



Technical Memorandum

FUNDAMENTAL RESEARCH CENTRE
BRITISH AMERICAN TOBACCO COMPANY LTD
Southampton England

No. TM 91-04-002

Subject **COMMENTS ON A RECENT PAPER BY FISCHER AND
CO-WORKERS ENTITLED "TOBACCO-SPECIFIC
NITROSAMINES IN CANADIAN CIGARETTES"**

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To

File

Date

8 April 1991

Index Terms

Tobacco Specific Nitrosamines; NNN; NAIB; NNK; Canada;
Tobacco Chemical Properties; Smoke Chemical Properties;
Mainstream Smoke; Cigarette Brands; Smoke Transfer;
Cigarette Ventilation; Burley Tobacco; Flue-cured Tobacco

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400703005

BATCo document for Province of British Columbia 21 April 1999

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400703006

BATCo document for Province of British Columbia 21 April 1999

WDE/BTM
8 April 1991

**COMMENTS ON A RECENT PAPER BY FISCHER AND CO-WORKERS
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TECHNICAL MEMORANDUM NO. TM.91-04-002

Author: W.D.E. Irwin

SUMMARY:

The paper by Fischer *et al* lists tobacco and mainstream smoke results for tobacco specific nitrosamines (TSN) in 25 Canadian cigarette brands.

This technical memorandum evaluates these results in respect to consistency with findings from previous internal and external research. The conclusion is that trends in the results are compatible with previous findings on variables which influence TSN levels in tobacco and smoke.

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INTRODUCTION

Sophia Fischer and co-workers have published a paper on the tobacco and mainstream smoke tobacco specific nitrosamine (TSN) levels in 25 Canadian cigarette brands (1). The purpose of this report is to evaluate their results in respect to consistency with findings from previous internal and external research. A review of this literature to end 1988 was published as a BAT (UK & Export) report in March 1989 (RD.2136, Reference 2). Findings from that review are used in this evaluation.

Fischer *et al* have published a number of other papers on tobacco and smoke TSN levels as indicated in the reference section of their Canadian study. These papers post-date the above review and five of them were evaluated in a BAT (UK & Export) Technical Memorandum in 1990 (TM.90-06-001, Reference 3). These five papers are References 11-14 and 16 as ordered in the reference section of the Canadian study.

Abbreviations

Abbreviations as used in the Fundamental Research Centre (FRC) will be used in this report. In two cases these differ from those used by Fischer. Tobacco specific nitrosamines will be abbreviated "TSN" rather than "TSNA". Nitrosoanatabine will be abbreviated "NAiB" rather than "NAT". Other abbreviations do not differ. However, Fischer refers to a composite nitrosoanabasine/nitrosoanatabine as "NAB/NAT". NAB level is usually very low compared with nitrosoanatabine (2) and therefore this report will abbreviate this composite as "NAiB".

Fischer's paper (1) will now be evaluated under three headings, TSN transfer, ratios of individual TSN to each other and TSN/tar ratios.

TSN Transfers

It is usual practice in the FRC and in most external literature to record the TSN content of tobacco as nanograms or micrograms TSN per gram tobacco. Fischer *et al* have recorded tobacco results as nanograms per cigarette. Without knowing tobacco weights it is not possible to compare the TSN contents of the tobaccos from the 25 brands. However, the percentage transfer of the three TSN can be calculated on an approximate basis from the mainstream and tobacco results. The calculation is approximate if transfer is defined as the mainstream delivery divided by the TSN content of that portion of the tobacco rod which is consumed during smoking i.e. the rod length minus 8 mm in this case. With the available information, the TSN content of the whole tobacco rod must be used in the denominator, but this is satisfactory for comparison of TSN transfers within a given brand.

"Transfer" is a misnomer in this calculation because some mainstream TSN are derived by pyrosynthesis during smoking as well as by distillation, see page 43 of the review of nitrosamine literature (2). That review concluded that most of the mainstream NNN and NAIB was derived by distillation but rather more NNK was derived by pyrosynthesis. The TSN transfers of the 25 brands are recorded in Table 1.

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TABLE 1

TSN TRANSFERS

Brand	Transfer (%)		
	NNN	NAIB	NNK
1	1	2	1
2	1	2	1
3	1	1	2
4	1	2	2
5	3	4	5
6	5	6	6
7	4	5	6
8	4	4	5
9	5	6	7
10	8	8	11
11	8	8	10
12	7	7	10
13	6	6	8
14	7	8	10
15	8	8	10
16	8	9	11
17	9	10	11
18	9	9	12
19	9	9	12
20	11	11	14
21	11	12	15
22	10	11	14
23	8	9	11
24	10	11	15
25	8	8	12

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The increase in transfer with tar delivery (see Table 1 of the paper) is obvious and expected, given that the TSN are contained in the particulate phase and are subject to reduction by the same design variables (e.g. tobacco weight, filtration and ventilation) as tar. The Review (2) concluded that filtration and ventilation reduce TSN by approximately the same amount as for nicotine.

Comparisons of the transfers of the three TSN within each brand also indicate the expected pattern. There is little difference in boiling points between the three TSN (2) and hence no obvious reason to expect different transfers. However more NNK pyrosynthesis should lead to higher "transfers" and this is a consistent feature of Table 1.

To conclude on transfers, the results in Table 1 are consistent with prior expectations.

NAI_tB/NNN and NNK/NNN Ratios for Tobacco and Mainstream

The three TSN are determined from the same smoking and gas chromatography runs. Hence errors in these ratios may well be less than the errors in the individual TSN results. Fischer notes in her paper that NAI_tB and NAB are derived from anatabine and anabasine respectively. NNN is recorded as being derived from normicotine and nicotine. However, consideration of other information (2) suggests that NNN is derived mainly from normicotine. It is also probable (2) that the majority of all three TSN in mainstream smoke is derived by distillation of the same TSN from tobacco.

With these assumptions and the transfer data in Table 1, one would expect a good relationship between the above ratios in mainstream smoke and tobacco. Further, because there is more normicotine in Burley tobacco than in Virginia tobacco, relative to the other alkaloids, one would expect the lowest NAI_tB/NNN and NNK/NNN ratios from brands 1, 2 and 6 which have the highest nitrate contents.

Figures 1 and 2 are MINITAB plots of mainstream and tobacco NAI_tB/NNN ratios and mainstream and tobacco NNK/NNN ratios respectively. The symbols A-Y correspond to brands 1-25. Where two data points are similar, MINITAB records these as "2", rather than as the individual letters.

The figures confirm that brands 1, 2 and 6 (A, B and F) have the lowest ratios. Fischer makes a similar point in her paper. The results are consistent with prior expectations.

Figure 2 shows a better linear relationship than Figure 1. This is slightly surprising based on FRC experience which suggests greater variability in NNK results than for the other two TSN. This may be due to NNK being eluted towards the end of the gas chromatography run. The good linear relationship of Figure 2 will not have occurred by chance and suggests no problem in NNK reproducibility in Fischer's work.

TSN/Tar Ratios

These are recorded in Table 2 and give the quantity in nanograms of NNN, NAIB and NNK delivered for each milligram of tar. (Tar values were taken from the pack information). The table is divided into the tar categories in Fischer's paper.

One value of such ratios is that they take out much of the variation in TSN deliveries due to design differences. Thus the bottom three tar categories show little difference in TSN deliveries when "normalized" to equal tars. NNN/tar ratio is in the range 2-3 ng/mg. NAIB/tar and NNK/tar ratios are in the range 4-7 ng/mg. Tar is a fairly good predictor of TSN level for these categories. Tar is not a good predictor for the very low tar category for the following reasons. The highest NNN/tar ratios occur with brands 1,2 and 6 which probably contain the highest proportions of Burley tobacco and highest nicotine and NNN levels in the tobacco. From Reference 2 and elsewhere, Burley tobacco also contains higher levels of anatabine and NAIB than Virginia tobacco, though the difference is less marked than for nicotine and NNN. Hence the high NAIB/tar ratios for brands 1,2 and 6 are as expected. The highest NNK/tar ratio occurs with brand 4 which probably also has the highest NNK tobacco level, based on the quantity in the cigarette.

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TABLE 2

TSN/TAR RATIOS

Brand	TSN/tar ratio (ng/mg)		
	NNN	NAIB	NNK
1	13	21	10
2	11	16	6
3	4	9	9
4	6	15	18
5	3	7	9
6	10	16	8
7	5	10	11
8	4	8	8
9	3	6	6
10	3	7	7
11	2	5	6
12	2	5	6
13	3	6	6
14	3	6	6
15	3	5	6
16	3	5	6
17	2	5	5
18	2	5	6
19	2	5	5
20	2	5	5
21	2	5	6
22	2	4	5
23	2	4	4
24	2	5	6
25	2	4	5

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However, it is obvious that the above considerations do not provide a complete explanation of the higher TSN/tar ratios in the very low tar brands. Two other factors may be operating. Firstly, the balance of the evidence (2) suggests that ventilation reduces TSN to a similar extent to that for nicotine, i.e. less than for tar. Therefore, increasing ventilation should increase TSN/tar ratios. There is some evidence in Table 2, across all four tar categories, of increasing TSN/tar ratios with increasing ventilation (and decreasing tar). Secondly, greater errors might be expected in measuring the lower TSN deliveries from the very low tar cigarettes. Confusion between "signal" and "noise" could lead to overestimates at lower deliveries.

To conclude on TSN/tar ratios, the results in Table 2 are compatible with expectations based on precursor and ventilation levels, with the possibility that some part of the higher ratios in very low tar products could be due to methodology factors. This possibility is conjecture only.

Other Comments

Parts of the summary and main text of Fischer's paper demonstrate some inexperience of the TSN literature and of cigarette design and its influence on smoke deliveries. The summary refers to the "unusual" good correlation between tar delivery and ventilation ratio. There is nothing unusual about this correlation, other things being equal. This inexperience has adversely affected the clarity of the analysis of the reasons behind the various trends in the results.

CONCLUSIONS

This Technical Memorandum has calculated and examined various ratios based on Fischer's results. The aim was to check that trends were compatible with prior information from the internal and external literature.

In all cases these trends were as expected and therefore strengthen previous teachings as well as validating Fischer's analytical results.

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