## Bill Russell, Rex Burch and the Three Rs

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In *The Principles of Humane Experimental Technique*, Russell & Burch explained how the Three Rs can be used to diminish or remove the inhumanity inevitably involved in animal provide experimentation. They concluded that "*Replacement* is always a satisfactory answer, but *Reduction* and *Refinement* should, whenever possible, be used in combination". Many of the commonsense insights in *The Principles* are as relevant today as they were in 1959. However, their warnings about the limited value of models in general, and, in particular, the danger of succumbing to the high-fidelity fallacy (whereby it is assumed that the best models for humans are always placental mammals, because they are more like humans than other animals), appear to have largely gone unheeded. Of particular importance is their discussion on toxicity testing, which they saw as one use of laboratory animals "which is an urgent humanitarian problem, for it regularly involves considerable and sometimes acute distress". How, then, can it be that mammalian models are still routinely used in attempts to detect chemical carcinogens and reproductive toxins, despite the fact that the relevance to humans of the data they has not been, and perhaps could never be, satisfactorily established?