Optimal Coating Process Parameters for a, Fully Formulated, Acrylic-Based, Enteric, Film Coating System

OBJECTIVES

- Identify the sensitivity of each response variable to the independent process variables.
- Determine the optimal coating process parameters.
- Demonstrate the overall applicability of a developmental film coating system.

METHODOLOGY

Materials

The developmental film coating formula was a fully formulated powder containing Eudragit L100-55 (supplied by Degussa) and other pharmaceutically acceptable additives including Yellow#6 lake pigment.

The coating dispersions were prepared using distilled water.

Experimental Design Software

The experimental design and data analysis were conducted using D.o.E. Fusion software supplied by S-Matrix Corp. (Eureka, CA).

Experimental Design Parameters

- Independent Variables:

Exhaust Heat (ºC)	30-35
Fluid Delivery Rate (grams/minute)	60-80
Pan Speed (rpm)	10-15
% Solids (in Water)	20-30

- Response Variables
  - Tablet Surface Roughness
  - Aspirin Dissolution
  - Standard Enteric Disintegration
  - Stressed Enteric Disintegration
  - Coating Process Efficiency

Number of Experimental Runs: 32 with 4 replicate pairs

Dispersion & Coating

- Dispersion Preparation:
  Silverson Hi-Shear Mixer: L4RT-A
  RPM: 10,000
  Duration: 10 min/run
- Coating Equipment/Conditions:
  24” O’Hara Labcoat II
  Spray Guns: 2 Spraying Systems Co (1/8-VAU-SS)
  Air caps: VA1282125-60-SS
  Atomization Air: 35 psi (2.4 bar)
  Pattern Air: 35 psi (2.4 bar)
  Pan Charge: 14 kg
  Inlet Air Flow Rate: 250 $ft.^3$/minute (7.1m^3/min)

Tablet Samples Used:

⇒ 325 mg

⇒ Sub-coat: Opadry II®, high performance film coating system, Y-30-18037 (theoretical 2% weight gain)

- Acrylic Coating Weight Gain: theoretical 10% for each run

Analytical Methods

Dissolution:	USP "Delayed-Release Aspirin Tablet" Monograph Q (pass) = 80% dissolved in 90 minutes Results expressed as time required for 80% of the aspirin to dissolve ("DT-80%")
Enteric Disintegration (ET):	Modified USP <701> using 50 rather than 6 tablets pH 1.0 (0.1 N HCl) for 1 hr Pass = no signs of disintegration
Stressed Enteric Disintegration (SET):	Friabilation (50 Tabs, 4 min, 100 revolutions) ET protocol subsequently followed
Surface Roughness:	Determined by MicroPhotonics (Allentown, PA) Average roughness (Ra) determined on five tablets/run
Coating Process Efficiency:	% Efficiency = $\frac{100*(\text{theoretical - actual weight gain})}{\text{theoretical weight gain}}$

RESULTS

Table 1. Replicate Pairs Indicated by R1-R4 Designations

Run No.	Exhaust Heat	FD Rate (g/min)	Pan Speed (rpm)	% Solids	DT-80% (min)	Coating Efficiency (%)	SET % Pass	Roughness
1	30	60	15	20	48	75	68	0.91
2 (R1)	33	70	13	25	36	74	64	1.19
3	35	70	13	25	39	74	44	1.2
4	30	80	10	30	46	85	80	1.47
5	35	60	15	20	48	76	76	1.02
6	30	80	15	30	41	82	74	1.21
7 (R2)	35	80	15	25	43	78	38	1.24
8	34	75	14	28	44	76	42	1.17
9	35	80	15	20	42	77	72	1.04
10 (R3)	35	70	15	30	25	73	34	1.32
11	35	80	15	30	32	75	64	1.47
12 (R3)	35	70	15	30	27	69	36	1.31
13	33	70	10	25	28	72	70	1.27
14 (R4)	35	60	10	30	24	65	22	1.43
15	30	80	10	20	42	77	98	1.06
16	35	80	13	30	40	72	54	1.48
17	34	65	11	23	53	64	52	1.18
18	35	80	10	30	41	68	42	1.51
19	30	60	15	30	32	67	18	1.21
20	35	60	15	30	28	64	14	1.29
21 (R4)	35	60	10	30	27	71	26	1.52
22	35	60	10	20	39	75	74	1.18
23	31	65	11	28	40	79	54	1.25
24 (R1)	33	70	13	25	40	78	68	1.2
25	30	70	13	25	41	81	74	1.09
26	35	80	10	20	46	79	92	1.18
27	30	80	15	20	57	90	100	0.92
28	30	60	10	20	38	79	88	1.05
29	34	65	14	23	32	76	50	1.13
30 (R2)	35	80	15	25	41	79	38	1.22
31	34	70	12	30	25	68	74	1.51
32	34	70	12	25	28	70	90	1.28

General Observations

- ET performance was insensitive to process conditions.
    - 98-100% of the tablets from each run passed
- All tablets were smooth; however, discernible differences in roughness were measured.
- No tackiness was observed in any of the runs.
- The standard deviation for each response variable measurement was < 5% based on replicate pair data analysis.

Key for Graphs:

LB = lower bound for selected independent variable
UB = upper bound for selected independent variable

Figure 1. Coating Efficiency vs. % Solids and Fluid Delivery Rate

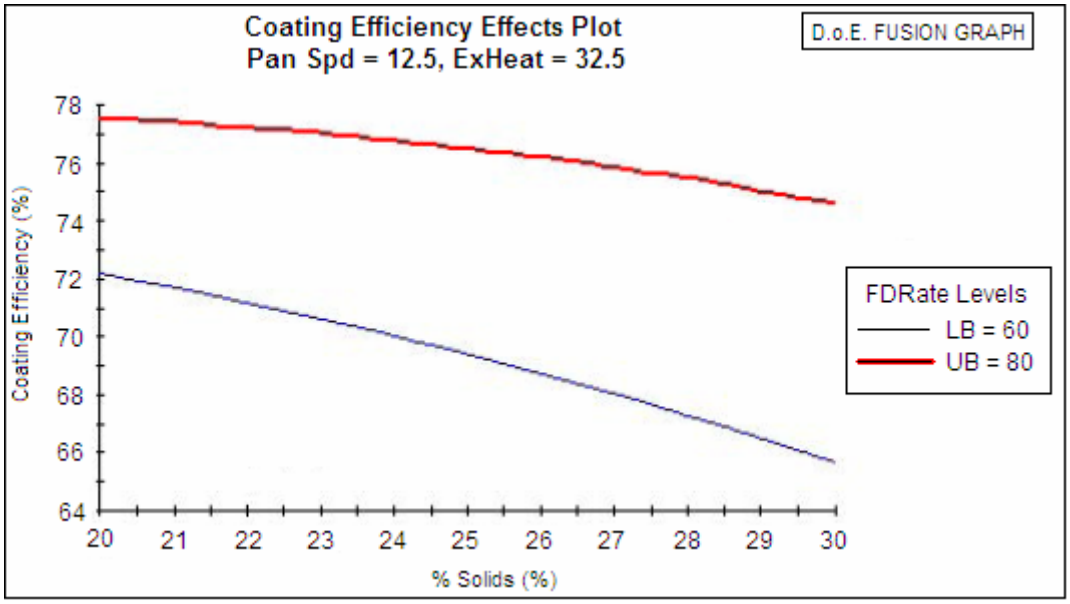

Figure 2. Coating Efficiency vs. Pan Speed and Exhaust Heat SET Performance vs. % Solids and Fluid Delivery Rate

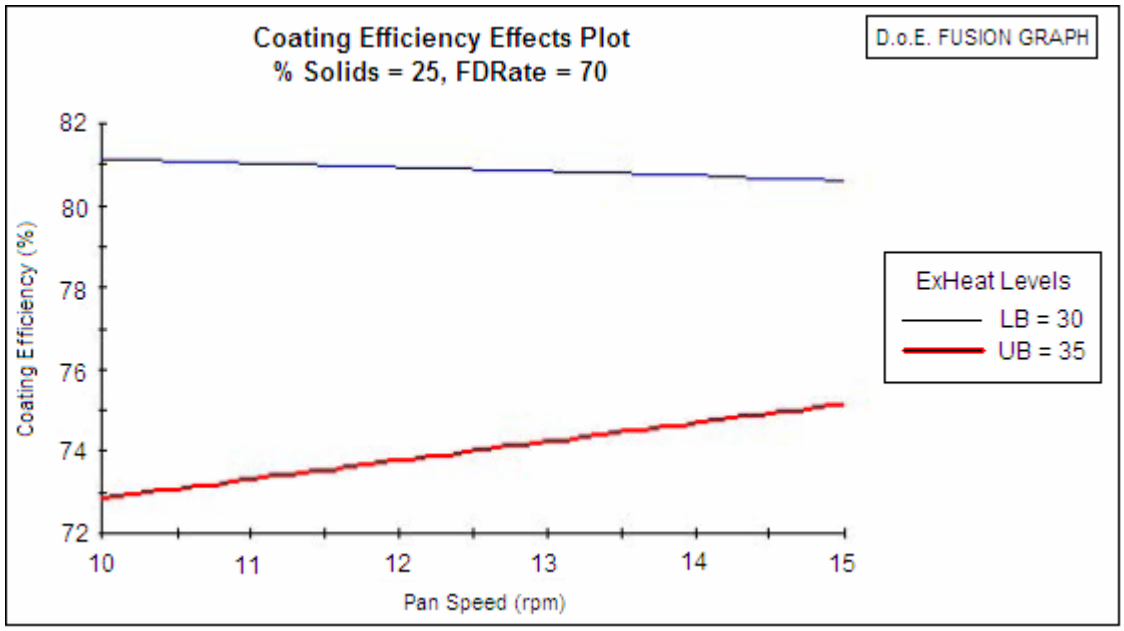

Figure 3. SET Performance vs, Solids and Fluid Delivery Rate

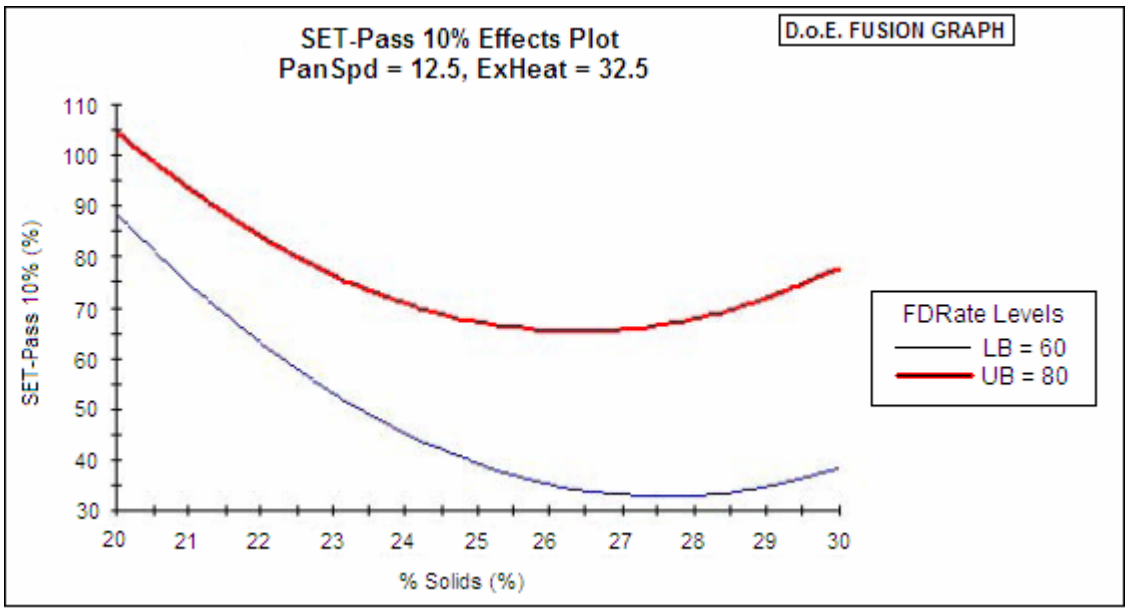

Figure 4. SET Performance vs, Pan Speed and Exhaust Temperature

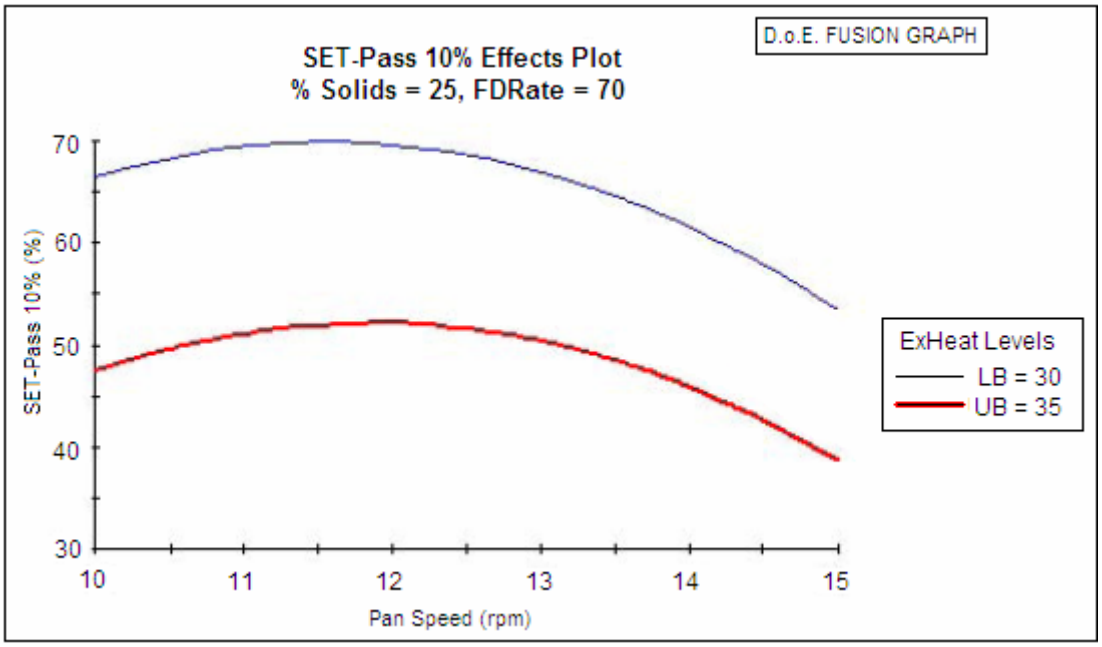

Figure 5. Surface Roughness vs. % Solids

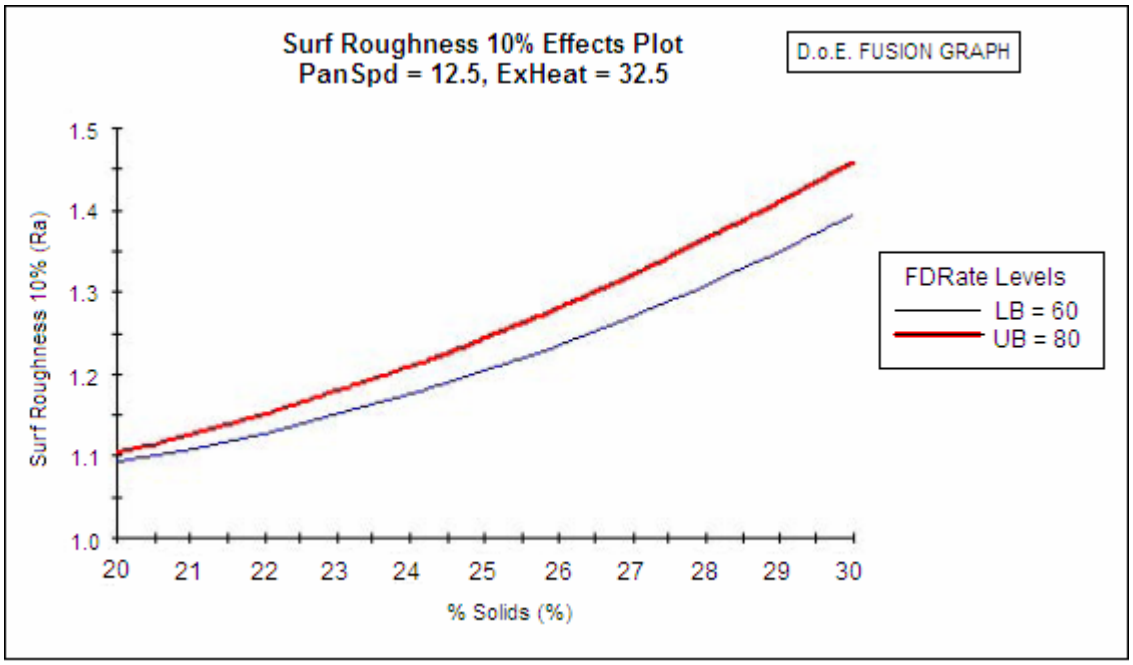

Figure 6. Fluid Delivery Rate Surface Roughness vs. Pan Speed and Exhaust Heat

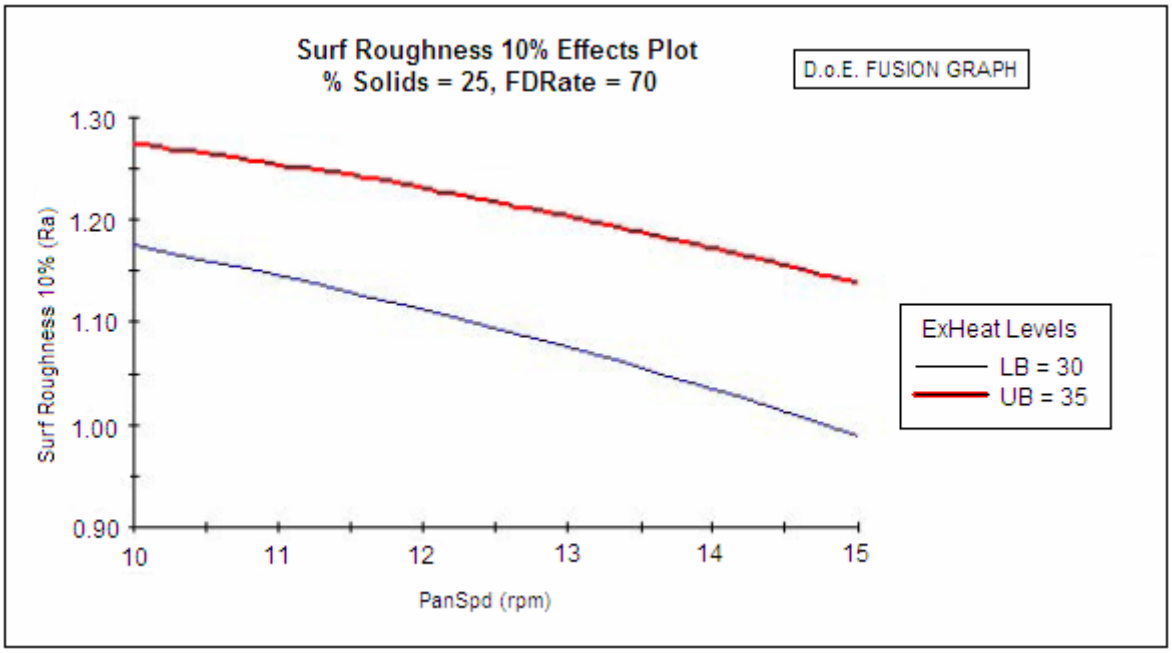

Figure 7. Dissolution Time vs. Pan Speed and Exhaust Heat

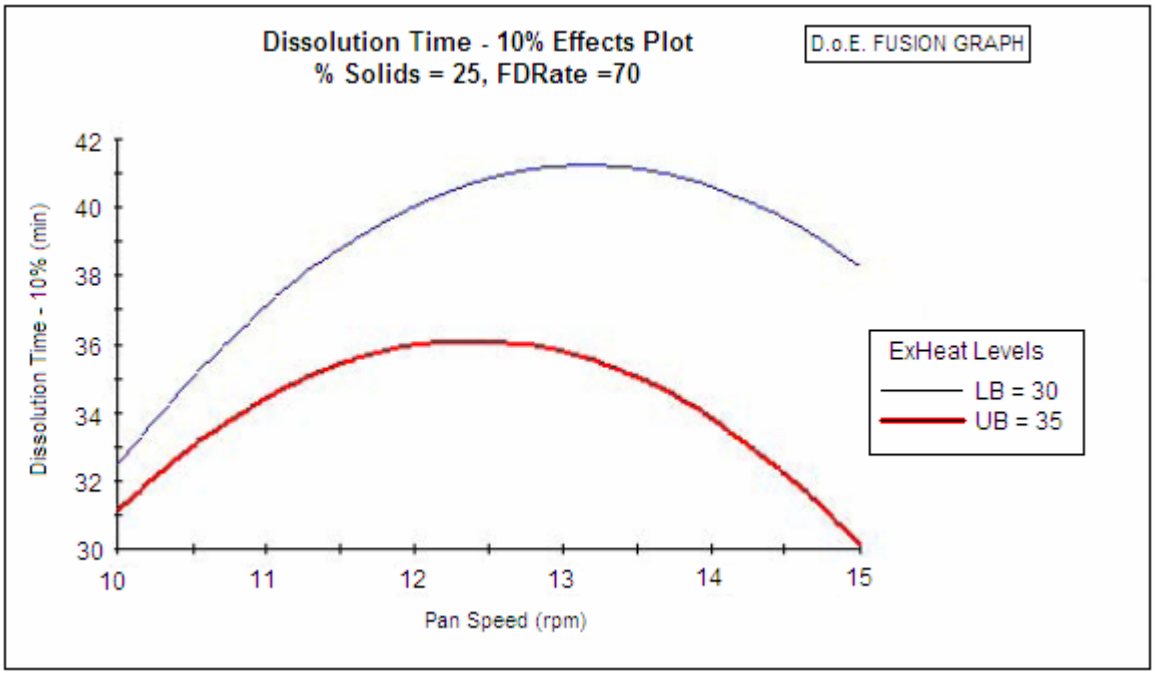

Figure 8. Dissolution Time vs. % Solids and Fluid Delivery Rate

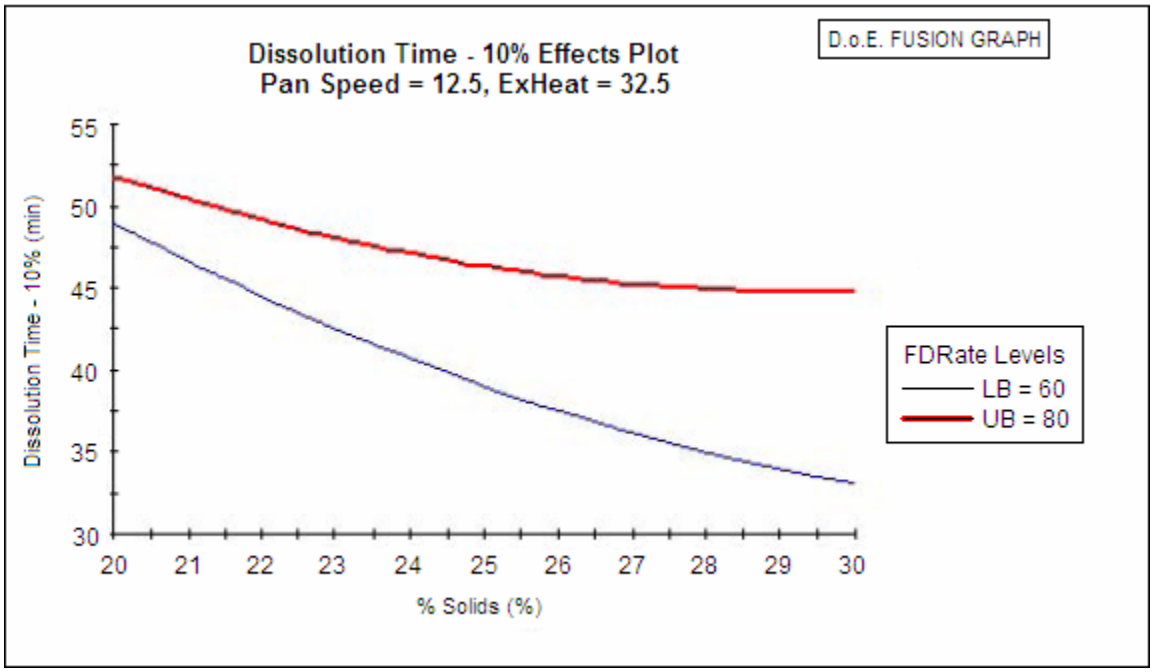

Table 2. Coating Parameters Optimized for Coating Efficiency (as calculated by D.o.E. Fusion)

Parameter	**Value**
% Solids	20
Fluid Delivery Rate (g/min)	80
Pan Speed (rpm)	15
Exhaust Temperature (C)	30
Predicted Coating Efficiency Response = 87%	
Actual Coating Efficiency (Run #27) = 90%	
(Parameters used in Run #27 were identical to those listed above.)	

Table 3. Run # 27- Response Variable Values

Response Range		**Run # 27**
Response Variable	For All Runs	Result
ET (% Pass)	98-100	100
SET (% Pass)	14-100	100
DT-80% (Minutes)	25-57	57
Roughness (Ra)	0.91-1.52	0.92
Coating Efficiency (%)	64-90	90

CONCLUSIONS

Coating process efficiency is maximized when:

- % solids and exhaust temperature are minimized
- Fluid delivery rate and pan speed are maximized

The SET pass rate and dissolution time were also maximized under the same conditions, since the amount of polymer applied to each tablet increased as the coating efficiency increased.

Surface roughness was minimized under these conditions due to the reduced incidence of spray drying.

The developmental film coating formula can be applied under high productivity conditions to obtain tablets which pass the USP Delayed Release Aspirin criteria.

Reprint of poster presented at AAPS – Nov 2000.