R3.1 Biodistribution

A physiological distribution test is prescribed, if necessary, for certain radiopharmaceutical preparations. Specific requirements are set out in individual monographs. The distribution pattern of radioactivity observed in specified organs, tissues or other body compartments of an appropriate animal species (usually rats or mice) can be a reliable indication of the expected distribution in humans and thus of the suitability of the intended purpose. The individual monograph prescribes the details concerning the performance of the test and the physiological distribution requirements, which must be met for the radiopharmaceutical preparation. A physiological distribution conforming to the requirements will assure appropriate distribution of the radioactive compounds to the intended biological target in humans and limits its distribution to non-target areas.

Selection of animals

The animals used in this test are healthy animals, drawn from uniform stocks that have not previously been treated with any material that will interfere with the test. If relevant, the species, sex, strain and weight and/or age of the animals are specified in the monograph. Unless otherwise stated, mice weigh not less than 20g and not more than 30g; rats weigh not less than 150g and not more than 250g; and guinea pigs (especially for cardiac radiopharmaceuticals) weigh not less than 250g.

Method

Where applicable, reconstitute the test preparation according to the manufacturer’s instructions. In most cases, dilution immediately before injection may be necessary to ensure optimal radioactivity count characteristics. Unless otherwise stated, inject the specified dose (x) of the radiopharmaceutical preparation into the caudal vein of three animals previously weighed and, where necessary, warmed to room temperature under an infrared lamp.

Swab the injection site with cotton wool and retain the cotton wool and the residual dose in the syringe after injecting for counting (y) and (z) respectively.

Actual injected dose (a) = x-(y+z).

Immediately after injection, place each animal in a separate cage that is designed to allow collection of excreta and to prevent contamination of the body surface of the animal. After the time period specified in the monograph, kill the animals. Collect a sample of blood by cardiac puncture and record the weight of the sample. Dissect out the required organs and tissues, e.g. gall bladder, liver, stomach, intestines, bones and kidneys and place in separate labelled counting tubes. Remove the tail above the injection site and place in a labelled counting tube. Prepare three dose standards (0.2ml) in counting tubes. Count remaining organs and standards in an automatic gamma-well counter or other suitable device. Determine the percentage of injected radioactivity in all organs according to the following formula: 100 x (A/a) where: A = radioactivity in organ; a = actual injected radioactivity.

The percentage of radioactivity in blood is determined according to the formula:

$$[100x(C/Ws) \times 0.07 \times (Wr)] / a$$

where C = Radioactivity in specimen of blood; Ws = weight in grams of blood specimen and Wr = weight in grams of animal. (Normally blood is approx. 7% of total body weight.)

Calculate the physiological distribution and express as the percentage of the injected dose/gram wet weight of tissue. Tissues are counted in optimally calibrated gamma counters.

Specification

The preparation meets the requirements of the test, if the distribution of radioactivity in at least two of the three animals complies with the criteria specified in the monograph. Disregard the results from any animal showing evidence of extravasation of the injection (observed at the time of injection or revealed by subsequent assay of tissue radioactivity).