Contribution to Panel Discussion on
"In vitro alternatives in toxicity testing"
BIBRA Annual General Meeting, 9 February 1989,

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Panel: Dr George Elton (Vice-Chairman, SCF) [Panel Chairman]; Dr Diana Anderson (Assistant Director, BIBRA); Dr John Ashby (Research Associate, ICI); Professor Bryn Bridges (Director, MRC Cell Mutation Unit and Chairman, CoM); Dr Richard Carter (Chairman, CoC); Professor Peter Elias (Consultant, Federal Research Centre for Nutrition, Karlsruhe, Germany); Dr Sharat Gangolli, (Director, BIBRA) and Dr Francis Roe (Member, CoT)

(1) Dr Francis Roe

I should like to make some general points about this meeting. Ten years ago nobody would have mentioned non-genotoxic carcinogenicity, and yet it is now a respectable concept . We must now ask how important is non-genotoxic carcinogenicity in comparision with genotoxic carcinogenicity? From looking at the animal studies, many of the tumours that might be classified as non-genotoxic relate to physiological disturbances, and short-term tests can identify these. However,

(2) Dr Francis Roe

"You cannot draw such a clear relationship between hyperplasia and cancer. I think David Clayson was looking at cell turnover rates. Increased cell turnover is probably more relevant to future cancer risk than simple hyperplasia. In pathological terms one would never be more than slightly suspicious of simple hyperplasia unless dysplasia was present also."

(3) Dr Francis Roe

"Twenty years ago I think regulators and industry tended to regard each other in low esteem and had little appreciation for each other's objectives, but now, especially with the forum provided by organisations such as ILSI, BIBRA and CITT, industry is more co-operative and the regulators are wiser. Nowadays the regulators are better informed of the standard of science that is available and of the need for flexibility. Thus, provided that the science is good, they are not unwilling to consider alternative tests."

(4) Dr Francis Roe

"The usefulness of *in vitro* tests as replacements depends on whether one is undertaking primary screening or some other investigation. I do not see any prospect for primary screening to be able to replace animals completely, and I do not think it would be morally right in the present state of knowledge to judge safety or toxicity solely on the basis of *in vitro* tests. If, however, one is looking at a specific activity of a chemical based on its structure or other aspect, then I think there is a lot of scope for the use of *in vitro* methods, and it may be possible to do without animal tests in the case of a chemical or group of chemicals if their toxicity is established by the use of these alternatives."

(5) Dr Francis Roe

We are inclined to express our feelings according to the old maxim that where you cannot get rid of an offending substance you reduce exposure as far as possible. We also live with the American concept that a chemical is either completely safe or completely unsafe - a carcinogen or a non-carcinogen. But if we are going to be faced with all the difficulties of long-term bioassays and the public feeling against animal experimentation then we have got to be realistic and bridge the gap between the completely safe and unsafe, perhaps with labelling. We should be able to express a degree of uncertainty about safety but give a realistic form of labelling that gives some concept of level of risk between one extra cancer in 200 million people and absolute certainty of cancer. It is a question of giving guidance to people and I think we need this approach because we have a shortage of test facilities, and many people now regard it as unethical to continue carrying out tests of somewhat dubious value.