MEMORANDUM

LIMITED

TO PERSONNEL DIRECTLY CONCERNED

59086

To: R. Stevens Case: 59087 Date: March 29, 1954 Page: 1

Subject: Liggett & Myers Conference on March 25, 1954

Morning Session

Personnel Present: Dr. F. R. Darkis, Dr. E. J. Hackney, Dr. M. E. Hobbs of Liggett & Myers Tobacco Co.; Dr. S. E. Cairncross, Mr. R. F. Lar: Dr. W. Machle, Dr. H. O. McMahon, Mr. R. Stevens, and Mr. R. L. Swaine of Arthur D. Little, Inc.

Dr. Darkis opened the meeting by stating his reasons for requesting this conference (1) after Mr. B. F. Few had approved the budget he asked for information on two specific items, these items dealt with the section of our informational survey and biology program; (2) Liggett & Myers believes they want a biology program that will have for its purpose the obtaining of technical data. He stated that this biology program would be helped by our survey program getting information as to how to best set up the biology program. Liggett & Myers also believes that most of our work on filters should be directed under our biology program and not the item under which it appears in our estimate. Dr. Darkis explained that VIII in our budget was set up under Liggett & Myers advertising budget and is to be used only concerning advertising. It would be a short term, quick result type of experiment. Mr. Stevens remarked that this memorandum listing our estimated expenditures was given to Mr. Few in order to acquaint him with the magnitude of our program and the allocation of funds of this program under a definite item was by no means frozen. For example, the use of our Operation Research team should probably be under VII and not VI. A copy of this memorandum in question is reproduced below.

Below are listed the estimates you requested for the current year on the various Liggett & Myers projects

		Approx. Billing in 1953	Est. Billing for 1954
I.	General Consulting Service (57978)	24,000	24,000
II.	Cardinal and Allied Projects (——) (Base Case 58689; Bacteriology 57997; Quarterly Reports 58530)	30,000	15,000
III.	Flavor (57996)	80,000	84,000
IV.	F. T. C. Program (58731)	80,000	15,000
V.	ADL Smoking Group (58495)	30,000*	30,000*
VI.	Investigation of Current Research (59086)	—	200,000*
VII.	Biological Research (59087)	—	250,000*
VIII.	Study of Smoke and Allied Projects (1-4839) (Filter program, investigation of particles, analytical and biological study of smoke components and tobacco products)	—	150,000
	Total	$244,000	$768,000

* These estimates include expenses

From hmm/ R. L. Swaine:4

Mr. Stevens said we are aiming at a preliminary report within three months concerning filters that might be useful for advertising. Along with this we intend to carry out a broader program on filters that would feed information into our biology program as listed under VII or restating it, the program under filters would have two objects (1) obtaining of information for biology by long term studies; (2) obtaining of information useful in advertising in short term studies.

Dr. McMahon then discussed his program in more detail. He stated that you would first look at the filter problem itself before trying to study smoke with its peculiarities. He believes that the filter could be studied by either using natural tobacco smoke or by using DOP of specific particle size. The use of natural smoke would employ greater knowledge about the smoke then we now have. If DOP is used, this knowledge is not necessary and simple optical devices could be used to measure filter efficiency. For example, the use of a Tyndall beam with natural smoke may mean nothing unless all the smoke is of a uniform particle size, however, if DOP is used the measurements are immediately meaningful. Dr. McMahon stated that because of the non-uniformity of filters, the statistical procedure should be used. It is possible that full information of uniformity on filters would be helpful to both Mr. Few and our biology program. This same method could be used to study cigarettes as filters themselves. Dr. McMahon stated there are several things that could be done fairly quickly on the study of natural tobacco smoke. These would include (1) the use of impact separators yielding rough separation. From this information a rough particle size distribution could be obtained; (2) the use of thermo precipitators with lowered temperature. Optical and electron microscopes would augment this study; (3) the use of electrostatic precipitators. In connection with this, we would use a collector plate in the flow path of the smoke on a micro basis. Here again it is possible to use the electron microscope. The above mentioned methods would lead to photographic presentation of data.

Dr. Hobbs interrupted to state that on the basis of Mr. Few's request for meaningful data, the use of DOP appears to him to be more of a research tool than a means of fulfilling Mr. Few's request. Dr. Hobbs pointed out that DOP has fewer particles per cc. than does natural smoke. He agreed, however, with Dr. McMahon that all measurements must be made on a statistical basis. Dr. Hackney concurred with the need for a statistical measurement. He stated that a manufacture of filters is more closely controlled than the manufacture of cigarettes.

Mr. Stevens wondered if Mr. Few might not be able to use this information on the lack of variability of the Liggett & Myers filters.

Dr. Hobbs questioned as to what you would do with the material you would get out of impaction. He questioned as to whether you could get photographs of impaction particles. He stated that the medium particle size of tobacco smoke is about 0.5 microns. In connection with particle size, Dr. Hobbs stated that Dr. Nelson at N. Y. U. is doing work on inhalation and inhalation retention and its relation to particle size.

Dr. Hackney volunteered the specific figures on the variation of the filter efficiency of Liggett & Myers filters which will be available to Dr. McMahon.

Dr. Hobbs said that it was definitely undesirable to use tobacco smoke instead of DOP in any and all measurements of our filters.

Mr. Stevens stated that actually, the cost of Dr. McMahon's program is not tremendous. Dr. McMahon figured that work on DOP would take about three months at $2000 per month and that he defintely needed the information on filters before ADL could make any meaningful statements.

At this point Dr. Darkis stated that ADL must be the judge of the program. He summarized the program as being (1) it would take some two to five months to complete; (2) we would have the information that Mr. Few wanted; (3) that ADL would be able to back up this information if necessary; (4) at the end of the time limit the project would end. He felt that Dr. Hobbs and Dr. Hackney would be of help to ADL in this project. Mr. Stevens said that within three months we would make a package of all information we would have concerning filters and give this information to Mr. Few. That our groupswork on this project would keep in close touch with Liggett & Myers. Dr. Darkis again emphasized the importance of having something that the eye can see.

Literature

The next topic under discussion was that of our literature survey. Dr. Machle stated that studies are now going on at the American Cancer Society and National Institute of Health that are related to the epidemiology of smoking to lung cancer. Dr. Machle reviewed the present status of lung cancer and stated that he intends, while he is in Europe, to get a European pathologist who would keep a check on European work. At this point the meeting was adjourned for lunch.

Afternoon Session

Personnel Present: Dr. F. R. Darkis, Dr. E. J. Hackney, Dr. M. E. Hobbs of Liggett & Myers Tobacco Co.; Dr. S. E. Cairncross, Dr. W. Machl Mr. R. Stevens, Mr. R. L. Swaine of Arthur D. Little, Inc.

The afternoon session opened with a discussion of the Wynder experiment. Dr. Machle suggested that Dr. Wynder's experiment should be repeated not only to attempt to reproduce the same results, but a means of checking our own techniques and obtaining important leads. Dr. Hobbs said he believed Dr. Graham used many br however, has publicly mentioned only that a definite brand was used. The name of this brand is not known. Mr. Stevens said that we must repeat Dr. Wynder's experiment using L&M's, Chesterfield, Camel, and Brand X. Where Brand X is the brand Dr. Wynder used, it was suggested that concurrently we do experiments on the same brand using improved techniques. Dr. Machle stated that there were two

types of projects. One was the check and standardized experiment; the second the search and identification experiment. It was agreed that ADL will completely repeat Dr. Wynder's experiment using all of his techniques. Before the experiment is started Dr. Machle is to go to Dr. Wynder and inform him that we are repeating his experiment and to ask for all information that he can give us. This information must be in writing.

(Dr. Fieser joined the conference at this point). Dr. Fieser stated that he has done much work on chlorestrol. Using this as a background and knowing of Dr. Wynder's acetone soluble fraction, he had made acetone extracts of tobacco. Dr. Fieser presented extracts of Chesterfield, Lucky Strike, as well as, the previous extract of Old Gold. He stated that these had been extracts with the use of both ether and acetone. The larger amount had been extracted from Old Gold and the least from Lucky Strike. Dr. Fieser suggested experiments on the smoking and collecting of tar of previously extracted cigarettes. The material obtained would be subjected to biology testing.

Dr. Hobbs stated that in Durham they have some information on the use of extraction of tobacco particularly with methanol. Dr. Fieser stated that the infra red spectra of tar shows something peculiar. Dr. Hobbs stated that Liggett & Myers has information on the infra red spectra on many tar fractions. These fractions show a compound C-55. Dr. Fieser said he did not believe that this long chain hydrocarbon C-55 is a cancer producing substance. Dr. Hobbs said that although they have found many pyridine bases and phenol, they have never found napthalene or any other compound with two benzene rings in tobacco smoke.

Dr. Fieser questioned the composition of the presence of sterols in tobacco. Dr. Hackney implied that there were none if any sterols present. Dr. Fieser replied that although he did not suspect a sterol, as such, he would suggest a sterol oxidation product that would be an active cancer producer. Dr. Fieser told of natives in India getting cancer of the mouth with beetle nuts only when they also chewed tobacco.

Dr. Fieser specifically asked if nicotine was carcinogenic. Dr. Hobbs replied that N. Y. U. says "no". Dr. Fieser stated that he believed one could take out nicotine and other alkaloids by using ion exchange resins. Dr. Hobbs replied that they are now using ion exchange resins at Duke University. Dr. Hobbs further stated that the most active fraction at N. Y. U. in their separation studies appears to be an ester. N. Y. U. has a report on these fractions but apparently does not plan to publish it. It is however, possible that Dr. Hobbs may obtain copies of this report. Dr. Hobbs offered to Dr. Fieser any information that Liggett & Myers has that might be helpful to him.

Dr. Fieser questioned phenols in tobacco. Dr. Hobbs replied that phenols are present not only in the tobacco but in the smoke, and papers have been published on phenols in smoke. According to Dr. Hobbs, apparently the only inclusive study on the chemical composition of tobacco has been on the presence of inorganic substances in tobacco.

Dr. Fieser asked specifically if arsenic is in tobacco. Dr. Hobbs replied "yes". In answer to Dr. Cairncross' question, Dr. Hobbs stated that he did not know of any chlorinated hydrocarbons in tobacco.

Dr. Fieser questioned the use of blends of tobacco. Dr. Darkis replied that although the majority of American cigarettes sold today are blends, this doesnot hold true all over the world. For example, the Swiss smoke Maryland-type tobacco. Dr. Darkis stated that the chemical composition of each specific type of tobacco varies from each other type and that each manufacturer varies his own blend. He stated, however, that American blends usually contain 45%-65% flue-cured, 20%-45% burly, 2%-5% Maryland, and 5%-10% Turkish. In reply to Dr. Fieser's question, Dr. Darkis said that in the flue-cured process the tobacco doesnot reach over 200° F. Dr. Darkis stated that flue-curing is the most drastic process of treating tobacco and that the first forty-eight hours of the process probably sees the greatest amount of change. The enzymes in flue-cured tobacco are curtailed but not necessarily killed.

Dr. Fieser specifically questioned the carry-over of tobacco mosaic virus. Dr. Darkis replied that if a leaf of tobacco in the field has tobacco mosaic virus the finished cigarette made from this leaf will also contain the virus.

Dr. Fieser asked what the temperature was in the burning zone of the cigarette. Dr. Hackney replied that the temperature is 600 - 850° C., however, the temperature is normal 1" back of this burning zone. Dr. Hobbs said, obviously, this presents a complicated pyrolis problem.

Dr. Hackney stated that the gaseous phase of the tobacco smoke has aldehydes and unsaturation.

Dr. Cairncross told of his experiment with old and new cotton rope where the smoke from old weathered rope could be inhaled without discomfort whereas the new rope caused considerable irritation.

Dr. Hobbs volunteered that if one wanted to just get the hydrocarbon out of smoke one could use silica jell. He then outlined a simple smoking machine to Dr. Fieser that is nothing more than a 105 cc. syringe attached to a three-way tube using alpha cellulose to remove all except the gaseous phase. Dr. Hobbs asked specifically of Dr. Fieser if he knew of any compound that had an ester that

was cancer producing. Dr. Fieser replied he knew of none. Hydrolized urethanol gives a butyric acid odor. Dr. Hobbs again remarked on the ester fraction of the compound obtained during the screening tests at N. Y. U. which was cancer producing.

In connection with screening tests Dr. Machle remarked that certain substances will reduce the number of subaceous glands in mice however, the number of subaceous glands in man are not reduced. He also stated that certain subaceous injections are used in a screening method. It was his opinion that the tar used in the Wynder experiment would be too toxic for injection. Dr. Machle also questioned the value of bubbling air through acetone solution of tar as practiced by Dr. Wynder.

At this point, Dr. Fieser asked as to the kind of cigarettes used in the Wynder experiment. Dr. Darkis replied that he did not know. Dr. Fieser then remarked he felt that it was imperative to repeat Dr. Wynder's experiment using Chesterfield and then again with the same brand used by Dr. Wynder. Dr. Darkis agreed that it was necessary to find out what cigarette was used, and to repeat his entire experiment. However, he cautioned that Dr. Wynder may have changed his techniques in the middle of the experiment. We, therefore, must know the actual operating conditions and not just those conditions that were published. If Chesterfield turns out to be negative and "X" as positive, it would then be possible to say that by using Dr. Wynder's techniques Chesterfield did not produce cancer in mice.

Dr. Fieser volunteered to find out the name of Brand X, however, it was agreed that he would tell Dr. Rhoads about his working for Liggett & Myers and ADL.

Dr. Darkis was requested by Mr. Stevens to check and see if it is necessary to keep absolutely secret that work we are doing for Liggett & Myers. If we do not hear from Dr. Darkis we will assume that the need for great secrecy is not present.

Dr. Darkis replied that Liggett & Myers has not dealt with any cancer agencies or has talked with any, however, they have been indirectly informed that they should support these various cancer agencies. This is not the opinion of Liggett & Myers. Dr. Machle questioned as to Dr. Rhoads having an active interest in work at N. Y. U. Dr. Fieser believed he did, in an advisory capacity. Dr. Fieser quoted in a letter received from Dr. Rhoads dated March 3, 1954, N. Y. U. was having tests done on human lung sections and human skin. Dr. Machle stated that it was his impression that N. Y. U. was independent and not responsible to Dr. Rhoads. Dr. Rhoads is, however, on the advisory board of the Damon Runyon Cancer Fund. All work at N. Y. U. is under Dr. Nelson with advice from tobacco industries.

Dr. Fieser asked if it was possible for the tobacco industry to support cancer agencies. Dr. Darkis replied that it was Liggett & Myers policy that they could get more work done by using an agency such as ADL. He stated that it was his opinion the committee for the tobacco companies is not working too effectively on cancer. This may, in part, be due to the fact that the committee must not work on one brand but all twenty brands. Dr. Machle expressed the opinion that if the American tobacco companies did what the English did to support the cancer fund it would take at least twenty years before any results could be obtained. Dr. Darkis agreed pointing out that although tobacco companies have some able scientists none of these men are on the committee concerning the cancer problem and that of all the tobacco companies, Reynolds and the American Tobacco Co. are the only ones in a position to make any contributions, moneywise, of any importance.

Dr. Darkis pointed out that Liggett & Myers major concern is to produce cigarettes that the public will use and then to make these cigarettes the best possible from a health standpoint. Dr. Darkis continued that the talk of cancer has reduced the sales of cigarettes. He then made the following points: (1) in Liggett & Myers opinion the information linking smoking and cancer is weak; (2) they do not believe in the use of negatives or in tearing down other peoples' work; (3) the work must be done on Liggett & Myers products; (4) it would be good if absolute proof could be found indicating that tobacco is safe to use and not a cause of lung cancer.

Mr. Stevens indicated to the group that Dr. Fieser wanted to be assured of a sound and complete program before he joined our group. He indicated that ADL has been associated with another program and it was completely sound. He stated that obviously Liggett & Myers wanted to sell cigarettes so we must get over the hurdle of linking smoking and lung cancer. Dr. Fieser questioned what would happen if the problem were solved. Dr. Darkis replied that no tobacco company could have an exclusive on this and that the advantage to Liggett & Myers would come in the first six months after solution. Dr. Fieser stated he believed it was a "swell problem" and he was glad to be able to work on it.

Dr. Hobbs stated he was not particularly worried about the chemistry as much as the physiology. Dr. Fieser stated that during his work on anthroquinones they had found it all-right in chickens but not any good in humans. However, seeing that it was a metabolic process they had found a way to interfere with the metabolism in man.

Dr. Machle said, obviously, you cannot get the answer with mice. But by using mice you can satisfy people, otherwise, it would be necessary to wait at least thirty years and watch the death rate change.

With reference to testing small fractions of tar, Dr. Hobbs suggested that instead of testing of all chromatographic fraction, gross testing should be employed, that is, to test the acetone soluble fractions etc.

It was agreed that we would set up machines to smoke in a similar manner as those used by Dr. Wynder, and would obtain tar from L&M's, Chesterfield, Camel, and Brand X. (1) We would use the total tar obtained and test these on animals; (2) we would then study fractions from each tar taken on the cigarette fractions; (3) would try non-smoked fractions of tar. All agreed that these were only the initial studies of our program but should be done before more detailed studies are undertaken.

Dr. Darkis stated that if we can eliminate or reduce the cardinogenic agent in smoke we will have made real progress.

Dr. Fieser said that in the Harvard laboratory they would explore each fraction of tar for new compounds. Should ADL do this? Mr. Stevens replied he would like ADL to do this first, however, Dr. Fieser is free to do exploratory work in his own laboratory.

Dr. Machle stated that there are twelve places doing fraction studies on tobacco smoke. He therefore, suggests any logical shortcuts or hunches be tried realizing that we still must do the long term study. Dr. Darkis agreed to this and again stated we first must repeat Dr. Wynder's work, getting started on this at once and then repeat his work using better procedures.

Dr. Hobbs stated that there is now a program in process at Duke University on the study of smoke for its own sake, that has nothing to do with cancer. They expect to have complete analysis on the gaseous phase of smoke completed in two years.

Dr. Machle pointed out that 270 g. of material are necessary to treat thirty mice for one year. Dr. Hackney answered that one of their smoking machines would give 30 g. of tar for every eight run operations therefore, we would have no trouble. Upon this statement, the meeting was adjourned.

R. L. Swaine

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