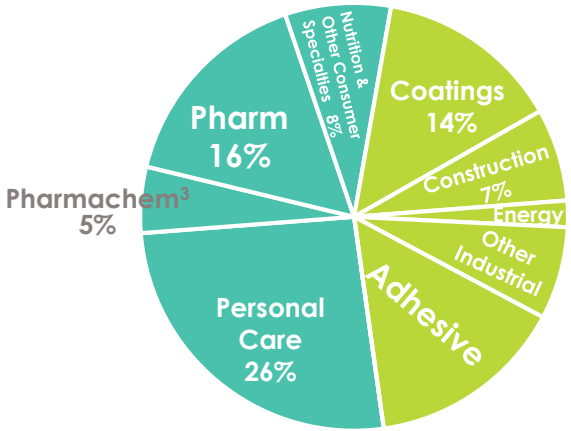
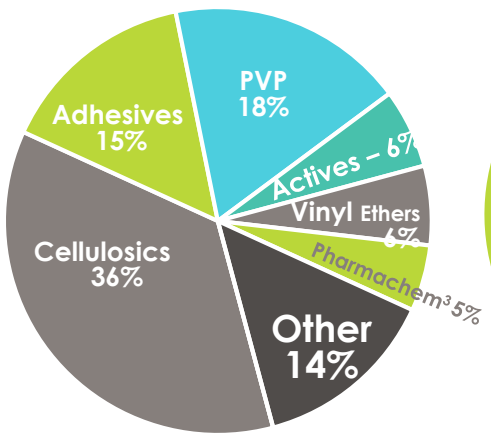
Ashland

A global leader of cellulose ethers, vinyl pyrrolidones and biofunctionals

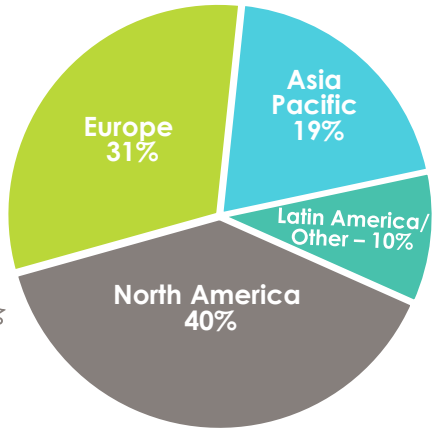
Sales by Market[1]



Sales by Product



Sales by Geography[2]



For 12 Months Ended September 30, 2017

Sales: $2.2 billion

[1] Within the Sales by Market chart above, Industrial Specialties are presented in green and Consumer Specialties are presented in blue.

2 Includes Pharmachem's sales for the period May 17, 2017 through September 30, 2017, the period for which Pharmachem was owned.

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global network of pharma technical centers

North America
- Wilmington,
- Delaware

Europe
- Düsseldorf, Germany
- Istanbul, Turkey

Asia Pacific
- Hyderabad, India
- Shanghai, China

Latin America
- São Paulo, Brazil
- Mexico City, Mexico
- Buenos Aires, Argentina

Each regional center has core competencies in oral solid dosage formulation technologies

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Cellulosic Products	Application											
	Tablet Binding	Modified-release Matrix Former	Tablet Film Coating	Drug Solubilisation	Direct-compression Tableting	Disintegration	Lyophilisation Solubiliser	Liquid Rheology Modification	Suspending Agent	Stabiliser	Crystallisation Inhibitor	Hot-melt Extrusion
Klucel™ hydroxypropylcellulose	✓	✓	✓		✓							✓
Benecel™ methylcellulose and Hypromellose	✓	✓	✓	✓	✓			✓			✓	
Natrosol™ 250 hydroxyethylcellulose		✓						✓				
Aquasolve™ Hypromellose acetate succinate			✓	✓								
Aqualon™ ethylcellulose	✓	✓	✓									
Aqualon and Blanose™ sodium carboxymethylcellulose			✓				✓	✓	✓		✓	

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Vinyl pyrrolidone Products	Application											
	Tablet Binding	Modified-release Matrix Former	Tablet Film Coating	Drug Solubilisation	Direct-compression Tableting	Disintegration	Lyophilisation Solubiliser	Liquid Rheology Modification	Suspending Agent	Stabiliser	Crystallisation Inhibitor	Hot-melt Extrusion
Plasdone™ S-630 copovidone	✓		✓	✓								✓
Plasdone povidone C grades				✓			✓	✓	✓		✓	
Plasdone povidone K grades	✓			✓				✓			✓	
Polyplasdone™ crospovidone				✓		✓						
Pharmasolve™ N-methyl-2-pyrrolidone				✓								

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Products	Application											
	Tablet Binding	Modified-release Matrix Former	Tablet Film Coating	Drug Solubilisation	Direct-compression Tableting	Disintegration	Lyophilisation Solubiliser	Liquid Rheology Modification	Suspending Agent	Stabiliser	Crystallisation Inhibitor	Hot-melt Extrusion
Cyclodextrins												
CAVAMAX*, Cavitron™ and CAVASOL* cyclodextrins				✓			✓			✓		
Film coating systems												
Aquarius™ film coating systems			✓									
Viatel™ bioresorbable polymers												
Poly(D, L-lactide), Poly(L-lactide), Poly(D, L-lactide-co-glycolide), Poly(ε-caprolactone), Poly(L-lactide-co-ε-caprolactone)		✓		✓								✓

*Registered trademark owned by Wacker Chemie AG. Ashland acts as a worldwide distributor for Wacker.

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Aquarius™ Genesis film coating systems general features and benefits

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Aquarius™ Genesis ultra high-solids film coating systems

- The traditional coating polymers are HPMC and PVA, but their inherent high viscosity limits their application for high solids, high productivity coatings
- Ashland has developed an ultra **high-solids coating** that can be used in a commercial process at up to 35% solids **without compromising aesthetics**

Aquarius Genesis is:

- designed for use in both continuous processes and traditional coating equipment with shorter application times
- specially formulated with unique properties that provide a **strong film** with **high adhesion** and **smooth appearance**
- designed for higher solids content coating, which can **increase productivity** and take advantage of coating machine speed while assuring good tablet appearance

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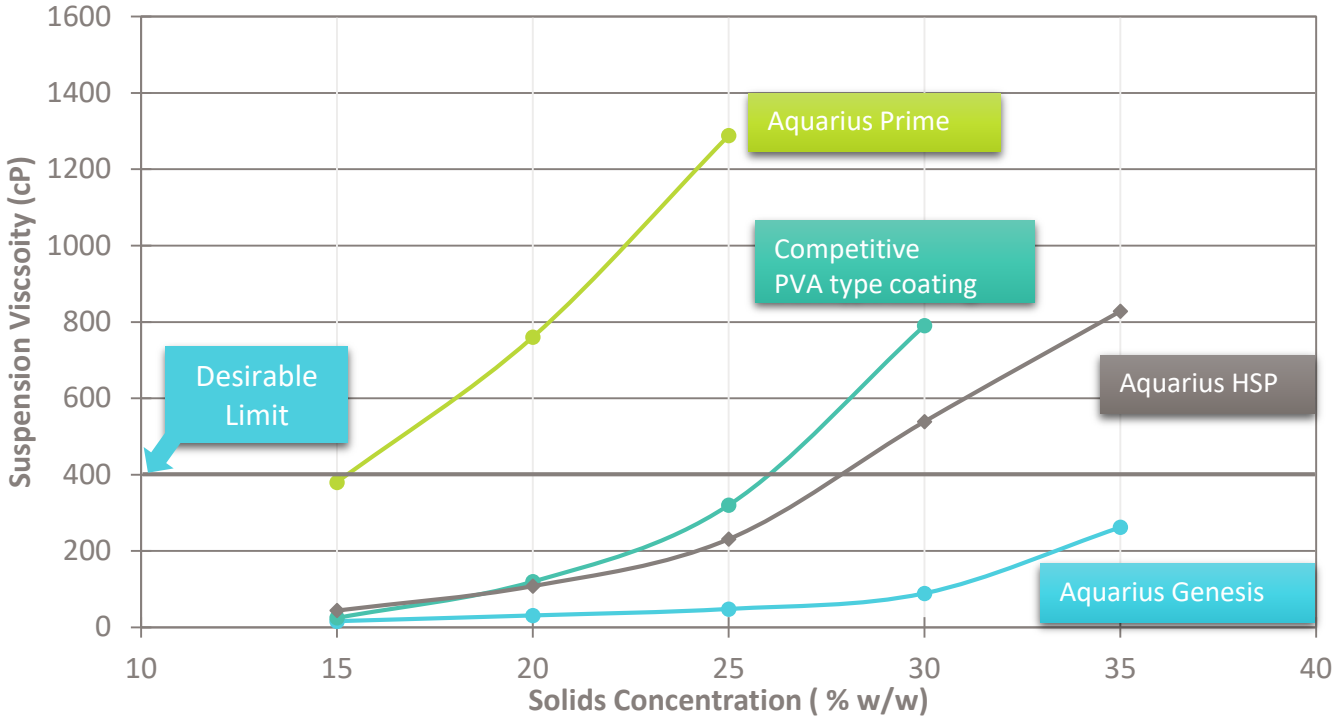
Aquarius™ Genesis film coating systems general features and benefits

Facilitates significant processing advantages, such as:

- Higher solids content in the range of 20–35% w/w solids for pigmented coatings with viscosities in the range of 100–300 cP
- Faster processing times increase manufacturing capacity, reduce the need for capital investment, and lower energy costs. Coating processing time can be reduced up to 65%
- Lower processing temperatures are crucial in heat sensitive APIs, or in tablet formulations with dissolution characteristics negatively affected by relatively higher aqueous coating process temperatures
- Improved coverage enable lower weight loadings and reduced raw material costs
- Non tacky coating characteristics prevent surface to surface interactions known to be problematic during handling and packaging

Aquarius™ Genesis film coating systems coating suspension viscosity



Even at high solids levels up to 35% w/w, the viscosity of the formulation remains low, allowing faster spray rates to help achieve higher coating efficiency

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important features & benefits

- Ultra High-Solids
- High Gloss System
- Clear Crisp Logo
- Improved Adhesion
- Smooth finish

- Reduced Cycle Time
- Improved Productivity
- Reduced exposure to stressful process conditions
- Reduced Process Time
- May Reduce Energy Costs

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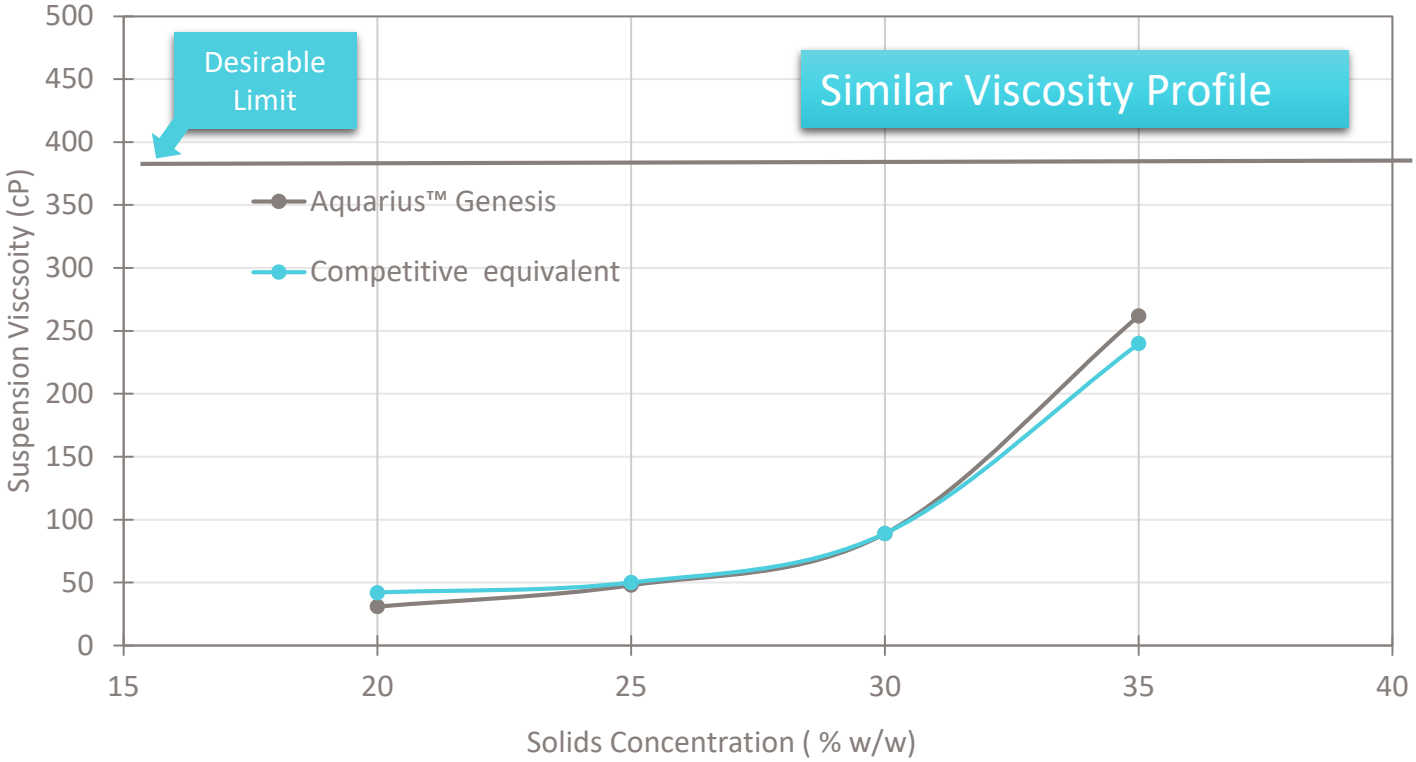
competitive testing

viscosity profile



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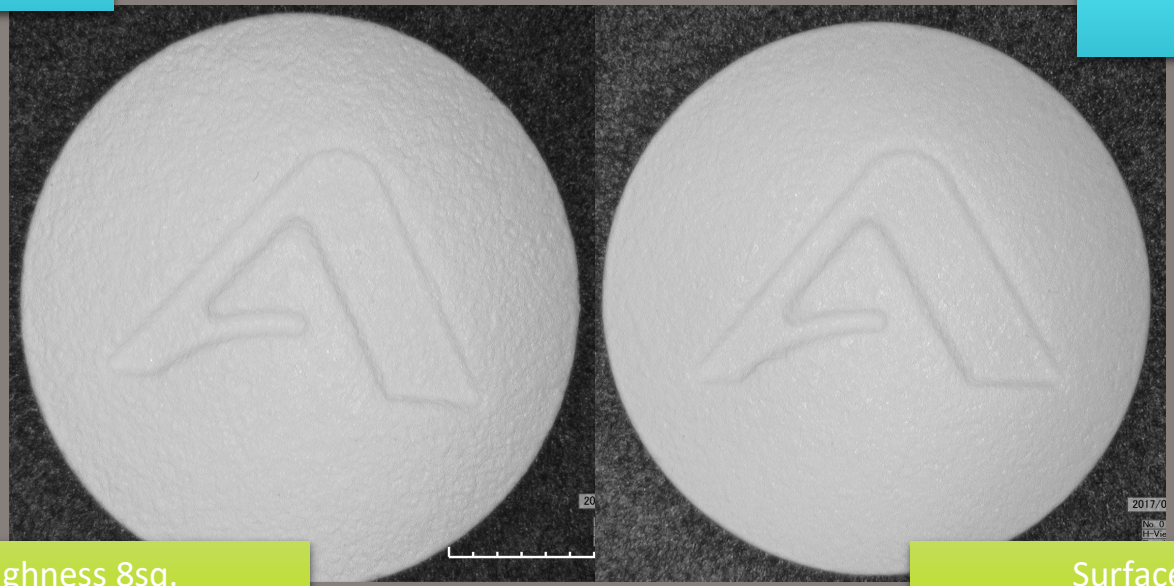
competitive testing
35% solids

Competitive Coating

Ashland's Coating
Aquarius Genesis



Surface Roughness 8sq.
Gloss 65 gu

Surface Roughness <5sq.
Gloss 88 gu

Glossier looking tablets and lower surface roughness at high solids when coated at the same processing conditions

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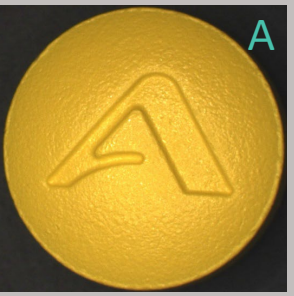
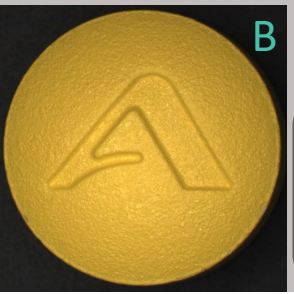
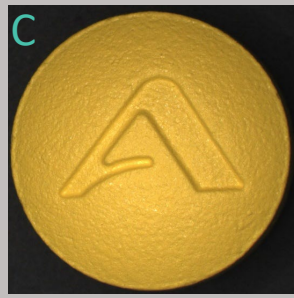
Aquarius™ Genesis film coating systems

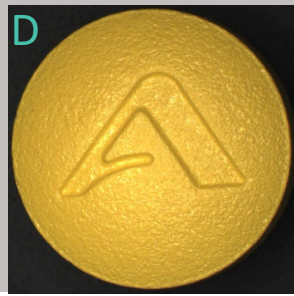
Tablet Surface Roughness and Gloss





#	Solids (% w/w)	Tablet Surface Roughness (µm)	Gloss (glu)
A	25.0	2.8	130
B	30.0	3.5	110
C	32.5	4.2	96
D	35.0	4.8	88





High solids coatings together with short processing times typically result in coarser tablet coating finishes. In contrast, the coating finish for Aquarius Genesis remains smooth.

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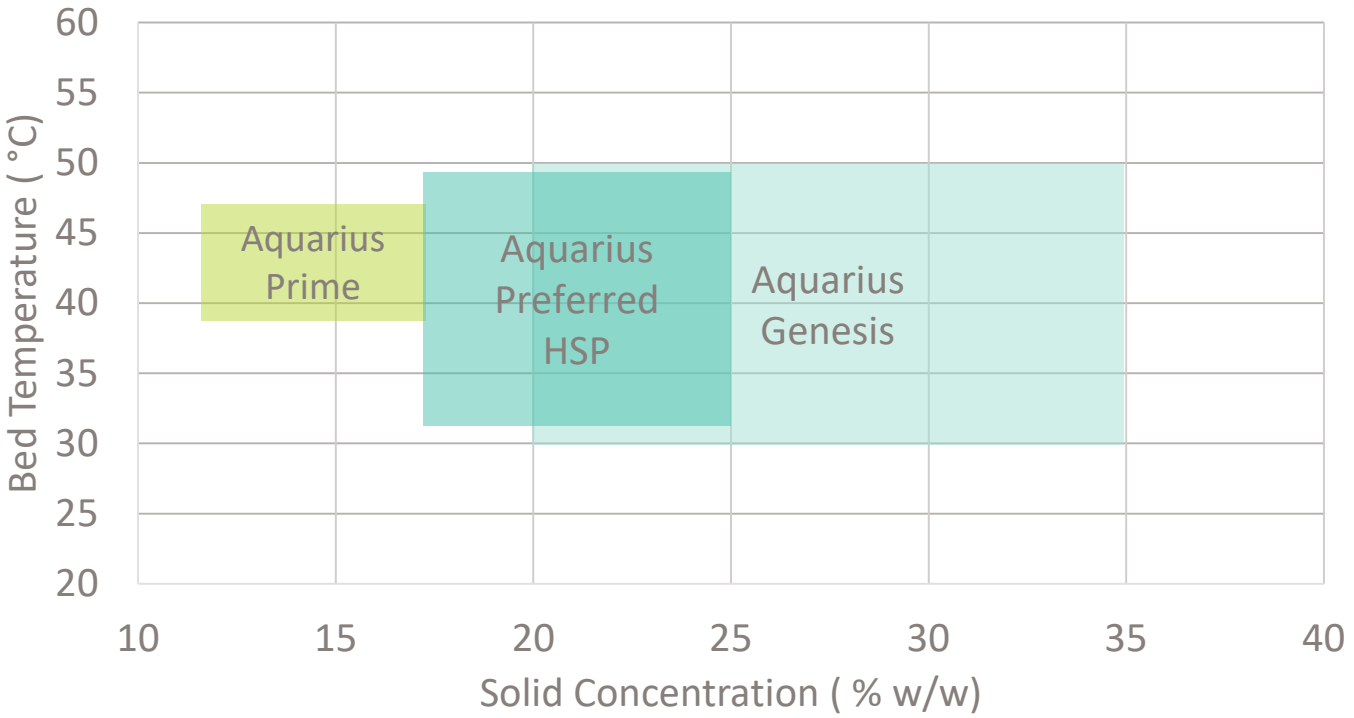
wider processing window



High solids enable faster application of films, quicker attainment of color uniformity and all coated tablets have a uniform, defect-free finished appearance.

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Aquarius™ Genesis film coating systems

scale-up coating trials

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scale-up coating trials: equipment

A. O'Hara Labcoat IIX

50 kg scale

B. Thomas Engineering Accela-cota

400 kg scale

C. GEA Consigma Coater

10-100 kg/hr scale

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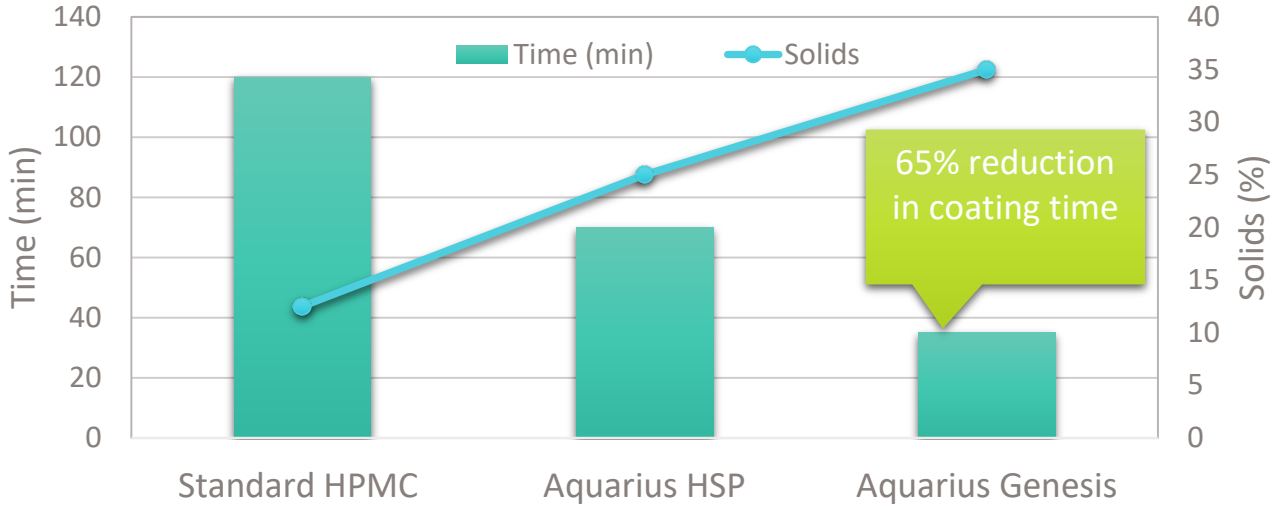
film coating comparison

500 mg tablets/O'Hara Labcoat IIX coater/30" coating pan/40Kg batch

At the typical 3% weight gain, coating weight gain was achieved faster compared to alternative systems. This improved processing means tablets were exposed for significantly less time to the tumbling, heat, and moisture, associated with coating.



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Thomas Engineering 60” Accela-Cota

Process Parameter	Aquarius Prime	Aquarius Genesis
Coating pan	60” Pan	
Spray guns(s)	Five Spraying Systems (1.2 mm fluid nozzle)	
Pan loading (kg)	400 Kg	
Coating solids (% w/w)	12.5	35
Inlet temp. (°C)	**68**	**58**
Product temp. (°C)	42-44	42-44
Exhaust temp. (°C)	44-46	44-46
Atomizing air (bar)	2.5 - 2.8	2.5 - 2.8
Pattern air (bar)	2.5 - 2.8	2.5 - 2.8
Pan speed (rpm)	5	
Process air vol. (cfm) ($m^3 h^{-1}$)	2500	
Spray rate (g min^{-1})	400	600
Coating Time (minutes)	**240**	**62**

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Aquarius™ Genesis film coating systems:

results from GEA ConsiGma continuous coating trial

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principles of continuous manufacturing

Continuous manufacturing is based upon speeding up of conventional batch processes.

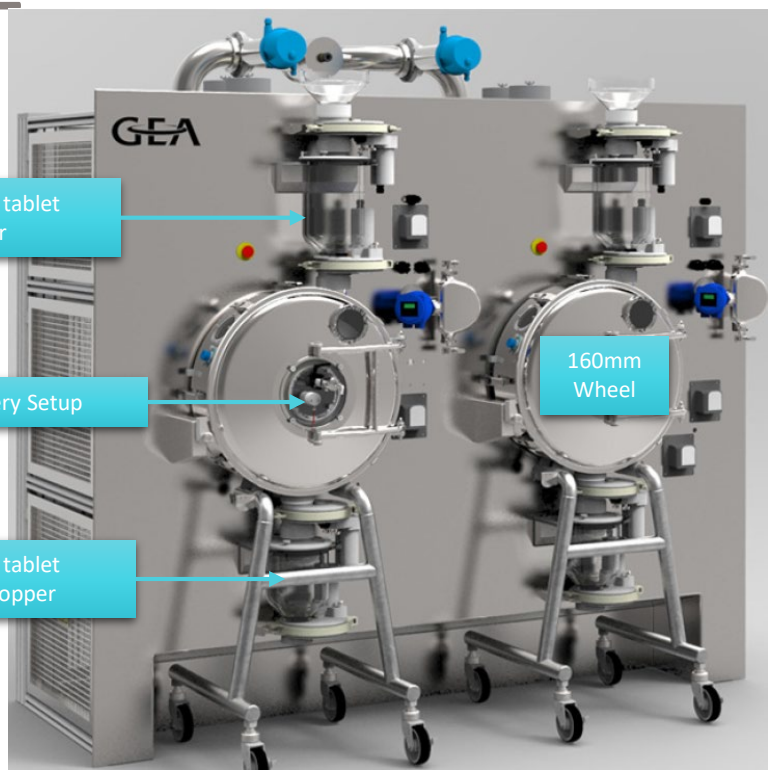
Typical processing time in the continuous processing chain

- Wet granulation in 3 to 5 seconds
- Fluid bed drying in 12 to 17 minutes
- Blending steps in 1 to 2 minutes
- Tablet coating needs to match 12 – 17 minutes, ideally faster

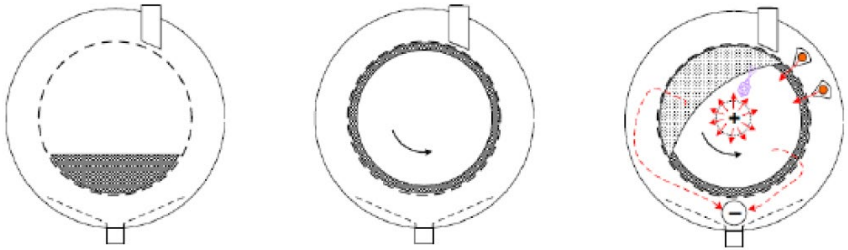
To achieve this requirement, new coating systems are needed for faster spraying and quicker drying while still maintaining acceptable aesthetics.

GEA ConsiGma coater

twin wheel configuration



- High speed semi – continuous coater
- ConsiGma coater fitted with a 160mm wheel
- Supports 10-100 kg/hr continuous tableting line



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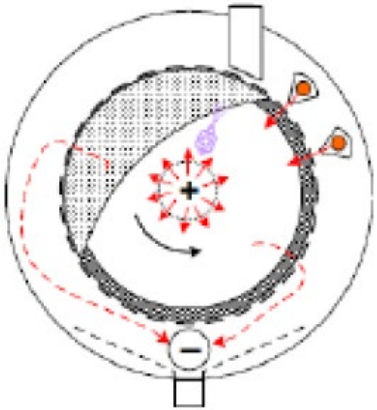
reducing drying time requires higher solids

….. But high solids usually results in rough surfaces.



Hence, optimized **Aquarius™ Genesis film coating systems**

Ultra high solids → very fast drying (~5mins) → Smooth finish

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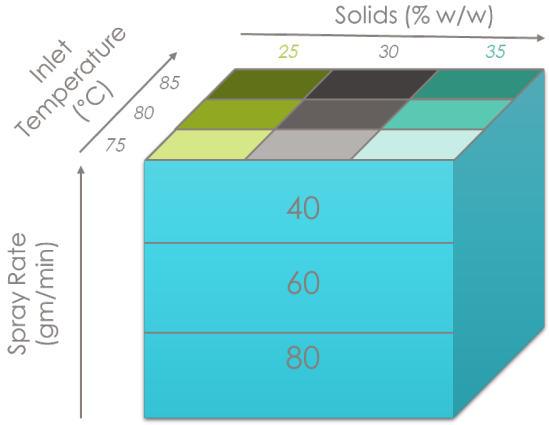
GEA ConsiGma coater trial

experimental conditions

- Convex round shape, 450mg, placebo tablets (3 kg batch size)
- 26 coating trials
- DOE methodology was used to evaluate the effect of
  - spray rate (40-80gm/min),
  - inlet temperature (75°C- 85°C), and
  - solids (25% - 35%)

Responses measured at 3% weight gain

- Surface roughness,
- Gloss and
- Color uniformity



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DOE parameters

Solids Conc. (% w/w)	Inlet Temperature (°C)	Spray rate (gm/min)	Run Order	Spray Time (min)
35	85	80	1	3.21
35	75	40	4	6.43
35	75	60	11	4.28
35	80	60	13	4.28
35	85	60	14	4.28
35	80	40	23	6.43
35	80	80	24	3.21
32.5	80	60	16	4.62
32.5	85	80	17	3.46
30	75	40	5	7.50
30	60	60	6	5.00
30	75	60	8	5.00
30	75	60	9	5.00
30	75	60	10	5.00
30	80	60	18	5.00
30	80	40	19	7.50
30	80	80	20	3.75
30	85	60	21	5.00
30	85	80	22	3.75
25	75	60	2	6.00
25	80	60	3	6.00
25	85	80	7	4.50
25	85	60	12	6.00
25	75	40	15	9.00
25	80	40	25	9.00
25	80	80	26	4.50

Coating trials achieved a 3% weight gain in 3 minutes - 9 minutes depending on the spray rate and solids concentration.

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GEA ConsiGma coater throughput

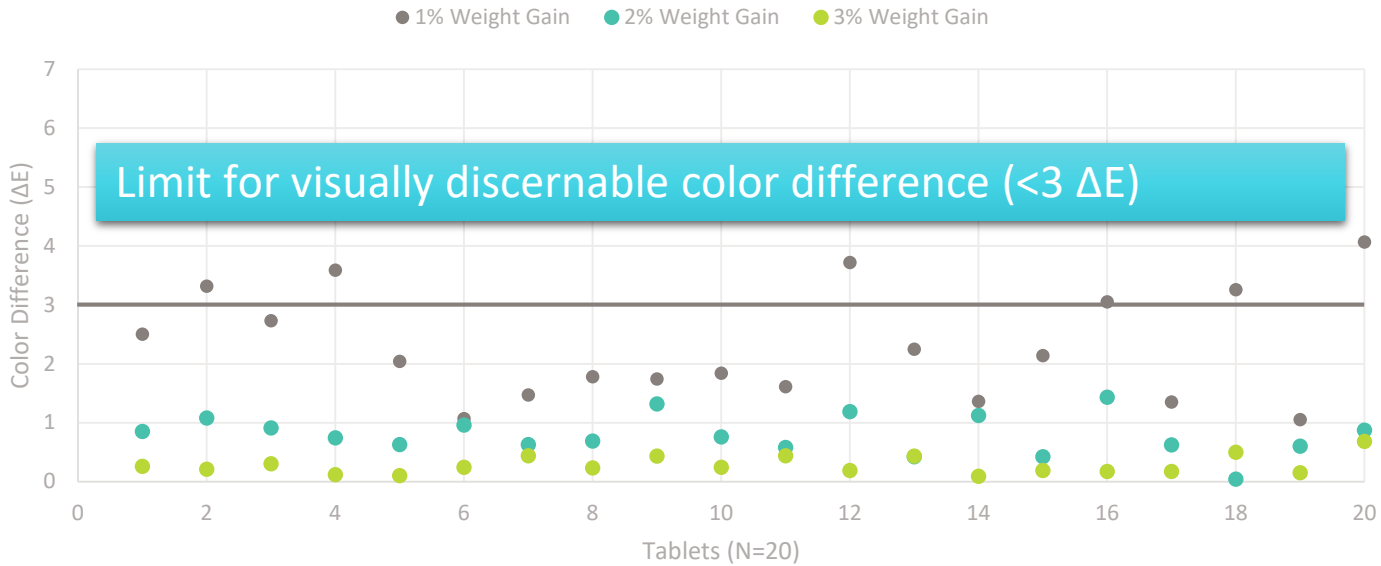
Solids (%)	Weight Gain (%)	Spray Rate (%)	Coating Suspension (gm)	Coating time (min)	*Setup time (min)	Throughput rate (kg/hr)	Twin Wheel Configuration Throughput rate (kg/hr)
25	3	60	360	6.0	2	30	60
25	3	80	360	4.50	2	40	**80**
30	3	60	300	5.0	2	36	72
30	3	80	300	3.75	2	48	**96**
32.5	3	60	277	4.62	2	39	78
32.5	3	80	277	3.46	2	52	**104**
35	3	60	257	4.28	2	42	84
35	3	80	257	3.21	2	56	**112**

Trials showed increased output with increased spray rate and solids content

* Load, preheat, dry and discharge

typical color variability chart

high-speed ConsiGma coating run at 35% solids



Color uniformity improved with increasing weight gain of coating, with color difference values reaching <1.2 ΔE from 2.0% WG

$$\Delta E^*_{CMC} = \sqrt{\left(\frac{L^*_2 - L^*_1}{lS_L}\right)^2 + \left(\frac{C^*_2 - C^*_1}{cS_C}\right)^2 + \left(\frac{\Delta H^*_{ab}}{S_H}\right)^2}$$

L – Lightness
C – Chroma
H - Hue

Measured using Datacolor spectrophotometer

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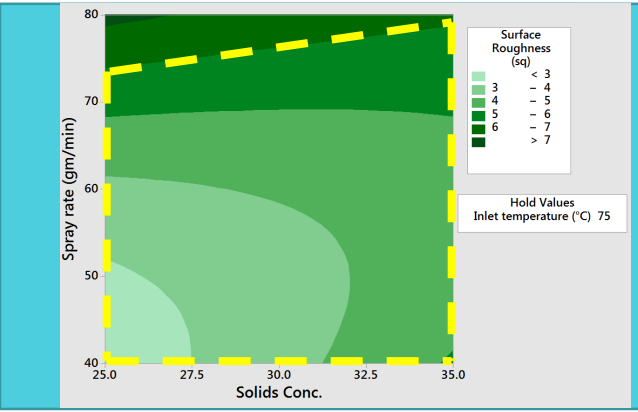
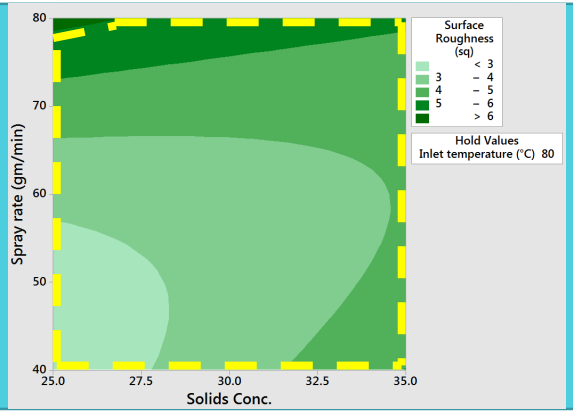
effect of spray rate and solids concentration on surface roughness

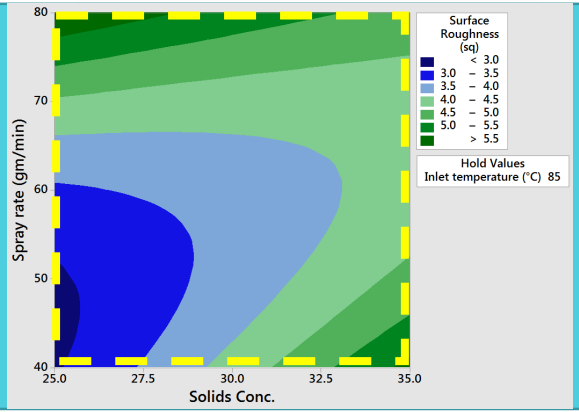
Inlet Temperature 75°C



Inlet Temperature 80°C



Inlet Temperature 85°C



In most cases, the new system had low surface roughness (< 6 sq. µm) except under very dry or wet conditions.

Recommended Window of Operation

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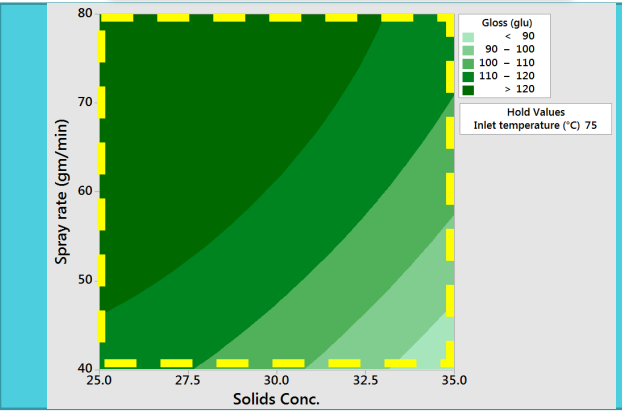
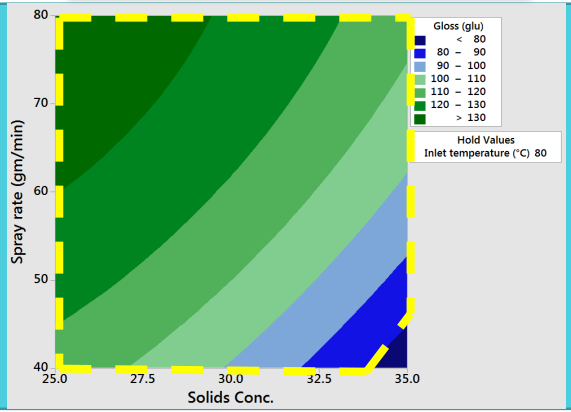
effect of spray rate and solids concentration on gloss

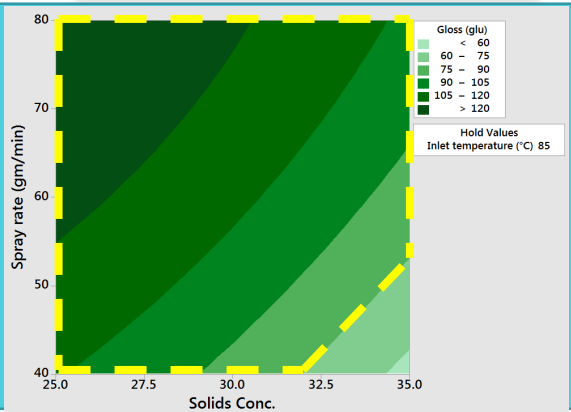
Inlet Temperature
75°C



Inlet Temperature
80°C



Inlet Temperature
85°C



In most cases, the new system had high gloss (> 80 glu) except under very dry conditions.

Recommended
Window of Operation

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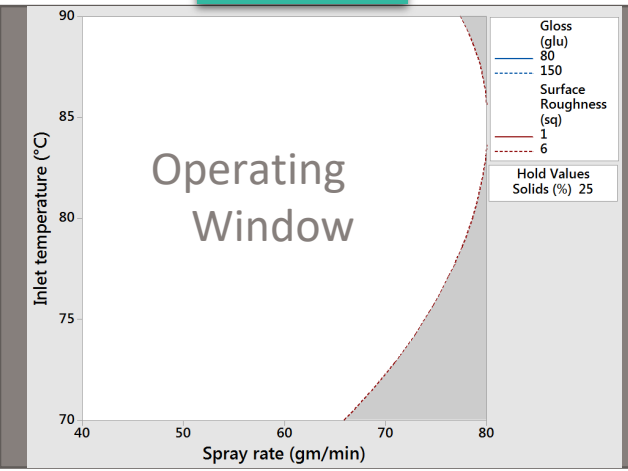
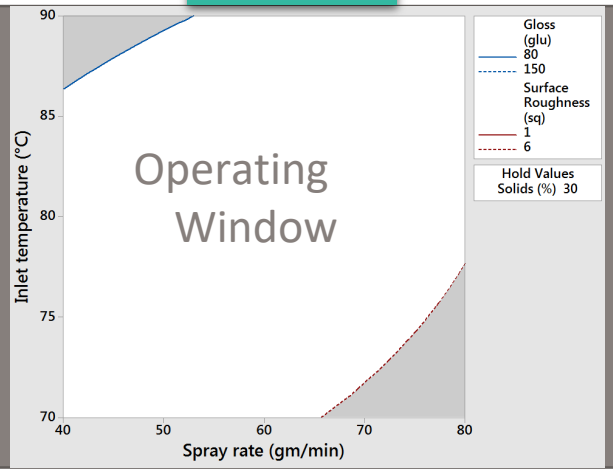
optimal operating window for gloss and smoothness

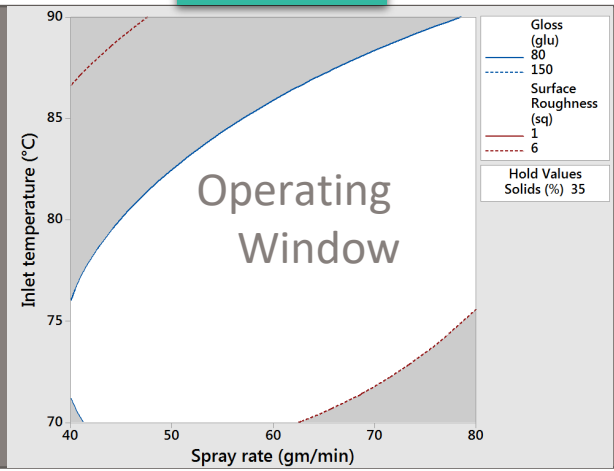
Solids 25%



Solids 30%



Solids 35%



Wide operating window across a range of temperature and spray rates resulting in acceptable surface rough ness and gloss

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summary

- The trials were successful with a total of 26 different experiments completed in < 2 days
- Most of the coating runs resulted in high quality appearance and significant process efficiencies
- Demonstrated high solids coating while meeting or surpassing acceptance criteria for elegance
- The increased solids concentration allowed the ConsiGma Coater to achieve higher throughputs than with traditional coating material

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Aquarius™ Genesis film coating systems

Specialized coating systems designed to improve:

- Process economics
- Product appearance
- Film adhesion and smoothness
- Product stability

Benefits:

- Potential cost and energy savings
- Reduce exposure of tablet cores to stressful process conditions
- Excellent adhesion
- Minimize moisture ingress to tablets

Aquarius Genesis film coating system shows improved productivity, good appearance and color stability characteristics, and is an excellent candidate for further testing in continuous processes.

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