Adaption of "Protocol for MSC cultivation in MSC-Brew GMP Medium"

<table>
<thead>
<tr>
<th>Product</th>
<th>REF</th>
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</thead>
<tbody>
<tr>
<td>MSC-Brew GMP Medium, 500 mL</td>
<td>170-076-326</td>
</tr>
<tr>
<td>MSC-Brew GMP Basal Medium, 500 mL bag</td>
<td>170-076-315</td>
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<td>MSC-Brew GMP Medium, 2 L</td>
<td>170-076-325</td>
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<tr>
<td>MSC-Brew GMP Basal Medium, 2000 mL bag</td>
<td>170-076-322</td>
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<tr>
<td>MSC-Brew GMP Supplement II</td>
<td>170-076-320</td>
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<tr>
<td>MSC-Brew GMP Supplement I</td>
<td>170-076-323</td>
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<tr>
<td>MSC-Brew GMP Supplement R I</td>
<td>170-076-316</td>
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</table>

**Category of change:** Adoption of documentation

**Current State:** Document does not contain the newest products. Also there was a change in the formulation of MSC-Brew GMP Supplement I (170-076-323) which has not been addressed herein, yet. Furthermore, the document contains some typos.

**Planned change:** Adaption of "Protocol for MSC cultivation in MSC-Brew GMP Medium" in order to include new products.

After incorporation of changes into section 1.2, it shows the following MSC-Brew GMP Medium components (the remaining listing remains unchanged):

MSC-Brew GMP Medium 2000 mL Order no. 170-076-325  
MSC-Brew GMP Basal Medium, 2000 mL bag (#170-076-322)  
4× 5.0 mL MSC-Brew GMP Supplement I 100× (vial) (#170-076-323)  
4× 5.0 mL MSC-Brew GMP Supplement II 100× (vial) (#170-076-320)

MSC-Brew GMP Medium 500 mL Order no. 170-076-326  
MSC-Brew GMP Basal Medium, 500 mL bag (170-076-315)  
1× 5.0 mL MSC-Brew GMP Supplement I 100× (vial) (170-076-323)  
1× 5.0 mL MSC-Brew GMP Supplement II 100× (vial) (170-076-320)

TGF-β1 is now included into the formulation of MSC-Brew GMP Supplement I (170-076-323), the customer does not need to add this component himself, so TGF-β1 will be removed from section 1.2 Reagent and instrument requirements.

The following components have to be removed from the cultivation protocol in section 2.1:
- MSC-Brew GMP Supplement RI (# 170-076-316)
- human TGF-β1 (e.g. Human TGF-β1, premium grade, # 130-095-067)
Adaption of "Protocol for MSC cultivation in MSC-Brew GMP Medium"

Section 2.1 Preparation of MSC-Brew GMP Medium will be changed to the following:
For preparation and usage of complete MSC-Brew GMP Medium please refer to the data sheet of MSC-Brew GMP Medium 2000 mL 170-076-325 and MSC-Brew GMP Medium 500 mL 170-076-326.

The following bracketed remark that is highlighted as “Note” in section 2.4. “Cryopreservation of human MSCs will be also removed from the MSC cultivation protocol: (the addition of TGF-β1 is not necessary for freezing)

In addition, some typos will be corrected.

Please beware that the MSC cultivation protocol can be downloaded from the website only. The cultivation protocol is not physically enclosed into product deliveries to the customer.

**Justification/ Evaluation:**
There is no change of raw material, testing or manufacturing process. Therefore no impact on the performance, quality and safety of the affected product could be identified.

**Estimated Implementation**
Q2/2022

Please share, if applicable, this information with relevant staff in your organization. If there are any further questions, do not hesitate to contact us.

04.May.2022
Manager QA Audit/Customer/Supplier
Miltenyi Biotec B.V. & Co.KG