FURTHER READING

Australian Pharmaceutical Manufacturers Association. Code of Conduct of the Australian Pharmaceutical Manufacturers Association. 13th ed. Sydney: Australian Pharmaceutical Manufacturers Association Inc; 2000.

Roughead EE, Harvey KJ, Gilbert AL. Commercial detailing techniques used by pharmaceutical representatives to influence prescribing. Aust N Z J Med 1998;28:306-10.

Sandhu GS, Day RO. Factors affecting prescribing in general practice – a role play. Med J Aust 1992;157:621-2.

Day R. Pharmaceutical company promotion: striking a balance [editorial]. Aust N Z J Med 1998;28:291-3.

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Self-test questions

The following statements are either true or false (answers on page 111)

3. Pharmaceutical promotion has no effect on prescribing patterns.
4. The Code of Conduct of the Australian Pharmaceutical Manufacturers Association covers the interaction between health professionals and drug company representatives.

Your questions to the PBAC

I note the list of generic brands in the 'New drugs' section of each edition. I wonder how many will have the same bioavailability as their competitors?

The matter of bioavailability is of concern to my patients who frequently speak of coercion to accept a strange brand currently stocked in the pharmacy. The reported variability of effect experienced by patients, for example in swapping brands of frusemide, cannot be lightly dismissed as anecdotal.

I am very doubtful that equal weights of drugs translate to bioequivalence, but would be pleased to be reassured that this is so. If generic drugs are not bioequivalent, then the parties concerned should be aware of the differences.

Perhaps *Australian Prescriber* could provide a service to its readers by documenting the bioavailability studies done on each generic registered for inclusion on the Pharmaceutical Benefits Scheme? The name of the testing laboratory, its ownership, the techniques used, the quality control standards employed and the number of samples taken, should all be on the public record and available to all.

John Mackellar
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Dr Leonie Hunt, Drug Safety and Evaluation Branch, Therapeutic Goods Administration, comments:

The Therapeutic Goods Administration (TGA) is the body responsible for the registration of medicines in Australia, including generic equivalents of prescription medicinal products. Applications for generic products, which are claimed to be essentially similar to an innovator product, must include bioavailability data which demonstrate that the proposed product is bioequivalent to a leading brand of the medicine available in Australia. Guidance in relation to how a bioequivalence study should be conducted is available to sponsors of medicinal products in the document issued by the Commission of the European Communities entitled 'Investigation of Bioavailability and Bioequivalence'. Further information is available from the TGA web site (www.tga.health.gov.au/) and the Committee for Proprietary Medicinal Products web site (www.eudra.org/humandocs/humans/qwp.htm).

In general, a comparison of the time course of the blood concentrations of the drug resulting from administration of the two brands to a group of volunteers is required. Comparison of the rate and extent of absorption of the drug from the two products is conducted by a statistical analysis using internationally recognised methods. A decision whether to register the generic product is then made taking these results into account. Modified-release products, such as delayed-release tablets and slow-release tablets, may require studies to be conducted under a variety of conditions to confirm equivalence. Where there is any doubt as to the bioequivalence of the two products, the TGA is able to seek advice from the independent expert committee, the Australian Drug Evaluation Committee.

The actual data sets, on which decisions to register individual products are made, may contain commercially confidential information. They are not usually available to the public.

Associate Professor R. Moulds of the Executive Editorial Board, comments:

Dr Mackellar's concern is a common one. The regulatory processes outlined by Dr Hunt are good at ensuring the plasma concentrations of a generic drug are similar to those obtained with the 'innovator' brand of the drug, usually the market leader. The limits allow for differences of no more than 20% in the overall plasma concentration versus time curves of the two drugs.

It is a more difficult question whether or not such allowable differences might be noticed by a patient. The intraindividual variation in plasma levels of a drug when it is taken on different occasions is usually greater than 20%. So a patient will probably only genuinely notice a difference between various brands of a drug if they also notice a difference when they take the same brand on different occasions.

A patient is also only likely to notice a difference between brands if the drug has a steep concentration-effect curve, so that a 20% change in concentration results in a significant change of effect. Few drugs have such a steep curve.

There are very few clear examples where differences between brands of a drug are clinically important. One very important exception, however, is that of warfarin, and patients should not shift from one brand of warfarin to another.