PhD in Chemical Engineering

Research Title:

Spectroscopy techniques as PAT monitoring tools for the development of biopharmaceutical product processes

Funded by	Merck Serono SpA

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Context of the research activity	Merck-Guidonia site is center of excellence for the development of new biological entities (NBEs) and new chemical entities (NCEs) with the purpose of contributing to patient's health. Drug Products (DP) can be delivered as liquid or freeze-dried presentation. The proposed PhD program, in collaboration with Merck, will be about the implementation of PAT tools based on spectroscopy techniques (e.g. Raman, NIR) in biopharmaceutical drug product process development. Spectroscopy techniques have proven to be useful tools in a vast number of fields, including pharmaceuticals. Spectroscopy analytical techniques have been increasingly implemented at different stages of drug discovery and development; this includes formulation and process analytics in late phase drug product development. In the frame of this PhD program it will be investigated how spectroscopic techniques can be introduced as in situ/in process monitoring PAT tools for various pharmaceutical unit operations and processes including freeze-drying. Large datasets can be generated using spectroscopic techniques demanding multivariate data analysis approaches like principal component analysis (PCA), partial least square regression (PLS) and partial least square discriminant analysis (PLS-DA). Data analysis will be part of PhD program.

	The design of surrogate solution for use in biopharmaceutical drug product process development will be part of PhD program. The manufacturing process for such formulated protein solutions typically consists of several unit operations such as thawing of the drug substance, compounding of the bulk drug product solution, sterilization, filling, lyophilization (where applicable), crimping, visual inspection, and packaging. A low-risk approach to development of these processes would be to perform studies at full scale using the same equipment used in clinical or commercial production. Since there are limitations on the supply of expensive drug substance for use in development studies, one solution could be the use of surrogate solution without the active molecule in the drug product process development and in the technical runs carried out at large scale.
Objectives	**Objective 1.** Implementation of Raman spectroscopy and/or additional spectroscopic techniques in biopharmaceutical drug product process development. ○ Training and Familiarization with Raman spectroscopy and/or additional spectroscopic techniques ○ Training on drug product manufacturing process for biopharmaceuticals ○ Identification and monitoring of process steps (e.g. mixing; freeze-drying) in which Raman spectroscopy and/or additional spectroscopic techniques can be introduced with focus on critical quality attributes potentially affected by process unit operation **Objective 2.** Data analysis and management of spectra generated by spectroscopic techniques. ○ Training and familiarization with multivariate analysis and the software able to carry out the analysis (e.g. SIMCA) ○ Development of model suitable to predict the behavior of quality attributes which can be affected by drug product manufacturing process and model integration in PAT manager (e.g. SynTQ) **Objective 3.** Development of surrogate solution for use in biopharmaceutical drug product process development. ○ Surrogate design for use in both lab-scale process development studies and at-scale technical runs using the production equipment ○ Surrogate formulation development to meet the desired attributes identified in the surrogate phase design

Skills and competencies for the development of the activity	- Chemical engineering background - Knowledge of basic statistics and spectroscopic techniques (e.g. Raman, NIR, UV-VIS) - Knowledge of modeling principles - Literature scouting - Protocol and report issuing