

# Development of an Index for Mainstream Tobacco Smoke Based on Chemical Composition

## Introduction and Methods

For the past 30 years, Health Canada has funded contract research related to the chemical composition of tobacco, tobacco smoke and environmental tobacco smoke. In July 1997 a project was commissioned to characterize the toxicity of mainstream tobacco smoke in support of proposed expanded reporting requirements (1-3). Six products were selected for the study including 4 commercially available Canadian cigarettes (market share about 20%), an American product which primarily heats tobacco and the Kentucky reference cigarette, 1R4F. The products, their codes for figure references, and approximate sales figures may be found in the following table.

Brand Code	Product Type	Sales (1995)
FC1	Flue-cured commercial Canadian	4%
FC2	Flue-cured commercial Canadian	13%
FC3	Flue-cured commercial Canadian	3%
FC4	Flue-cured commercial Canadian	?
KR	Kentucky reference cigarette 1R4F	N.A.
TH	American tobacco heating cigarette	?

Yields of 42 constituents in 8 groupings were determined under standard Federal Trade Commission (FTC) type smoking conditions and a second protocol which required taping of the filter, and a puff volume of 56 ml of 2 second duration every 26 seconds. Constituent monitoring included aromatic amines, such as 4 aminobiphenyl, miscellaneous organics including compounds such as 1,3-butadiene, 8 carbonyls including formaldehyde and acrolein, phenolics such as phenol and catechol, tobacco specific nitrosamines which were determined under contract by the American Health Foundation, and trace metals including arsenic and mercury. These were selected based on published properties (toxicity/carcinogenicity), and lists of toxic compounds such as that which has been compiled by Dr. Hoffmann (4,5). The methods are available from Health Canada and are mandated under the proposed regulations regarding emissions reporting (see Health Canada, Health Protection Branch Information Letter No. 819 dated June 10, 1998). A list of groupings along with the individual constituents can be found in figure 1.

## Results

The data set resulting from the analyses has been used to address three issues.

1. There is now a regulatory requirement, in at least two jurisdictions, for the use of two smoking regimens. The issue of predicting yields under non standard conditions is of importance in this context since suitable prediction equations could reduce the amount of work involved in meeting these requirements. Dr. Borgerding and others (6,7) have proposed equations for the prediction of "tar" nicotine and CO yields. The same approach can now be used for other constituents of interest.
2. The use of "tar" as an indicator variable for other tobacco smoke constituents has been suggested on numerous occasions (see, for example, ref. 8). The data from this project provides another opportunity to examine this issue.
3. The committee that looked at the FTC methodology (9) has recommended the use of simple graphical methods for communicating yield data. This becomes all the more important when faced

with the prospect of reporting on over 40 constituents most of which have no significance for the general public.

## A Comparison of Yield Under Standard and "Intense" Smoking

Smoking under "average" or "intense" conditions results in an increase in yield (**10**). This is not surprising since increasing the puff volume or decreasing the puff interval results in an increase in the amount of smoke taken for analysis (see figure 2). For example, in the present study the average volume of smoke taken for analysis under standard conditions was 344 ml (standard deviation, 33 ml) and 845 ml (standard deviation 107 ml) under "intense" conditions for an average ratio of 2.5 (i.e. intense/standard)<sup>1</sup>. Some variation in this ratio was anticipated due to product differences, random variation in puff number within a product and the effect of different smoking machines. For example, analyses for NO required the use of a single port smoking machine, while 'volatiles' utilized a 20 port rotary machine, and "tar" a linear SM 400 smoking machine.

In terms of individual constituents, the variation in yield ratio is much greater; again for a number of reasons (figure 3). These include normal analytical variation, the possibility of a condition/yield interaction and the other factors noted previously. Consequently, it is noteworthy that the observed average ratio of 2.3 is very close to the expected value of 2.5. This reinforces the conclusion drawn previously from results for "tar": namely, that for many compounds it may be possible to predict yields under non standard conditions by adjusting for differences in smoke volume (**11**). This point was communicated in 1986 by a former Canadian Health Minister in a press release in which yields of "tar" nicotine and CO were reported in units of mg/litre rather than mg/cigarette. To quote the press release "...yields per litre estimate the maximum amount of toxic substances per cigarette to which some smokers are exposed (**12**)". It is important to point out that the "maximum" referred to by the Minister, was obtained without resorting to a second set of testing conditions.

## "Tar" as a Predictor of Other Smoke Constituents and the Rank Order Issue

The relationship of carbon monoxide (a gas phase constituent) to "tar" was investigated by regressing the corresponding Canadian yield data obtained in a 1997/98 survey. The relationship is linear with a slope of 1.0 (i.e. 1.0 mg CO per mg "tar") and a very good fit to the regression line particularly for those brands with "tar" yields less than or equal to about 12 mg. There is more scatter for higher "tar" brands in this data set but there is no evidence for a 'break' in the regression relationship (figure 4).

A similar data set from 1978 presents a somewhat different picture. In this case, the slope of the regression line is 50% higher (i.e. slope = 1.5 mg CO per mg "tar") for those 22 brands with a "tar" yield of 12 mg or less. For the 80 brands with "tar" yields in excess of 12 mg, the correlation between "tar" and CO was non significant (Pvalue > 0.01). Thus in 1978, the relationship between yields of "tar" and CO was not constant over the "tar" range (figure 5). This has changed over time. For those brands with yields less than about 12 mg, the slope of the regression line has decreased from 1.5 to 1.0 so that the numbers for "tar" and CO are now virtually identical. For the remainder, there is a highly significant relationship where previously there was none. One possible explanation for the change lies with another former Canadian Minister of Health who, in 1983, asked the Canadian cigarette manufacturers "...to reduce carbon monoxide yields so that by 1984, the level of carbon monoxide does not exceed the level of tar for any brand of cigarette (**13**).". Based on these results, it is reasonable to conclude that useful predictive relationships between "tar" and other variables do exist for some brands. However, these relationships may change in response to government pressures and/or the introduction of new technologies.

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<sup>1</sup> Results for the cigarette which primarily heats tobacco have not been included in these calculations. In many cases yields for this brand approached the detection limits for the method under both test conditions resulting in ratios for many constituents which were highly variable.

A related issue is that of the rank order of brands based on yield and how this might be affected by changes in smoking conditions. For example, consider yields of phenol for the 6 brands examined in this project. As illustrated in figure 6, the functional relationship between yields under standard conditions and those under intense conditions is not the same for all 6 brands; the slope of the line for the Kentucky reference cigarette (1R4F) is different from that of the flue-cured (FC) cigarettes. Secondly, Brand FC3, which ranks as the lowest under standard conditions, is not the lowest under intense conditions.

This is not the case with respect to yields of carbon monoxide. Here it appears as though a single function would be adequate to describe the "tar", CO relationship for all 6 brands (figure 7). In addition, it is apparent that the rank order of the 4 flue-cured brands based on yields of CO is not affected by changing the smoking conditions. Based on these results and those presented previously (14), it is reasonable to conclude that some brands change rank when testing conditions change and some do not depending on which constituent and which brand are being considered.

## Development of Simple Methods for the Communication of Yields

Surveys of Canadian smokers have demonstrated that they continue to be confused regarding the meaning of the numbers for "tar" nicotine and CO which appear on every package of Canadian cigarettes (15,16). Smokers and non-smokers alike continue to view the numbers which appear on all packages of Canadian cigarettes in absolute terms in the same way as they view other content labels. And yet, the many measurements of human smoking behaviour have demonstrated that yield to smokers is too variable to be represented by any one number. The committee that examined the FTC method recognized this problem. They concluded, among other things, that "A simple graphic representation should be provided with each pack of cigarettes sold in the United States and in all advertisements (9). One possibility is to take advantage of the unique colour of "tar" and to produce a scale which depicts the relationship between the two variables (17). Consumers would then be able to estimate their mouth level exposure by breaking the filter off of the residual tobacco column and comparing the colour of the tobacco end of the filter to the scale. This type of scale has the advantage of demonstrating to the smoker that his/her "tar" exposure is highly variable and depends on how the cigarette is smoked. Given this confusion, methods for the communication of the results from any proposed additional reporting requirements must be given careful consideration. In fact, one could make the argument this aspect merits as much or greater attention than the test methods themselves.

Another graphical possibility is as follows. To begin, 42 smoke constituents have been listed in a circle in alphabetical order beginning with acetaldehyde and ending with 2-amino naphthalene (figure 8). This is the key for two star plots; one which summarizes yields under standard conditions and one which expresses relative concentrations under 'intense' smoking conditions<sup>2</sup>. Under standard smoking conditions, there are three distinct patterns, one for the tobacco heating cigarette, one for the Kentucky reference cigarette and one for the flue-cured cigarettes (figure 9). Within the flue-cured group, brand FC1 is distinguished by its smoke selenium content. The tobacco-heating cigarette is remarkable due to its high filter efficiency and small 'footprint' while the Kentucky reference cigarette stands out because of relatively high values for lead, arsenic and nitric oxide. Differences among the brands become more prominent under non-standard smoking conditions; a phenomenon that has been noted previously (18). Under these conditions, the Kentucky Reference cigarette now stands out along the dimensions of Pb, As, HCN, NO and filter efficiency and the tobacco heating cigarette along the three dimensions of "tar", CO and ammonia (figure 10). Yields of chromium and formaldehyde distinguish brand FC2 from the other 3 brands of flue-cured tobacco cigarettes. While star plots are useful for detecting groupings, the depiction is relative and depends on which products are included in the mix. Also it is unlikely that they would be understood by the majority of consumers. Unfortunately numerical summaries for each and

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<sup>2</sup> Recall that a star plot is a visual means of comparing different observations in a relative sense for all the variables at once. Each star is a-polygon drawn so the distance of the vertices from the center point represents that observation's values in relation to the other variables. The shortest ray is used to plot the smallest value in each variable and the longest ray to plot the largest value.

every constituent, such as that suggested by Dr. Jeff Harris (9) will not solve the problem since a comparative base is not at hand.

This difficulty could be overcome if all of the yield data were to be combined in a single number that was related, in some way, to potential health effects. One possibility would be an exposure index which takes into account both constituent concentration and relative toxicity. This is the approach was taken by the RJ Reynolds Tobacco Company in the characterization of the smoke produced by Premier (19) and has also been used, more recently, in support of Massachusetts regulations regarding tobacco products (20). A similar calculation was carried out using the data generated in this project. The steps involved are as follows:

1. Determination of yields under standard or non standard smoking conditions.
2. Determination of the smoke volume (i.e. puff volume x puff number) and conversion to concentration/m<sup>3</sup>.
3. Calculation of a 15 minute weighted average exposure (puff number x 2 seconds/puff x concentration/m<sup>3</sup>)/(900 seconds).
4. Division by the corresponding ACGIH 15 minute short term exposure limit values (STEL's).
5. Summation over all constituents.

In summary, a relative exposure index (REI) is defined to be the summation of the ratio of the observed concentration in tobacco smoke to a 15 minute short term exposure limit (21).

Although the procedure is straightforward, there were difficulties due, primarily, to a lack of information.

1. Not all constituents have ACGIH STEL's.
  - OSHA or NIOSH STEL's were substituted
  - ACGIH 8 hr TWA substituted
2. Some constituents are A1 carcinogens and do not have STEL values.
  - Smallest tabled ACGIH STEL used (i.e. Be, 0.0005 mg/m<sup>3</sup>)
3. Some constituents have not been listed (e.g. tobacco specific nitrosamines or TSNA's)
  - not included in the calculation

Consequently the relative exposure index reflects the contribution of only 28 out of a possible 42 tobacco smoke constituents. The results from this calculation have been displayed, graphically, in figure 11<sup>3</sup>. The effect of the weighting procedure is evident from an examination of the values for acetaldehyde (average smoke yield of 521 ug/cig) and acrolein (average smoke yield of 55 ug/cig). When the yields are weighted by STEL's, the relative contribution of acetaldehyde to the index (REI, 0.74) is less than 20% of that calculated for acrolein (REI, 4.4). This reflects the fact that the toxicity of acrolein is much greater than that of acetaldehyde; a point which is lost when results are presented in the traditional manner that leaves relative importance to the imagination of the reader.

Considering the remaining 26 compounds, it is evident that most contribute very little to the value of the index. Specifically, on average 90% of the value of the index is comes from 8 compounds. These have been listed in the following table.

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<sup>3</sup> When examining this figure please remember the many assumptions which have gone into the calculation and the fact that the two American cigarettes represented there are not typical of what is sold in the United States. Thus it would be unfair and unreasonable to assume toxicological differences between American and Canadian cigarettes based on either this data set or this calculation

**Individual Contributions to the  
Relative Exposure Index**

<b>Index No.</b>	<b>Compound</b>	<b>Amount</b>
1	Acrolein	26%
2	BaP	16%
3	Formaldehyde	16%
4	Hydroquinone	9%
5	HCN	8%
6	Benzene	5%
7	Crotonaldehyde	5%
8	Acetaldehyde	4%
	<b>Total</b>	<b>89%</b>

There are also marked differences among product types. For example, in the case of the tobacco-heating cigarette, about 40% of the value of the index is attributable to acrolein while only 5% is due to the presence of formaldehyde. Nitric oxide contributes a little over 3% to the values for both the tobacco heating cigarette and the Kentucky reference cigarette but only 0.3% to the average value for the flue-cured products.

In summary:

1. An index (REI) has been constructed for 28 tobacco smoke constituents based on the ACGIH model for determining TLV's for mixtures.
2. REI values ranged from 1.8 to 25.4 and identified three cigarette types: Tobacco heating, 1.8; American blended, 14.6 and Canadian flue-cured, 24.3 (average).
3. REI is largely independent of smoking conditions but increases with the number of constituents.
4. As currently constructed eight compounds accounted for 90% of the value of the index.
5. The calculation of an REI suffers from a number of difficulties, the most important of which is the lack of adequate data and the assumption of additivity.
6. The purpose of the REI, as currently constructed, is to stimulate debate and foster further research.

As reporting requirements increase communication issues become critically important. In fact, in our opinion this question merits as much thought, attention, and effort as the methodologies themselves. It is in this spirit that a relative exposure index has been calculated and not as a definitive device for the toxicological characterization of tobacco products.

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