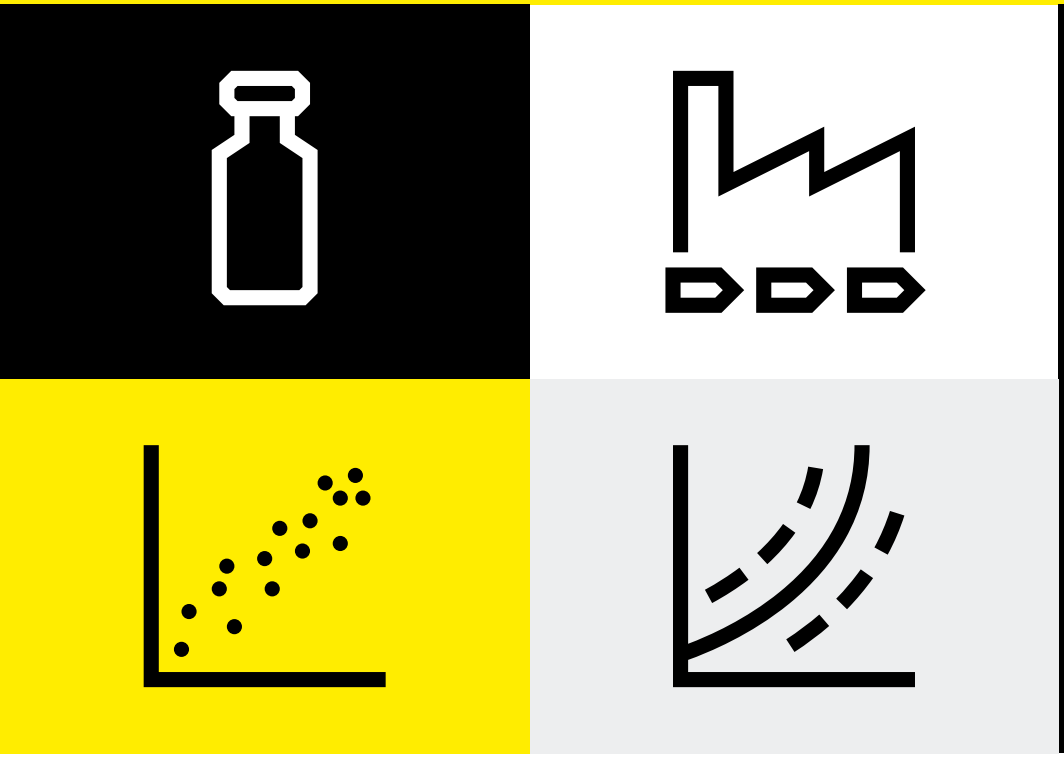
SARTORIUS

Batch-to-Batch Consistency

of CellGenix® GMP & Preclinical Cytokines



Technical Note

The quality, safety and efficacy of cell therapies are significantly influenced by the raw (ancillary) materials used in manufacturing. We prioritize safety and reliability to provide the highest quality products for clinical *ex vivo* cell processing.

Executive Summary

Inconsistent product performance of raw materials causes deviations in the cell therapy manufacturing process. It is unlikely that you will be able to use the same raw materials batch during all stages from early clinical studies to commercial manufacturing. It is therefore crucial to choose raw materials with a high and reliable batch-to-batch consistency. This will allow you to plan your manufacturing process as accurately as possible and save time and cost of goods on incoming controls and revalidations.

To make sure your manufacturing process is not influenced by using different batches of GMP and preclinical cytokines, we have performed batch-to-batch consistency studies for our key CellGenix® growth factors and cytokines. These studies demonstrate that our batch-to-batch consistency is very high over the full range of production.

Meanwhile batch-to-batch consistency of critical raw materials is emphasized in different regulatory guidelines. Examples are Ph. Eur. General Chapter 5.2.12 ("... ensure that the production process is under control and consistently produces raw materials of consistent quality."), and the ISO 20399:2022

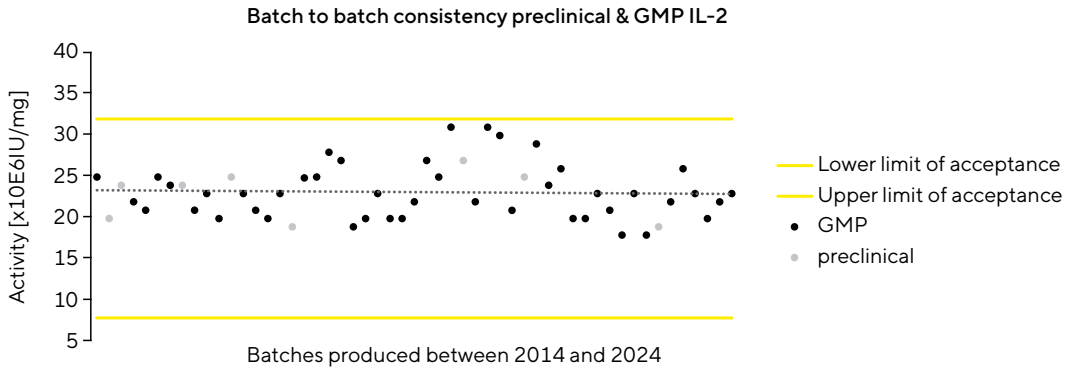
Batch-to-Batch Consistency Studies

To confirm our batch-to-batch consistency we have compared the activity and purity of different batches produced at Sartorius CellGenix over several years. Exemplary test results are shown in figures 1 and 2 for CellGenix® rh IL-2 and CellGenix® rh Flt-3L.

Test Conditions

All growth factors and cytokines have been reconstituted following the instructions in the respective CoA. Cytokine activity was determined by performing a proliferation assay of the respective growth factor or cytokine in which the activity of each batch was measured against the reference standard (internal standard for CellGenix® rh IL-2 and NIBSC #96/532 for CellGenix® rh Flt-3L). Purity was determined using reversed phase HPLC and/or SDS-PAGE.

Figure 1: *Activity and purity of different CellGenix® GMP and preclinical rh IL-2 batches produced between 2014 and 2024.*

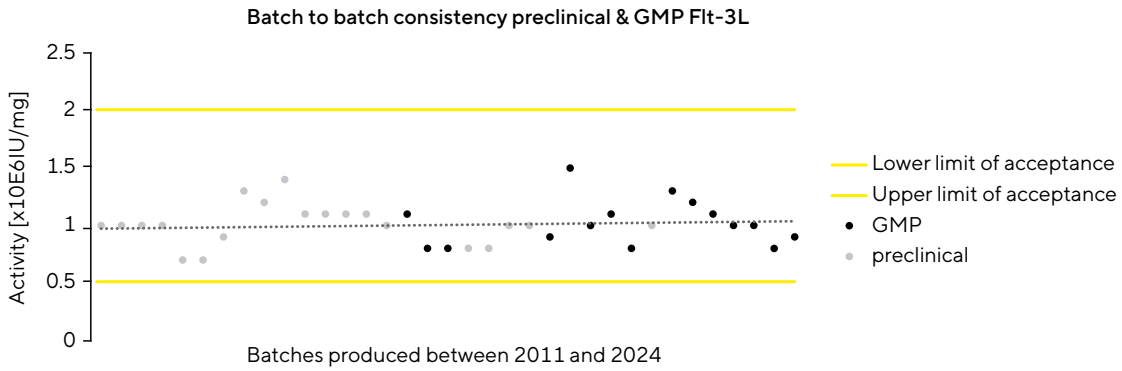


Activity GMP IL-2 [10E6 IU/mg]	
Mean	23.2
Standard Deviation	3.3
RSD [%], Relative Standard Deviation	14.1

Activity Preclinical IL-2 [10E6 IU/mg]	
Mean	22.9
Standard Deviation	3.1
RSD [%], Relative Standard Deviation	13.5

Purity GMP & Preclinical IL- 2 [%]	
Purity (all batches)	> 97

Figure 2: *Activity and purity of different CellGenix® GMP and preclinical rh Flt-3L batches produced between 2011 and 2024.*



Activity GMP Flt-3L [10E6 IU/mg]	
Mean	1.02
Standard Deviation	0.20
RSD [%], Relative Standard Deviation	20.02

Activity Preclinical Flt-3L [10E6 IU/mg]	
Mean	1.01
Standard Deviation	0.18
RSD [%], Relative Standard Deviation	17.57

Purity GMP & Preclinical Flt-3L [%]	
Purity (all batches)	> 97

As part of our assay validation studies, we determined the accuracy and precision of the proliferation assays that were used to determine the different cytokine activities. The relative standard deviations (RSDs) that were obtained in those validation studies correspond to the RSDs that were obtained in our batch-to-batch consistency studies. Accordingly, we can conclude that the observed variance of activity between the different batches is rather caused by assay variance than by variance in product quality.

Conclusion

The test results for different batches of CellGenix® GMP and preclinical rh IL-2 and CellGenix® GMP and preclinical rh Flt-3L demonstrate that the batch-to-batch consistency is very high over the full range of production. Observed minor variances between the different batches can be assigned to assay variance rather than a variance in product quality.

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

Sartorius CellGenix GmbH
Am Flughafen 16
79108 Freiburg
Phone +49 761 88889 0
Fax +49 761 88889 830
info-freiburg@sartorius.com

USA
Sartorius Stedim North America Inc.
565 Johnsom Avenue
Bohemia, NY 11716
Toll-free +1 800 368 7178

For more information, visit
sartorius.com

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