NHS Pharmaceutical Aseptic Services Group
www.pasg.nhs.uk

Version 2 – Updated 13th October 2016

NHS Guidance to Device Manufacturers introducing Neuraxial Syringes and Syringe Caps into the UK NHS on the Pharmaceutical Testing Requirements to allow Drug Storage in their Syringes

Informed from previous experience with the introduction into the UK market of proprietary non-luer neuraxial devices, this guidance document sets out the pharmaceutical testing requirements for syringes and syringe caps fitted with the new ISO neuraxial connector when used as drug storage devices for intrathecal chemotherapy, epidural and other drugs given by spinal injection.

Testing Requirements for Syringe & Cap combinations

1) Microbiological and physical integrity testing must be carried out as per 'Protocols for the Integrity Testing of Syringes 2nd edition April 2013' – NHS Pharmaceutical Quality Assurance Committee. This protocol is available to download here http://www.pasg.nhs.uk/test-requirements-for-neuraxial-syringes-for-drug-storage This will need to be undertaken for lock syringes for the full range of syringe sizes from each manufacturer. If it is intended that a manufacturer's slip syringes are suitable for drug storage then the same level of testing will be required as for lock syringes.

It is recommended that device manufacturers use an independent NHS testing laboratory familiar with the integrity testing protocol above to carry out this validation work. If a non-NHS laboratory is contracted by a device manufacturer, then it is recommended that this laboratory seeks advice from the authors below to ensure that they fully understand the requirements in terms of sample numbers, who does the filling and capping of the syringes etc.

2) Device manufacturers will need to demonstrate that their full range of syringes are in compliance with the British Pharmacopoeia Sterile Single-use Plastic Syringes monograph and testing method 3.2.8 as per Appendix XIX G. This monograph is available to download here http://www.pasg.nhs.uk/test-requirements-for-neuraxial-syringes-for-drug-storage

3) Within the testing criteria in 2) there is a UV absorbance test for extractables (method 2.2.25 as per Appendix II B. Ultraviolet and Visible Absorption Spectrophotometry – available to download here http://www.pasg.nhs.uk/test-requirements-for-neuraxial-syringes-for-drug-storage), but this is for 24 hours storage at 37C. The UK NHS requirements are that device manufacturers carry out extended testing for a minimum of 7 days at 4C & 20C to reflect normal hospital pharmacy practice (as well as at 37C for the same time period) e.g. at 1,2,5 & 7 days as a minimum. Some hospitals have a requirement for 14 day storage.

4) a) In order for hospital pharmacists to assess drug stability for drug solutions stored in neuraxial syringes, device manufacturers are asked to provide details of the composition of the plastics used for the barrel & plunger, the constituents of the rubber grommet & lubricant, and the method of sterilisation (Ethylene Oxide, gamma irradiation). In particular it would be helpful to know the vulcanising agents used in the grommet. If a particular brand of syringe is already in use for medicine storage in the UK, and the only change is to the nozzle design, such that the plastic/rubber composition and the non-nozzle syringe dimensions are unchanged, then this information would help the UK minimise testing requirements.

b) Device manufacturers are asked to inform NHS hospital pharmacists if at any time changes are made to the materials used, composition and sterilisation method of their syringes and caps in future as part of their change control processes to ensure suitability for continued drug storage in their devices before such changes are implemented.

c) Device manufacturers will need to demonstrate chemical stability for a range of drugs commonly stored in neuraxial syringes on a risk based approach. Stability testing must be undertaken in syringes with a relatively large surface area to volume ratio – 5ml is suggested as typically used for intrathecal chemotherapy and at a low concentration of the drugs listed below. This is to replicate the worst case scenario for adsorptive / absorptive drug losses. Chemical stability testing must be carried out as per 'A Standard Protocol for Deriving and Assessment of Stability Part 1 Aseptic Preparations (Small Molecules) 3rd edition December 2015' – NHS Pharmaceutical Quality Assurance Committee. This protocol is available to download here http://www.pasg.nhs.uk/test-requirements-for-neuraxial-syringes-for-drug-storage Testing must cover a 6 week period as a minimum for each drug in triplicate to allow assessment of the data and possible extrapolation to other drugs commonly stored in neuraxial syringes. The two drugs below represent the worst case scenario for stability:-

Fentanyl 2micrograms/ml & Bupivacaine 0.1% in Sodium Chloride 0.9% stored at Room Temperature 15-25 C
Hydrocortisone sodium succinate 1mg/ml in Water For Injections stored Refrigerated at 2-8 C

d) Syringes and caps used for chemical stability testing must be pre-sterilised using the same method for commercially available supplies (typically Ethylene Oxide or gamma irradiation). Where a manufacturer is providing both individually wrapped sterile packs and sterile triple wrapped packs of syringes and caps, and the sterilisation method is different for each, then both types of syringes must be submitted for stability testing as in 4c) above.

It is recommended that device manufacturers use an independent NHS testing laboratory familiar with the stability testing protocol above. If a non-NHS laboratory is contracted by a device manufacturer, then it is recommended that this laboratory seeks advice from the authors below to ensure that they fully understand the requirements of the testing protocol.

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