

2nd MEETING OF SCIENTIFIC RESEARCH GROUP
MONTREAL AUGUST 6th-8th 1986

Present:	Dr. R.E. Thornton	BAT Co. London
	Dr. S.R. Massey] Imperial Tobacco Ltd., Montreal
	Dr. M. Bilimoria	
	Mr. R.G. Nicholls	W.D. & H.O. Wills, Sydney
	Dr. G. Smith	BAT UKE, Southampton
	Dr. F. Knabjohann] BAT Cigaretten Fabriken, Hamburg
	Dr. F. Seehofer	
	Dr. J.G. Esterle	Brown & Williamson, Louisville, Kentucky
	Dr. G. Gori] Consultants
	Dr. W. Templeton	

Nicotine

Dr. Gori discussed the results of a behavioural study of 799 subjects carried out in the U.S.A., strongly pointing to nicotine as the basis of the smoking habit. For example plasma nicotine levels were almost constant, regardless of measured machine smoked delivery levels, as were the number of cigarettes smoked per day. Dr. Gori went on to discuss the possibilities for products in the future including changes in Tar/Nicotine ratios and nicotine aerosols. Dr. Gori said that further work to demonstrate that some of the effects of smoking were due to nicotine was still required.

In a broad look at nicotine toxicology, covering carcinogenicity, promoting activity, mutagenicity and a possible rôle in cardiovascular disease Dr. Gori considered the evidence that nicotine had activity to be equivocal at best and frequently weak or non-existent. Some good studies also existed in which no activity was seen (e.g. carcinogenicity). However he suggested that a repetition of a well planned study looking at carcinogenicity might be justified. Dr. Gori also commented on the multifactorial nature of cardiovascular disease.

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Dr. Gori considered that work in relation to diseases negatively associated with smoking might be justified, e.g. colon cancer, Alzheimer's disease etc.

Finally in regard to the allegation that nicotine was addictive, Dr. Gori said that this was a problem in semantics and pointed out that the reinforcing effects of smoking (and presumably nicotine) were entirely positive.

Dr. Templeton described the distribution of receptors for acetylcholine and the current status of work using materials such as α -bungarotoxin to probe for binding sites. It was now realized that α -bungarotoxin did not necessarily bind at the same sites as nicotine; implying, perhaps, that an endogenous ligand exists for such sites. However, since there is some binding of nicotine at "bungarotoxin" sites the possibility exists that the effects of nicotine might be enhanced by effects at the adjacent "bungarotoxin" receptors.

Studies of receptor sites using modern techniques of molecular biology were described. Brain acetylcholine receptors have been shown to possess 4 cysteine units at similar places. With regard to the human diseases (Parkinsons and Alzheimer's disease) it was pointed out that patients presenting were at an advanced stage of degeneration because the brain functioned even with 70% or so of neurons out of action.

With regard to the effects of smoking on cognitive performance more work was needed to clarify the research of Warburton which was rather isolated, particularly concentrating on nicotine and on whether it caused an intrinsic increase in performance.

Experiments in non-human primates did not support the view that smoking was addictive. Training non-human primates to smoke required a reward and water (a basic necessity of life) had to be used, and after removal of the reward the % of 'smokers' was as low as 2%. Attempts to classify materials such as nicotine, amphetamine, caffeine, heroin etc. showed that each material was unique.

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August 7th

Present: As on 6th August, but without consultants.

Delegates reviewed the previous day: it was agreed that the presentations by Dr. Gori and Dr. Templeton were of great value.

Agenda items:

1. No specific comments: a brief summary was given to those not present in Nice.
2. Terms of Reference agreed as written (with the addition of "interactions with the non-smoker" thereby including passive smoking).
3. Dr. Seehofer discussed his paper outlining plans for his visit to Japan. It was noted that the J.T.I. had approached U.S. companies for financial support towards their programme. Find plans, priorities to be discussed with RET in Hamburg. Visit should be between September and November 1986, probably of 2 weeks duration.
4. Agreed that passive smoking be included, but that additives, which relate specifically to products, should be considered separately.

The prime aim of the S.R.G. is to review the literature, identify gaps in knowledge, commission research and monitor the results. Individual companies could, of course, carry out their own research as appropriate but should place any work on the S.R.G. data base.

5. Funding. RET will write a paper for consideration in Sydney and individual companies would consider the position.
6. Grant Applications. Six applications had been received in the U.K. and were being considered in BATCo. Members agreed that 2 (Clamp and Carter) appeared to fall within areas which the S.R.G. had identified as deserving further work (see item 7). Ideally such applications would in future be considered by BATUKE, bringing the U.K. into the practice of local consideration typical of the rest of the group.

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7. It was agreed that work was desirable in the following areas:

- a) Nicotine receptors, to include the α -bungarotoxin receptor which might synergize the nicotinic receptor. This could include work on subjects such as Alzheimer's or Parkinson's disease which appear to involve degeneration of CNS mechanisms.
- b) Novel behavioural work, to complement the studies of Professor Warburton.
- c) Subject to views from consultants, it appears that the fate of nicotine is not fully accounted for. This may need further work, and at least a literature search.

8. This is being compiled.

9. A brief job description was circulated and accepted. As far as possible members would be kept in touch with progress. Target date for employment: late 1986.

10. There was an exchange of information on external activities, including funded research of passive smoking and the 1987 Nicotine conference to be held in Sydney.

11. Dr. Seehofer described his discussions with distinguished German scientists in which their views on smoking issues were solicited.

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