To whom it may concern

Freiburg, March 30th 2015

Change in analysis of GMP Grade CellGenix DC Medium

Order numbers 20801-0500, 20801-0100, 20901-0500, 20805-0500, 20905-0500 and 20905-1000

Dear CellGenix Customer,

CellGenix strives to provide you with highest quality products suitable for clinical therapy applications. Safety, performance and product consistency are our main concerns.

This is to inform you about current improvements in flow cytometry analysis of CellGenix DC Medium testing.

An important principle of flow cytometry data analysis is to selectively visualize the cells of interest while eliminating results from unwanted particles e.g. debris. This procedure is called gating and is a negative selection of unwanted events. As a general guide, this is done by size, which is estimated by forward scatter (FSC) - cellular debris is usually FSC-low. And dead cells often have lower FSC and higher side scatter (SSC) than live cells.

Before February 2015, flow cytometry analysis of CellGenix DC testing was performed without a gating procedure. In conclusion, debris has been integrated into the dot plot analysis and weakened the analysis. In order to find viable, single cell events and to increase quality of analysis a gating procedure was implemented excluding those events: debris exclusion by gating on low FSC and high SSC and dead cells exclusion by adding 7-Aminoactinomycin D (7AAD)* into the CD1a and CD83 marker measurement.

The concept of our functional quality assay in generating dendritic cells (DC) with CellGenix DC Medium is that DC are characterized by the percentage of all double positive cells (e.g. $CD1a^{+}CD83^{+}$) and single positive cells (e.g. $CD1a^{+}$, $CD83^{+}$). Results of DC can now directly be combined with the viable cells count.

Manufacturer

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As in the past, confirmation of test results of new medium batches are compared and confirmed by a simultaneously tested control medium. All product specifications remain unchanged, therefore neither safety nor efficacy of the product are compromised.

Please share this notification as needed with the appropriate staff in your organization. Should you have any questions, please contact customerservice@cellgenix.com.

* Fluorescent dye that appears to be generally excluded from live cells

Sincerely,

Susanne C. Schreiber
Head of QC Cell Culture Systems

Manufacturer

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