

10.0 ANIMAL WELFARE CONSIDERATIONS

10.1 Refinement, Reduction, and Replacement Considerations

ICCVAM promotes the scientific validation and regulatory acceptance of methods that refine, reduce, or replace animal use where scientifically feasible. Refinement, Reduction, and Replacement are known as the three Rs of animal protection. These principles of humane treatment of laboratory animals are described as:

- Refining experimental procedures such that animal suffering is minimized;
- Reducing animal use through improved science and experimental design; and
- Replacing animal models with nonanimal procedures (e.g., *in vitro* technologies), where possible.

Combes (2000) and Phillips (2000) recommended that adequate consideration be given to animal welfare concerns by careful development and validation of all proposed endocrine disruptor screening methods. With respect to the proposed use of *in vitro* ER TA assays as screening methods to detect substances that potentially exhibit estrogenic or anti-estrogenic activity, it is important to evaluate the current level of animal use in these assays, and to consider what opportunities exist for refining, reducing, or replacing procedures that use animals.

10.2 Use of Animals in *In Vitro* ER TA Assays

All of the *in vitro* ER reporter gene and cell proliferation assays addressed in this BRD utilize cultured whole cells containing estrogen-inducible gene expression systems and, therefore, do not require use of animals. From an animal welfare perspective, all of these *in vitro* cell-based assays are equally advantageous. However, because none of these assays has been validated for the routine testing of substances, further development and validation are required.

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