



Dose administration aids: Pharmacists' role in improving patient care

Haywood A¹, Llewelyn V², Robertson S², Mylrea M², Glass B²

¹ School of Pharmacy, Gold Coast Campus, Griffith University, QLD 4222

² School of Pharmacy and Molecular Sciences, James Cook University, Townsville, QLD 4811

REVIEW

Please cite this paper as: Haywood A, Llewelyn V, Robertson S, Mylrea M, Glass BD. Dose Administration Aids: Pharmacists' Role in Improving Patient Care. AMJ 2011, 4, 4, 186-192
<http://doi.org/10.21767/AMJ.2011.693>

Corresponding Author:

Professor Beverley Glass
School of Pharmacy and Molecular Sciences,
James Cook University, Townsville, QLD 4811
Email: beverley.glass@jcu.edu.au

Abstract

Dose administration aid (DAA) usage has become increasingly prevalent among populations worldwide and as such has become an important part of pharmacy practice. The evidence for the use of these aids has been favourable in Australia resulting in 2006 in a community based DAA program being considered by the Australian Government Department of Health and Ageing PPSAC (Professional Programs and Services Advisory Committee) and the first phase of this program implemented in October 2007. The program was established under the Better Community Health Initiative of the 4th Community Pharmacy Agreement between the Pharmacy Guild of Australia and the Commonwealth Government. The aim of this program is to reduce medication-related hospitalisations and adverse events through improved medication management and adherence by people in the community. The most common patient groups that access this service include the elderly, who are often on several different medications, and patients with cognitive disabilities who may have trouble understanding or remembering their dosage regimes.

Repackaging of a medication, involving removal from its primary packaging invalidates the stability guarantee of the manufacturer. It is in fact the role of the healthcare team to ensure optimal patient care by making an informed judgment as to the effect on the quality and safety of this repackaging process. Drug manufacturers, on the whole, tend to discourage repackaging of medications and there is little

quality data available to support this process. Indeed, only a small number of medications have been investigated for their stability following repackaging into DAAs, namely atenolol, paracetamol, frusemide, prochlorperazine, sodium valproate, aspirin (dosette boxes) and clozapine. This paper will review the repackaging of medications into DAAs and the role that the pharmacist plays in this process to improve patient care, in addition to presenting the Australian research that has contributed substantially to the body of information available internationally on the quality implications, relating to the stability of medicines repackaged into DAAs.

Key Words: Compliance (dose administration) aid, patient care, storage, repackaging, quality, safety

Background

Populations are increasing in age worldwide as are the number of medications prescribed for patients. An increasing number of these patients are receiving their medication in Multi-compartment Compliance Aids (MCCAs) or DAAs due to the benefits in terms of health outcomes and cost of healthcare. Despite the widespread use of these devices, there is little available data on the quality implications, based on the stability of these drug products when repackaged into such devices.¹⁻⁴

Compliance aids are devices which have been developed to assist patients in managing their medicines by arranging individual doses according to their prescribed dose schedule throughout the day.⁵ These aids have been used to facilitate medication administration to patients for over 30 years and their wider application has been strengthened by various government programs worldwide to facilitate their use.⁶ A community pharmacy contractual framework in the UK now places emphasis on assessing and providing practical compliance aids to all patients who fall within the protection of the Disability Discrimination Act 1995 and need help with medicine taking.⁷ The Australian Government Department of Health and Ageing has funded a number of professional programs and services under the Better Community Health Initiative of the 4th and 5th Community Pharmacy Agreements, including the DAA Program,⁸ where the dollar value was increased from nearly \$73 million to \$132 million. The objective of this program is to identify patients who will derive the most benefit from the supply



of a DAA, to develop a sustainable service and payment model capable of meeting the program’s aim and to trial the broader use of these aids within the community setting. The provision of a DAA service through community pharmacies is expected to reduce medication related hospitalisation and adverse events through improved medication management. This should result in improved quality of life and health status for patients, and have flow on benefits for the community by reducing the demand on aged care facilities and costs associated with adverse reactions to medication mismanagement.⁸

The *shelf-life* of a drug product may be affected by the intrinsic stability of the active pharmaceutical ingredient (API) and the excipients, the potential interactions between them, the manufacturing process, the dosage form, the packaging and the environmental conditions encountered during their transport, storage and use.^{9,10} A recent survey of 392 products revealed that, although some information regarding the potential stability of oral solid dosage forms in DAAs can be obtained from manufacturers, there is still a lack of short-term stability data for the transfer of drug products into these devices.¹ Thus, although the benefits of the use of these devices, in terms of both health outcomes and cost of healthcare have been reported,^{11,12} there is little available data regarding the shelf-life of drug products when repackaged.¹ The fact that there is little available stability data is significant considering the value of these aids, the investment in dollars and the extent to which they are being used to aid adherence. Although there are various published guidelines, such as the Pharmaceutical Society of Australia (PSA) Professional Practice Standards¹³ and Dose Administration Aids Service Guidelines and Standards for Pharmacists¹⁴ providing general guidance on stability issues related to the repackaging of oral solid dosage forms, a review article by Glass and colleagues¹⁵ published in 2009 was innovative in that it represented the first data and developed methodology on the stability of a series of drugs susceptible to environmental conditions, repackaged into DAAs.

The stability of a pharmaceutical product may be defined as the capability of a particular medicine, in a specified container, to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications. Pharmaceuticals are expected to meet specifications for identity, purity, quality and strength throughout their defined storage period. The stability of manufactured medicines is routinely confirmed by the drug manufacturers according to International Regulatory requirements,¹⁶ where stability studies on packaged medicines are conducted at real time, long term and accelerated conditions at specific temperatures and relative humidity (RH). This represents storage conditions experienced in the distribution chain of the climatic zone(s) of the country or region of the world concerned. Manufacturers’ packaging is designed to protect drug products from environmental factors encountered during storage, such as light, air (oxygen, carbon dioxide, other gases), and moisture while ensuring limited interactions between the product and the packaging material.

However, this does not guarantee the stability of API and the drug product on removal and repackaging into a DAA. Although the stability of a dosage form is often seen to be the responsibility of the manufacturer, this does not include removal from the original packaging. In electing to repackage a drug product into a DAA, healthcare professionals must consider the implications on drug stability of the transfer to a non-manufacturer pack.

Pharmacists thus rely largely on individual drug storage recommendations, available national guidelines for repackaging, e.g. in Australia,¹⁷ the UK¹⁸ and USA¹⁹, and their basic understanding of inherent drug substance stability to make case-by-case recommendations as to whether repackaging is appropriate.

Evidence of assuring quality patient care in practice – Australian studies

Despite the widespread use of these devices, there is little available data regarding the effect of repackaging and storage on the quality these drug products. Because of the lack of availability of data on the quality implications, in terms of stability on repackaging and storage of drugs in DAAs, the following Australian studies have contributed significantly to the body of evidence available on this repackaging process. The drug candidates were chosen for study because they are commonly repackaged into DAAs, because of their proven susceptibility to various environmental conditions and because of anecdotal evidence from the practice of problems encountered when these drugs are repackaged either from a patient or health professional perspective (Table 1).

Table 1: Summary of Australian research reporting on the stability of medicines repackaged into DAAs.

Active Ingredient	Stability considerations	Reference
Aspirin	Moisture sensitive	20
Clozapine	Oxygen sensitive	21
Frusemide	Light sensitive	22
Paracetamol	Moisture sensitive	23
Prochlorperazine	Light sensitive	24
Sodium valproate	Hygroscopic	6

Methodology

Physicochemical studies, including the determination of the drug content in the tablet (analysis by a validated high performance liquid chromatographic method) were performed on the repackaged tablets in a commonly used DAA at ambient (25°C; 60% RH), accelerated (40°C; 75% RH), and light (photostability testing according to the International Committee on Harmonisation [ICH, Q1B]) conditions,²⁵ over an appropriate period of time.

Physical characteristics of the tablets, namely; tablet weight uniformity, physical appearance, thickness, hardness, friability, disintegration and dissolution rates, were evaluated at time zero and at appropriate time intervals. A favourable outcome for these physical tests is

important as they reflect the drugs' ability to dissolve, be absorbed and exhibit bioavailability resulting in effective therapy. Since DAAs, when packed in a community pharmacy usually include a four week supply, stability data was collected over a minimum period of six weeks, to allow for repackaging in the pharmacy and delivery to the patient. In some studies, depending on the stability considerations for that particular drug candidate which needs to be taken in to account, additional storage conditions were investigated e.g. exposure of the DAA to fluorescent and window filtered sunlight. This is justified by the fact that although DAAs are commonly packed in a controlled room temperature environment (i.e. 25°C; 60% RH) they may however be subsequently exposed to increased temperature, humidity and light in-use, especially in rural and remote regions of northern Australia. All results were compared to control samples stored in the manufacturer's original blister packaging at the various environmental conditions and time periods employed.

Paracetamol is commonly repackaged into DAAs with the potential to degrade in the presence of moisture motivating its choice as a model drug to commence investigations into the effect on stability of drugs repackaged and stored in DAAs. Haywood and colleagues²³ examined the stability implications of repackaging a commonly used 500mg paracetamol tablet (Panamax, Sanofi Synthelabo). Samples were repackaged and stored under the conditions specified in the methodology. Results were very favourable for repackaging paracetamol, indicating that all requirements for the physicochemical stability were met with the paracetamol content within the required British Pharmacopoeial (BP) range of 95–105% of the labelled amount, for all storage conditions, even those conditions of high humidity.

The results of the study suggest that paracetamol tablets repackaged into a DAA offering sufficient protection from moisture would remain stable for a reasonable in-use period of approximately six weeks (i.e. allowing two weeks for advanced packing and delivery on a four-week supply).

Frusemide is commonly used in the treatment of cardiac failure and hypertension and likely to be a candidate for repackaging into a DAA. A study by Bowen and colleagues²² reported on the 'in-use' stability implications of repackaging this light sensitive medicine, namely 40mg frusemide tablets (Uremide, Alphapharm), and storing under the conditions specified in the methodology. In addition, packed DAAs were stored for eight weeks under conditions that reflected: 1) "home-environment" where DAAs were stored blister-side up in a bathroom exposed to a standard 60W tungsten bulb and indoor indirect daylight/ window- filtered sunlight; and 2) "pharmacy-environment" where DAAs were stored blister-side up on a bench top exposed to fluorescent lighting and indoor indirect daylight. Again the drug content was confirmed to be within the BP range of 95–105% for all storage conditions, including under ICH light conditions.²⁵

Although the physical stability was confirmed by all tests (weight uniformity, hardness, friability, disintegration, dissolution), under both controlled and in-use conditions, the

exposure to light in the pharmacy and under ICH conditions, even after one week resulted in a yellow colouration of the tablets. The progressive yellow discolouration of the tablets over an eight week storage period (Figures 1 and 2) was attributed to exposure to fluorescent lighting, which was not encountered under the 'home-conditions'. Although the colour change was noted as having negligible effects on the drug content and other physical parameters, such as dissolution of the tablets, it was considered an unacceptable change, since patients are likely to be concerned about a possible compromise in the quality of the medication, and this may have an adverse effect on patient acceptance and hence adherence.



Figure 1: Progression of colouration of frusemide tablets exposed to fluorescent lighting over an eight week period from left (week 1) to right (week 8)



Figure 2: Colouration of frusemide tablets after eight weeks of exposure to fluorescent light showing the exposed side of the tablet (left) and the bottom unexposed side of the tablet (right).

Prochlorperazine is a phenothiazine drug, widely used as an anti-emetic and is susceptible to oxidation to sulphoxide (a metabolite and a photodegradant) under the influence of light. The main metabolites and degradants of all phenothiazines are found to be inactive at the dopamine receptors. This, and the fact that prochlorperazine is reported to cause photosensitivity effects in patients, prompted an investigation into its repackaging into DAAs.^{26, 27}

A study by Glass and colleagues²⁴ reported on the physicochemical stability of repackaged 5mg prochlorperazine tablets (Stemetil, Sanofi-Aventis) under the storage conditions and time period specified in the methodology. In addition because of the instability of prochlorperazine to light, tablets were placed blister-side up on a bench top exposed to fluorescent lighting and indoor indirect daylight for 12 hours per day. Chemical (drug content) and physical stability was confirmed to be within BP limits (drug content within 95–105%) however, there were noticeable organoleptic changes in the tablets stored under in-use conditions, with a progressive grey discolouration over an eight week period, starting in week

2. The discolouration and the potential for the resulting photodegradants to cause adverse effects in patients suggest that the quality of this medication had been compromised.

Sodium valproate Recently Llewelyn and colleagues⁶ undertook a study on the stability of sodium valproate repackaged into DAAs and stored under various temperature and humidity conditions. The results of this study highlight the importance that accelerated conditions of temperature and humidity be taken into account, and that cognisance is taken from the fact that in different countries, and in fact within the same country, the climatic conditions might vary considerably. Medication therefore may be appropriately for repackaged in, for example, a temperate region such as London, Los Angeles or even Sydney, but repackaging that same medication in tropical or desert regions such as Darwin or Dubai may be completely inappropriate due to increased heat, humidity and light conditions. The results revealed that while the sodium valproate content in the tablets remained within an acceptable range under all storage conditions for eight weeks, the physical stability was not maintained, with unacceptable weight variation in the tablets, changes in their dissolution profiles and significant changes in their appearance, under accelerated conditions, due to the hygroscopicity of the API even after only three weeks (Figure 3). These results are significant because these accelerated conditions are not uncommonly encountered in northern Australia and other tropical regions worldwide.



Figure 3: Appearance of sodium valproate tablets after 21 days of storage at accelerated (40°C; 75% RH) (left), refrigerated (2–8°C) (middle) and controlled room temperature (25°C) (right) conditions.

Clozapine is an atypical antipsychotic used in the treatment of schizophrenia. Because of reports from hospital pharmacy practice about discolouration of returned clozapine tablets repackaged into DAAs, and the literature evidence that it is susceptible to oxidation,²⁸ the aim of this study was to evaluate both the chemical content and physical stability of clozapine tablets (Clopine, Hospira, and Clozaril, Novartis) repackaged into a DAA over a six week period. Although the physical stability was confirmed for all tests at room temperature (weight uniformity, hardness, friability, disintegration and dissolution), under accelerated conditions, the disintegration test did not meet the BP requirements. However the subsequent dissolution test was successful with 85% of clozapine dissolving in 45 minutes. The chemical stability (the clozapine content within the BP range of 90–110%) was also confirmed for all storage conditions, including for those light ICH conditions.²⁵ Based on the susceptibility to oxidation, in order to reproduce the colouration noted in the practice of samples returned by patients, a study was undertaken on a control sample, a sample packed six weeks

under simulated real conditions (exposed to ambient temperature and fluorescent light conditions) and a sample removed from the packaging and exposed to light and air on the bench beside the simulated real conditions samples.

The results shown in Figure 4, illustrate an extreme discolouration for the exposed tablets very similar to the anecdotal reports from practice. This result thus shows that clozapine, when correctly repackaged, maintained its physical and chemical stability for six weeks. Based on these further studies it is assumed that these reports were as a result of improper handling of these DAAs by patients. These findings highlight the importance of the role of the pharmacist providing patient care in advising on the correct handling and storage of their DAAs.



Figure 4: Photographic comparison of the colour of clozapine tablets from left to right: control, sample packed six weeks under simulated real conditions, and left out of packaging exposed to light and air on the bench (Clopine above and Clozaril below).

Aspirin (acetylsalicylic acid) in low-doses has been increasingly prescribed for primary prevention of stroke and acute myocardial infarction in the elderly. A recent study has shown that low-dose aspirin is a cost-effective option in primary prevention and that the majority of healthcare systems are more than willing to pay for any additional Quality-Adjusted Life Years (QALYs) gained.²⁹ It is often more cost-effective for patients to purchase standard dose (300mg) aspirin and to cut the tablet in half to achieve a “low-dose” equivalent. Tablet splitting or dividing has been an accepted practice for many years as a means of obtaining the prescribed dose of a medication and for cost-saving purposes.³⁰ However, the storage of split tablets is not well discussed in the literature and anecdotal evidence suggests that many patients or their carers split tablets in advance and then store the split tablets in bottles that previously contained the same medication, different medication or some other substance, or in a compliance aid such as a dosette box.³⁰ Due to stability concerns, patients and carers should be advised that when half a tablet is taken, the unused half should be immediately discarded, particularly with medicines that are known to be unstable when exposed to light and air.³⁰ Considering the above practices and the



fact that acetylsalicylic acid is rapidly hydrolysed to salicylic acid on exposure to moisture, the aim of this study was to assess the stability of aspirin tablets (Solprin [Dispersible Tablets], Reckitt Benckiser) when repackaged and stored under a number of 'in-use' conditions, both as a whole tablet and also when split in half. This is an important consideration as it is a decision to be made in practice by pharmacists or at home by patients and carers. The acetylsalicylic acid content remained within specifications (95–105% of labelled amount) for all except the accelerated storage conditions, with 93.4% of the drug remaining in this case and the salicylic acid content at 0.04% (BP limit 0.0006%). The split tablets did not display any additional degradation of the drug or increased amount of the degradant salicylic acid, when compared to the whole tablets under the same conditions. While the acetylsalicylic acid content remained within specifications under standard room conditions, it must be noted that the limit for the degradant has been exceeded under all conditions. Additionally there was some colouration and disintegration of the tablets, thus compromising the quality of this medication and suggesting that this practice of repackaging by patients is inappropriate.

Dispersible tablets are in fact listed as an example of tablets that should not be repacked into a compliance aid.¹⁷ This study in fact does confirm the instructions given that these tablets should not be removed from their original packaging and that if tablets are split, that the remaining half should be discarded.

Discussion

Various published guidelines, such as the Pharmaceutical Society of Australia (PSA) Professional Practice Standards¹³ and Dose Administration Aids Service Guidelines and Standards for Pharmacists¹⁴ have provided general guidance on stability issues related to the repackaging of oral solid dosage forms into DAAs and are summarised as follows:

- Medicines that are generally unsuitable for packing into DAAs include effervescent, dispersible, buccal, and sublingual tablets and significantly hygroscopic preparations.
- Medicines administered on an 'as required' basis are generally unsuitable for packing into DAAs since they may be taken unnecessarily on a regular basis or removed from the blister for use at an earlier or later stage, thus exposing the remaining contents to the environment.
- Cytotoxic preparations or other medicines posing occupational health and safety risks are generally inappropriate, however the risk-benefit of packing must be considered; for example, packing may be appropriate where non-adherence is considered to be a greater risk.
- Only devices that are well sealed and tamper evident should be used.
- The length of time taken for the end-to-end packing process should be kept to a minimum; tablets and capsules should be removed from the manufacturer's foil or blister pack immediately before the DAA is packed, and the DAA sealed immediately after it is packed.
- Any heat sealing methods should be used quickly and efficiently to minimise exposure of medicines to heat,

especially medicines that might be affected when the backing of a DAA is heat-sealed, for example, soft gel capsules.

- The packed DAAs should be stored in an area that is cool, dry and protected from light, and the time between packing and dispensing should be kept to a minimum.
- When a DAA needs to be transported by independent couriers or other means, consideration should be given to the likely storage conditions (e.g. exposure to heat, humidity, and moisture) and the length of time the DAA will be in transit.
- It is useful to maintain a list of medicines/medicine types that should not be removed from their original pack for packing in a DAA.

Recommendations

A flow chart for the quality management of DAAs in practice is shown in Figure 5. The following practical recommendations for ensuring the stability of medication repackaged in DAAs, arising from this review include: (i) selecting an appropriate brand of DAA for repackaging medicines that affords appropriate protection against air and moisture; (ii) protecting the DAA containing drugs susceptible to photodegradation from light in the pharmacy and in patients' homes, achieved by either storing the DAA protected from light and/or placing the DAA into a light-protecting sleeve (e.g. foil, cardboard); (iii) careful removal of tablets to prevent accidental rupture of adjacent blisters, thus exposing tablets to air and moisture; (iv) monitoring the DAA integrity during repackaging, dispensing and throughout the in-use period; (v) consideration of an appropriate location to store the DAA to avoid unnecessary exposure to light, heat, humidity and away from children if the device is not child-resistant; (vi) counselling patients on correct use and appropriate storage locations for their DAA; and (vii) following appropriate professional practice guidelines¹³.

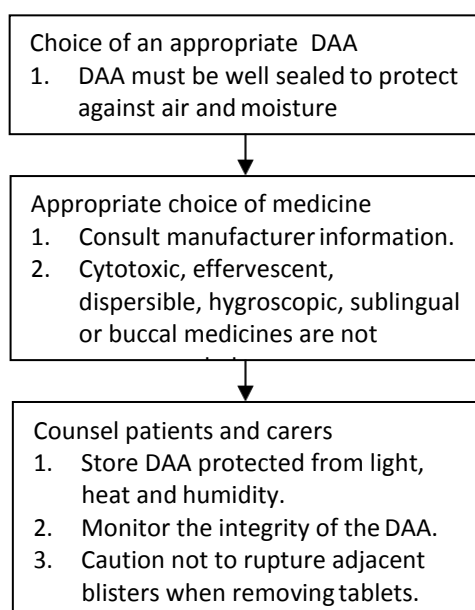


Figure 5: DAAs – Assuring quality in practice



Conclusions

This review, while highlighting the role of DAAs in improving the health outcomes for many patients, also provides further evidence to inform healthcare professionals, enabling them to assure the quality of medications repackaged into DAAs. This data serves to build on general guidelines (PSA) and provides some specific information on drugs at risk for repackaging into DAAs. For the light sensitive drugs, frusemide and prochlorperazine, the pharmacist's role in minimising light exposure during repackaging and counselling the patient is confirmed.

However, for hygroscopic drugs such as sodium valproate, without further investigation into the permeability of the DAA, caution should be exercised in repackaging into the DAA. This is confirmed by the guidelines which state that those preparations which are significantly hygroscopic should not be repackaged into DAAs.

Although this data provides an important contribution to the knowledge on the stability of drugs repacked into DAAs, it is important that it is adopted in context and does not detract from those procedures which for most drugs have the ability to improve the health outcomes for many patients.

This review presents the Australian research that has contributed substantially to the body of information available internationally on the quality implications relating to the stability of repackaging medicines into DAAs, and the important role that the pharmacist plays in this process of improving patient care.

References

1. Church C, Smith J. How stable are medicines moved from original packs into compliance aids? *Pharm J* 2006; 276: 75-81.
2. Nunney JM, Rayner DKT. How are multi-compartment compliance aids used in primary care? *Pharm J* 2001; 267: 784-9.
3. Walker R. Stability of medicinal products in compliance devices. *Pharm J* 1992; 25:124-6.
4. Ware GJ, Holford NH, Davison JG, Harris RG. Unit-of-issue medicine administration: time and cost-benefits in a geriatric unit. *Aust J Hosp Pharm* 1994; 24:329-32.
5. Australian Government Department of Health and Aging. Pharmacy: Dose Administration Aids Program - Fact Sheet. Accessed 19 January 2011. Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/ppasac-qa-daa>.
6. Llewelyn VK, Mangan MF, Glass BD. Stability of sodium valproate tablets repackaged into dose administration aids. *J Pharm Pharmacol* 2010; 62:838-43.
7. Chan K, Swinden J, Donyai P. Pilot study of the short-term physico-chemical stability of atenolol tablets stored in a multi-compartment compliance aid. *EJHP Sci* 2007; 13:60-6.
8. Pharmacy Guild of Australia. Professional Pharmacy Services: Dose Administration Aids. Accessed 19 January 2011.

Available from: <http://www.guild.org.au/pps/content.asp?id=1425>.

9. Aulton ME. *Aulton's Pharmaceutics. The Design and Manufacture of Medicines*. 3rd Ed. Edinburgh: Churchill Livingstone; 2007.
10. US Pharmacopeial Convention Inc. *US Pharmacopeia 33 - National formulary 28 <1191> Stability considerations in dispensing practice*. 2010.
11. Simmons D, Upjohn M, Gamble GD. Can medication packaging improve glycemic control and blood pressure in type 2 diabetes? Results from a randomized controlled trial. *Diabetes Care* 2000; 23:153-6.
12. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA* 2006 6; 296:2563-71.
13. Professional Practice Standards. Version 4. Standard 7: Dose Administration Aids Service: Pharmaceutical Society of Australia; 2010.
14. Pharmaceutical Society of Australia. Guidelines and standards for pharmacists: Dose administration aids service. July 2007. Accessed 19 January 2011. Available from: <http://www.psa.org.au/site.php?id=2065>.
15. Glass BD, Haywood A, Llewelyn V, Mangan M. Compliance aids and medicine stability: new evidence of quality assurance. *Curr Drug Saf* 2009; 4:74-8.
16. ICH Harmonised Tripartite Guideline. Stability Testing of New Drug Substances and Products Q1A(R2): ICH Steering Committee, Feb 2003.
17. Pharmaceutical Society of Australia. Guidelines and standards for pharmacists. Dose Administration Aids Service. Accessed 18 November 2010. Available from: <http://www.psa.org.au/site.php?id=2065>.
18. Royal Pharmaceutical Society of Great Britain. *Medicines, Ethics, and Practice: A Guide for Pharmacists*, Volume 27. London: Pharmaceutical Press, 2003.
19. US Pharmacopeial Convention Inc. *US Pharmacopeia 33 - National formulary 28 <681> Repackaging into single-unit containers and unit-dose containers for nonsterile solid and liquid dosage forms*. 2010.
20. Mangan M, Haywood A, Glass BD. Aspirin Repackaged: Caution in Practice. Proceedings of the Australasian Pharmaceutical Science Association Annual Conference. 2009.
21. Perks S, Robertson S, Haywood A, Glass BD. Stability of Clozapine Repackaged into Dose Administration Aids. Proceedings of the Australasian Pharmaceutical Science Association Annual Conference. 2010.
22. Bowen L, Mangan M, Haywood A, Glass BD. Stability of frusemide tablets repackaged in Dose Administration Aids. *J Pharm Prac Res* 2007; 37:178-81.
23. Haywood A, Mangan M, Glass BD. Stability implications of repackaging paracetamol tablets into Dose Administration Aids. *J Pharm Prac Res* 2006; 36:21-4.
24. Glass B, Mangan M, Haywood A. Prochlorperazine tablets repackaged into dose administration aids: can the patient be assured of quality? *J Clin Pharm Ther* 2009; 34: 161-9.



25. ICH Harmonised Tripartite Guideline. Stability Testing: Photostability testing of new drug substances and products Q1B: ICH Steering Committee, Nov 1996.
26. Moore DE, Tamat SR. Photosensitization by drugs: photolysis of some chlorine-containing drugs. *J Pharm Pharmacol* 1980; 32: 172-7.
27. Nejme M, Pilpel N. The effect of the photodecomposition of chlorpromazine on lecithin monolayers. *J Pharm Pharmacol* 1978; 30: 748-53.
28. Kohara T, Koyama T, Fujimura M, Tanaka H, Maeda J, Fujimoto T, et al. Y-931, a novel atypical antipsychotic drug, is less sensitive to oxidative phenomena. *Chem Pharm Bull (Tokyo)* 2002; 50: 818-21.
29. Annemans L, Wittrup-Jensen K, Bueno H. A review of international pharmaco-economic models assessing the use of aspirin in primary prevention. *J Med Econ* 2010; 13: 418-27.
30. Marriott JL, Nation RL. Splitting tablets. *Aust Prescr* 2002; 25: 133-5.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.