Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Australian regulatory guidelines for prescription medicines

Appendix 20: Supplementary guidelines for radiopharmaceuticals

June 2004

TGA Health Safety Regulation

About the Therapeutic Goods Administration (TGA)

- The TGA is a division of the Australian Government Department of Health and Ageing, and is responsible for regulating medicines and medical devices.
- 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.

Appendix 20: Supplementary guidelines for radiopharmaceuticals

In addition to the European Union guidelines adopted by the Therapeutic Goods Administration (TGA) sponsors should note the following points in respect of radiopharmaceuticals.

1. Specifications and control tests on the finished product

Specifications for radiopharmaceuticals (see Committee for Medicinal Products for Human Use (CHMP) guideline *Specifications and Control Tests on the Finished Product*[1]) apply at all times up to product expiry. The radioactive content, or radioactive concentration, is to be stated at the calibration date and time.

In general, it will not be practical to apply a release specification of ±5% for the radioactive component of ready-to-use radiopharmaceuticals.

2. Redispensing

Prior approval is required for redispensing of radiopharmaceuticals by any person or organisation other than the institution that will administer the product to a patient.

3. Product Information

- Radioactivity should be expressed in SI units.
- Where appropriate, radiation dosimetry information should be based on that of the International Commission on Radiological Protection (ICRP). It is recommended that the radiation doses provided in the table should be those delivered from the administration of the recommended maximum quantity of the radiopharmaceutical. Absorbed doses should be expressed in mGy.

  The effective dose should be calculated using the weighting factors given by ICRP 60, and expressed in mSv.

  Where a radionuclidic impurity may make a significant contribution to the radiation dose, the additional contribution to the effective dose resulting from the maximum allowable concentration of this impurity should be stated.

  If ICRP data are not available at the time of application, radiation dosimetry estimates should be based on clinical trial information in the submission. When ICRP data become available, these should be substituted for the sponsor's own information.
- Users should be advised to observe the National Health and Medical Research Council (NHMRC) *Code of practice for the disposal of radioactive wastes by the user* (1985)[2] published on the

[1] http://www.tga.gov.au/industry/pm-euguidelines-quality.htm
[2] http://www.arpansa.gov.au/rhs_pubs.htm

Australian Radiation Protection and Nuclear Safety Agency (ARPANSA) website as Radiation Health Series (RHS) (publication No. 13).

- Changes to the Product Information (PI) which provide conformity with the above (Section 3) are considered self-assessable, subject to general and specific conditions in Appendix 12 (*Changes to the quality information of registered medicines: notification, self-assessment and prior approval*).

- Changes to the PI which are consequent to new or amended monographs in the British Pharmacopoeia (BP) are also considered self-assessable, subject to general and specific conditions in Appendix 12 (*Changes to the quality information of registered medicines: notification, self-assessment and prior approval*), and provided they result in more restrictive statements in PI, that is, tighter limits. Changes which result in less restrictive statements in PI are not self-assessable and a Category 3 application must be submitted.

  An example of how a new or amended BP monograph can affect PI is the new limit for radionuclidic impurities in Thallous[^{201}Tl] Chloride Injection. Prior to the publication of the BP 1988 monograph, the USP monograph had been applied. The reduced limits for ^{202}T1 in BP 1988 also affected the estimate of the maximum radiation dose arising from the impurity ^{202}T1. PIs which included information on impurities and radiation dose due to impurities had to be changed.

4. Cyclotron-Produced radiochemicals for use in radiopharmaceuticals

Standard Operating Procedures (SOPs) should be provided for target preparation, isotopic purity of target materials, irradiation and processing, together with an indication of what validation has been conducted.

It is not necessary to provide redrafts of these SOPs when they are updated subsequent to registration. However, any changes to the method of manufacture are subject to Section B4 *(Manufacturing Method, Manufacturing Batch Size and Manufacturing Equipment for Finished Products*) in Appendix 12 (*Changes to the quality information of registered medicines: notification, self-Assessment and prior approval*). In brief, such changes must be approved in advance for sterile products but, for those few nonsterile radiopharmaceuticals, they may be self-assessable subject to the conditions specified in Appendix 12.

5. Radiopharmaceuticals based on monoclonal antibodies

Sponsors of new monoclonal antibody products that are intended to be labelled with 99mTc or other radionuclides, need not demonstrate that their product is compatible with all sources of the radionuclide available in Australia. It will be sufficient for regulatory purposes if compatibility is demonstrated with one approved source of the radionuclide available in Australia; if possible the market leader, and the compatible brand is mentioned in the PI document. Any additional compatibility claims in the PI should be supported by data.

If the product is incompatible with the market leader in Australia, this should be stated in the PI.

Any restrictions on the time interval since a ^{99}Mo/^{99m}Tc generator has been previously eluted or on the time after elution after which sodium pertechnetate [^{99m}Tc] should not be used for labelling should be stated in the PI.

Note: When a radiopharmaceutical is the subject of a monograph in the BP, new editions of the Pharmacopoeia, including Addenda, must apply from their effective date in Australia (which is advised in the Commonwealth of Australia Gazette). Any tests that have been agreed with the TGA, in addition to these in the BP, must continue to be applied.

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Reference/Publication #