Alkermes Pharma Ireland Ltd collaborate with Innopharma Labs to enable enhanced control of granulation, milling and spheronisation of a manufacturing process

I. Jonesa*, James Burkeb.

a Innopharma Labs, Ireland  bAlkermes Pharma Ireland Limited, Ireland

*corresponding author, email: jonesi@innopharmalabs.com

1.0 INTRODUCTION

Alkermes Pharma Ireland Ltd (Alkermes) and Innopharma Labs (Innopharma) have collaborated to integrate Innopharma’s eyecon™ particle characteriser within one of Alkermes’ centrifugal spheronisation manufacturing processes. Nine months later, this collaboration has generated yield and time savings for Alkermes.

Innopharma’s eyecon™ particle characteriser platform is designed to understand spheroid morphology, sphericity and size distribution. All three parameters are critical to the the manufacturing process. Coating processes for the purposes of extended release characteristics can also be affected by excessive variation in morphology, shape and size distribution. In addition, a subsequent sieving step to remove excessively large or small spheroids can affect yield if there is not a narrow size distribution of spheroids. Alkermes Pharmaceuticals have integrated the eyecon™ particle characteriser within their manufacturing process in order to fulfil Quality by Design QbD, Process Analytical Technology (PAT) and lean manufacturing
principles applied at the plant. Applying these principles has enabled enhanced understanding of a specific manufacturing process.

2.0 TECHNOLOGY OVERVIEW

The eyecon™ particle characteriser was developed by Innopharma and was launched in January 2011. It was tailor-made for the pharmaceutical manufacturing sector and is based on high speed 3-D machine vision which enables the capture of both the size and shape of pharmaceutical particles between 50 and 3000 microns. A continuous image sequence of the particles is captured using illumination pulses, with a length of one microsecond for freezing the movement of particles which are moving with a speed up to several meters per second. The illumination is arranged according to the principle of photometric stereo for capturing the 3-D features of the particles in addition to a regular 2-D image. The particle size is estimated from the images using the 2-D and 3-D information, applying novel image analysis methods and direct geometrical measurement. Both the minimum and maximum diameters of each spheroid are then used to determine the size distribution and shape characteristics. In addition, the method requires no contact with product and can be applied, for example, behind a view glass on a granulator, mill or spheroniser without physical modification of the process equipment.
3.0 MANUFACTURING PROCESS OVERVIEW

The IPDAS® (Intestinal Protective Drug Absorption System) is Alkermes’ multi-particulate drug delivery system which is currently applied in the manufacture of one of its commercial products.

A high density multi-particulate controlled release tablet technology, the IPDAS® System is designed for use with gastrointestinal irritant compounds.

Once an IPDAS® tablet is ingested, it disintegrates and disperses beads containing a drug in the stomach, which subsequently pass into the duodenum and along the gastrointestinal tract in a controlled and gradual manner, independent of the feeding state. The intestinal protection of IPDAS® technology is by virtue of the multi-particulate nature of the formulation, which ensures wide dispersion of irritant drug throughout the gastrointestinal tract. (Bhupendra. G. Prajapati, 2009)

Benefits offered by the IPDAS® technology include:

- High concentration multi-particulate formulation
• Minimizes local concentration effects - once ingested micro-particulates are dispersed throughout GI tract in a controlled and gradual manner independent of the feeding state.

• Immediate release and sustained release components for 24 hour duration

The key challenges for this IPDAS® process were

1. Excessive time required awaiting sieve analysis results;
2. Excessive coating activities to impart the correct dissolution profile for the product;

4.0 BENEFITS OF THE EYECON™ PARTICLE CHARACTERISER

Through the utilisation of the eyecon™ particle characteriser and the adaptation of QbD, PAT and lean manufacturing principles, Alkermes have now adopted a more robust analytical method and have qualified the system to make informed process decisions around the manufacture of their IPDAS® technology related products. Yield improvements of 8% have been realised and the expectation is that the use of the eyecon™ particle characteriser will reduce the cycle time for this type of product by 50%.

Paul Cruise, Engineering Director at Innopharma Labs has commented ‘We were delighted to collaborate with such an innovative partner as Alkermes. Their willingness to adapt new technology and to improve their process so effectively has been really impressive’

James Burke, Director of Manufacturing at Alkermes Pharmaceuticals stated ‘the eyecon™ particle characteriser has helped us understand our process at a new level. The ability to
acquire images and size distribution data of our spheroids in real-time is a significant improvement for this process. The savings we realized are tangible.’

Alkermes, Athlone (formerly Elan Drug Technologies) offer contract development and manufacturing services from their Athlone, Ireland facility. They specialise in lean technology transfer and robust manufacturing processes through the utilisation of QbD and PAT methodologies.

Innopharma Labs develop and distribute PAT analysers for the pharmaceutical industry. The eyecon™ particle characteriser can be used to understand and control various granulation, milling and spheronisation processes.

Innopharma Labs
Contact: Mike Mulcahy
E: mulcahym@innopharmalabs.com
W: www.innopharmalabs.com

Alkermes Contract Pharma Services:
Contact: Fidelma Callnan
E: fidelma.callnan@alkermes.com
W: http://www.alkermes.com/Contract-Services