Emergency Preparation of Eye Drops in Unlicensed Aseptic Units

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Written by:

Linda Hardy, Regional Quality Assurance Specialist Pharmacist, Yorkshire & the Humber
on behalf of the NHS Pharmaceutical Quality Assurance Committee

The author would like to acknowledge input from the NHS PQA committee members & MHRA Expert inspectors

Please feedback any comments to: linda.hardy5@nhs.net

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Edition 1	Issued September 2019
Edition 2	
Edition 3	
Edition 4	

Purpose and Scope:

1. This document aims to provide guidance to NHS Chief Pharmacists and Accountable Pharmacists working under the Section 10 exemption to the Medicines Act 1968 on the circumstances and potential risks that should be considered before preparation of eye drops is undertaken in unlicensed NHS Aseptics Units.

Background:

2. Drugs are commonly administered to the eye by topical application as eye drops. Most are licensed products or medical devices but certain eye drops are prepared aseptically from material supplied for injection. These are available as "Specials" from UK MS licence holders. The Royal College of Ophthalmologists and the UK Ophthalmic Pharmacy Group have produced Ophthalmic Specials Guidance on their use. See Appendix 1 and full document available via the following link:
   https://www.rcophth.ac.uk/2016/09/ophthalmic-special-order-products-august-2016-update/

3. Aseptic Preparation in the UK is only exempt from the licensing requirements of the Medicines Act 1968 providing five conditions are met. One of these conditions is that the preparation uses "closed" systems (MCA 1992). The preparation of eye drops, in particular the filling of eye drop bottles, is considered to be an "open" system due to the requirement to fill the bottle with the prepared solution via the open neck of the bottle. Therefore the filling of eye drop bottles should not occur in an unlicensed Aseptic Unit.

4. The availability of eye drops as "Specials" from licence holders has expanded in recent years, with approximately two hundred product lines listed on NHS Pro-File in 2019. As a result, the need for unlicensed preparation has reduced. For example, in the Yorkshire & the Humber region in 2005 more than 2,800 bottles of eye drops were prepared in unlicensed units and in 2018 the estimated number was around 20-30 bottles.

5. However, the supply of unlicensed "Specials" from the licensed compounding centres, both NHS and Non-NHS is limited and often subject to delay and interruption. This may result in unlicensed units occasionally being requested to urgently prepare extemporaneously compounded eye drops. This is usually considered to be a breach of one of the five conditions for exemption from licensing.

6. It is recognised that there may be clinical circumstances where urgent treatment will be required in the best interests of the patient, e.g. in order to potentially save sight when a licensed eye drop preparation or "Special" is not available to meet the need. The alternative may be to return preparation to the clinical area which would increase the risk of error and contamination.

7. MHRA Q&As for "Specials Manufacturer's":

7.1 In the document "Guidance for Specials Manufacturer's"(revision 1 January 2015) the MHRA assigns a higher risk to the preparation of aseptic products using "open" systems compared to "closed" systems and an increased level of environmental control is required to assure the quality of products prepared in open systems. The controls vary depending on whether the process takes place in an open fronted Laminar Air Flow Cabinet (LAFC) or in a pharmaceutical isolator.

7.2 In an LAFC, full compliance with Annex 1 (EU Guidance on Good Manufacturing Practice) is expected i.e. full gowning with no facial exposure and continuous particle counting during operations.

7.3 In an isolator, Annex 1 requirements must be met at rest and the isolator integrity must be checked prior to undertaking the open procedure. Goggles and face protection are not required.

8. Clinical Guidance and Guidance Note 14:

Clinical guidance on the use of eye drops and other eye preparations has been issued jointly by the Royal College of Ophthalmologists and the UK Ophthalmology Pharmacist Group (See Appendix 1). The guidance is written for primary care but the essential principles apply to the hospital setting and the recommendations are in line with the requirements of Guidance Note 14. This requires that "*a licensed medicinal product obtainable from normal distribution channels in a reasonable time should be considered available for use. If a licensed product becomes unavailable, it may be necessary for an unlicensed equivalent to be supplied. This should be seen as a temporary expedient and should not be taken as justification for long term supply. Supply in these circumstances should cease as soon as is practicable, following reinstatement of the licensed product".*

9. Guidance for Accountable Pharmacists on the circumstances and potential risks that should be considered before preparation of eye drops is undertaken.

9.1 The Accountable Pharmacist of the unlicensed unit should, before preparing an eye drop preparation using an open system, ensure that:

- the clinical situation requires urgent and potentially sight-saving treatment;
- a suitable eye drop prepared from a licensed unit is not available OR there will be an unacceptable delay in the commencement of treatment by obtaining a product from a licensed unit;
- the required medication cannot be delivered in an alternative presentation using closed system techniques e.g. pre-filled syringes;
- supply is a temporary expedient and must cease as soon as is practicable, i.e. as soon as a licensed product, or failing that a product made under a Specials Licence is available.

- the procedure is undertaken in a pharmaceutical isolator, the integrity of which is demonstrated prior to commencing filling i.e. a compliant leak test has been completed*.

**Where no pharmaceutical isolator is available, the procedure may be undertaken in a LAFC. This is a higher risk option and a short shelf life not exceeding 24 hours is recommended for eye drops prepared in this way.*

In addition:

- A deviation should be raised in the Pharmaceutical Quality System each time.
- A risk assessment should be performed and raised to the Trust Risk Register.

9.3 Shelf life considerations:

- The expiry period of the eye drop product prepared under these circumstances should be based on a knowledgeable assessment of the formulation of the preparation and the microbiological risk to the product, balanced against the expiry period required to meet the patient's needs until a product prepared under licence can be obtained. The shortest possible practical expiry period should be assigned to the eye drop product. This would not normally exceed 72 hours.

- In use, the eye drops should be assigned a 24 hour maximum expiry period.

9.4 Validation:

- The issue of whether to undertake a validation of eye drop bottle filling as part of the overall Validation Master Plan (VMP) for a Section 10 unit is controversial. Some units undertake a process validation to mimic the process and sterility testing on filled bottles. The completion of validation is recorded in the risk register entry as a risk mitigation procedure. This may be interpreted as "normalization" or "acceptance" of the preparation of eye drops into the usual product portfolio of the unit. Open system products may not be part of the regular range of "catalogue" products prepared; however, performing process validation to mimic all procedures is good practice.

- For Section 10 units preparing eye drop products occasionally the following validation approach is recommended:
- Prepare an additional bottle in each "batch" and send for sterility testing
- Complete an end of session broth fill at the end of the process
- Review the results and any process validations at annual quality review to feed into future risk assessments.

References:

- MHRA Q&As for “Specials Manufacturer’s”: revision 1 January 2015
- MHRA Guidance Note 14 (GN14) - The supply of unlicensed medicinal products (“specials”) June 2014
- MCA 1992 – Guidance to the NHS on the Licensing Requirements of the Medicines Act 1968 issued by the Medicines Control Agency September 1992
- Annex 1 (EU Guidance on Good Manufacturing Practice) - Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2017 10th Edn. Pub Pharmaceutical Press ISBN 978 0 85711 285 9

Appendix 1:

Clinical Guidance, Ophthalmic Special Order Products, August 2016

- When clinically appropriate and available, licensed products should always be prescribed and dispensed in preference to unlicensed products;

- Certain products e.g. sodium chloride 5%w/v eye drops and sodium chloride 5%w/w eye ointment are now available as prescribable medical devices throughout the UK, these should be prescribed in preference to unlicensed medicines;

- Where a preservative-free (PF) preparation is clinically necessary, licensed Single Dose Units (SDUs) or licensed multi-dose devices e.g. Tear-Lac® should be prescribed if available;

- Excipient intolerances should be included on the prescription (some licensed and unlicensed products including those labelled preservative-free contain potentially sensitising excipients);

- Multidose preservative-free preparations should only be used for a limited period once opened;

- Justified and validated in-use shelf lives should be provided by the manufacturer*;

- Single dose units should be used once only in accordance with the licence.