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A quality- by- design approach for the implementation of a manufacturing license change using a qualified scale- down process model

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A QUALITY- BY- DESIGN APPROACH FOR THE IMPLEMENTATION OF A MANUFACTURING LICENSE CHANGE USING A SCALE- DOWN PROCESS MODEL.

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Influenza vaccines are required to be re formulated every year to account for antigenic drift with recommendations coordinated by the World Health Organisation. This results in a short development cycle of only six months to be able to choose and characterise a suitable reassortant of a recommended strain and proceed to commercial manufacturing of the influenza antigen and vaccine product. Due to the ongoing healthcare crisis brought about the Covid-19 pandemic, the demand for influenza vaccines has increased rapidly requiring vaccine manufacturers to be able to meet this demand and be the first to market in the season. This has necessitated the implementation of novel approaches to increase antigen and vaccine product yield in a rapid and yet robust process development.

One of the potential yield improvements was the introduction of an optimised quantity of Hydrocortisone solution in the egg-based platform process at the inoculum stage for the Influenza A strains, which was already introduced and in use for Influenza B strains. In this presentation, we demonstrate the implementation of a scale-down modelling to support process changes and their subsequent regulatory approval.
To facilitate the implementation of this change to the manufacturing license with various regulatory bodies, we devised a protocol to produce representative antigen batches at scale-down (i.e., 1% scale from a qualified area to the commercial batches) at higher and lower Hydrocortisone input on a variety of Influenza A strains. A total of 11 batches executed with various hydrocortisone inputs and Influenza A seasonal strains showed that the resulting antigen met internal drug substance batch release specifications and showed yield increase of 9-24% across various seasonal Influenza A strains, which could potentially be higher at the commercial scale.

A collaborative approach was also established from the start with regulatory bodies allowing us to understand intricacies and consequences of this change to the manufacturing license. We were able to demonstrate agility during the implementation process due to constant dialogue, for example, demonstrating current label claim of the vaccine product with the new process and generation of ‘worst case’ toxicology data, in addition to routine requirements.

This change is currently under implementation and has received approvals in a short time that will allow us to proceed directly to commercial manufacturing result in savings and the opportunity to produce the needed flu vaccine supply without interruption instead of performing the costly and facility/time-consuming engineering runs