

FILE MEMORANDUM

September 25, 1974

DISCUSSION OF COLLABORATIVE BIOLOGICAL/BIOCHEMICAL RESEARCH

A further meeting took place on September 23, 1974, between Ms. J. Johnson, Dr. M.H. Bilimoria, Mr. R.S. Wade and Dr. T.A. Smith of ITPL, Drs. J.C. Hogg and S. Inoue of McGill and Dr. H.P. Witschi of Université de Montréal.

Four projects were discussed in the order given in the memorandum of September 19.

1. Transformation of Carcinogens by AHH:

In the actual experiment, six animals per dose level will be needed for statistical significance. A standard exposure of 5 cigarettes was accepted. The enzyme has to be obtained from whole lung homogenate or from its microsomal fractions. MHB referred to the possible use of a double beam spectrophotometer to distinguish between effects on different cytochromes of the P450 group, of possible relevance to cancer.

It was confirmed that after training by HPW at U. de M., the exposures and subsequent steps will be done at McGill.

2. Development of Protective Enzyme Systems

All four enzymes could possibly be measured on one lung. No one yet knows whether these enzymes will change due to smoke, and of course even if they do, the meaning of such change would be unclear. It was agreed that an exposure to smoke of 5 cigarettes would be sufficient, not 10-20 cigarettes as originally suggested. It was agreed that the best approach would be to take 1 lung (or lung lobe) per animal for microscopy, and homogenise the other in preparation for the enzyme assays. The techniques for the assays are simple to carry out, making this a much shorter study than Project 1. HPW suggested that straight forward histology would be the best approach at first.

3. Biosynthetic Processes in Tracheal Mucosa

HPW believes this technique will be quite difficult to develop. He will oversee this development stage at U. de M. Then the method can be transferred for the exposures and experiments to McGill. It may be possible to get the tracheal mucosa samples from the animals used in Project 2.

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#### 4. Signs of Lipid Peroxidation in Membranes of Specific Cells

Again this will be a difficult technique to get working, but once successful, it could be the most rewarding project. A good, pure cell population will be needed for this, and methods for obtaining such a population are available in the literature.

#### OVERALL PROGRAMME

JCH believes that this programme can be managed without too much difficulty. It involves at least one year's work. It was agreed that an application for a grant should be worked out for initially one year for the preliminary studies, with the written understanding that, if successful, a further grant for a longer period would be required.

A proposal from RSW was accepted, that JCH should submit the application for a CTMC grant as coming from McGill, with MHB and JJ participating through ITPL, and HPW acting as a consultant. This will be kept entirely divorced from JCH's present grant which he hopes to get renewed for 3 years (With this he hopes to progress from animal lung examinations to study of surgical samples of human lungs). The reimbursement of HPW would be done directly from the CTMC.

Working under his MRC grant, HPW does not have to worry about getting materials for assays over the next 2 years. If the project is successful and long-running, then the politics of such a system would be uncertain. Previously MRC would not allow grantees to get money from elsewhere, but regulations are now more flexible.

JCH should have no problem in working out his required budget. He is presently employing a man half-time for animal exposure, and the proposed work could be handled by simply employing the same man full-time. A further budget would then be needed for materials for microscopy. JCH suggested that JJ, MHB and HPW visit McGill to assess what equipment would be needed there for the biochemical work. This visit is arranged for September 30, (similarly, we must consider what equipment, if any, is required here for the related biochemical work).

In preparation for the grant application, HPW will prepare for JCH an expanded version (with references) of his outline list of project proposals as soon as possible. JCH will then put this together in an overall proposal. A copy of this will be sent to R.M. Gibb before JCH submits it formally through McGill to CTMC.

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If the CTMC should turn down the application, JCH indicated that it now appears possible for work to be carried out in the Pathology Dept. at McGill and supported by an individual company with the arrangements being made through the McGill Contracts Office (as is common in certain other faculties).

Priorities for Projects were discussed briefly. JCH was more interested in Project 1, and would tend to put that first. However, in terms of animal exposure and microscopy, there is no reason why all 4 should not be handled, so that the order of priority could be dependent on the biochemistry.

RSW reported that Dr. Binns had been contacted on the importance of deciding on a smoking machine for animal exposure, and it was agreed that it would be best if Southampton and Montréal were to use the same type of machine. HPW mentioned that he had asked Dietrich Hoffmann about inhalation machines. The latter's advice had been that the only suitably versatile one worth considering was the Dantenwill smoker.

On the question of publication of results, JCH said that McGill always insists on open publication of results. There would be no problem in joint authorship with HPW of the U. de M. or with MHB and JJ of ITPL (JCH quoted an example of a model of emphysema being passed to McGill from Merck-Frosst).



TAS/cp

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