Assessment of the stability of citrate-buffered flucloxacillin for injection when stored in two commercially available ambulatory devices: INfusor (Baxter) and Accufuser® (Woo Young Medical), a study compliant with the NHS Yellow Cover Document (YCD) requirements

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INTRODUCTION

- Outpatient parenteral antimicrobial therapy (OPAT) services in the UK predominantly use antimicrobial agents that can be given via a short, once daily infusion, for convenience.
- These agents are often broad-spectrum. Beta-lactam antibiotics are often unsuitable in OPAT due to the frequency of dosing and their poor stability in aqueous solutions for extended infusion.
- The buffering of beta-lactam antibiotics has been shown to improve stability.[1]
- A continuous infusion of a beta-lactam, such as flucloxacillin, could maximize PK/PD parameters, promote stewardship by use of narrow-spectrum agents, and potentially improve patient outcomes.
- Ambulatory devices that allow a 24-hour infusion period are available in the UK; however, there are no open access data to support the extended stability of antibiotics in these devices.[2]
- The British Society for Antimicrobial Chemotherapy is commissioning the stability testing of selected antibiotics in two devices to NHS Yellow Cover Document standards,[3] with the aim of making stability data open access and freely available.
- Here we present the results of the first such study on flucloxacillin.

METHODS

- After assessing the influence of buffers and pH on the degradation rate of flucloxacillin, we determined that the drug could be stabilised in low strength citrate-buffered saline, circa pH 7.
- The stability of 10 and 50 mg/ml flucloxacillin sodium injection in two brands (Accufuser® and INfusor LV) of 24 hour ambulatory devices was assessed with a diluent of saline buffered with sodium citrate 0.3% w/v using a fully validated, stability-indicating, HPLC method.
- Samples were visually inspected for the presence of particles or discolouration. The pH of the solutions was monitored, as was the presence of sub-visual particles.
- The test period was up to 14 days at 2-8°C, then a 24 hour 'in use' period at 32°C. Tests were carried out in triplicate at both concentrations in both devices.

RESULTS

- The devices tested are shown in Figure 1.
- All flucloxacillin solutions throughout the study period remained colourless, clear in appearance and free from visible particles. Sub-visible counts remained within acceptable limits throughout the study.
- There was a trend towards lower pH of the solutions over the course of the study, which was accelerated at the end of the study by storage at the elevated temperature.
- Results showed that flucloxacillin concentrations remained greater than 95% of the zero-time concentration for at least 14 days (Figure 1).

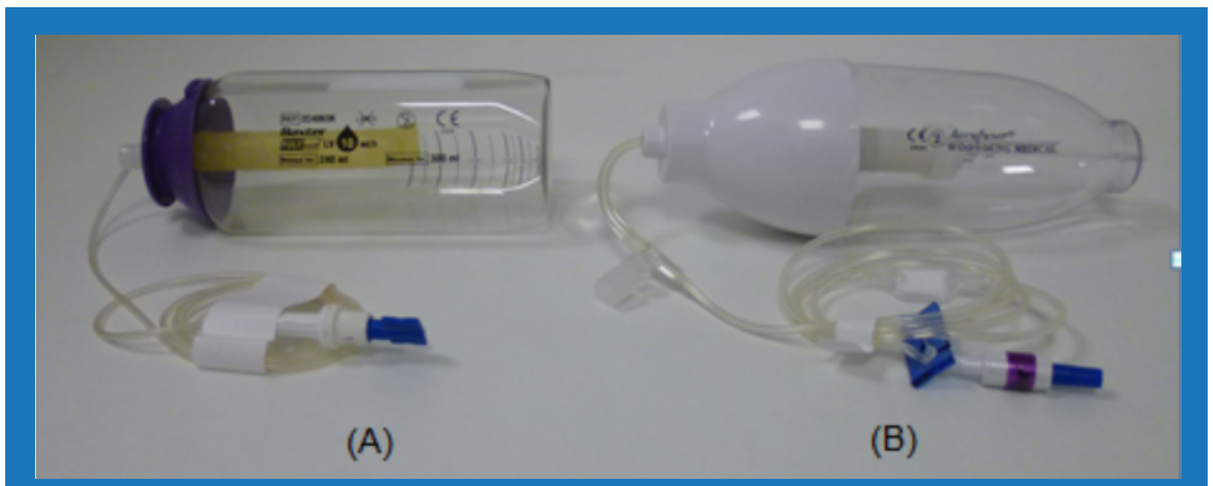

FIGURE 1. (A) INfusor LV10 pump (Baxter); (B) Accufuser® pump (Woo Young Medical)

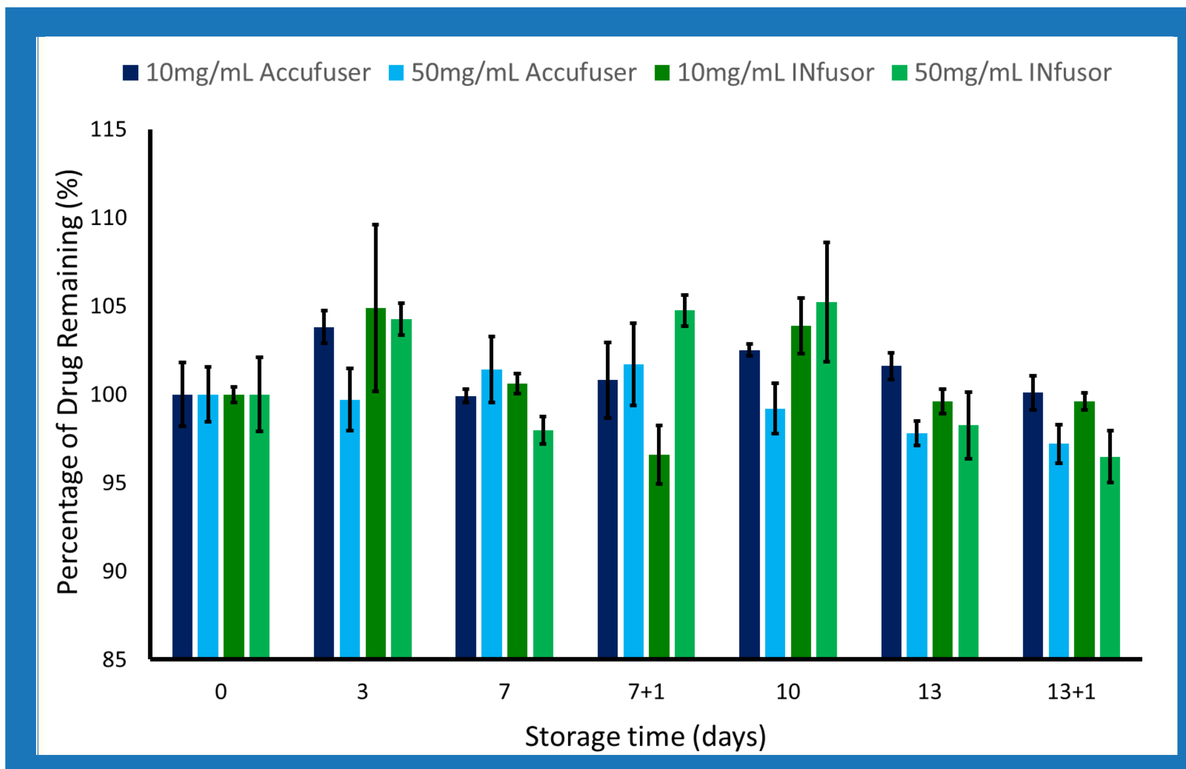

FIGURE 2. Amount of flucloxacillin remaining after storage for up to 14 days (13 days' at 2-8°C, plus up to 24 hours at 32°C)

CONCLUSIONS

- Flucloxacillin can be stabilised in low strength citrate-buffered saline circa pH 7.
- Citrate-buffered flucloxacillin infusion in two ambulatory devices available in the UK, passed full stability studies in accordance with the requirements of the NHS YCD.
- A shelf life of up to 13 days' at 2-8°C, followed a body-worn infusion period of up to 24 hours at 32°C, can be assigned (for the two ambulatory devices studied).
- This study was funded through the BSAC Antimicrobial Drug Stability Programme and has been submitted for peer review. Links to open access publication will be available via the BSAC Drug Stability website http://www.bsac-dsp.com/

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