In-line monitoring and analysis of fluid-bed pellet coating processes using **PATVIS** APA

10th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
PBP WORLD MEETING

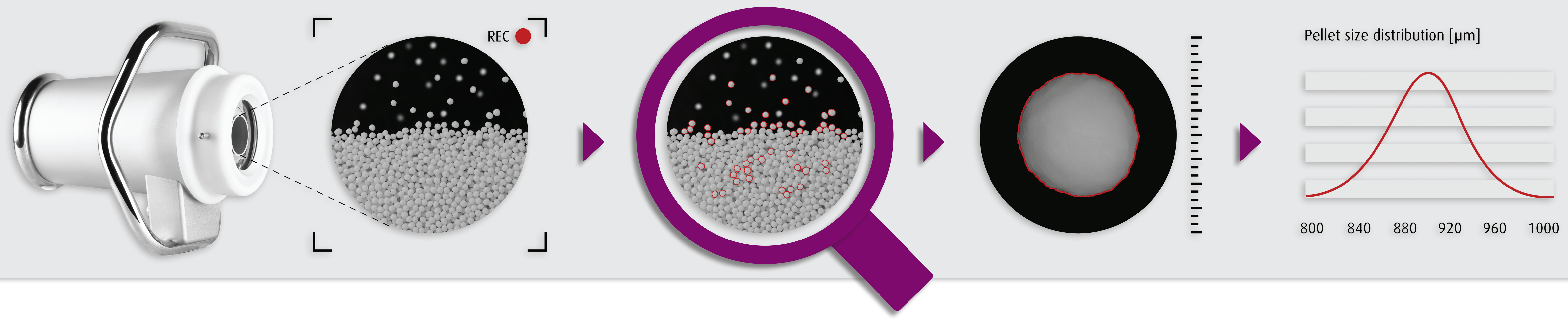
D. Kitak[1], G. Podrekar[1], C. Funaro[2], G. Mondelli[2], G. Bertuzzi[2], B. Likar[1,3], D. Tomaževič[1,3]
[1] Sensum, Computer Vision Systems, Tehnološki park 21, 1000 Ljubljana, Slovenia
[2] IMA S.p.A. Active Division, Via I Maggio 14, 40064 Ozzano Emilia, Bologna, Italy
[3] Laboratory of Imaging Technologies, Faculty of Electrical Engineering, University of Ljubljana, Tržaška cesta 25, 1000 Ljubljana, Slovenia

AIM

The aim of this study was to evaluate the performance of **PATVIS** APA (Sensum, Slovenia), a visual inspection system designed for in-line monitoring and analysis of pellet coating processes, on a fluid-bed coater. In particular, the pellet size was measured in real-time, from which the pellet coating thickness was estimated and compared to the final coating thickness determined by batch weight gain as a reference method.

INTRODUCTION

Coating is one of the most commonly employed processes within manufacturing of solid oral dosage forms [1]. Fluid-bed coating with a draft tube insert is the preferred method for coating pellets [2]. The main parameter that characterizes both the state of the coating process and the product is the coating thickness. It is especially important in active and functional coatings [3] and represents one of the most important critical quality attributes that should be routinely monitored [4].



MATERIALS AND METHODS

MATERIALS

The coating formulation was composed of hydroxypropyl methylcellulose (9.36%), polyethylene glycol (0.29%), riboflavin (0.13%) and deionized water (90.22%). The sugar pellet cores had a size distribution in the range of 850-1000 µm.

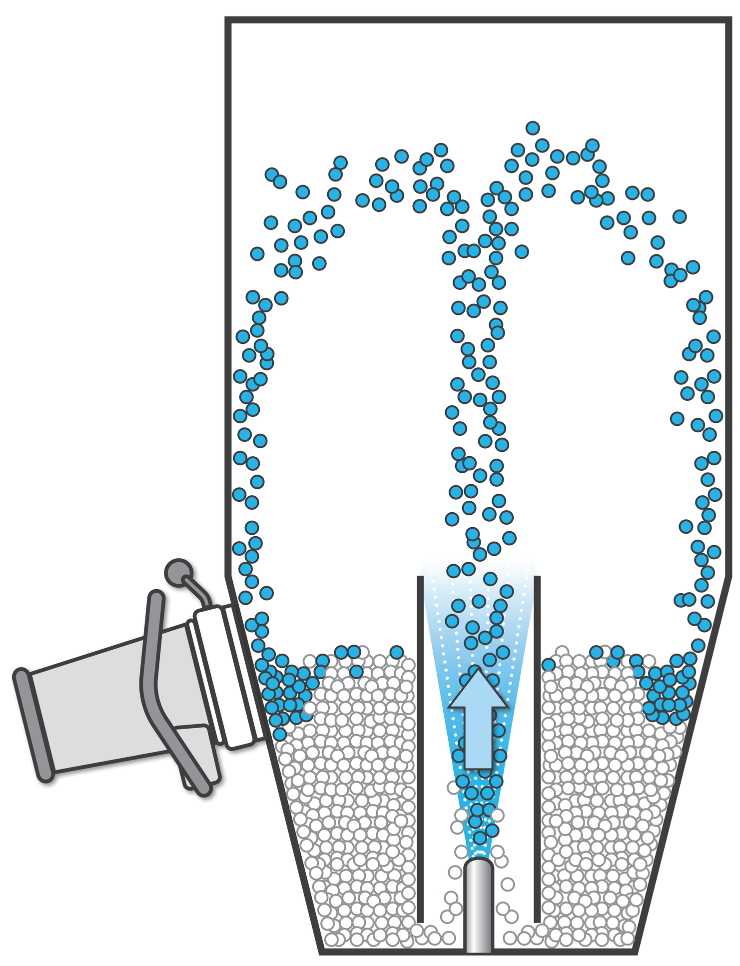
METHODS

COATING

Five coating processes were performed in the pilot-scale fluid-bed coater ARIA 120 (IMA, Italy) in the bottom-spray configuration (Table 1).

MONITORING

The image acquisition was performed through an observation window of the coater. Images were acquired at 100 frames per second, giving a 200 000 pellets sample size in a two minute sampling interval.



COATING THICKNESS ESTIMATION

The coating thickness was estimated from the difference between the medians (d_{50}) of the measured pellet size distributions at coating-start and coating-end time points.

Table 1: Process parameters (Tin, Qin = Temperature and quantity of the fluidizing air; SR = Spray rate; AP = Atomization pressure; CD = Column distance; WG = Theoretical weight gain)

Batch	Size [kg]	T_{in} [°C]	Q_{in} [m³/h]	SR [ml/min]	AP [bar]	CD [mm]	WG [%]
1	50	70	800	80	2	28	10
2	25	70	800	150	3	28	5
3	50	55	800	150	2	35	5
4	50	70	500	80	3	35	5
5	25	55	500	80	2	28	5

RESULTS AND DISCUSSION

Table 2: Final coating thickness estimation

	Coating thickness [µm]		Difference [µm]
Batch	**PATVIS** APA	Weight gain	**PATVIS** APA-Weight gain
1	15.0	14.5	0.5
2	7.6	7.6	0.0
3	7.6	7.1	0.5
4	5.8	6.0	-0.2
5	9.0	8.4	0.6
Root mean square (RMS)			0.42
Coefficient of determination (R^2)			0.99

PATVIS APA shows good correlation and minimum discrepancy with reference to the batch weight gain method, even for very thin film coatings (Table 2).

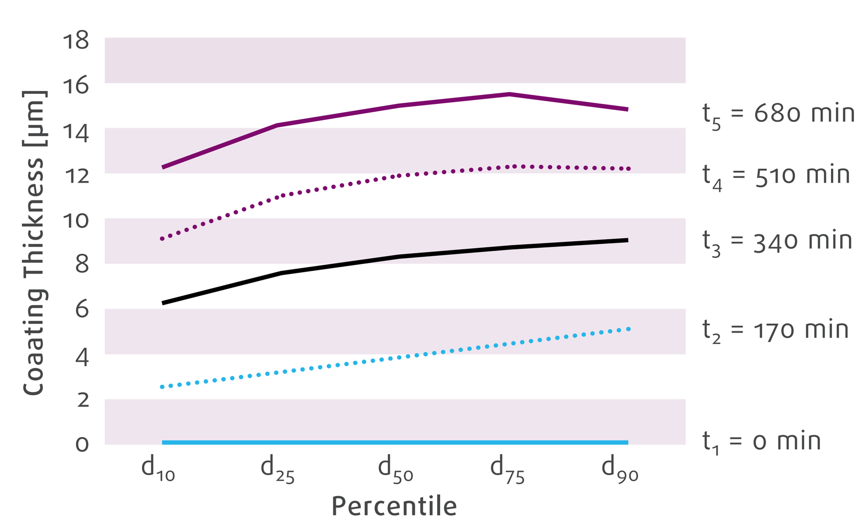


Figure 2:
Evolution of the coating thickness gains for batch 1

The evolution of the coating thickness gains (Figure 2) indicates that smaller pellets receive a lesser amount of coating material, which is consistent with previous findings [5].

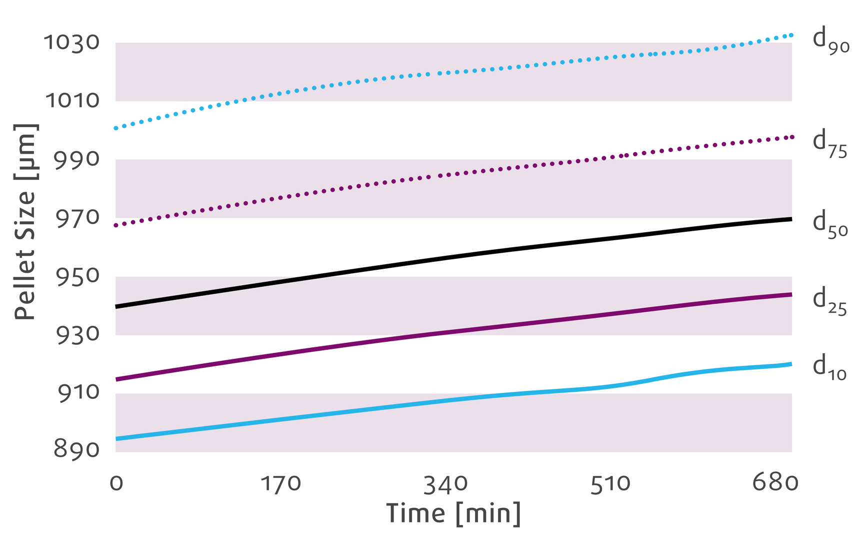


Figure 1:
Progress of the pellet coating process for batch 1

A clear trend in pellet growth throughout the coating process is evident for all the observed percentiles of the size distribution (Figure 1).

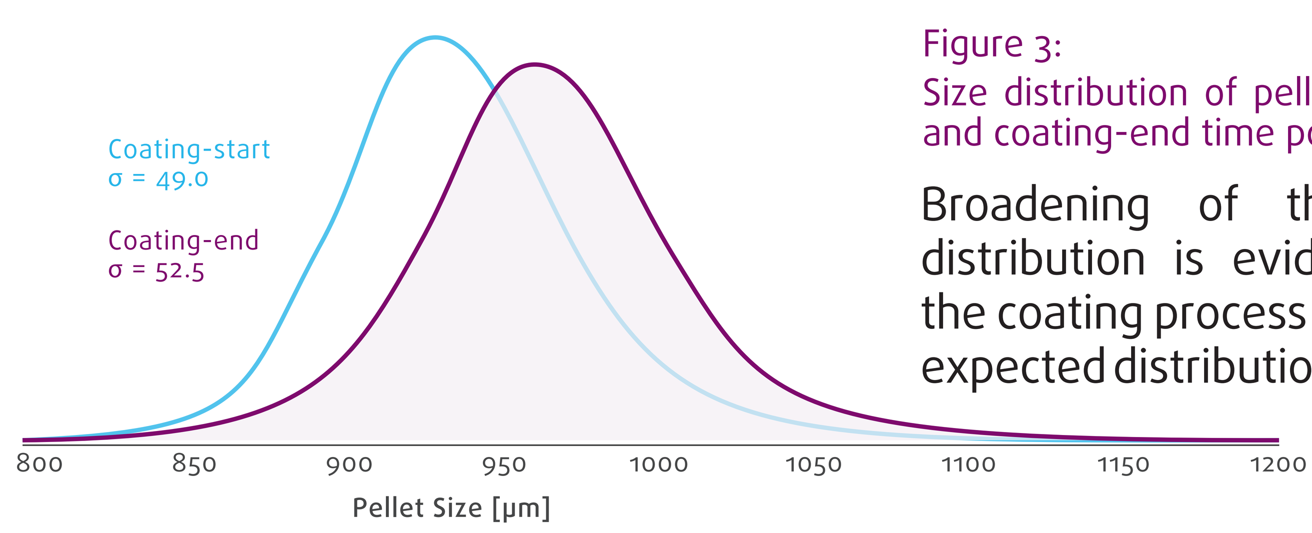


Figure 3:
Size distribution of pellets at coating-start and coating-end time points for batch 1

Broadening of the pellet size distribution is evident throughout the coating process in addition to an expected distribution shift (Figure 3).

CONCLUSION

Results show the potential of **PATVIS** APA as a process analytical technology (PAT) tool for more in-depth understanding, controlling and optimisation of pellet coating processes.

PATVIS APA revealed process footprints in the form of pellet size and the underlying size distribution, enabling effective process end-point detection and intervention.

1. Porter SC. Coating of tablets and multiparticulates. In: Aulton, ME (Ed), Aulton's Pharmaceutics: The Design and Manufacture of Medicines. London: Churchill Livingstone; 2013. p. 912.
2. Teunou E, Poncelet D. Batch and continuous fluid bed coating – review and state of the art. J Food Eng. 2002 Aug;53(4):325–40.
3. Knop K, Kleinebudde P. PAT-tools for process control in pharmaceutical film coating applications. Int J Pharm. 2013 Dec 5;457(2):527–36.
4. Kucheryavski S, Esbensen KH, Bogomolov A. Monitoring of pellet coating process with image analysis—a feasibility study. J Chemom. 2010 Jul 1;24(7-8):472–80.
5. Luštrik M, Dreu R, Šibanc R, Srčič S. Comparative study of the uniformity of coating thickness of pellets coated with a conventional Wurster chamber and a swirl generator-equipped Wurster chamber. Pharm Dev Technol. 2012 Jun 1;17(3):268–76.