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Appendix 3. Guidelines for compounding of Avastin.

1. Avastin (bevacizumab, Roche) is an off-label agent used for intraocular injection in the eye but it is registered for a non-ocular indication and is therefore available at pharmacies and wholesalers.
2. Avastin needs to be compounded into smaller aliquots for delivery by intraocular injection.
3. The compounding must be performed to the standard required by the injecting doctor who bears the ultimate responsibility for the patient's welfare. This compounding into smaller units may be performed by a compounding pharmacy where this is available and readily accessible, otherwise the agent needs to be aseptically drawn up to avoid contamination which could lead to endophthalmitis.
4. This compounding must be performed with an aseptic technique in a clean environment by an experienced operator, who is usually a qualified pharmacist, sister or the doctor himself. In order to have the optimal environment for compounding so that the risk of endophthalmitis is minimized the following methodology is advised:
5. The experienced operator is somebody who performs this function on a regular basis. The procedure should take place in a theatre with the compounder gowned and wearing gloves and a mask.
6. Puncturing of the multidose vial must be performed once only. This is in order to avoid blunting the needle that will be entering the eye and to reduce the risk of contamination/infection. A multidose spike or needle is inserted into the Avastin bottle e.g. a Clave multidose vial access spike (product number: 011-cs-50; ICU Medical SA). Sterilisation filters between the vial and syringe should be avoided as the active drug may bind to the filter.
7. From a 100mg/vial with 4ml volume, it should be possible to draw up at least 20 injections with a volume of 0.1 mL in a sterile syringe which will be reduced to 0.05ml

(injection dose 1.25mg/0.05ml) at the time of injection. This syringe may be an insulin syringe with a pre-attached needle (but that has not punctured the vial) or a syringe with a cap to which a needle is later attached. The syringes should then be each individually placed in an opaque packet that is sealed and dated. These are then refrigerated. Syringes should be submitted for microbiological analysis (culture) from every batch that is drawn up from a vial and then released for use when culture is found to be negative.

8. The aliquots of Avastin are stable when refrigerated for up to 3 months but then ongoing sterility testing is required.
9. A detailed accountability log with the drug batch number and patient names should be kept.
10. For patients requiring bilateral injections, aliquots from different batches should be used.

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Academic Advisory Committee of the South African Vitreo-retinal Society. October 2013