Stability of paracetamol tablets repacked in dose administration aids for prn use: implications for practice

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PARACETAMOL TABLETS REPACKAGED INTO DOSE ADMINISTRATION AIDS AND STORED UNDER BOTH AMBIENT AND ACCELERATED CONDITIONS ARE STABLE FOR 12 MONTHS.

INTRODUCTION
Paracetamol is a valuable first-line drug for relieving mild to moderate pain and has been successfully combined with opioids for the management of severe pain.1,2

Dose administration aids (DAAs) are used to safely manage medication for patients in their homes and for residents in aged care. The level and type of care often determines which medicines are repackaged and the type of DAAs used. High-care facilities administer when necessary (pro re nata [prn]) medicines from the primary packaging, while their regular, non-prn medicines are often packed in DAAs. Low-care facilities, where registered or enrolled nurses are not always available to administer medications, will utilise repackaged prn medicines, as per the Guidelines for Medication Supply to Residential Aged Care Facilities (RACFs).1 In such facilities, paracetamol is one of the most commonly repackaged prn medicines, with two paracetamol tablets packed into each blister of a prn DAA.

Despite this, only a limited number of medicines have been investigated for stability, following repackaging into DAAs and the stability of these repackaged medicines has not been investigated for a 12-month period.

Paracetamol, subsidised under the Australian Pharmaceutical Benefits Scheme, is supplied in quantities of 100, or 500 for patients with chronic arthropathies. For patients with an infrequent need for paracetamol, this may necessitate disposal and replacement of large quantities of medicine every eight weeks. Frequent replacement of prn DAA packs that may contain viable medication places additional cost on the patient, and extra workload and cost on the RACF and Pharmacy.

Haywood et al. have reported on the physicochemical stability of paracetamol tablets repackaged into DAAs and stored for three months. Therefore the aim of this study was to investigate the physicochemical stability of paracetamol tablets repackaged into DAAs stored for 12 months.

METHOD
Physicochemical stability studies were performed at baseline,
### Physical stability

Appearance was evaluated organoleptically in comparison to the original samples. Tablet weight, friability hardness and thickness were analysed using appropriate equipment as described in appendices XII and XVII of the *British Pharmacopeia*.

Disintegration was determined with purified water used as the medium. Disintegration tests were performed using a phosphate buffer (pH 5.8) dissolution media (900 mL) maintained at 37 ± 0.5°C. Samples were withdrawn at two, four, 10, 20 and 25 minutes and assayed for paracetamol content according to the test for disintegration for paracetamol tablets described in the *British Pharmacopeia*.

All physical tests are described in the previous study by Haywood et al.

### Chemical stability

High performance liquid chromatography (HPLC) was used to quantify paracetamol in the presence of its degradants and tablet excipients. Twenty tablets were ground to a fine powder and replicate samples containing 100 ± 5mg paracetamol were weighed, diluted appropriately with mobile phase and filtered through a 0.45μm filter (Millipore) prior to analysis.

#### RESULTS

**Physical stability**

No organoleptic changes were observed for any of the samples over the 12-month period under ambient or accelerated conditions, with no significant change (p > 0.05) in tablet weight uniformity, hardness or thickness, demonstrating that moisture...
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![Graph showing dissolution rate profiles of repackaged paracetamol tablets under accelerated conditions (40°C; 75% RH) for 12 months (mean ± 95% confidence interval; n=6).]

**FIGURE 1:** Dissolution rate profiles of repackaged paracetamol tablets under accelerated conditions (40°C; 75% RH) for 12 months (mean ± 95% confidence interval; n=6).

**DISCUSSION**

This study has shown that paracetamol tablets repackaged into a DAA, offering sufficient protection against moisture, will remain stable for up to 12 months, including under accelerated storage conditions (40°C, 75% RH). However, DAs may be subjected to a reasonable amount of handling and accidental rupture of blister seals may occur, allowing the tablets to be exposed to increased levels of humidity. Since the DAs in this study were also stored in a dark climate chamber, pharmacists should caution carers to store DAs appropriately away from light as paracetamol is required to be protected from light. This could include storage inside lockable cabinets, medicines trolleys and within medicine storage areas, which aligns with RACF Guidelines.

In conclusion, this study provides data that paracetamol tablets repackaged into DAs and stored under both ambient and accelerated conditions are stable for 12 months. Pharmacists will therefore be able to make risk-benefit assessments and recommend a 12-month expiry on these paracetamol tablets.