Aseptic Media Fill Investigation

Investigation # _____________

Part I. Product and QC Lab Test Data:

Media Fill for Product/Container Closure System: ______________________________

Batch Code and Number: ______________________________________________________

Media Type/Lot #/Expiration Date: ___________________________________________

Volume of Media/Bulk Tank: _________________________________________________

Fill Volume: _______________________________________________________________

Date Filled: _______________________________________________________________

Date Incubated: ____________________________________________________________

Temperature Incubated: ____________________________________________________

Incubated by: _____________________________________________________________

<table>
<thead>
<tr>
<th>Environmental Monitoring</th>
<th>Location</th>
<th>Results- Count &amp; ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particulates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air Samples/Settling Plates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodac Plates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personnel Monitoring</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Media Growth Promotion Test: Passed/ Failed

Reference Lab Notebook/Page: ________

Media Fill Results:

<table>
<thead>
<tr>
<th># of Containers</th>
<th>Date</th>
<th>Inspected By</th>
<th># Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th># of Containers</th>
<th>Date</th>
<th>Inspected By</th>
<th># Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># of Containers</td>
<td>Date</td>
<td>Inspected By</td>
<td># Positive</td>
</tr>
<tr>
<td>-----------------</td>
<td>------</td>
<td>--------------</td>
<td>------------</td>
</tr>
</tbody>
</table>

Media Fill: Passed/Failed/Invalidated

Notification of QA/Who/Date/Time: ______________________________________

**Part 2: Risk Based Assessment:**

Identify all positive containers to species level: ______________________________

Determine if any positive containers have cracks or other integrity defects: __________

Dosage Form of the Product: Injectable_______ Ophthalmic_______ Topical ________

Sterility Test Results ________________________________________________________

Possible sources of specific organism recovered______________________________

Was the organism(s) found in any environmental test samples? _________________

Other dates specific organism was recovered and location ______________________

Is the product capable of sustaining growth of the organism?____________________

Did this media fill cover all appropriate interventions? Any new ones? ____________

Media Fill history for this product/container/closure system: ____________________

Date of Last Media Fill for same container/closure system: ______________________

If current Media Fill failed, list all batches filled on same line since the last passed media fill:

List may be attached.

________________________________

____________________________________

____________________________________

Is there more sampling that needs to be done to find root causes?
Describe______________________________________________________________

List possible root causes:
______________________________________________________________

______________________________________________________________

______________________________________________________________

What is the most probable root cause? ____________________________________

______________________________________________________________
Are experiments needed to confirm? ____________________________________________
List batches to be put on-hold: ________________________________________________
_________________________________________________________________________
Written By/Date: ______________________ Approved By (QA)/Date: _________________

Attach Appendix A- Production Data:
Attached By/Date: __________________________
Reviewed By (QA)/Date: ________________

Part 3. Final Quality Assurance Assessment:
Corrective Action: What should be an immediate action? Are more media fills needed, and if so how many? How should batch disposition be impacted?
_________________________________________________________________________
_________________________________________________________________________
Preventive Action: What needs to be done to prevent a recurrence of the event?
_________________________________________________________________________
_________________________________________________________________________
Follow-up to ensure effectiveness of actions _____________________________________
_________________________________________________________________________

Written By/Date: _________________________ Approved By/Date:____________________
QA notes/Batch Disposition Decision: __________________________________________
QA approval/Date:________________________
Appendix A. Production Data for Media Fill Investigation:

This section must be filled out by Production Staff:

Date/Time Media Prepared: __________________________

Media Prepared By: _____________________________

Formulation Tank: ______________________________

Filtration Date/Time: ____________________________

Filter Pre & Post Integrity Test Results: ________________

Holding Tank: _________________________________

Holding Tank SIP Date: _________________________

Filling Room number: __________________________

Filling Machine #: _____________________________

Filling Line Equipment Sterilized Date/Time: __________

   Autoclave # __________________

   Adequate Cycle _Yes/No Explain___________________

List All Cleaning/Disinfecting Staff: _____________________________

List All Sterile Operators: _________________

List All Microbiology Technicians: ______________________________

List All Maintenance Technicians: ______________________________

Start Time of Filling Media: ____________________________

Line speed: ______________________________________

List of number of containers filled each shift: _______ Total: ____________

List of number of rejects found each shift: _______ Total: ____________

End Time of Filling Media: ____________________________ Total Time: ________
### Interventions:

<table>
<thead>
<tr>
<th>Type</th>
<th>Date</th>
<th>Time</th>
<th>Operator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight/Volume adjustments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filling needle change</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Addition of components</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in personnel</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shift Change</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EM Sampling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other: List below</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Prepared By/Date: ____________________

Approved by (Manufacturing)/Date: __________