Real Time Quality Control of ATMPs Fabrication Using White Light Spectroscopy

B Wacogne[1,2], N Vaccari[2], M Belinger-Podevin[2], C Koubevi[2], A Rouleau[2], and A Frelet-Barrand[2]

[1]*INSERM CIC1431, CHRU Besançon, Besançon, France*
[2]*FEMTO-ST institute, Univ. Bourgogne Franche-Comté, CNRS, Besançon, France*
Contact Email: bruno.wacogne@univ-fcomte.fr

The fabrication of Advanced Therapy Medicinal Products presents many difficulties, among which the fight against the contamination of the bacterial culture. Also, the production can last several days, and the whole process takes place in a clean and sterile environment. Numerous samplings of the bioreactor's content are made to perform regular quality controls. The goal is to monitor cell growth and detect any contamination. Drawbacks are a delayed result of the control and an added risk of new contaminations due to samplings. All these difficulties explain the enormous cost of these new drugs, which prohibits their distribution to the largest number of patients. A way of reducing cost is to automate the fabrication as much as possible. To this end, a real-time and sampling-less cell growth monitoring and quality control method may help. Indeed, real-time monitoring avoids a certain number of possibly deleterious bioreactor content sampling. Maybe more importantly, in situ quality control may help stop the fabrication as soon as something unwanted occurs in the bioreactor. Although old, white light spectroscopy can be easily integrated into the bioreactor's environment and allows sampling less, real-time and closed system analysis of the cell growth.

In this conference, we present simple white light spectroscopy means to simultaneously monitor T-cell growth and detect contaminations in real-time. Methods are based on the mathematical description of T-cell and bacteria absorption spectra shapes. T-cell concentrations are measured with uncertainties below 10% (equivalent to sampling-based techniques), and contamination can be detected a few hours after it occurred (to be compared to at least one day currently). Implementing such a system would be of great interest in terms of research, industrial manufacturing and more importantly, in terms of benefit to patients.