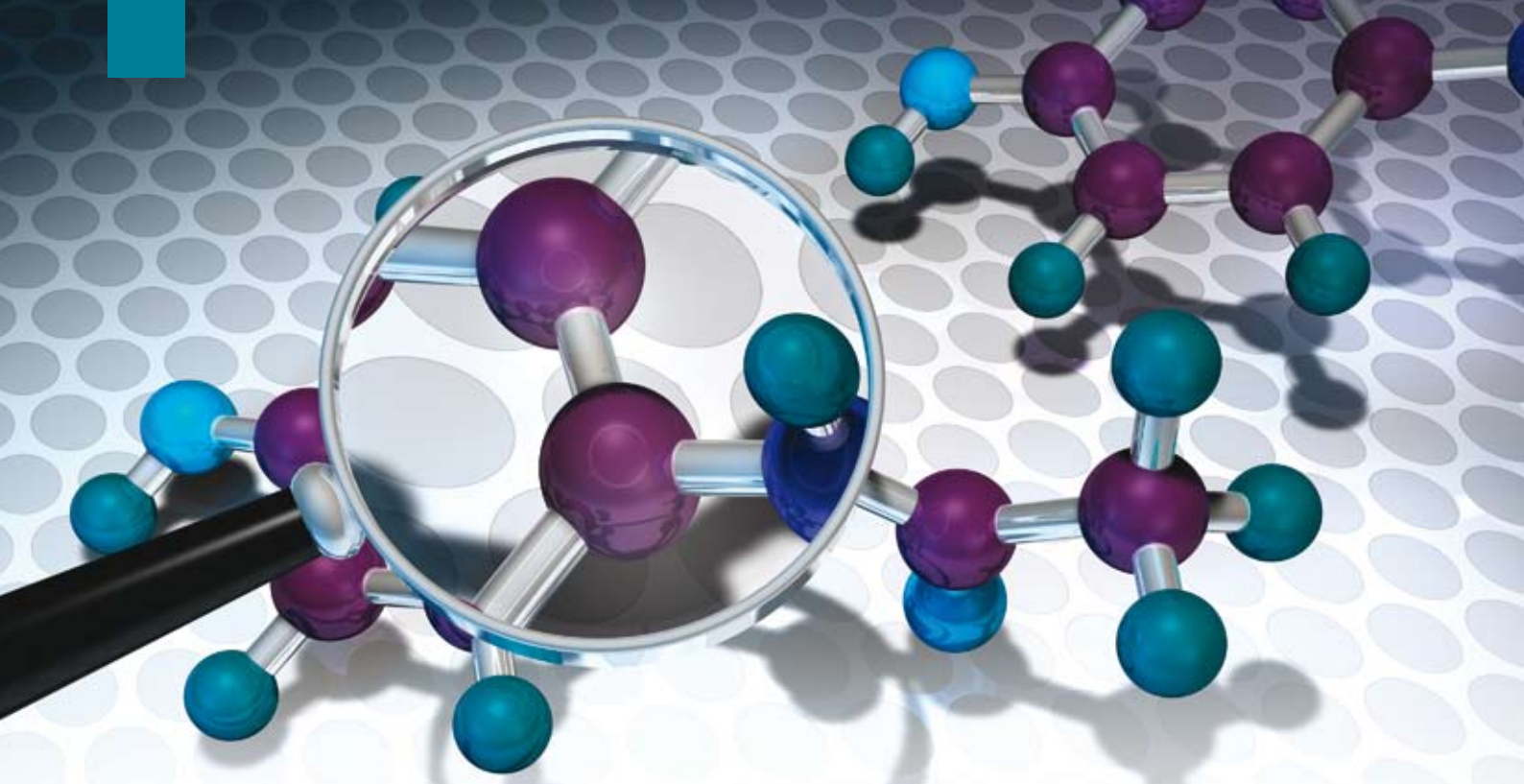

The regulation and oversight of Generic Medicines in New Zealand

In New Zealand, Medsafe is responsible for the regulation of generic medicines. This involves evaluating the manufacturing processes, assessing product quality and evaluation of bioequivalence study reports.

Medsafe regulations are based on current international best practice. New Zealand regulation is consistent with most (if not all) overseas regulators.

In the wake of recent high profile medicine brand changes, pharmacists, general practitioners and patients have raised a number of questions about the regulation and oversight of generic medicines. We put these questions to **Dr Stewart Jessamine** and **Dr Enver Yousuf** from Medsafe.

Q **Do our methods and standards in NZ comply with international standards such as those used in the USA and Europe?**

A The quality, safety and efficacy evaluations for generic medicines used by Medsafe follow processes that are at least as stringent as those in the USA, Europe and Australia.

The basic requirements for approval of generic and innovator medicines are the same. The generic medicine manufacturer is not required to repeat the safety and efficacy studies conducted by the developer of the original product. In approving a generic medicine, Medsafe relies on previous findings that the innovator product is safe and effective, both in terms of the excipients and active ingredients.

The generic version must have the same dosage form, strength, route of administration, and conditions of use as the innovator product. The applicant must show that a generic product delivers the same amount of its active ingredient in the same amount of time as the trade-name counterpart. This bioequivalence is critical for drawing the conclusion that both the original and generic medicines will produce similar therapeutic results.

With respect to bioequivalence testing, Medsafe may in fact go further than some countries in that the pharmacokinetic data provided by the applicant is taken and recalculated to ensure that it fulfils the criteria for bioequivalence.

In addition to bioequivalence testing, Medsafe, in common with other agencies, also require that comparative dissolution testing is performed on a generic medicine. This test is designed to determine that the generic tablet or capsule will perform in the same way as the innovator formulation under a variety of conditions e.g. pH. Demonstrating that dissolution is the same for two medicines gives an indication that the active substance is made available for gastrointestinal absorption in the same way.

Q For how long has compliance with these standards been in place, i.e. have there been any significant changes in standards or approval processes in the last few years?

A Medsafe work to the same standards as other international regulatory authorities. These standards have been in place for the last 30 years but are reviewed on a regular basis.

Q Who conducts the bioequivalence studies? Are they done in New Zealand?

A Very few bioequivalence studies are undertaken in New Zealand. Because the studies are cross-over studies and subjects are their own controls the results may be extrapolated to any population regardless of where the original study was conducted.

Q Do manufacturers usually supply the results of their own bioequivalence studies or do they sub-contract to other agencies?

A Manufacturers supply their own data; more often than not the manufacturers have contracted a clinical research centre to undertake a bioequivalence study on their behalf.

Q What safeguards are in place to assure quality and validity of the bioequivalence data provided ?

A Regardless of where they are undertaken, bioequivalence studies must have been undertaken according to 'Principles of Good Clinical Practice' and the samples analysed according to 'Principles of Good Laboratory Practice'. The manufacturers self-certify that this was the case and this is open to audit at any point. This system of self-certification is used by regulatory authorities overseas including the FDA, and the TGA as well as by Medsafe.

Q If two medicines are confirmed to be bioequivalent is it possible for differences in therapeutic effect or adverse effects to occur?

A Bioequivalence is a statistical test and is derived from population pharmacokinetics. It is feasible that at an individual patient level, for a very small proportion of patients, changes in formulation may lead to differences in bioavailability. For the majority of these patients any differences should be clinically insignificant.

Q Are the medicines data sheets for generics always the same as the innovator product? What process is in place to assure this?

A The datasheets for generic medicines do not have to be identical to the innovator, but they should be

consistent with that for the innovator product. The datasheet for the generic medicine cannot contain more indications or any less safety information than those for the innovator product. Datasheets are checked as part of the evaluation process and changes to them requested as appropriate.

Q **If there are reports of adverse events (including reduced therapeutic effects) to the Centre for Adverse Reactions Monitoring (CARM), what is done with this information, and at what stage would the registration of the generic be reviewed?**

A CARM receives spontaneous adverse event reports including those associated with brand switches. These reports are analysed and held on a database. Medsafe meet weekly with CARM who raise any signals that may have been identified as a result of their monitoring. Where necessary, reports are reviewed by the Medicines Adverse Reaction Committee (MARC) who provides advice to Medsafe regarding steps that should be undertaken to minimise the risk to the public.

Advice provided by MARC could range from ongoing monitoring with changes to the datasheet through to the recommendation that the medicine is removed from the New Zealand market.

Q **Are there any safety issues with generic medicines?**

A As part of the dossier submitted by the generic medicine manufacturer, safety data from bioequivalence studies are provided. Any difference between the safety profile of the innovator and generic medicine is reviewed and questions raised as necessary. Details of all excipients and non-active compounds are provided and these may differ from the innovator product. However, the toxicological profile of all excipients is checked in order to ensure their approved use for this purpose.

For further information about Medsafe see the Medsafe website:
www.medsafe.govt.nz