TCH-027

MEDIA FILL TO VALIDATE THE ASEPTIC PREPARATION OF SODIUM BICARBONATE INTRAVENOUS INFUSION

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BACKGROUND

Sodium bicarbonate is an alkalinizing agent and is indicated for treating acute or cronic metabolic acidosis.The dose of bicarbonate required for the treatment of acidotic states must be calculated on an individual basis, and is dependent on the acid-base balance and electrolyte status of the patient.In severe acidosis, sodium bicarbonate has been given intravenously by contiuous infusion usually as a 1,26% (150 mmol/litre) solution or by slow intravenous injection of a strong (hypertonic) solution of up to 8,4% (1 000 mmol/liter) sodium bicarbonate.For the correction of acidosis during advanced cardiac life support procedures, doses of 50 mmol of sodium bicarbonate (50 ml of 8,4% solution) may be given intravenously to adults.Frequent monitoring of serum-electrolyte concentrations and acid-base status is essential during treatment of acidosis.
The substance is thermolabile and when heated in solution it gradually changes into sodium carbonate. That's why we prepared the Sodium Bicarbonate Intravenous Infusion aseptically, according to the standard operating procedure.

PURPOSE

To validate the performance of aseptic processes used to produce our sterile product and to meet GMP Requirements, i.e. to comply with the "law", twice per year we are performing media fill (process simulation studies)

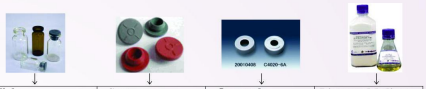
MATHERIALS AND METHODS

Media Fill Protocol

- **Key elements to be taken into account include:**

•Number and frequency of runs
•Medium culture (to replace the product)
•Number of units filled
•Container (vial) size
•Fill volume
•Line speed (or filling speed)
•Duration of fill
•Operators shifts
•Monitoring activities
•Interventions –both routine and non-routine-
•Incubation method
•Acceptance criteria

Media fills are simulating the whole process in order to evaluate the sterility confidence of the process. Process simulation includes formulation (compounding), filtration and filling. Important factors in the process are: personnel (number, shift changes, fatique), sterility test for sterilized components (bottles, stoppers), frequency, media fill sizes, acceptance criteria, environmental monitoring. We select the growth medium and prepared the bulk media as the same process as routine production including filtering process and number of units (the batches is smaller than 1000).Then all units were incubated at 20-25 ˚C for 14 days.



Vials	Stoppers	Overseals	Dispense Medium Powder
↓	↓	↓	↓
Wash	Wash	Wash	Prepare Solution
↓	↓	↓	↓
Sterilize	Sterilize	Sterilize	Steril filtration

↓

Fill / Stopper / Seal Aseptically
↓
Inspect
↓
Incubate
↓
" Read " Results

RESULTS

After the incubation period of the media filled containers they were visually examined for microbial growth.

Relation between observed number of failures and upper 95% confidence limit

Observed number of failures	0	1	2	3	4	5	6	7	8	9	10
Upper 95% confidence limit	3	4,74	6,3	7,75	9,15	10,51	11,84	13,15	14,43	15,71	16,96

The maximum contamination rate that can be expected with a 95% certainty for an observed frequency of failures can be calculated according to the following formula:

Contamination rate=Upper 95% confidence limit/Number of filled unitsX 100%

The contamination rate was zero, so, the accepted contaminations rate is less than 0, 1.

CONCLUSION

With media fill we evaluate the aseptic assembly and operation of the sterile equipment, qualify the operators and assess our technique, and demonstrate that the environmental controls are adequate to meet the basic requirements necessary to produce Sodium Bicarbonate Intravenous Infusion by aseptic processing.