post shooting debriefing for officers and their spouses. Law enforcement family services and counseling for families of police killed in the line of duty.

The pervasive nature of job related stress in law enforcement was highlighted in 1986 when a nationwide assessment of law enforcement training needs found that State and local officers in all types and sizes of agencies ranked the need for training in personal stress management as the highest priority.

The law enforcement family support programs places heavy emphasis on family well-being.

All to often, the work of the law enforcement community is overlooked. Everyday, they risk their lives to keep our neighborhoods safe. Everyday, they struggle to uphold justice fairly and equitably. Every day, they work vigorously to remove those who work to terrorize our communities. This hard work places a heavy personal burden on them and their families.

Law enforcement is the single most stressful and dangerous occupation, requiring life and death decision all in a days work. Last year, nearly 160 officers were killed in the line of duty and another 300 took their own lives.

Our police dedicate their lives to and serving our communities. We must do what we can to aid these brave citizens and their families who sacrifice so much for us.

My amendment is fairly funded by reducing the Motor Vehicle Theft Prevention Program to the level it was funded in fiscal year 1995. The committee had zero-funded the family law enforcement programs and I believe this is a more equitable distribution of funds in this time of fiscal constraints. I appreciate the support of the chairman and the ranking member for this amendment and hope my colleagues will join us in aiding the families of our Nation's police.

Mr. ROGERS. Mr. Chairman, if the gentleman will yield, I accept the amendment.

Mr. MOLLOHAN. If the gentleman will yield, we have no objection, Mr. Chairman.

The CHAIRMAN. The question is on the amendment offered by the gentleman from Maryland [Mr. HOYER].

The amendment was agreed to.

Mr. ROGERS. Mr. Chairman, I move that the Committee do now rise.

The motion was agreed to.

Accordingly the Committee rose; and the Speaker pro tempore (Mr. HAYWORTH) having assumed the chair, Mr. EWING, Chairman pro tempore of the Committee of the Whole House on the State of the Union, reported that that Committee, having had under consideration the bill (H.R. 2076) making appropriations for the Departments of Commerce, Justice, and State, the Judiciary, and related agencies for the fiscal year ending September 30, 1996, and for other purposes, had come to no resolution thereon.

SPECIAL ORDERS

The SPEAKER pro tempore. Under the Speaker's announced policy of May 12, 1995, and under a previous order of the House, the following Members will be recognized for 5 minutes each.

TOBACCO AND AMERICA'S YOUTH

[Additional statements to Mr. WAXMAN's Testimony, in the RECORD of Monday, July 24, 1995.]

January 8, 1969.

OBJECTIVES AND PLANS—1600

[By Dr. P.A. Eichorn and W.L. Dunn, Jr.]

OBJECTIVE 1

To establish different thresholds for menthol level in cigarettes and identify optimum menthol level or levels.

Plan

Complete study already initiated by April 1.

OBJECTIVE 2

Attempt to develop research addressed to following questions:

(a) How much reduction in TPM delivery can we expect the typical smoker to tolerate over the next five years?

(b) Can we forecast the stabilization level in the percentage of the U.S. population who smoke cigarettes?

(c) Is there any product that can potentially replace the cigarette in need-gratification?

Plan

Non-schedulable. The task is one of problem solution in research design.

OBJECTIVE 3

To develop instrumentation and procedures for monitoring the psychophysiological state and responsivity of the free-roaming human and apply this technology to a study of the psychophysiological state and/or responsivity of cigarette smokers relative to non-smokers.

Plan

(1) Instrument acquisition and calibration by May 1, 1969.

(2) Hard-line preliminary runs with human subjects completed by December 31, 1969.

OBJECTION 4

To attempt to teach a rat to seek the inhalation of cigarette smoke.

Plan

An informal small-scale (no budget) exploration in which principles of operant conditioning will be applied to teaching the rat to inhale smoke first through reinforcement of the act by food or shock avoidant reward and ultimately through the reinforcing effect of the psychopharmacological effects of the inhaled smoke. No definite conclusion anticipated in 1969.

To: Dr. H. Wakeham
From: W. L. Dunn, Jr.
Date: August 1, 1969
Subject: A Trip Report—Discussions with Prof. Lazarsfeld on the Study of Discontinuing Smokers

I spent six hours with Dr. Paul Lazarsfeld on Wednesday. Following lunch together, I sat with him in his office in the Sociology Dept. of Columbia University, later attending as his guest a status conference on the on-going drug addiction study for New York State. The conference was held in the off-campus building housing the Bureau of Applied Social Research. I met several of his doctoral staff members and observed the graduate student interviewing staff as they participated in the conference proceedings. I was favorably impressed.

We have made great strides towards initiating the exploratory study of the experiences of smokers in their efforts to discontinue the habit. The agreed upon calendar of events calls for Dr. Lazarsfeld to submit a proposal to P.M. R&D prior to August 15. In turn I agreed to make immediately available to him copies of pertinent articles from the R&D Smoking and Health library, to be followed by a background bibliography of broader scope. Thereafter, pending acceptance of his proposal, dialogue between P.M. R&D and BASR staff will be addressed to the development of interview format and content.

I anticipate that his proposal will consist of a study of recidivists and cohort groups of abstainers, the latter consisting of one month, three-month, six-month and one-year abstainers. Subjects will be selected on a post-hoc basis, that is, their efforts to abstain will precede their entry into the study. Interviews will be retrospective probings into their daily lives during the period from the date of discontinuation to the date of the interview. The initial interviews will be loosely structured, with subsequent waves increasingly structured and focused. The progressive sharpening of the interview is to the achieved through Prof. Lazarsfeld's characteristic research style; a series of conferences in which interview material from new batches of interviews is studied in great detail for clues to pay-dirt, with subsequent interviews altered accordingly. I saw this approach in operation in the drug-addiction conference. In its current application it appears to be highly effective. I can see no reason why It should not be as effective for the proposed study.

We also discussed the idea of a steering committee. We noted the various forms this might take:

1. An unstructured group of consultants to Prof. Lazarsfeld as principle investigator.
2. A formally structured advisory group to the project.
3. The Board of the Stress Institute (in this case the Stress Institute would likely be the sponsor of the project).

He seemed equally amenable to all three, though expressing fascination with the third alternative. He pointed out that the task of creating an institute would require heavy commitment of time on someone's part over a period of many months.

As men of repute to advise, he is agreeable to Hans Selye (whom he does not know) and he suggested Prof. Stanley Schacter, a social psychologist of Columbia University who has recently been studying the effects of adrenalin on perceptual processes. We further agreed upon the wisdom of an additional psychologist closer to the physiological front. I named Dr. Frank Finger of the University of Virginia, widely known among psychologists and active in various governing bodies of the American Psychological Association. Another prospect that just occurred to me is Joseph D. Matarazzo, Chairman, Dept. of Medical Psychology, University of Oregon Medical School and writer of the source review of smoking psychology in 1960.

He displayed pleased surprise at our interest in the development of theory, although at this point it would be difficult to say whether this was diplomacy or genuine interest.

I also met and spoke briefly with George Brooks, his staff man formerly with Elmo Roper, confidante of Jet Lincoln, and key man in the series of smoker attitude surveys conducted in the early '60's by Roper for Philip Morris.

RYAN/DUNN ALTERNATE—THIRD VERSION OF BOARD PRESENTATION—DELIVERED WITH ONLY MINOR CHANGES (FALL 1969)

Gentlemen of the Board and guests:

Once again it is my pleasure to appear before you and to make this traditional annual presentation of Philip Morris Research Center activities. Before talking about that particular aspect of the program that I have selected for this year's presentation, let me

make a few remarks about the Research Center in general. You have before you a new brochure on Research at Philip Morris. In it are details about our people and the facility, but here are some figures I think you will find of interest. Our present staff numbers about 330 persons. We occupy 125,000 ft. of floor space. Our budget for this year is $6 million, of which about 25 percent goes into research, 50 percent into product development and 25 percent into technical services to other departments.

I have selected our psychology program to talk about this year. In terms of people and budget it is relatively inconsequential, which partly explains why it has never been mentioned before. We are proud of the fact that we are the only company in the industry that has the discipline of psychology represented amongst its research staff; and we think it only proper, in view of the climate of the times, that we concern ourselves with the topic of the psychology of smoking.

In order to bring you up to date, let me first review the highlights of accomplishments on this front during the past few years.

1. We have established a consumer research facility called our Product Opinion Laboratory. This consists of about fourteen people, mostly pretty girls, who have as their chief task the collecting of opinions and judgments about our new products. The judgments are made by different types of people, depending on the stage of product development and the degree of expertise required. Thus, preliminary taste and flavor profiles are supplied our chemists and development engineers by three small groups of highly trained experts. Products slightly further along the development trail are evaluated by a larger groups of less expert Research Center employees, supplemented by a group of about eighty Richmond housewives who smoke cigarettes in an office near a shopping center. Further screening is available from about 1500 members of civic clubs and community organizations who are called on when we want a quick test from a more representative group of non-experts. And finally, products approaching the test market stage of development are evaluated by a national cross section of American consumers, chosen from some 35,000 people who represent 15,000 families.

So, funneled through our little group of consumer research people, there is a continuous flow of consumer responses to guide the Research Center and Marketing people of making product decisions.

Apart from their routine product testing, they have also reported a number of interesting findings that are worthy of mentioning.

2. Some Highlights:

A. One study has demonstrated that a cigarette manufacturer presumably P.M.—can increase the reconstituted-tobacco component of the cigarette blend to 30 percent without significantly altering the taste and subjective properties of the smoke. The implications of dollar savings here are obvious.

B. Another study demonstrated rather dramatically that the menthol coolness ascribable to our competitor's Kool cigarette is attributable to its name and brand image rather than to the taste of the smoke, per se. When the Kool cigarette was compared to our Marlboro Menthol with the brand identify concealed, menthol smokers, including regular Kool smokers, could not tell the difference. When these same smokers smoked these same cigarettes in their regular packages, most of the menthol smokers chose the Kool cigarette to be the cooler smoking.

C. In a third study a thousand smokers were asked to compare cigarettes made of aged tobacco with cigarettes of unaged tobaccos. They had no preference, suggesting that the aging process does not significantly alter the taste of the cigarette from the consumer's point of view. This means we have more latitude in maintaining a tobacco inventory than was heretofore appreciated.

D. All the medical research on how much people smoke has used the smoker's estimate of how many cigarettes he smokes a day. We've always known this to be a crude measure, but a recent P.M. study has made it possible to show how very crude it is. Our chemists have developed a means of measuring residual nicotine in the filter of a cigarette. From this can be precisely calculated how much TPM passed through the filter and into the smoker's mouth. We had 2500 filter smokers save their butts for us for one week, and from the residual nicotine measurements, obtained an average daily TPM intake value for each smoker: The slide before you shows the relationship of the daily intake value with the smoker's estimate of how many cigarettes he smokes per day.

There are two important political as well as scientific implications from this study.

1. The index of smoking level in health surveys as determined by the number of cigarettes people say they smoke is a very unreliable measure of actual smoke intake, and

2. The prediction of smoker intake from the FTC tar value for the brand smoked is also very unreliable.

E. From the study of smoke intake we developed the hypothesis that a smoker will tend to seek his own level of smoke intake whether he smokes filter cigarettes, long cigarettes or skinny cigarettes. A study to test this hypothesis has just been completed. We had about 150 filter smokers volunteer to smoke only the cigarettes we gave them for six weeks. For the first two weeks they all received cigarettes delivering 20 mg of TPM. Beginning the third week, half the group were supplied with cigarettes delivering 25 mg and the other half were given cigarettes delivering 15 mg. They were not informed of the switch nor did they know anything about the purpose of the study. They were kept on the high and low TPM cigarettes for four weeks. During the entire six weeks they saved their butts. Daily intake values were calculated from the residual nicotine in the butted filters.

The slide tells the story. Initially there was an increase in daily intake for those shifted to the 25 mg cigarette, and a decrease for those shifted to the 15 mg cigarette. But notice that they returned toward their original level of intake after 2 weeks on the new cigarette. It would appear that smokers do modify their smoking habits in order to maintain a preferred intake level. [Illegible]

So much for the past. Recently the psychology program has added a new emphasis. Most of our attention in the past has been focused upon the cigarette. Now we are beginning to concentrate on the smoker himself. We are addressing ourselves to that simple but fundamental question, ''Why do people smoke?''

I must admit to some embarrassment when I say I don't know the answer to this question. It is even more embarrassing to the psychologists on my staff. But I can tell you this . . . . despite the voluminous research and pseudo-sophisticated theories, there is not a scientist alive who can give an explanation backed up by fact.

First we have to break the question into its two parts: (1) Why does one begin to smoke? and (2) Why does one continue to smoke?

There is general agreement on the answer to the first part. The 16 to 20 year-old begins smoking for psychosocial reasons. The act of smoking is symbolic; it signifies adulthood, he smokes to enhance his image in the eyes of his peers.

But the psychosocial motive is not enough to explain continued smoking. Some other motive force takes over to make smoking rewarding in its own right. Long after adolescent preoccupation with self-image has subsided, the cigarette will even preempt food in times of scarcity on the smoker's priority list. The question is ''Why?''

One of the obvious ways to approach the problem is to ask the smoker himself why he smokes: When you do this (and Leo Burnett did this about 10 years ago for P.M.) the smoker will either parrot an advertising slogan or give you one of these responses: (1) It relaxes me.

(2) It stimulates me.

One way to interpret this is to conclude that different people are affected in different ways by the inhalation of smoke. We are inclined, however, to ascribe this apparent duality of effect to an inability on the part of the smoker to describe smoke-produced sensations.

Another obvious way to approach the problem is to search for differences between smokers and non-smokers. This strategy has been more fruitful. The research effort in England and the U.S. over the past 15 years has yielded the following findings:

A. Personality Differences—Smokers are:
(1) More gregarious.
(2) More extroverted.
(3) More business oriented.
(4) Greater sense of time urgency.
(5) More competitive.
(6) More mobile (jobs, residences).
Generally more aggressive and risk oriented.

B. Physiological Differences:
(1) Smokers have faster heart rate.
(2) Eat more.
(3) Drink more—beer, whiskey, coffee.
(4) Have higher oxygen metabolism.
(5) Weigh less.
Generally more active, faster living.

C. Psychological Differences—Smokers exhibit:
(1) More anxiety.
(2) More emotional disturbance.
(3) Higher accident and injury rate.
(4) More suicide.
(5) Lower grades in school.
Generally more tense and emotional.

A third way to approach the question is to search for the immediate effects of smoke inhalation upon the smoker. This approach also has been fruitful. Here are the changes in human body function which follow smoke inhalation. All of these changes have been reported by at least two independent researchers:

Cigarette smoke effects:

Increased pulse rate; Increased cardiac output and coronary flow; Lowered skin temperature in hands and feet; Adrenalin released into blood stream; Increased blood flow in skeletal musculature; Reduction in pattellare reflex magnitude; Nerve impulse transmission facilitated through autonomic nervous system; Arousal center in brain stem excited, causing arousal patterns in the electrical activity of the cortex; Blood sugar level increases.

Now what can be said about all of these findings?

As for the differences between smokers and non-smokers, one might summarize with these three general observations:

1. Cigarette smoking is more often a habit among more responsive, more arousable, more anxious people than among the less responsive or more tranquil people.

2. More cigarette smoking is to be found among people whose life careers expose them to pressures and crises.

3. A smoker smokes more during the more stressful moments of his day or during stressful period of his life.

One might expect from these differences to find that people are attracted to smoking because it acts as a tranquilizer in a stressful situation, as some told Leo Burnett. Indeed this reason for smoking has been hypothesized by a number of other investigators. But in our experimentation whenever we have attempted to confirm this hypothesis, we have found exactly the opposite effect. For example, in studies using excessive muscle tension as a measure of psychological arousal we have observed that smoking increases rather than decreases muscle tension.

We are of the conviction, in view of the foregoing, that the ultimate explanation for the perpetuated cigarette habit resides in the pharmacological effect of smoke upon the body of the smoker, the effect being most rewarding to the individual under stress.

We cannot view the smoke as a tranquilizer; most of its effects on body function suggest arousal. We can see on all the benefits of smoking when bored, not yet fully awake, etc.—it arouses you when you need to be aroused. However, we do not yet understand how an additional source of stimulation could be rewarding to an aroused person in a stress situation. We are beginning to work on this problem.

Currently we are making exploratory measures of bodily indices of emotion and arousal. We are measuring heart rate, respiratory rate, the electrical resistance of the skin and muscle tension. At the moment our subjects are wired to a polygraph recorder; we plan to develop the techniques and instrumentation to measure these indices remotely by radio signal.

Our ultimate intent is to monitor the smoker under real life conditions, under conditions of experimentally induced stress and under conditions of tobacco-deprivation.

This is basic exploratory research, but we would hope for fallout in the way of information applicable to the design of our smoking products and also information that could be used in a public relations program to counter that of the American Cancer Society.

To: W.L. Dunn, Jr.
From: F.J. Ryan
Date: December 23, 1969.
Subject: Proposed Research Project: Smoking and Anxiety

It seems likely that cigarette smoking is affected by stressful situations, but we have little experimental evidence of such a relation. We reason that stressful situations produce states of anxiety within the smoker, and know that he seeks anxiety-reducing palliatives in order to feel more comfortable. Smoking may be one of these palliatives. However, not only are the mechanisms by which tobacco smoke might serve as a palliative not completely clear, but we do not even know whether people smoke more under stress than under nonstress. We wish to conduct the research outlined below in order to clarify the matter and lay the ground work for later study. It is discouraging to realize that we have so little data available that we must start at the very beginning but start we must.

Title: Smoking Under Conditions of Shock Produced Anxiety

Purpose: To show cigarette smoking is more probable in stress situations than in nonstress situations.

Importance: Most research in smoking emphasizes its negative qualities. This project is interested in one of the advantages of smoking, its use as an anxiety reducer.

Nontechnical Summary: We will warn people that they're going to get a harmless but annoying shock while we note changes in (a) amount of smoking, compared to no shock days and in (b) frequency of puffs during the interval between warning and shock. The smoking, the warning, and the shock will all be embedded in a simple discrimination task. Our cover story will be that we are interested in ''smoking and judgment.'' (We need to disguise our real interests in order to prevent subjects from telling us what they think we want to know.)

Predicted Results: (a) Number of puffs on cigarettes will be highest on days when shock is administered, lowest on days when shock is not administered. (b) The distribution of puffs on shock days should be different from the distribution of puffs on no shock days. E.g., either a greater percentage of puffs may occur between the warning and the shock on shock days than in a similar interval on no shock days, or it may be that we will find puffing is postponed until after shock administration.

The Subjects: We prefer to use non-employees for this research. A ready supply of college age subjects can be had from VCU and the University of Richmond. We will pay for the services of both males and females, all volunteers over 21 years old. Each subject will be asked to sign a paper stating that he understands the general conditions of the experiment, and it will be made clear that the subject can withdraw from the experiment at any time, including the middle of a session. They will be paid $2 for participating in each session, plus about $1.50 in rewards for correct responding. In the course of several sessions they can earn $15, including a bonus for completing a series of sessions.

Shock Intensity: Shock intensity will be adjusted for each subject according to the subject's pain threshold. The shock will be painful, but tolerable. Depending on the subject, this will require shock currents of from half a milliamp up to three and a half milliamps. Shock administration will be via a constant amperage shock source controlled by relay equipment. Safety precautions include (1) an isolation transformer, (2) fuses in both shock leads, and (3) a limited time of administration through the contacts of a precautionary timer. The latter unit would limit shock duration to T_1 seconds in case the shock administration circuit should fuse shut.

The Discrimination Task: A series of slides containing different shapes will be presented by a modified Carousel projector. Odd numbered slides will contain a single shape, even numbered slides two shapes. The subject's task will be to decide which of the two shapes presented on the even numbered slide most closely resembles the shape shown on the preceding odd numbered slide. (The shapes can be varied in number of enclosed dots, number of sides, color, area, etc., and there may or may not be irrelevant characteristics also present.) Whenever the correct choice is made, the subject will be rewarded with a token. At the conclusion of the session the accumulated tokens can be exchanged for money over and above the amount paid for participation. Whenever an incorrect choice is made, a warning tone will sound. The tone will last for T_2 seconds. Tone offset will, on shock trials, be accompanied by a brief presentation of shock to the subject's fingers.

Noshock-day Procedures: On days when the subject is to receive no shock he will be treated exactly as on shock days, but he will be told truthfully that he will receive no shock. No pretesting shocks will be administered on these days, and incorrect choices will produce only the tone.

Shock-day Procedures: The subject will receive pre-test shock to find his appropriate shock intensity. His incorrect responses will produce the warning tone. The probability, p, that the tone will terminate in shock will always be above zero, but need not be 1.00 (certainty). It might be more anxiety producing to have p values of less than 1.00, for we suspect that uncertainty of punishment may be more disturbing than certainty of punishment. Accordingly, we will have two different shock-day procedures, one of which p=1.00 and one in which $p \cong .50$, or some other value less than 1.00.

The Subject's Response: The subject's overt task is to throw a left switch or a right switch to indicate that the left or right stimulus is most like the previous stimulus. Action of these switches will produce electrical impulses which in turn will deliver shock or reward, depending on the state of other routing switches. The routing switches will be set by photocell relays, operated by lights shining through holes in the plastic slide mounts of the modified Carousel projector. The relays and switches will start and stop various timers, which will in turn control the sequence of events. Subjects will be asked to abstain from smoking for a period of time prior to the test session, and will be asked to smoke during the test session. Puffing will be observed by the monitoring experimenter, who will throw a switch to mark each puff. The placement of puffs within the intervals between other events can be read directly off a polygraph record. (If a satisfactory puff monitor can be produced by the electrical engineers at U. Va. then its output can replace the experimenter/observer's switch.)

Later Research Plans: It is possible for us to monitor a number of concurrent physiological variables during the test session, such as Heart Rate, GSR, perhaps EMG, depending on our developing interests.

Charge Number: 1600
Program Title: Consumer Psychology
Program Leader: W. L. Dunn, Jr.
Period Covered: September 16—October 15, 1971

Project Title: Psychology of Smoking
Project Leader: W. L. Dunn, Jr.

The Conference on Motivation in Cigarette Smoking is on schedule.

Project Title: Miller Brewing Work
Project Leader: Anne Ferguson

A new augmenting smoking panel is being selected and the beer panel is receiving refresher instruction. Both activities are being undertaken with the consultative assistance of Barbara Hall Ellis.

Project Title: Methods Studies
Project Leader: W. L. Dunn, Jr.

Replication of SIC–1 (preference justification effect) is in the field. The study of alternative field test designs was mailed out but has been aborted and will be rerun due to package coding errors.

Project Title: Smoking Profiles: A Pilot Study
Project Leader: Frank Ryan

Several improvements in the puff monitoring system have made it less obtrusive. Some preliminary measures have been made on college students in the shock research project, and additional measures have been made on R & D personnel to aid in calibration of the system. When five additional models are made, they will have slightly different specifications. The range of flow rates by the orifice is such that we will have to use different models for different smokers, but we should be able to handle 9/10 of the smokers we are likely to meet. (See the reports of the Program on Human Smoking Simulation, Charge Number 4008)

Project Titles: Shock I, II, III, and IV
Project Leader: Frank Ryan

We continue to gather data on the puffing behavior of local college students (Shock

IV). The first study of this type (Shock I) indicated that personality affected the puff rates of the 16 students in a shock and heart rate experiment. The second study (Shock II) replicated the procedures of the first but omitted the heart rate measures. Assigning 21 new students to one of three groups on the basis of their personality scores and the data of the first study, we predicted that the three groups would rank low, moderate, and high in number of puffs. The data supported the hypothesis, the means being 9.1, 10.6 and 12.0 puffs for the three groups.

At third variation (Shock III) of the procedures has now been completed and the data analyzed for 23 new students. The results suggest that personality factors, particularly the Anxiety factor, account for most of the puffing in our test situation under our tests conditions (note the qualifiers.) The correlation between the personality factors and puff rate is very high, and further research will undoubtedly lead to lower but more stable figures.

We are very much encouraged by the tend of these findings, because they bear on the hypothesis that different types of people have different tar and nicotine intakes.

Project Title: Preferred Tar Reduction Procedure
Project Leader: Frank Ryan

Planning is underway for a study of consumer preferences among the different procedures which lower FTC Tar delivery. Cigarette models will be chosen in November, and mailout target date is February 20, 1972.

Project Title: Cigarette TPM Difference Limens
Project Leader: T.R. Schori

Twenty R & D employees have been run as subjects in this study which was designed to determine what constitutes a just-noticeable-difference in cigarette TMP. The data suggest that smokers are very poor at making such discriminations. We are instigating a slight change in our approach to the problem to see whether our procedure is insensitive or whether in fact smokers are unable to discriminate.

Charge Number: 1600
Program Title: Consumer Psychology
Period Covered: January 15-February 15, 1972

Project Title: Preferred Delivery Reduction
Written by: Frank Ryan

We are comparing five cigarettes, each delivering about 14 mg. tar from a Marlboro 85 blend. Each achieves its tar reduction in a different fashion. The models are: No air dilution, high RTD; moderate air dilution, moderate RTD; high air dilution, low RTD; a paper/CA filter; and an extended tipping paper. Prototypes have been made which are reasonably homogeneous and close to the 14 mg. target, and mailout cigarettes have been ordered. Panelists will be selected from known Marlboro smokers after POL National repolling is complete.

Project Title: Shock V
Written by: Frank Ryan

(a) Additional subjects will be screened to test our personality-puff rate data with new slides.

(b) We plan to reintroduce electric shock in studies this spring.

(c) The apparatus is currently tied up in the smoking profiles pilot work.

Project Title: Smoking Profiles Pilot Study
Written by: Frank Ryan

Students with known puffing patterns (e.g., number of puffs and puff intervals) are evaluating the difficulty of the slides used in Shock I-V while smoking with the human smoking recorder. We are looking for differences in puff behavior attributable to the cigarette holder mouthpiece, tubes, recorders system, etc.

The first test we plan to run with this apparatus will compare puffing behavior on two different types of very different cigarettes. Our present plans are first to test a high delivery 85 mm against a low delivery 85 mm vs. 100 mm of comparable draw.

Project Title: Puffing vs. Judgment
Written by: Frank Ryan

We will ask our students to rate two vastly different experimental cigarettes, using standard SEF callots, to see whether those who take many puffs are as responsive to smoke characteristics as those who take few.

Project Title: Perceived Attributes of Cigarettes
Written by: T.R. Schori

This study was designed to determine major cigarette characteristics as perceived by smokers by means of a factor analytic technique. Ballots are in process of being mailed to a representative panel of 800 smokers.

Project Title: Smoking and Low Delivery Cigarettes
Written by: T. R. Schori

This is a two part study. Cigarettes for Part 1 (TNT-2) are in the process of being mailed out. Cigarettes for Part 2 (TNT-3) are currently being developed.

Project Title: A Comparison of the Effect of Caffeine and Cigarette Smoking
Written by: T. R. Schori

Smokers were tested in each of 3 conditions: placebo, caffeine, and cigarette smoking. Eleven measures of arousal were collected. A discriminant analysis indicated that these three groups differed from one another in terms of the eleven measures considered simultaneously. A report will be written shortly.

Dr. P.A. Eichorn
W.L. Dunn, Jr.
Quarterly Report—Projects 1600 and 2302
October 5, 1972

SEX–III

Twelve hundred of the original 2400 filter smokers who participated in the SEX–I study in 1968 are, at the time of this writing, saving butts for R&D analysis. We will be attempting to relate change in smoke intake to other variables, notably change in available TPM in the cigarette smoked.

Publication of Smoking Behavior: Motives and Incentives.—Because of editing difficulties with one author, the volume is now likely to be delayed until January, 1973.

Participation in Ford Motors Keep-Well Campaign.—The Medical Department of Ford Motor Co. will be launching an exploratory study of a Prophylactic Program to Reduce Cardiovascular Illness among Employees. We will collaborate in the design and data collection. The study is in the early planning stage.

Miller Brewing.—We are providing ongoing consultation and testing services to this subsidiary in the evaluation of its beer products.

The Schachter Studies.—We are collaborating closely with this investigator and providing technical support to the research activities in the Psychology Dept. of Columbia University. A significant theoretical contribution to the understanding of cigarette smoking is believed imminent from this effort.

Puffing Behavior.—We have begun gathering puffing data among student college smoking various brands of cigarettes and little cigars. Intake variables (puff frequency, interpuffing intervals, puff volume, etc.) should prove related to product preferences, FTC tar and nicotine delivery, etc. The human smoking recorder is used to monitor the puffing while subjects watch slides.

Personality and Puffing.—We continue to observe differences in puffing behavior related to personality variables. The effect seems clearer among male subjects than among females.

Shock and Smoking.—Data collection will resume in October at a new location (POL). We need to develop a different stressor as fear of shock is scaring away some of our more valuable subjects.

Sustained-Performance and Smoking.—In this two-part study, we are evaluating psychomotor performance of smokers, deprived smokers, and nonsmokers over time (3 hours). Part 1, concerned with complex task performance, has been completed. The subject's task consisted of five subtasks which had to be performed simultaneously. These subtasks were: a meter monitoring subtask (6 meters), a light monitoring subtask (4 lights), a visual choice reaction time subtask, an auditory choice reaction time subtask, and a mental arithmetic subtask.

In terms of all five subtasks, the subjects showed significant improvements in performance over time. No significant differences in performance were found between the three smoking conditions except in the auditory subtask where smokers displayed the best performance. This latter finding suggests the possibility that smoking enhances auditory sensitivity and we are currently looking into this possibility. As we had found in previous studies, smokers had fewer significant mood changes (as measured by the Nowlis Mood Scale—a paper and pencil device to measure transient mood states) than did nonsmokers or deprived smokers. This suggests that smokers are more emotionally stable in this sort of test situation than are nonsmokers or deprived smoker.

MULTIPLE DISCRIMINANT ANALYSIS: A REPEATED MEASURES DESIGN VIRGINIA JOURNAL OF SCIENCE, 23, 62–63, SUMMER, 1972. SCHORI, T.R., AND TINDALL, J.E.

Menthol Cigarette Studies.—Two menthol cigarette studies are underway. The first is designed to delineate the images possessed by various of the menthol cigarettes currently on the market. This is a questionnaire type study using national roster panelists.

The second type is a smoking test. It is designed to identify nicotine and menthol parameters which make for optimal acceptability of menthol cigarettes. This study has a three-stage design. The first stage is designed to identify those nicotine delivery levels which we might reasonably wish to consider for menthol cigarettes. Having identified these nicotine delivery levels, in stage 2 we will determine combinations of nicotine and menthol which make for optimal acceptability. And then in stage 3, cigarettes with these combinations will be tested against current brands of known quality and sales potential.

Bay Area Study.—Marketing, for the past few months, has been trying to improve the image of Multifilter in the San Francisco Bay Area and San Jose. In this study, we are trying to determine whether this attempt to improve Multifilter's image has been successful. We are doing this by means of a mailout to smokers in these areas.

Tar and Nicotine Studies.—We have done a number of nicotine to tar ratio studies. Development is continuing to try to make cigarette models with various levels of tar and nicotine using our low nicotine tobacco. When we get successful models, we will go out to a national panel in an attempt to determine combinations of tar and nicotine which make for optimal acceptability.

In addition, a local panel of smokers will test these cigarettes for nine weeks in order to determine the effect of tar and nicotine on cigarette consumption when both tar and

nicotine deviate downward from that to which the smokers are accustomed. This is a follow-up of TNT–1.

Dr. P. A. Eichorn
W. L. Dunn, Jr.
Five-year Objectives and Plans for Project 1600
September 25, 197

OBJECTIVE I

Identify as many as possible of the short-term psychological and psychophysiological phenomena attendant upon the smoking of a cigarette.

Plans.—To expand the scope of the present psychology research program to include studies of the immediate, short-term effects of cigarette smoking as manifested through changes in autonomic, perceptual, cognitive and central nervous system processes and motor performance.

OBJECTIVE II

Advance scientific knowledge of the motivation sustaining the cigarette smoking habit.

Plans.—(1) To further observe the smoking-induced changes identified under Objective I under varying degrees of psychological tension, from relaxed calmness to anxiety, in order to study the interaction effects of smoking and tension upon psychological function.

(2) To conduct studies in which the dependent variable is rate of smoking and the independent variable is a situational factor affecting the smoker's level of vigilance or tension, testing the hypothesis that rate of smoking is a function of vigilance or tension level.

(3) To research the question, ''Can the smoking habit be sustained in the absence of nicotine?'' Other strategies may be developed, but one now being explored is to attempt to identify which components of the smoke, in gross fractions, effect the heart rate change associated with inhalation of whole smoke.

(4) To coordinate the industry-sponsored conference on the motivational mechanisms of cigarette smoking scheduled for January, 1972.

(5) To prepare a review paper on the psychodynamics of cigarette smoking.

OBJECTIVE III

Forecast trends in cigarette smoking behavior and preferences for guidance in cigarette development.

Plans.—(1) To design a test for determining the smoker's tolerance for reduction in tar delivery over time in terms of rate, increments and limits of reduction.

(2) To elucidate the role of nicotine as a factor in determining cigarette acceptability in terms of absolute levels and relative to other smoke components.

(3) To more systematically observe puffing profiles of smokers across various cigarettes via use of the mobile recording system developed for P.M. by the Engineering School of the University of Virginia.

OBJECTIVE IV

Establish the psychological units of detectable difference for the basic dimensions of cigarette smoking including tar, nicotine, RTD, menthol and TFP.

Plans.—Since methodological obstacles have severely limited our progress on this front to date, we must concentrate on devising research procedures for circumventing these obstacles.

OBJECTIVE V

Improve the validity and reliability of our standard product testing procedures, and reduce the lagtime between service request and report of findings.

Plans.—(1) Continue, as in the past, to test out new research designs and procedures.

(2) Incorporate data retrieval, processing and reporting innovations into our routine procedures as they become available and appropriate.

Charge Number: 1600
Program Title: Consumer Psychology
Program Leader: W.L. Dunn, Jr.
Period Covered: October 16–November 15, 1971

Project Title: Psychology of Smoking
Project Leader: W.L. Dunn, Jr.

The Conference on Motivation in Cigarette Smoking is continuing on schedule.

Project Title: Methods Studies
Project Leader: W.L. Dunn, Jr.

The study of alternative field test designs (TRI–2) is in the field. SIC–2 (preference justification effect) is now in analysis.

Project Title: Shock IV
Project Leader: Frank Ryan

Data collection continues in this series of experiments on student smoking behavior. Nearly 100 students have been tested in the four series to date. We are seeking additional tasks for them to perform in order to broaden the scope and generality of our findings.

Project Title: Desire to Smoke
Project Leader: Frank Ryan

All available college subjects will fill out a questionnaire rating their desire to smoke in each of 22 hypothetical situations. One of Eysenck's colleagues has postulated that there are two types of smokers: one smoker smokes in quiet situations to raise the level of his central nervous system arousal, a second smokes in tense situations in order to reduce their arousal level. The published data suggest that males had their highest desire in quiet situations, females in stressful situations. This may be related to male extroversion and female introversion factors, so Eysenck has suggested that extroverts smoke to increase arousal, while introverts smoke to reduce arousal. We'll compare the rated desire to smoke with our existing personality profiles of these students to check out the hypothesis.

Dr. P.A. Eichorn
W.L. Dunn, Jr.
Quarterly Report—Projects 1600 and 2302
January 5, 1973

SEX-III—Data collection completed. Analysis in progress. Preliminary analysis reveals a 10% reduction from 1968 to 1972 in available tar among cigarettes smoked and commensurate reduction in mean daily intake.

Ford Motor's Keep-Well Campaign.—No progress to report. The study at Ford has been delayed.

The Schachter Studies.—A pilot study at the Columbia University laboratory has revealed a 30% increase in cigarette consumption (number smoked) over normal consumption when on a regimen of high level Vitamin C dosage. A comparable regimen with sodium bicarbonate did not result in the predicted reduction in consumption.

The Neal Miller Studies.—A pilot study at the Rockefeller University laboratory suggests that the elicited attack behavior in cats is markedly moderated when the animal has been injected with nicotine. The high nicotine dosage level, however, demands caution in any interpretation.

Puffing Patterns.—Data continues to be collected on puffing behavior relative to the type cigarette being smoked.

Bay Area Study.—Discontinued. The study was judged to be of a non-R&D nature and Marketing Research funds were not available for its support.

The Effects of Smoking on Heart Rate Variability.—Three studies are in the initial stages for determining what effect, if any, smoking has upon the magnitude of shifts in arousal level, with heart rate being used as the index of this psycho-physiological state. The study involving the telemetry of heart rate, delayed because of technical problems and laboratory relocation, is about to enter the recording phase. Heart rates of R&D smokers, under smoking and abstention conditions, will be sampled over working hours. A second study is being initiated in which a small sample of R&D employees will record their heart rates on portable tape units while driving to and from work under smoking and extended abstention conditions. A third study is being formulated in which volunteer subjects will be subjected to intensive and varied activity programs designed to be fatiguing and/or frustrating and extending over a 24-hour period in which no sleep will be permitted. The effects of deprivation of food, of water and of smoking will be observed in terms of heart rate measures and performance efficiency. The scheduling of these latter two studies is contingent upon the assembly of the portable heart rate recording device, the critical element of which is the sensor-transducer component. The critical measure is the variance of heart rate over time.

Tar & Nicotine Studies.—Cigarettes are scheduled to become available for these studies in January.

Fourteen Choice.—There are various ways for lowering TPM to 14 mg. Which yields the preferred cigarette? After extensive experimentation, adequately controlled samples of the six selected cigarettes have been provided in sufficient quantity for local testing. This testing will begin in January, to be followed by national field testing.

Black Menthol Panels.—Recruitment of both local and national black menthol smokers is underway.

Menthol-tar Combinations.—Experimental models of the cigarettes needed for this study are being made. When the specifications are met, the cigarettes will be produced and the study initiated.

Tar-nicotine Combinations.—Here also the execution of the study is contingent upon the design and production of cigarettes which meet the specifications demanded.

Charge Number: 1600
Program Title: Smoker Psychology
Project Leader: W. L. Dunn, Jr.
Period Covered: January 1—January 31, 1973
Date of Report: February 9, 1973

Project Title: Smoking and Rate of Learning Alpha Control (A new study)
Written by: W. L. Dunn

Alpha brain wave (8–12Hz) dominance is associated with states of tranquility and meditation. Alpha is recordable with appropriate electronic circuitry (EEG) and can be used to trigger auditory or visual stimuli as signals of alpha presence above predetermined threshold levels. These biofeedback signals can facilitate the learning of alpha control in human subjects.

As part of our continuing search for the motivationally relevant effects of smoking, we are investigating the influence of smoking upon the rate of acquisition of alpha wave control. Using smoking subjects and alternating smoking and non-smoking learning sessions (daily sessions of 3 to 5 minutes) we will test for differences between the two conditions in terms of cumulative time of alpha dominance.

Project Title: Richmond Product Placement Panel
Written by: M. E. Johnston

Plans for establishing a local roster of 1500 to 2000 smokers, including much needed Marlboro, hi-fi and black menthol smokers, are being put into effect.

Project Title: The Delivery of Inhalation Impact via Other Vehicles than Nicotine
Written by: W. L. Dunn

It has been observed that when the filler of a commercial type cigarette is denicotinized, the inhalation impact of that cigarette is lost. In collaboration with Hind and Gellatly, we are investigating the capability of a denicotinized 100% uncased burley cigarette to deliver impact. If there is found to be residual impact, we will attempt to build an acceptable cigarette around denicotinized uncased burley.

Project Title: Optimum Mode of Tar Reduction
Written by: Frank Ryan

A five-pack handout is now in local distribution. Results will be used to determine feasibility of national mailout.

Project Title: Arousal and Smoking
Written by: Frank Ryan

The effect of smoking or non-smoking on the arousal mechanisms of the central nervous system is being monitored throughout the day by measuring heart rate activity. Samples of activity are taken throughout a week of smoking, and then throughout a week of non-smoking. Several employees have volunteered to quit smoking for a week and then resume, but not all will be usable.

In addition, heart-rate recordings while commuting to work will be collected under smoking and extended abstention conditions.

Project Title: Puffing Behavior on Different Brands
Written by: Frank Ryan

Final subjects are now being run. Preliminary data indicates puffing at little cigars is different from puffing at cigarettes and that Marlboro and Winston are smoked similarly. This appears to be a useful procedure, but it takes a long time to gather any significant amount of data. We may change our standard task to enable us to use the same smokers more often.

Project Title: Cigarette Variability
Written by: Frank Ryan

A pack handout will be made in late February to test the effect of cigarette variability on consumer response. Warren Claflin's group has provided the cigarettes.

Project Title: Personality and Puffing Behavior
Written by: Frank Ryan

A report is being prepared on this topic covering progress to date.

Project Title: *Smoking and Spare Mental Capacity*
Written by: T. R. Schori

This is a study in which we are looking for differences in spare mental capacity between smokers, smokers-deprived, and nonsmokers using a cross-adaptive loading task technique. With this technique, subsidiary task difficulty is dependent upon primary task performance in such fashion that primary task performance is made comparable over groups while subsidiary task performance becomes an indication of spare mental capacity.

Project Title: *SEX–III Analysis*
Written by: T. R. Schori

Data analysis continues. The first draft of the report will be complete February 14.

Project Title: *JND–2*
Written by: T. R. Schori

This is a follow-up of JND–1 in which we are interested in whether smokers can detect differences in two cigarettes varying in tar delivery by 5 mg. They were unable to do so in the original study. The cigarettes are in the field. Ballots are starting to trickle in.

Project Title: *Smoking and Sustained Performance*
Written by: T. R. Schori

Report in progress.

Project Title: *Menthol Cigarette Image (HN–1)*
Written by: T. R. Schori

Report in progress.

Project Title: *Acceptability and Low Delivery Cigarettes (II)*
Written by: T. R. Schori

Awaiting cigarettes.

Project Title: *Economic Analyses*
Written by: Myron Johnston

The following analyses were completed:

1. Projections of Weighted Average Tar Deliveries (requested by Steve Fountaine). Extrapolations of trend lines of weighted average tar deliveries basedoon three different time periods and two methods of computation (logarithmic and arithmetic).

2. Weighted average tar deliveries of 85mm and 100mm filter cigarettes calculated separately (requested by Al Udow).

3. Calculation of simple average tar delivery and range of delivery levels available to the American public, 1954–1972 (requested by Dr. Wakeham).

4. Percent who smoke cigarettes by occupation and age (requested by Dr. Fagan and Mr. J. Lincoln).

5. Attitudes of R&D professionals to the speakers at the evening seminars for the past two years (requested by Dr. Fagan for the Evening Seminar Committee).

Project Title: *Smoking Patterns as Related to Status Inconsistency*
Written by: Myron Johnston

Several computer runs have been made and we are in the process of analyzing and writing up the results of our findings to date. Status inconsistent smokers report higher consumption rates than status consistent smokers according to preliminary data. Our panel data confirms the findings of other studies that smoking is inversely related to income, occupation and educational attainment (the components of socio-economic class).

Project Title: *Acquisition of Marlboro Smokers from Market Research Department*
Written by: Myron Johnston

HTI has been having computer problems but we have been promised delivery of the names and addresses of 500 Marlboro smokers by February 12.

Project Title: *Product Usage—Pipe Tobacco (requested by Marketing Department through Bill Corsover).*
Written by: M.E. Johnston

Several computer tabulations have been run and I am ready to begin the analysis of the data.

Charge Number: 1600
Program Title: Smoker Psychology
Project Leader: W.L. Dunn, Jr.
Period Covered: May 1–31, 1974
Date of Report: June 10, 1974

Project Title: *Alpha Brain Waves and Smoking*
Written by: W.L. Dunn

Data collection complete. Analysis in progress.

Project Title: *Inhalation Controls*
Written by: W.L. Dunn

Instrumentation is nearly complete. Electronic problems have been resolved and mechanical valving of airways appears to be in working order. The nose mask is causing some delay in that we recently became aware of a shrinkage problem with the silicon rubber material used in fabricating the mask. An alternate curing agent (on order) is supposed to solve the problem.

Project Title: *Puffing Behavior*
Written by: F.J. Ryan

We have begun gathering data on the effects of intercigarette interval on puffing behavior. Students smoke cigarettes either 10 or 60 minutes apart while working on paper and pencil tasks and reading into the delayed feedback tape recorder. We expect to see differences in behavior as a function of the intercigarette interval. It is not clear whether these differences will be in average puff volumes, durations, and flows, or in number of puffs, total puff volume, and interval between puffs. Our previous research suggests that average puff volume, puff duration, and flow rate of the smoke are relatively insensitive to external conditions, each smoker having his own preferred response pattern which interacts with the physical characteristics of the cigarette rod at the time of the puff to determine the puff volumes, etc. Therefore we suspect that the major differences will appear in the number of puffs taken, interpuff interval, and total volume of smoke.

Project Title: *Relationship Between Smoking and Personality*
Written by: F.J. Ryan

Some children are so active (or ''hyperkinetic'') that they are unable to sit quietly in school and concentrate on what is being taught. In recent years it has been found that amphetamines, which are strong stimulants, have the anomalous effect of quieting these children down and enabling them to concentrate in the face of distractions which otherwise would have disrupted their attention. Many children are therefore regularly administered amphetamines throughout grade school years. The wisdom of such prescription is open to question, and some published reports have suggested that caffeine, in the form of coffee or tea for breakfast, would produce the same end result. We wonder whether such children may not eventually become cigarette smokers in their teenage years as they discover the advantage of self-stimulation via nicotine. We have already collaborated with a local school system in identifying some such children presently in the third grade; we are reviewing the available literature on the topic; and we may propose a prospective study of this relationship. It would be good to show that smoking is an advantage to at least one subgroup of the population. Needless to say, we will not propose giving cigarettes to children.

Project Title: *Smoking and Mental Concentration*
Written by: F.J. Ryan

Embedded in the puffing behavior study mentioned above is the study of the effects of smoking on performance with the delayed feedback tape recorder. The students read passages into a microphone connected to a tape recorder while hearing their own voice over earphones either as they say each word or slightly after they say each word. The latter (delay) condition disrupts normal speech patterns, sometimes causing stuttering, word blocking, slurring, dropped final word-endings, etc., and seems to slow reading rate by 15% of more. One strategy adopted by readers under delay circumstances is to ignore the sound of their own voices and hence to pay no attention to what they are reading. We test for this by asking questions about the material read. To the extent that smoking aids in concentration we should see performance improvement when reading in the delay condition after having had a cigarette compared to reading when no cigarette has been smoked for an hour.

Project Title: *DL–2*
Written by: T.R. Schori

Panelists smoked a Marlboro Control and three low delivery cigarettes, averaging less than 10 mg tar, at three levels of RTD varying upwards from 4.8 inches. The most interesting finding was that these low delivery

cigarettes were as acceptable as the Marlboro Control. A report is being written.

Project Title: *Smoking, Arousal, and Mood*
Written by: T.R. Schori
The data acquisition phase of this study is nearly over.

Project Title: *MN–3*
Written by: T.R. Schori
This is the second in a series of studies designed to determine what nicotine and menthol parameters will optimize consumer acceptability (of various subsets of the menthol smoker population) of menthol cigarettes. These cigarettes are ready to go out to a national panel.

Charge Number: 1600
Program Title: Smoker Psychology
Project Leader: W.L. Dunn, Jr.
Period Covered: February 1–28, 1975
Date of Report: March 10, 1975

Project Title: *DTR–2*
Written by: W.L. Dunn
A dual field study of RTD/tar interaction and assessment of three modes of presentation. Data in analysis.

Project Title: *Inhalation II*
Written by: W.L. Dunn
An attempt to monitor all of the behavioral mechanisms available to the smoker for regulating exposure to smoke under conditions of varied delivery levels. The study will require the simultaneous recording of (a) the puff profile, (b) nose/mouth inhalation ratio, (c) total inhalation volume and (d) retention time. We are engaged in solving the instrumentation problems.

Project Title: *Puffing Following Deprivation*
Written by: Frank Ryan
Data collection continues, will end this month.

Project Title: *Constant Volume Puffing*
Written by: Frank Ryan
To see what cues govern the size of puffs we will ask smokers to attempt to take puffs of identical volume at different places on the rod, while manipulating delivery and RTD of the products being smoked.

Project Title: *Hyperkinesis as a Precursor of Smoking*
Written by: Frank Ryan
The size of our prospective study should be increased to a base of about 6,000 children when a local school system extends its student evaluations three more grades this spring.

Project Title: *Annual Monitoring of Cigarette Acceptability*
Written by: Frank Ryan
The tentative design of this study is as follows: once a year we will have five different products evaluated by a large panel of smokers.
The evaluation will be on a 9-point acceptability scale, ranging from Dislike Extremely to Like Extremely.
The products will range from 8 mg FTC tar to 20 mg FTC tar in 3 mg steps. All will be nonmenthol.
The panelists will be chosen from the POL National Roster. Both sexes and a wide variety of ages will be used, with over-sampling of younger smokers whose preference criteria may not yet be well established. We do not have data on the number of years panelists have been smoking, so we will ask that question on the ballots, and then make analyses by age, number of years smoking, as well as delivery range of current own product. Myron Johnston is cross tabulating the POL panel now to get us up-to-date information on the number of panelists in different age and sex categories in the available subject population. (Nonfiltered menthol smokers will be excluded.)
Test is tentatively scheduled for late October to early November.

Project Title: *Smoking and Risk-taking in a Simulated Driving Task*
Written by: T.R. Schori
The data acquisition phase is complete. We have started to analyze the data.

Project Title: *The Betta Study*
Written by: T.R. Schori
Having gotten our first group of fish, we are preparing to determine nicotine dosage effects. Subsequently, we plan to test 30 Bettas at each of 3 nicotine levels (the lowest being 0 nicotine). We will make observations of exploratory activity and hooding behavior (aggressive behavior) on each Betta at each dosage on several occasions.

Project Title: *Miscellaneous*
Written by: T.R. Schori
Menthol Cigarette Preferences of Blacks: cigarettes are in storage awaiting the availability of the RP Black menthol panel. Low Delivery Cigarettes: Another Look at the Influence of Delivery Information on Subjective Evaluations: cigarettes are ready and should go out shortly to a National POL panel. There are two conditions in this study. In the first panelists will make blind ratings of a Marlboro control and a 9 mg tar cigarette while in the second condition the cigarettes will be identified as to their tar and nicotine deliveries.

PHILIP MORRIS RESEARCH CENTER—BEHAVIORAL RESEARCH ANNUAL REPORT APPROVED BY W.L. DUNN & DISTRIBUTED TO H. WAKEHAM ET AL.—JULY 18, 1975

We have arranged the 1600 activities for this report into the three status sections: Completed, In Progress and Planned.
Under each status section the individual studies are grouped under the three objectives of the Behavioral Research Laboratory: I. To learn more about why people smoke. II. To learn more about how people smoke. III. To further identify what people want to smoke.

COMPLETED STUDIES

I. The effect of smoking on risk-taking in a simulated driving task (Jones and Schori)

Smokers are reported to have more traffic accidents than nonsmokers. There are several possible explanations. First, the studies that have been conducted have made no attempt to control certain important extraneous variables. For meaningful comparisons of smokers and nonsmokers, it is essential that quantity and quality of driving exposure be considered. The higher alcohol consumption of smokers is another example of an uncontrolled variable that could influence accident data. Second, it could be that smoking adversely affects driving performance. The results of studies in this area are not conclusive. Furthermore, it is not known whether inferior motor performance significantly increases accident rates. Our interest has been in a third possibility: That smokers are more willing to take risks than nonsmokers, resulting in higher accident rates among smokers. Therefore, an investigation was conducted to determine experimentally whether smoking condition (smoking, smoking-deprivation and nonsmoking) affects an individual's degree of willingness to take risks. The task used was designed to simulate an actual car passing situation, varied as to the degree of risk involved in making the pass.
The subject was seated in front of a panel on which lights represented the movement of cars in the inner and outer lanes of a race track. The subject's task was to pass the car ahead of his car (lead car) without crashing into an approaching car. It was emphasized to the subject that in order to do well on the task it was necessary to take risks. The necessity of risk-taking was increased by the random increases in the speed of the approaching car. A performance contingent monetary bonus was used to motivate the subject to perform well on the task.
There were 15 college students subject in each of the three smoking conditions. Smokers were randomly assigned to either the smoker or smoker-deprived condition. Performance data were collected on the following dependent variables: response latency, number of pass attempts, number of backout attempts, number of successful passes, number of crashes, and amount of good time (the amount of time not immediately behind the lead vehicle or in a crash condition).
The performance data were analyzed by means of a two-way multivariate analysis of variance in which both Smoking Condition and Trials were treated as independent variables. We analyzed for treatment effects in terms of all dependent variables simultaneously while taking into consideration their interrelationships.
Significant differences were detected as a function of trials. The nature of the trials effect was such that it can be concluded that the accuracy with which subjects evaluated potential risk improved with practice, a finding which may have practical implications for driver training programs. However, no differences were detected as a function of smoking condition or the smoking condition trials interaction. Thus, it can be concluded that in this simulated car passing task nonsmokers, smokers-deprived, and smokers did not differ in their willingness to take risks.

I. Delayed audio feedback (Ryan and Lieser)

In the last annual report we commented briefly on a then recent study not yet completely analyzed. It had been undertaken to see whether cigarette smoking, which should have stimulating and frustration reducing characteristics, would improve vocal performance under conditions of delayed audiofeedback.
In delayed audio feedback subjects speak or read aloud into a microphone connected to a special tape recorder. The subject's voice is relayed to his earphones either as he speaks (immediate feedback) or a fraction of a second after he has spoken (delayed feedback). Most people are unaware of the fact that our speech behavior depends in part on hearing what we are saying as we say it. Even fraction of a second delays can therefore cause stammering, speech blockage, slurred words, slower speech, louder speech, etc.
The speech problems cause speakers to become more tense, and the extra tension seems to make the problem even worse.
We reasoned that smoking cigarettes might reduce tension and speed up behavior, so that after a smoke speakers would read faster and make fewer errors under delayed feedback than they made before smoking.
We found that as expected:
(1) smoking increased post-cigarette speech rate (by about 8%) under both feedback conditions; and (2) smoking decreased the total number of speech errors under the delayed feedback condition, but (3) the magnitude of the effect was not great because (4) our headphone speaker volume was not loud enough.
Because this is an easy experiment to conduct, we will replicate it piecemeal in the future (at higher output volumes) using as subjects college students who have come to the laboratory to participate in other projects and have either finished earlier than expected or have been excused from participation because of apparatus failures.

II. Smoking behavior following deprivation (Ryan and Lieser)

This study was conducted to answer two question: What effect does short-term smoke

deprivation have on number of cigarettes subsequently consumed? and What effect does short-term smoke deprivation have on subsequent puffing behavior?

By ''short-term deprivation'' we mean being in a No Smoking condition for two hours when smoking would otherwise be an appropriate act. Thus we are indirectly testing the effects of various state laws, local ordinances, and business establishment decisions which forbid smoking in various places: buses, stores, theatres, waiting rooms, schools, etc.

Our subjects were 20 college students who visited the Research Center on two separate days during each of which they spent 4 hours taking multiple-choice tests, memorizing facts, free associating to nonsense words, filling out personality tests, and (less frequently) talking with the experimenter about miscellaneous topical matters during a 15-minute break period which split the 4-hour session into two 2-hour parts. The situation was therefore like that of study and testing periods, although it required more concentrated work than most students normally perform.

A dozen other students were tested in portions of this study, either in a pilot work or during the project itself, but were excluded from the results here presented either because we suspected they were not smokers or at best very light smokers, or because we made slight changes in procedure. All these omitted subjects followed the same general smoking patters reported here.

On one of the days the students were allowed to smoke as often and as much as they wished (ad lib) from a free supply of their own brand of cigarettes placed prominently on the table before them.

On the other day they were forbidden to smoke during the first 2 hours (deprivation) and then allowed to smoke ad lib during the next 2 hours. Prior to the beginning of each 4-hour period, they smoked one of their own brand cigarettes through a PM Human Smoking Recorder system. The computer output describing these two smokings was used to calculate the 2-day average puff volume on nonlighting puffs for each smoker. No other cigarettes were monitored by recorder, but number of cigarettes smoked, interval between cigarettes, number of puffs, taken, and interval between puffs were noted by observer(s) in an adjoining room watching the subject via closed circuit TV. From the nominal nicotine delivery of a 35 cc puff on each brand listed in CI reports, given the size of an average puff from the recorder output, and having counted the number of puffs taken during the session, we were able to approximate nicotine intake during the sessions.

This also assumes that puffs outside the recorder are like recorded puffs, and that deprivation does not affect puff volume. We can't do anything about the first assumption, but in a prior study in which effects of one hour of deprivation on a subsequent single cigarette was evaluated, we saw no volume change after deprivation although there was an effect on number of puffs and interpuff interval which explains the choice of variable in the present work.

Twelve of the students were males, eight were families, and half of each gender group smoked menthol.

The results are summarized in Tables 1, 2 and 3 and in Figs. 1 and 2.

TABLE 1—EFFECTS OF DEPRIVATION ON NUMBER OF CIGARETTES SMOKED, NUMBER OF PUFFS TAKEN, AND ESTIMATED NICOTINE INTAKE (ALL SMOKERS)

	Number of cigarettes	Total No. of puffs	Estimated group nicotine intake (mg)
First 2 hours ad lib	79	621	79.73
Second 2 hours ad lib	74	608	78.74
2 hours post deprivation	95	832	106.50

TABLE 2—EFFECTS OF DEPRIVATION ON SUBGROUPS: MENTHOL VERSUS NONMENTHOL; MALES VERSUS FEMALES

	Number of cigarettes		Total No. of puffs		Estimated group nicotine intake (mg)	
	Menthol	Non-menthol	Menthol	Non-menthol	Menthol	Non-menthol
First 2 hours ad lib	43	36	340	281	43.75	35.98
Second 2 hours ad lib	39	35	323	285	42.43	36.31
2 hours post deprivation	47	48	415	417	54.10	52.40
	12 Males	8 Females	12 Males	8 Females	12 Males	8 Females
First 2 hours ad lib	45	34	321	300	42.09	37.64
Second 2 hours ad lib	44	30	341	267	45.13	33.61
2 hours post deprivation	56	39	459	373	59.68	46.82

TABLE 3—CONSUMPTION POST–DEPRIVATION AS A PERCENT OF SECOND TWO HOURS AD LIB AND OF TOTAL 4-HOUR AD LIB DATA; WITH SECOND TWO HOURS AD LIB COMPARED WITH FIRST TWO HOURS AD LIB TO SHOW THE CONTRAST

[In percent]

		Number of cigarettes	Total number of puffs	Estimated group nicotine intake (mg)
Post deprivation vs. second two hours ad lib	All Smokers	128	137	135
	Menthol	121	128	127
	Non-menthol	137	146	144
	Males	127	135	132
	Females	130	140	139
Post deprivation vs. all four hours ad lib	All Smokers	62	68	67
	Menthol	57	64	63
	Non-menthol	58	74	73
	Males	63	70	68
	Females	61	66	66
Second two hours ad lib vs. first two hours ad lib	All Smokers	94	98	99
	Menthol	91	95	97
	Non-menthol	97	101	101
	Males	98	106	197
	Females	88	89	89

Tables 1 and 2 show that behavior and nicotine intake were strikingly similar during each of the two sessions of the ad lib smoking day. This similarity is stressed further at the bottom of Table 3, which shows the second two hours' behavior as a percentage of the first. We shall consider these two periods as essentially equal in their effect. However, because the design suggests that the post-deprivation period should be compared to a comparable period of free smoking, we concentrate our attention on the difference between the post-deprivation measures and those of the second two hours of the ad lib smoking day.

The data in the tables show that number of cigarettes consumed increased 28% from 74 to 95, that number of puffs taken increased 37% from 608 to 832, and that total estimated nicotine intake increased 35% from 78.74 to 106.50 mg after the deprivation period.

The effect of No Smoking situations of 2-hour durations is to increase subsequent consumption by anywhere from 28% to 37% depending on the measure taken.

On the other hand, in only a two-hour period smokers do not make up the entire smoke deficit created by a No Smoking situation. Comparing their consumption during the combined deprivation-smoking period of one day with their normal 4-hour smoking behavior, (see second block of entries in Table 3) they only take about ⅔ the puffs and ⅗ of the cigarettes they would normally have taken.

TABLE 4.—MEAN NUMBER OF PUFFS FOR 9 ''LIGHT'' SMOKERS (1 PACK OR LESS) AND ''HEAVY'' SMOKERS

[Over one pack a day]

	Light	Heavy
First 2 hours ad lib	22.7	37.9
Second 2 hours ad lib	21.6	37.6
Post Deprivation	36.1	46.1
Increase Post Deprivation in percent	67	23

The effects of the deprivation were not the same on all smokers. They were proportionally much stronger on the light smokers than on the heavy smokers. That is because the heavier smokers spent so much time smoking that they could not increase their consumption as much as the light smokers could. There are several ways to classify the smokers of this study as ''light'' or ''heavy''; they all show the same type of effect. In Table 4 we show the number of puffs taken by light and heavy smokers classified by their answers to the question ''How many cigarettes do you smoke each day?'' On the consent form which all subjects filled out. Those nine who smoked a pack or less increased the number of puffs they took by 67% following deprivation, while for the eight who report smoking more than a pack a day the increase was only 23%.

A second-and perhaps more objective—way to classify the subjects is by the number of cigarettes they smoked during the first two hours of the ad lib day. Breaking these into three groups, who smoked less than four, four, or more than four cigarettes during the first two hours we make the interesting observation that after deprivation the light smokers smoked as moderate smokers normally do and the moderate smokers smoked as heavy smokers normally do (Table 5).

To overgeneralize from small samples is always dangerous, but it is tempting to suggest that establishing a No Smoking situation-with the well-intentioned (?) goal of cutting back smoke consumption makes people heavier smokers than they would otherwise be. (It must be understood, however, that there is a net reduction, and that the data for the increase are based on only two hours of observation. This is not a slogan that can be used without reservation.)

TABLE 5.—MEAN NUMBER OF PUFFS FOR LIGHT, MODERATE, AND HEAVY SMOKERS CLASSIFIED BY NUMBER OF CIGARETTES SMOKED DURING FIRST TWO HOURS OF AD LIB DAY

	Mean number of puffs/smoker		Percent of increase
	Second two hours	Post-deprivation	
8 Light (less than 4 cigts.)	20.6	33.9	65
7 Moderate (4 cigts.)	33.7	44.3	31
5 Heavy (more than 4 cigts.)	41.4	50.2	21

Will the increased smoking rate following deprivation be continued beyond the two-hour period? This is an important question, and it is impossible to answer based on the data obtained. However, we have some clues which are suggestive.

Plotting the cumulative total smoke volume (in ccs) across the four-hour ad lib period we see that intake accumulates in a near linear fashion across time, an observation we have already made in a different form by noting that first and second two-hour behavior was almost identical. Similarly we see a near linear accumulation of smoke volume during the two-hour deprivation period. The slope of the post-deprivation line is steeper than that of the control day

* * *

Assuming the linearity to continue, then we can project both lines to an intersection point which represents equal volumes accumulated under the two condition. For the present data this intersection occurs about 7½ hours after our observations stopped, implying that it will take a smoker 9½ hours to make up the intake he loses because of two hours of deprivation. It therefore seems unlikely that a group of smokers would be able to make up their deficit during a day, and would undoubtedly not be able to make up deficits which occurred late in the afternoon or early evening.

Personality Differences.—Examining the personality scores of our subjects we note that those who are high in anxiety tend to take more puffs than those who are low in anxiety. The correlation between the two variables is +.58. Given the obvious relation between puffs and nicotine delivery, it is not surprising that anxiety was also positively related to nicotine intake: r=+.56. Both these correlations are significant at the .05 level.

III A Comparative Evaluation of Three Methods For Field Testing Cigarettes—Accession Number 75–105 (Dunn and Martin)

Recently the New Cigarette Products Division demonstrated that they could provide any tar delivery and RTD combination within the 12 mg to 20 mg tar delivery range and 4″ to 6″ RTD range, and do so with good approximation to target specifications. This achievement made possible a critical comparative study of several alternative field test methods. Using high and low tar delivery levels, and high and low RTD levels, we tested the four combinations (High-High, Low-Low, Low-High and High-Low) against a control, middle-of-the-array, Marlboro-like cigarette, using three field testing methods.

The design of the study permitted a comparative assessment of the three methods and gave information about the influence of tar delivery and RTD changes on subjective response to cigarettes.

The most significant finding was that a method which permitted the testing of as many as four experimental cigarettes on a single mailout, with judgment based upon a 2-pack sample, was as sensitive and as potentially useful in cigarette testing as the standard field testing procedure. Recommendations for further investigation of the technique are made in this report, with proposals for data treatment that promise to yield additional useful information from field tests.

We also concluded that a 5 mg reduction from the 17 mg tar delivery norm is clearly detectable to the average regular filter smoker, but he is tolerant of this reduction. He is not so tolerant of tar delivery increases.

RTD changes of ±1″ from the 5″ norm appear to have little influence upon overall acceptability. The 1″ increase is clearly detectable; that 1″ decrease did not appear to be so.

III. Further evaluation of delivery information influence on subjective acceptability of a low delivery cigarette (Martin and Schori)

Cigarettes at two delivery levels (15 mg and 8 mg) were rated on acceptability and strength by National POL nonmenthol smokers. One panel of 500 rated the cigarettes with no delivery informatioon supplied. A second panel of 500 rated the cigarettes with tar and nicotine delivery levels clearly marked on the packs and on the ballots. The purpose of the test was to determine the effect of delivery information upon the subjective ratings of cigarettes at two distinctively different delivery levels.

With no information provided, the strength difference was clearly detected and the higher delivery cigarette was rated more acceptable.

The judgment of those panelists who were given delivery information contrasted sharply with the judgments of the no-information group. The low delivery cigarette was rated the more acceptable. The difference between the strength ratings of the two cigarettes, so evident under the no-information condition, was wiped out under the information condition, such that the two cigarettes were rated as being of equal strength, despite the fact that the panelists were told that the higher delivery cigarette delivered 80% more tar and nicotine.

We see two phenomena at work in these results:

(1) Given a cigarette ''blind,'' a smoker will judge it largely on its own merits—given vital information along with the cigarette, the smoker's hedonic judgment of the cigarette will be confounded by socially learned value judgments, e.g. ''low delivery is healthy and good.''

(2) The smoker will move his rating on a physical attribute scale toward that end of the scale that corroborates his hedonic judgment, e.g., the cigarette rated more acceptable will be rated toward the ''strong'' rather than the ''weak'' end of the strength scale. This is the halo effect, a force we believe to be so pervasive in product testing that the validity of any judgment of the physical attributes of a product rendered in company with a preference or acceptability judgment of that product must be held suspect.

The practical implication of these findings is that a real marketing advantage is gained by calling attention to the delivery values of low delivery values of low delivery cigarettes, the effect being greatest among those smokers most likely to buy the low delivery cigarette anyway.

III. Menthol cigarette characteristics as perceived by blacks and whites (Martin, Jones and Schori)

The black menthol smoker is an important segment of the menthol market, yet all of the PM national field tests of menthol cigarettes have been conducted with virtually all white panels. What with some 500 black menthol smokers having become available with the advent of the RP[3] panel, the opportunity was afforded to study the black response to menthol cigarettes. We were interested in determining whether the two loosely defined ethnic groups differed in their assessments of variations in two important parameters of menthol cigarettes.

The study consisted of two runs, the second intended to be a partial replication. Because of unintended significant differences in the menthol levels of the two sets of cigarettes, the results of the two runs cannot be pooled but must be treated separately. Table 6 contains the critical values for the cigarettes.

TABLE 6.—THE CIGARETTE SPECIFICATIONS IN THE TWO BLACK MENTHOL RUNS

	Nicotine/Menthol	
	First Run	Second Run
Low Nicotine Low Menthol	.84/.48	.85/.48
Low Nicotine High Menthol	.82/.62	.71/.62
High Nicotine Low Menthol	1.08/.48	1.17/.36
High Nicotine High Menthol	1.12/.76	1.12/.80
Control	.92/.46	.70/.36

Table 7 gives the essential information about the panelists. Note that in the second run only black respondents were used.

TABLE 7.—THE PANELISTS USED IN THE TWO BLACK MENTHOL RUNS

[The parenthesized value is the percent useable return]

	First Run		Second Run	
	Black	White	Black	White
Number	250 (36)	350 (50)	405 (54)	0
Source	RP[3] Menthol	Nat. POL Menthol	RP[3] Menthol	.....

Two packs of each of the five cigarettes were provided in a carton mailout in both runs.

The ballots were identical in both runs, with ratings obtained for each cigarette on Acceptability, Strength and Menthol Level.

In the first run, where both white and black smokers were responding, the two groups were apparently detecting the menthol level differences among the cigarettes. It is to be noted, however, that black males and black Kool smokers were apparently not detecting these differences.

In the second run, with slightly larger differences in the menthol levels, all of the black subgroups were differentiating in terms of menthol levels.

There is some evidence that the blacks were less sensitive to ''strength'' differences than the whites. But the strength rating is of itself interesting in that panelists were reacting to menthol level as well as tar level when recording their strength ratings, i.e. menthol level ratings and strength ratings are probably not meaningfully distinguishable as discrete subjective variables in menthol cigarette tests. Also of interest is the observation that the variation in nicotine delivery level had no influence upon strength ratings.

Both groups of panelists in the first run were responding more favorably (higher acceptability ratings) to the lower level of menthol. These findings were not supported, however, in the second run, for here we find the black smokers were finding all of the cigarettes equally acceptable, despite the fact that the menthol differences among the cigarettes were greater than in the first run.

Thus the first run finding that a lower menthol delivery is more acceptable among menthol smokers is made equivocal, especially for the black smoker.

What with the observation that the response of blacks may be less differentiating than whites and what with the questionable representativeness of a Virginia sample for the national market, it would seem feasible to establish a larger, national roster of black smokers especially for the evaluation of menthol candidates:

III. Mixed pack study (Ryan)

As deliveries drop we reasoned that eventually they could reach a point where all the cigarettes in a pack would be unsatisfying. The inclusion of some high delivery cigarettes in a pack would therefore give the smokers at least occasional feelings of satisfaction and should lead to a preference for a mixed pack over a homogeneous pack with the same tar and nicotine delivery per pack. Pilot testing with RP[3] subjects twice indicated slight preferences for a mixture. Therefore a POL national field test of two different packs of 11 mg tar cigarettes was conducted in which one pack consisted of 20 cigarettes each delivering about 11 mg and the other pack was half made up of 8 mg and half of 14 mg cigarettes.

A total of 309 respondents (most of whom were low delivery smokers) answered the usual ballot questions giving a 9-point rating of each pack type, a preference, and so on. Observed rating and preference differences favoring the homogeneous pack did not reach statistical significance; but since we began the study hoping to show that the mixed pack would be preferred and get higher ratings, we have concluded that this idea should be rejected. this may, of course, be because the smokers found either the 14 or 8 mg model in the mixed pack unacceptable in flavor after taste, or in some other characteristic such as satisfaction.

There were a few interesting inversions in the ratings by 242 HiFi and 67 other than HiFi smokers: For example, the HiFi smokers thought the mixed pack stronger than the homogeneous (responding to the 14 mg?) and the non-HiFi smokers thought the homogeneous stronger than the mix (responding to the 8 mg?).

No one commented on the fact that the mixed pack consisted of different cigarettes.

In general the panelists rated all the cigarettes rather high—5.3 for the mix and 5.6 for the homogeneous pack—but many complained about them all burning too rapidly, being dry, and having a long filter. Several noted that the two-part paper filter broke or came apart.

The idea may still be feasible, but not with the cigarettes we used at the levels we tested.

STUDIES IN PROGRESS

I. Nicotine as a modulator of CNS arousal (Dunn, Martin and Jones)

Several investigators participating in the 1973 St. Martin Conference on ''Motivation in Smoking'' reported data suggesting that smoking in humans or nicotine injection in animals may have the effects of reducing aggressivity in overt behavior. Schachter also reported at that conference a greater tolerance for pain among smokers when allowed to smoke. There is also the readily observable, commonly acknowledged fact that smokers at a greater rate when under stress. These and other observations imply the influence of nicotine upon some control mechanism governing affective responsivity, the net effect upon overt behavior being to reduce the intensity of the emotionally-toned response, or raise the threshold for the elicitation of that response.

We have singled out aggressive behavior for study quite frankly because of the practical significance of the suspected effect of nicotine. If indeed, nicotine lowers the intensity or raises the threshold for a form of socially unsanctioned behavior, such as aggression, to demonstrate that effect could be of considerable consequence to the smoker and his protagonists.

We have a trio of studies in progress, all aimed at observing the effect of nicotine upon aggressive behavior in subhuman species. The species, or the individual animals, have been selected for their innate aggressivity in a form readily elicitable and readily quantifiable. The aggressive pattern is observed in the normal state of the animal and following the administration of nicotine. With proper controls, and with no change in baseline behaviors, (i.e. frequently recurring behaviors other than aggressive), any reduction in the aggressive responses can be attributed to the nicotinic effect specific to the aggressivity.

This rationale is common to all three of the studies. At the Laboratory of Comparative and Physiological Psychology at Ohio State University we have had a guiding hand in designing studies of the influence of injected nicotine upon the predatory attack of cats upon mice. At the Psychology Department of Rockefeller University, the influence of injected nicotine upon the predatory attack of rats upon mice is being investigated at our request. And at R&D we are observing for the influence of low concentrations of nicotine in the ambient water of male *Betta* fish upon their mirror display behavior.

Only preliminary observations are available, but in the two extra-R&D studies these are encouraging. The cats and rats are ceasing their attacks. Whether the base-line behaviors are remaining unchanged is now the subject of greatest interest as the data is being gathered.

In house, the toxicity phase of the *Betta* testing has been completed. We established that the LC_{50} was greater than 10 ppm and less than 100 ppm v/v, using distilled nicotine base. The S in the 10 ppm solution was almost completely inactive, but would respond to prodding. The S in the 100 ppm solution was dead within 2 minutes. A possible avoidance pattern to the stimulus was noticed at 1 ppm. This will be the solution used as the higher concentration in the effects study. The lower concentration will be 0.1 ppm. These preliminary observations have indicated a possible differential effect of nicotine, whereby aggressive display is decreased and other base-line behaviors (e.g. air gulping) remain the same.

Thirty male *Bettas* of approximately the same age are being established in a housing tank for approximately one month. The fish will be calibrated (base line air gulping and display activity) before the effects study starts. Each fish will be in each of the three solutions for three test periods. Test days and solutions will be randomized. Measurements to be made will be number of times gill erection occurs, duration of gill erection and number of air gulps.

I. Personality, smoking, and stimulus deprivation (Ryan and Lieser)

We are interested in the problem of why some people smoke and others do not. The personality research of Hans Eysenck offers one clue. Eysenck points out that the level of activity in our central nervous system affects our performance efficiency. If it is too low or too high we perform inefficiently. Somewhere in between high and low there is an optimal point at which our bodies work at their best. This optimal point is markedly higher for some people than for the average man, while for still other people it is much lower than it is for the average. He hypothesized that in order to maintain optimal efficiency a person who is chronically below optimum level will seek to increase his CNS activity level. One way to do this is by seeking out stimulating situations—such as parties, music, sporting events, etc. which increase the amount of social and environmental stimulation to which he is exposed. These probably increase the amount of adrenalin in the system, which increases the CNS activity. Another way to increase CNS activity would be to consume socially approved chemicals which would have a similar effect on the body—such as the stimulant drugs caffeine and nicotine.

In fact it has been reported that people who (theoretically) seek out such stimulation, called extraverts because they are outward directed, are also more apt to be smokers than are those who avoid such stimulation, called introverts because they are inner directed.

In our next project we are testing this hypothesis by placing extraverts in a stimulus deficient environment (a dark, very quiet room) and watching to see whether they will seek stimulation (by working to turn on flashing lights and sounds) than will a group of introverts. Extraverted smokers who are smoke-deprived (or nicotine deprived) should be more in need of stimulation than those who have just finished smoking several cigarettes.

Similarly the hypothesis that introverted smokers will be *less* likely to work for stimulation after smoking cigarettes than when smoke deprived, for the extra input from smoke will tend to bring them close to the point where any extra environmental stimulation would make them feel uncomfortable. Hence they would be content with the status quo.

Thus an extension of the existing hypothesis predicts one type of difference in behavior for one group of people and the opposite type of behavior for another group—which always makes a nice study. (Actually we're

not as convinced of the effect on the introverts as the foregoing suggests. They may respond similarly whether smoking or not, depending on how content they are with the quiet dark situation.)

I. Hyperkinetic child as a prospective smoker (Ryan)

We hypothesize that the characteristics of smokers and hyperkinetic children so closely resemble each other that in the past hyperkinetics were almost sure to become smokers. Thus we could account for some of the differences between smokers and nonsmokers by the disproportionate representation of this special subgroup in the adult smoking population compared to the adult nonsmoking population.

We have undertaken a long term prospective study to identify the hyperkinetic and borderline hyperkinetic youngsters in the Chesterfield County school system, and to see whether they become smokers. All the children in one grade level were tested last year but the school system did not continue their testing this year to include extra grades. This was due to the reorganization of the system by a new superintendent with its concomitant personnel and morale problems and readjustment of priorities. Because school systems *must* (under Virginia law) identify all problem children of all types, we expect to greatly expand the data base next year.

We did manage to check the reliability of last year's pupil ratings by having new teachers rerate a previously rated subsample. The correlation was satisfactorily high (+.86), suggesting that teachers agree on what constitutes problem behavior as defined by the questionnaire used.

I. Smoking and aggression (Jones)

The simulated driving test used in the risk-taking study has been modified so that college student subjects will receive inaccurate feedback regarding their performance on the task. It is expected that a student who is being paid for successful passing will respond aggressively if his successful passes are incorrectly recorded as crashes.

There will be 30 subjects tested in each of the three smoking conditions (nonsmoker, smoker-deprived, and smoker). Both groups of smokers will be instructed not to smoke at all the day they are to report to the laboratory. They will be told that urine samples will be taken to verify their abstinence. All subjects will be in the laboratory for at least an hour before the actual testing session begins, during which time they will fill out information forms, take a personality test and complete a Nowlis Mood Scale. Those in the smoker group will be permitted to smoke ad lib during this period and will be required to smoke one cigarette before each trial of the driving task. Smokers-deprived, however, will not be permitted to smoke until the entire experiment has been completed.

All subjects will have a 10-minute practice session before beginning two 20-minute trials. The first trial will be with accurate feedback so that baseline measurements may be obtained before inaccurate feedback is introduced. The smoker-deprived group will be given a third trial with inaccurate feedback. The group will be divided, with half of the subjects remaining deprived and the other half being permitted to smoke. All subjects will be given a Nowlis Mood Scale after each trial.

Subjects will be observed through a one-way mirror, verbal behavior will be coded, and the force with which they push the response buttons will be recorded as a measure of aggressive behavior. College student pilot subjects will be brought in so that observational techniques can be perfected.

III. Lowe delivery cigarettes and increased nicotine/tar ratios, a replication (Jones and Martin)

This test is a replication of a study (74–088) in which a 10.7 mg tar cigarette with a .12 nicotine/tar (N/T) ratio was found to be comparable to a Marlboro control in both subjective acceptability and strength. The three experimental cigarettes deliver approximately 10 mg tar with N/T ratios of .07, .10 and .13.

These cigarettes and a Marlboro control have been sent out to 300 RP[3] smokers and returns are beginning to arrive. Panelists were asked to smoke the four cigarettes in any order they wish and to rate each cigarette on a acceptability scale and a strength scale before beginning to smoke the next cigarette code. In the event that the panelists smoke the cigarettes in the order suggested by the rating scales, all possible presentations of the rating scales for the four cigarettes will have been used an equal number of times.

III. A low delivery cigarette with impact and flavor (Jones and Martin)

This is the first study in the 5–6 mg tar delivery program being carried out in collaboration with Paul Gauvin, Barbro Goodman, and Willie Houck. The purpose is to evaluate the relative influences of blend (Standard Marlboro blend vs 50% burley blend), burley spray (100% vs. 50%), and filter system (cellulose acetate filter vs. paper/cellulose acetate filter) on smoke impact and acceptability of cigarettes in the 5 to 6 mg tar range.

Panelists will be asked to smoke the eight experimental cigarettes and a Marlboro control in any order they wish and to rate each coded cigarette on an impact scale and an acceptability scale before beginning to smoke another cigarette code. The cigarettes have been released and should go out shortly to 400 RP[3] smokers.

PLANNED STUDIES

I. Conference on the regulatory influence of nicotine on human behavior (Dunn)

An international conference on the regulatory influence of nicotine upon behavior has been proposed to the cigarette industry. We would hope that these studies on aggression could be reported at that conference, as well as studies of the influence of smoking upon other emotionally toned response patterns. The interest of prospective sponsors has yet to become great enough to provide the impetus for approval and support.

I. Is learning affected by nicotine? (Ryan and Lieser)

Some reports in the animal literature suggest that nicotine facilitates at least some aspects of the learning process. Recently Andersson and Post have reported that nicotine interferes with human learning in at least one task situation—the learning of a long list of nonsense syllables. We are unhappy with this report and unconvinced by its evidence, which appears to have some internal inconsistencies (e.g. a first nicotine cigarette *slows* learning, a second speeds it up); as well as some flaws in design (e.g. the control nicotine free cigarette used was Bravo—we prefer denicotinized tobacco); the ''smokers'' were *very* low intake people whom we would not classify as regular smokers (we prefer heavier smokers); both cigarettes smoked were the same type (we would have included switch groups); the list of syllables was very difficult (we would prefer a difficult and an easy list); only a few smokers were used; total smoke intake was unmeasured, etc. We're repeating the study (In part because we have student subjects already on hand in the lab who are participating in the Personality, Smoking and Stimulus deprivation study) essentially as run together with some of the corrections suggested above. We feel a responsibility to see that the published report is corrected if it is in fact wrong. The smoking studies in psychology journals contain too much unchallenged and unreplicated junk which has passed editorial review because the findings conform to editorial biases against tobacco. Sooner or later the accumulation of this unchallenged sloppy work will be used against us. We aren't interested in picking fights, but . . . .

II. Inhalation patterns (Dunn and Levy)

Following our preliminary run reported at the November Project Review, we decided to continue this work. In the preliminary runs we measured gas volume drawn in through the nose upon smoke inhalation, as well as that drawn in through the mouth. We did not measure puff volume, nor retention time, two measures that we now view as essential. We have also come to believe that the smoking of our subjects must be monitored over a period of many hours rather than during the smoking of a single cigarette. These two decisions force the experimentation into a new realm of complexity in terms of instrumentation and logistics. We have installed an observation room that permits complete control of sensory input. We plan to have our subjects remain in this room for four to eight-hour periods, measuring all parameters of smoking behavior throughout the period while varying factors suspected to be determinative of dosage. Some preliminary work on the additional instrumentation has been accomplished, but full scale resumption of the work has been delayed until the arrival in September of the new member of our staff, a physiological psychologist.

Our objective in this part of our program is to demonstrate the degree to which the smoker's absorption of smoke components is a function of his smoking behavior as opposed to his absorption being a function of what is made available to him in the cigarette smoke.

III. Annual cigarette monitoring (Ryan)

Cigarettes with tar and nicotine deliveries only a few years ago though much too low for public acceptance are now selling in the billions. Is the public's taste actually changing, so that even lower delivery cigarettes may soon become acceptable?

We lack data on the relative acceptability of cigarettes of different delivery evaluated by the same smokers. No broad studies of this type have ever been conducted here. To fill the data gap we have had Marlboro rods attached to five different filter systems to produce 85 mm nonmenthol cigarettes with nominal deliveries of 20, 17, 14, 11, and 8 mg tar, which we will ask a National POL panel to evaluate annually. The filter systems, whose characteristics were chosen by W. Houck and W. Claflin, represent the draw and other characteristics of typical cigarettes now marketed at these delivery levels.

The actual deliveries are: 19.6, 17.6, 14.3, 10.5, and 7.9 mg tar; 1.22, 1.10, 0.93, 0.74, and 0.59 mg nicotine per cigarette, respectively.

Smokers will be asked only to rate the acceptability (on a labeled scale from 1–9) of the five products in a blind test, basing their evaluation on two packs of each type sent them as a carton mailout. A variety of possible outcomes can be foreseen. In any given year different acceptabilities are expected for the five cigarettes, with the most acceptable being the one which most resembles and the lowest being the one which least resembles the smoker's own brand—if the smoker bases the acceptability of the unbranded models on cues based on their resemblance to his own brand. To the extent that he has some other criterion, then the evaluations

will differ from this model. For example, if he likes taste but has chosen to smoke a low taste cigarette for obscure reasons (e.g. health? advertising campaigns? imitating his friends?) then he should give higher acceptability ratings to the high delivery models than to the low delivery models, no matter what his own brand is. The reader can speculate for himself on how other possible demographic or smoking history variables might be expected to affect the acceptability ratings.

To be sure that a wide variety of demographic characteristics are present we will poll a large sample from the POL National panel, oversampling young subgroups to insure reasonable returns.

Although basic information of interest can be gathered from the returns of any given year, our principal interest will be in the acceptability change from year to year.

III. Low delivery cigarettes and RTD (Jones)

A study is being planned in collaboration with some people in Development in which the question of the influence of RTD level upon acceptability and strength ratings of low delivery cigarettes will be further explored. Based upon the recommendations given in a previous report (75–105), the multiple monadic testing procedure will be used. After cigarette models are designed and cigarettes made, they will be sent out to a large panel of National POL smokers.

III. Perceived attributes of cigarettes, a replication (Jones)

Two studies have been conducted concerning smoker perceptions of regular filter (72–088) and menthol (73–027) cigarettes. It seems that with the recent interest in longer (120 mm) cigarettes, smokers' ideas about cigarettes may have shifted such that they place more emphasis on length than they did previously. In addition to possible changes in what cigarette attributes are considered important, there have been brands introduced since the previous studies were completed (e.g. Marlboro Lights, Winston Lights, Kool Milds) which may have filled what at that time appeared to be gaps in the market (e.g. low in delivery, high in flavor). Therefore, plans are being made to replicate the perceived attributes studies.

Charge Number: 1600
Program Title: Smoker Psychology
Project Leader: W.L. Dunn, Jr.
Period Covered: April 1–30, 1977
Date of Report: May 13, 1977

Project Title: Regulator Identification Project
Written by: C.J. Levy

Twenty-five college student smokers have been smoking high and low delivery cigarettes for two weeks at home. These students are now coming in to our Franklin Street office on four separate occasions to smoke under more controlled conditions.

Project Title: Low Nicotine Cigarettes
Written by: C.J. Levy

Forty-eight R&D smokers compared two types of cigarettes in a booth test. Both cigarettes were made from tobacco which had been treated with steam and ammonia by Fran Utsch's group. The cigarettes (control and experimental) delivered 20.0 mg tar, 0.40 mg nicotine and 19.9 mg tar, 0.87 mg nicotine, respectively. The nicotine delivery of the experimental cigarettes was increased using nicotine citrate. No significant differences were found between the two cigarettes in this test.

Eighteen (out of 23) smokers who previously identified the experimental cigarette as producing more inhalation impact than the control were subsequently asked to smoke the cigarettes on three more occasions. Only three of these smokers consistently identified the experimental cigarette as producing more inhalation impact. Eight identified it twice and seven identified it only once.

We conclude from these tests that there are no dramatic differences between the cigarettes when tested using a paired comparison methods, even through the experimental cigarette delivers twice as much nicotine.

Project Title: Measurement of Smoke Inhalation
Written by: C.J. Levy

(a) We are continuing to collect chest expansion data using a mercury strain gauge. We are currently working out calibration procedures with the assistance of Dr. Farone.

(b) In another approach we have brought in Dr. Eli Fromm of Drexel University as a consultant to advise in the development of a device for unobtrusively monitoring smoke inhalation under normal smoking conditions.

Project Title: Annual Monitoring
Written by: F.J. Ryan

We sent cigarettes to 4,000 panelists. All but 128 were delivered. Ballots have been returned from 2,953 people, a return of 76%. Not all of these will be usable. At least 197 (or 6.7%) have incomplete data or will be voided for various reasons: being smoked through an extra filter, or by a smoker who had a cold, or by a nonsmoker, etc. At least 125 more ballots (or 4.2%) were returned by people who had switched to menthol brands since last being polled.

Ballots are now being coded and a preliminary report should be ready by mid-June.

Project Title: Verbal Learning and Smoking
Written by: F.J. Ryan

Only two more subjects are needed to complete the data gathering phase of this study.

Project Title: Perceived Smoke Strength and Interpuff Interval
Written by: F.J. Ryan

We have screened 25 R&D smokers to find 20 who can detect differences in strength between cigarettes of widely varying delivery. They will be asked to rate the apparent strength of a 9 mg cigarette smoked at long or short interpuff intervals. If short interpuff intervals increase apparent strength, then we may be able to account for the increased puff count sometimes observed on low delivery products.

Project Title: Hyperactivity
Written by: F.J. Ryan

To test our hypothesis that hyperactive children are more likely to become cigarette smokers than nonhyperactives, we have begun pilot research for two prospective studies in collaboration with others interested in hyperactivity. Together with Dr. Ron David, a pediatric neurologist at MCV, we are identifying a group of his patients who are known to have their hyperactive or impulsive behaviors reduced by drugs (e.g. Ritalin) and a group which does not respond to drugs. Together with Dr. Al Finch, research psychologist at the Virginia Treatment Center, and Dr. Howard Garner, VCU, we are identifying a group of patients treated with Ritalin or other stimulants, and a group of controls with nonhyperactive behavior problems. In both cases we will later contact the children to see whether they have become smokers, comparing the incidence of smoking among these groups with the incidence in the nonhyperactive school population.

In return for access to their files we are helping our colleagues find (1) the variables which account for drug-responding and nonresponding (Dr. David) and (2) the effect of miscellaneous treatments on later adjustment to school and society (Drs. Finch and Garner). Neither of these colleagues is being financially supported.

Project Title: Patterned Cigarette Paper
Written by: E.C. Gay

A second consumer evaluation of patterned papers was conducted using eight designs printed in green. A clear winner emerged as top choice of respondents across and within all subgroups. It has a ''light'' overall appearance, with a ''small'' ''plain'' design according to panelists. Additional evaluations are programmed to evaluate still other patterns, with first and second choices from each heat to compete in a final runoff evaluation later.

Charge Number: 1600
Project Title: Smoker Psychology
Period Covered: February 1–28, 1978
Project Leader: W.L. Dunn
Date of Report: March 10, 1978

Project Title: Smoking and Learned Helplessness
Written by: C.J. Levy

We continue to collect data. We are having some difficulty recruiting the male smokers needed to complete the study.

Project Title: Smoking of Low Nicotine-Cigarettes
Written by: C.J. Levy

We have received the analytical data on our experimental cigarette. The nicotine-fortified cigarette delivers 1.34 mg of nicotine, and the low-nicotine cigarette delivers 0.14 mg of nicotine. We are currently recruiting R&D smokers for our study.

Project Title: Smoking Parameters Study
Written by: F.P. Gullotta

A follow-up on the completed heart rate study is being implemented. In addition to heart rate, respiration and puff measures will also be recorded. Data collection will begin in one to two weeks and the study should be completed in five to six weeks.

Project Title: EEG
Written by: F.P. Gullotta

Neither the EEG/Polygraph nor the computer has arrived. The EEG will be shipped from Quincy, MA this week. It is anticipated that the computer will arrive within a month.

A meeting has been arranged with Mr. D. Derr of Coulbourn Instruments to discuss the purchase of auditory and somatosensory evoked potential modules to be used in studies planned for the second half of 1978.

Project Title: Smoking Diary Study
Written by: F.J. Ryan

Butt collection is complete. Although 33 students completed the study, we expect to discard a few because their results appear affected by influenza or chronic unreliability. We have switched full-flavor smokers to low delivery and back, or switched low-delivery smokers to full flavor and back. The data consist of butt counts, butt lengths, nicotine in filler analyses, time of day each cigarette was smoked, and proportion of day spent in various activities.

We are interested in the extent to which smoking behavior changed when cigarette delivery changed. We are seeking (1) to find the extent to which nicotine need governed behavior and (2) to find the extent to which stimulus situations controlled the behavior. Data evaluation will be a lengthy process.

Project Title: Hyperkinetic Children
Written by: F.J. Ryan

Obstacles presented by school systems and physicians concerned with the various ''privacy acts'' passed by state and national legislatures have made it very difficult for us to conduct studies using school and medical records of minors. Therefore we have stopped our activities in this area.

Project Title: Annual Monitoring

Written by: F.J. Ryan

The second ''mailout'' of the annual monitoring cigarettes is now firmly scheduled for the end of March. Ballots are essentially the same as last year. We will contact about 2700 of last year's panelists, plus 1300 supplementary people who smoke full-flavor or low-delivery nonmenthol filter cigarettes. Ballots are to be returned on or before April 21.

Project Title: Exit Brand Cigarettes
Written by: F.J. Ryan

A report has been written outlining the findings of the Exit-Brand Study.

PHILIP MORRIS RESEARCH CENTER—BEHAVIORAL RESEARCH ANNUAL REPORT (PART II) APPROVED BY T.S. OSDENE & DISTRIBUTED TO H. WAKEHAM ET AL.—NOV. 1, 1974

This is the second of a two-part annual report covering the research activities under Charge No. 1600. The first part was prepared by Frank Ryan in August, 1974, and included accomplishments by him. This second part has been prepared by Tom Schori and Bill Dunn and summarizes accomplishments in their respective areas:

OBJECTIVES

Our objectives under 1600 are threefold:

I. To learn more about why people smoke.

II. To learn more about how people smoke.

III. To further identify what people want to smoke.

For each of these objectives we have formulated hypotheses which guide our research effort. For the sake of clarity, the studies being reported on are designated by a three-part prefix. The first symbol is a Roman numeral designating the objective being pursued, the second symbol is a letter of the alphabet identifying the hypothesis being tested and the third symbol is an Arabic number which identifies the study.

Below we set forth in sequence the three objectives and list the working hypotheses under each objective:

I. To learn more about why people smoke.

IA. Cigarette smoke improves efficiency in the performance of complex psychological tasks.

IB. Cigarette smoking attenuates, modulates or otherwise influences emotional arousal such as to be gratifying or rewarding to the smoker, thus reinforcing the smoking act.

II. To learn more about how people smoke.

IIA. Smoking patterns vary as a function of changes in cigarette and the smoke it generates.

IIB. Dose-control continues even after the puff of smoke is drawn into the mouth.

III. To further identify what people want to smoke.

IIIA. There are optimum combinations of critical variables in smoke composition.

IIIB. Deterioration in cigarette acceptability can be minimized when reducing tar deliveries by not reducing or changing other critical properties.

IIIC. More effective ways can be developed for obtaining consumer response to cigarettes.

From this point on we will present the individual studies of 1600, grouping them by progress status in three sections:

1. Completed

2. Data Being Collected

3. Preinvestigative (conceptualization and instrumentation)

The Ryan studies will be cited with page references to his portion of the annual report.

COMPLETED STUDIES SINCE JULY, 1973

IAI—(Dunn and Martin)—THE INFLUENCE OF CIGARETTE SMOKING UPON THE VOLUNTARY CONTROL OF ALPHA TYPE ELECTROENCEPHALOGRAPHIC ACTIVITY (Accession No. 74–075)

Observations suggest that there are links-between brain wave frequencies and psychological levels of alertness. The highly aroused human will display brain activity at the upper end of the 1–30 Hz range. When drowsy or sleeping, the dominant activity will be at the low end of the spectrum. The 1–30 Hz range has been divided somewhat arbitrarily into four bands, each band associated with a reasonably circumscribable psychological state. The beta band, including all signals exceeding 13 Hz, is linked to the state of alert responsiveness to external stimulation. Those ranging from 8 to 4 Hz, the theta waves, correspond to the drowsy, sleepy states of mind. Delta, less than 4 Hz, is seen in deep sleep states. The alpha waves (8–13 Hz) are the most interesting in that these appear to be dominant when the subject is in a relaxed but awake meditative state, not unlike the states thought to characterize the meditating Indian yogi.

Thus, if one seeks to induce the ''alpha state'' in oneself, the effort can be facilitated by the auditory signal linked to a dominant alpha frequency. It is not clear how the gradual increase in control occurs, but it is a matter of observation that the increase does occur and that the feedback signal is facilitative.

In that we here at P.M. R&D are intent upon identifying psychological changes induced by smoke inhalation, it occurred to us that we should determine whether smoking has an influence upon achieving the alpha state. We considered it not unreasonable to anticipate a smoking effect upon rate of learning of the control of alpha activity, or even more likely an effect upon time on target during a fixed period of observation. We did not arrive at this position by way of a conceptual model, at any rate not in any formal, deductive manner. Perhaps at some pre- or sub-conceptual state there is an intuitive belief that we should be paying attention to the more subtle psychological functions having to do with alertness and concentration as possible points at which we may find smoke inhalation having some facilitative effect. In any event we had no preconceptions as to what effect, if any, smoking might have upon the acquisition and maintenance of the alpha-state. Long inured to the elusiveness of smoke inhalation effects upon psychological state or function, we have come to proceed in a pragmatic way by sinking shafts here and there for signs of smoke-induced change. Either facilitory or inhibitory effect would be a welcome clue.

Nineteen R&D smokers, with sensing electrodes and headphones in place, sat in daily 10-minute sessions learning to keep the auditory tone on by maintaining a dominant alpha brain wave pattern. These sessions were continued until on-target time had plateaued. Nine subjects were allowed to smoke freely prior to session, and ten abstained from the preceding evening's bedtime. This was Phase I for which we had the following objectives:

1. To bring all subjects to a plateau level in maintaining the alpha state.

2. To observe for differences in learning rate between those smoking prior to the observation period and those abstaining from smoking.

3. To observe for differences in learning rate between introverts and extroverts.

4. To observe for correlations between certain measures of personality traits and acquisition rate in maintaining a dominant alpha pattern.

Mean time-on-target in the first session was 69%, with a range from 15% to 93%. The high base line of 69% for the first session was a surprise. It was also an unanticipated constraint on the study in that little latitude was left for improvement in performance. Mean time-on-target at plateau was 82%. Introverts performed better than extroverts, both initially and at plateau. We concluded after a thorough analysis that whether or not a smoker smoked immediately preceding observation had no discernible effect upon acquisition rate, not initial, nor final performance levels. Certain personality traits, as measured by the Cattell 16 PF Scales were found to be correlated with performance improvement, but these are of little interest for our purposes here. (See Table 4 of Accession No. 74–075.)

Having plateaued, a subject entered Phase II. Sixteen of the original 19 subjects completed Phase II. All subjects were pooled, each serving as his own control. There was a 5-minute pretreatment, 3-minute treatment and 5-minute post-treatment sequences. The pre- and post-treatment periods were alpha time-on-target periods. The 3-minute treatment period was a cigarette smoking and a dry-puffing period on alternate days. Each subject went through six such days, 3 experimental (smoking) and 3 control (dry-puffing).

Although there was a 2 to 1 tendency for introverts to improve and a 2 to 1 tendency for extroverts to worsen as a result of smoking, our numbers are simply too small and our performance values too variable to allow us to draw any inferences other than that all of the differences observed were but the result of change fluctuations.

Thus we have been unable to relate any of the measures pertaining to alpha control to cigarette smoking. Note that we did not look for differences between smokers and nonsmokers, since our interest was in the immediate effect of smoke inhalation.

We did make the passing observation in Phase II that there appeared to be some disruption during the initial part of the post-treatment (smoking) five minutes of observation. Not anticipating such transient, short-lived effect, we were not prepared to record anything other than cumulative performance over the whole of the five minutes. So we plan to follow up on this observation by running a few subjects under conditions in which we can record time-on-target for briefer time intervals. The results of this briefer study will be reported separately.

IA2—(Ryan and Lieser)—Effects of smoking and delayed audio-feedback on speech behavior

(See pp. 6–8—Behavioral Research Annual Report, Part I, Accession No. 74–065)

IA3—(Schori and Jones)—Smoking and attentional capabilities

Smokers, smokers-deprived, and nonsmokers performed a tracking task while simultaneously performing a cross-adaptive loading task. The loading task automatically varied in difficulty such that it utilized that portion of the subject's total attentional capacity which was not needed for satisfactory tracking performance, i.e., his spare attentional capacity. In this fashion, the size of the total work load (tracking and loading tasks combined) was individually tailored to utilize each subject's entire attentional capacity. No differences were found among groups either in tracking or loading task performance. Therefore, it was concluded that smokers, smokers-deprived, and nonsmokers expended similar amounts of attentional effort in performing the tracking task and, thus, smoking condition did not affect the size of the workload which could be handled. Reference: 73–123, September, 1973.

IB1—(Ryan and Dunn)—Heart rate change under arousal conditions among smokers and nonsmokers

The Emory-Ryan hypothesis predicts reduction in magnitude of heart rate increment under smoking conditions. We did an exploratory study in which arousal was induced by physical exercise, using smokers and nonsmokers whose heart rates were radio-telemetered to a nearby recorder. The study was aborted when we observed no difference in heart rate increments for the two group of subjects.

IB2—(Schori and Jones)—Smoking, arousal, and mood change

In this study smokers, smokers-deprived, and nonsmokers were required to solve multiple choice problems (mathematical problems adapted from the College Boards and the Graduate Record Examination) which were rear-projected onto a screen. When the subject had solved a problem, he indicated his response by pressing the button—just below the rear-projection screen—that corresponded to the alternative he had chosen. Each subject, on different days, performed the task at 3 problem presentation rates, i.e., slow-paced, self-paced, and fast-paced. Performance of smokers-deprived was definitely better (that is, they responded both more quickly and more accurately to the problems presented) than either nonsmokers or smokers—the latter two groups exhibiting comparable performance. That the smokers-deprived performed better, without going into detail, was explained in terms of two factors in combination: (1) simply being deprived of cigarettes; and (2) the nature of the task itself.

No differences in personality profiles were found between nonsmokers and smokers (which for this analysis included smokers-deprived). This may not be too surprising. When personality differences between nonsmokers and smokers have been reported, it has generally been based upon large scale samplings of heterogeneous populations—not from small relatively homogeneous populations such as our college student sample. Furthermore, even when large heterogeneous populations are sampled, differences in personality characteristics that have been reported are very slight. In agreement with most literature on the topic, heart rates of smokers were substantially higher than those for nonsmokers and smokers-deprived, viz., an increase in heart rate of 10–11 beats/min. could be attributed to smoking.

We had expected that mood change would be more prevalent under the slow and fast-paced conditions than under this self-paced condition. However, this is not what we observed. Instead, mood change, i.e., changes in affect, was much more prevalent (more significant mood changes occurred) under the self-paced condition. Smokers, though, did experience less mood change than did nonsmokers or smokers-deprived—which in agreement with similar findings of other investigators does suggest that smoking actually may act to temper emotional reactivity. Draft manuscript, October, 1974—the technical report should be out shortly.

IIA1—(Ryan)—Puff three—Chained puffing (see p. 1, Accession No. 74–065)

IIA2—(Ryan)—Puff four—Puffing behavior at 30-and 60-second puff intervals (see p. 2, Accession No. 74–065)

IIA3—(Ryan)—Puff five—Puffing behavior changes on cigarette cut to different lengths (see pp. 2–4, Accession No. 74–065)

IIA4—(Schori and Jones)—Does the smoker compensate for changes in delivery in order to regulate intake? (TNT–4)

Winston smokers from the RP[3] panel smoked 7 different cigarettes each for 1 week. There were 6 experimental cigarettes, with tar ranging from 8.2 to 14.6 mg and nicotine ranging from .28 to .90 mg, and a Marlboro control. The number of cigarettes smoked/day and the amount of rod consumed per cigarette (mm) were recorded from saved butts. If the smoker does change the number of cigarettes smoked or amount of rod consumed to maintain relatively constant intake as changes in cigarette deliveries occur, this should be evident as deliveries both increases and decrease from his accustomed levels. However, we found no evidence of any such regulatory behavior, i.e., they failed to compensate for the decreased availability of tar and nicotine by changing either the number of cigarettes which they smoked or the amount of rod consumed from each cigarette. In the face of mounting evidence (of which this study is an instance) that smokers do not alter consumption rates sufficiently to support the intake constancy hypothesis, this hypothesis must be viewed with skepticism unless some other mechanism for regulating intake can be discovered. Reference: 74–078, August, 1974.

IIIB1—(Schori and Jones)—Smoking and low delivery cigarettes (TNT–3)

Smokers from the POL National Panel were required to smoke 14 mg tar cigarettes at .30, .75 and 1.20 mg nicotine, 11 and 8 mg tar cigarettes at .30 and .75 mg nicotine, and a Marlboro control. The 14 mg tar/.75 mg nicotine cigarette (a cigarette with proportional reductions in nicotine and tar) was accorded an acceptability rating equivalent to that of the Marlboro control. The other experimental cigarettes, however, did not compare very favorably to Marlboro in acceptability. Reference 73–129, October, 1973.

IIIB2—(Schori and Martin)—Low delivery cigarettes and increased RTD (DL–2)

Smokers in an R&D handout test and in an RP[3] test smoked a Marlboro control and three low delivery cigarettes—averaging less than 10 mg tar—with RTDs varying upwards from 4.8 in. We has predicted, based upon earlier data, that increasing the RTDs of low delivery cigarettes would make them subjectively appear stronger. However, this is not what we found The Marlboro control was given the highest mean strength rating. The next highest strength rating was ascribed to the low delivery cigarette with the 4.8 in RTD while the lowest mean strength rating was given to the low delivery cigarette having the highest RTD. Although there can be other interpretations of this finding, it appears most likely that the variations in strength ratings among the low delivery cigarettes reflect their variations in RTD.

The most interesting finding had nothing to do with the relationship between RTD and cigarette strength. It was the fact that the Marlboro control, in comparison to the low delivery cigarettes was not the most acceptable cigarette to the smokers. Thus, it may be possible to make cigarettes delivering less than 10 mg tar which will be just as acceptable to high delivery smokers as a standard Marlboro—a finding similar to those that we have reported earlier in conjunction with studies of smoker response to cigarettes of somewhat higher deliveries than those of the present study. Reference: 74–054, June, 1974.

IIIB3—(Schori and Martin)—Low Delivery Cigarettes and Increased Nicotine/Tar Ratios (DL–1)

In this study, we compared 3 low delivery cigarettes (in the 10 mg tar range) to a Marlboro control. One of these cigarettes, i.e., the 10.7 mg tar, .12 nicotine to tar (N/T) ratio cigarette, was comparable to the Marlboro in terms of both subjective acceptability and strength. In other words, that cigarette was perceived to be a full-flavored low delivery cigarette. Although we previously have had cigarettes, in this tar delivery range, which achieved parity with Marlboro in acceptability, this is the first time that such a cigarette has achieved parity in both acceptability and strength. However, we cannot be certain whether the high N/T ratio was an essential factor in that cigarette being perceived as a full-flavored cigarette. And obviously we do not wish to increase N/T ratios unless it is absolutely necessary to do so in order to make full-flavored low delivery cigarettes. Reference: 74–088, September, 1974.

IIIC1—(Schori and Jones)—A Method for Field Testing a Distinctively Flavored Candidate

In response to a specific need, we developed a general testing methodology for consumer tests of novel cigarette products. The methodology itself is currently being evaluated in an actual product test. Reference: Memo to Filosa, April, 1974.

IIIC2—(Schori)—Analyzing Descriptive Panel Data

Having recommended a different approach for analyzing descriptive panel data, we continue to do these descriptive panel analyses on a regular basis.

IIIC3—(Schori and Jones)—A Procedure to Identify Gaps in an Existing Product Market

We prepared this paper to present at the ASTM Symposium this fall (based upon an earlier report—72–088, June, 1972). However, it was felt that the material covered in the paper was of a proprietary nature and, therefore, was not suitable for outside release. Reference: Unpublished manuscript, September, 1974.

OUTSIDE PUBLICATIONS:

Schori, T.R. & Jones, B.W. Smoking and multiple-task performance. *Virginia Journal of Science*, in press.

Schari, T.R. & Jones, B.W. Smoking and work load. *Journal of Motor Behavior*, in press.

DATA BEING COLLECTED:

IA4—(Schori and Jones)—The Relationship Between Smoking and Risk-Taking Behavior

It has often been suggested that smokers take more risks than do nonsmokers. This notion, though, has been based upon non-experimental data (e.g., the fact that smokers have more traffic accidents than nonsmokers). And such data do not take into consideration certain critical factors. For instance, they do not take into consideration possible differences in exposure between smokers and nonsmokers which could explain their differential traffic accident rates. Therefore, the present investigation was designed to determine experimentally whether smoking condition (i.e., smoking, smoking-deprivation, and nonsmoking) actually does affect the individual's degree of willingness to take risks. The task itself is a simulated driving task.

IIA4—(Ryan and Lieser)—Puff six-Puffing behavior following long and short intervals (see pp. 8–9, Accession No. 74–065)

IIA5—(Ryan and Lieser)—Smoking following cigarette deprivation

We want to know whether smokers who are deprived of smoke—by being in a ''no-smoking'' area or situation—will make up for this smoke deficit when they leave the ''no smoking'' area.

We will observe number of puffs and number of cigarettes smoked in a two-hour control period, and compare these figures with those observed in a two-hour period following two hours of smoke deprivation.

IIBI—(Dunn and Martin)—Patterns of smoke inhalation

We are investigating the manner in which the puff of smoke in the mouth is introduced further into the respiratory system.

We became interested in this aspect of smoking behavior through earlier work on the problem of dose control. Since 1968 when we undertook SEX–I, an extensive field study of the quantity of smoke taken into the mouth, we have been investigating the extent to which the smoker regulates intake and the manner in which he regulates intake.

A general premise in our theoretical model of the cigarette smoker is that the smoking habit is maintained by the reinforcing effects of the pharmacologically active components of smoke. A corollary to this premise is that the smoker will regulate his smoke intake so as to achieve his habitual quota of the pharmacological action. As circumstances and body state vary, so will vary the desired level of action. Also as the concentration of the active agents in the smoke varies, so will vary the amount of smoke taken in.

Seeking confirmation of our model, since 1968 we have been measuring intake levels while systematically varying circumstances, body state and smoke composition. We have observed changes in the predicted directions, but the magnitude of the changes has always fallen far short of that change necessary to infer that the smoker is exercising quota regulation of intake. Others have reported similar investigations with similar findings.

Recent observations have led us to question whether the indices of intake which have been investigated to date are, in fact, the appropriate indices to be measuring. We have counted the number of cigarettes smoked, we have counted the number of puffs taken, we have measured amount of rod consumed and we have obtained reasonably accurate estimates of how much smoke is actually taken into the mouth over extended periods of time.

All of these measures fall short of determining the amount of smoke brought into contact with the absorbing surfaces within the lungs. We now have evidence that with some smokers a good portion of the smoke of a given puff never goes beyond the mouth, it being retained in the mouth to be expulsed ahead of that portion which was inhaled. Furthermore, we have good evidence that the gas inhaled following the drawing of a puff from the cigarette is not exclusively the air/smoke mixture introduced through the mouth. A greater or lesser amount of air is introduced through the nose, mixing at the pharyngeal junction of the nose and mouth with the air/smoke mixture being swept in from and through the mouth.

These observations have made us aware of a heretofore unnoticed mechanism that has the potential of affording the smoker a wide latitude of control over the amount of smoke he brings into contact with the absorption sites.

It has been our purpose in this, the first of an anticipated serie of studies, to systematically observe the inhalation patterns of smokers. We are measuring flow rates and volumes of air drawn through the mouth and air drawn through the nose while varying tar and nicotine levels in the mainstream smoke. If the smoker is seeking his quota of the pharmacologically active ingredients, and the regulatory mechanisms available at the post-puff levels are being used toward this end, then we would expect to find directional changes in the ratio of air drawn in through the nose and the air/smoke mixture being drawn in through the mouth, and/or changes in the total inhalation volume.

The problem has required the fabrication of novel apparatus. With much trial and error we have devised a means of independently measuring the rate and volume of air drawn in through the two orifices as the smoker inhales immediately following the drawing of a puff of smoke into his mouth. We have designed and constructed a face mask of silicon rubber which contains a cavity for the nose and a cavity for the mouth. These cavities are sealed off from ambient air and from each other when the subject's face is in position. The mask is rather massive and self supporting, yet flexible enough to effect a good seal with a face. The mask is rigidly mounted on a plexiglass sheet. Leading off behind the plexiglass sheet are two ⅜'' i.d. tygon tubes, one connecting the mouth cavity to a flow rate sensor and the other connecting the nose cavity to a second flow rate sensor.

The sensors responding to flow rate are hot wire anemometers. The voltage changes in these sensors reflecting air flow are processed through electronic circuitry to be finally recorded on polygraph paper in terms of flow rate and air volume. The system is calibrated such that quantified flow rates and volumes in cc can be read directly from pen deflections.

Seated before the apparatus, the subject takes a puff from his cigarette inserts his face into the mask, inhales, withdraws from the mask and exhales in normal fashion. The only part of the sequence occurring with face in mask is the inhalation.

We have used twelve volunteer R&D pack-a-day-plus smoker of regular filter cigarettes. Each subject smoked one cigarette at the mask in the morning and afternoon of each workday. The study ran for three weeks. On the first week they smoked their regular cigarettes. On the second and third weeks they smoked Commanders and Carltons, with a split-group balanced order. The cigarette designated for a given week was smoked continuously by the subject from the first session on Monday to the last session on Friday.

Data collections has been completed and the analysis is underway. The results available at the time will be reported at Project Review on November 8.

Data collection has been completed and the analysis is underway. The results available at the time will be reported at Project Review on November 8.

IIIA1—(Schori, Jones and Martin)—Menthol cigarette preferences of Blacks and whites (MN–3)

Black menthol smokers have generally been inadequately represented in our National menthol cigarette tests. In fact, our National POL Panel, for all practical purposes, is a White panel since nonwhite returns from product tests probably rarely exceed 3% of the total returns. Since there is considerable evidence which suggests that Blacks and Whites may differ in their likes and dislikes in menthol cigarettes, the present investigation was designed to identify Black and White preferences for menthol and nicotine deliveries in Alpine-like cigarettes. Accordingly, Black menthol smokers (from RP^3) and White menthol smokers (National POL panelists) were required to smoke and rate 4 experimental Alpine-like cigarettes (which delivered two levels of nicotine at each of two levels of menthol) and an Alpine control. The lower level of nicotine, for the experimental cigarettes, was slightly lower than Alpine. The lower level of menthol was comparable to that of Alpine.

The results from the first run of this test have been analyzed, but questions have been raised about the reliability of the data. The study is to be replicated before the report is finalized.

IIIB/C1—(Dunn and Martin)—A field test of systematically varied tar and RTD levels in which three methods of cigarette presentation are compared

This study has been in process since November of last year, its execution being delayed by difficulties in fabricating cigarettes with the required tar/RTD combinations. The proper combinations have recently been achieved by Messrs Houck and Claflin, and the test is awaiting its turn on the RP^3 panel.

STUDIES IN THE PREINVESTIGATIVE PHASE:

A Prefatory Note: It has been well established that one of the differences between smokers and nonsmokers is that smokers will tend as a group to display more aggressivity. There have recently been some suggestions in the literature that those individuals prone to aggression may have learned that smoking facilitates the control of these tendencies; and that it is for this reason that one finds a higher incidence of aggression prone individuals within a smoking population than within a nonsmoking population.

If this interpretation is correct, then one would expect to find that when the smoker is allowed to smoke freely, his display of aggression in an aggression-inciting situation will be at a level comparable to that of nonsmokers, but when deprived of the opportunity to smoke for a period of time before and during observation, his display of aggression will be manifestly higher than that of nonsmokers.

We recognize, however, that any observed increase in aggressivity when deprived of cigarettes may be as readily explained as the emergence of reactions to deprivation, not unlike those to be observed upon withdrawal from any of a number of habituating pharmacological agents.

The Behavioral Research Laboratory is initiating a series of studies on aggression in smokers. Collectively, the studies will be aimed at (1) observing for differential aggressivity under free-smoking vs. deprived smoking conditions and (2) if increased aggression under deprivation is observed, differentiating between personality-related aggression and deprivation-induced aggression.

Our strategy for distinguishing between the personality-related and deprivation-induced aggression is premised upon the logic that if the aggression is personality related, then it should be observable (1) among prospective smokers, and (2) among abstaining smokers whose period of abstention has extended beyond the withdrawal period.

Study IB1 (Schori and Jones) is designed to induce aggressivity in order to determine if, indeed, differential aggressivity under free-smoking and deprived smoking conditions is observable. Study IB2 (Dunn and Martin) is designed to observe for aggressivity the abstaining smoker whose abstention has extended beyond the period in which deprivation-induced behaviors are likely to be present. Study IB3 (Ryan and Lieser) is a longitudinal study attempt to observe for personality-related or trait aggressivity in the prospective smoker.

IB1—(Schori an Jones)—Smoking and aggression

This study is designed to evaluate the influence of smoking condition on both aggression and performance in a complex task situation at 3-levels of failure-induced frustration. The task is a slightly modified version of the simulated driving task that is being used in the ''Smoking and Risk-taking'' study.

IB2—(Dunn and Martin)—Bruxism suppressed by smoking

Bruxism in medical cryptology, is but the habitual act of grinding the teeth. In a recent experiment aimed at treating the habit through the application of biofeedback principles, an enterprising psychologist at Claremont Graduate School, Dr. John Rugh, devised an unobtrusive, totable electronic package which emitted an audible signal whenever the tension in jaw muscles exceeded a preset threshold level. The package embodied a sensor whose output voltage correlated with the electrical activity of the muscles over which it was placed, an IC amplifier and the auditory signal generator. Without the device teeth grinding has been occurring at a subconscious level. The buzzer brought the behavior to the subject's attention, making it more accessible to voluntary control. Daily use of the device proved effective in the reduction of teeth grinding.

Our interest in this investigation is two fold: The relationship between jaw muscle contraction and psychological tension has relevance to smoking dynamics. Hutchinson used the measure of jaw muscle tension as an index of psychological tension in a 1970 study funding by P.M. R&O. The measure was more specifically interpreted by this investigator as an index of covert aggressive responsivity. Hutchinson put smokers into frustrating task situations and recorded the EMG signals at the jaw. He reported less muscle tension (ergo, less anger) under smoking than under abstaining conditions.

Secondly, it occurred to us that the total package may have another application to our continuing study of the motivational factors in cigarette smoking. It may make it possible to circumvent a methodological problem over which we have agonized for some time.

The problem is this: In order to properly assess the influence or cigarette smoking upon some specified behavior one must observe that behavior in the same subject undersmoking and nonsmoking conditions. If, for example, one wished to determine whether smoking influences visual accuracy, one would obtain measures of the subject's acuity immediately following the smoking of a cigarette and at some other time obtain the same measures following a period of abstention from smoking, the period being sufficiently long to clear the organism of the pharmacological effects of the smoke. Any observed difference, one might argue, would be a function of the effect of the smoke upon the smoker. But such an argument assumes that the abstaining smoker is in his normal, i.e., non-smoke-influenced state. This assumption is open to challenge. The counter argument is that, if the period of abstention is sufficiently long to allow for the metabolic clearing of the agents taken in from cigarette smoke, then that period has been sufficiently long also for the onset of any deprivation effects.

Our methodological problem lies in our inability to distinguish between those behavioral changes that reflect return to some non-smoke-influenced baseline on the one hand and those changes which are the individual's response to smoke deprivation on the other hand. Thus Hutchinson's reported increase in jaw muscle tension in abstaining smokers could as readily be the emergence of behavior which had been suppressed by smoking or the onset of behavior specific to the smoke-deprived state. We need some means of distinguishing between these two possible classes of response to cessation of smoking.

We would expect behavior specific to smoke deprivation to peak rapidly following cessation of smoking and diminish gradually thereafter, dropping out entirely at some later point in time as the former smoker's system accommodated to a nonsmoking regimen.

On the other hand, if the observed behavioral change is due to the re-emergence of patterns suppressed by smoking, we would expect the behavioral change to peak fairly rapidly following discontinuations, as in the case of deprivation-specific behavior, but then plateau at peak and remain constant.

Here, then, are two distinctive time-related patterns. Were we able to continuously monitor the behavior beginning a week before ceasing to smoke and continuing for a month or more thereafter, the data should allow us to confirm or refute the Hutchinson observation that the jaw clenching rate is altered by ceasing to smoke and further, if confirmed, classify the altered rate as either withdrawal-specific behavior or baseline behavior characteristic of the individual when not smoking.

If we were to establish that the behavior is characteristic of the smoker when not smoking and not merely a transient response to deprivation, the implications are profound. Following Hutchinson's interpretation of jaw clenching as a covert manifestation of anger, we would have in hand our first clear-cut positive effect of cigarette smoking—the inhibition of anger.

If, on the other hand, the alteration were to prove to be limited only to the time period immediately following cessation, the implications would not be so profound but there would remain the possibility of some important inferences. The duration of the altered rate would reflect the duration of the deprivation period. The determination of the time interval would establish how long observations must be delayed following ceasing to smoke in order to study the uncontaminated non-smoke-influenced behaviors for comparisons with smoke-influenced behaviors.

The totable EMG unit lends itself nicely to the collection of the data. After substituting an electronic counter for the signal generator, we will be able to record either continuously, or by periodic sampling, the frequency with which jaw clenching occurs. A simple graphic plotting of jaw clenching rate over time should make it possible to evaluate the pattern of change and thus establish the nature of the altered behavior.

Our major problem will be to recruit enough regular smokers willing and able to abstain from smoking over the five or more weeks required.

We are corresponding with two laboratories (in the Psychology Departments of Harvard University and Claremount Graduate School) on the details of instrumentation.

IB3—(Ryan and Lieser)—The hyperactive child as prospective smoker (see pp. 9–12, Accession No. 74–065)

This is an intriguing theoretical derivation of an hypothesis which predicts that today's hyperactive child is tomorrow's smoker.

A Final Note to the Series of Aggression Studies: We are considering modest financial support to two university laboratories whose programs include studies immediately relevant to the question of the influence of smoking upon aggression. Neal Miller's laboratory at Rockefeller University is prepared to investigate further the nicotinic mechanisms in the brain of the rat, there being already some evidence that nicotine does reduce irritability and aggression while its withdrawal has the opposite effect.

At Ohio State University two psychologists are eager to follow up leads pointing to the inhibitory influence of central nicotinic systems on the aggressive behavior in cats.

IB4—(Dunn and Martin)—The influence of smoke inhalation upon accommodating to distracting stimulation, using the control of brain wave patterns as an index of accommodation

A group of investigators at Melbourne University in Australia have reported that smokers accommodate (or become inured) to distracting stimulation more rapidly while smoking than while deprived. Maintenance of alpha brain wave dominance in the face of such stimulation was used as the index of accommodation. When not accommodated, alpha dominance was lost when distracting stimulation was presented. When accommodated, alpha dominance was not disrupted by the stimulation. The reported observation is exciting because of its theoretical significance and because, as reported, it was a very clean effect induced by smoking. We are displeased with the lack of rigor in the design of their experiment, so our purpose is to replicate the experiment with better controls and improved conditions of observation.

IIIB4—(Schori and Jones)—Manipulating smoke impact in very low (<8 mg tar) delivery cigarettes

How can we achieve full-flavored very low delivery cigarettes? We feel that the main hinderance to doing so is our inability to achieve sufficient smoke impact in very low delivery cigarettes. Therefore, although ultimately we would like to develop a marketable one, this study (which is being conducted in cooperation with Willie Houck and Paul Gauvin) is designed to assess the relative influences of various factors on smoke impact in very low delivery cigarettes. Specifically, the relative influenced of blend (standard Marlboro blend vs. 50% burley blend), burley-spray (100% vs. 50%), and filter system (cellulose acetate filter plus high dilution vs. paper/cellulose acetate filter plus zero dilution) on smoke impact in cigarettes within the 5 to 6 mg tar range).

IIIB5—(Schori and Jones)—A low delivery full-flavored candidate (Opus I)

In an earlier study (74–053, June, 1974), three low delivery cigarettes, averaging less than 10 mg tar, were found to be comparable in acceptability to the Marlboro control. Because of the obvious practical significance of that finding, we felt that it was necessary to follow up that study in order to determine whether with our current capabilities we can reliably make low delivery cigarettes which are just as acceptable to the smoker as Marlboro. Accordingly, we attempted to remake the most promising low delivery candidate from the earlier study. That candidate is to be compared to a Marlboro control by high delivery RP^3 smokers.

IIIB6—(Schori and Jones)—A low delivery full-flavored cigarette (Opus 2)

In an earlier study (74–088 and IIIB3 above) a low delivery cigarette which delivered 10.7 mg tar—with a nicotine to tar ratio (N/T) of .12—was found to be comparable to a Marlboro both in acceptability and strength, i.e., this cigarette was perceived to be a full-flavored cigarette. We were not positive however, that the high N/T ratio was the primary determinant of the smokers' favorable perceptions of this cigarette. Therefore in this study we will make three 10 mg tar cigarettes with N/T ratios of .07, 110, and .13—insuring that tar is constant over cigarettes—and a Marlboro control. From this test, we will be able to determine: (1) whether we can reliably make full-flavored cigarettes in the 10 mg tar range; and (2) whether a relatively high N/T ratio is essential in order to do so.

IIB2—(Dunn and Martin)—Continuation of the investigation of inhalation patterns

A number of questions have been raised by the initial inhalation study. We plan to continue these observations in order to determine what, if any, aspect of the inhalation pattern is relatable to smoker characteristics and cigarette characteristics.

''PME Research: 1972–1974'' Gustafson & Haisch

* * * [Indicate deleted material]

HUMAN SMOKING HABITS—(or: the impact of our products on the smokers)

The thoughts on cigarette design which we have developed so far and which we are realizing in the trials of the Teams of ''Thermodynamics of Adsorption Processes,'' ''Intersection of smoke with Cysteine,'' and ''Product Research'' are our response to developing trends and public pressures.

Further input into this research is provided by the wants, references and needs of the smoker. Under the direction of Mr. Bourquin we have planned, executed and analyzed several studies on human smoking habits.

At the planning stage, the objectives and goals as well as the scope and depth of the study were set by asking some relevant questions. The answers to these questions are needed to match consumer profiles and product relevance, to provide information on certain aspects of ''Smoking and Health'', and for future prototype development.

How much nicotine does the smoker want?

2. Does the smoker compensate for nicotine delivery in a low nicotine cigarette?

3. What are the actual delivery levels of important brands?

4. Does nicotine delivery depend on the social situation of the smoker?

5. Do well defined classes of cigarettes fit well defined classes of smokers?

6. How can an increased smoke impact be achieved with a low delivery product?

The first study was executed with the cooperation of the marketing department in Germany. The stumps of 27 major brands were collected at various locations and offices. To calculate filter efficiency and nicotine consumption the nicotine deposit in the filter was measured. (The German study must be regarded as incomplete as the pilot study was never followed-up by a proper scale investigation.)

The results and conclusions gave us possible solutions to some marketing problems and set the limits for product modifications.

The most frequent nicotine yield was 0.4 to 0.5 mg of nicotine per cigarette. This yield is not dependent upon the nicotine content of the tobacco and is not related to the nicotine yield under Coresta (machine) smoking conditions. The difference between nicotine yields obtained under standard laboratory procedures and yields obtained under ''real'' smoking conditions is explained by the existence of a compensation mechanism in the smoker. This compensation mechanism seems to be in operation for a proportion of the consumer population to adjust the nicotine yield to their needs or liking.

* * * [Indicate deleted material]

[From Philip Morris, Richmond, Virginia]

To: Dr. T.S. Osdene
From: W.L. Dunn
Subject: Quarterly Report—January 1–March 31, 1995
Date: March 25, 1975

Inhalation Studies.—All work has been held up for the installation of the sound- and electromagnetically-insulated room. The room has arrived and is to be in April.

A Field Test of RTD and Tar Influences on Acceptability with Three Methods of Cigarette Presentation.—Analysis is underway.

Conference on the Regulatory Influence of Nicotine on Human Behavior.—Proposal has been presented to the industry. Awaiting decision to proceed.

FRANK RYAN'S REPORT

Puffing Following Cigarette Deprivation (Puff Seven).—Ongoing. We are observing number of cigarettes smoked and total puffs taken by college students smoking their own brands during a critical two-hour period. Preliminary data suggest that more cigarettes are smoked and more puffs taken when the observations follow a two-hour deprivation period than following two hours when smoking is permitted.

Mixed Pack Study.—Ongoing.—A national mailout is scheduled for early April in which High Filtration panelists will compare a 10 mg cigarette to a mixture of 7 and 13 mg cigarettes. The object of the test is to see whether the intentional inclusion of some more flavorful cigarettes in a pack of low delivery cigarettes will affect product ratings.

Personality, Arousal and Smoking.—Planning.—Following Eysenck's suggestion that smokers seek stimulation to increase the arousal level of their central nervous system whereas introverts avoid stimulation, we will look at the effects of smoke deprivation on extroverted smokers in a sensory stimulation deprived situation and compared to nondeprived and nonsmoker groups, as well as to introverts.

Equal Puff Volumes.—Planning.—In this smoke recorder study smokes will be instructed to take either puffs of a constant volume or constant duration. Cigarette characteristics will be changed from time to time to see if volume changes follow. The purpose of the study is to find some of the cues which control puff volume changes.

TOM SCHORI'S REPORT

The Effect of Smoking on Risk-taking in a Simulated Passing Task.—Data analysis is complete. The report is in preparation.

Smoking, Arousal, and Mood.—A manuscript for publication has been prepared.

The Influence of Nicotine on Aggression in Fish.—This is a new study in which the Beta, an innately aggressive fish, is to be treated with varying concentrations of nicotine in tank water. We will be observing for differential effects upon aggressive display behavior and some control behavior which is to serve as an index of general activity level.

Menthol Cigarette Preference of Blacks.—Cigarettes with two nicotine and two menthol levels have gone out to 350 Black RP^3 menthol smokers. This is a modified form of the original study, the results of which proved difficult to interpret.

Low Delivery Cigarettes: The Influence of Delivery Information on Subjective Evaluations (II).—Cigarettes are ready and should go out shortly to 2 National POL panels. This is a follow-up on a smaller scale study (RP^3) the results of which suggested that smokers responded favorably to being provided the information that the cigarettes were low delivery.

A Low Delivery Cigarette with Impact and Flavor.—The 5–6 mg tar delivery program being carried out in collaboration with P. Gauvin is proceeding nicely. Models for the 8 experimental cigarettes have been developed and the cigarettes are now being made.

SEPTEMBER 8, 1975.

Prof. STANLEY SCHACHTER,
Dept. of Psychology, Columbia University, Schermerhorn Hall, New York, NY.

DEAR STAN: Welcome back and thanks for your letter. And thanks for your solicitation of my critique of your manuscripts. I'd be delighted. I wouldn't view it as an imposition because, after all, I am responsible for the Company having provided you with those modest sums and therefore have vested interest as well as personal interest in your output.

As for your Marlboro question, we've tracked sales vs. nicotine over the past five years and have concluded that there is no discernible relationship. Interestingly, the concern grew from an hypothesis antithetical to your own. Market Research is burdened with attempting to explain a slipping sales increment. The robust 15% annual increase which we'd come to view as the norm became 10% from 1973 to 1974 and recent figures are of the order of 7%, if my memory serves me well.

Some have interpreted this as the inevitable leveling off. Although we cannot fit any kind of explanatory equation using nicotine as a predictor, we cannot of course rule out the possibility that the Marlboro smoker is responding to nicotine reduction by switching to other brands. But your manner of putting the question implies that you would have predicted a sales increase. You neglected to take into account that the smoker has other options than merely increasing the number smoked.

My own prejudice is that the smoker is oblivious at the conscious level to major changes in the composition of his smoke, but not wholly unresponsive. I am more of the belief that we have many ways in which to accommodate to a variable smoke, and perhaps the least of these is to smoke more cigarettes. For too long investigators have relied on measures relatable to the cigarette (number of cigarettes, number of puffs, butt length) as consumption rate indices. True enough, the number smoked is an infallible index of cigarette consumption, but we should be thinking more in terms of cigarette consumption. Cumulated puff volume tells us more, but even this is but a measure of smoke taken into the mouth. The ultimate index is how much passes over into the bloodstream, a not so readily monitored phenomenon. We're now looking at the fate of the smoke entering the mouth; how much goes down, how much comes back out, and related behavioral events that we anticipate finding to be dose-regulating mechanisms of remarkable precision and sensitivity.

Thus to accommodate to the 15 percent reduction in available Marlboro nicotine, the smoker who was getting 50 percent of the available nicotine over into his blood from the Marlboro delivering 1.1 mg of nicotine into a smoking machine now must get 59 percent of what the current Marlboro offers him. He can take bigger puffs, or inhale more from the supply drawn into the mouth (we have varying quantities of residual smoke in the mouth at the end of an inhalation) or for more efficient extraction of the goodies, he can draw it in deeper or hold it longer.

So we're looking at respiratory behaviors. I have a physiological psychologist joining the staff this month. Instrumentation is the big challenge at the moment.

Send the manuscripts.

Regards,

WILLIAM L. DUNN, Jr.,
Principal Scientist.

Charge Number: 1600
Program Title: Smoker Psychology
Project Leader: W.L. Dunn, Jr.
Period Covered: January 1–31, 1976
Date of Report: February 10, 1976

Project Title: Smoke Inhalation Study
Written by: Carolyn Levy

Our new apparatus which allows the subject to puff on a cigarette while his face is in the mask is almost operational. We are remaking the rubber masks in order to give the subjects better access to the mouthpiece.

In order to determine if the delivery of a cigarette is reduced by the new apparatus, two Marlboro monitors were smoked through the apparatus on the twenty-port smoking

machine. For comparison purposes, two monitors were also smoke through the regular smoking profile recorder mouthpiece. The TPM deliveries (17 puffs) were 38.2 and 38.4 mg. Thus, we get comparable deliveries with the two different pieces of apparatus. In addition, these deliveries are not appreciably different from what would be expected from smoking the monitors in the regular fashion on the smoking machine.

Our next study will again use R&D smokers. Cigarettes delivering 18, 15.7 and 13.3 mg of tar have been made, holding puff counts and RTD's approximately constant.

Project Title: Regulatory Identification Program

Written by: Carolyn Levy

We are ready to begin our first attempt to identify nicotine regulators and non-regulators among our smoking student population. In selecting our initial subjects we hypothesized that those who smoke more than 30 cigarettes per day of a high delivery brand (>15 mg tar) would more likely to regular than those who smoked less than 10 cigarettes per day of a comparable brand. Thus we have two groups: likely regulators and likely non-regulators.

In order to measure daily nicotine intakes, the subjects will smoke at home and save butts for three weeks. During Week 1 they will smoke their own brands. During Weeks 2 & 3 they will smoke high and low delivery products in a counterbalanced order. The relevant dependent variables are number smoked per day and the nicotine residual in the butts. We expect that daily nicotine intakes will be more product-dependent for non-regulators and more product independent for regulators.

After this butt saving period, the smokers will come to the lab for four sessions. Session 1 will be used to familiarize the subjects with procedures and apparatus. During Sessions 2-4 we will measure their smoking behavior while smoking own brand, high and low delivery products. In order to reduce the number of variables that are free to vary in the smoking situation, we will tell our subjects when they will smoke a cigarette, how many puffs they may take, and where along the rod these puffs will be taken. We want to find out if we can ''force'' our potential regulators to modify their puff volumes, inhalation volumes, and/or smoke retention times in order to obtain their usual nicotine dose. On the other hand, we do not expect the potential non-regulators to modify their smoking behavior under these circumstances. When not smoking, all subjects will be occupied with time filling tasks.

This initial study will enable us to assess the relevance of consumption data to regulation. That is, are heavy smokers more likely to regulate than light smokers? In addition, we would like to determine other factors that are correlated with regulation so as to improve our ability to predict which smokers will be regulators.

Project Title: Smoking of Nicotine Free Cigarettes

Written by: Carolyn Levy

Due to a delay in equipment set-up, we have been unable to obtain denicotinized tobacco. Hopefully we can begin this study in one or two months.

As an alternative to denicotinized tobacco, we have look into the possibility of having cigarettes made from a strain of tobacco that is naturally low in nicotine. Our comparison cigarette would also be made of this tobacco with nicotine citrate added to bring the nicotine content up to ''normal.'' This tobacco should be available by the end of February.

Project Title: Annual Monitoring of Cigarette Preferences

Written by: F.J. Ryan

As a preliminary test of our ballot and procedures, five non-menthol cigarettes—delivering 8, 11, 14, 17, and 40 mg of tar and .6, .7, .8, 1.0, and 1.2 mg nicotine—were sent to 300 RP[3] panelists who rated them for acceptability. Usable replies were received from 232 (77%) of the panel.

A preliminary analysis of returns based on incomplete data suggests that the differences in ratings were small, as seen in Table 1, but illustrative.

* * * [Insert notation for deleted material]

[From Philip Morris, New York, NY

To: Mr. J.J. Morgan

From: Al Udow

Subject: Why People Start To Smoke

Date: June 2, 1976

At the end of last week I gave you some material intended to answer Cliff Goldsmith's question on why people start to smoke. Because we should have this information at our disposal, this document summarizes the data available, and cites references.

There are surprisingly few hard facts on the question of the initiation of smoking. Most of those who write on the subject of smoking tend to rely on the statistical work of Daniel Horn and the National Clearinghouse for Smoking and Health. Others offer opinions without sources or data to back them up.

The best summary of the situation may be an entry by Matarazzo. Joseph D. Matarazzo, of the University of Oregon Medical School has written widely on smoking. He is the primary author of the entry on smoking in The International Encyclopedia of the Social Sciences (1968).

His summary of the factors involved in the initiation of smoking is as follows:

These studies consistently have identified parental smoking as one of the most important predisposing factors in smoking among school-age children. As mentioned above, most smokers appear to have begun smoking between the ages of 10 and 18. If both parents smoke, the probability that their children will begin to smoke is several times that of children with nonsmoking parents. When only one parent smokes, the incidence of smoking among the offspring falls midway between that of the other two groups. Published data also suggest a higher frequency of smoking among children with older siblings who smoke.

The relationship of some other sociopersonal factors to initiation of the smoking habit is less clear-cut. In general, the studies suggest that youngsters' beginning to smoke is related to: (a) curiosity about smoking; (b) conformity pressures among adolescents; (c) need for status among peers, including self-perceived failure to achieve peer-group status or satisfaction; (d) the need for self-assurance; and (e) striving for adult status (see the reviews by Hochbaum 1964; Horn 1963). However, it is difficult to measure the strength of such needs, as well as their relative influence, and therefore these relationships should be considered tentative.

The basis for his, and many other statements is a publication of the National Clearinghouse of Smoking and Health (1972) which reported on two surveys of teenagers, numbering 4931 and 1968 and 2640 in 1972. Their conclusions are based largely on statistical inference.

The report concludes:

While there are many factors in the environment of the child that influence his taking up, or not taking up, the smoking habit, the one that has by far the most influence is the smoking behavior of those around him . . .

In households where both parents are present, the teenager is much more likely to be smoker if the parents smoke. In fact, if both parents smoke the teenager has about twice the likelihood of being a smoker than if neither parent smokes, the rates are 18.4%and 9.8% respectively. Those with one parent who smokes fall in between, with a rate of 13.8%

We find a striking relationship between the behavior of the older members of the family and that of the younger members. In homes where both parents are present, boys with an older brother or sister are twice as likely to smoke if one or more of the older siblings smoke than if none smoke (30.0% and 13.1%). The relationship is even stronger among girls, with a four to one ratio; 24.8% of girls with one or more smoking older siblings are smokers while only 5.6% of those with older siblings, none of whom smoke, have taken up the habit.

When the combined effect of smoking of parents and older siblings is considered, the concept of family patterns is reinforced. The lowest level of smoking is found among teenagers who live in households where both parents are present and neither smokes, and who have older siblings, none of whom smoke. Less than one in twenty have become regular smokers (4.2%). This compares with one in four (24.9%) in families with at least one parent and one older sibling who smoke. The older sibling, as would be expected, is more likely to smoke if he has a parent who smokes. It is impossible to determine precisely what are the relative effects of parental and sibling smoking on the teenager. However, we do see that he is more likely to smoke if the older sibling smokes and the parent does not than if the parent smokes and the older sibling does not. We cannot discount the influence of either; they interact with each other, and as they do, the family pattern is established.

[Not legible]

Harold S. Diehl, M.D. (1969), of the American Cancer Society quotes liberally from David Horn of the National Clearinghouse for Smoking and Health. Much of what he says is stated authoritatively without source or supporting data.

''For children who see their parents, teachers, other adults, and older brothers and sisters smoking, the desire to be like them, to be grown-up, constitutes a strong incentive to try it themselves. Studies show that children are much more likely to smoke if their parents smoke.'' (No source given)

''Many boys and girls start smoking to show their independence, as a symbol of revolt against authority, to feel sophisticated and grown-up, to be ''one of the crowd'', to gain social status, to have something to do.'' (No source given)

''The advertisers of cigarettes exploit this urge by creating an image of a smoker as an outstanding athlete; a handsome, virile outdoor man; nonchalant campus leader; a man who succeeds; a sophisticated, charming young woman.'' (No source given)

''For some smokers the motions and movements associated with smoking seem to have a soothing, pleasurable effect, similar to the chewing of tasteless objects such as pencils, straws, or chewing gum after the flavor is gone. It also seems that some of the satisfaction derived from smoking—particulary of pipes and cigars—is related to watching the smoke. Few people enjoy smoking in the dark, and blind men rarely smoke.

For persons who are self-conscious and insecure smoking provides an activity and something to do with their hands that takes their minds off themselves. Many accept the image created by cigarette advertisements of cigarette smoking as a symbol of poise, self-confidence, and social success. But once one

becomes dependent upon cigarettes, habituation or addiction are impelling drives to continue.'' (No source given)

Dr. Daniel Horn, Director of the National Clearinghouse for Smoking and Health, says that people smoke cigarettes for one or more of the following reasons: (1) for stimulation, such as to get started in the morning; (2) because of addiction; this smoker ''must have'' a cigarette after a certain amount of time has elapsed; (3) to reduce negative feelings, such as distress, anger, or fear; (4) out of habit—a behavior pattern followed almost involuntarily; (5) for oral gratification—the satisfaction derived from something in the mouth; and (6) for pleasurable relaxation—to enhance positive feelings, such as after a good dinner.

A paper by Meyer, Friedman and Lazarsfeld (1972) given before the Conference on Motivation Mechanism of Cigarette Smoking provides some qualitative insight into the initiation of smoking which may be abstracted as follows:

Many smokers, particularly ''white collar'' started in rebellion against their parents. Another theme is that of emulating friends and relatives. Peers provide especially important role models to emulate and partners with whom to rebel.

The theory is offered that when youngsters of smokers start to smoke, they are helping to deny that their parents are in danger. Also, when offspring of smokers take up the practice themselves, they are striking back at their parents' hypocrisy, and at the same time, making a connection with them.

The Encyclopedia Americana (1969) says that the way smoking begins is not fully understood and then attempts to explain it:

The beginning of smoking and the processes by which it becomes a habit are complex and not fully understood. In large part, the habit stems from psychological and social drives; the individual smoker does what others around him do. Physiological and possibly constitutional factors may play a lesser role. There is little doubt that the physiological effects strengthen the habit. Nicotine, one of the many substances pharmacologically active in tobacco smoke, exerts its effects on the heart and the nervous system in particular. Smoking of one or two cigarettes causes an increase in the heart rate and a slight rise in blood pressure. The effect on the nervous system is predominantly tranquilizing and relaxing.

Relationships between smoking and a number of psychosocial and economic variables are apparent, but no simple explanation is evident. It is obvious, however, that smoking as a behavior has become interwoven with the complex culture and environment of modern society.

Start of the Habit. The smoking pattern is established relatively early. Before 12 years of age less than 5 percent of boys and 1 percent of girls smoke, but soon thereafter a steady increase begins. In the 12th grade, from 40 to 55 percent of children are smokers, and by the age of 25 years about 60 percent of men and 36 percent of women have acquired the habit. The increase in the percentage of smokers continues into the fourth decade of life.

Among the reasons why children take up the habit are their desire for adult status and their need to conform to social pressures exerted by other children. In striving for status and self-assurance, children may imitate their parents or famous people. The association between the smoking habits of parents and children is strong and many-sided. More children smoke in families where both parents smoke than in families where neither parent smokes. In adolescent and adult life, similar factors involving the individual's need and his environment appear to play a role in the beginning of smoking.

Although no differences in intelligence between smoking and nonsmoking children have been established, smokers are more frequent among those who fall behind in scholastic achievement.

Personality and Other Factors. No clearly defined ''smoker's personality'' has been established. Furthermore, no personality characteristic is found exclusively in either the smoker or the nonsmoker. Certain personality factors—among them extroversion, neuroticism, and increased psychosomatic complaints—have been found to be slightly more common in smokers.

Stressful situations occurring in an environment favorable to smoking may contribute to the starting of the smoking habit, as well as to its continuation. For instance, some men begin smoking in the tense days of their first job. Smokers consistently report that they tend to smoke more when under tension.

Both more smokers and more early starters are found in the unskilled working classes. White collar, professional, managerial, and technical occupations contain fewer smokers than craftsmen, sales persons, and laborers. Smokers are reported to change jobs more often than nonsmokers. Another socioeconomic factor, income does not seem to be as consistently and positively related to prevalence of smoking as to the quantity of cigarettes consumed. A relationship does exist between smoking and educational level, but it seems likely that this relationship is really based on occupation, because those occupations associated with higher education usually show a smaller prevalence of smokers.

Social pressures undoubtedly delayed the acquisition of the smoking habit by women. Increased cigarette consumption by women began in the 1920's, and the rate rose rapidly during and after World War II. Although the habit has been prevalent among women for a shorter period, the percentage of women who smoke has been increasing faster than the percentage of men who smoke.

Kozlowski and Harford (unpublished) cite a 1959 British study by Bynner based on 5601 adolescent school boys in Great Britain which concludes that the important influences that lead to the initiation of smoking are: (1) number of friends who smoke (2) anticipation of adulthood (3) parental permissiveness toward smoking (4) whether or not deterred from smoking by danger of lung cancer.

The Yankelovich organization (1976) undertook a study for the American Cancer Society by means of interviews with 826 teenagers and young women.

Their conclusions about the teenage smoker suggest some correlates (though not exactly reasons) of the beginning of smoking. They say:

The Profile of the Teen-age Girl Smoker: The profile of the teen-age girl smoker counters the image of a socially ill-at-ease youngster turning to cigarettes as a means of being thought of as more sophisticated or as a needed prop for handling social situations. Instead, it is the teen-age girl smoker who is at ease socially, very put together, and with full confidence in herself. Parties and social gatherings are her metier. One measure of both her sophistication and her value structure is the fact that 31% have already had sexual relations.

It is instead the nonsmoker who tends to be quieter, far less self-assured, more involved with athletics, school activities and clubs—but more likely in her spare time to be reading or watching television.

Rebelliousness and Smoking: Cigarette smoking among teenage girls, however, does appear to be highly identified with an antiauthority rebellious syndrome. Among teen-age girls who smoke 25% use marijuana regularly compared to 3% of the nonsmokers; 81% of the smokers drink and 32% drink at times to get drunk compared to 42% of the nonsmokers who drink or 4% who drink to get drunk. One out of four teenage girl smokers have run away from home compared to 10% of the nonsmokers. Despite the widespread acceptance of cigarettes, and the acknowledgement of smoking by parents and school authorities, the old ''wood shed'' image of cigarette smoking lingers on—while the concept of not smoking of nonconformity or rebellion against advertising, big business, society, has not yet caught on.

Teen-age Girl Smokers and Peer Relationships: Peer relationships, long identified as a major factor in teen-age smoking, continue to operate as a dominant influence. Teen-age smokers flock together and have more respect for the opinions of their own peers than for authorities. There is, however, an opposite side to the story as well. For the current study indicates that all teen-age girl nonsmokers are not homogeneous but rather divide into two almost equal groups. It is easy to explain why over half of the nonsmokers (55%) do not smoke—for they are not influenced by the new values, but are very traditional in their views and outlook. They are strongly religious and respectful of authority and they shy away from their peers who smoke, use marijuana and are part of the new values. The other group of nonsmoking teenagers are very different for they share many of the same values as the smokers—and are highly exposed to the total smoking environment. We call them the ''Vulnerables'' for, on the surface, they appear to be ready candidates for the next wave of new smokers. One out of two of the ''Vulnerables'' report that half or more of their male friends smoke; a third indicate that most of the girl friends smoke. A majority have one or more parents who smoke. They see more women smoking now than in the past. Yet they do not smoke. Instead they have found consciously or unconsciously, some strong barriers to smoking. These are the importance of being in control of one's own life; and emphasis on physical fitness and well-being; concern about the addictive nature of cigarettes, and perhaps most of all, by becoming militant antismokers—people who are angered by other smokers, upset by smoke filled rooms and ready for increased regulation of smoking. In other words, they are finding a cause—and a new peer identification.

Information on the motivation that leads to a continuation of smoking comes from a special study done for Philip Morris (Brand, 1971). Smokers first answered the question ''Why do you smoke'' with platitudes such as:

—gives me something to do with my hands
—relieves tensions
—goes well with a social drink
—settles my stomach after a heavy meal
—helps me to relax
—just an automatic habit
—keeps my weight down

But on deeper probing, the circumstances in which smoking occurs may be generalized as follows:

1. As a narcotic, tranquilizer, or sedative. Smokers regularly use cigarettes at times of stress.

2. At the beginning or ending of a basic activity. This would cover such activities as entering or leaving a room, starting or finishing a job, going into a party or leaving one, starting a telephone conversation or a personal visit.

3. Automatic smoking behavior. Heavy smokers, particularly, light up at intervals without much thought, and often without realizing what they are doing.

It should be noted that there was scarcely any unprompted reference to smoking for ''taste'', or ''flavor'', until it was suggested—and then everyone agreed that it was the major element in smoking satisfaction.

[From Philip Morris, Richmond Virginia]

To: Dr. T. S. Osdene
From: W. L. Dunn
Subject: Rationale for Investigating the Effects of Smoking upon Electroencephalographic Phenomena
Date: December 22, 1976

The pharmacology of nicotine and tobacco smoking is very complex (Larson et al., 1961; DiPalma, 1971; Goodman & Gilman, 1970), Nicotine acts on the cardiovascular nervous gastrointestinal and endocrine systems. Armitage, Hall, and Morrison (1968) and Jarvik (1970) have provided evidence for nicotine as the pharmacological basis of tobacco smoking. It is obvious that we need much more research to unravel the relative importance of the multiple actions of nicotine in doses inhaled during tobacco smoking. In agreement with these investigators, it is my basic premise that one of the many reasons people smoke tobacco is that it contains nicotine. An extension of that premise is that the doses of nicotine inhaled produce definite, mild, and transient neuropsychopharmacological effects which are positively reinforcing and thus promote repetition of smoking. These effects include: (a) modulation of conditioned behavior; (b) mixed depression and facilitation of the neural substrates of reward; (c) transient (in minutes) EEG and behavioral arousal crudely reminiscent of d-amphetamine but pharmacologically quite different; and at the same time (d) skeletal muscle relaxation. Edward F. Domino, in Dunn (Ed.) Smoking Behavior: Motives and Incentives, 1973.

In addition to the four classes of neuropsychopharmacological effects cited by Domino, there has more recently been added a fifth class: modulation of unconditioned, innate aggressivity. Philip Morris, one can remark in passing, funded the research establishing this fifth class (R. Hutchinson at Fort Custer State Home, Michigan; G. Berntson at the Ohio State University; and Robert Waldbilling at Rockefeller University).

It is important to note that all of these effects are attributed to the action of smoke components on the central nervous system. It is also essential to know that it is the consensus of investigators that the reinforcement of the smoking act is the effect of smoke component action in the central nervous system. It behooves us, therefore, to seek an ultimate, explanation of cigarette smoking among the nicotine- or smoke component-related events of the central nervous system.

These effects can be studied in various ways. One way is to observe the post-treatment behavior of both animals and humans, such as we have been doing for some years with humans in the Behavioral Research Laboratory. Another way is to monitor treatment effects as they occur within the brain via the monitoring of the electrical activity of the brain. Such monitoring can be done in a passive, nonobtrusive manner by means of the electroencephalograph. This instrument is essentially an array of microsensitive sensors attached to a multi-channel recording device. EEG technology, combined with the analytic capabilities of the computer, now permits some localization of signal source and the differentiation of complex wave patterns into their simpler component elements. The smoke effects of EEG patterns were reported as early as 1958 (Hauser, H., et al., EEG changes related to smoking. Electroencephalography and Clinical Peurophysiology, 1958, 10, 576). Barbara Brown, in Dunn (Ed.) Smoking Behavior: Motives and Incentives, 1973, reviewed this literature.

The continually improving technology has recently led to the isolation of an intriguing wave pattern which appears to be the c.n.s. correlate of the psychological state of anticipatory alertness. This is a vaguely defined concept because of the difficulty of reducing it to operational terms. Attempts have been made to more accurately delineate the state by resorting to such terms as vigilance; arousal, readiness to respond, etc., but it has remained an elusive, though undeniably real variable in psychology. The identification of an observable and quantifiable correlate of this immensely important psychological factor is, indeed, a welcome development. This EEG phenomenon has been labeled the contingent negative variation (CNV). First observed by Walter Grey in 1964, the CNV has been found to occur most intensely in an expectancy situation (having been given an alerting signal, ready to respond to execution signal).

During the past two years Prof. John W. Thompson, and Dr. Heather Ashton at the University of Newcastle Upon Tyne have been observing the effects of smoking upon the CNV. At the Zurich Conference in September 1976 they reported observable, replicable changes in the CNV upon smoke inhalation and nicotine injection (papers available in manuscript form). They relate these changes to the subjectively reported stimulating and relaxing effects of smoking, but with speculative inferences. The association of smoking and CNV patterning appears to be real, but further study is needed. Judgmentally, however, the area has great potential for yielding up observations related to why people smoke cigarettes. The Research Center of B.A.T. in Southampton, England, has already established an EEG laboratory to study the relationship.

EEG research is not usually considered to be the domain of the psychologist. On the other hand, it is not the proprietary domain of any existing discipline. Psychologists are as prevalent, however, as any other specialists as users of the instrument, as they have pursued their investigations of sleep, dreaming, hypnosis, behavioral responses to exogenous agents, psychopathology, intelligence, learning, etc. It is inappropriate to think in terms of EEG research, except in those not so frequent instances of pure research into the nature of the phenomenon. More properly, electroencephalography should be viewed as a technology for monitoring otherwise unmonitorable events of direct psychological significance. Since we have already hypothesized a relationship between smoking and arousal (my paper at the Zurich Conference), and since the CNV is apparently the neural correlate of arousal, to initiate studies which entail the monitoring of the CNV seems mandated by our corporate and scientific responsibility.

Accordingly, we have in our plans for 1977 the creation of an EEG facility. The leading contender for the open position in the Behavioral Research Laboratory is a man specialized in the field, having already established two such units. He estimates the cost to be $35,000, this including the required dedicated computer. The required observation chamber with Faraday cage is already in service.

Charge Number: 1600
Project Title: Smoker Psychology
Period Covered: October 1–31, 1977
Project Leader: W.L. Dunn, Jr.
Date of Report: November 11, 1977

Project Title: Psychophysiology of Smoking
Written by: F.P. Gullotta

Initial data gathering has been completed in the study on the effects of cigarette smoking on heart rate. Statistical analysis is now in progress. Additional data will be obtained when the new experimental cigarettes which are being manufactured for Dr. Levy are received.

Project Title: Smoking and Learned Helplessness
Written by: C.J. Levy

Complete data have been collected on 41 subjects thus far. We hope to finish data collection by February.

Project Title: Smoking of Low Nicotine Cigarettes
Written by: C.J. Levy

We are still awaiting our new batch of cigarettes.

Project Title: Habit and Need Cigarettes
Written by: F.J. Ryan

Although nicotine intake appears a critical mainstay of tobacco consumption, not all people smoke for nicotine on all occasions. Many of a smoker's cigarettes are undoubtedly smoked to be sociable, to occupy his hands, to give him an excuse to rest, or for some other nonnicotinic reason. Such cigarettes are smoked not because of some internal cues triggered by the nicotine level in the smoker's body but because of the presence of external cues which have in the past been associated with smoking.

To the extent that these external cues tend to occur regularly in the smoker's day, many of his cigarettes will be smoked out of habit (i.e., will be conditioned responses triggered by external cues) rather than out of any nicotine need (i.e., will be conditioned responses triggered by internal cues). All these cigarettes contribute to the total nicotine in the system, so that a cigarette smoked out of habit will delay the time until a cigarette is smoked out of need.

When a smoker switches from a high nicotine cigarette to a low nicotine cigarette, or vice versa, it is the nicotine input of these habit cigarettes which makes it impossible for us to predict what changes in consumption will occur from our knowledge of the deliveries of the two products. If many cigarettes have been smoked out of habit, then the past nicotine intake may have been higher than needed, so that lowering delivery may still not lower it enough to cause extra cigarettes to be smoked. Similarly, if nicotine delivery is increased, because many cigarettes will continue to be smoked out of habit, the increased nicotine will not cause many fewer cigarettes to be smoked.

It stands to reason, therefore, that two groups of smokers—one which smokes many cigarettes out of habit and few out of need and a second which smokes few out of habit and many out of need—would respond differently to shifts in nicotine delivery.

To test the reasoning of this argument we are beginning a two-part project. The first seeks to distinguish those smokers who smoke many cigarettes from habit and few from need from their opposites. The second part will switch the two groups from high (or low) nicotine-cigarettes to low (or high) nicotine cigarettes. The smokers who smoke mainly from habit should show little or no compensation (titration), whereas those smokers who smoke mainly from need should show relatively more compensation.

Groups will be identified by the regularity with which critical stimulus situations elicit smoking—which means by the extent to which they are ''habit'' smokers. Nonhabit smokers will be assured to be ''need'' smokers.

Regularity of behavior will be evaluated from a diary kept by each smoker, showing the time of day when each cigarette was

smoked and the events taking place at the time. Nicotine intake will be determined from butt residues.

VCU students will serve as subjects, making regular visits to our Franklin St. quarters to leave butts and pick up cigarettes. We will seek as many smokers as possible, and then try to use the extremes to make up the two groups.

To: Dr. T.S. Osdene
From: W.L. Dunn
Subject: Behavioral Research Accomplishments—1977
Date: December 19, 1977

A Summary of 1977 Accomplishments

Making reference to the Plans and Objectives for 1977 as written December 1, 1976, we have succeeded some and failed some; happily more of the former than the latter.

Our successes: We have—

(1) Acquired a third principal researcher.

(2) Structured the group into three delineable programs each headed by a principal investigator.

(3) Established an EEG facility (to be fully instrumental during the first quarter of 1978).

(4) Moved aggressively into comparative behavior studies.

(5) Nearly completed an extensive study of learned helplessness.

(6) Reported the first run of the Annual Monitoring Program.

(7) Done an analysis of quitting as a function of brand last smoked.

(8) Shown that we can distinguish between regulator and nonregulator smokers and that after being deprived, the regulators do indeed try to make up for lost intake.

(9) Shown that acute, but not chronic, administration of nicotine will alter an animal's behavior consistent with the Berntson hypothesis that nicotine raises the pain threshold in rats.

(10) Gotten preliminary indications that we can use a nicotine/saline discrimination task as a tool for studying central nervous system mechanisms associated with smoking.

(11) Acquired a consultant.

(12) Completed a study of stimulus-seeking among introvert vs. extravert smokers.

(13) Completed a study of smoking effects upon learning nonsense syllables.

(14) Effected an arrangement with a university affiliated hospital for injecting nicotine in humans for discrimination studies.

Our failures: We have not (1) Developed a workable technique for unobtrusive monitoring of smoke inhalation patterns. (2) Obtained satisfactory batches of low nicotine and nicotine fortified cigarettes for a more definitive study of smoke intake regulation. (3) Carried out investigation of nicotine self-administration in rats. (4) Gotten completion reports of funded work by Dr. Robert Weldbillig. (5) Articulated the two-factor theory of smoking behavior.

Behavioral Research Accomplishments in Detail
Smoking and Learned Helplessness—Levy

Hiroto and Seligman (1975) have reported that college students who were subjected to inescapable loud noise or unsolvable discrimination problems showed deficits in performing subsequent tasks involving escape from loud noise or anagram solution; they were helpless.

Those experimental situations which are effective in producing helplessness are frustrating and stressful. We contend that smoking helps smokers cope with stressful situations; such that smokers perform better in high arousal situations than nonsmokers or deprived smokers. We therefore have hypothesized that smokers will be affected less by a situation devised to induce helplessness than nonsmokers or deprived smokers.

Before beginning data collection using smokers as well as nonsmokers, we conducted a series of pilot studies using approximately sixty nonsmokers. The purpose of the pilot studies was to verify that we could induce helpless behavior in our lab using local college students. As a result of the pilot studies, we modified our procedures considerably. In the final pilot study we had usable data on 23 subjects (12 males and 11 females). The results are summarized below:

Decandent Measures	Treatment	
	Helpless	Control
X Latency to solution (sac.)	47.5	[1] 28.9
X No. of failures to solve	6.3	[1] 4.1
X Trials to criterion	14.2	[1] 10.0

[1] <.05, one tailed t test

Subjects in the helpless group took longer to solve the anagrams, failed to solve more anagrams and ''caught on'' to the pattern later in the task when compared to the control subjects. Therefore, we were successful in producing a helplessness effect in our lab.

In March we began collecting data on smokers and nonsmokers and now have complete data on 43 subjects. We anticipate completing this study by February, 1978. One problem that has slowed data collection considerably is our requirement that subjects must score at least 115/150 on the Ammons & Ammons Quick Test (a short IQ test). In our pilot work we determined that this cutoff was necessary since subjects with poor verbal skills find it difficult to solve the anagrams used in this study.

Smoke Inhalation Studies—Levy & Dunn

During the past year we have been trying to devise a technique by which we can unobtrusively monitor smoke inhalation. Our initial attempt was to have Frank Watson's group construct a piece of equipment modeled after one described in a June, 1967, issue of *Science.* This apparatus sensed changes in the antero/posterior diameters of the rib cage and abdomen to estimate changes in lung volume. Unfortunately design problems forced us to abandon this approach.

In cooperation with Dr. Farone, we explored the alternative of using a mercury strain gauge to measure chest expansion during smoke inhalation. We found that chest expansion correlates quite well with volume of inhaled air (r=+0.95). We can improve this correlation by adding in a correction factor which takes the person's chest expansion just prior to inhalation into account. A major shortcoming of the strain gauge is its relative insensitivity.

Having not found a workable technique for monitoring smoke inhalation patterns unobtrusively, we called in Dr. Eli Fromm, a bioelectronics expert from Orexel University. Dr. Fromm proposed using an impedance pneumograph, involving pot-holder-like woven silver electrodes placed in sub-axillary positions on the chest. These electrodes are part of an impedance sensing electronic circuit. Previous work by Fromm and others had established that the volumetric changes associated with respiration altered the thoracic impedance. We have been unable to develop this technique to even an evaluative stage, since the voltage change, although discernible, has not been sufficiently distinguishable from background noise.

We continue to actively search for usable technology.

Regulator Identification Program—Levy

We have hypothesized that some people smoke for nicotine, and that these people try to obtain a relatively constant amount of nicotine from their cigarettes. On the other hand, people who do not smoke for nicotine would not be expected to regulate. We have been conducting studies to identify those people who are nicotine regulators among our smoking student population.

In our most recent study we wanted to determine if regulators and nonregulators would respond differently to smoke deprivation. After smoking high and low delivery cigarettes at home for two weeks, fifteen smokers came to our lab on four separate occasions. Each subject smoked the high and low delivery cigarettes under nondeprived and overnight deprived conditions. Based upon ''at home'' smoking data, 11 of the smokers were determined to be regulators, while 4 were nonregulators. When these subjects came to the lab and smoked under more controlled conditions, we found that 9 of the regulators obtained more nicotine from their cigarettes when overnight deprived than when nondeprived. On the other hand, only 1 of the 4 nonregulators responded to smoke deprivation by obtaining more nicotine from their cigarettes. Thus it appears that regulators and nonregulators do respond differently to smoke deprivation.

Smoking of Low Nicotine Cigarettes—Levy

We have been trying to obtain cigarettes made from denicotinized tobacco to use in a study which will look for changes in people's smoking behavior when they're shifted to a low nicotine cigarette, with tar delivery held constant. We plan to use a nicotine fortified cigarette made from denicotinized tobacco as our comparison cigarette. We have had problems in getting the nicotine level of the nicotine fortified cigarettes back up to normal.

As part of this study we are trying to see if smokers can easily discriminate the nicotine fortified cigarettes from the low nicotine cigarettes. Forty-eight R&O smokers compared two of these cigarettes, one delivering .40 mg nicotine and the other .87 mg nicotine. Over all smokers no significant differences were found between the two cigarettes. Only three smokers were able to identify unequivocally the nicotine fortified cigarette as producing more inhalation impact. We concluded that there were no dramatic organoleptic differences between these two cigarettes, even though the nicotine fortified cigarette delivered twice as much nicotine.

Nicotine as a Mitagator of Stress—Levy

During the past several months we have been looking at the effects of nicotine on post-stress learning deficiencies in rats. In one study using 24 rats we found that an injection of nicotine (.2 mg/kg) five minutes prior to a shock avoidance task in a shuttle box significantly increased the rats' latencies (in seconds) to cross the barrier if they had been stressed with a cold swim thirty minutes before. A control condition, identical to the experimental condition except for a warm rather than cold swim, produced no such latency difference. These results are consistent with Gary Berntson's finding that nicotine increases the pain threshold in rats as measured by the tail flick test.

In a second study we looked at the effect of chronic nicotine treatment on rats' shuttle box performance following cold swim stress. We had hypothesized that injecting rats with nicotine hydrogen tartrate (.5 mg/kg) four times daily for six weeks would enhance their ability to cope with stress. In order to test this hypothesis we chronically injected twenty-two rats with either nicotine or saline for six weeks. On test day six rats from each injection condition were stressed with a four-minute cold swim (2°C) and five from each injection condition were given a four-minute warm swim (28°C). Thirty minutes post-swim each rat was tested in a shock avoidance task. Rats that were stressed with the cold swim took significantly longer to cross the barrier in the shuttle box than rats

given the nonstressful warm swim. Rats chronically injected with nicotine that were stressed with a cold swim did not perform better than the saline injected cold swim rats. In addition, the behavior of saline- and nicotine-injected warm swim rats did not differ. Thus the latency effect produced by nicotine under acute conditions was not produced under chronic conditions.

Nicotine Discrimination Learning by Rats—Levy

During the past few months we have been exploring the feasibility of using a nicotine-saline discrimination task as a tool for studying the central nervous system effects of nicotine. To date, seven rats have been trained to discriminate a nicotine injection (.2 mg/kg) from an injection of isotonic saline. These rats are currently being tested with R-(+)=nicotine (.2mg/kg and 2 mg/kg) as the bartrate salt to see if the central nervous system effects of R-(+)-nicotine are similar to those of S-(−)-nicotine. Our data suggest that R-(+)-nicotine at a dose of .2 mg/kg is more like saline than S-(−)-nicotine. However, at a dose of 2 mg/kg the R-(+)-nicotine is similar to S-(−)-nicotine.

Another group of eight rats is currently being trained to discriminate nicotine (.4 mg/kg) from saline and will be tested using tobacco alkaloids such as anabasine and nornicotine.

The Annual Monitoring Study—Ryan

We completed first Annual Monitoring study, providing the baseline data with which later Monitoring studies will be compared. This research asked a large national panel (N–2711) to rate five cigarette models for strength and acceptability. The cigarettes tested had nominal deliveries of 5, 9, 16, 17, and 21 mg FTC tar, with commensurate nicotine values.

The 13 and 17 mg models had the highest acceptability ratings, the 5 mg model had the lowest acceptability rating, the 9 and 21 mg models being of near-equal, intermediate acceptability. The strength ratings increased with delivery, the 5 mg being rated weakest and the 21 mg rated strongest.

Of greatest immediate interest was the observation that relative acceptability was dependent on the delivery of the smoker's own brand. Thus, the ultra-low delivery brand smokers (Now and Carlton) gave high acceptability ratings to the lowest test brand, with systematically declining ratings to higher delivery brands; the Merit and Kent Golden Light smokers gave their highest rating to the 9 mg model, with systematically declining acceptability to the higher delivery models, and the full flavor smokers top rated the 19 mg model, with declining ratings to the lower delivery models.

It is impossible to decide from this single test whether smokers have assorted themselves into brand loyalties on the basis of preexisting tastes (i.e.—people who like weak cigarettes gravitate towards weak cigarettes by trying available brands until they meet one that fits their taste, while people who like full flavor sample until they end up with a full flavor brand) or whether having been smokers of a certain brand for some time for unspecified reasons they consider other deliveries less acceptable to the extent that they differ from their accustomed brand's delivery.

Stimulus Seeking Among Smoker and Nonsmoker Introverts and Extraverts—Ryan

We completed study of stimulation-seeking behavior among smoker and nonsmoker introverts and extraverts. The data suggest that nonsmoker extraverts seek more stimulation than nonsmoker introverts as Eysenck has suggested. It had been hoped that smoke extraverts would respond differentially when allowed to smoke and when smoke deprived, in that the effects of nicotine in the system would cut down on the smoker's need for external stimulation, but the differences were inconsequential. Whether allowed to smoke or deprived of smoke, the smoker extraverts sought about as much stimulation as the nonsmoker extraverts.

Smoking Effects Upon Learning Nonsense Syllables—Ryan

We completed study of effects of smoking low nicotine and moderate nicotine cigarettes on the learning of nonsense syllables and words. The data fail to substantiate the hypotheses that smokers would be worse than nonsmokers, or that smoking moderate delivery cigarettes would retard rote learning more than smoking low delivery cigarettes. The observed smoke differences are best attributed to chance.

A Theoretical Model of Cigarette Smoker Motivation—Ryan

We developed theoretical position relating total daily cigarette consumption to two types of stimuli: internal stimuli caused by deficits or surfelts of nicotine (or some unknown smoke components) and external stimuli which habitually trigger or inhibit smoking regardless of internal cues.

The adoption of this point of view by members of the staff will lead us to recognize that apparent failures of nicotine compensation model may not in fact be failures at all, and that nicotine compensation is a real phenomenon which is masked by the fact that smokers smoke many cigarettes out of habit rather than need. We began testing the theoretical model to determine the extent to which situational cues rather than nicotine need determine the smoking behavior of college students. This study is in progress.

Establishment of an Electroenceonalographic Laboratory—Gullotta

The major objective this year has been to set up a functioning psychophysiology laboratory. Setting up the physical work space was relatively easy, since it merely required the modification of the existing sound-attenuated chamber.

Selecting and acquiring the equipment is taking more time. A Grass model 780, EEG machine, with eight EEG channels and five polygraph channels was selected. This instrument will be capable of monitoring many physiologic functions including EEG, EMG, heart rate, respiration, temperature, etc. It is scheduled to be delivered in mid-January 1978. Grass has loaned us a machine for the interim. A research model photostimulator has also been ordered from Grass. It will be used in visual evoked response studies.

A techtranix-5111-storage-oscilloscope and a-C-5A ascilascope camera has been received. They will be used both for general laboratory procedures and to provide graphics for the computer system.

A computer system has been decided upon and ordered. After a great deal of investigation, thought and discussion, a Data General Micro Nova system was selected. It will be interfaced with the Level 6 and Sigma 9 systems and will provide the capability for planned investigations.

We have developed and obtained legal approval for an informed consent form. This was necessary in order to bring students into the laboratory for experiments involving psychophysiological monitoring.

Periodic trips to the EEG laboratory at MCV were undertaken to gain experience in recording the EEG patterns in humans. The staff at MCV has proven extremely cooperative and helpful in this regard. It is also anticipated that this source will be of potential use on future research projects.

To date, over twenty EEG recordings have been performed on approximately a dozen PM R&O employees as preliminary work.

A Heart Rate Study—Gullotta

This study was undertaken to assess the effects of two experimental cigarettes on heart rate. The two cigarettes were both denicotinized Marlboro-like blends, the experimental version having had nicotine citrate sprayed on before making. The control delivered approximately 0.3 mg and the experimental 0.7 mg of nicotine. Tar content and RTO did not vary.

R&D employees were used as subjects. In the experiment, they smoked the two experimental cigarettes and regular Marlboros. In addition, controls consisting of puffing on an unlit cigarette and not inhaling a lit cigarette were employed.

With 10 subjects, the heart rate changes were seen to be positively related to available inspired nicotine; the greatest increment occurred on smoking regular Marlboros, the least change occurred under control (no smoke) conditions and an intermediate change occurred with the 0.3 mg nicotine cigarette. Results with the 0.7 mg nicotine experimental cigarette were ambiguous. Additional data are being collected.

Exit Cigarette Brands—Ryan

Available data based upon the exit brand (last brand smoked) of people who have quit smoking (nonmenthol filter cigarettes within a year prior to being polled, suggest that the proportion of such quitters who smoked low delivery brands is about twice as great as the market share of those cigarettes would indicate.

Our data do not enable us to determine whether this means that low delivery cigarettes enable smokers to wean themselves from nicotine, or whether it means only that people who are concerned about their health (and so smoke low delivery, ''safer'' cigarettes) are more likely to quit smoking than are those who are *not* concerned about their health. The study, rather than providing answers, prompts us to ask more specific questions.

Acquisition of a Behavioral Research Consultant

Prof. Gary Berntson of Ohio State University has become affiliated with our program as a consultant. Prof. Berntson's own research program has been partially funded by PM R&O for several years.

Other Extra PM Work Promoted by PM R&O

(A) Dr. Rosecrans at MCV—With protracted intervals between steps, we reached the point in November of granting a nominal sum of money to underwrite a study of human ability to discriminate between nicotine and no-nicotine bodily states. The delays have resulted from the reluctance of the MCV Ethics Committee to approve the infection of nicotine in human studies. The initial study will be of smoke inhalation where control and experimental cigarettes are minimally distinguishable organoleptically although differing in nicotine deliveries.

(B) Prof. Bernston at Ohio State—With supportive PM R&D funding, this investigator has completed two studies in 1977. He reported to the Annual Meeting of the Psychonomic Society that nicotine (O. 16–0.50 mg/kg) greatly reduced pain sensitivity to thermal stimulation in the rat as measured by the tail-flick test and the hot-plate test. This finding and preliminary findings of other studies suggest that nicotine may selectively reduce visceral pain without reducing somatic sensitivity.

Prof. Bernston has obtained authorization by the Ohio State University Ethics Committee to pursue this line of investigation

with humans, with implicit approval to inject nicotine. We are requesting that he conduct the nicotine discrimination work originally discussed with Rosecrans, in view of his capability of injecting nicotine in humans.

In a study with cats he found evidence that the basic sensory sensitivity of the animals remained unaltered by nicotine, as well as their motor responsivity, such that previously reported changes in aggressivity induced by nicotine now appear more clearly to be centrally mediated.

(c) Or Kazlowski at Wesleyan-University—This investigator reported completion of a study partially supported by PM R&D funds (1976) in which he observed no changes in puffing behavior as a function of experimentally induced changes in buccal pH.

To: Dr. T. S. Osdene
From: J. I. Seeman
Subject: Nicotine Program
Date: March 15, 1978

This summary and evaluation represent the cumulative influences of a number of discussions with Carolyn Levy and Ted Sanders and myself. However, these conclusions may not in every respect correspond directly to the ideas of CL and TS.

An effective nicotine program must include both peripheral and CNS bioassays. The former are being preferred under contract, and we must await the full reports before being able to make conclusions either about the results or the testing program itself. It is clear that CNS studies represent the most complex, state-of-the-art concepts. Ultimately, the isolation and characterization of the nicotine CNS receptors are the major goal. Many steps must come first. These include (1) pharmacological location of sites of nicotinic action using both cannulae and various tissue sections; measurement of electrochemical activity following drug administration; (3) various techniques including photoaffinity labeling and binding studies as aids at receptor isolation (4) receptor identification and characterization (against and antagonist activity).

Currently, Abood has begun work involving a ''prostration syndrome.'' He is initiating synthetic work aimed at preparing suitable photoaffinity labels. Goldstein, at the present, has not applied his ''bag of opiate tricks'' in the nicotine area and is doing only T-maze behavioral studies. He is unquestionably going to pursue the nicotine-receptor question vigorously.

Ultimately, we and others (perhaps we have not considered in detail ''the others'' except for Abood and Goldstein) will be successful in the ''steps.'' What can be requested at the present in terms of ''outside help'' is clearly limited by what is available.

I believe that we should rely on C.L. for all behavorial studies. This will undoubtedly require more rats and testing equipment. However, the behavorial work is key to the testing program.

Binding studies with DeVries at MCV can be initiated. He is currently interested in a variety of nicotine CNS receptors. Metabolism work which Castagnoli would give use information with respect to biological stability of any analogues.

For the present, I cannot believe that ''we should cancel'' any opportunities with Goldstein who is clearly by-far the most sophisticated experimentalist and theoretician of the outside investigators. I have some suggestions relative to our initial response to his current request for materials.

In summary, I believe that the key note in this memo is that we must devise not a shopping list for todays needs but a policy for the program as a whole.

To: Dr. T. S. Osdene
From: J. I. Seeman, C. J. Levy, and E. B. Sanders Nicotine Program: Specific Implementations
Date: March 31, 1978

The memo of March 21, 1978 to you from us outlined in detail the long-term nicotine program, including sections on (a) receptor isolation, identification and characterization; (b) pharmacokinetics; (c) CNS testing (behavorial aspects); (d) peripheral bioassays; (e) synthetic organic chemistry; (f) chemical property evaluations; and (g) smoking studies.

The purpose of this memo is to specifically detail the additional experiments needed in the immediate future, with the assumption that projects already in progress will continue at their present rate.

A. CNS Behavorial Testing

Nicotine discrimination, self-administration and tolerance studies will enable us to examine the cueing and reinforcing properties of nicotine and nicotine analogues in rats. These are the state-of-the-art biossays for central nervous system activity which we believe will serve as useful models of human smoking behavior. Implementation will require an additional 400–500 sq. ft. of laboratory space for animal housing and testing facilities, one-half technician, one B.A. professional, and $15,000–20,000 of capital expenditure for housing and testing purposes.

T. S. Osdene
Nicotine Program: Specific Implementations
March 31, 1978
Page 2

B. Molecular Basis of Nicotine Pharmacology

We must begin to gain expertise in experimentation dealing with nicotine receptor technology. Initial studies will involve the determination of nicotine and nicotine analogue binding with various biological membranes. Studies of this type are currently being performed at a number of academic institutions. For example, Prof. George DeVries has contacted us suggesting a possible collaboration along these lines; he will conduct the biological studies on our nicotine analogues. In this particular case, no request for financial support has been made. It is possible that other collaborations may require such aid. We suggest initiating these experiments on a modest scale through the aid of outside collaborations. Should results be particularly interesting and important, we can then consider in-house experimentation.

C. Nicotine Analogue Preparation and Chemical Evaluation

This work involves the preparation of the analogues and physical and chemical evaluation of their properties. Significant continued reliance on the Analytical Division is necessary, and in certain areas, increased responsibilities by them will be necessary. A.B.S. professional is necessary to serve as back-up to this work.

Please note that surgical procedures will be required for certain of the behavorial studies.

It is important to reemphasize that better communications with the peripheral bioassay evaluation group in Germany must be established, and that shorter response time for our questions and our bioassays is essential. Additional and/or replacement bioassays must be required by this group.

Finally a decision with regard to collaboration with Dr. Abood is in order.

RESEARCH AND DEVELOPMENT FIVE YEAR PLAN—1979–1983

September 1978

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IV. Fundamental studies of the product and its users

Fundamental research at R&D consists of long-range investigations aimed at discovering basic scientific principles about the nature of our product, its components and its users. We seek essential knowledge which can be applied to the practical problems of cigarette design.

Objectives	Strategies
To extend our knowledge of nature of tobacco and smoke.	Continue to study the precursor/product relationships in tobacco and smoke Analyze the chemical interactions of smoke on physiological systems Study the relationship of cigarette paper composition to smoke delivery, principally carbon monoxide and nitrogen oxides Continue to study smoke flavor and how to manipulate it to achieve desired subjective response Investigate tobacco characteristics that affect expandability Refine analytical methods for tobacco and smoke components, using the most advanced instrumentation possible
To extend our knowledge of the nature of water in tobacco.	Evaluate changes in tobacco expandability and filling power as a function of moisture-absorbing utility
To extend our knowledge of the nature of combustion and pyrolysis.	Refine models of cigarette combustion Apply cigarette combustion and pyrolysis models to the design of cigarettes
To control gas phase constituents ...	Continue research on control of gas phase constituents including carbon monoxide, nitrogen oxides, hydrogen cyanide, and acrolein Learn more about smoke aerosol and how to manipulate it to improve product quality
To identify the smoke components sustaining cigarette smoking and describe the motivational mechanism.	Monitor changes in smoking behavior as a function of changes in the composition of smoke

We will continue to coordinate multidisciplinary research to determine the role of water in tobacco filling power. Specifically, we hope to learn how to manipulate the water in tobacco in order to change and control filling power. Emphasis will be placed on water exchange processes which occur in ordering, reordering and expansion. Information developed from this program will be applied to improve the economics of our manufacturing processes.

In our program on cigarette pyrolysis and combustion, we seek knowledge which will contribute to the design of cigarettes with controlled delivery. We are investigating the mechanics of how specific compounds are formed in smoke. Experiments are being conducted in the kinetics of smoke generation as a function of the physical and chemical properties of the cigarette.

We have recently intensified investigations of the physical and chemical properties of smoke aerosol. This work is relevant to filtering specific tar elements and modifying subjective response to smoke. By altering filter geometry, we have noted a change in subjective response without changing tar delivery. We will continue to explore ways of changing filter design and hence the pattern of mainstream smoke.

Nicotine may be the physiologically active component of smoke having the greatest consequence to the consumer. Therefore, we are studying the differences in physiological effects between nicotine and its analogues to determine the mode of nicotine action. If acquired, this knowledge may lead to a substance which will produce the known desirable nicotine effects and greatly diminish any physiological effects of no benefit to the consumer.

Fundamental Studies of the Product and Its Users (continued)

[From Philip Morris, Richmond, Virginia]

To: Dr. T.S. Osdene
From: W.L. Dunn

Subject: Plans and Objectives—1979
Date: December 6, 1978

All of the effort of the Behavioral Research Laboratory is aimed at achieving this objective: To understand the psychological reward the smoker gets from smoking, to understand the physchophysiology underlying this reward, and to relate this reward to the constituents in smoke.

The rationale for the program rests on the premise that such knowledge will strengthen Philip Morris R&D capability in developing new and improved smoking products.

In pursuit of this knowledge, three somewhat independent lines of investigation are underway:

1. The effects on nicotine and nicotine-like compounds upon animal behavior.

2. The effects of smoke and smoke constituents upon the electrical activity in the human brain.

3. The effects of changes in smoke composition upon puffing behavior, inhalation behavior and descriptive statements by the smoker.

Animal Behavior Studies (Levy, Young and Rowsey)

A major objective of the comparative research effort is to develop behavioral tests which are sensitive to the effects of nicotine and can be used to screen nicotine analogues for central nervous system (CNS) activity. The studies which aim to meet this objective as well as the objective of learning more about the reinforcing properties of nicotine are described below.

1. *Nicotine Discrimination*. In this test rats are trained to discriminate nicotine injections from saline injections based upon the CNS effects of the injections. We have been using this test to screen a variety of nicotine analogues and plan to continue doing so during 1979. This test is important because it allows us to determine if test compounds produce cues (subjective effects?) similar to those of nicotine.

2. *Tail Flick*. Nicotine has been shown to have analgesic properties as measured by the tail flick test, and apparently this effect is centrally mediated (Sakley and Berntson, 1977). We have completed some tests using this procedure and will continue doing so in an effort to determine if it can be used as a preliminary quick and objective screen for analogues.

3. *Monitoring of Motor Activity*. Stolerman, Fink and Jarvik (1973) have reported that the depression of spontaneous locomotor activity can be used to monitor the development of tolerance to nicotine in rats. We plan to explore the feasibility of using a similar test to screen analogues for nicotinic activity and also to evaluate cross tolerance between nicotine and nicotine analogues.

4. *Prostration Syndrome.* A prostration syndrome in rats has been described by Abood, Lowy, Tometsko and Booth (1978) which appears to be mediated by central noncholinergic nicotinic receptors. This simple behavioral response is elicited by the intraventricular administration of 2–10 μg of (−) nicotine bitartrate. We plan to implant rats with cannulae in the lateral ventricles and then inject a variety of nicotine analogues into the brain to determine if they elicit the prostration syndrome.

5. *Nicotine Self-Administration*. A few recent studies have demonstrated that intravenous nicotine is reinforcing to rats since they can be taught to self-administer it. (Hanson, Ivester and Morton, 1977; Lang, Latiff, McQueen and Singer, 1977). We plan to replicate these studies to determine a) if this behavior can be blocked by cholinergic antagonists, b) if it is dose-responsive and c) if it will extinguish rapidly when saline is substituted for nicotine. We feel that this paradigm may be a useful animal model of human smoking behavior.

6. *Rat EEG.* If time permits, we plan to collect some preliminary data in which the dependent variable will be the rat's ongoing EEG activity. The purpose of this type of study will be to a) compare the effects of nicotine on the rat and the human brain and b) determine if we could use data of this type to evaluate the nicotinic properties of nicotine analogues.

Electroencephalographic Studies (Gullotta and Spilman)

The major objective of all of the studies to be conducted in the neuropsychology laboratory is to understand the interrelationships between cigarette smoking and the human brain. In so doing, we hope to further elucidate how and why people smoke. The studies outlined below are directed toward achieving these goals.

1. *The Effects of Cigarette Smoking on the Early, Late and After-Discharge Components of the Visually Evoked Response.* To date data accumulation is approximately eighty percent completed. We should finish running subjects in January. Statistical analysis of the results will be a lengthy process, but it is anticipated that the analyses will be completed by the end of the first quarter of 1979. A completion report will be written at that time.

2. *A Search for Other Evoked Responses which are Sensitive to Cigarette Smoking.* We wish to identify a number of dependent measures which change following cigarette smoking. Evoked responses seem to be a fruitful area of research. The precise nature of the research we will engage in will depend on the results of the current VER study; however, three avenues of investigation seem likely:

A. *Visually Evoked Responses from Association Cortex*. We are currently studying VERs recorded from the primary sensory cortex. However, VERs may also be recorded from other areas of the brain, including the ''association cortex.'' Evoked responses recorded from association areas are particularly sensitive to and modifiable by behavioral variables such as attention, learning and cognition. Since cigarette smoking has been suggested to influence these variables, association VERs might provide important information about the neuronal circuitry involved.

B. *The Auditory Evoked Response.* The evoked response to pure tones delivered to the auditory system is quite sensitive to pharmacological intervention. Several studies on the effects of cigarette smoking or nicotine administration on the AER has been done, but the results are ambiguous. Some researchers find no changes in AERs following smoking or nicotine administration, whereas others report decreases. It is important to know whether and how this measure is influenced by cigarette smoking.

C. *The Somatosensory Evoked Response.* Very little evidence exists regarding the effects of cigarette smoking or nicotine administration on the somatosensory evoked response to either electrical or vibratory stimulation. This response, however, seems to be very sensitive to many classes of pharmacologic agents and behavioral states. It is possible, therefore, that the SER might be a very responsive index of cigarette smoking.

3. *The Effects of Cigarette Smoking on the Electroencephalogram.* Numerous studies have shown that both cigarette smoking and nicotine administration result in EEG activation, followed at various intervals, by EEG synchronization. However, those studies employing cigarette smoking as the independent variable have certain methodological shortcomings which need to be rectified. We propose replications of these studies using more appropriate controls.

4. *Long-Term Smoke Deprivation and the Electrical Activity of the Brain*. In terms of the electrical activity of the brain, there can be little doubt that smokers and nonsmokers are very different. It is also true that the brains of deprived smokers are quite different from the brains of both nondeprived smokers and nonsmokers.

Were the brains of smokers always different from nonsmokers, or did the brains change in some fashion following experience with tobacco? These are difficult questions to answer. Yet, some insight into these questions might be gained by a study which followed quitters over long intervals. Such a study would necessarily be a long-term longitudinal endeavor. We would need to solicit volunteers who were intending to quit, accumulate prequitting baseline CNS measures, then restudy these individuals periodically for as long (within reason) as they remain quitters.

5. *A Comparison of Three Routes of Nicotine Administration on Physiologic Function.* We have discussed this study with Dr. Arthur Ryan and he has agreed to lend us the medical personnel necessary to carry out this study. In addition he has agreed to be available for consultation as needed.

In essence, this study involves a comparison of three different methods of nicotine administration: inhalation, ingestion, and intravenous injection. The dependent measures would probably be the EEG, VER, heart-rate, blood pressure, and blood nicotine levels. A small group (five or six) of subjects will be used and will be brought into the laboratory between six and eight times. Dependent variables will be measured prior to and at several intervals, subsequent to nicotine administration.

This experiment should help answer several important questions. For example, what is the relationship between blood nicotine levels and CNS activity? How soon following a given method of nicotine administration are effects seen in the CNS, and for how long? How are the human studies employing cigarette smoking similar to or different from animal studies employing nicotine injection?

Smoking Behavior Studies (Ryan and Eaust)

The focused objective of this area of study is to relate the intake of nicotine and its presence in the body to the occurrence of other behaviors, including subsequent smoking behavior.

Question 1. *To what extent is the presence of nicotine in smoke detectable by smokers?* To answer this question we need to conduct two types of studies and make two types of measurement. The study types will be (A) an absolute threshold study, in which smokers will be given ''nicotine-free'' and very low nicotine cigarettes and asked whether they contain nicotine. The subjects' ability to verbalize the presence of nicotine is the first type of measurement. As a second type of measurement we will look for a change in heart rate (HR), which is customarily associated with nicotine intake in most deprived smokers. It is possible that there would be a physiological (HR) effect at a level different from the level at which verbalization takes place.

Study (B) will be a difference threshold study, in which we try to find how small an increment (or a decrement) of nicotine in smoke can be detected as an increase (or a decrease) by the smoker. If the just noticeable difference (JNO) is small, the nicotine delivery of cigarettes may be expected to play a more important role in the evaluation of cigarette acceptability than if the just noticeable difference is large. Again we will

make 2 types of measure—subject ratings that this cigarette has more nicotine than that cigarette, and a monitoring of heart rate. The heart rate changes should not be important in this case, for the subjects will be getting nicotine from each cigarette. However, we may see differential HR increases while smoking the first of the two cigarettes being compared.

Question 2. *To what extent is the ability to detect the presence of nicotine in smoke masked by other smoke components?* There are three ways to answer this question: One is to present the nicotine without the smoke, a second is to hold the nicotine delivery constant while varying the quantitative amount of other smoke components (e.g. FTC tar), and the third is to add qualitatively different smoke components (e.g. menthol or anise flavoring). Since all three approaches involve novel manipulations in the smoke (aerosol) delivered to the smoker, we anticipate that the year's efforts devoted to this question will be consumed in the experimentation required to develop the cigarettes.

Question 3. *To what extent does the presence of detectably more or detectably less nicotine in smoke affect the acceptability of low delivery cigarettes?* This question is related to the optimal nicotine/tar ratio, a problem we have addressed before at higher delivery levels. Implicit in the second question was the assumption that nicotine's effect may be different at different tar deliveries, for its detectability is expected to be different depending upon the masking effect of the tar borne flavors. Consider the following table of 85 mm brands arranged by FTC tar delivery:

Product	Nicotine	FTC Tar	Nicotine/ Tar
Carlton	.20	1.5	.125
Now	.22	1.8	.122
True	.44	4.8	.092
Decade	.45	4.9	.092
L&M	.64	7.4	.086
Tareyton Light	.71	7.6	.093
(Kent) Golden Light	.71	7.7	.092
Spirit	.90	8.0	.112
Merit*	.66	8.3	.080
Viceroy Xtra Mild	.86	9.1	.095
Real	.87	9.1	.096
Raleigh Lights	.86	9.2	.093
Parliament*	.78	9.3	.084
Camel Light	.97	10.0	.097
Vantage	.87	10.7	.081
Marlboro Light*	.82	11.4	.072
Kent	1.04	12.6	.083
Winston Light	1.11	13.5	.082
Doral	1.13	13.8	.082
L&M	1.01	14.7	.069
Tareyton	1.01	14.8	.068
Raleigh	1.02	15.6	.065
Lark	1.26	17.4	.072
Marlboro*	1.12	17.8	.063
Camel	1.38	18.8	.073
Winston	1.41	19.6	.072

The table suggests that Philip Morris brands (asterisked) have *lower* nicotine/tar ratios than do other brands with about the same FTC tar delivery. Marlboro has the lowest ratio on the list, Marlboro Lights has the lowest ratio among brands delivering less than 14.0 mg tar, and Parliament has the second lowest and Merit the lowest ratio among brands delivering less than 10 mg tar. The table also suggests that nicotine/tar ratios go up as tar goes down, and that our competitors' brands such as Golden Light, Now and Spirit (in test market) seem to be higher in nicotine delivery than we would otherwise expect from our own experience with low delivery cigarettes. The reason for the low PM ratios seems to lie in tobacco processing procedures. The reason for the high ratios at low tar may be that high efficiency filters catch relatively more tar than nicotine when compared to low efficiency filters, and that this effect is enhanced by air dilution. We suspect that in some cigarettes the use of high alkaloid blends may also be an important contribution to the higher ratios.

It appears therefore that the mechanics of cigarette engineering and the deliberate decisions of our competitors are such as to suggest that *high* nicotine/tar ratios be used at ultra low tar levels. But traditionally our brands have been successful with *low* ratios. Whether this will bear true at a very low FTC tar delivery as it has been heretofore at higher deliveries, we do not know. We have heard some people suggest that low tar cigarettes may need nicotine supplements to be rated acceptable. On the other hand, we have heard others suggest that people who smoke low tar products want as little tar and nicotine as they can get, which suggests that a *low* nicotine/tar ratio might be preferred. Still others feel that ratio size won't make any difference at all, that ''all you have to do'' is get the smoker accustomed to a cigarette and he'll come to call its characteristics his preferred characteristics.

To shed further light on this problem we will evaluate low delivery experimental cigarettes in the 5–7 mg FTC tar range but with nicotine levels which are discernibly higher than, equal to, and lower than the typical level expected of cigarettes in this range (which would be .53 mg). To determine how much higher or lower we must go, we'll consult the results of the JNO study and the absolute threshold study.

One of the reasons for conducting the JNO study now becomes apparent, for it would make no sense to ask smokers whether they preferred cigarette A or cigarette B if A and B could not be told apart.

Question 4. *Tar delivery being the same, what are the behavioral consequences of smoking low nicotine rather than high nicotine cigarettes?*

This question will be answered by conducting a series of shift studies using cigarettes of similar low tar but differential nicotine deliveries. The low nicotine delivery will ensure that total nicotine in the system remains at or near the nicotine need threshold, thus maximizing the proportion of the day's cigarette consumption which is smoked out of need and minimizing the nicotine augmentation from those cigarettes which are smoked out of habit.

The results may shed light on the manner by which nicotine control is achieved.

Question 5. *To what extent do ''mouthfeel'' factors affect the taste and acceptability of cigarettes?* We begin to answer this broad question by asking a narrower one: To what extent does salivation affect the taste of cigarettes?

We ask the question because low tar triers often complain that low tar products taste ''hot and dry.'' This may mean that the smoke is in fact hot and dry, but it is more likely to mean that the smoker's mouth is hot and dry—which suggests that salivation could affect the sensation.

We will investigate this by sampling the saliva quantity present in the mouth during and after smoking cigarettes of differential delivery. Both nonmethols and menthols will be used as it is possible that menthol may affect salivation.

If saliva flow is found to be relatable to delivery, then we can investigate compounds which may counter the effect.

Annual Monitoring Study. We have twice presented a large national panel with five widely differing types of cigarettes to be rated on acceptability, seeking to find whether low delivery cigarettes are becoming more acceptable. So far the evidence, based on the changes from 1977 to 1978, is slim. We will repeat that test in the spring of 1979, examining changes since '78 and since baseline data in '77.

Diary Study. We will finish our first diary study during January, '79. Only data analysis and final writing remains to be done. It is possible that we will employ this technique again, but with fewer subjects selected from a nonstudent population.

Inhalation Studies (Dunn)

We have failed to find convincing evidence of regulation of smoke intake when observing number of cigarettes smoked, puffing patterns, etc. Nor have we found such evidence when looking at inhalation measures in the laboratory. Nevertheless there are compelling reasons to suspect that the smoker does accommodate his smoking behavior to smoke composition. We suspect that the regulation occurs in inhalation patterns and that the regulation was obscured by the laboratory conditions under which we made our earlier observations. We did, in fact, establish that the smoker has great latitude in altering intake at the inhalation level. Inhalation is the final volitional act whereby the smoke is transported from the mouth to the site where smoke constituents cross the tissue barrier to enter the bloodstream.

Our working hypothesis remains that the smoker does alter inhalation in response to cues of smoke composition and that these alterations can be observed under natural smoking conditions if recording procedures are made sufficiently unobtrusive.

Our objectives for 1979 are two-fold:

1. To complete development of an electronic recording device for continuous, unobtrusive monitoring of smoke inhalation (collaborative with Electrical Engineering).

2. To apply the recording device to the investigation of smoke inhalation patterns and those variables which influence them.

We have established the following criteria to be satisfied before the device is judged acceptable:

1. Measures are demonstrated linear within operating range.

2. Measures can be calibrated with spirometer.

3. Baseline drift over 6 hr. period controlled or compensated.

4. Extraneous variables controlled.

5. Monitoring can run continuously for 6 hours.

6. Body movement error minimized and residual effect randomized.

7. Smoke laden inhalation peak is labeled.

8. Obtrusiveness judgementally not distorting smoking behavior.

We will initiate the following sequence when the device becomes available:

Preliminary Exercises

Procedural refinements and development of criteria for subject's habituation to device.

Study 1 (N=4)

Establish Smoker's Inhalation Profile in terms of:

1. Inhalation volume
2. Retention time
3. Depth (Volume/Vital Capacity)
4. Σ daily inhalation volume
5. Puff interval
6. cigarette interval

Study 2 (N=4)

Investigation of state variables influencing profile parameters:

1. Heart rate
2. Heart rate Δ
3. Preceding cigarette interval (controlled and uncontrolled)

Study 3 (N=4)

Inhalation profile changes as a function of smoke composition changes:

1. Nicotine varied—tar constant
2. Tar varied—nicotine constant

To: Dr. T.S. Osdene
From: W.L. Dunn
Subject: Plans and Objectives—1980
Date: January 7, 1980

In our 1979 Plans and Objectives report we stated that there were three somewhat independent lines of investigation underway. These were:

1. The Comparative Psychology Program—Studies of the effects of nicotine and nicotine-like compounds upon animal behavior.

2. The Electroencephalography Program—Studies of the effects of smoke and smoke-constituents upon the electrical activity of the human brain.

3. The Experimental Psychology Program—Studies of the effects of changes in smoke composition upon puffing behavior, inhalation behavior and the judgmental statements of smokers reacting to those changes.

These three programs are being continued through 1980.

We are adding a fourth area of investigation this year:

4. The Social Psychology Program—Studies of cigarette smoking as a psychosocial phenomenon. Sandra Dunn, Ph.D., Research Psychologist, will be responsible for this new program.

Our aim in this new program will be to contribute to the understanding of how cigarette smoking and the social process influence one another. We will be interested, for example, in how social change effects changes in the behavior, attitudes and self-perception of the smoker, and how, conversely, cigarette smoking can have psychosocial consequences through its manifest involvement in the social situation, and also through its central-nervous-system-mediated effects upon the coping abilities of the smoking social participant.

Details of the three original lines of investigation follow. It is premature to set down concrete plans for the social psychology program. Our initial efforts in 1980 will be to formulate those plans.

I. The Comparative Psychology Program—Levy Replacement, Carron and Allen

The two major objectives of the comparative psychology program are 1) to develop and use animal behavior tests to screen nicotine analogues and 2) to learn more about the reinforcing properties of nicotine. Studies designed to meet these objectives are described below.

Nicotine Discrimination

In this test rats are trained to discriminate nicotine injections from saline injections based upon the CNS effects of the injections. We have been using this test to screen nicotine analogues and plan to continue doing so during 1980 because it has proven to be an extremely sensitive and reliable test.

Tail Flick

Nicotine has analgesic properties as measured by the tail flick test (Sahley and Berntson, 1977). We have done extensive testing of (−)- and (+)-nicotine using this test. Unfortunately the data were highly variable due to the rats' severe agitation after the nicotine injections. During 1980 we plan to administer nicotine and nicotine analogues intraventricularly in an effort to obtain more reliable data.

Prostration Syndrome

A prostration syndrome in rats has been described by Abood and his coworkers (1978). This response is elicited by rapid intraventricular administration of 2–10 μg of nicotine. We have begun to routinely administer nicotine and nicotine analogues intraventricularly and to rate the resultant prostration. During 1980 we plan to continue using this test to screen analogues. In addition we plan to begin video taping the test sessions, and (in collaboration with F. Gullotta) record from the dorsal hippocampus during testing.

Place Preference

Mucha and Van der Kooy (1979) have reported that a place preference paradigm may be used to demonstrate the rewarding properties of morphine. We plan to use a similar paradigm to examine the rewarding effects of nicotine. Rats will be given nicotine injections in one distinctive environment and saline injections in another distinctive environment for several days. Following this training procedure, the rats will be given a choice between the two environments, and the time they spend in each will be the dependent variable. If the rats spend more time in the environment paired with the nicotine injections, this will suggest that the nicotine was reinforcing to them.

Nicotine Self-Administration

If the reinforcing properties of nicotine cannot be readily demonstrated using the place preference paradigm described above, we will try to get rats to self-administer nicotine through indwelling intravenous catheters using a procedure similar to that of Hanson and his coworkers (1977). If we are successful if getting rats to self-inject nicotine, we plan to determine a) if this behavior can be blocked by cholinergic antagonists, b) if it is dose-responsive and c) if it extinguishes when saline is substituted for nicotine.

II. Electrophysiological Program—Gullotta and Frankovitch

We hypothesize for this program that the smoking act is perpetuated by the salutory effect of smoke inhalation upon certain discrete as yet unspecified neural functions. We take as a premise that the effect will be present and observable in the EEG correlates of these neural functions. Our objectives in all of the following proposed studies therefore are to determine 1) if the effect is discernible in any of the various monitorable EEG patterns and if so 2) whether further knowledge of the nature of the effect can be inferred from its EEG manifestation.

Auditory Evoked Potentials and Cigarette Smoking

This study was begun in late 1979 and should be competed during the first quarter of 1980. It was initiated by reports in the literature which suggest that both nicotine administration and cigarette smoking may influence auditory evoked responses.

In a study using cats as subjects (Guha & Pradhan, 1976) it was found that low doses of nicotine enhanced auditory EPs, while high doses depressed them. In a study using humans as subjects (Friedman, et al., 1974) it was found that cigarette smoking tended to depress auditory EPs. It is extremely important to further investigate the effects of cigarette smoking on auditory EPs. If cigarette smoking does, in fact, depress auditory EPs, this would imply that nicotine has selective effects on the CNS (recall that several reports have indicated that cigarette smoking enhances *visual EPs*).

Cigarette Smoking and the Standard Electroencephalogram

Numerous studies have shown that both cigarette smoking and smoke deprivation affect the EEG. Cigarette smoking results in EEG changes associated with arousal, while smoke deprivation results in the high amplitude, low frequency waves associated with drowsiness.

The EEG studies that have been reported thus far generally fail on one or two accounts. First, most studies have only examined EEG changes occurring over very few cortical areas. Second, the majority of these studies have used rather crude data analysis techniques.

As part of our ongoing program, we have placed electrodes over central, posterior and temporal brain areas and have recorded ongoing EEG activity. We are now in the process of developing a spectral analysis program, which will allow us to perform power spectral density analyses of ongoing EEG data from a number of brain loci under varying conditions of smoking and smoke deprivation.

Central Gating and Cigarette Smoking

Cigarette smoking appears to have opposite effects on visual and auditory evoked potentials. While visual EPs are enhanced by smoking, auditory EPs appear to be depressed. First, nicotine, rather than being a general stimulant, may be exerting a selective influence on brain structures. Second, perhaps nicotine somehow participates in the gating of information by the brain. This gating phenomenon was eloquently demonstrated in 1959 by Hernandez-Péon and has been often replicated. It could be that visual EPs are enhanced at the expense of auditory EPs.

It is possible that cigarette smoking (via nicotine) allows for selective attention in the visual mode by damping input from other sensory modes. We propose to investigate this possible relationship by using cross-modal evoked potentials. Visual and auditory EPs will be recorded in the same experiment, while attention is varied by instructional set.

Cigarette Smoking and Learning by the Brain

A number of studies have shown that cigarette smoking may facilitate certain types of learning. The mechanisms by which this facilitation is accomplished remain to be clarified. The following study may shed light on this problem.

When a dim flash of light is presented to a subject, an evoked response is recorded over specific visual projection areas. No responses are recorded from the auditory cortex. If, however, the dim flash of light is repeatedly paired with a tone, an evoked response to the flash alone will gradually develop at the auditory cortex. This type of learning is called classical conditioning and it is the fundamental building block of many ''higher'' forms of learning.

We propose to study the effects of cigarette smoking on the rate at which an EP develops at the auditory cortex to light flash. If smoking accelerates the rate at which conditioning occurs, these data would help explain why smoking facilitates certain types of learning.

Cigarette Smoking and Somatosensory Evoked Potentials

We have two reasons for wanting to investigate the effects of cigarette smoking on somatosensory evoked potentials. First, we wish to find out whether smoking influences this response. No literature currently exists on this topic. Any data gathered would increase our understanding of how cigarette smoking influences brain systems mediating behavior. Second, and more importantly, we wish to investigate the proposed analgesic properties of nicotine.

Animal studies from our laboratory (Levy) and other (Berntson) suggest that nicotine may have analgesic effects on certain types of pain. Analgesics affect somatosensory EPs in known ways. If cigarette smoking influences these EPs in a similar fashion, this would be correlative evidence for cigarette smoking possessing analgesic properties in humans.

III. The Experimental Psychology Program—Ryan and Jones

Objective 1: To gain better understanding of the role of nicotine in smoking.

First Approach: To further evaluate the smoker's ability to detect nicotine differences among cigarettes.—The first phase

of this research was conducted in 1979, when we found that 9 of 10 smokers could detect nicotine differences (at 6 mg tar levels) if nicotine deliveries differed by 50%. In the second phase of this research we will extend the investigation to cigarettes at the 12 and 17 mg tar levels. These cigarettes have been ordered and should be made in January. We are looking into the possibility of a third phase, in which nicotine detectability is examined at near zero tar levels.

Second Approach: Examine smoker preference for nicotine delivery in very low tar cigarettes.—The first phase of this project consists of having consumers rate the strength and acceptability of 6 mg tar cigarettes with detectably different nicotine contents above and below the levels found in normal 6 mg models. Should it be possible to make ultra low tar models with markedly different nicotine deliveries (see above) then a second phase investigation will examine acceptability and strength ratings for cigarettes with detectably different nicotine deliveries at near zero tar. (We understand that M.A.H. Russell is engaged in similar research in England.)

Third Approach: Examine the changes in body nicotine content pre and post smoking.—Our theorizing on the role of nicotine suggests that cigarettes will be smoked whenever body nicotine content drops below a certain (unknown) level. We can detect nicotine's presence in saliva, where its concentration probably reflects its concentration in blood and tissues.

We are engaged in systematic investigation of the changes in salivary nicotine content as a function of the time since smoking and magnitude of intake. Our first goal is to find the growth and decay curve of salivary nicotine concentrations after different amounts of smoking. As a second step, we will relate the salivary concentrations to the concentration of nicotine in the blood. We have had preliminary discussion of the latter problem with Dr. Arthur Ryan, in our medical Department, and, depending on our ability to identify the salivary growth and decay date, will make a series of blood and saliva concentration measures later in the year. The exact procedure is as yet undecided, but the data will be gathered from a few volunteer subjects under medical supervision.

Assuming that salivary nicotine concentrations will reflect blood nicotine concentrations, we can then proceed to a fourth stage in the research, relating the easily obtained salivary concentrations to the urge to smoke.

Fourth Approach: Identification of two smoking population subgroups, one of which has greater nicotine needs than the other.—We have described these people in the past as compensators and noncompensators, and attempted to define them by their consumption changes when nicotine deliveries were moderately shifted. However, we've had no great success in the identification to date. Now we may have two extra tools to use: commercial PM cigarettes of ultra low tar and nicotine, and salivary nicotine concentrations. Others, principally at Columbia University, have suggested that shifts to ultra low nicotine cigarettes produce the same type of psychological stress behaviors as quitting. We therefore propose a shift study in which smokers are shifted to an ultra low brand, and the key dependent variable becomes the presence or absence of the withdrawal syndrome. Those who show evidence of nicotine dependence and those who do not can then be used to test our hypotheses on the relationship of salivary concentration to smoking behavior.

Objective 2: To better understand the mechanisms controlling cigarette acceptability.

First Approach: We will continue the *Annual Monitoring of Cigarette Acceptability* for a fourth year. This will exhaust our supply of available cigarettes at 5, 9, 13, 17, and 21 mg tar. It would seem reasonable to change this project slightly in 1981 by adding a 1 mg tar cigarette and dropping the 21 mg model when the next batch of cigarettes is made.

Second Approach: We have noted that some cigarettes produce a greater saliva flow than other cigarettes. This may in part be attributed to the role of nicotine and in part to PTO but it appears also in part related to the presence of other flavorings in the smoke (e.g. menthol). We intend to investigate this phenomenon more systematically, examining the effects of RTD, menthol, WS, etc.

Inhalation Studies—Jones

A method for monitoring respiration has been developed to permit further research on the nicotine titration hypothesis. The question has been asked: When given cigarettes with differing nicotine deliveries, do smokers alter their smoking behavior to regulate or ''titrate'' the amount of nicotine taken up via inspiration of smoke? The Respitrace Calibrator will be used to address this question, investigating whether smokers alter inhalation patterns when smoking cigarettes with differing nicotine deliveries.

In a series of preliminary trials using 5 subjects, respiratory transducer recordings have been shown to correlate with spirometer readings on the order of .92+, including readings taken up to five hours after calibration. The relationship consistently has been identified as linear. We have isolated several variables which influence the accuracy of the measurements, and they are being controlled—positioning of the tunic on the abdomen and rib cage, posture when taking the readings, slippage of the tunic, etc.

Several other variables are currently under investigation.

Plans for 1980 are as follows:

1. Further procedural refinement of the present system. A study of the sensitivity of the calibrator to gain values is planned, as well as development of criteria for the subject's habituation to the device.

2. Procedural refinement for the mobile apparatus which is on order for spring of 1980. These investigations will parallel the work that has been done on the present system, determining the accuracy of the recordings as compared with a standard, identifying extraneous variables and working toward their control, investigating baseline drift across a single day and the variability between days.

3. Application of the mobile Respitrace to research on the nicotine titration hypothesis as detailed in Plans and Objectives, 1979.

Dr. T. S. Osdene

M. C. Bourlas distributed to R. Seligman et al.—

Analytical Research Division—1980 Plans and Objectives

Date: January 16, 1980

A summary of the major Plans and Objectives for the Analytical Research Division is presented below. A more detailed description may be found in the accompanying memos.

The establishment of basic, fundamental research programs and the continuation of these programs to the applied and development stages will be a primary goal for the Analytical Research Division. In addition and of equal importance will be the continuation of providing technical service to the Research and Development staff, the PM Leaf Department as well as PM International whenever our services are required.

I. NUCLEAR AND RADIOCHEMISTRY

The Nuclear and Radiochemistry Group has been charged with the responsibility for the use of radioisotopes and radiation to study how cigarette smoke is formed and is transported out of the cigarette. In order to accomplish this task, the group will be investigating mechanisms of smoke formation by being engaged in labelled precursor-product studies, labelled tracer studies, neutron activation analyses and radiation effects research. The group will continue to maintain the Health Physics responsibility which includes environmental monitoring of the natural radioisotopes. The preparation of labelled tobacco via biosynthesis will also continue in order to accomplish our isotopic studies.

Distribution of effort—fundamental studies, 80 percent; technical services 20.

II. FOURIER TRANSFORM INFRARED EVOLVED GAS ANALYSIS (FT–IR–EGA) SYSTEM

The study of smoke constituents generated during pyrolysis or combustion is important if cigarette deliveries are to be manipulated and controlled. These studies involve establishing the conditions when smoke products form, the rate at which they form, and the effects of secondary factors, such as heating rate and oxygen content, on their formation. For this purpose a FT–IR–EGA System has been developed. The technique will be employed to examine gases generated during tobacco decomposition.

This computer controlled system permits the simultaneous determination of major gas phase constituents and the effects of tobacco processing, expansion and blending. The system will be used to evaluate the denitration processes, effects of oxygen on the thermal degradation of tobacco and, in general, various physicochemical approaches to reduce gas phase components.

Distribution of effort:	*Percent*
Fundamental Studies	50
New Product Development	25
Technical Services	25

III. TUNABLE DIODE LASER (TDL) SYSTEM

While a clear picture of the thermal behavior of tobacco is being obtained with the EGA System (above), the TDL System is being developed to monitor both mainstream and sidestream gas phase components under actual smoking conditions.

The increased resolution and sensitivity of the TDL System will permit us to investigate two major areas: 1. The first involves monitoring certain gas phase components in mainstream and, 2. The second is the profiling of gases within a single puff.

In the area of filtration and filter development, changes in dilution as a function of puff number become important. With the TDL system puff-by-puff profiles of many gas phase constituents can be obtained for evaluation of the effect of dilution on gas phase reduction.

A clear understanding of dilution of filtration mechanisms can be greatly facilitated by a detailed knowledge of the rate of delivery of a smoke component within an individual puff. Because of limited detector response time, the profile within a single puff of smoke could not be investigated utilizing conventional infrared instrumentation. Using tunable diode lasers a method will be developed which will allow puff-by-puff variations and the single puff profile of gas phase constituents to be simultaneously recorded.

Major gases which will be monitored included NH_3, acrolein, CO, NO, NO_2 and HCN.

Distribution of Effort:	*Percent*
Fundamental Studies	50
Cost Savings	20
New Product Development	20
Technical Services	10

77. PATTERN RECOGNITION ANALYSIS (PRA)/CHEMOMETRIC CHARACTERIZATION OF TOBACCO

The ability to recognize and measure differences in competitor's cigarettes is essential in the design of our own products and in maintaining a clear view of the changes in the cigarette market. The approach taken to obtain the required analytical information has been to develop the necessary methodology to quantitatively measure individual components of tobacco and smoke. This single parameter approach (tar, nicotine, water, PG, RTD, etc.) has permitted us to establish a significantly large data base for comparison purposes. However, the complexity of tobacco processing, changes in filter design, application of new flavors, changes in cigarette dilution, and various alterations made to the tobacco (expansion, denitration) have required that approaches be established and employed to characterize and differentiate between various tobaccos and tobacco blends. Multi-variate data analysis in the form of pattern recognition analysis (PRA) is a versatile tool for extracting information from a well defined data base and is in fact the approach which will be taken to classify tobaccos.

The long-range goal for PRA is to interrelate flavor quality, that is, subjective responses, with analytical data. In our attempts to achieve this goal, computer manipulation techniques and sampling procedures are currently being tested and refined.

Distribution of Effort:	Percent
Fundamental Studies	20
Cost Savings	20
Methods Development	40
Technical Services	20

V. NUCLEAR MAGNETIC RESONANCE (NMR) LABORATORY

Conformational analysis of tobacco and smoke components and those organic compounds which have either flavor or biological implications will continue to occupy the bulk of the activities in the nuclear magnetic resonance laboratory. To this end, strategies have been designed and computer programs written in order to extend the ^{13}C T_1 analysis already completed for nicotine to other compounds. This analysis will yield information regarding internal and overall motion a well as conformational details. An extension of these investigations will be to study a variety of menthol derivatives to establish both the conformation and relative configuration at asymmetric centers.

Distribution of Effort:	Percent
Fundamental Studies	60
Technical Services	40

VI. MECHANISMS OF TOBACCO EXPANSION—CHARGE NO. 8204

Project No. 8204 will concentrate its efforts on the changes occurring in the non-water fraction of tobacco as a function of expansion. Investigations to date have emphasized the water fraction and its changes upon expansion, however, this has not yielded the complete picture with regard to the mechanism of expansion. Our involvement in this project will be to coordinate efforts in four major areas—

(A) Investigations into the interactions of salts and their distribution within the tobacco cell wall with expansion. Particular attention will be given to calcium. The method of investigation will be the measurement of the rates of cation extraction with various solvent systems using atomic absorption techniques.

(B) FT–IR evolved gas analysis of the various expanded samples, to study the changes in specific tobacco components upon expansion (i.e., sugars, cellulose, pectin, etc.).

(C) EPR studies of the free radical content of expanded samples to gain insight into the effects of heat and air on the tobacco constituents.

(D) SEM microstructural studies in order to access physical cell wall damage as a function of the method of expansion.

These investigations are in various stages of completion at the present time and will be continued throughout 1980.

Distribution of effort:	Percent
Fundamental Studies	70
Cost Savings	10
Methods Development	20

VII. ANALYTICAL RESEARCH NECESSITATED BY LOW TAR CIGARETTES

A. Significance and Use of Gas Phase (OGPP) Data

As our products aim toward lowered tar deliveries, gas phase delivery assumes a role of greater importance. The techniques employed in the chromatographic separation of tobacco and smoke constituents and subsequent chemometric characterization of tobacco have been shown to provide data that his previously been inaccessible. This data will be correlated with cigarette variables such as blend composition, filter effectiveness, paper types and flavor systems.

B. Significance and Use of Profiling Whole Smoke by Gas Chromatography

The techniques developed for production of high resolution gas chromatographic separation of gas phase components will be applied to whole smoke, especially for the ultra-low tar delivery models.

C. Analytical Procedures Developed for Low Tar Cigarettes

Efforts will be made to develop analytical procedures for the evaluation of low tar cigarettes since the procedures now in use were developed for cigarettes yielding relatively gross amounts of tar. These new procedures will be directly correlatable with the FTC tar number.

An automated computerized technique towards this end is being investigated using the 2-propanol extract of TPM needed for the nicotine and water determination.

Distribution of Effort:	Percent
Fundamental Studies	40
Methods Development	40
Technical Services	20

VIII. SUPPORT EFFORTS

A. Leaf

Support in this area will be given as a cooperative function with other divisions of R&D as well as areas outside R&D. The changes in the chemistry of aging tobacco as well as chemical changes caused by cultural practices and storage variation will be monitored. In addition to established analytical procedures, some methods development and/or modification will be necessary.

B. Manufacturing

Support will continue to be given to Manufacturing to assist them in problem areas involving tobacco processing. Particular effort is anticipated in the area of tipping paper problems. A great deal of effort will be expended to develop an on-line optical porosity monitor which will be interfaced with the existing laser perforator.

C. International

Support for International is expected to continue. This requested support will be in the form of on-site education and training in the operation of instrumentation as well as troubleshooting. Significant in these areas is the automated determination of TPM, H_2O, nicotine and tar.

NUCLEAR AND RADIOCHEMISTRY OF SMOKE—PLANS AND OBJECTIVES (1980)

I. PRECURSOR-PRODUCT STUDIES

These studies are divided into two broad areas—A. Naturally occurring materials present in the finished cigarette. Examples are the following: 1. What are the major smoke products from tobacco polyphenols? 2. Is nicotine transferred at the same rate from bright, burley, ET, stems, etc.? 3. How much CO is formed from each ingredient in the cigarette? Do the various tobaccos contribute their equal shares to the CO? Does the calcium carbonate in the paper contribute to the CO formed? How much do the sugars, humectants, etc., contribute?

B. Added materials and their contribution to smoke. These are broken down into several areas.

1. Flavor release compounds—Selected candidates will be prepared, labelled and the contribution of each part of the compound to smoke determined. This type of study must be conducted for every new material added to our cigarettes in order to insure that we know what is produced in the smoke stream.

2. Distillable flavors/additives—These materials must also be studied to determine their contributions to smoke in order to ascertain what products are derived from the precursors added.

II. LABELLED TRACER STUDIES

This area will be divided into research and service A. Service—In this area, efforts will be in the use of labelled compounds to determine isolation schemes and recoveries from ours and other projects' research studies. Examples are:

1. The use of ^{14}C–NNN to determine recoveries and to calculate absolute amounts delivered.

2. The use of labelled rutin to establish recoveries (if any) from smoke.

3. The use of neutron activation analysis (NAA) to determine Br and C1 levels in submitted samples.

B. Research 1. Labelled materials will be selectively placed within the cigarette at known locations, and these used to determine smoke formation mechanisms, dilutions and deliveries. 2. Neutron Activation Analysis will be used to follow the fate of the inorganics during smoke formation, i.e., how are the inorganics transferred into smoke, and how do they affect smoke formation?

III. SMOKE FORMATION AND COMPOSITION STUDIES

A. Smoke Aerosol Studies—It has already been demonstrated that the chemical composition of MS nonvolatile smoke is different for different smoke particle sizes. This has important considerations in giving the *smoker maximum impact*. If the desired flavors can be enriched into those particle sizes which have maximum lung retention (or mouth retention if desired), overall concentration in the total smoke can be kept to a minimum. The data will allow us to accurately state just how much of each smoke component in each particle size range comes from each labelled cigarette constituent.

B. Use basic smoke formation knowledge to regulate the delivery of selected smoke constituents. Examples are 1. The use of selected flavor components on the cigarette periphery to give ''enriched'' TPM in the MS. 2. The use of solid center tobacco cores to ''block'' the formation and transfer of CO to the MS smoke.

IV. ENVIRONMENTAL RADIOLOGICAL MONITORING

A. Monitor all naturally occurring radioisotopes in our tobaccos and finished cigarettes. These data will be used to monitor any increase in naturally occurring materials in our future tobaccos due to environmental factors similar to Three Mile Island.

B. Conduct all defensive studies regarding naturally occurring isotopes, i.e., the ^{210}Pb-^{210}Po problems of the past, etc.

V. GREENHOUSE FACILITY

The greenhouse facility will provide support in the following areas:

A. Establish the techniques and produce labelled plant materials which will provide the major source for all of the labelled smoke studies at R&D.

B. Provide fresh green tobacco plant materials to all Research & Development projects and other PM departments, as requested.

C. Provide a liaison with R&D , the Leaf Department, Tobacco Industry Committees, commercial companies, Federal and State Agricultural Research agencies, and growers, on a cooperative basis, to test and evaluate any necessary materials and/or tobacco deemed in the best interest of the company.

D. The preparation of all experimental labelled cigarettes in support of all ongoing research studies utilizing Carbon-14 and Nitrogen-15.

VI. MASS SPECTROMETRY LABORATORY

The existing mass spectrometers will be utilized in support of both ongoing and planned Research programs. These programs include the MC Materials Evaluation Program, the synthesis of tobacco flavorants and the evolved gas analysis program which entails the determination of the gases evolved from thermally degraded tobacco. Particular emphasis will be placed using mass spectrometry in tobacco product/precursor studies and especially the nitrogen containing components.

Since the present hardware and software are nearly fully extended, the primary activities over the coming year will be in the area of system investigations. Continuing studies include the denitration, and expansion processes, cellulase treatment, and baseline studies on individual tobacco constituents. The baseline data will also be used in correlation studies on the effects of physical factors (heating rate, flow rate, etc.) on constituent decompositions. Other planned investigations include the effect of genotype and fertilizer application on ammonia and other nitrogenous materials in burley tobacco. Also, the correlation between formic acid evolution and molecular weight of cellulose will be explored further.

SPECTROSCOPY/CHROMATOGRAPHY SECTION

I. *Tobacco and Filler*

A. Tobacco Expansion

OBJECTIVE: Develop data base designed for defining tobacco expansion as functions of physical and chemical parameters

ACTIVITIES:

(1) Investigate salts' interactions and their distribution within the tobacco cell wall using atomic absorption

(2) Study changes in tobacco components using FT–IR and Evolved Gas Analysis

(3) Coordinate efforts of Charge No. 8204

B. Blend Composition

OBJECTIVE: Quantitative discrimination of cigarette blend components

ACTIVITIES:

(1) Investigate and determine optimum methods for sample preparation and analysis by $(GC)^2$

(2) Establish degree of difference of total blend components

(3) Apply chemometric techniques

II. *Smoke*

A. Chromatographic/Chemometric Characterization

OBJECTIVE: Application of chemometric techniques in extraction of information from smoke analyses

ACTIVITIES:

(1) Develop procedures for profiling wholesmoke

(2) Investigate use of mass spectral data as a ''third dimension'' in GC smoke profiling

(3) Apply ARTHUR to profiled data for correlation with sensory evaluations.

B. Tunable Diode Laser (TDL)

OBJECTIVE: Application of TDL to understanding of parameters affecting smoke component formation and delivery

ACTIVITIES:

(1) Determine mechanism of incorporation of water oxygen atoms in nitric oxide

(2) Quantitate NH_3, NO_2, NO, and acrolein in whole smoke

(3) Develop programs for on-line dedicated computer processing of TDL data

(4) Construct single puff profile (within puff) monitors for CO

(5) Develop infrared laser monitor for routine puff-by-puff quantitation of NH_3

III. *Other*

A. Optical Porosity Monitor

OBJECTIVE: Provide accurate on-line measurement of porosity of laser perforated tipping paper

ACTIVITIES:

(1) Design and build prototype laser monitors for optically measuring porosity of tipping paper

(3) Develop system for tracking perforations as to positioning of holes.

B. Automation

OBJECTIVE: Increase accuracy and capacity for routine GC analyses

ACTIVITY: Apply automaton to routine GC analyses with dedicated or time-shared on-line data collection and report generation

C. Flavor Release Compounds—NMR Studies

OBJECTIVE: Increased understanding of the synthesis and reactions of potential flavor release compounds (in collaboration with Yoram Houminer)'

ACTIVITIES:

(1) Determine stability of methyl pyrazine anions through NMR studies of deuterium exchange kinetics of methyl protons

(2) Examine the conformation of pyrazine ethanols by coupling constant analysis and by studying the effects of various substituents on proton chemical shifts

(3) Assign ^{13}C and ^{1}H spectra of alkyl pyrazines using coupling constant measurements and lanthanide shift reagents

D. Conformation of and Kinetics of Internal Rotation in 2, 4-dimethyl Nicotine

OBJECTIVE: Understanding the energetic factors which determine the solution conformation of tobacco alkaloids

ACTIVITY: Measure the rotational barriers on 2, 4-dimethyl nicotine by ^{13}C NMR lineshape analysis; analyze conformation from coupling constants and Nuclear Overhauser effects

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SPECIAL INVESTIGATIONS

The following is a list of plans and capital instrumentation needed by the above section in 1980.

I. *Tobacco and Filler*

A. Complete Development of HPLC Determination of Solonesol in Tobacco and/or Smoke

OBJECTIVE: To assist the flavor transfer group in their evaluation of the lipid portion of the blend for flavor characteristics.

Project Chiefly Concerned—2306

B. HPLC Study on Turkish Tobacco

OBJECTIVE: To do a cumulative collection of selected HPLC peaks from Turkish tobacco extracts for reconstitution into cigarettes. The cigarettes will be subjectively evaluated and the peaks of interest will be identified. This will be a cooperative effort with development.

Project Chiefly Concerned—2306

C. Liquid CO_2 Extraction of Tobacco

OBJECTIVE: To investigate the utility of the apparatus for analytical extractions, particularly for the lipid portion of tobacco. To do HPLC on the extracted material and compare it with other extraction techniques.

Projects Chiefly Concerned—1901, 1503, 8401, 2306

D. Amino Acid Analysis

OBJECTIVE: To determine individual amino acids and peptides on samples of green leaf, cured leaf, expressed juices and protein hydrolysates. The Dionix amino acid analyzer will be used to replace the long tedious gas chromatographic procedure.

Projects Chiefly Concerned—8205, 1503, 1901

E. Organic Acids in Tobacco by HPLC

OBJECTIVE: To develop an HPLC procedure for the determination of organic acids in tobacco. The procedure could replace the tedious extraction and derivatization steps required before the gas chromatographic readout. A 0.5% dicyclohexylamine ion-pairing agent will be the eluting solvent and a C_{18} column will be used.

Projects Chiefly Concerned—1503, 1901

F. Tobacco Protein Analysis

OBJECTIVE: To investigate the proteins in tobacco and smoke. Emphasis initially would be directed toward the separation of tobacco glycoprotein by GPC and HPLC.

Projects Chiefly Concerned—6900, 6906, 6908

G. Amino Sugars in Tobacco and Reaction Flavor Mixtures

OBJECTIVE: To determine the amino sugars formed from the reaction of sugars and amino acids and/or ammonia. The approach will be investigation of the reaction of ninhydrin with amino sugar, making appropriate correction for amino acids.

Projects Chiefly Concerned—8401, 2305

H. Fluoride Selective Ion Electrode for Ionizable Fluoride

OBJECTIVE: This method will be developed in response to a request from Park 500 for a fluoride determination in potassium nitrate crystals isolated from CEL.

Project Chiefly Concerned—8205

I. Evaluation of the Microwave Moisture Meter for Leaf

OBJECTIVE: To assist the Engineering Department in the evaluation of their prototype microwave moisture.

Project Chiefly Concerned—8204

II. *Smoke*

A. Aldehydes in Smoke

OBJECTIVE: To extend the isocratic HPLC determination of aldehydes in smoke with the gradient capability of the new Hewlett-Packard HPLC to achieve better resolution of the peaks.

Projects Chiefly Concerned—8101, 6908

B. FTC Tar by TPM Fluorescence

OBJECTIVE: FTC tar measurement by fluorescence will be made for the study of filter efficiency, sidestream/mainstream ratios and puff X puff data on low delivery cigarettes.

Project Chiefly Concerned—8101

C. Electrochemical Analytical Techniques for Smoke Analysis

OBJECTIVE: These techniques should be investigated as a quick and selective way of determining aldehydes, ketones, alcohols, acids, volatile metals or any material capable of oxidation or reduction.

Projects Chiefly Concerned—6908, 1503, 1901

D. Gel Permeation on Whole Smoke Condensate

OBJECTIVE: To make a comparison of GPC profiles of WSC from cigarette types. The feasibility could be determined on the Waters 202 HPLC using microstyrogel columns and THF solvent. Possibly the isolated PAH fraction could thus be enriched making easier any future analytical determinations of PAH's.

Project Chiefly Concerned—6908

III. *Cigarette Paper*

A. Completion of Tipping Paper Ink/Adhesion Problem

OBJECTIVE: To determine from one lot of paper to another and to be able to correlate these differences with performance on the cigarette maker.

Project Chiefly Concerned—8205

B. Citric Acid in Cigarette Paper

OBJECTIVE: To develop a simple HPLC procedure for citrates in cigarette paper to replace the present gas chromatographic procedure. The procedure will be developed on the new Hewlett-Packard 1084b HPLC. The old DuPont 820 HPLC will be dedicated for this determination.

Project Chiefly Concerned—8101

GENERAL ANALYTICAL CHEMISTRY

I. *General*

A. Provide accurate, precise analytical service as needed to personnel of R&D and other PM departments with a target turnaround time of seven work days or less per request.

B. Consult with the above personnel in order to advise them on ways of obtaining meaningful analytical data to aid them in meeting current and future project objectives.

II. *Tobacco Leaf, Filler, Reconstituted Materials and Process Slurries*

A. Investigate HPLC methods for separation and/or quantitation of (in order of priority):

1. Polyphenols
2. Major and minor alkaloids
3. Sorbate salts and sorbic acid in filler

B. Incorporate a nitrite nitrogen procedure into the nitrate nitrogen method.

C. Conduct a rigorous investigation into all aspects of the petroleum ether solubles method in order to develop a more efficient procedure.

D. Adapt the rapid procedure for hot water solubles to the determination of cold water solubles.

E. Develop a rapid accurate direct method for low levels of insoluble solids in process slurries to aid in improving accuracy of material balance studies.

F. Improve precision, accuracy and sensitivity of the sorbic acid method.

G. Total Nitrogen Determination

1. Maintain contacts with the manufacturer of the LECO NP–28 to lower maintenance requirements and reduce downtime.
2. Investigate the feasibility of the determination of insoluble nitrogen on the LECO NP–28.
3. Investigate other methods of total nitrogen determination, such as pyrolysis-chemiluminesence.
4. Do a critical study of the effect of conditions such as the salt concentration of digests on the values obtained in the Kjeldahl total nitrogen method using the Technicon block digestor.

H. Investigate conditions which affect the reproducibility of barium sulfate crystal formation in the turbidometric sulfate method.

III. *Smoke*

Evaluate the method for NH_3 in mainstream wholesmoke by comparison with values obtained by the infrared spectroscopy group on the diode laser IR spectrometer, with the development of a low cost diode laser instrument capable of routine operation as a goal.

IV. *Miscellaneous*

A. Methods Manual

1. Document all methods in routine use in the General Analytical Section.
2. Consider ways of evaluating circulated manuals for accuracy of content.
3. Utilize computer capabilities for manual indexing and updating.

B. Computer/Microprossor Applications

1. Utilize the existing microprossor or the computer for the automation of the weighing of petroleum ether extractables.
2. Expand the availability of computer-generated hard copy reports.

C. Instrumentation

1. Keep abreast of new developments in HPLC technology to update present equipment, especially new detection systems.
2. Optimize all AutoAnalyzer systems to increase speed and accuracy and decrease reagent use.

D. Personnel Education

1. Continue rotation and cross-training of professionals and technicians.
2. Develop a training program for technicians providing instruction in laboratory skills (complete with written material) necessary in our laboratory.
3. Develop a program of education of both the analyst and submitter so that work performed is both meaningful and necessary.

E. Conduct an extensive study of laboratory organization to determine what changes (e.g., flex time) might result in more efficient operation, then implement those changes.

F. Assume responsibility during the first quarter of 1980 for the receiving, coding, collating and transmittal of samples and data from sources outside of R&D.

BIOCHEMICAL RESEARCH

To: Dr. T.S. Osdene
From: W.F. Kuhn
Subject: Plans and Objectives for 1980—Biochemical Research Division
Date: January 7, 1980

The attached documents are the Plans and Objectives prepared by the individual project leaders in the Biochemical Research Division. These reports represent the areas of research to be explored in 1980 under each charge number. Each project leader prepared his report from the input he received from his colleagues coupled with his own goals for the coming year.

The overall objectives of the Division are threefold and remain essentially the same as outlined in previous reports. First, develop an integrated program for control of insects which infest stored tobacco, processed filler and finished cigarettes. Second, establish a matrix or battery of *in vitro** bioassays for the evaluation of the biological effects of smoke products and apply these assays for the investigation of biological, chemical, and physical parameters of cigarette smoke. Third, develop methods for the collection, isolation, identification and quantitation of tobacco and cigarette smoke components which affect the *in vivo* and/or *in vitro* bioactivity. The main areas of endeavor are highlighted below.

CHARGE NUMBER 1101—ENTOMOLOGICAL RESEARCH

Our effort on cigarette beetle physiological studies will be continued. This emphasis stems from the trend to eliminate the use of highly toxic or residual pesticides as control agents and increase the use of mechanical and physical methods to achieve the desired result. This effort will be focused on: (1) the effect of relative humidity and low temperatures toward beetle growth; (2) the investigation of the comparative attractiveness to the beetle of various colors from the visible spectrum; (3) the initiation of studies on the use of feeding inhibitors; *e.g.*, Neem nut extracts, as possible repellents; (4) the efficacy of pyrethrin alone as a larvicide; and (5) the evaluation of commercially available sex pheromones of the cigarette beetle and the tobacco moth. (Japanese scientists have published the synthesis of a chemical reported to be the sex pheromone of the cigarette beetle.)

The research program on the application of an insect growth regulator, methoprene, was highly successful. These results led to the initiation of a large commercial application trial (16,000 hogsheads) of KABAT—5% methoprene in ethanol—to strip and stem. We will monitor the treated tobacco materials for the presence of cigarette beetles and methoprene residue. These hogsheads will be used to evaluate the effects of various control practices (methoprene only, methoprene+DDVP fogging and methoprene+DDVP fogging+PH_3 fumigation) in separate warehouses. The HTI results of both methoprene treated Marlboro filler and Benson & Hedges filler in relation to appropriate controls will be completed. We will assist in the transfer of KABAT application techniques to Stemmery personnel as the use of material is more widely used throughout Philip Morris, U.S.A.

We will continue to provide consultation and technical service to other Departments within the Company. Such effort will focus on the efficacy of DDVP fogging in warehouses, methyl bromide vacuum fumigation at lower dosages and on-site examinations within PM, USA and upon request.

Distribution of effort:	*Percent*
Fundamental studies	30
Cost savings	45
Technical services	25

CHARGE NUMBER 6906—BIOLOGICAL EFFECTS OF SMOKE

In the coming year, the goals of this group reflect our decision to learn more about the existing, developed assays rather than focus our attention on the interests of the company to emphasize the former at the expense of the latter. Since our resources are finite, we cannot engage in both endeavors and adequately contribute to the understanding of effects of smoke components in biological systems.

MAMMALIAN CELL SYSTEMS

The principal goal of the L5178Y mouse cell (thymidine kinase mutation) assay will be to define parameters which determine the activity of whole smoke condensate (WSC). To accomplish this goal, three lines of investigation will be pursued. First, the WSC derived from cigarettes which contain filler variants of the LTF–IIIA formula will be tested. Second, acid, base and neutral fractions isolated from WSC will be evaluated as well as the testing of fractions derived from synthetic mixtures of pure compounds to define the application of the exponential dose-response curves. In addition, WSC will be ''spiked'' with a known chemical of high activity to trace its distribution, recovery and potential interaction with isolates smoke components. Third, the effect of variable microsomal protein (S9) on the activity of positive control chemicals and WSC will be studied. The objective of this effort will be to determine how the relative activities of various WSCs are influenced by changes in the amount of available, exogenous mammalian metabolism.

Although investigations on the measurement of sister chromatid exchange (SCE) were suspended last year, investigations on this phenomenon will be resumed. Successful establishment of this assay will provide a second genetic endpoint in the L5178Y cell system as well as provide an additional assay for evaluating the biological effects of smoke products.

Literature reports indicate that smoke products are weak initiators but moderate promotors in the two-stage model of carcinogenicity. By measuring the degree of metabolic cooperation between tymidine kinase proficient (TK+/−) and tymidine kinase deficient (TK−/−) cells in the presence of trifluorothymidine, it may be feasible to develop an *in vitro* assay for promotors with L5178Y cells. Investigations will be conducted to explore this phenomenon in the coming year.

The major goal of the baby hamster kidney (BHK) assay will be to establish the system

with positive and negative control compounds. Experiments designed to identify the causes of problems encountered to date are under investigation. Failure to resolve these problems in our facilities may require a visit to Dr. J.A. Styles' laboratory at ICI in England to gain ''hands on'' experience in conducting this bioassay.

NONMAMMALIAN SYSTEMS

Our efforts in the *E. coli* differential toxicity assay will be directed toward the hypothesis that aldehydes in smoke are causally related to activity. This study is closely coupled to the development of a method for aldehydes in smoke by personnel of the smoke condensate studies group.

The major thrust in the yeast mitotic gene conversion assay will continue to refine our knowledge of the determinants of WSC activity. We plan to study the activity of TPM as a function of puff volume initially which may lead to additional studies on activity *versus* puff interval and/or frequency. Additionally, the water soluble and insoluble fractions of WSC will be tested along with the components present in the acid, base, and neutral portions of WSC. On a continuing basis, the pyrolyzate formed at 620 °C from filler of various cigarettes will be tested. In particular, the higher activity of RCB *versus* RL is especially important.

Various investigations involving the application of the *Salmonella*/microsome assay continue to require about 50% of the total personnel effort of this project. In this regard, we plan to study the TPM activity as a function of puff volume, duration and frequency. THe feasibility of testing pyrolyzed materials in the assay was demonstrated in 1979. We plan to continue this effort this year. Studies of whole smoke and gas phase activity (direct exposure of plates in a chamber) in this assay will be suspended while the principal investigator is on LOA. However, some work will be done on the activity of whole and gas phase smoke collected directly in solvent (DMSO) filled traps. Although this study is not as elaborate as the chamber-exposure technique, it should provide valuable information about the activity of gas phase.

We plan to pursue the extensive study of the base fraction, acid/neutral fraction and WSC activity of 14 model cigarette types. We will continue the investigation of components responsible for the base fraction activity of burley cigarettes. In this regard model compounds such as amino α- and γ-carbolines will be studied.

We will continue to test potential cigarette additives and WSC from new cigarette candidates as requested. We anticipate that this effort will receive increased emphasis in the coming year.

Another specific goal will be to prepare an internal Salmonella/microsome assay methods manual to document all procedures involved with this assay.

Distribution of Effort:	*Percent*
Defensive Research	90
New Produce Development	10

CHARGE NUMBER 6908—SMOKE CONDENSATE STUDIES

The primarily defensive nature of this research effort necessitates a continual monitoring of developments in the literature related to the biological activity of smoke components. Achievement of this project's goals require close coordination of research efforts with those of charge number 6906 which were expressed in the previous section.

More emphasis will be placed on condensate collection studies since these methods may affect the overall research effort. Collection of WSC in Elmenhorst cold traps (ECT) or impaction-traps (IT) will continue, along with processing, for in vivo testing. The collection of samples for in vitro and chemical studies has been expanded to ECT, IT, TPM pad, gas phase, and collection in liquids. Some of these collection methods will require further development. We plan to design and apply sidestream smoke collection systems in the coming year. A longer range study of a glass cascade impaction trap for a particle size profile is planned. Satisfactory separation of discrete particles will lead to the chemical and biological evaluation of each size fraction.

A system will be established for controlled pyrolysis or combustion of filler for chemical and/or *in vitro* bioassay investigations. The evaluation of a series of marcs isolated from flue-cured tobacco is planned.

Major improvements in chromatographic separation procedures are anticipated. Achievement of this objective will permit the investigation of new areas of smoke condensate chemistry as well as more thorough evaluation of studies conducted previously. Toward this objective, extensive modification of the PE–900 gas chromatograph (gc) for use with fused silica columns is underway. A law pressure liquid chromatographic (lc) system was designed and will provide a flexible preparative or isocratic analytical lc system. Major emphasis of this system will be directed toward the reversed phase chromatographic evaluation of the base fraction from burley WSC. The acquisition of a high performance liquid chromatograph will provide sufficient capability to develop new methods for the isolation of smoke components of biological importance.

The procedure for volatile nitrosamines is well developed and will be applied to smoke products upon request. We plan to apply the methodology to correlate tobacco precursors with nitrosopyrrolidine in smoke. Investigation of nitrosamines in sidestream smoke and processed WSC will be investigated. Development of methods for the characterization of nonvolatile nitrosamines will be pursued. Initial studies will concentrate on mainstream smoke, but may be extended to sidestream smoke later this year.

The isolation and identification of active components in the base fraction of WSC has proven difficult. However, the high microsome dependent (*Salmonella*) activity in this fraction requires our continued attention. We will pursue this goal using the improved chromatographic equipment described previously as well as use of model compounds for enhanced improvements in fractionation and identification procedures. From studies of a series of 14 cigarette types, we hope to better understand the influence of filler composition on base fraction activity and yield. In addition, this evaluation should enhance our knowledge of the relative amounts of some specific components in WSC from these various tobacco types. Planned chemical studies include: pattern recognition analysis of gc data *versus in vivo* and/or *in vitro* bioactivity; quantitative hplc procedure for quinoline in WSC will be developed and extended to additional aza-arenes in these fractions; a method will be developed for harmane and norharmane in the base fraction as well as methods for the determination of amino α- and γ-carbolines (tryptophane pyrolysis products). Cigarettes have been prepared by adding proline, tryptophane or pheylalanine to LTF-IIA filler. A study of the active base fraction components from these simple model systems is planned with emphasis on the tryptophane added sample.

Work will continue on the fractionation of bright tobacco. Increased emphasis will focus on the chemical components of each marc and extract, particularly the amino acid composition of protein fractions and the nature of the nonprotein nitrogen components.

There are additional areas of interest which do not fit into the research endeavors discussed above and thus are of lower priority. The utility of gel permeation chromatography will be explored for WSCs and condensate fractions. The effect of added sugars or sugar-amino acid reaction products in modulating the activity arising from proteins and amino acids in tobacco will be studied. It has been stated that a tobacco glycoprotein may be transferred into smoke (Becker's work). If so, an understanding of the parameters controlling this transfer would be beneficial. A capability for isolation of such material will be developed.

Distribution of Effort:	*Percent*
Defensive Research	80
Fundamental Studies	10
Technical Service	10

To: Mr. W. F. Kuhn

From: R. A. Pages

Subject: Project Charge Number 6906 (Biological Effects of Smoke)—Plans and Goals for 1980

Date: December 20, 1979

1. *INTRODUCTION*

The objectives of Project Charge Number unchanged.

(a) To develop a battery of short-term assays to evaluate the potential b effects of cigarette smoke product

(b) To conduct research investigations to generate an understanding of and control of cigarette smoke * * * in each in vitro assay.

(c) To conduct tests on potential new products or additives upon request assist in the evaluation and inter * * * of the results obtained.

The original objectives of the project above) presented us with a formidable challenge. * * * challenge, we developed a strategy regarding the and evaluation of in vitro assays at PM. Implement strategy led to the successful development to sev * * * detect and measure the in vitro activity of cigar * * * condensate. With that success, we first discovered objective b and then came to recognize its ultimate importance to our program. Thus, it became apparent that the intelligent application of in vitro tests and the interpretation of their results could be carried out only when sufficient knowledge had been obtained about the many factors (cigarette, chemical, and/or biological) which together determine the level of cigarette smoke product activity. This was vividly illustrated when we were faced with trying to interpret the meaning of diametrically opposite results obtained with the same test material in different assays.

Against this background, we will now present our plans for 1980. This year, as in prior years, we have had to make difficult and risky decisions. This is because it is self-evident that: time is precious; our resources, both human and material, are finite; and we cannot do everything if everything we do is to be done well. Accordingly, our plans reflect an imbalance between learning more about our existing, developed assays and the development of additional, new assays. In our judgment, it is in the best interests of PM that we continue to emphasize the former at the expense of the latter.

2. *PLANS AND GOALS FOR 1980*

A. *L5178Y MOUSE CELLS*

1. *Thymidine Kinase Mutation*

The principal goal of work with this assay in 1980 is to try to define some of the parameters which determine WSC activity. Although this assay system for WSC has been established for almost two years, we do not yet know anything about the nature of WSC activity. (Tests on the Model II and URLS variant WSCs conducted during 1979 did not

provide any new insights into this question.) We therefore propose to pursue three lines of investigation in the coming year.

(a) *LTF–IIIA Variants*—The Model I WSC results have consistently shown that LTF–IIIA yields a WSC which is significantly more active that LTF–IIA WSC. Following the approach so successfully used in the *Salmonella*/microsome and *E. coli* assays, we will test the WSCs derived from cigarettes which contain filler variants of the LTF–IIIA formula. Enough filler is already available for these studies, but it will be necessary to fabricate handmade cigarettes for smoking in order to standardize cigarette paper porosity and filtration parameters. We intend to begin these studies no later than the second quarter of 1980 and to pursue them on a continuing basis thereafter. Our specific goal is to try to relate WSC activity to the presence (or absence) of particular precursors in the LTF–IIIA formula.

(b) *WSC Fractions*—Previous studies of fractions have been limited to a cursory examination of the H_2O soluble and insoluble portions of 2R1 WSC (both fractions were active). We intend to exhaustively examine the question of activity in WSC fractions on a continuing basis during 1980. These studies will include: tests of the acid, basic, and neutral fractions from one or more Model I WSCs; the testing of fractions derived from synthetic mixtures of pure compounds in order to define how to use the exponential dose-response curves.

(c) *Activity as a Function of S9 Concentration*—Almost all prior work with this assay has involved tests conducted at a single, arbitrarily selected, level of microsomal protein (S9). Because it is well established that the amount of S9 can have a dramatic effect on the level of activity observed in many short-term *in vitro* assays, we propose to investigate this phenomenon in the L5178Y TK mutation assay. Initial experiments will involve studies of the activity of our positive control compounds—B(a)P and 2-acetylaminofluorene. We will then investigate WSC activity *versus* S9. These studies will necessitate the conduct of assays simultaneously at different concentrations of WSC *and* S9. The specific goal of the experiments will be to determine how the relative activities of different WSCs and their respective dose-response curves are affected by changes in the amount of exogenous mammalian metabolism. Depending on the degree of success attained with testing WSC fractions at a single S9 level, these studies may also be extended to fractions tested at multiple S9 concentrations. This work will be initiated no later than the second quarter of 1980 will proceed throughout the remainder of the year.

Prior to initiating the three programs outlined above, in the first quarter of 1980, we expect to conclude three ongoing investigations. The first is the evaluation of the utility and effectiveness of a modified cloning procedure which is expected to simplify the conduct of the assay. The second is the evaluation of a series of selected WSC-induced, trifluorothymidine (TFT) -resistant mutants to verify that they are indeed TK-deficient (TK−/−). The third is the drafting of a special report to document the conclusions reached after an extensive review of the data generated on positive and negative control compounds over the last three years. By doing this, we are hopeful of being able to establish objective quality assurance criteria which can be used to help us decide: when this assay is performing satisfactorily; what is the acceptable level of variation; and when is a test sample active or inactive in this assay.

2. Sister Chromatid Exchange (SCE)

Work on the development of an assay based on the measurement of a second genetic endpoint, SCE, in L5178Y cells was suspended in May, 1979. As time permits, we plan to resume this effort on a part-time basis. Based on the information gathered in recent months, we are absolutely confident that we can successfully establish the SCE assay in our laboratory and that we can detect WSC activity by that method. If and when we are able to resume the SCE work, we expect to take advantage of the advice of Dr. David Kram (G. Washington University) by accepting an invitation to spend several days in his laboratory to obtain ''hands on'' experience with the SCE assay.

3. Metabolic Cooperation

As time permits, we plan to conduct studies to measure the degree of metabolic cooperation between TK+/− and TK−/− cells in the presence of TFT. These exploratory studies are designed to examine the feasibility of the possible development of an *in vitro* assay for promoters in L5178Y cells along the lines pioneered by Trosko and co-workers (*Science*. 206:1089–1091; 1979 November 30).

B. *BHK CELL TRANSFORMATION*

The principal goal of our efforts on this assay in 1980 (as it was in 1979) is to reproducibly establish the assay system with positive and negative control compounds. The results obtained in 1979 were moderately encouraging in that we were able to obtain several cell clones which appear promising for use in the assay. Several sources of difficulty were identified with the published assay protocol—some of which appear to be related to the quality of sera, media, *etc.* Major obstacles remain to be overcome, however, before satisfactory responses are obtained with positive control compounds and a usable assay protocol is available in our laboratory. Experiments designed to further identify the causes of problems and variables in this assay will be continued during the first and second quarters of 1980. If success has not been achieved by that time, strong consideration will be given to trying to arrange a visit to the laboratory of Dr. J. A. Styles at ICI in the UK in order to try to get some ''hands on'' experience in one of the few places that has been able to get this assay to work.

C. *E. COLI DIFFERENTIAL TOXICITY*

The principal goal for work with this assay in 1980 is to definitively test the hypothesis that aldehydes in smoke are causally related to activity. This is a collaborative effort with various personnel of Project Charge Number 6908.

In 1979, methodology was developed to test either whole smoke or TPM and gas phase in this assay. Additionally, experiments were begun to study the activity of several low molecular weight aldehydes in the liquid culture version of this assay. These experiments will be completed in the first quarter, 1980. Concurrently, 6908 personnel are exploring various possibilities for analyzing and quantitating the aldehydes in cigarette smoke. The ultimate test of the aldehyde hypothesis is contingent upon successfully coupling analytical chemical methods with the *in vitro* assay on common samples. Pending further progress on aldehyde method development by 6908 personnel, we intend to continue to investigate cigarette smoke activity as a function of physical cigarette parameters which are known to affect aldehydes in smoke (*e.g.*, carbon filters). The specific goal of these studies will be to accumulate additional circumstantial evidence in support of the aldehyde hypothesis. This will be done on a continuing basis throughout 1980.

D. *YEAST MITOTIC GENE CONVERSION*

Our major goal in the yeast assay work in 1980 is to continue to refine our knowledge about the determinants of WSC activity. Excellent progress was made in 1979 based upon the results of tests on: the Model III WSCs and TPM; WSC fractions; and some cigarette filler pyrolyzates. We plan to continue efforts in all of these areas in 1980. Because many of the studies which are of interest in the yeast assay will also be conducted in the *Salmonella*/microsome assay, we anticipate that there will be extensive interaction and coordination with other personnel within 6906 and 6908 a well. Hopefully, this will minimize duplication of effort(s) whenever possible.

1. *WSC/TPM Activity versus Smoking Parameters*

We intend to follow up our Model III cigarette studies by measuring the activity of TPM as a function of puff volume. These experiments will be conducted in the first quarter, 1980, and may lead to additional studies such as TPM activity *versus* puff interval and/or frequency. Further comparisons between TPM and WSC activity in the yeast assay will also be conducted on additional model cigarettes.

2. *WSC Fractions (with 6908)*

We are interested in testing fractions derived from the H_2O soluble and insoluble portions of WSC—both of which were found to be active in experiments conducted in 1979—particularly the base and acid/neutral fractions (Activity detected in the base fractions would extend our observations of an association between filler nitrogen and WSC activity in this assay.) Because studies already underway in the *Salmonella*/microsome assay involve testing the bases and acids/neutrals prepared directly from various WSCs (see below), our initial efforts in the first quarter, 1980 will be directed toward testing some of those samples in the yeast assay as well.

3. *Cigarette Filler Pyrolyzates (with 6908)*

The results of feasibility studies conducted during 1979 demonstrated that samples prepared by heating cigarette filler in air at 620° C were active in the yeast assay as well as in the *Salmonella*/microsome assay. Thus, the acquisition of pyrolysis equipment by 6908 personnel to evaluate the potential of this method of generating samples for *in vitro* testing may also provide valuable information about the filler determinants of WSC activity in the yeast assay. In this connection, we are especially interested in investigating the higher activity of RCB *versus* RL. These studies will be conducted on a continuing basis throughout 1980.

E. *SALMONELLA/MICROSOME ASSAY*

Various investigations involving the application of this assay will continue to make up about half the total efforts of the personnel of the project. The majority of these studies will be devoted to developing a better understanding of the determinants of WSC activity, although we also anticipate increased demands for testing WSCs and additives at the request of J.L. Charles.

1. *TPM Activity versus Smoking Parameters*

Extension of the Model III WSC studies will be conducted by testing TPM from the Model III cigarettes during the first quarter, 1980. Upon completion of that work, we intend to study TPM activity (unfiltered PMKRC cigarette) as a function of puff volume. Depending on the results obtained, it may be important to also study the effects of changes in other smoking parameters such as puff interval and/or frequency. In continuation of our expanded efforts to study TPM activity, it may also be necessary to test the Model II cigarettes.

2. *Cigarette Filler Pyrolysis (with 6908)*

We were sufficiently encouraged by the results of extensive feasibility studies conducted during 1979 to strongly urge and support the acquisition of pyrolysis equipment by 6908 personnel. We are hopeful that this equipment will be set up during the first

quarter so that intensive studies can begin to establish the relationship between various pyrolysis conditions (*e.g.*, temperature, air *versus* nitrogen, *etc.*) and activity in this assay. (As indicated above, section 2.D.3, there is great interest in exploring the application of this method to generate samples for testing in other *in vitro* assays.) The ultimate goal of theses investigations will be to determine how pyrolysis can be used to evaluate the activity of samples for which cigarette fabrication is not feasible—particularly the extracts and marcs of bright tobacco and RCB feedstock. Pyrolysis studies will be continued throughout 1980.

3. *Whole Smoke and Gas Phase Studies*

Studies of whole smoke activity in this assay as originally conceived (exposure of prepared agar plates in a chamber) will be suspended while the principal investigator is on leave. However, it is likely that some work will be conducted during the first and second quarters, 1980 to investigate the *Salmonella*/microsome activity of whole smoke and gas phase samples prepared by the methods developed for the *E. coi* assay—*i.e.*, by collection in solvent (DMSO) filled traps. While not as elegant as the chamber-exposure technique, it is likely that such experiments will provide valuable information regarding the activity of gas phase smoke components.

4. *WSC versus Base Fraction Activity (with 6908)*

Already in progress is an extensive study of the base fraction, acid/neutral fraction, and WSC activity of 14 model cigarette types. The study should be completed in the first quarter, 1980. At that time, we expect to be able to answer several important questions: *What is the relationship between WSC specific activity and the specific activity and concentration of the base fraction? Do the components recovered in the weakly active acid/neutral fraction have an effect on base fraction activity; i.e., are there any interactions? Does the presence of high concentrations of nicotine in the base fraction (30–60% of the fraction is nicotine) have any effect on the microsome-dependent activity of the high activity compounds that are present in that fraction?*

5. *Fractionation of WSC Bases (with 6908)*

The isolation and identification of individual components which may be important determinants of burley WSC activity remains the specific goal of this program. Further progress in this effort is dependent on the development of improved separation and identification methods by 6908 personnel. Plans have been formulated to investigate various separation procedures in conjunction with the use of model compounds such as amino-α and γ-carbolines. In addition, we also plan to study the activity of selected fractions as a function of different levels of S9 to ascertain if the low accountabilities of activity sometimes observed is due to the use of single, nonoptimal levels of S9 in routine tests. All of the studies will be ongoing throughout 1980. * * *

7. Assay Standardization and Quality Assurance

In 1979, a series of steps was taken to improve our internal quality control over the conduct of the assay. These included: greater interaction and coordination on a regular basis between all members of the project involved in using the assay; the use the common cell stocks and samples of positive control compounds; standardization of assay methodology of conform to the most recent recommendations of Ames and co-workers; and more careful monitoring of interexperiment variations of spontaneous backgrounds, cell titers, and positive control activities. These efforts will be continued and expanded in 1980. It is our specific goal to prepare an internal, *Salmonella*/microsome assay methods manual which will document in detail all phases of the conduct of the assay at PM including data processing and analysis *via* the R & D computer. We expect to complete the initial draft of the manual in the second quarter of 1980 and then to continually update it whenever changes in protocol or procedures are made.

F. PERSONNEL

We have received authorization to hire a new person for our group in 1980. In view of the rather ambitious program outlined above and in keeping with our basic philosophy on current priorities as outlined in the Introduction above, our plans are to hire an Associate Scientist A in the second quarter of 1980. The new person will be assigned to work under the supervision and direction of more experienced personnel in one of the assay areas outlined above. Exactly which area will be decided upon at the end of the first quarter of 1980.

3. *SUMMARY OF PLANS AND GOALS FOR 1980*

Assay/Activity

A. *L5178Y Mouse Cells: Time*

1. *TK Mutation*

Verify WSC-induced, TFT-resistant mutants are TK: 1st quarter

Modified Cloning Procedure: 1st quarter

Develop and publish quality assurance criteria for assay: 1st quarter

LTF–IIIA variants-filler: 2nd quarter composition *vs.* WSC activity: and continuing

WSC fractions: 2nd quarter and continuing

WSC activity *vs.* S9 concentration: 2nd quarter and continuing

2. *SCE*

Establish assay: as time permits

3. *Metabolic Cooperation*

Feasibility studies: as time permits

B. *BHK Cell Transformation*

Establish assay protocol with positive and negative control compounds: continuing

C. *E. coli Differential Toxicity*

Aldehydes in smoke *vs.* activity: continuing

Test model compounds in liquid culture assay: 1st quarter

Activity *vs.* physical cigarette parameters: 2nd quarter and continuing

Mehtod development—aldehyde analysis (by 6908 personnel): continuing

D. *Yeast Mitotic Gene Conversion*

TPM activity *vs.* Puff volume: 1st quarter

Base *vs.* acid/neutral fractions of WSC: 1st quarter and continuing

Cigarette filler pyrolyzates: continuing

e. *Salmonella/Microsome Assay*

TPM activity *vs.* puff volume: 1st quarter

Cigarette filler pyrolyzates: continuing

Whole smoke and gas phase activity of solvent trapped smoke: 2nd quarter

WSC *vs.* base fraction activity: 1st quarter;

Fractionation of WSC bases: continuing

Additive and WSC testing: as requested

Research studies of additive testing: 2nd quarter

Assay standardization and quality assurance Methods: continuing

Manual: 2nd quarter

To: Mr. W.F. Kuhn
From: R.N. Ferguson
Subject: Plans and Objectives for 1980 (Charge Number 6908)
Date: December 18, 1979

I. INTRODUCTION

The project continues to have several interrelated goals:

(a) to develop and apply methods to identify and quantitate components of cigarette smoke which relate to biological activity,

(b) to use cigarette models to relate chemical composition to biological activity including precursor/product relationships,

(c) to develop or improve methods for collection of cigarette smoke and apply these to collection and processing of smoke condensate for *in vivo, in vitro,* and chemical testing.

The primarily defensive nature of this research necessitates a continual monitoring of developments in the literature related to the biological activity of smoke components. These goals also require a close coordination of our research efforts with those of Charge Number 6906—Biological Effects of Smoke.

During the last year, considerable progress was made in nitrosamine studies, in base fraction components, in liquid and gas chromatography methods, in pyrolysis, and in an aldehyde procedure. The complexity of WSC remains the major challenge to advances in these areas of interest. Another problem is the large number of areas requiring our attention. This is due to the considerable number of potentially active components known or suspected in WSC.

II. RESEARCH PLANS

A. Condensate Collection and Processing

More emphasis will be put on condensate collection studies since these methods are a key part of our research.

Collection of whole smoke condensate by Elmenhorst cold trap (ECT) or impaction trap (IT) procedure will continue, along with processing, for *in vivo* testing. This involves gc analysis and concentration testing on these samples. Selected ECT or IT trapped and processed samples will be checked for volatile and nonvolatile nitrosamines.

The collection of samples for *in vitro* and chemical study has been expanded to ECT, IT, TPM pad, gas phase, and collection in liquids. Some of these methods will require further development. In addition, design and application of sidestream collection systems has begun. Considerable effort will be required to develop satisfactory methodology in the coming year.

A study of volatiles not collected (IT) or lost during processing (ECT) has also been initiated and will continue. A longer range study of a glass cascade impaction trap for a particle size profile is planned. This could be extended to chemical and biological evaluation of each size fraction.

A system will be set up in the coming year for pyrolysis or combustion of filler and collection of the smoke for either chemical or *in vitro* assay. After the equipment has been obtained an extensive check of conditions will be made for possible correlation of pyrolyzate and WSC biological activity. The application of this methodology to evaluation of a series of bright marcs is also planned.

B. Chromatography

Improved separation procedures will allow both the investigation of new areas and more complete investigation of areas previously studied.

Extensive modification of the PE–900 for use with fused silica capillary columns is progressing.

The Sigma 3 gc, which is coupled to the du Pont 21–490 mass spectrometer, has capillary capability. To permit the exploitation of this feature on the 21–490 ms will require considerable effort due to limitations in the ms system. Acquisition of capillary capability for the gc/ms/ds, if possible, will be a significant advance in our capabilities.

A low pressure lc system has been designed and will provide a flexible preparative or isocratic analytical chromatography system. Major initial emphasis will be on reversed phase chromatography applications to base fractions from X6D3IM (burley) WSC.

It is anticipated that a number of new hplc separations will be made possible by the acquisition of a second high performance, gradient analytical lc system in 1980. This will

provide sufficient capability both to develop new methods and to put developed methods into routine use on the present instrument (Spectra Physics 3500B).

Droplet counter-current chromatography is a method not previously investigated for WSC fractionation. An effort toward a collaborative evaluation of the methods potential in areas of interest to us will be made.

C. Nitrosamines

The procedure for volatile nitrosamines is well developed but application of this technique on new samples will continue. The general method will also be applied to correlation of tobacco precursors with nitrosopyrrolidine in smoke. Work with sidestream and processed WSC is also planned.

We have been delayed in development of methods for nonvolatile nitrosamines by sample load but work in this area will be initiated in the first quarter of 1980. Of interest is N-nitroso nornicotine (NNN), 4-(N-methyl-N-nitrosoamino)-l-(3-pyridyl)-l-butanone (NNK), and N-nitrosanatabine (NAB). A hplc has been interfaced to the thermal energy analyzer (tea) for these analyses, but we also will explore the possibility of using gc/tea for these so called nonvolatile nitrosamines. Initial work will concentrate on mainstream smoke, but extension to sidestream is possible in the future.

D. Base Fraction of X6D3IM (burley)

The isolation and identification of individual active base fraction components has proven difficult. Nevertheless, the high microsome dependent activity shown by these fractions requires a further effort at identification. Of particular importance will be the improve chromatography methods described in section B. Further use of model compounds is planned for improvement in fractionation and identification procedures.

E. Model Cigarettes: Chemical Studies versus Salmonella Activity

A series of 14 cigarettes (varying tobacco fillers) has been selected for a number of chemical evaluations. In addition, the *Salmonella*/microsome activity of each WSC and base fraction will be evaluated. We hope to better understand the influence of filler parameters on base fraction activity and yield and also the levels of some specific components in WSC from various tobacco types. Planned chemical studies include: a) TMS derivatization of the WSC and capillary gc profile generation. Pattern recognition analysis of data *versus in vivo* estimated activity and/or *in vitro* activity. Use of the gc profile method on base fractions. b) The quantitative hplc procedure for quinoline in WSC will be applied. The determination of additional aza-arenes in these fractions is also a possibility. c) A procedure for harmane and norharmane in the base fraction will be developed. This hplc procedure will also be applied to the set of model WSCs. d) A gc method for nicotine will be applied to the base fractions. e) We hope to be able to develop an hplc method for amino $\alpha-$ and $\gamma-$ carbolines (tryptophane pyrolysis products) in the base fraction. When available, this procedure will also be applied to the model WSC samples.

In addition to these studies, cigarettes have been prepared by adding proline, tryptophane, or phenylalanine to LTF–IIA (nitrogen free) filler. A study of the active base fraction components from these fairly simple model systems is planned with emphasis on the tryptophane spiked sample.

F. Bright Tobacco Extraction

Work is continuing on the fractionation of bright tobacco in order to study the effect of removal of various classes of nitrogen containing compounds. Increased emphasis will be on the chemical components of each marc and extract, particularly the amino acid composition of protein fractions and the nature of the nonprotein nitrogen components.

When acceptable pyrolysis conditions are available, this method will be used for evaluation of each marc.

G. MW 288

The positive identity of this smoke component has remained unsolved, primarily due to our problems with selective ozonolysis and derivatization of model compounds. A synthetic approach to this compound is being pursued by Dr. Edwards. We are considering the possibility of the preparation of a crystalline derivative suitable for an x-ray structure study.

The cuticular wax of bright and burley tobacco has been obtained. We hope to establish that duvatrienediols produce MW 288 under appropriate thermal conditions. Further, we expect to find out if each isomer of duvatrienediol leads to one specific MW 288 isomer.

H. E. coli Assay and Aldehydes

The *E. coli* assay has previously defied attempts to determine which components of smoke are principally responsible for activity. This may no longer be the case. Evidence has been accumulated that some aldehydes are highly active in the assay. Progress has been made in trapping and derivatizing both whole smoke and gas phase smoke. An hplc method for the dinitrophenyl-hydrazones of reactive carbonyl components is almost finalized. We will attempt to definitely establish the quantitative importance of the smoke aldehydes in this assay.

I. Additional Areas

There are a number of additional areas of opportunity and interest which do not fit into the areas already discussed or are of lower priority for study. Investigation in at least some of these areas is planned as time allows.

(a) Some initial work has been done with activity in fractions in the yeast assay. We wish to find the types of components responsible for the activity seen in WSC by fractionation studies.

(b) LTF–IIA plus phenylalanine-continuation of gc and gc/ms studies for products from phenylalanine in model cigarettes.

(c) Develop methods for N-heterocycle analogs of PAHs in smoke.

(d) Further study of the red material formed in ECT smoke of nitrate cigarettes and see if addition of NO to smoke will produce this band on ECT.

(e) Explore the utility of gel permeation chromatography both for WSCs and for condensate fractions.

(f) Explore the effect of added sugars or sugar-amino acid reaction products in modulating the activity arising from proteins and amino acids in tobacco.

(g) Study the mass spectra of geometric isomers of aldehyde O-methyloximes.

(h) A tobacco glycoprotein may be transferred to smoke. If so, an understanding of the parameters controlling this transfer would be of great use. A capability for isolation of such material will be developed.

(i) Fluorescence is a very useful tool in a number of areas. Additional evaluation of the utility of fluorescence for studies of smoke components and evaluation on commercial instrumentation needs to be made.

(j) Is 3-nitro-5-(3′-pyridyl)-pyrazole formed on ECT collection of smoke from high nitrate cigarettes?

(k) Develop and apply chemical/physical indicators of estimated *in vivo* biological activity.

III. CONCLUSION

These plans and objectives represent some redefinition of the project's goals. There is more emphasis on the development of smoke collection technology and its impact on WSC chemistry. Also greater emphasis is on chemistry coupled to actual *in vitro* (particularly *Salmonella*/microsome) activity rather than estimated *in vivo* activity has been dropped as a research goal. Finally, capillary gc and various hplc methods have been given a high development priority in our planning.

IV. PLANS

Activity; Timetable

A. Condensate Collection, Preparation, Analysis

1. Current Test Samples: Ongoing*

2. ECT and IT for *in vitro* and chemical study: Ongoing

3. Alternate collection—TPM, solvent impaction, sidestream: 4th qtr., 1979 through 4th qtr. 1980

4. Volatiles and semivolatiles lost in collection and processing: complete 2nd qtr.

5. Pyrolysis setup and experimentation: Initiate; 1st qtr.

B. Chromatography

1. Capillary gc on PE 900

(a) Derivatized WSC: Complete 3rd qtr.

(b) Fractions: Initiate 2nd qtr.

2. Evaluation of capillary gc/ms: 1980

3. Low pressure lc system: Assemble 1st qtr.

4. Analytical hplc

(a) New system installation: 1st quarter

(b) New methods development: Ongoing

(c) Gel Permeation: 1980?

C. Nitrosamines

1. Volatile nitrosamines: Ongoing

2. Nonvolatile nitrosamines: Initiate 2nd qtr.

D. MW 288

1. Structure: Complete 3rd qtr.

2. Duvatrienediols as precursors: Complete 4th qtr.

E. *Salmonella*/microsome assay

1. X6D3IM base fractions: Ongoing

2. Base fractions from Model cigarettes

(a) Yield and activity: Complete 1st qtr.

(b) Chemical constituents: Initiate 1st qtr.

3. Bright tobacco marcs and extracts: Ongoing

4. LTF–IIA plus additives: 1980

F. Aldehydes and *E. coli* activity: Complete 3rd qtr.

G. WSC fractions and yeast assay: Initiate 1st qtr.

H. Additional Areas

1. Chemical predictors of EBA: In 1980 as time permits.

2. Polycyclic nitrogen heterocycles

3. Red bands in ECT smoke

4. Tobacco glycoprotein

5. Application of fluoresence

6. Basic ms studies—oximes

7. Sugar effect on WSC activity

8. Droplet counter current distribution

*Completion in 1980 is not anticipated for any ongoing projects.

To: Dr. E.B. Sanders

From: J.I. Seeman

Subject: Plans and Objectives for 1980 (Charge 2500)

Date: January 4, 1980

Work for 1990 will be focused in three general areas; alkaloid and nicotine chemistry, flavor chemistry, and flavor-release chemistry. In addition, we will continue to perform assistance to other units upon request in such areas as custom synthesis and general organic chemistry.

I. Alkaloid and Nicotine Chemistry (Chavdarian, Secor, plus one).

A. Objectives

1. To develop a fundamental understanding of the mechanisms by which nicotine and other tobacco alkaloids interact with peripheral and central nervous system receptors.

2. To determine if nicotine analogues can be designed which exhibit differential activity at different receptors.

3. To develop procedures to synthesize nicotine analogues and isotopically labelled nicotine analogues.

4. To investigate the possible correlation of structural and chemical parameters with biological behavior.

5. To perform, in a collaborative fashion, pharmacological testing of nicotine and its analogues with a goal of deriving structure-activity relationships.

6. To develop an effective insecticide(s) through collaborative testing of nicotine analogues; in this conjunction, the mode of action(s) of these compounds will be investigated.

7. To aid other groups with problems related to tobacco alkaloids.

B. Synthetic Studies

1. Preparation of Optically Active Nicotinoids

a. Procedures will be developed which will allow the separation of racemic nornicotine derivatives into their enantiomers. This will involve the HPLC purification of, a.g., nornicotine urethanes which are diastercomeric by virtue of the nornicotine condensation reagent.

b. We have already shown that 6-methylnicotine and 6-butylnicotine can be formed in high yield from nicotine by reaction with methyllithium and butyllithium respectively. This procedure will be extended to other 6-substituted nicotinoids.

c. Microbiological reduction of 3-acetylpyridine has been shown to result in the optically active alcohol. Attempts to convert this alcohol to the corresponding amine will be made. If successful, this procedure will be applied to an asymmetric norcotinine synthesis.

d. We have found that cotinine can be alkylated and carboxylated at C-4′. The products can subsequently be reduced to 4′-substituted nicotinoids which are optically active by virtue of asymmetry of cotinine. This work will be extended to a few additional analogues.

e. 5-(3-Pyridyl)butyrolactone, obtainable from procedure I.B.1.c. above, may be convertible to active norcotinine with ammonia.

f. The microbiological reduction of imines (e.g., myosmine) to saturated amines (e.g., nornicotine) may result in an optically active product. There are no examples of such a reduction in the literature. This will be examined.

2. Preparation of Pyridine-Substituted Analogues

a. 5- and 6-Substituted nicotinoids will be prepared by a variety of methods, including the reaction of nicotine with alkyllithium reagents (c.f. I.B.1.b.) and routes involving synthesis of substituted nicotinonitriles and methyl nicotinates. These will also include heterosubstituted nicotinoids. Optically active 6-hydroxynicotine will be prepared from microbiological oxidation of nicotine. This material will be used as the key intermediate in the preparation of 6-alkoxy and 6-acetoxy derivatives.

b. Nicotine 6-carboxylic acid and nicotine 5-carboxylic acid and their corresponding esters will be prepared.

c. 2,4-Dimethylnicotine and selected deuterated analogues will be prepared for mechanistic studies.

3. Preparation of Pyrrolidine Substituted Analogues

a. HPLC purification will be performed to purify numerous isomeric methylated nicotinoids.

b. 2′-Substituted analogues will be prepared by addition of organometallic reagents to N′-methylmyosmine perchlorate.

c. A number of N′-substituted nornicotines in their enantiomeric forms (c.f. I.B.1.a.) will be prepared.

d. 4′-Substituted nicotinoids will be prepared (c.f. I.B.1.d.).

e. Additional examples of 3′-alkylnicotines will be prepared by condensation of 3-pyridinecarboxaldehyde and Michael acceptors.

f. Anatabine will be prepared from the reaction of 3-pyridyllithium (or 3-pyridylmagnesium bromide) and 2-cyano-Δ^4-piperidine.

g. Simple syntheses of nicotyrine will be investigated, for example, by the reaction of 3-pyridyllithium with a protected 4-hydroxypyrrolidinone.

h. Δ3′-4′-Dehydronicotine will be prepared, either by reduction of methylnicotyrine (c.f. I.B.3.g.) or dehydration of 4′-hydroxynicotine (c.f. I.B.l.d.).

4. Preparation of Bridged Nicotines. This type of nicotinoid represents the most difficult challenge in the synthesis of nicotine analogues. In the past year, one member of this class has been prepared in a one-step procedure from tropinone and β-aminoacrolein.

Note that the carbon atoms which have the ''bold-faced'' dots can be interchanged with the pyridine nitrogen atoms of these compounds to produce isomeric bridged compounds. Ideally, the preparation of the ''pairs'' of compounds will be successful.

5. Ring-Ring Shifted Nicotinoids. A number of compounds falling into this class have already been prepared.

C. Mechnistic Studies

1. Kinetic experiments and stereochemical evaluations of the alkylation of a wide variety of nicotinoids with iodomethane and possibly other alkylating agents will continue. These experiments are aimed to allow an understanding of the steric, electronic, stereoelectronic, and conformational features present in these systems. Implementation of the totally automated conductivity system is anticipated to be a milestone in such kinetic investigations.

2. Protonation studies will continue to allow the evaluation of the conformation of the N-methyl group in these nicotine analogues.

3. NMR studies will be used as in the past to derive conformational information about these molecules.

4. Theoretical calculations (INDO, Ab Initio) will be performed to give information regarding conformation, electron distribution, polarizability, etc., of these molecules.

5. Kinetic studies involving a-cyanoamines will be performed.

D. Microbiological Studies. In collaboration with B. Semp, a number of studies involving the use of microbiological techniques to perform a variety of synthetic operations will be investigated (c.f.I.B.l.c.; I.B.l.e.; I.B.l.f.; I.B.2.a.). Also included will be an attempted large scale preparation of nornicotine from nicotine.

E. Pharmacological.

l. Efforts will continue to obtain peripheral and central nervous system data on our compounds. Some of this will be with the aid of C. Levy and her associates.

2. Partition coefficients and pK_a data are needed for our compounds.

F. Insecticidal. More racemic and optically active nicotine analogues will be submitted for in-house and collaborative testing.

To: Those Listed Dr. T.S. Osdene, Dr. E.B. Sanders, Dr. W.L. Dunn, Mr. J.L. Charles, Dr. J.I. Seeman

From: R.B. Seligman

Subject: Nicotine Receptor Program—University of Rochester

Date: March 5, 1980

As you know, we have been supporting the subject program for the past year, and Dr. Abood has visited with us several times during this period. I would like an *independent written* evaluation from each of you concerning the benefits this program brings to our Research Center.

Please transmit these reports to me by March 21.

To: Dr. R.B. Seligman

From: J.L. Charles

Subject: Nicotine Receptor Program—University of Rochester

Date: March 18, 1980

Nicotine is a powerful pharmacological agent with multiple sites of action and may be the most important component of cigarette smoke. Nicotine and an understanding of its properties are important to the continued well being of our cigarette business since this alkaloid has been cited often as ''the reason for smoking'' and theories have been advanced for ''nicotine titration'' by the smoker. Nicotine is known to have effects on the central and peripheral nervous system as well as influencing memory, learning, pain perception, response to stress and level of arousal.

It is not surprising that a compound with such a multitude of effects would have properties which are considered undesirable by the anti-smoking forces. Claims are made that nicotine in cigarette smoke can induce chest pain and irregularities in cardiac rhythm when a person with a compromised cardiovascular system smokes or when persons with cardiac disease are exposed to high concentrations of side stream smoke.

For these reasons our ability to ascertain the structural features of the nicotine molecule which are responsible for its various pharmacological properties can lead to the design of compounds with enhanced desirable properties (central nervous system effects) and minimized suspect properties (peripheral nervous system effects). There are many opportunities for acquiring proprietary compounds which can serve as a firm foundation for new and innovative products in the future.

The above is an excerpt from an introduction to the nicotine program which I wrote on 12/1/78. My views have not significantly changed since that time. I believe that nicotine does play an important role in the smoking process. How important that role is remains to be determined. The receptor program at the University of Rochester is an integral part of the nicotine program and can be justified in a number of ways. An initial thought was that Dr. Abood would have the knowledge and techniques to perform screening of nicotine analogs for CNS activity. The synthesis group has created a number of interesting compounds which are now being screened by Dr. Abood. In addition Dr. Abood was to carry out fundamental studies on sites and mechanisms of action of nicotine in the brain. That research is in progress.

I sat in on an additional meeting with Dr. Abood and Drs. Sanders, Seeman, and Chavdarian during Dr. Abood's last visit. I found the discussions to be useful and felt that Dr. Abood was doing some very interesting work which can ultimately be of benefit to Philip Morris. I also utilized Dr. Abood as a consultant during that visit and he made some good suggestions and I thought the time was well spent.

In summary, the nicotine receptor program at the University of Rochester is an integral part of our overall nicotine program. The combination of basic research on the pharmacology of the nicotine receptor combined with the capability to screen nicotine analogs for CNS activity complements our internal synthetic and behavioral efforts in the nicotine program. The program is justified in my view as a defensive response to the anti-smoking forces criticisms of nicotine and also as fundamental research into the nature of our product and how it affects

our customers, the smokers. This entire program involves complex technological problems and the benefits to be derived from the program will not be realized immediately. Indeed the benefits will necessarily be of a long-term nature and may have direct bearing on our market position in a 10–15 year time frame. However, if we do not have the basic research results this program will provide we will not be in a position to respond if and when the pressures to change do occur.

To: Dr. R.B. Seligman
From: E.B. Sanders
Subject: Nicotine Receptor Program—University of Rochester
Date: March 21, 1980

Dr. Leo Abood's collaboration with the Research Center has been extremely beneficial to the nicotine program. His assistance has impinged on four different areas; namely, direct assistance to the Behavioral Research Group, assistance in interpreting peripheral testing results, providing us with current information regarding work concerning nicotine pharmacology at other locations, and direct hands on work in setting up binding assays for nicotine analogues synthesized by members of Charge Number 2500.

Dr. Abood's interaction with the Behavioral Research Group has been of crucial importance in establishing the ''prostration syndrome'' test. The value of this particular technique to the nicotine program cannot be overstated in that it is the first biological response to nicotine that does not appear to be mediated by a cholinergic receptor. The original charge of the nicotine program was (1) to ascertain if the central and peripheral effects could be ''separated'' and (2) to design a nicotine analogue which would have CNS activity equivalent to nicotine with little or no peripheral effect. Since it has been well-established that nicotine's peripheral effects are cholinergic, the discovery of a non-cholinergic central receptor provides us with reason to believe in the ultimate success of the program.

Future work involving the ''prostration syndrome'' must unequivocally establish the non-cholinergic nature of the receptor and must explore the role that the ''prostration syndrome'' receptor plays in the psychology of smoking. Leo's expertise, involving his experience in the necessary methodology as well as his work in attempting to characterize the natural neurotransmitter for this receptor, is crucial to the vigorous prosecution of this work.

For several years we have been receiving data on peripheral screening of our nicotine analogues from Germany. The quality of the work has been consistently of the highest calibre. On the other hand, the German laboratory has been of minimal assistance regarding interpretation. The problem is a combination of our lack of pharmacological sophistication coupled with the large distance between Richmond and Cologne. We have existed with this problem for some time since it would be virtually impossible to match the good service we are getting elsewhere. Leo Abood's association with Philip Morris has consequently filled a void. Not only have we been able to get a better handle on both the meaning of a given test result but possible interesting follow-up tests on certain analogues as well.

Dr. Abood has occupied a position of preeminence in neuropharmacology for some time. Consequently, he has contacts with virtually all of the laboratories working on various aspects of nicotine pharmacology, throughout the country. These contacts have benefitted us by keeping us abreast of interesting current developments as well as in more direct ways. The best example of the latter involves the direct assistance Leo is providing us in carrying out binding assays for our synthetic analogues. Leo has obtained a sample of purified nicotinic receptor from Torpedo and has established the experimental conditions for assaying binding to the receptor. We are now in the process of sending out the first set of compounds. This assay will allow us to differentiate between compounds which bind to the nicotinic receptor but do not activate it and those compounds which do not bind. With this information we hope to get a clearer picture of the nicotinic receptor.

In summary, I feel that we have benefitted considerably from Leo's association with the Research Center, and I trust that this association will continue.

To: Dr. T.S. Osdene
From: W.L. Dunn
Subject: Plans and Objectives—1981
Date: November 26, 1980

INTRODUCTORY NOTES

The Behavioral Research Laboratory effort is organized into programs which reflect to a large degree the subdisciplines of the responsible psychologists. On the one extreme of the psychological spectrum is the social psychology program of Dr. Sandra Dunn. On the other extreme is the behavioral pharmacology program of Dr. DeNoble. Ranging between are the experimental psychology program of Mr. Ryan, the electrophysiology program of Dr. Gullotta and the smoke inhalation program of Miss Jan Jones. Each of these programs is but a varied attach upon the overall objective of the Behavioral Research program: To contribute useful knowledge about the response of the smoker to the cigarette and its smoke. The results may prove useful in developing a new product, or improving an existing product, or in the defense of the company from legislative or litigative harassment.

ELECTROPHYSIOLOGY PROGRAM . . . Gullotta and Shultz

Objectives:

It is our belief that the reinforcing properties of cigarette smoking are directly relatable to the effects that smoking has on electrical and chemical events within the central nervous system. Therefore, the goals of the electrophysiology program are to: (I) Determine how cigarette smoking affects the electrical activity of the brain, and (II) Identify, as far as possible, the neural elements which mediate cigarette smoking's reinforcing actions.

Planned Studies

I. SPECTRAL ANALYSIS OF THE ELECTROENCEPHALOGRAM

We have proposed this study in the past but, due to technical problems, we have been unable to undertake it. We are finally in a position to begin.

Numerous studies have investigated the effects of cigarette smoking and nicotine administration on the electroencephalogram (EEG) of man and other animals. Although there is some degree of concordance among the results of these studies, many points are yet to be resolved. For example, with regard to the human literature, an early study showed that cigarette smoking produced low amplitude, fast EEG activity. Another study, however, found that smoking did not increase low amplitude fast activity and, indeed, slowed certain EEG frequencies. A number of other examples of this type can be found in the literature.

It seems likely that most of the controversies could be resolved by a more systematic analysis and quantification of the EEG. Therefore, we plan to spectrally analyze EEG data from a variety of electrode locations under varying smoking and deprivation conditions.

II. Animal Electrophysiology

We have discussed with Dr. DeNoble the possibility of a collaborative effort to study the effects of nicotine and nicotine-like compounds on the electrical activity of the rat brain. This would involve EEG recordings from surface and deep structures within several experimental paradigms. It would also involve the use of evoked potential technology. Some technical problems must be solved before such a program can be initiated. Our early efforts will be aimed at addressing these technical considerations.

III. The Effects of Cigarette Smoking on Pattern Reversal Evoked Potentials

This study is well under way and will be completed in early 1981.

We have previously demonstrated that cigarette smoking increases the amplitude of the late components of the visual evoked potential to flash stimulation. However, since flash stimulation activates nonspecific brain structures (e.g., reticular formation, association cortex, etc.) as well as specific structures (e.g., primary visual cortex), we were unable to determine with certainty whether the enhancement we observed was due specifically to increased receptivity to visual information.

Pattern stimulation avoids the problems associated with flash by activating primarily visual structures. Therefore, we are using pattern reversal evoked potentials to checkerboard stimulation to study the effects of cigarette smoking on visual information processing.

IV. Cigarette Smoking and the Habituation of Pattern Reversal Evoked Potentials

It is commonly reported that cigarette smoking facilitates one's ability to concentrate. Concentration implies sustained attention to simulation. We are interested in the possibility that we might gain insight into the processes involved by employing evoked potential techniques.

When, within a given session, sensory evoked potentials are repeatedly measured, there is a decrement in the response over trials. We interpret this decrement as a decrease in the sensitivity of the system to incoming sensory information. We can then ask whether cigarette smoking alters the rate at which this decrement occurs. If smoking retards the rate at which the evoked potential decreases in amplitude over trials, we will have demonstrated one manner in which concentration might be facilitated by cigarette smoking.

We have recently been gathering pilot data on this subject employing pattern reversal evoked potentials. If our data look encouraging we will mount a full-scale investigation in early 1981.

V. *Cigarette Smoking and the Brainstem Auditory Evoked Potential*

Recently, a new class of evoked potentials have been described. These are the acoustic and sematosensory brainstem (far-field) evoked potentials. One of the advantages of these brainstem potentials relative to the more traditional forms of recording is that the neural generators of the components are better known. For example, it has been shown that Peak I of the auditory brainstem response is due to VIIIth nerve activity, Peak II to activity of the cochlear nucleus, etc..

In this experiment we will be employing brainstem auditory evoked potentials in an attempt to ascertain sites and modes of action for centrally active smoke constituents. We chose the auditory potential because (1) there are nicorinic cholinergic synapses within the system and (2) it has recently been shown that, in rats, systemic nicotine administration alters certain components of the response.

THE BEHAVIORAL PHARMACOLOGY PROGRAM . . . DeNoble

Objectives

I. To develop a better understanding of the behavioral pharmacological actions of nicotine, particularly the action which reinforces smoking behavior.

II. Develop the empirical evidence which differentiates nicotine from the classical abuse substances.

III. Use behavioral pharmacological methods for evaluating the nicotine-likeness of nicotine analogues.

Planned Studies—I. Nicotine Self-administration

A successful development of the technique for establishing self-administration of nicotine in an animal has important implications for all three objectives of our behavioral pharmacology program.

We have developed that technique, making it quite clear that nicotine can function as a positive reinforcer for rats. We will use the technique (1) in studying the reinforcing action of nicotine, (2) in differentiating nicotine from the classical abuse substances, and (3) in evaluating analogues.

We will undertake as many of the following essential self-administration studies in 1981 as time permits:

(1) Examine the dose-response curve under various schedules.

(2) Examine the effects of cholinergic antagonists upon self-administration.

(3) Determine substitutability of selected analogues.

(4) Demonstrate, in pursuit of Objective III, that (a) nicotine self-administration does *not* interfere with on-going behavior and (b) that termination of nicotine availability for self-administration does not produce behavior impairment, or alter self-administration of other reinforcers (food, water, saccharine, etc.).

II. The Nicotine-Induced Prostration Syndrome

The prostration syndrome, first reported by Leo Abood as a gross behavioral response to the intraventricular infusion of nicotine, has been used routinely for several years in our program of nicotine analogue evaluation.

Although the prostration syndrome is a reliable screen for behaviorally active nicotine analogues, the rating scale developed by Dr. Abood provides only descriptive interpretation of the compounds' effects, and does not permit a determination of possible prolonged changes in CNS activity. We have begun using scheduled controlled behavior to evaluate the effects of intraventricular injections, since measures based upon this behavior have been shown to be more sensitive than activity rating scales, and provide a more stable nicotine baseline from which to evaluate CNS recovery times for nicotine analogues.

We have recently observed in conducting these studies that there is a diminution of the effect of nicotine over repeated administrations. Diminution will occur even with a 7 day interval between the first and the second administration, and observation difficult to explain simply in terms of the development of metabolic tolerance. We may be observing instead an instance of behavioral tolerance. We are currently designing a study which should more accurately characterize the development of tolerance.

We will also be conducting studies in which the effects of the selective blockade of neural structure will be reflected in the behavioral components of prostration, anticipating that these observations can further our knowledge about the sites of action of nicotine.

III. Discrimination Studies

We will continue to use the now standardized discrimination technique to evaluate nicotine analogues. We are currently investigating a dose-response curve approach, a modest variant on the standard procedure.

THE EXPERIMENTAL PSYCHOLOGY PROGRAM

Objectives

1. To gain a better understanding of the role of nicotine in smoking.

2. To study basic dimensions of the cigarette as they relate to cigarette acceptability.

Planned Studies—I. Salivary Nicotine

Speculation suggests that smokers modify smoking behavior to maintain certain levels of nicotine in the blood. Historically this has been the basis of nicotine titration hypotheses. Knowledgeable consideration of the issue suggests that the changes in level may be more important than the absolute levels—that the input of nicotine from a cigarette creates a ''spike'' which is the summation of the discrete puff-induced spikes.

We now have the ability to measure via gas chromatograph the level of nicotine in saliva. Observations from previous work with salivation and smoking suggest that systemic nicotine in saliva tracks with systemic nicotine in the blood. We plan to use the g.c. measure to:

A. Monitor the appearance and decline of nicotine in saliva following smoking. This will shed light on the question ''Does a low systemic level of nicotine trigger the smoking response.'' The question can only be answered if measures are made many times. Therefore, we will:

B. Observe changes in salivary nicotine level across time and smokings, relating the changes to the delivery of cigarettes smoked and the time since prior smokings. The data will bear upon the issue to the extent that salivary nicotine reflects tissue and blood levels of nicotine. This must be confirmed by means of:

C. A correlational study of the salivary nicotine with blood nicotine. This is awkward research to perform because the taking of blood samples is so intrusive and objectionable to participants and because it requires medical supervision. Therefore, we will postpone this segment of the research until it is evident that there are some systematic changes in the salivary nicotine data. We have made some preliminary contacts with our medical staff, and they will support us when needed.

II. There are tentative plans for one other project in which nicotine will be delivered intravenously in different sized spikes of different duration, to yield a broader picture of the role of the spike, the level, and the reinforcement characteristics of the substance. The execution of this project is contingent upon the execution of study I–C above, since both involve the dosing of numerous subjects with nicotine.

III. Other smoking related research

1. Role played by Cigarette Firmness in determining cigarette acceptability. Much attention has been paid to the problem of maintaining the firmness of our cigarettes at a level consistent with the image of a high quality product. We have recently found that a trained panel's evaluations of firmness are highly correlated with the firmness data provided by the Firmness-while-smoking machine and our compacimeter procedures. However, we know neither the relative importance of firmness to the consumer (compared to other characteristics of the cigarette's appearance) nor the most desirable firmness level. We will try to find out.

IV. Support for other projects, within R & D and within behavior research, will be provided, as necessary.

SOCIAL PSYCHOLOGY PROGRAM S. Dunn

Objectives

I. To gain a better understanding of the role of social psychological factors in shaping cigarette smoking behavior.

II. To apply social psychology techniques to the study of cigarette acceptability.

Planned Studies—I. *Exploratory Study on Psychosocial Determinants of Smoking Behavior*

As an initial approach to the problem, we have designed a one-on-one interview including both objective questions and in-depth probes. This interview is an intensive two-hours of data gathering, ranging across a spectrum of social, personality, attitudinal and situational dimensions. The dimensions were chosen for inclusion because of their potential relevance to smoking behavior. Items included in the questionnaire/interview schedule can be subsumed under these headings:

1. Emotional state and responsivity.
2. Stress-handling mechanisms.
3. Situational determinants and cues.
4. Socio-cultural influences.
5. Health concerns and smoking.

Interviewees are being drawn from among the population of 45 year-old, white, college-educated, upper-middle class women, half of whom smoke high-delivery cigarettes and half of whom smoke ultra-low delivery cigarettes. Focus on these groups will also provide data on women smokers and on the factors determining choice of delivery level.

The data obtained will be subjected to a statistical analysis designed to identify the underlying higher order factors. The nature of these factors, and the extent of their influence upon smoking behavior will provide the basis for further studies. The analysis is scheduled for completion by the end of the first quarter of 1981. Upon completion of this analysis we will generate hypotheses testable under rigorous, laboratory-controlled conditions.

II. The Influence of Cigarette Firmness Upon Cigarette Acceptability

Mr. Ryan has reported a study of the correlation of subjective firmness with measures obtained on the Firmness-while-smoking machine and on the compacimeter. The question has been raised as to what relevance, if any, these measures have to cigarette acceptability. We are designing a study that will address this question. The study will incorporate interview techniques of social psychology rather than rely upon conventional marketing research survey methods.

III. THE INHALATION MONITORING PROGRAM . . . Jones

Objective: To determine in what manner the smoker altersimulation patterns in response to changes in the chemical composition of cigarette smoke.

Planned Studies—I. Instrumentation

A. *Exploratory research using the new recording system.* The literature on smoke-laden inhalation research is limited, and that which does exist suffers from severe technological constraints. Our inhalation monitoring system provides us with the advanced technology necessary to acquire fundamental information about inhalation behavior. We are immediately concerned with establishing valid and reliable criteria for determining when a subject's inhalation patterns have

stabilized—at what point we are seeing a reproducible representation of the subject's inhalation behavior. In designing our experiment we must determine what would be sufficient time within each period of data collection for the smoking behavior to stabilize, before introducing a new experimental condition. Other information which is related to experimental design involves what happens to baseline behavior, established on a smoker's own cigarette, following experimental conditions. Is there a return to baseline inhalation behavior or will the baseline readjust? Carry-over effects resulting from the use of repeated measures may occur and must be taken into account.

B. *Programming a dedicated minicomputer for data display and analysis.* The MINC/DECLAB minicomputer, expected to arrive early in 1981, will be used to store and display the quantities of information collected. Following our programming efforts, the computer will be customized to handle the high-speed analyses required for our specific needs.

II. Experiment # 11: Does the smoker demonstrate compensatory inhalation behavior in response to changes in the nicotine content of cigarette smoke?

The experimental design is repeated measures with an ABACA format—a powerful method for examining what happens to inhalation patterns when a smoker switches between cigarettes of high, low, and ultra-low nicotine delivery. Baseline measures will be taken on the smoker's own low delivery cigarette until we observe stable behavior. The smoker will then switch to an ultra-low or high delivery experimental cigarette for two weeks, the order of presentation being balanced across subjects. Following each experimental condition, the smoker will switch back to his own cigarette to re-establish baseline behavior. Our primary interest is in comparing one inhalation parameters of Condition B with Condition C, demonstrating differences due to nicotine delivery of the cigarette smoked. The other 3 conditions will mainly serve to make this information meaningful.

We will be collecting data for approximately 2 months on each subject. The study will begin early in 1981 and is expected to continue throughout the year.

The SPEAKER pro tempore. Under a previous order of the House, the gentleman from New York [Mr. TOWNS] is recognized for 5 minutes.

[Mr. TOWNS addressed the House. His remarks will appear hereafter in the Extensions of Remarks.]

The SPEAKER pro tempore. Under a previous order of the House, the gentleman from Florida [Mr. GOSS] is recognized for 5 minutes.

[Mr. GOSS addressed the House. His remarks will appear hereafter in the Extensions of Remarks.]

FRENCH NUCLEAR TESTS

The SPEAKER pro tempore. Under a previous order of the House, the gentleman from American Samoa [Mr. FALEOMAVAEGA] is recognized for 5 minutes.

Mr. FALEOMAVAEGA. Mr. Speaker, once again I take the floor to express to my colleagues and to the American people my deep disappointment with a decision made recently by the President of the Government of France to explode eight nuclear bombs in the South Pacific, and each bomb explosion is ten times more powerful than the nuclear bomb dropped on the city of Hiroshima.

Mr. Speaker, I have just learned from media reports that some 47 parliamentarians from Australia and 11 from New Zealand, and several more parliamentarians from Austria, Japan, Denmark and Germany—all plan to travel to French Polynesia to protest the proposed nuclear testing program by the French Government which will commence in September of this year.

Mr. Speaker, I want to offer my support and commend the parliamentarians of all these countries for their commitment and convictions to tell the French government leaders that France's proposal to explode eight nuclear bombs is just plain wrong and contrary to the wishes of some 28 million men, women and children who live in this region of the world.

Mr. Speaker, I also would like to make an appeal to my colleagues to join me by traveling to French Polynesia and let the French Government know that nuclear testing in the middle of the Pacific Ocean is an outmoded, ridiculous, and simply a dangerous undertaking not only for the marine environment but the lives of the millions of men, women and children who live in the Pacific region.

Mr. Speaker, the President of France recently proclaimed that France was the homeland of the Enlightenment, and I have no doubt that some of the world's greatest thinkers—men of reason—men who appreciate and value human rights, and who respect the rights of others.

Mr. Speaker, again I ask—what possible reason is there to justify President Chirac's decision to explode eight nuclear bombs? He said in the interest of France—but what the concerns and higher interest of some 170 nations of the world that recognized the dangers of nuclear proliferation—the dangers of nuclear bombs being exploded in an environment that changes constantly because of seasons climatic conditions that produce earthquakes, hurricanes, cyclones; and another real serious danger to these French nuclear explosions, Mr. Speaker, is we have no idea what is going on below the base of this volcanic formation.

After some 139 nuclear explosions for the past 20 years inside the core of this volcanic formation—something has got to give—and if radioactive leakages start coming out of this volcanic formation within the next 10 years or even 50 years—my problem, Mr. Speaker, is that the 60 million French citizens living in France are going to continue enjoying the good things of life like drinking their French wines, while the millions of people who live in the Pacific are being subjected to radioactive contamination—let alone some 200,000 Polynesians, Tahitians, who incidentally are also French citizens—all, Mr. Speaker, are going to be the victims. Is this fair, Mr. Speaker?

Can Mr. Chirac honestly look at himself in the mirror—every morning and keep saying to himself that it is okay to nuke those islands out there in the Pacific, and that the lives of 200,000 French citizens in the Pacific are not important to the Government of France? What arrogance, Mr. Speaker.

Mr. Speaker, in the minds of millions of people around the world—the Government of France has committed a most grevious error by authorizing an additional eight nuclear bomb explosions to take place in certain atolls in the South Pacific.

Mr. Speaker, I would like to make this special appeal to my colleagues on both sides of the aisle and to my fellow Americans—make your voices heard—support the concerns of the millions of men, women, and children in the Pacific and around the world who do not support French nuclear tests—call and write letters to the Congress and the French Embassy here in Washington, DC—tell the leaders of France that exploding 1.2 million tons of TNT in an ocean environment is both dangerous, insane, and utter madness.

Mr. Speaker, tomorrow the House Committee on International Relations will consider House Concurrent Resolution 80, which expresses the strong sense of the Congress for recognition of the concerns of the nations of the Pacific region—a recognition also of the environmental problems that will attend these additional nuclear bomb explosions—and to call upon the government of France to stop these nuclear tests since about 70 percent of the people of France do not want nuclear tests to take place, and countries from Asia, the Pacific region, the Western Hemisphere, Europe—all do not want France to resume nuclear testings.

Mr. Speaker, I ask my colleagues to support House Concurrent Resolution 80, which already has the support of Members from both sides of the aisle.

Mr. Speaker, I include the following for the RECORD:

U.S. DOUBTS FUEL FEAR OF COLLAPSE ON NUCLEAR TEST BAN—PHYSICISTS MEET TO REINFORCE STAND

(By Charles J. Hanley)

Weeks before they light the fuse in the far Pacific, the French have set off an explosion of global protest with their plan to resume nuclear weapons testing.

But the nuclear future may depend less on what happens on a Polynesian island in September than on the outcome of a secretive meeting last week at a California resort, where leading physicists gathered to try to help a wavering U.S. government take a stand on a global test ban.

These latest developments—a decision in France, indecision in America—have suddenly cast a shadow over international negotiations to conclude a comprehensive test ban treaty by late 1996.

The Polish chairman of those talks in Geneva sounds worried.

''It's possible,'' Ludwik Dembinski said of reaching the goal. ''But it will be very difficult.''

Fifty years after the first atomic test explosion in New Mexico, on July 16, 1945, the