Requirements on pre-fillable glass syringes

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Purpose.

Pre-fillable glass syringes are used for modern drug formulations containing peptides, antibodies and DNA fragments. The composition of such drug containing solution is often very sensitive to side reactions with the packaging materials used, leading in its worst case to a complete inactivation of the active ingredients. Since some year's silicone oil as well as Tungsten residues are known as catalytic substances which can result in such stability problems with parenteral drug compositions. The presentation will highlight the latest requirements on the inside siliconization of pre-fillable syringes as well as state of the art technology for the reduction of Tungsten residues in modern glass based drug delivery systems.

Methods.

Atomic Absorption Spectroscopy (AAS) was used to characterize the quantity of silicone sprayed into the glass barrel. A study was done to characterize the optimal silicone quantity as well as the best distribution inside the glass barrel for biopharmaceutical drug compositions to be filled into glass syringes. Within this study syringes from 0.5 ml filling volume size to 3 ml were analyzed for their silicone content. Homogeneity of the inside silicone distribution was analyzed by glass dust testing and AAS measurement. Interactions between protein based drug molecules with silicone were characterized by gliding force measurements on filled syringes dependent on the silicone quantity per barrel (0,4 - 1,6 mg)

Tungsten residues were tested after extraction with dilute nitric acid by ICPMS (Inductively Coupled Plasma Mass Spectroscopy) on different syringe formats produced using Tungsten containing and Tungsten-free forming tools.

Results.

The AAS measurements yields an intra batch precision (<5%CV) and accuracy (>10%) from production batch to production batch for the total silicone quantity and distribution. Gliding force measurements indicated a lower level of silicone of 0,4 mg required for injection usability, which is improved up to 0,8 mg and did not yield further improvement over 1,6 mg. Protein based drug compositions did not show an effect on aggregation for silicone quantities between 0,4 and 0,8 mg. Over 0,8 mg an increase of the gliding force of 40% was identified which results from aggregation.

Tungsten residues on standard processed syringes were detected to in average 50 ng per syringe with a standard deviation of 15 ng. Under such Tungsten conditions, modern biotech drugs are none or only low affected. The usage of Tungsten free forming technology generates complete Tungsten residue free syringes.

Conclusion.

Useful silicone levels for glass made pre-fillable syringe configurations were determined. The Tungsten contaminations of syringes out of the standard as well as out of the Tungsten residue improved production process were analyzed. Both together offer the optimal combination for the packaging material parenteral biopharmaceutical drug formulations are requiring today in order to avoid stability issues.