COMPUTATIONAL X-RAY TOMOGRAPHY TECHNIQUES AS DEVELOPMENT TOOLS FOR NASAL AND PULMONARY DEVICE OPTIMISATION

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INTRODUCTION

Understanding of quality and interactions between assembled components of nasal and pulmonary devices with their corresponding formulations (liquids or powders) are critical to the development process of aerosol products. Recent advances in computational x-ray tomography has led to the availability of this non-destructive development tool[1] for the in-situ study of medical devices; providing critical information and allowing detailed analysis of nasal and pulmonary devices to optimize aerosol product development. Two examples are discussed here, the first details the improved understanding of powder retention in a dry powder inhaler device (DPI) and the second relates to the optimisation of a nasal spray pump actuator. In both cases solutions were found as a result of x-ray analysis which helped resolve development issues that would not have been so easily resolved using current investigative techniques.

MATERIALS AND METHODS

An X-Tek HMXST CT system[2] with the following settings was used for this study: 160kV microfocus x-ray system, 360° imaging with max. 4 images/degree, image size 200 x 200mm, magnification up to 160x, precision 0.01mm and 3D image collection times of ~1.5 hours. The software used for generating 2D images was X-Tek (UK) standard software and for 3D images a Digisense (France) software package. The 3D images can be viewed in any cross-section required and can be easily manipulated by the operator, Other software features include viewing of individual components by material density resolution (e.g. different plastics, rubber or metal components), dimensional measurements and importation into computer aided design (CAD) systems for comparison with engineering drawings or to generate stereo lithography files.

ANALYSIS AND RESULTS

DPI powder holdup investigations – during the development of the Valois Prohaler® DPI, it was noted that certain powder formulations had a tendency to be held up in the device engine leading to compromised emitted dose (ED) and fine particle fraction (FPF) performance. Using 3D x-ray tomography analysis it was possible to locate and qualitatively assess the areas of powder holdup in the device in-situ with this non-destructive technique (Fig 1). The output of this analysis led to the optimization of the device in terms of engine design, airflow path and resistance, following input of the information into a computational fluid dynamic model. The result was reduced powder holdup in the device and improved ED and FPF performance (Table1).

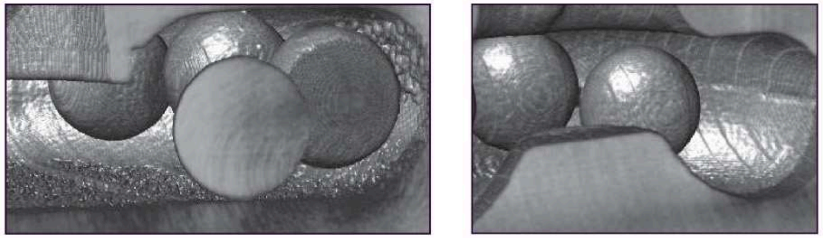

Figure 1. DPI powder holdup pre-optimization (left) and absence of powder holdup post-optimization (right).

	Emitted Dose (% of Fill Dose) mean (SD)	FPF (% < 5.8 µm of ED) mean (SD)
DPI pre-optimisation	61 (10)	26 (3)
DPI post-optimisation	82 (9)	33 (2)

Table 1: DPI performance improvements following optimization as a result of x-ray analysis.

ANALYSIS AND RESULTS...CONTINUED

Nasal actuator molding optimization – the introduction of new large scale tooling from small scale (8 cavities) to industrial scale (32 cavities) molds revealed issues of incomplete cavity filling during plastic injection molding leading to "air pockets". These can lead to weakness in certain thick walled areas of plastic components located furthest from the plastic liquid injection points. In turn this can lead to the reduction of the liquid channel path in the actuator head which can impact aerosol spray performance. Detailed x-ray analysis allowed easy location and quantification of these issues. This information was then used in computational molding simulation tools in order to optimize the molding process (temperatures, injection points, plastic liquid flow paths and cavity designs) leading to the optimal production of robustly molded nasal actuator components (Fig 2).

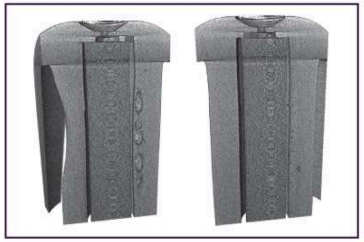

Figure 2. Improvements in nasal actuator moulding quality a result of optimisation following x-ray analysis (left ⇨ right).

CONCLUSIONS

Computational x-ray tomography is a powerful tool to aid product development. It has contributed key technical information in building the knowledge and design space during the application of quality by design principles for several inhalation devices in development. This non-destructive tool allows the collection of valuable information, in-situ, for a range of device materials (plastics, rubbers, metals) whilst allowing the study of the devices in the presence of their formulations; whether they be aqueous based, pressurized liquids or powders.

REFERENCES

1. Stuart, A. (2009), "The role of x-ray computed tomography as an investigation tool in hardware design", Dalby, R.N., Byron, P.R., Peart, J., Farr, S.J., Suman, J.D. and Young. P. (eds), Respiratory Drug Delivery 2009, 213-216
2. URL website, http://www.xtekxray.com (visited January 07, 2010)