

RJR CONFIDENTIAL

R.J.Reynolds Tobacco Company
Winston-Salem, NC 27102

INTER-OFFICE MEMORANDUM

RJR

January 23, 1985

TO: Dr. G. R. Di Marco

SUBJECT: Weekly Highlights
Biochemical/Biobehavioral
For Week of January 14-18, 1985

ITEMS FOR WEEKLY BRIEF

Scientific Affairs

• Environmental Tobacco Smoke (ETS)

Issues regarding federal funding were discussed at a meeting of the Environmental Tobacco Smoke (ETS) Advisory Committee. The National Cancer Institute (NCI) is currently funding ETS at \$500,000. This amount is expected to increase. The Environmental Protection Agency (EPA) has allocated an additional ceiling of two million dollars to fund ETS research.

A critique of the Repace and Lowrey (EPA) analysis of ETS originally written by Dr. Sorel Schwartz of Georgetown University for submission to the Office of General Counsel, EPA has been rewritten by Dr. Colucci at the request of the Tobacco Institute.

• Future Meetings

The American Society of Testing Methods (ASTM) has announced a subcommittee organizational meeting on "Measurement of Indoor Air Quality", March 12-13, 1985, Philadelphia. ASTM has been asked by the Consumer Federation of America to develop standards for indoor air quality.

ITEMS OF GENERAL INTEREST TO R&D

Biobehavioral Research

• Nicotine Pharmacology

Dr. Robinson attended a seminar by Dr. Hayward (UNC-Chapel Hill) at BGSM last week. Dr. Hayward employs hypothalamic preparations to study endocrine response to electrical and chemical stimulation. Dr. Hayward has found that endocrine responses of the preparations are seen only when nicotine is injected directly into the supraoptic

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nucleus and not when it is added to the cell-bathing medium. This may explain some anomalous results observed by Robinson and Deadwyler in their work with the hippocampus.

Rats are now housed in the small animal facility. Binding assays of nicotine with membrane preparations from whole rat brain and selected brain subregions will begin immediately.

- Psychophysiology of Smoking

Dr. C. D. Spielberger (U. South Fla.) visited Dr. Gilbert on January 18th to discuss development of questionnaires for the peer assessment of personality.

- Blood Chemistry

An RIA assay for ACTH, run with a commercial kit, showed excellent agreement with expected values.

- Smoke Component Dose

Negotiations with Respitrace, Inc., suppliers of our respiration monitoring equipment, re the schedule for software modifications required, have resulted in an agreement for a six-month time-frame for effecting the changes. This allows time for us to test the equipment and to advise as to the efficacy of the changed software.

Scientific Affairs

- Environmental Tobacco Smoke (ETS)

Dr. Tony Colucci and Mr. Mike Davidson of Jacob, Medinger & Finnegan met with Drs. D. Sterling and D. J. Moschandreas of the Illinois Industrial Toxicology Research Institute (IITRI). They solicited proposals to determine the reliability of questionnaires to quantify ETS exposure by individuals and to develop a personal nicotine monitor, respectively. These projects are to be conducted for the ETS Advisory Committee of the Tobacco Institute.

- Additives

Pyrolysis data from triethylene glycol did not reveal any unusual compounds. In-house comparisons of smoke from Winston and Marlboro brands were reviewed since Marlboro contains triethylene glycol as a humectant. Traces of diethylene glycol were found in the pyrolyzate (700°C) from an in-house study and 5.0 µg/cigarette was found in the smoke from Marlboro. High concentrations of Diethylene glycol have been reported to cause bladder tumors in rats due to formation of calcium oxalate crystals in the bladder. The tumors are probably the result of mechanical irritation and not the result of primary carcinogenesis. Routine analytical tests for aldehydes, benzo(a)pyrene, carbon monoxide, cyanide, nitrous oxides, and phenols

along with triethylene glycol concentration in smoke have been requested before final approval of this additive. A review of in-house data suggests that transfer of triethylene glycol from the tobacco to the smoke may be greater than either propylene glycol or glycerin.

The flavor division recently reformulated a flavor containing N-methyl pyrrolidinone for RJR MacDonald (Canada). It is a natural constituent of tobacco. This compound is approved by the Hunter - Froggatt Committee, Great Britain, and the German government. The compound has not been approved for use by any United States government agencies. We are currently compiling the literature on this compound.

- Fiberglass

Owens-Corning Fiberglass has initiated an epidemiological study to examine the effects of smoking and fiberglass exposure. This study will be conducted by Dr. Phil Enterline, University of Pittsburgh, and will be completed in approximately 2 years.

Toxicology

- Training for the HGPRT/CHO assay (Chinese hamster ovary assay for gene mutation). Substances tested thus far include standard mutagens (ethyl methane sulfonate and dimethyl-benzanthracene). Testing of cigarette smoke condensate has been initiated.
- Dr. Burger visited laboratories and animal facilities in Pennsylvania and New Jersey. These laboratories included Exxon, Mobil, Smith Line and French, and McNeil laboratories.


A. Wallace Hayes

AWH:bm

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