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Department of Health and Ageing
Therapeutic Goods Administration

Labelling and packaging practices: A summary of some of the evidence

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TGA Health Safety
Regulation

Historical consultation document

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Ageing, and is responsible for regulating medicines and medical devices.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <www.tga.gov.au>.

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Medication errors and the role of labelling

It has been estimated that the rate of medication related hospital admissions in Australia is around 2-3%, with as many as 30% of unplanned geriatric admissions being associated with an adverse medicines event. Approximately 50% of these admissions are considered potentially avoidable (Runciman et al, 2003; Roughead & Semple, 2009). In addition to hospitalisations related to adverse medicine events, there are thought to be over 400,000 general practitioner visits annually in Australia for addressing medication errors (Safety and Quality Council, 2002; Runciman et al, 2003).

It is difficult to more precisely determine the actual rate of adverse drug events, particularly those associated with labelling errors (Winterstein et al, 2002) as many may go unreported due to lack of severity or due to embarrassment of making an error with self-medication (Evans et al, 2006). Data collection is complicated as there are multiple ways of reporting adverse drug events and there is not a single central repository or analysis of adverse drug events that are reported in Australia (Safety and Quality Council, 2002; Runciman et al, 2003).

Taking these data limitations into account, it has been reported in the literature that medication misadventure resulting in hospitalisation in Australia is estimated to cost \$660 million annually (Roughead & Semple, 2009). A number of factors have been identified as contributing to the medication errors which occur in either a hospital or acute care setting or in the community or home setting (Weingart et al, 2000; Safety and Quality Council, 2002; Taylor et al, 2009a, Taylor et al, 2009b).

Factors contributing to medication errors include:

- environmental (distractions, lighting, level of activity) and personnel factors (not taking enough care, failure to confirm, fatigue, communication failure)(Weingart et al, 2000; Pharmaceutical Defence Limited, 2008);
- a lack of co-ordination between health care professionals in the care setting (Lu and Roughead, 2011);
- process or system failures between prescribing, transcribing/verifying, dispensing and administration (Senders, 1993; Leape et al, 1995; Safety and Quality Council, 2002).

Labelling and packaging issues either contributed to these errors or were the source of error in some instances (Cohen, 1995; Jensen et al, 2004; Hellier et al, 2006; Gernerin et al, 2007). Unsafe pharmaceutical packaging, nonexistent warning systems, look-alike labelling and poorly conceived drug nomenclature have been identified as major contributing factors to medication errors (Cohen, 1995).

The comprehensive review by Hellier et al (2006) of evidence-based research in related areas such as food and chemical labelling and more general warnings research considered design characteristics such as font size, colour, signal words and language and the effect of these on performance variables including compliance, understandability and discriminability; and discussed the relevance of these factors to medicine labels. The authors concluded that signal words, colour, format and wording are the design variables that have the most consistent effect on user outcomes. The outcomes that were likely to be

most relevant to reducing medication errors were those that relate to product noticeability and discriminability and those that relate to compliance.

Jensen et al (2004) developed evidence-based recommendations for the minimisation of errors in intravenous drug administration. Specific recommendations regarding labelling and packaging included standardisation of font, size, colour and information included on the labels of ampoules and the avoidance of similar packaging and presentation of drugs.

Labelling and packaging, may adversely affect patient safety and adherence to instructions by increasing the difficulty of finding and comprehending information (de Somer and Trofimov, 2011; Shrank et al, 2007a). In the US, poorly designed prescription drug labels are reported to account for approximately 1/3 of errors investigated by the US Pharmacopoeia, and is due, at least in part from confusion caused by the label (Shrank et al, 2007b). Furthermore, the observation that many patients receive no information from a health care provider except the instructions on the label highlights the importance of the medication label (Holt et al, 1992, Shrank et al, 2007b).

Shrank et al (2007a) conducted a systematic review of the published literature to evaluate the evidence regarding optimal content and format of prescription labels that might improve readability, understanding and medication use. The evidence about label format supported the use of larger fonts, lists, headers and white space, using simple language and logical organisation to improve readability and comprehension.

References

- Chermak TE & Lambert BL, Descriptive analysis of primary package labels from commercially available prescription solid oral dosage form drugs. *J Am Pharm Assoc*, 2009;49:399-406.
- Cohen MR, Drug product characteristics that foster drug-use system-errors. *Am J Health-Sys Pharm*, 1995;52:395-399.
- De Somer E & Trofimov I, Medicine Partnership of Australia – Packaging and labelling of pharmaceuticals and consumer safety - A survey of the literature, 2011.
- Evans SM, Berry JG, Smith BJ et al, Attitudes and barriers to incident reporting: a collaborative hospital study. *Qual Saf Health Care* 2006;15:39-43.
- Gernerin P, Perneger T, Chopard P et al, Drug Selection errors in relation to medication labels: a simulation study. *Anaesthesia*, 2007;62:1090-1094.
- Hellier F, Edworthy J, Derbyshire N & Costello A, Considering the impact of medicine label design characteristics on patient safety. *Ergonomics*, 2006;49:617-630.
- Holt GA, Dorcheus L, Hall EL, et al, Patient Interpretation of Label Instructions. *American Pharmacy*, 1993;NS32:58-62.
- Jensen LS, Metty AF, Webster CS et al, Evidence-based strategies for preventing drug administration errors during anaesthesia. *Anaesthesia*, 2004;59:493-504.
- Leape LL, Bates DW, Cullen DJ et al, System analysis of adverse drug events. *JAMA* 1995;274:35-43.
- Lu CY & Roughead E, Determinants of patient-reported medication errors: a comparison among seven countries. *Int J Clin Pract*, 2011;65:733-740.

Pharmaceutical Defence Limited Annual Report 2008.

Roughead E & Semple S, Medication safety in acute care in Australia: where are we now? Part 1: a review of the extent and causes of medication problems 2002-2008. *Australia and New Zealand Health Policy* 2009; 6:18.

Runciman WB, Roughead EE, Semple SJ & Adams RJ, Adverse drug events and medication errors in Australia. *International Journal for Quality in Health Care*, 2003; 15 (supp 1):i49-i59.

Safety and Quality Council, Second National Report on Patient Safety: Improving Medication Safety. July 2002.

Senders JW, Theory and analysis of typical errors in a medical setting. *Hospital Pharmacy*, 1993;28:505-508.

Shrank W, Avorn J, Rolon C & Shekelle P, Effect of content and format of prescription drug labels on readability, understanding and medication use: a systematic review. *Ann Pharmacother*, 2007a;41:783-801.

Shrank WH, Agnew-Blais J, Choudhry NK et al, The variability and quality of medication container labels. *Arch Intern Med*, 2007b;167:1760-1765.

Taylor D, Robinson J, MacLeod D et al, Therapeutic errors among children in the community setting: nature, causes and outcomes. *Journal of Paediatrics and Child Health* 2009;45:304-309.

Taylor D, Robinson J, MacLeod D et al, Therapeutic errors involving adults in the community setting: nature, causes and outcomes. *Australian and New Zealand Journal of Public Health*, 2009;33:388-394.

Weingart SN, Wilson R, Gibberd RW & Harrison B, Epidemiology of medical error. *BMJ* 2000;320:774-7.

Winterstein AG, Sauer BS, Hepler CD & Poole C, Preventable drug-related hospital admissions, *Ann Pharmacother*, 2002;36:1238-1248.

Active ingredient prominence

Research conducted by the Consumers Health Forum (2009) identified strong demand from consumers for improved prominence of the active ingredient on both prescription and non-prescription medicines and has argued that this could lead to improved safety and quality use of medicines. Together with improvements to labelling, through increased active ingredient prominence, it is recognised that health literacy and education are important factors for reducing the risk of confusion associated with medicines (Sorensen et al, 2005; Consumers Health Forum of Australia, 2009).

The potential for confusion of prescription medicines is increasing as the number of generic alternatives proliferates; proliferation which is fostered by government incentives to use generic medicines (McLachlan, Ramzan & Wilne, 2007; Ortiz, Simons & Calcino, 2010).

The greatest risk associated with confusion of this type is overdose, either from the patient not realising two medicines are the same, or from duplicate prescriptions when healthcare professionals also may not have recognised that two medicines are the same (Sorensen et al, 2005; Graudins & Dooley, 2010; Carney et al, 2011, Lalor, 2011).

Whilst much of the work in this area refers to confusion associated with prescription medicines, awareness of the active ingredient impacts on the quality use of medicine and safety of consumers of all classes of medicines (Consumers Health Forum of Australia, 2009; Lalor, 2011).

Consumers also report having trouble with compound medicines, such as cold and flu preparations, as these preparations could have paracetamol or aspirin, which may have negative health consequences for some people (Consumers Health Forum of Australia, 2009).

For further discussion regarding paracetamol and non steroidal anti-inflammatory drugs (NSAIDs) see "[Warnings statements for paracetamol and ibuprofen](#)".

References

Carney SL, Gazarian M, Denholm JT et al, What's in a name? Brand name confusion and generic medicines. *MJA*, 2011;195:650-651.

Consumers Health Forum of Australia, Equal prominence of active ingredient and proprietary names on labels for prescription medicines. Consumers Health Forum of Australia, Canberra, 2009.

Graudins LV & Dooley MJ, Generic medicines literacy – minimising the potential for patient confusion. *MJA*, 2010;193:427.

Lalor D, Medicines Labelling. *Australian Prescriber*, 2011;34:136-138.

McLachlan AJ, Ramzan I, Wilne RW, Frequently asked questions about generic medicines. *Australian Prescriber*, 2007;30:41-43.

Ortiz M, Simons LA, Calcino G, Generic substitution of commonly used medications: Australia-wide experience, 2007-2008. *MJA*, 2010;192:370-373.

Sorensen L, Stokes JA, Purdie DM, et al, Medication management at home: medication-related risk factors associated with poor health outcomes. *Age and Ageing*, 2005;34:626-632.

Look-alike sound-alike errors

The existence of confusing drug names is considered one of the most common causes of medication error and is of concern worldwide, with many drug names looking or sounding like other drug names. It has been recognised by the WHO as a significant issue to be addressed (WHO, 2007).

There are numerous published examples of errors attributed to look-alike sound-alike names, labels and packaging (Teplitsky, 1969; Hargett et al, 1977; Lessard, Mathieu & Farfard, 1993; USP Quality Review, 2001; Drug Topics, 2003; Reines, 2005; Dunlop, 2009; Kay, 2011; O'Donoghue, 2012). A recent Australian review was conducted by Ostini et al (2012), with the objective of developing strategies to enhance patient safety and minimise clinical risk associated with look-alike sound-alike names. From the 32 publications reviewed, Ostini et al (2012) identified that a multi-faceted approach involving all aspects of the medication process, from manufacture, prescribing, dispensing and through to administration, is required to minimise the risks to consumer safety from this issue and labelling more broadly.

Table 1, from the review, summarises potential ways to minimise harm from medications.

Table 1: Minimising potential patient harm from medication (Ostini et al, 2012)

Group	Recommended actions
Prescribers	<ul style="list-style-type: none"> Inspect actual medicines a consumer is taking, especially when adverse events occur, and be vigilant for possible confusion due to similar names Report errors to the relevant government agency/ regulatory authority Use INN, if possible, or the national generic name when prescribing Issue computer-printed prescriptions if possible; any handwritten prescriptions should be clearly written, using uppercase letters, and never abbreviated medicine names Check unfamiliar names of medicines that patients report they are taking
Consumers	<ul style="list-style-type: none"> Assume more responsibility for educating themselves about medicines they are taking, and asking questions of their health professionals Take actual medicines along to consultations with prescriber or pharmacist Tell each new prescriber about all medicines being taken Report any suspected medication adverse events to their pharmacist and prescriber

Group	Recommended actions
Pharmacists	<ul style="list-style-type: none"> • Check that consumers recognise all the medicines they are taking • Discuss all medications with consumers, including likelihood for any confusion due to similarly named medicines • Clearly differentiate storage areas for medications with LASA names • Include alerts on shelves for medications known to be at risk for mix-ups due to similar names • Ask consumers for old containers when filling a new prescription • Report errors to the relevant government agency/regulatory authority • Liaise with prescribers, advising on potential for medication mix-ups due to LASA medication names • Instigate systems for always double checking prescriptions
Pharmaceutical companies	<ul style="list-style-type: none"> • Conduct market research on potential names with consumers, prescribers and pharmacists • Use available software (using orthographic and phonetic approaches) to test for LASA names and choose alternatives least likely to be confused with medicines already available • Cooperate in international process of choosing new names and be prepared to change brand names, worldwide, if necessary to avoid medication safety issues • Use the same INN (generic) name when naming new formulations • Emphasise INN above the brand name in all labelling, packaging and consumer or prescriber information
Regulatory authorities	<ul style="list-style-type: none"> • Government agencies should use more regulatory muscle to enforce naming that does not risk patient safety • Enforce use of INNs, rather than requiring different names in different jurisdictions • Harmonise international use of proposed new proprietary names • Use databases to compare existing names with proposed names (using software to test orthographic and phonetic LASA proposed names), so possible name confusion can be predicted and avoided by not becoming registered medications

The recommendation of a multifaceted approach is supported by the previous studies of Cohen (1995), Hoffman & Proulx (2003), Berman (2004) and Emmerton & Rizk (2012). All of these reviews recognised the risk potential at the various stages of the medication cycle and the need to consider behaviour at each step.

In the approvals stage of the medication cycle, electronic screening of look-alike sound-alike names is considered to be most effective using a combination of orthographic and phonetic measurements, such as that developed by Kondrak and Dorr (2006) and used by the US Food and Drug Administration. This approach to preventing medication errors

caused by confusion between similar drug products is further analysed and discussed by Lambert et al (2004).

Prescribing and dispensing are the next steps in the medication cycle where errors may result from look-alike sound-alike names. As the likelihood of name confusion is reduced by the distinctiveness of the name, it has been suggested that use of the active ingredient and brand name, should be used when referring to medicines with known potential for confusion (Berman, 2004).

Tall man lettering is another method of differentiating confusable names, using capitalisation of letters within the medication name (Australian Commission on Safety and Quality in Healthcare, 2011a). A number of studies have been conducted to evaluate the effectiveness of tall man lettering in error reduction (Filik et al, 2004; Filik et al, 2006; Gabriele, 2006; Van de Vreede et al, 2008; Filik et al, 2010; ISMP, 2011; Australian Commission on Safety and Quality in Healthcare, 2011a). Many of these studies found that the use of tall man lettering may have reduced selection error due to similar names being easier to distinguish (Filik et al, 2004; Filik et al 2006; Van de Vreede et al, 2008). However, in many of these studies a standardised version of tall man lettering was not used, and capitalisation may have been applied in a variety of ways, and there was no consistency in the evaluation methods (Gerrett et al, 2009; Australian Commission on Safety and Quality in Healthcare, 2011b). Furthermore, the capitalisation was found to be only of real value when participants were aware of the purpose of tall man lettering (Filik et al, 2006; Gabriele, 2006; ISMP, 2011; Ostini, 2012). Concerns were also raised regarding the potential reduction in effectiveness of tall man lettering that may result if it is over-used (Gabriele, 2006; ISMP, 2011; Australian Commission on Safety and Quality in Healthcare, 2011b).

For these reasons the Australian Commission on Safety and Quality in Healthcare (2011a), recommended use of the National Tall Man Lettering Standard in prescribing and dispensing software to assist pharmacists and doctors reduce the risks associated with look-alike sound-alike drug names, but not more widely. Only medicine names included on the standard list of tall man names would be incorporated into medical software.

From a consumer perspective, the risk associated with look-alike sound-alike names, in the final step of the medication cycle, is best reduced through education and awareness, in particular in relation to the active ingredient, as well as the indication or illness a medicine for which a medicine is being taken (Ostini, 2012).

References

Australian Commission on Safety and Quality in Health Care, National Standard for the Application of Tall Man Lettering. Australian Commission on Safety and Quality in Health Care, Sydney 2011a.

Australian Commission on Safety and Quality in Health Care, Evaluating the Effect of the Australian List of Tall Man Names. Australian Commission on Safety and Quality in Health Care, Sydney 2011b.

Berman A, Reducing medication errors through naming, labelling and packaging. *Journal of Medical Systems*, 2004;28:9-29.

Ostini R, Roughead EE, Fitzpatrick CMJ, et al, Quality Use of Medicines – medication safety issues in naming; look-alike, sound-alike medicine names. *International Journal of Pharmacy Practice* 2012; doi: 10.1111/j.2042-7174.2012.00210.x (first published online 18 May 2012).

- Cohen MR, Drug product characteristics that foster drug-use system-errors. *Am J Health-Sys Pharm*, 1995;52:395-399.
- Dunlop C, Medicinal mishap: Atropt-Azopt Substitution, *Australian Prescriber*, 2009;32:138-139.
- Emmerton LM & Rizk MFS, Look-alike and sound-alike medicines: risks and 'solutions'. *Int J Clin Pharm*, 2012;34:4-8.
- FDA Safety Page, Generic Name Confusion, Drug Topics, 2003;October:90.
- Filik R, Purdy K, Gale A & Gerrett, Drug name confusion: evaluating the effectiveness of capital ("Tall man") letters using eye movement data. *Social Science & Medicine*, 2004;59:2597-2601.
- Filik R, Purdy K, Gale A & Gerrett, Labeling of medicines and patient safety: evaluating methods of reducing drug name confusion. *Human Factors*, 2006;48:39-47.
- Filik R, Price J, Darker I, et al, The influence of Tall Man Lettering on drug name confusion. *Drug Safety*, 2012;33:677-687.
- Gabriele S, The role of typography in differentiating look-alike/sound-alike names. *Healthcare Quarterly*, 2006;9 88-95.
- Gerrett D, Gale AG, Darker IT et al, Tall Man Lettering Final Report of the use of tall man lettering to minimise selection errors of medicine names in computer prescribing and dispensing systems. ITQ Invitation Reference No: ER 07-0612. Loughborough University Enterprises Ltd. National Health Service, United Kingdom.
- Hargett NA, Ritch R, Mardrossian J, et al, Inadvertent substitution of acetohexamide for acetazolamide. *Am J Ophthalmology*, 1977;84:580-583.
- Hoffman JM & Proulx, Medication errors caused by confusion of drug names. *Drug Safety*, 2003;26:445-452.
- ISMP Medication Safety Alert, ISMP Updates is list of Drug Name Pairs with TALL Man Letters, ISMP Medication Safety Alert Posted 02/08/2011.
- Kay, E (ed), Coversyl and Coumadin: new packaging to reduce potential for dispensing errors. *Australian Prescriber*, 2011;34:48.
- Kondrak G & Dorr B, Automatic identification of confusable drug names. *Artificial Intelligence in Medicine*, 2006;36:29-42.
- Lambert BL, Yu C, Thirumalai M, A system for multiattribute drug product comparison. *Journal of Medical Systems*, 2004;28:31-56.
- Lescard MR, Mathieu M, Fafard M, Similarity of drug labels predisposes to drug errors. *Can J Anaesth* 1993;40:1109-11.
- O'Donoghue N, Look-alike/sound-alike confusion could be lethal: study. *Pharmacy News*, 21 May 2012.
- Reines SA, Look-alike sound-alike drug errors with Reminyl and Amaryl. *Am J Health-Syst Pharm*, 2005;62:35-36.
- Tepltisky B, Confusing drug names. *JAMA*, 1969;207:2440.
- US Pharmacopeia, USP Quality Review: Use Caution – Avoid Confusion, March 2001, No 76.

Van de Veerde M, McRae A, Wiseman M, Dooley MJ, Successful introduction of tallman letters to reduce medication selection errors in a hospital network. *J Pharm Pract Res*, 2008;38:263-266.

WHO Collaborating Centre for Patient Safety Solutions, Look-Alike Sound-Alike Medication Names. *Patient Safety Solutions*, 2007;1: Solution 1.

Historical consultation document

Over-the-counter medicines

Label formats and lettering

Research has found that consumers prefer to have medicine information presented under headings and in a list format with 'white space' on the packaging clearly differentiating the information (Wogalte & Vigilante, 2003). The most important information is generally regarded as being: active ingredient and what the drug is used for, how to take (dosing instructions), and outcomes and hazards associated with the drug. The remaining information on the packet could cover inactive ingredients, storage instructions, manufacturer information and the bar code (Vigilante and Wogalter, 1997; Morrow et al, 1998; Shrank et al, 2007).

Information presented in standardised schemas has also been found to be better recalled by consumer groups, as it allows consumers to rapidly find information they require and compare products (Vigilante and Wogalter, 1997; Morrow et al, 1998, Shrank et al, 2007).

A systematic review of randomised controlled trials, observational studies and of label format found that the use of larger fonts, lists, headers and white space, simple language and logical organisation may all improve readability and comprehension of prescription medicine labels (Shrank et al, 2007). These authors noted that when optimizing label format, use of lists, headers and white space enhance readability and the content should be organised in a schema that patients use to understand medication information. Wogalter & Vigilante (2003) found that line spacing (white space) made simulated over-the counter medicine labels easier to read and paragraph style separation between sections of text helped consumers differentiate the different parts of the label.

In a study of prescription medicine labels, which could also be applied to OTC medicine labels, Sundar et al (2012) argued that proper and informative labelling is a promising and important tool in the prevention of adverse drug events. In particular they found that understanding consumers' attentive behaviour, which is attracting the consumer's attention, is crucial for developing effective medicine labels. There is a need for consistency in format and content and labels need to effectively attract attention to ensure information is more effectively conveyed (Lalor, 2011; Sundar et al, 2012). As previously discussed, the often limited interaction between consumers and healthcare professionals when purchasing non-prescription and prescription products further highlights the importance of the label (Holt et al, 1992; Shrank et al, 2007). The study by Holt (1992) raised serious concerns regarding the assumptions associated with dosage instructions. The variety of responses to commonly used dosage instructions indicated that the instructions may not be as simple and clear as authorities consider them to be. Holt suggested that the assumptions regarding common label language be re-examined since the availability of non-prescription products is, in part, based on the assumption that label instructions are sufficiently clear that intervention by health professionals is unnecessary.

Watanabe (1994) has suggested that lettering on OTC medicine labels should be at least 1.2 mm in vertical height (or 20/40 Reduced Snellen visual acuity level) and should have no more than 40 characters per inch (approx 16 characters per cm). Along with the importance of letter height, horizontal compression had a significant effect on readability and should be a major consideration in defining readability (Watanabe, 1994). Shrank et al noted that there are limitations regarding space for increased font size, however this

should not be used as justification for not using the largest possible font size (Shrank et al, 2007).

A study by Murty et al (2007) evaluated the effectiveness of the 1999 FDA-mandated standardised format called “Drug Facts” for the labelling of over-the-counter-medicines, and compared three labelling formats, the old, new and simulated. They found that consumers preferred the label format with a larger font size over those currently available. In addition, it was noted that the new OTC drug labels may not be easy for some consumers to use and understand, although they are an improvement over old unstandardised labels. It was concluded that manufacturers should look beyond the mandatory minimum font size (FDA 6 point) and develop strategies to improve comprehension of information on OTC medication labels (Murty et al 2007).

Label language

In addition to the physical presentation of information on a label, the language used to convey that information was also a significant factor in medicines safety and quality use of medicine (King et al, 2011). Poor understanding of medication labelling or failure to recognise the consequences of exceeding a maximum recommended dosage may lead to unintentional overdoses. (King et al, 2011). In a study of paracetamol by these authors, it was found that consumers had poor recognition of which products contained paracetamol.

Brand name confusion

Consumer confusion has also been reported regarding similar branded names of OTC products. It takes a degree of awareness for the consumer to realise that similar branded products may contain different medicines or different combinations of medicines. Some products may have slightly different names reflected by use of suffixes but the brand name may confuse patients as it does not reflect the active ingredient in the product. This confusion may lead to accidental poisoning (Aronson, 1994; Alambo, 2010).

Paediatric and elderly patients

A study by Lokker et al (2009) investigated factors associated with the understanding by caregivers of the importance of age of the child and dosing instructions on labels for paediatric OTC cough and cold medication. It was found that label language and graphics can lead to inappropriate interpretation of the appropriate dose (Lokker et al, 2009).

There are also issues with the readability of OTC labels for the elderly population. As OTC labels are the primary source of information for consumers, older people need medication information in large font and easy-to-understand language so that they can use the medications independently. Lack of adequate information and knowledge about OTC medications can cause drug misuse, overdose, and abuse leading to hospitalisations, morbidity and even mortality (Pawasker and Sansgiry, 2006).

A survey conducted by Holt et al (1992) found that despite US FDA requirements that OTC labelling be written in sufficiently simple language, dosage instructions were often misinterpreted, further highlighting the need for clear, simple and tested instructions. A similar situation exists in Australia, with statements such as “take two tablets twice a day”

correctly interpreted by 71% of consumers with adequate literacy and by as few as 33% with literacy problems (Lalor, 2011).

References

- Alambo, D, Mistaken identity: some OTCs look alike but are very different. Consumer Health Information Corporation 2010.
- Aronson, JK, What's in a brand name? *BMJ*, 1994;308:1140.
- Holt GA, Dorcheus L, Hall EL, et al, Patient Interpretation of Label Instructions. *American Pharmacy*, 1993;NS32:58-62.
- King JP, Davis TC, Bailey SC et al, Developing consumer-centered, non-prescription drug labelling, a study in acetaminophen. *Am J Prev Med*, 2011;40:593-598.
- Lokker N, Sanders L, Perrin EM, et al, Parental Misinterpretation of Over-the-Counter Cough and Cold Medication Labels. *Pediatrics*, 2009;123:1464-1471.
- Morrow DG, Leirer VO, Andrassy JM, Hier CM and Menard WE, The influence of list format and category headers on age differences in understanding medication instructions. *Experimental Ageing Research*, 1998;24:231-256.
- Murty S & Sangsiry S, Consumer comprehension of OTC Medication Labels and the scope for improvement in font size. *J Pharm Technol*, 2007, 23:207-213.
- Pawaskar MD & Sangsiry SS, Over-the-counter medication labels: problems and needs of the elderly population. *JAGS*, 2006;54:1955-1956.
- Shrank W, Avorn J, Rolon C & Shekelle P, Effect of content and format of prescription drug labels on readability, understanding and medication use: a systematic review. *Ann Pharmacother*, 2007;41:783-801.
- Sundar RP, Becker MW, Bello NM & Bix L, Quantifying age-related differences in information processing behaviours when viewing prescription drug labels. *PLoS ONE*, 2012;7:e38819.
- Vigilante WJ & Wogalter MS, The preferred order of over-the-counter (OTC) pharmaceutical label components. *Drug Information Journal*, 1997;31:973-988.
- Watanabe RK, The ability of the geriatric population to read labels on over-the-counter medication containers. *J Am Optom Assoc*, 1994;65:32-37.
- Wogalter MS & Vigilante WJ, Effects of label format on knowledge acquisition and perceived readability by younger and older adults. *Ergonomics*, 2003;46:327-344.

Warning statements for paracetamol and ibuprofen

A number of studies have discussed the occurrence of hepatic toxicity associated with high doses of paracetamol, with many suggesting that the underlying cause is due to self-dosing with paracetamol beyond the toxic threshold (Roumie & Griffin, 2004; Graudins & Gazarian, 2006; Wilson et al, 2010; King et al, 2011; Bond et al, 2012). In 2008, it was reported that paracetamol was the single most commonly taken drug in overdose that lead to hospital presentation and admission in Australia (Daly et al, 2008).

In some cases overdosing is intentional, resulting from suicide attempts, but for approximately 2/3 of cases (King et al, 2011), overdose and subsequent liver damage occurs for various reasons including:

- A perception of safety due to the OTC status of the medicine being taken
- Lack of awareness of the potential for liver damage
- Long-term suprathreshold dosing, including from administration of paracetamol in a combination of products (headache tablets, osteoarthritis tablets, cold and flu medicines)
- Due to perceived safety of the medication, continual increase in the dose of paracetamol taken until pain is relieved. This is of particular concern when it has been reported that 50% of patients achieve good to excellent headache relief at 650 mg, 65% at 975 mg and 75% at 1300 mg (the recommended dose is 1-2 500 mg tablets, with a maximum daily dose of 8 tablets (4000 mg)) (Bond et al, 2012).

It was commonly acknowledged that there is a need to educate the public on the dangers of OTC analgesics, in particular those containing paracetamol (Roumie & Griffin, 2004; Bond et al, 2012; Wilson et al, 2010). It was suggested by Roumie and Griffin (2004) that this may be achieved by appropriate counselling from healthcare professionals as well as labelling appropriate for the minimal literacy levels of the community. Suggestions for alternative methods to display information to improve understanding and awareness included larger print, clearer identification of the active ingredient, simpler instructions and graphical displays of risk (Roumie & Griffin, 2004). It has also been suggested that with the high prevalence of over-the-counter use of paracetamol, a consumer-centred approach to developing icons and messages to promote awareness and safe use of paracetamol could benefit consumers. Additionally, partnerships among health services researchers, industry and government should be formed to identify optimal ways to improve product labelling and educate the public on the meaning of icons and the importance of safe use of these medicines (King et al 2011).

In a study examining OTC analgesic use and comprehension in older adults, Roumie and Griffin (2004) found that more than 60% of people could not identify the active ingredient of their pain reliever. Similar observations were made in a study of adolescents, which as well highlighting the lack of understanding regarding OTC analgesics, also discussed the risk of failing to associate an active ingredient with a brand name and the subsequent potential for unintentional overuse (Wilson et al, 2010). In a study by King et al (2011) which endeavoured to develop a consumer-focused label for paracetamol, it was suggested that the cause of unintentional overdoses was likely the result of poor understanding of medicine labelling or failure to recognise the consequences of exceeding the maximum daily dose. The study highlighted poor recognition of products containing

paracetamol, recognition of brand name rather than active ingredient and the implications of that when there are a considerable number of products containing paracetamol available (King et al, 2011).

The Acute Liver Failure Study Group compiled data (1998-2005) on more than 500 paracetamol-related acute liver failure cases showing that the number had increased considerably since 1998. Half the cases were due to self-harm and half were unintentional. The data showed that most unintentional overdose patients repeatedly exceed the package labelling limits of 4 grams and that this group frequently (62%) used opiate-paracetamol combinations. In addition, 38% had taken more than one paracetamol-containing agent simultaneously. Improving education and labelling might help decrease use of multiple preparations and perhaps make individuals more mindful that paracetamol can cause serious liver damage (Lee 2007).

Gaps in knowledge and understanding of carers of young children regarding the paracetamol and its safety may also result in unintentional misuse and harm (Graudins & Gazarian, 2006). Reasons identified for misuse of paracetamol in children included a lack of awareness of:

- Appropriate indications
- Potential for toxicity with a single acute overdose or from sustained administration of supratherapeutic doses
- Availability of many different strengths and formulations and the appropriateness for the age of the child
- Need to avoid adult strength preparations in children.

These factors highlighted the need for consumer oriented information to aid the understanding and awareness of carers administering these medicines (Graudins & Gazarian, 2006).

Whilst ibuprofen overdose can occasionally produce serious toxicity with some rare severe adverse events, the risk of life-threatening symptoms from ibuprofen overdose is considered to be low (Hall et al, 1988; McElwee et al, 1990).

However, ibuprofen can occasionally result in serious toxicity complicated by metabolic acidosis, renal insufficiency and/or renal failure necessitating prolonged dialysis.

It has been reported that there is also a lack of awareness of the active ingredient in ibuprofen products by consumers for whom ibuprofen is contraindicated, and therefore the potential for adverse events to be experienced following use of these products (Roumie & Griffin, 2004).

When considering warning design, to complement consumer-centred labels, research has identified a number of features that should be considered (Wogalter et al 2002; Laughery, 2006). These factors include:

- Salience – prominence or conspicuousness of the warning
- Wording – including a signal word for getting attention, identification of the hazard, explanation of the consequences and directions for avoiding the hazard. For effectiveness, this requires careful balance between completeness and brevity
- Layout and placement – including consideration of ways to increase the available surface area
- Pictorial symbols – providing they have been tested for comprehension and understanding.

Wogalter et al (2002) discuss research-based guidelines for warning design (e.g. signal codes, colour, symbols, and text/context), placement (location within product instructions) and how to enhance the usability of designs by considering factors internal to the user (eg beliefs, perceptions of risk, stress). Evaluation methods have also been developed that can be used to measure the effectiveness of warnings such as the degree to which warnings are communicated to recipients and the degree to which they encourage or influence behavioural compliance.

References

- Bond GR, Ho M, Woodward RW, Trends in hepatic injury associated with unintentional overdose of paracetamol (acetaminophen) in products with and without opioid: an analysis using the National Poison Data System of the American Association of Poison Control Centers, 2000-7. *Drug Safety*, 2012;35:149-157.
- Daly FFS, Fountain JS, Murray L et al, Guidelines for the management of paracetamol poisoning in Australia and New Zealand – explanation and elaboration, A consensus statement from clinical toxicologists consulting to the Australasian poisons information centres. *MJA*, 2008;188:296-301.
- Graudins LV & Gazarian M, Promoting safe use of paracetamol in children. *Journal of Pharmacy Practice and Research*, 2006;36:297-300.
- Hall AH, Smolinske SC, Kulig KW & Rumack BH, Ibuprofen Overdose – A prospective study. *West J Med*, 1988;148:653-656.
- King JP, Davis TC, Bailey SC et al, Developing consumer-centered, non-prescription drug labelling, a study in acetaminophen. *Am J Preventative Med*, 2011;40:593-598.
- Laughery KR, Safety Communications: Warnings. *Applied Ergonomics*, 2006;37:467-478.
- McElwee NE, Veltri J, Bradford DC & Rollins DE, A prospective, population-based study of acute ibuprofen overdose: complications are rare and routine serum levels are not warranted. *Annals of Emergency Medicine*, 1990;19:65-70.
- Roumie CL & Griffin MR, Over-the-counter analgesics in older adults: a call for improved labelling and consumer education. *Drugs Ageing*, 2004;21:485-498.
- Weiss S, Compliance packaging for over-the-counter drug products. *J Public Health*, 2009;17:155-164.
- Wilson KM, Singh P, Blumkin AK et al, Knowledge gaps and misconceptions about over-the-counter analgesics among adolescents attending a hospital based clinic. *Academic Pediatrics*, 2012;10:228-232.
- Wogalter MS, Conzola VC, Smith-Jackson TL, Research-based guidelines for warning design and evaluation. *Applied Ergonomics*, 2002;33:219-230.

Small containers

Space availability on a medicine label has significant impacts on readability of the information, although in general, small containers are usually not given separate consideration in studies of medicines labelling effectiveness. Beyond medicine labelling, there has been some investigations of alternative labelling for small containers and the impact on behavioural compliance, as discussed below in the work of Wogalter and Young (1994). In a study that was designed to compare two alternative label designs, tags and wings, with the conventional labelling for their effect on behavioural compliance on a very small container of glue, Wogalter and Young (1994) found that the tag design had a greater compliance than the other labelling methods, when measuring compliance of participants. The findings suggest that alternative designs can enhance warning communication and compliance, particularly if they are used to provide greater surface area for information.

In a comparison of guidelines for labelling anaesthetics, Merry et al (2011) identified a number of factors that can provide guidance for developing suitable labelling requirements for small containers. In particular, they highlighted the lack of legibility of information on ampoules, suggesting that separate consideration of requirements for this type of packaging may be appropriate. It was suggested the focus of labels should be on legibility, ease of identification and avoidance of look-alike labels, rather than information for quality control of medication manufacture and distribution.

Merry et al (2011) also suggested there should be a consistent approach to addressing colour coding, container size, background, font size and type, look-alike sound-alike names and poorly legible labels, which have all been implicated in medication errors. The work advocated a coordinated approach to clear, consistent presentation of the active ingredient and concentration in each container.

References

Merry AF, Shipp DH, Lowinger JS, The contribution of labelling to safe medication administration in anaesthetic practice. *Best practice and research clinical anaesthesiology* 2011;25:145-159.

Wogalter MS & Young SL, The effect of alternative product-label design on warning compliance. *Applied Ergonomics*, 1994;25:53-57.

Blister strip labelling

Ambiguous labelling of blister strips has been implicated in medication errors (Guchelaar, Kalmeijer & Jansen, 2004, Rev Prescrire, 2011;). Guchelaar et al (2004) discussed how a section of a blister strip containing two tablets labelled with 'Zelitrex 500' (valaciclovir) caused confusion among health care professionals, with many being unclear whether the 500 referred to the amount of active ingredient in a single tablet or the total amount of active ingredient in the two tablets together. It was reported that a patient being treated with medication packed in this manner was given two tablets twice a day, equating to 1000 mg twice a day, instead of 500 mg twice a day). It was found that the labelling of the blister and the packaging of two tablets together contributed to the misadventure. Similar examples were cited in Rev Prescrire (2011).

In a paper proposing a packaging design blister strips for optimal compliance, Weiss (2009) identified discarding of packaging containing directions, warnings and dosing instructions as one of the contributory factors to the misuse of OTC medicines. Weiss (2009) suggested that optimal compliance packaging should:

- keep the instructions, warnings and dosing directions attached to the blister strip at all times
- increase the surface area of the packaging without adding bulk
- organise the pills into logical, unit-of-use sets or rows (for example per-dose maximum or per-day maximum)
- limit the number of pills in a unit-of-use package to coincide with the instructed maximum dose and maximum days of use for a specific product.

An article in Rev Prescrire (2011) noted a new packaging design where the box, blister pack and information leaflet for a paracetamol OTC product could not be separated. This design ensured that the patient leaflet remained on hand throughout the use of the product, and that a blister pack containing another drug could not accidentally be put into this box.

References

Guchelaar HJ, Kalmeijer MD & Jansen MEP, Medication error due to ambiguous labelling of a commercial product. *Pharm World Sci*, 2004;26:10-11.

2010 drug packaging review: identifying problems to prevent errors. *Rev Prescrire* 2011;31:142-145.

Weiss S, Compliance packaging for over-the-counter drug products. *J Public Health*, 2009;17:155-164.

Historical consultation document

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