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Geneve, le 25 June 1986

Dear Dr. Heck:

We were pleased to have you visit our facility yesterday. We hope that you found our discussions and the tour of the laboratory to be informative. We are enclosing the brochures, sample protocols, and articles that you requested while you were here. We hope that you now feel as we do, that our 18 years of tobacco related research experience and state of the art technology make us without doubt the best qualified contract laboratory to carry out this type of research.

As we mentioned during your visit the cost estimates for the standard protocols in Swiss Francs are, 60,000 and 225,000 respectively. However we would like to emphasize, that when these studies are done as part of a multistudy program, the cost per study could be substantially decreased. The main endpoint in these studies would be the microscopic pathological evaluation of the tissues of the respiratory tract.

Other endpoints which we commonly use in smoking studies, that strengthen the interpretation of results and facilitate the ability to make interstudy comparisons are as follows: 1) respiration physiology measurements, especially the comparison of spontaneous breathing in animals both before and during exposures. This measurement can be used as an estimator of the relative quantities of aerosol deposited in different exposure groups, and also as an indicator of the irritancy potential of test substances. Other tests of respiratory function, such as forced expiratory maneuvers, airway resistance and lung compliance can indicate long term changes in function. These functional changes can be correlated with structural changes in the lung using morphometric methods for the evaluation of lung tissue. 2) exposing animals to smoke from radiolabelled cigarettes, allows us to determine the dose of smoke to the lung and clearance rates of the particles from lungs. This assay is particularly valuable when respiration physiology measurements are made in the same animal before and during exposures. C-14

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DOT is normally used, but other suitable labels can be used as well. 3) measurements of plasma nicotine and blood carboxyhemoglobin levels are useful for matching exposure groups when different products are being tested. These measurements can be correlated with nicotine and carbon monoxide levels measured in the whole smoke during exposures, thus indicating absorption efficiencies.

In addition to mainstream smoking studies, we also have the capability of doing sidestream smoke exposures, with fresh or aged smoke. Outside the area of smoking studies, we can perform inhalation studies with liquid or solid materials that may, for example be used as additives to products. Also in the area of inhalation, we have developed models of lung disease, which are useful for looking at the reactions of sensitive groups exposed to inhaled materials, and in the development of better products.

In areas other than inhalation toxicology testing, we have active programs in mouse skin painting (GENCAR colony), Ames mutagenicity testing, and the micronucleus test (with exposures done by oral, injection, or inhalation routes).

If you have an interest in any of the assays briefly discussed here, we can provide additional information and cost estimates upon request. Dr. Richard White will be contacting you after he returns from his vacation to provide you with detailed information about his areas of research, particularly with his animal model of emphysema.

Best regards to you, and good luck to Tom Vollmuth in his new position with you.

Very truly yours,

David M. Bernstein, Ph.D.  
Group Leader

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Enclosures mentioned

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