Biopharmaceutical production is a growing area of the pharmaceutical industry and cell culture is a key process in the production of many biopharmaceuticals. The cell culture media used for the growth of cells plays an important role in the quality and efficiency of biopharmaceutical production. A non-destructive, reliable, efficient and cost effective method to analyze complex cell culture media is extremely important to ensure high quality process control.

Raman spectroscopy is an analytical technique capable of providing highly detailed chemical information about a variety of samples. It is non-destructive, fast and requires little to no sample preparation. Many pharmaceutical companies have adopted Raman spectroscopy as an effective and efficient technique for raw material identification, in-process analysis and final product authentication. Handheld and portable Raman devices are qualifying that incoming raw materials are both the correct material and meet sufficient quality. The USP and EP now recognize Raman spectroscopy as a viable technique for compendial identification.

Fluorescence from cell culture media is a common problem associated with handheld Raman analyzers using 785 nm laser excitation sources. When present, fluorescence interference is typically orders of magnitude higher than the Raman signal, preventing successful chemical identification and/or analysis. Fluorescence can be significantly reduced via the purposeful selection of a Raman spectrometer’s excitation laser’s wavelength. Four synthetic cell culture media were analyzed with Rigaku Raman FirstGuard™ Spectrometers using both 785 nm and 1064 nm laser excitations (Figures 1 – 4). The 785 nm spectra show significant fluorescence, making it difficult to obtain reliable and specific information about the sample. In contrast, the 1064 nm spectra show clear Raman peaks that can be used to reliably distinguish different media. Figure 5 shows the Raman spectra from two cell culture media, both of which are versions of a minimum essential medium developed by Harry Eagle, that have only small differences in their components. Clear differences can be seen in these Raman spectra and when a correlation analysis was performed these two media could be accurately and reliably distinguished.

**Figure 1.** Comparison of 785 nm and 1064 nm excitation Raman spectra of cell culture medium; Minimum Essential Medium developed by Harry Eagle.

**Figure 2.** Comparison of 785 nm and 1064 nm excitation Raman spectra of cell culture medium; Minimum Essential Joklik Modification.

**Figure 3.** Comparison of 785 nm and 1064 nm excitation Raman spectra of cell culture medium; Medium 199.

**Figure 4.** Comparison of 785 nm and 1064 nm excitation Raman spectra of cell culture medium; Dulbecco Modified Eagle Medium.

**Figure 5.** 1064 nm laser excitation Raman spectra of two slightly different modifications of Minimum Essential Medium Eagle.