**The Principles of Humane Experimental Technique**

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## CHAPTER 4

## THE SOURCES, INCIDENCE, AND REMOVAL OF INHUMANITY

The three chief principles stated...

## Contingent Inhumanity and the Problem of Scale

Before commencing the three analyses, one important principle deserves mention. In some procedures, refinement may go so far as virtually to abolish the incidence of direct inhumanity. But under certain conditions there may remain an irreducible minimum, sometimes considerable, of contingent inhumanity. The chief of these conditions is the case where very large numbers of animals are employed daily in a single laboratory (Russell, 1957a).

As this number passes a reasonable level, imperfect handling, injection, housing, and general husbandry becomes virtually inevitable, in the absence of prohibitively large staffs and premises. This will be so with the best will and skill in the world on the part of experimenters and technicians.

This is the significance and rationale of the construction of Table 16 (q.v.)--the number of animals used annually per laboratory. Three compartments of the table contain figures over 5,000: mice in N laboratories, and mice and rats in Group III laboratories. The most serious case is that of mice in Group III, which amounts to an average of over 100 per laboratory per diem. Size of laboratory staff, an obviously relevant factor, is not taken into account, but there is little doubt that in some of these laboratories the number per diem per member of staff must be passing the critical level, though some of the resulting difficulties may be overcome by automation.

Much of this last usage is associated with the assay of insulin. Apart from the more general and comprehensive groupings (such as toxicity testing), and with the exception of TB diagnosis (including milk) and the combined human pregnancy tests, insulin assay is in fact the largest single item on the list of purposes to which animals were applied in 1952 (cf. Tables 6, 10, and 18). This assay is concentrated in a very few laboratories, and may be regarded as a test case. It is far from certain that the present method of insulin assay (based on clonic or tonic convulsions and death in mice) is directly humane, for all or any of the subjects. Human analogy here is both conflicting and of uncertain application. But clearly even if the direct humanity of the procedure were above reproach, the inescapable risk of contingent inhumanity of husbandry and experimental conditions would remain. This assay should, therefore, be high on the list of candidates for replacement or reduction. We must recall also that, husbandry apart, there may always be a finite penetrance of contingent inhumanity due to the procedure itself, and this will be absolutely appreciable when, as here, the overall numbers are large. It would be illustrated in the present example by the possibility that some mice might experience conscious distress at or just before convulsion (cf. Croft, 1952b).

In general, then, in cases such as this (which may multiply as the total scale of experimentation rises--Figure 1b), refinement is never enough, and we should always seek further for reduction and if possible replacement. Still more generally, replacement is always a satisfactory answer, but reduction and refinement should, wherever possible, be used in combination. The principle may be borne in mind throughout the succeeding chapters.

Against this general background of fact and principle, we shall proceed to set the positive features of the subject: the removal of inhumanity by the three modes of Replacement, Reduction, and Reference.