Quality control test for Sterile formulations

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Basic quality control tests

- 1) Sterility Tests.
  2) Pyrogen Tests.
  3) Leaker Tests.
  4) Particulate matter testing.

Sterility tests

Sterility means complete absence of all viable Micro-organism. It is an absolute term. The methods which are used to perform sterility tests are

a) Direct transfer method

b) membrane filtration method

Direct Transfer method:-

It is an traditional sterility test method which involves a direct inoculation of required volume of a sample in two tests tube containing a culture medium that is FTM, SCDM. This method is simple in theory but difficult in practice when the demand for repetition in opening container, sampling Transferring, and mixing increases causes potential fatigue to the operator and detoriation in operator technique. So chances of Accidental contamination is there.

Membrane Filtration method

It is more popular and widely used method over direct transfer method. This method basically involves filtration of Sample through membrane filters. The filtration is assisted under Vacuum, After filtration completion the membrane is cut into 2 halves and one halve is placed in two test tubes containing FTM, SCDM medium

Pyrogen Test

Pyrogens are products of metabolism in microorganisms Gm-ve bacteria produces most potent pyrogens. These are lipopolysacchrides chemically and heat stable and are capable of passing through bacteria retentive filter. When these pyrogens are introduced into a body they produce a mark response of fever with body ache and vasoconstriction within an onset of 1 hour. Basically there are test performed to detect the presence of pyrogens in sterile parenteral products they are a) Rabbit Test b) LAL Test

Rabbit test

This test basically involves the injection Sample solution which is to be tested into a Rabbits Which are use as test animals through ear vein. The Temperature sensing probe (Clinical Thermometer, Thermosistor or similar probe) into a rectum cavity of Rabbit (3) at the depth of 7.5 cm the test solution must be warmed at 37 degrees prior to injection. Then Rectal temperature is recorded at 1,2,3 hr subsequent to injection.

The solution is judged to be non pyrogenic if no single rabbit show rise in temperature of 0.5 degree

LAL test

It is an recently developed in vitro test method for pyrogen utilizing gelling property of lysates of amebocytes of limulus polyphemus which is found only at specific locations along the east coast of North America and along southeast Asia. It is derived from horse shoe crab, The basic procedure is the combination of 0.1 ml of test sample with LAL Reagent after incubation for 1 hr at 37 degree Celsius the mixture is analyzed for the presence of Gel clot. The LAL Test is positive indicating that the presence of endotoxin. Its applications are mainly to Pharmaceutics, Biological, devices, disease states, food, and validation of heat cycles. This method has several advantages of Rabbit test they are Greater sensitivity and reliability specificity, less variation, wider application, less expensive and simplicity

Leaker Test

- The leaker test is intended to detect incompletely sealed ampoules, so that they may be discarded. Tip sealed ampoules are more prone to leak than pull sealed. In addition to that crack my present around seal or at the base of ampoule as a result of improper handling leakers are usually detected by producing negative pressure within the incompletely sealed ampoule usually into a vacuum chamber while those ampoule are submerged into a colour dye solution of 0.5 to 1% methylene blue. Vials and bottles are not subjected to such leaker test because rubber closure is not rigid however bottles are often sealed while vacuum is pulled so that bottle remains evacuated during its shelf life

Particulate matter testing

Particulate matter is primary concern in the parenteral products given by I.V. Route, all parenteral products should be free from insoluble particle. Further U.S.P. states that GMP Requires that all containers be visually inspected and that with visible particle be discarded. It is found that formation of pathologic ganulomes in vital organs of body can be traced to fiber, rubber fragment and other solid present in intravenous solutions. The visual inspection is done by holding the ampule by its neck against highly illuminated screens. White screens for the detection of black particle and black screens for the detection of white particles to detect heavy particles it may be necessary to invert container but care must be exercised to avoid air bubble. The instrumental methods are based on principles of light scattering, light absorption, electrical resistance as in coulter counter. A method which utilizes a video image projection could detects a moving particle without destruction of product unit