The Role of Technical Services in Delivering an OPAT Service in North Wales

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Introduction

What is OPAT?

OPAT is Outpatient Parenteral Antimicrobial Therapy, this treatment facilitates patients to receive intravenous antibiotics in their own home. By enabling this OPAT can improve the patient experience, reduce strain on family and friends and reduce exposure to co-morbidities often associated with lengthy hospital stays. For a healthcare provider there are many advantages these include improvements to patient flow, the release of nursing time, additional bed days and reduced costs. However despite the advantages for patients healthcare providers uptake in the UK has been slow due to clinical, financial and logistical concerns (1). Much work has been carried out to help minimise these concern (2).Due to the high risk, difficulty and time intensive nature of producing the filled elastomeric devices required in a hospital aseptic unit, provision of this treatment is reliant on Contract Manufacturers. This is costly, introduces a delay between prescription and treatment, and as recently demonstrated does not have a robust or reactive supply chain, with lead times often longer than treatment times which reduces confidence in the service.

What do we want to do?

Technical Services departments are well placed in order to help over come some of these barriers to starting an effective OPAT service. Automation is becoming more widely employed in aseptic units and offers the chance to batch manufacture devices thus decreasing the manufacturing times of devices and reducing the strain on aseptic manufacturing technicians. Additionally most commercially available products are supplied with a 13 day refrigerated and 1 day 32oC shelf life, this shelf life is not conducive to the long term storage of treatment courses and limits the availability of the devices with manufacture required after a prescription is received. If the shelf life was extended then dose could be prepared and stored within the pharmacy so they are ready when a patient requires them.

OBJECTIVE

Technical Services within BCUHB in North Wales wanted to determine whether the latest in automated filling technologies could be employed in order to safely and efficiently batch manufacture Flucloxacillin 8g/ 240 mL elastomeric devices with an extended shelf life that would facilitate the expansion of the OPAT service within the Health Board.

METHOD

Advantages of Automation

Time studies were carried out whereby the production of equivalent batches using current manual aseptic manufacturing techniques and semi-automated manufacturing method were timed. Initial assay results and volume of fill studies were used to determine the validity of the method

HPLC Method Development

A stability indicating HPLC method was developed in accordance with ICH Q2.

Stability Study

Figure 1: Gri-Fill 4 and example elastomeric devices

Stability studies were carried out in accordance with the guidance set out in the NHS Yellow Cover Document. Batches of the EasyFlow elastomeric devices (Adriamed, Pescara) were stored under the following conditions: 4°C, 25°C/ 40%, and 32°C 60%. The study will continue until the testable product is depleted or 2 time points after the degradation limit is reached

RESULTS

HPLC Method Development

An analytical method was developed that was shown to be stability indicating. It is linear across a concentration range of 0.002 g/mL to 0.066 g/ mL. All impurities given in the BP are detectable to 0.002 g/mL with baselines resolution to the primary flucloxacillin peak

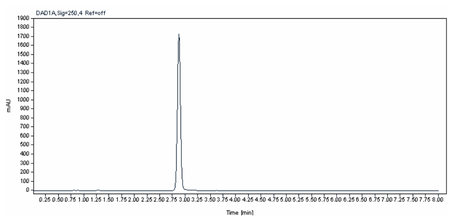


Figure 2: Sample flucloxacillin chromatogram

Table 1: Flucloxacillin Stability Indicating HPLC Method Parameters	
Run Time	8.00 minutes
Wavelength	250 nm
Flow Rate	1.0 mL/ min
Injection volume	5.0 µL
Column	C18 100 x 4.6 mm 2.6 µm 100 Å
Mobile Phase A	Acetonitrile
Mobile Phase B	10 mM di-sodium orthophosphate pH 2.5
Column Temperature	30.0 °C
Needle Wash	Methanol

Time Studies and Manufacturing Validation

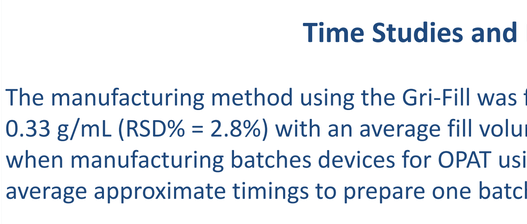
The manufacturing method using the Gri-Fill was found to produce devices with an average concentration of 0.33 g/mL (RSD% = 2.8%) with an average fill volume of 240 mL (RSD% = 0.35%). Operators were timed when manufacturing batches devices for OPAT using manual techniques and when using the Gri-Fill 4. The average approximate timings to prepare one batch of 4 devices are given below:

- Manual filling: 5 hours
- Semi-Automated filling: 1 hour

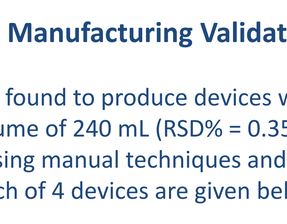
Manufacturing Development and Stability Study

Throughout the stability study the appearance, pH, sub visible particle count, assay and related substances have been assessed (n=4 for each storage condition).

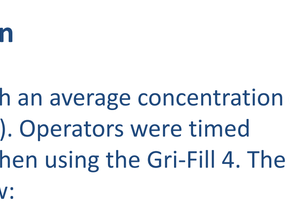
Graph 1: Assay % Relative to T0 for Refrigerated Samples



Graph 2: Assay % Relative to T0 for 25°C/ 40%



Graph 3: Assay % Relative to T0 for 32°C/ 60%



Appearance, pH and particle counts are all currently within limits outlined by the British pharmacopoeia for flucloxacillin injectable preparations. Current assignable shelf lives at each storage condition are:

- 4°C: 16 days
- 25°C/ 40%: 2 days
- 32°C 60%.: 2days

CONCLUSION

This study into the use of semi automated in-house manufacture of elastomeric devices for OPAT within technical services can realise the following benefits:

- **Manufacture devices in 20% of the time when compared to traditional manual methods**
- **Increased shelf life when compared to commercially available products, potentially up to 200%.**
- **Manufacture doses for 30% the cost of commercial purchase**
- **Reduce time to dose from 24 hours to 0 hours.**

IMPACT

Introduction of semi-automation to Technical Services facilities can enable a sustainable cost effective supply of elastomeric devices that overcomes many of the barriers to entry of these services. The efficiencies gained by using these automated techniques enables the capacity within manufacturing units to be released.

The indication from the on-going stability study that the shelf life can be improved over what is currently offered provides the ability to prepare and store devices well in advance of patient requirement, reducing the time from prescription to treatment and enabling better work management in the aseptic units. Additionally the additional confidence being provided by the 25°C may overcome some hesitations towards the logistics of patient supply and home storage. This is in line with the Welsh Government's 'A Healthier Wales' plan.

In-house manufacture by Technical Services enables the benefits, to patients in regard to quality of life and exposure of co-morbidity and benefits to the healthcare provider included increased patient flow, additional bed space and nurse time, to be realised in a more cost effective manner. These highlight the benefits of innovation within Technical Services on the patient experience. The table below uses BCUHB costing estimates to provide information the cost of treatment for an example 2 week treatment course of IV flucloxacillin.

Table 2: Estimated Cost of Treatments				
Method of Treatment	**Days in Hospital**	**Cost of Stay (£)**	**Cost of Treatment (£)**	**Total Cost of Patient (£)**
In - Patient	14	7490	490.00	7980.00
OPAT	1	535	1613.50	2148.50
Technical Services OPAT	0	0	474.00	474.00

Further Work

The stability study presented on this poster in currently in currently in progress and will continue as stated in the method section.

The next stage in the work presented here is to expand the stability study to cover a variety of manufacturer's elastomeric devices, thus improving the robustness of the service provided by introducing contingency.

Additional antimicrobials will be assessed for stability dependent on the requirements of the proposed OPAT service.

References

1. Chapman, ALN. (2013). 'Outpatient parenteral antimicrobial therapy clinical review', BMJ, 346.
2. British Society for Antimicrobial Chemotherapy; Outpatient and Parenteral Antimicrobial Therapy (OPAT) BUSINESS CASE MODELLING TOOLKIT
3. Welsh Government – A Healthier Wales: Our Plan for Health and Social Care. https://www.basw.co.uk/system/files/resources/180608healthier-wales-mainen.pdf

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