Optimization of Upstream Processing for manufacturing of SCF bacterial pellet and SCF unpurified bulk

<table>
<thead>
<tr>
<th>Product</th>
<th>REF</th>
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<tbody>
<tr>
<td>MACS® GMP Recombinant Human SCF, 10 µg</td>
<td>170-076-149</td>
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<tr>
<td>MACS® GMP Recombinant Human SCF, 100 µg</td>
<td>170-076-133</td>
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**Category of change:** Improvement of manufacturing process

**Current State:** The manufacturing of MACS GMP Recombinant Human SCF is carried out according to implemented procedures. Below, the part of the procedure that is affected by the change is detailed:

Currently, upstream production (*E. coli* fermentation) takes place in minimal medium and expression of the recombinant SCF is induced using lactose. The lactose is of animal origin. A certificate of origin (CoO) is provided for the MACS GMP Recombinant Human SCF.

**Planned change:** To avoid using material of animal origin during the manufacturing process, the production procedure of MACS GMP Recombinant Human SCF will be optimized as follows:

**Instead of lactose, IPTG will be used to induce the expression of the recombinant SCF protein.**

As IPTG is chemically defined and not of animal origin, a revised certificate of origin (CoO) will be established, that states that no material of animal origin is used as raw material for the MACS GMP Recombinant Human SCF.
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**Justification/Evaluation:**

According to the internal Animal Origin Policy, Miltenyi Biotec aims, wherever technically possible, to avoid the use of materials of human, animal or viral origin for the manufacture of medical devices and MACS GMP products.

Induction of recombinant protein expression using IPTG is a well-established protocol and will align the optimized production process of MACS GMP Recombinant Human SCF with the Animal Origin Policy of Miltenyi Biotec.

An extended risk assessment for the process change in question was performed. Usage of IPTG for induction of protein expression is a well-established and known process that will not impact the quality of the product, therefore no new or additional risks were identified in the optimization of the manufacturing process.

The Product Quality Certificate (PQC) remains unchanged.

**Estimated Implementation:**

Q4/2022

Please share, if applicable, this information with relevant staff in your organization.

If there are any further questions, do not hesitate to contact us.

14.Mar.2022

Manager QA Audit/Customer/Supplier
Miltenyi Biotec B.V. & Co.KG