Impact of Steam and Gamma Processing on Extractable

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Abstract—In Pharma application various elastomeric components are used as primary packaging and fluid transportation. Several methods are available for sterilization and among all steam & gamma sterilization are most suitable methods for elastomeric components. In this study the effect of steam & gamma sterilization has been compared with non sterile components. Steam and gamma which has been used as a source for sterilization that may affect the molecular chain & crosslink density of elastomeric components. This study serves to help understand the potential deterioration of physical and chemical properties, the possible impact to functionality and the potential changes to the extractable/leachable profile as a result of sterilization.

Keywords: Steam, Gamma, Extractable

I. INTRODUCTION

To study and test the extract of elastomeric component which are used as primary packaging in pharmaceutical industry is subject of interest. Some extractable are desire and some extracts are undesirable.

Extractable: - Extractable are chemical species / compounds that can be extracted from a primary container or component material (e.g. the elastomeric or plastic components) into drug or biological product & contaminate and/or cause various potential issues. Extractable are mostly generated by interaction between products and their packaging over time, usually under extreme conditions e.g. the presence of strong solvents or elevated temperatures.

Leachables: - Leachables are compounds that leach into the drug or biological product from the container-closure system such as the elastomeric or plastic components, or coatings of the container and closure system. Leaching is mainly as a result of direct contact with the formulation under normal conditions of use. Leachables are typically a subset of extractables, and have potential to affect the product in various ways.

Extractables and Leachables:

Extractables may be different than Leachables due to:
- Different extracting conditions
- Different time frames
- A particular Extractable or Leachable can occur in more than one component of the container-closure system e.g. Calcium from both plastic resin and elastomer Container-Closure System
- The sum of the packaging components that together contain and protect the dosage form. This includes both primary and secondary packaging components.

Sources of extractables and Leachables:
- Plastic components - Vinyl Monomer & Plasticizers e.g. Phthalates. These are added to plastics to make them more flexible and can be found throughout the manufacturing process and in packaging materials - carcinogenic.
- Rubber: Nitrosamines, Vulcanizing Agents, Accelerators, polynuclear aromatic hydrocarbons (PAHs) - carcinogenic
- Many drug products are distributed / administered in packages made of plastic and rubber components: phthalates, PAHs, or nitrosamines could potentially come into contact with the drug product and be harmful.
- Inks & adhesives from labels, coatings, antioxidants, catalyst residues, organic oligomers, heavy metals.
- Metered-dose inhalers (MDIs), dry-powder inhalers ( DPIs), and nebulizers can be complex because they may be constructed from a myriad of plastic, rubber, and stainless steel components.

Fortunately, information on potential leachables may be obtained from the known ingredients of the rubber and plastic materials.

For example:
- Thiurams, diethiocarbamates, and ercaptobenzothiazoles are commonly used sulphur-containing curing agents in rubber manufacturing; hence, they are potential leachables in the drug product where sulphur-cured rubber is used.
- Polybutylene terephthalate (PBT) is a widely used polyester plastic in medical device and MDI valve components.
- PBT oligomers and other residuals or degradants can be similarly leached from the valve components fabricated from this material.

Methodology:
- Collecting the halobutyl rubber stoppers and compound for the same, then prepares samples of steam sterilized stopper and gamma sterilized stopper and carry out the extraction for testing as mentioned in IP. Then carry out the counting of extractable by using GC and spectrophotometer. Compare the no of extractable found in unprocessed, steam sterilized rubber stoppers and gamma sterilized rubber stoppers.

Sample preparation:
Steam sterilization parameters:
- Temperature :- 121°C
- Holding time :- 60 minutes
- R.H. :- less than 60%

Gamma sterilization parameter:
- Energy level:- 25 KGY

Test results:

<table>
<thead>
<tr>
<th>No of extractable</th>
<th>No of extractable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unprocessed</td>
<td>28</td>
</tr>
<tr>
<td>Steam sterilized</td>
<td>24</td>
</tr>
</tbody>
</table>

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Table. 1: Test results of extractable

<table>
<thead>
<tr>
<th></th>
<th>36</th>
<th>37</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma sterilized(25 kGy)</td>
<td>28</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>Unprocessed</td>
<td>24</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>Steam</td>
<td>36</td>
<td>37</td>
<td>36</td>
</tr>
</tbody>
</table>

II. CONCLUSION

To examine how the extractable profile is impacted by sterilization processes and to compare the steam process to the gamma process, sample extracts were prepared and subsequently analyzed via a variety of analytical techniques. Comparing to the control, the RP-HPLC results shows a decrease in antioxidant (BHT) content. The antioxidant (BHT) content further decreased in the samples irradiated at 25 kGy. The antioxidant inhibits polymer degradation by scavenging radicals and is intended to be a sacrificial ingredient. Its consumption in the irradiated samples indicates degradation of the polymer that could result in potential loss of desired properties. Headspace analysis illustrates that extractables increase with increasing gamma energy level. Comparing to the control, the ICP results show a decrease in magnesium content in steam processed sample but an increase in magnesium content with increasing irradiation energy. Gamma irradiation caused a noticeable increase in the total number of extractables detected. The increase in the number of extractables coincided with an increasing gamma energy level.

REFERENCES

[1] WHO Glossary
[6] “IARC vol 60”