

Discussions on Canadian Biological Programme
held at Imperial Tobacco Ltd., July 14, 1982

Present: Dr. P.J. Dunn)
 Mr. R.S. Wade)
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1. On account of the success of the collaborative programme at McGill it was recommended that the research activity with McGill continue along with specific projects which complement the CAC biological programme. The present programme should consist of the following main areas of research.
 - a) the ambient smoke programme, already underway, and the subject of collaboration with Dr. Ecobichon of McGill University. This is funded by C.T.M.C.
 - b) a programme of work aimed primarily at identifying compounds in smoke responsible for mutagenic activity but also intended to supply some information on the range of activity in different products/different ways of smoking. This to be an I.T.L. study.
 - c) the development of a micronucleus test, to be used in conjunction with lung tissue. To be funded by C.T.M.C., as already submitted and agreed.
 - d) any necessary work to complete the AHH studies in pregnant animals.
2. In developing the new areas of work (b) and (c) it was agreed that the mutagenicity studies should take first priority in terms of effort allocation.

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3. It was agreed at the 1981 Research Conference that there was a need for increased understanding of the effect of product changes on biological activity, and of the related chemical composition/biological activity interface.

Although these areas have been studied extensively over the years, limited progress has been made. However, the utility of the Ames test in producing a rapid assessment of mutagenic activity makes this the most promising approach towards meeting the objectives listed above.

4. Specifically tobacco smoke condensates would be subjected to limited fractionation procedures and the biological activity of each fraction, and of the whole smoke determined by the Ames test. The smoke condensates would be prepared as follows:

- a) from different tobacco types
- b) from different smoking regimes
- c) from sidestream smoke
- d) and possibly from different products (design parameters changed)

5. 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 would 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.

6. This implies a 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.

7. Such a study would complement the deproteinization programme proposed within the group which would be carried out by GR & DC.

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8. Although success in identifying active components cannot be guaranteed by this approach, it is felt that the chances are considerably greater than for the fractionation procedures of the 1960/70's (skin painting techniques and inferior analytical chemistry). The duration of skin painting (1-2 years) prevented effective response to "blind alleys".

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9. It would be desirable to contact the group's mutagenicity consultant, Prof. B.A. Bridges, for any information on the fractionation of motor car exhaust condensate, an area in which he is known to be active, and which may be relevant, in that nitrogen containing compounds of high activity are reputedly present in such condensates. The project also implies close collaboration between Montreal and Southampton and on-site discussions between the participating scientists will be required.

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In any event Dr. Bilimoria would carry out a literature review before starting work, since there are some published studies in this area.

10. The fact that sidestream smoke appears to have similar activity to mainstream smoke (but a very different chemical composition) is alone sufficient to merit further work on sidestream smoke, which will also be studied at Southampton although fractionation procedures are not envisaged.

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11. The possibility of removing mutagenic compounds will depend on their identity. For example, it is not easy to control or remove the aromatic polycyclic hydrocarbons in smoke. If, however, mutagenic activity were associated with N- containing compounds the chances of removal/control are somewhat greater.

July 16, 1982.

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