

# THE EFFECT OF CONSECUTIVE BATCH PROCESSING ON PARTICLE SIZE AND THERMAL BEHAVIOR IN A HIGH-SHEAR GRANULATOR

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## PURPOSE

To determine the effect of consecutive multi-batch high-shear granulation processing on:

- 1) particle size and
- 2) thermal processing characteristics.

## METHODS

Two controlled release formulations (A & B) and one immediate release formulation C were used in this study. Formulations and process parameters are shown in Tables 1 and 2. Formulations A and C were designed to produce large granules and formulation B was designed for small granules. Three batches of approximately 37.5 liters of each formulation were granulated one after the other in a 75-liter high-shear granulator (Vector GMX-75). Mixer blade speed during pre-mix and water infusion times was 210 rpm, and 330 rpm during the wet-mass (or high shear) time. The change in product temperature ( $\Delta T$ ) during the wet-mass time was monitored. After granulation, a portion of the batch was oven dried overnight at 90°C. The remaining portion was dried with 65°C air using a fluid-bed dryer (Vector FL-M-15) until the product was less than 2.5% moisture content. Sieve analyses were performed to determine the arithmetic mean diameters ( $D_{50}$ ) for oven and fluid bed dried granules.

Table 1 – Formulations

Dry Ingredients	Controlled Release A	Controlled Release B	Immediate Release C
HPMC, K 100 M	30%	--	--
HPMC, K 4 M	--	30%	--
Starch 1500	--	--	15%
MCC, 50M	--	--	30%
Lactose	70%	70%	55%
Total Weight (Kg)	15.70	16.59	18.34
Bulk Density (g/cc)	0.423	0.447	0.489

Table 2 – Processing Parameters

Process Parameters	Controlled Release A	Controlled Release B	Immediate Release C
Pre-Mix Time	3 minutes	3 minutes	3 minutes
Water Infusion Time	10 minutes	8 minutes	8 minutes
Water Added (% , Kg)	35.7% , 8.7 Kg	28.1% , 6.5 Kg	24.7% , 6.0 Kg
Wet Mass Time	5 minutes	7 minutes	7 minutes
Time Between Consecutive Batches	6 to 9 minutes	8 to 9 minutes	6 to 8 minutes

## RESULTS

CR Formulation A Summary

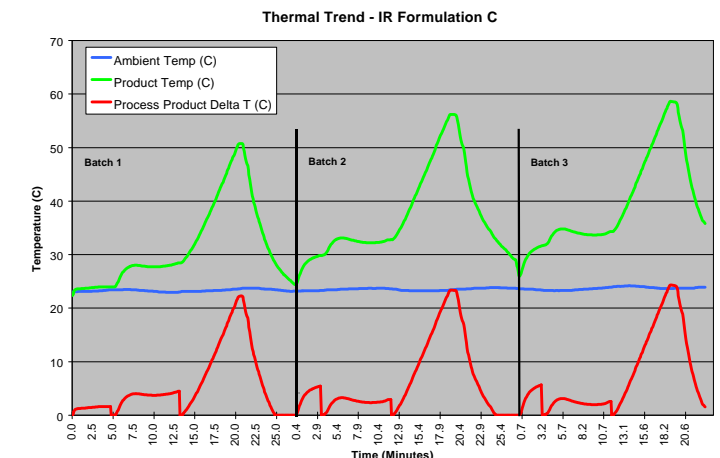
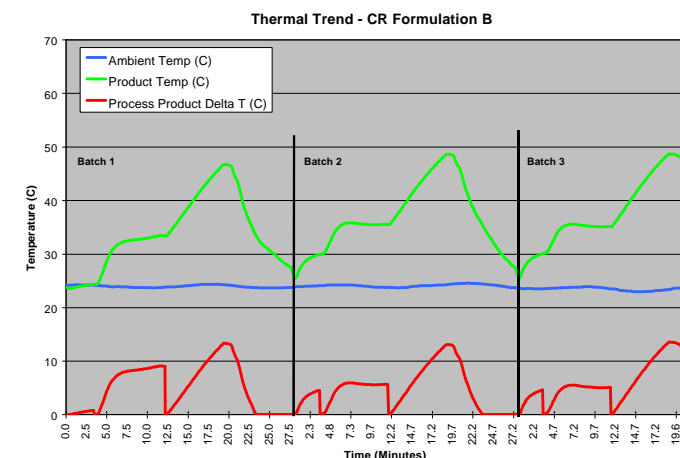
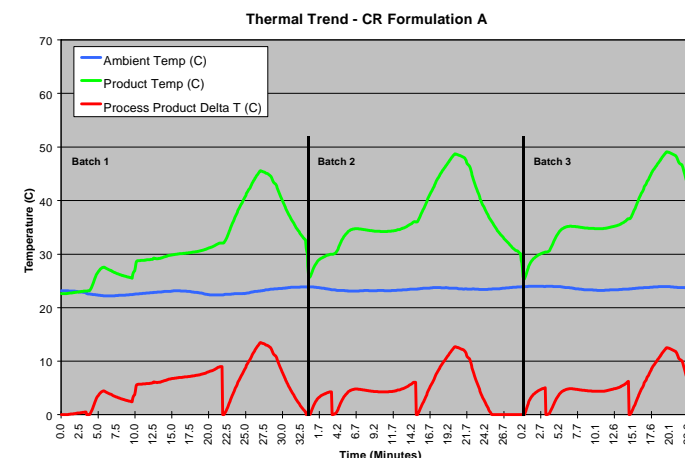
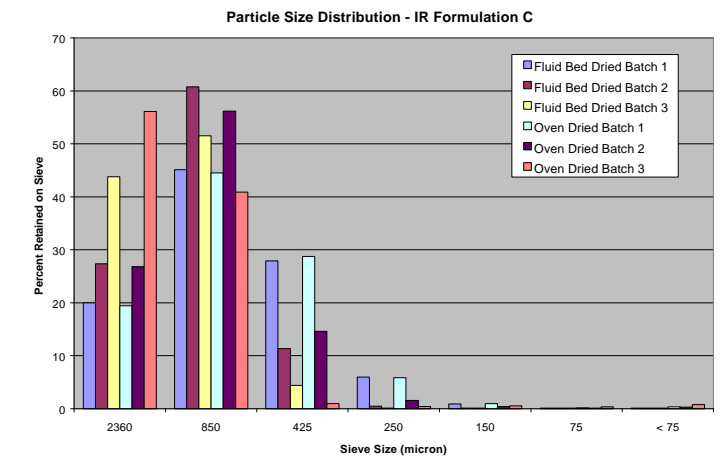
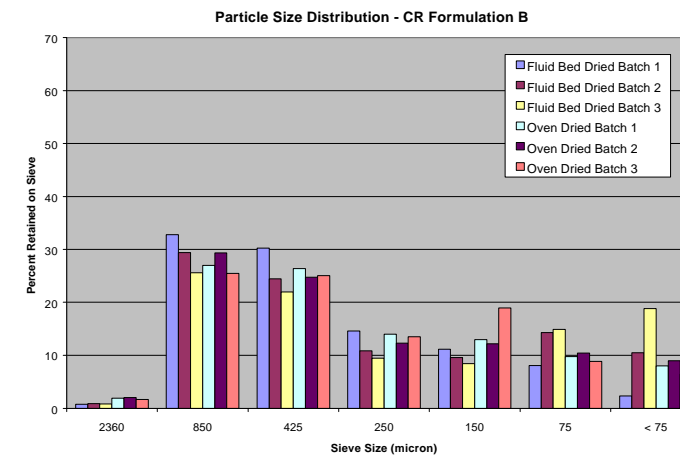
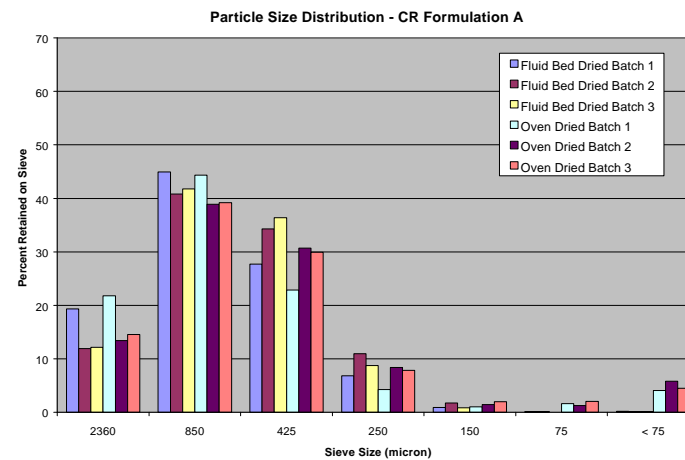
Parameter	1st Batch	2nd Batch	3rd Batch
D50 (Oven), $\mu\text{m}$	1182	1056	1054
D50 (FB), $\mu\text{m}$	1148	1040	1064
$\Delta T$ , °C	13.3	12.3	12.3

CR Formulation B Summary

Parameter	1st Batch	2nd Batch	3rd Batch
D50 (Oven), $\mu\text{m}$	761	794	721
D50 (FB), $\mu\text{m}$	826	790	767
$\Delta T$ , °C	13.3	13.0	13.4

IR Formulation C Summary

Parameter	1st Batch	2nd Batch	3rd Batch
D50 (Oven), $\mu\text{m}$	1147	1377	1545
D50 (FB), $\mu\text{m}$	1157	1444	1525
$\Delta T$ , °C	21.8	22.9	24.0



## CONCLUSIONS

Consecutive batch processing had no significant effect on  $D_{50}$  for the controlled released granulations in this study. However, consecutive batch processing did result in an increased  $D_{50}$  for the immediate release granulation. The change in product temperature during wet mass ( $\Delta T$ ) appeared to remain relatively constant for the controlled released formulations, but increased slightly for the immediate release formulation. The correlation coefficient between  $D_{50}$  and  $\Delta T$  for the immediate release formulation was 0.97. When processing multiple, consecutive, batches of a product similar to the immediate release formulation, the product temperature rise during the wet mass time should be taken into account if consistent particle size is important.

## ACKNOWLEDGMENT

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