WORLD INFORMATION

ANIMAL EXPERIMENTATION AND THE SEARCH FOR ALTERNATIVES AT THE RIVM

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RIVM-Institutional Center for Alternatives to Animal Testing

Introduction

One of the main tasks of the RIVM is the execution of research in the field of public health. In the investigations carried out within this framework animal experiments are of vital importance. The statistics reveal that 108.522 living animals were used at the RIVM alone in 1989, which is about 10.7% of the total numder of laboratory animals (1.010.919) used in the Netherlands in that year. The various purposes of the use of laboratory animals, both at the RIVM and in the Netherlands, are specified in Figure 1.

It is part of the RIVM policy and strategy to reduce the number of animals, this for ethical, political and scientific reasons. A significant reduction has been achieved in the last decades, amongst others due to organizational measures and an increased ethical awareness of the individual scientist. Moreover, emphasis has been given to the development and implementation of alternative methods. These methods include all the opportunities to replace *in vivo* by *in vitro* studies, to *reduce* the number of animals used to a minimum to achieve goals and to refine animal experiments so that suffering of the animals is minimized. Replacement, reduction and refinement, as a basis for Good Laboratory Animal Practice has become well known as the 3R concept[1].

The search for alternative methods at the RIVM

Several alternative methods have been developed at the RIVM in the past. Some even had major im-

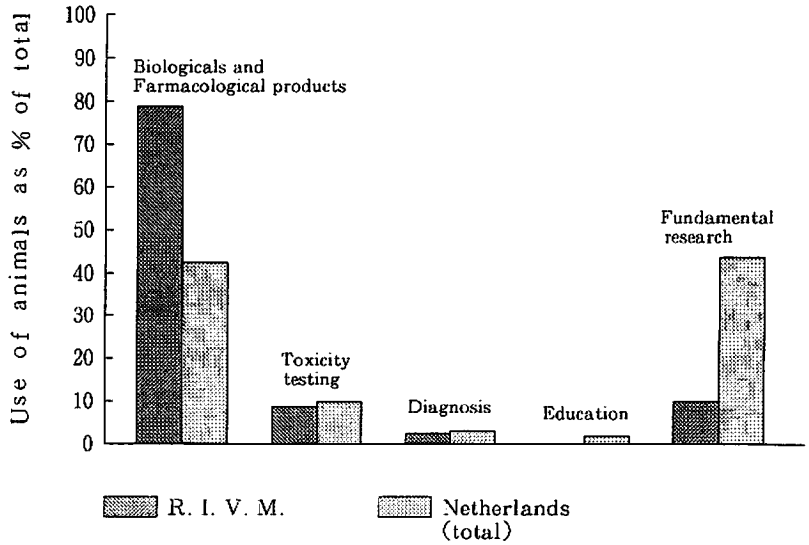

Fig. 1. Purposes of experiments using laboratory animals (%) at the RIVM and in the Netherlands. Data from 1989.

pact as they found international recognition and acceptance. To mention are the microcarrier principle in the culture of vaccine virus[2] and the *in vitro* VERO cell test as a replacement for the lethal challenge procedure in potency testing of batches of diphtheria toxoid[3]. Current RIVM activities in the field of replacement, reduction and refinement are quite divers. A number of the projects under study are spported by the major grant-giving agency on alternatives in the Netherlands; the "Platform for Alternatives to Animal Experiments". They include:

- an investigatory literature search for possibilities of replacing, reducing animal experimentation in the quality control of pharmaceutical products. This study is done in close cooperation With Organon BV.
- the development of a DNA-hybridization technique for the determination of Clostridium botulinum Type C and D.
- the development and validation of *in vitro* methods as an alternative to the *in vivo* NIH potency test in mice for the quality control of inactivated rabies vaccine.
- the optimalization and validation of *in vitro* methods for the identification of teratogenic substances.
- the development of *in vitro* techniques in the quality control of toxoid vacines.

Other, non-subsidized activities in the field of replacement, reduction and refinement are conducted in various laboratories of the RIVM. To give a few examples: at the laboratory of Toxicology bioassays using cultures of hepatocytes and thyroid gland cells are under investigation and at the laboratory for Carcinogenicity and Mutagenicity short-term in vivo assays are evaluated as an alternative to the long-team carcinogenicity test.

One of the spin-offs of the above-mentioned activities was a short-course on in vitro techniques in the quality control of bacterial vaccines, initiated by the WHO and organized at the RIVM in November 1990. Proposals formulated at this course will be used for a modification of the WHO requirements on bacterial vaccines.

The Institutional Centre for Alternatives to Animal Testing (ICAAT)

Although total replacement of animals is not considered a realistic achievement in the immediate future, futher reduction and refinement of the use of animals through the development of alternative methods is seen as a recognisable and attainable goal. The board of directors of the RIVE endorse this view and have supported the initiative to establish an institutional centre for alternatives to animal experimentation This centre has been set up in January 1991 and is the first of its kind in the Netherlands. The organizational structure of the centre is still in status nacendi but most probably will consist of a coordinating staff of two or three members and a contact persons in each department of the RIVM.

The main objective of the institutional centre is to increase the efficiency of 3R research activities at the RIVM. More specifically, the aims of the Centre are:

- to encourage the use of alternative methods whenever appropriate.
- to promote the development and validation of alternative methods and to give coordinative support when necessary.
- to create an institutional centre of expertise on laboratory animals, animal models and a lternatives to animal experimentation which can be consulted both at an institutional level and from the outside.
- to organize institutional conferences, workshops and symposia.
- to advise the board of directors with regard to animal experimentation and alternatives t o animal testing as well as proposing measures taken by the board.

The ICAAT will stimulate establishment of identical centres at other locations in the Netherlands as well participate in the establishment of a national and a European Centre[4]. Besides it will actively participate with foreign organizations such as ZEBET (Zentrale Erfassungs- und Bewertungsstelle fur Ersatz- und Erganzungsmthoden zum Tierversuch) of the Bundesgesundheitsamtes in Berlin, the Center for Alternatives to

Animal Testing (CAAT) at the Johns Hopkins Medical Institutes, Baltimore, USA and the Fund for the Replacement of Animals in Medical Experiments, Nottingham, U.K..

It is believed that the ICAAT can play a modest, but important role in encouraging the use of alternatives.

References

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