Production of Tyto-cartridges new production line Cologne

Product | REF
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MACS GMP Tyto Cartridge | 170-076-011

Category of change: Change of production line

Current State: The cartridge for the MACSQuant Tyto Cell Sorter System, MACS GMP Tyto Cartridge (170-076-011) is currently produced at Miltenyi Biotec Bergisch Gladbach.

Planned change: In order to meet the increasing demand for MACSQuant Tyto Cartridges, a new production line was set up in Cologne (Germany). Main differences of the new production line are:
  - A higher degree of automation
  - The introduction of laser welding to replace ultrasonic welding of Top/Base and capillary adhesive bonding of Interposer/Base.

These differences aim at improving process reliability, product quality and safety.

For the changeover to laser welding minor design changes have to be made to Top, Base and the two Interposer variants.

- **Base**
  - The welding geometry of the current Base has to be tapered for ultrasonic welding (à energy-direction transmitter geometry). This taper is not required in laser welding, so the geometry has been made wider and flat (see next page).

- **Top**
  - To fit the welding geometry of the Base, the Top has a corresponding groove which has been made wider in the laser welding variant. In addition, the position of the luer connectors was shifted so that the incident laser beam can reach the underlying welding geometry without interference (see next page).

- **Interposer**
  - In the current design the channels and compartments are surrounded by a thin barrier so that the glue does not penetrate. These have been made wider for laser welding because they serve as a joining surface here. As an example, only the Interposer for the MACS GMP Tyto Cartridge is shown on the next page but the same applies for the Interposer of the MACS GMP Tyto Cartridge HS.
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<table>
<thead>
<tr>
<th>Current Design</th>
<th>New Design</th>
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</thead>
<tbody>
<tr>
<td>Current Base</td>
<td>Base for laser welding</td>
</tr>
<tr>
<td>Current Top</td>
<td>Top for laser welding</td>
</tr>
<tr>
<td>Current Interposer (IP24)</td>
<td>Interposer for laser welding (IP27)</td>
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**Process**

- **Laser welding instead of ultrasonic welding**
  Due to the vibration-based principle, ultrasonic welding generates particles and abrasion marks on the Top (due to the contact of the sonotrode). The geometry of the Base also does not allow for uniform sound propagation in the welding area, so the weld has some critical spots. In laser welding, the (vibrationless) energy input can be controlled spatially, thus achieving uniform and particle-free welding.

- **Aminodextran instead of HMDSO**
  To improve the wetting of the Interposer it is currently coated with HMDSO. Since the coating has a higher melting point than polycarbonate, laser welding does not work. Therefore, a new coating process based on Aminodextran - which melts at a significantly lower temperature - is introduced.
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- Laser absorbing dye on joining surfaces of Base Polycarbonate, of which Top, Base and Interposer are made, does not absorb the utilized laser radiation naturally. To achieve the absorption necessary for welding the joining surfaces of the Base are coated with the dye Clearweld.

Justification/Evaluation:
The aforementioned design changes have no influence on the compatibility with the Tyto instrument. The functional elements of the affected component are not changed, so there are no additional risks to be expected with regard to the performance of the cartridge.

Production in Cologne takes place under the same conditions as in Bergisch Gladbach in terms of clean room class (ISO 8) and quality management system (according to ISO 13485). The clean room is qualified as well as the installed monitoring system. Accordingly, no risks were identified.

There is no change to quality release testing.

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.

29. Jul. 2022
Manager QA Audit/Customer/Supplier
Miltenyi Biotec B.V. & Co.KG