



## Life through a lens; novel quantitative cell imaging

LGC scientists, in collaboration with leading tissue engineering companies, have developed a rapid, quantitative imaging approach to measure the quality of cells in tissue engineered products in order to improve manufacturing, storage and transportation processes.

Assessment of 3D cell distribution during the manufacture of tissue engineered products.



## The Requirement

Tissue engineering is an emerging healthcare technology which uses cells, engineering and materials to manufacture functional replacement tissues which can be used in clinical applications. As with any pioneering new technology, regulation is critical for product quality, safety and development. However the novel aspects that make the future of tissue engineering so promising also make complying with regulation more challenging. The European Medicines Agency (EMA) guidelines require cells to meet a minimum quality for market authorisation. However, making even routine cell measurements, such as viability assessment, proves challenging in the complex environment contained within a tissue engineered product. This is because the cells are often manufactured in a 3-dimensional (3D) biomaterial matrix which is not compatible with standard measurement assays.

## The Solution

Manufacturing processes can affect cells by imparting stresses which they would not normally be exposed to in their natural corporeal environment. This may trigger stress responses in the cells which affect cell behaviour and can, in extreme cases, lead to apoptosis (cell death) affecting cell viability and the overall quality of the final product. Determining these responses is challenging, so development and validation of assays is critical to establishing an accurate measure of product quality.

Fluorescent probe technologies are now routinely used in cell biology to study important cellular events but are usually only applied to cells growing in monolayer or in suspension. However, LGC has succeeded in validating the use of fluorescent probes, in combination with laser scanning confocal microscopy (LSCM), to enable multiplexed analysis of cells within 3D tissue engineered products. Different fluorescent probes can be combined to measure biological processes such

as active metabolism, indicating viable cells, DNA intercalation indicating damaged or dead cells, and the production of reactive oxygen species, which is linked to cell stress. In combination with LGC's custom designed image processing platform, measurements can be made both in 3D and in real-time.

## Impact

Using this approach, scientists at LGC have demonstrated how cell viability and cell stress change, not only in response to manufacturing processes, but also during storage and transportation. This information can be used to minimise the stress placed upon the cells allowing production and distribution processes to be optimised, thus improving product quality and consistency. This has the potential to support the needs of the tissue engineering industry by providing a valuable tool to characterise cellular products and ensure a controlled consistent manufacturing process that meets the expectations of the regulators.

Dr. Christopher Bravery, Director of Consulting on Advanced Biologicals says "Regulatory authorities require that products can be manufactured consistently and that every dose can be guaranteed to be potent when delivered. Viability, morphology and phenotype are all important cellular characteristics that cannot easily be confirmed in 3D tissue constructs. This methodology developed by LGC fills a technology gap that is holding back tissue engineering since quality cannot otherwise be confirmed without destroying the product."

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