

Restricted

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I.T.L. Biological Programme

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At the 1981 Research Conference it was agreed that there was a need for an increased understanding of the effect of product changes on biological activity and the related chemical composition/biological activity interface.

Although these areas have been studied extensively over the years, only limited progress was made due, in part, to the type of test procedures used. However, the utility of the Ames test has now been recognised and represents a valuable tool in the study of the biological activity of tobacco smoke.

The I.T.L. contribution to the Group Biological Programme is as follows:-

1. In-House Studies

Mutagenicity studies to investigate the contribution of a range of factors on Ames biological activity. Tobacco smoke condensate will be subjected to limited fractionation procedures and the biological activity of each fraction and of whole smoke determined. The factors that will be considered are:-

- (i) Smoking regime i.e., human versus standard machine smoking.
- (ii) Different tobacco types including reconstituted materials.
- (iii) Product design.

By analysis of the matrix of results it should be possible to determine whether or not there are any consistent activity/fraction patterns. Subsequently an attempt will be made to characterize biologically active fractions. However, this work would, of necessity, have to be carried out at Southampton since the necessary analytical techniques are only available there. This implies a

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commitment from GR & DC towards this project, although the analytical work would probably not commence until mid 1983; probably the HPLC expertise available within the biological sciences group would be used to separate components of active fractions, with a view to analysis by appropriate analytical procedures such as FTIR, MS etc.

Such a study will complement the deproteinization programme proposed within the group which will be carried out by GR & DC. Earlier work in ITL has shown that Ames mutagenicity is highly correlated with both the protein and total nitrogen content of tobaccos.

It is desirable that contact be made with the group's mutagenicity consultant, Prof. B.A. Bridges, regarding information on the fractionation of motor car exhaust condensate, an area in which he is known to be active. This may be relevant since nitrogen containing compounds of high activity are reputedly present in such condensates. The project also implies close collaboration between Montreal and Southamton and on-site discussions between the participating scientists will be required. Dr. Bilimoria will be conducting a literature review before starting work, since there are some published studies in this area.

In addition, the study will include an examination, including fractionation, of sidestream smoke condensate. The fact that sidestream smoke appears to have similar activity to mainstream smoke (but very different chemical composition) merits further investigation. Sidestream smoke is also being studied in Southampton, however, fractionation procedures are not envisaged.

2. C.T.M.C. Funded Studies with Dr. Ecobichon at McGill University

- (i) Work will continue on the investigation of the effect of smoke exposure on perinatal animals. These studies are aimed at seeing whether exposure to cigarette smoke results in smoke components reaching the pups, and if so, whether via the placenta or breast milk. Arylhydrocarbon hydroxylase will be used as the biochemical indicator.

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- (ii) A programme of work on exposure of animals to ambient smoke has been initiated. This programme will also use arylhydrocarbon hydroxylase as the indicator.
- (iii) Work to develop a micronucleus test is anticipated. The object is to obtain a short-term site specific test for tobacco smoke.

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