Extractable and Leachable Testing In Prefilled Syringes Components

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Abstract—In prefilled syringes (PFS) two words are namely Leachable and Extractable are becoming a centre for discussion in therapeutic protein produces to patients. So understanding and testing of leachable and extractable of prefilled syringe components is of utmost requirement in parental drug delivery formulation development.

Keywords: Rubber Plunger, Leachable, Extractable, Parental Drug delivery formulation development.

I. LEACHING TYPE
Leachable 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.

Leachable are typically a subset of extractable, and have potential to affect the product in various ways.

II. HOW EXTRABLES AND LEACHABLE DIFFER FROM EACH OTHER
1) Different extracting conditions
2) Different time frames

Particular Extractable or Leachable can occur in more than one component of the container e.g. Calcium from both plastic resin and elastomer

III. WHAT IS PREFILLED SYRINGES?
“PFS (Pre-filled Syringes) is a pre-measured single-dose ready-to-use injectable for parenteral drug delivery”

IV. MANUFACTURING PROCESS OF PFS?
Pfs components which cn contribute to Extractable and Leachable.

A. Glass
Type I borosilicate glass is commonly used to make prefilled syringes and it may contain various inorganic oxides such as boron, silicon, calcium. Sodium, potassium, iron oxide may not pose a direct toxicological risk but migration of glass dissolution, pitting, stress, surface weathering or erosion corrosion effects may lead to particle formation.

B. Rubber Material
Rubber Plunger, Luwertips, Needle Shield) The plunger and Luwertips are Made from Bromobutyl Formulations, needle Shields are made from a Latex Free Polyisoprene Rubber Compounds.

The Rubber components also comes in a Direct Conact with Formulations, e.g. Rubber Plunger Top surface is remain contact with a different formulations or solvents so due to this storage any residue from plunger which can causes a toxicological effects to a formulations or may cause a protein formation which is toxic in nature.


C. Silicone Oil
Silicone oil is applied to coat the barrel inside surface, rubber plunger outer surface and Metal Canulla outer Surface.

Silicone oil is polydimethylsiloxane and function as a lubricant allowing the plunger guide smoothly within the barrel to inject a Drug. As the deman for prefilled syringes and automated injection devices increases, so does the important of understanding silicone oil. Functionally silicone oil is not a major concern for manual injections.
since a nurse r a doctor is capable of applying the necessary forces to push the plunger to end point. However a spring can provide a fixed amount of of forces and unanticipated friction may cause the plunger to stall before complete drug delivery.

Silicone oil is a inert insoluble in water it may interact with in a formulation causing a protein aggregation,droplets and particles

Ideally the silicone oil application process should balance the need to minimise the quantity of silicone oil also. The silicone oil distribution is non uniformly distributed with least amount located near needle end of syringe.

D. Syringe Pin-Tungsten Pin:

Lee obvious sources of PFS extractable are contamination from tools that were used to manufacturer and process syringes. Glass syringes are made from Cutting and molding Glass tubing at high temperature. Heated glass incontact with various processing tools like a Canulla Fix sizes is made at more than 1,200 Degree C. now a tungsten pin is used to make a size for Canulla capillary, and at 150 >c a tungsten metal comes in contact with air and it cinvert as Oxide as white substance residue in the syringes.

These residue may survive the syringe washing step and may contact the drug upon syringe filling and storage.

E. Hypodermic Needle

The attached hypodermic needle is made if stainless steel. Inorganic metal is used in stainless steel formulation such as Fe, Cr, Mn,Ni and Mo may Leach from a Syrynge and may be a toxic in nature.

V. ANALYTICAL TECHNIQUES FOR TESTING OF EXTRACTABLE AND LEACHABLE

Analytical characterization and quantitation techniques associated with organic and inorganic chemicals are commonly used to analyse extractable/leachable. Gas chromatography mass spectrometry(GCMS), solid phase micro extraction (SPME) – GCMS, liquid chromatography (HPLC), and nuclear magnetic resonance (NMR) spectrometry techniques are used to analyze unknown organic extractable compounds. Inductively coupled plasma mass spectrometry (ICPMS) can be used to identify and quantitate inorganic metallic elements. Evaporative light supplemental detection (ELSD) can be supplemental to HPLC and suitable for oligomers/polyomers and non-chromophores molecule analysis.

VI. CONCLUSION

To sum up ,PFS components and residues from processing tools may leach organic and inorganic chemicals into formulated drugs. Leachable information is often not readily available from the syringe manufacturer promoting drug manufacturers to initiate extractable and leachable investigation. Leachable from PFS may have contributed safety concern related to protein aggregation, particle formation and toxicological risk factors. Identifying extractable and leachable provides key information enabling safety assessment that addresses toxicology and drug quality impact for evaluating PFS

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