



Scope for regulation of cigarette smoke toxicity according to brand differences in toxicant emissions

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Abstract

Aims To explore the scope for regulating to reduce the toxicity of manufactured cigarettes sold in New Zealand (NZ), based on published toxicant emissions by brand.

Methods Internet searches of published cigarette smoke emissions of 13 toxicants chosen on risk assessment principles, for 20 British Columbian, 15 Australian brands, and one NZ brand, Holiday Extra-mild (HEM), tested by Health Canada intensive smoke machine method at Labstat Inc, Kitchener, Ontario, as a ratio of toxicant to nicotine yield. We estimated relative overall smoke toxicity per disease group and per brand, after adjusting for the published cigarette-attributed mortality fractions for cancer, cardiovascular, and respiratory disease.

Results After allowing for nicotine yield, filter ventilation, and compensatory over-smoking, there were significant differences between brands, with the NZ brand estimated to be the most toxic. Low-yield cigarettes (<0.9 mg nicotine ISO) were estimated to be on average 19% more potent overall than medium-yield cigarettes ($p < 0.01$). Of toxicants identified and measurable in smoke; 1,3-butadiene accounted for 45% of cancer potency; hydrogen cyanide for 89% of cardiovascular; and acrolein for 97% of respiratory potency—these three toxicants accounting for 65% of identified brand potency. Individual toxicant emissions varied across brands by a factor of 1.5 for carbon monoxide, to 32 for lead. Compared with HEM, one Canadian brand, 'Export A full flavor', carried a 37% lower cancer risk. This lower risk was largely due to differences in nicotine yield, lowering the toxicant/nicotine ratio.

Conclusions Cigarettes, unregulated, are unduly dangerous. Though many smoke toxicants cannot yet be quantified, risk assessment based on current data suggests that regulation could partly reduce identifiable cancer risk, and possibly eliminate the *excess* cardiovascular and respiratory toxicity of HEM, when compared with regular Canadian brands. The first goal should be to reduce emissions of the leading three toxicants, in addition to more effective charcoal filters. Tobacco smoke, unlike unburnt or non-smoking tobacco, contains toxic gases and trillions of reactive oxygen species molecules per puff, and will remain inherently harmful. Regulation could usefully part-reduce smoke toxicity exposure for continuing smokers, while not relenting on efforts to assist smokers and society to be quit of smoking.

Since 1990 in New Zealand, the Smoke-free Environments Act has provided powers at Section 31 to regulate harmful constituents 'contained in or generated in the smoke' of tobacco products, once the harmful constituents are named in regulations. The Ministry of Health's regulatory review of the regulations in 2004 included consultation for regulations needed to give effect to Section 31, which also gives powers to remove fire accelerants from paper, and to reduce the nicotine content of cigarettes. Improved nicotine delivery devices are needed,¹ and more effective

smoking cessation methods. This paper, however, confines itself to the regulated reduction of cigarette smoke toxicity.

Until now, the New Zealand comprehensive tobacco control programme² has focused on reducing prevalence and consumption. A national quit campaign began in 1999. A law change in 2003 banned smoking in all workplaces and hospitality venues from December 2004. Smoke toxicity per cigarette, has however, escaped policy attention.

This paper explores the feasibility and scope for reducing the toxicity per cigarette with respect to cancer, cardiovascular, and respiratory diseases. Scope for reducing toxicity seemed considerable—by the ISO machine test, tar varied 100-fold among New Zealand brands;³ and carcinogen NNK nine-fold among Marlboro brands from 30 countries.⁴ What was lacking was a method of assessing the combined risk from the various toxicants, and of scoring the overall toxicity of each brand. Smoke constituents include toxicants, such as carbon monoxide (CO), other vapour phase gases, particulates (tar); and the main addictive constituent, nicotine.

Cancer risk—Ethylene oxide, a known human carcinogen, has been found in the vapour phase of cigarette smoke of fumigated and unfumigated tobacco⁵ and in cigarette smoke,⁶ but has not been tested alongside other smoke carcinogens, even in British Columbia. Also un-quantified is the contribution of tumour promoting agents (such as free radicals) in the smoke stream, which almost certainly increases the cancer potency of the mixture in relation to the sum of its individual carcinogens.

Respiratory disease risk—Toxicants, such as aldehydes and acrolein, paralyse respiratory cilia, and work with reactive oxygen species (ROS), estimated at 10¹⁴ molecules per puff, to kill alveolar and bronchial epithelial cells.⁷ ROS in the vapour phase exist so briefly that their measurement is not possible, and may account for considerable unmeasured toxicity.

Cardiovascular disease risk—Nicotine on its own increases heart rate but not cardiovascular risk—in a randomised controlled trial of 3900 smokers chewing nicotine gum over 5 years, neither its use nor its dose was associated with cardiovascular hospitalisation or mortality rates.⁸ Hydrogen cyanide (HCN) inhibits cytochrome-c oxidase, blocking the cell from using its oxygen; the nervous system and the heart are particularly sensitive. For this reason, the Californian Environmental Protection Agency website assesses HCN as the most potent cardiovascular toxicant in smoke.⁹ Sublethal doses can result in vascular lesions and myocardial toxicity in animals.¹⁰ In fire victims, HCN may potentiate the hypoxic effect of CO. HCN in plasma has a half-life of only 14 minutes¹⁰—so that smoking should seldom lead to rising HCN levels during the day. Much less is known of the effects of small repeated exposures.

Cigarette smoking carries a 10-fold excess sudden-death risk, unmatched by any other coronary risk factor, and a 3.6 fold excess risk of myocardial infarction.¹¹ This risk is not due to nicotine as such⁸ or to oral tobacco, which has a disputed effect if any on cardiovascular risk.¹² Carbon monoxide, hydrogen cyanide, and nicotine, by increasing demands on the heart via the sympathetic nervous system, all tend to create a deficit of usable oxygen in the myocardium. Cigarette smoking and oral snuff both increase plasma cotinine—but only smoking facilitates the formation of thromboxane A₂ which enhances platelet stickiness and aggregation.¹³

Free radicals in smoke, through increasing platelet aggregation, platelet activation, and inflammation, also play a critical role in cardiovascular disease.¹⁴ Cigarette smoking also inhibits the formation of endothelial nitric oxide, which normally protects the endothelium from platelet aggregation; fresh cigarette smoke contains 100–600 mcg of nitric oxide per cigarette, which oxidises to nitrogen dioxide over a few minutes. Nitric oxide smoke emission is proportional to the nitrate level in unburnt tobacco,¹⁵ but was not ranked as a smoke toxicant.⁹

Identification of leading toxicants—The leading smoke toxicants identified⁹ are largely products of combustion, and in the gas phase, rather than in the particulates. Most of the estimated toxicity⁹ was found to have come from a limited number of constituents in the smoke.¹⁶ The usual cellulose acetate filter traps particulates, but not gases.

Method of testing—Regulation of cigarette smoke emissions for harm reduction purposes requires a method of inter-brand comparison which reflects the inhaled volume of mainstream smoke and the resultant toxicant exposure of the smoker. Since 1990, New Zealand regulations have prescribed the ISO smoking machine method (see Glossary) for measuring emissions as the basis of tar ratings on the side of the cigarette pack. This method tends to underestimate the average amount of mainstream smoke inhaled per cigarette from all cigarettes, and particularly from low yield cigarettes.

The smoker's toxicant exposure is correspondingly underestimated:

- Across 32 studies, American smokers took an average 43-ml puff on average every 34 seconds.¹⁷ No puffing data on New Zealand smokers were available.
- In low yield (nicotine and tar both lowered) brands, smokers inhale more per puff (compensatory smoking) than with medium yield or 'full flavour' brands,¹⁸ thus increasing toxicant exposure above that indicated by machine-measured emissions.
- Ventilated filters used in low tar brands since the 1990s, contain tiny perforations in the filter, through which air is drawn, diluting the mainstream smoke. Smoking machines take standard-sized puffs, so ventilated filters reduce machine-measured tar, and CO per puff, a marketing advantage.
- In contrast, smokers tend to respond to ventilated filters by taking larger puffs as above, and/or in the case of very low yield cigarettes, by blocking the vents with their fingers or lips, inhaling more toxicant than the machine readings indicate.¹⁹

Method

Selection of emission measurement methods that approximate human smoke exposure—To obtain a machine reading to better approximate human smoking, and in the absence of puffing measurements for New Zealand smokers, the machine smoking formula used in this paper to compare brands, is: toxicant exposure equals toxicant yield (as tested) divided by nicotine yield (as tested). The machine smoke test used was the Health Canada intensive method (see Glossary).

Estimation of toxicity of the emissions—The state of California has recognised over 800 compounds as causing cancer, of which the 158 found in cigarette smoke were reviewed.⁹ Of these, cancer potency units (the greater the CPU the greater the cancer risk at a given dose) were available for 40 known or suspected human carcinogens.

CPUs were multiplied by per cigarette smoke emissions and divided by 20m^3 , the daily breathing rate, to estimate the cancer risk index (CRI) for each carcinogen. For other diseases, 17 toxicants with published reference exposure levels (RELs) were found: the lower the REL the greater the risk at a given dose. Yield levels divided by RELs, and by 20m^3 , measured the non-cancer risk index (NCRI) for each non-cancer toxicant.

Selection of brands—We included all commercially available filter-tipped manufactured cigarette brands with published emissions data from intensive machine smoking, tested at the same independent laboratory—Labstat Inc, Kitchener, Ontario —19 medium nicotine brands (15 British Columbian, four Australian brands), and 17 low nicotine brands (five British Columbian, 11 Australian, and New Zealand’s top-selling low nicotine brand, Holiday Extra mild²⁰).

The overseas data were from overseas websites.^{21,22} The Canadian brand ‘Players Premiere king size’ was not included, as that brand is no longer sold; its nicotine yield was 1.87 mg—apparently unacceptable to Canadian smokers.²³ Eclipse, a brand that ‘heats rather than burns’ tobacco, Omni, a cigarette including palladium in its tobacco, and many other brands were excluded due to the lack of full published toxicant emission data based on intensive smoking machine methods.²⁴

Selection of toxicants—To compare brand toxicity, we selected the top 10 carcinogens with the highest cancer risk index per cigarette per day¹¹ (Table 1) after eliminating acetamide, thought to act through a non-genotoxic mechanism of carcinogenesis. For cardiovascular and respiratory risk, we included the known toxicants⁹ as listed in Table 2.

For cardiovascular toxicity, hydrogen cyanide, carbon monoxide, and arsenic⁹ were included, but cresols (a separate and therefore expensive test accounting for 7% of cardiovascular toxicity) were omitted, as was phenol (0.5% of cardiovascular toxicity). Some toxicants had multiple toxic effects, so that 13 toxicants, as listed in Table 1 and 2, were sufficient to compare brands: carbon monoxide, hydrogen cyanide, arsenic, lead, cadmium, and chromium; acetaldehyde, acrolein, and formaldehyde; and butadiene, acrylonitrile, benzene, ethylene oxide, and NNN. Cancer potency estimates were not available for NNK. Ammonia and pH were measured, but not used to estimate the free base form of the nicotine. Nicotine was noted (not as a toxicant) to permit estimation of toxicant to nicotine emission ratios, as a measure of toxicant exposures.

Estimation of toxicity by cause-of-death grouping—The Californian Environmental Protection Agency database lists each toxicant’s target disease groupings.¹⁰ Based on the toxicant emissions in each brand’s smoke, the cancer, cardiovascular, and respiratory risks were calculated for different brands, separately for ISO and for intensive machine testing. For example, the cardiovascular risk index was estimated as in Table 2 as the sum of NCRI for hydrogen cyanide, arsenic, benzene, and carbon monoxide in the mainstream smoke of that brand, with cresols and phenol not measured on this occasion.

Estimation of overall brand toxicity—We then weighted the relative toxicity estimate for each disease group according to each group’s relative contributions to New Zealand cigarette mortality in 2000, whereby 39% of cigarette deaths were attributed to cancer, 26% to cardiovascular, and 25% to respiratory mortality. Another 10% were due to other medical causes of death, which have not been attributed to specified toxicants.²⁵

For each brand and disease group, we standardised the toxicity against the average toxicity of the 15 British Columbian medium nicotine brands under intensive machine smoking, scored as 1.00—based on the fact that British Columbia was the only jurisdiction which had published tests on all brands sold. To estimate the scope for toxicity reduction for smokers of the popular New Zealand HEM brand, we compared its toxicity with that of the least toxic of the other 36 brands reviewed.

Table 1. Carcinogenic toxicants in the smoke of New Zealand Holiday Extra-mild cigarettes, 2002

Toxicant (V=mainly in vapour phase; P=mainly in particulate phase)	Cancer potency factor (mcg/m ³)-1	Yield of toxicant in mainstream smoke mcg per cigarette, intense method	Toxicant fraction of total cancer toxicity %*
1,3 Butadiene (V)	0.00017	94.6	44.6
Acrylonitrile (V)	0.00029	18.7	15.1
Acetaldehyde (V)	0.0000027	1198	9.0
Benzene (V)	0.000029	80.7	6.5
Formaldehyde (V)	0.000006	150	2.5
Ethylene oxide (V)	0.000089	9	2.2
Cadmium (P)	0.0042	.0557	0.65
NNN (P)	0.0004	.0187	0.02
Lead (P)	0.000012	.0397	0.01
Arsenic (P)	0.0033	0.00163 [#]	0.01
Others identified, not measured for this brand ^{**}			19

* Fraction based on ISO readings, Fowles and Dybing 2003.⁹ Table 1 www.tobaccocontrol.com; # Arsenic was present but not quantifiable. The value given is half of the lowest detected amount in the smoke of Canadian brands ** Estimated risk includes approximately 19% from carcinogens of known potency not measured for this cigarette (Based on reported ISO yields for all carcinogens⁹ Table 1) Of the top 10 carcinogens,⁹ acetamide and N-nitrosopyrrolidine were not measured. Chromium was present but not quantifiable.

Table 2. Cardiovascular and respiratory toxicants in the smoke of New Zealand Holiday Extra mild cigarettes, 2002

Toxicant (V=mainly in vapour phase; P=mainly in particulate phase)	Reference exposure level for minimum toxic effect (mcg/m ³)	Yield of toxicant in mainstream smoke mcg per cigarette, intense method	Toxicant as percentage of total group toxicity %
Cardiovascular:			
Hydrogen cyanide (V,P)	3	282	89.1
Arsenic# (P)	0.03	0.00163	0.05
Carbon monoxide (V)	10,000	26400	2.5
Benzene (V)	60	80.7	1.3
Cresols (V)	4	NM (19.7#)	7.0**
Phenol (V)	600	NM (26.1#)	0.05**
Respiratory:			
Acrolein (V)	0.02	148	97.1
Acetaldehyde (V)	9	1198	1.8
Formaldehyde (V)	2	150	1.0
Acrylonitrile (V)	2	18.7	0.12
Cadmium (P)	0.01	0.0557	0.07
Chromium (P)	0.0008	NQ	0
Others (dioxins, nickel)			.0003

NQ= Not quantifiable; NM=Not measured; *Arsenic was detected, but was not quantifiable. The value given is half of that of the lowest level detected in the smoke of Canadian brands; # Machine smoke measured under ISO conditions. Fowles and Dybing 2003.⁹ **Fraction based on ISO readings, from Fowles and Dybing 2003.⁹ Table 1 www.tobaccocontrol.com

Table 3. Top three ranking smoke toxicants of manufactured cigarette brands, tested by the intensive method; estimated identifiable cancer, and overall toxicity by brand.

Brands by country (number tested)	Nicotine yield mcg/cigarette, mean, SD=standard deviation, (range)	Acrolein mcg/cigarette, mean SD, (range)	Hydrogen cyanide mcg/cigarette mean, SD (range)	1:3, Butadiene mcg/cigarette, mean, SD (range)	Identifiable cancer toxicity relative to Canadian medium- nicotine brand average mean, SD (range)	Identifiable overall brand toxicity relative to Canadian medium-nicotine brand average=1.00 mean, SD (range)
Low nicotine brands						
NZ (1) HEM	1.8	81	155	52	0.55	1.39
Australia (11)	1.9 SD 0.26 (1.5-2.2)	62 SD 6.9 (53-73)	124 SD 15.2 (102-143)	48 SD 4.8 (39-55)	0.50 SD 0.05 (0.42-0.57)	1.18 SD 0.10 (1.00-1.33)
British Columbia(5)	2.3 SD 0.51 (1.7-2.9)	64 SD 12.8 (44-81)	123 SD 28.6 (92-155)	30 SD 4.2 (26-52)	0.42 SD 0.05 (0.37-0.48)	1.10 SD 0.16 (0.90-1.27)
Medium nicotine brands						
Australia (4)	2.4 SD 0.11 (2.3-2.5)	40 SD 15.7 (25-59)	98 SD 7.9 (88-106)	38 SD 3.8 (34-43)	0.40 SD 0.03 (0.36-0.43)	0.92 SD 0.06 (0.88-1.00)
British Columbia (15)	2.8 SD 0.32 (2.2-3.2)	57.2 SD 9.3 (43-77)	104.0 SD 12.1 (79-123)	34.1 SD 8.8 (23-47)	0.39 SD 0.06 (0.32-0.51)	1.00 SD 0.11 (0.85-1.24)
Export A FF (least toxic)	2.9	47	79	33	0.35	0.85
% change HEM to Export A FF	59	-42	-49	-37	-37	-39

HEM = Holiday Extra-mild brand, 0.6 mg nicotine yield on ISO testing; Export A full flavor, a Canadian cigarette, 1.3 mg nicotine yield on ISO testing; Low nicotine ≤ 0.9 mg yield on ISO smoke machine test condition; Medium = 0.9 to 1.3 mg nicotine, ISO; Except for nicotine values, all values are nicotine-adjusted (toxicant value divided by nicotine value, both measured under intense smoking condition); **Note:** The small number of Australian and New Zealand brands tested may not be representative of their markets: the New Zealand brand was higher, and the Australian brands lower, than the average for Canadian brands = 1.00. In British Columbia all main brands on sale were tested.

Results

- The mainstream smoke of all cigarette brands studied contained the same leading carcinogenic, cardiovascular, and respiratory toxicants in their smoke.
- Of the measurable, identifiable toxicants, the three most significant in all brands studied were acrolein, butadiene, and hydrogen cyanide. These three accounted for 65% of overall identifiable toxicity.
- Toxicants in the vapour phase accounted for over 80% of the HEM cigarette's toxicity. Overall, toxicants in the particulate phase (for which tar is a proxy measure) accounted for no more than 18% of overall cigarette smoke toxicity.
- The 13 toxicants tested accounted for 81% of identifiable cancer risk, 99.5% of identifiable cardiovascular toxicity, 99.9% of the identifiable respiratory toxicity, and 83% of the overall identifiable cigarette smoke toxicity
- For Canadian regular brands, the ratio of intensive to ISO emissions approximately doubled, with less increases for some heavy metals. Arsenic was detected in measurable quantity in one brand's smoke only, from Canada.
- The toxicant/nicotine ratio was virtually the same by either ISO or intensive method for medium and low nicotine cigarettes considered as a combined group. Under intense smoking conditions, HEM tar was 33 mg per cigarette, HEM nicotine 1.8 mg; and the tar/nicotine ratio 18, the highest for any brand. Samples of HEM purchased 6 months later, under intense machine smoking conditions, tested tar at 29 mg, nicotine 1.7 mg; tar/nicotine ratio 17. (ISO results for both samples were 9 mg tar, 0.6 mg; ratio 15).
- The tobacco-specific nitrosamine NNN for HEM in Table 1, and its ratio to nicotine was the lowest among all 37 brands.

Table 1

Four carcinogens accounted for 76% of the identifiable cancer risk of HEM: 1,3-butadiene (45%); and acrylonitrile, acetaldehyde, and benzene, a further 31%. Ethylene oxide, a known carcinogen, is included here—using the reported value of 9 ug/cigarette.⁵ To allow for identifiable carcinogens not measured, we left 19% of the carcinogenic risk unattributed to any toxicant, on the basis of published CPUs and ISO emissions.⁹ Using published tables based on ISO smoking conditions,^{9, Table 1} 87% of the identifiable carcinogenic risk was in the vapour phase, and 13% in the particulate phase.

Cancer risk based on CRIs versus cigarette cancer mortality—We updated the previous estimate⁹ of the percentage of cigarette cancer deaths accounted for by CRIs, using lifetime lung cancer risks from the American Cancer Society's Cancer Prevention Study II in the 1980s, against CRIs estimated using intensive smoking machine testing results from Table 1, otherwise using yield data from ⁹Table 1 scaled upwards to mimic intensive smoking, using the intense to ISO ratio (2.15) for summary CRIs for emissions as reported for Canadian regular cigarettes. On this basis, approximately 35% of lifetime cigarette cancers (lung and other sites) were explained by CRIs (27% of lung cancer in men, and 76% of lung cancer in women).²⁶

Table 2

Hydrogen cyanide was found in both vapour and particulate phases. Its very low REL indicated that even one cigarette smoked was sufficient to exceed this threshold and produce a toxic effect. Hydrogen cyanide made up 89% of the identifiable and measurable cardiovascular toxicity of HEM mainstream cigarette smoke, and carbon monoxide only 2.5%. For respiratory toxicity, acrolein, and cadmium were the most toxic per unit weight but when the quantity in smoke was considered, acrolein made up 97% of the estimated respiratory toxicity of HEM smoke. Vapour-phase toxicants contributed over half of cardiovascular toxicity and virtually all of respiratory toxicity.

Table 3

For the three most powerful toxicants, HEM had the highest toxicant/nicotine ratios among the 37 low and medium nicotine brands. On toxicant emissions alone, it was not the highest. The overall toxicity per brand in the far right column attributes 10% of relative toxicity to those toxicants (unknown, so not reducible by any known means) responsible for 'other medical' causes of death.²⁵ This accounts for the somewhat lower reductions obtained in the last column, compared with the second to last column for cancer.

The lead level in HEM smoke was second highest of 37 brands at 40 nanograms per cigarette, and the highest for lead/nicotine. In contrast, HEM gave the lowest NNN/nicotine ratio. The NNN/nicotine ratio varied by a factor of 6.4 between brands. Nicotine varied among medium nicotine brands from 0.9 mg to 1.3 mg per cigarette when tested under ISO smoking conditions (not shown in Table 3), and varied more, from 1.5 to 3.2 mg per cigarette, under intense machine smoking.

Among low nicotine brands, nicotine varied from 0.4 mg to 0.89 mg under ISO smoking conditions, and from 1.5 to 2.9 mg under intense smoking conditions. Thus under intensive smoking conditions, 'low' and 'medium' nicotine cigarettes gave similar values and ranges for nicotine yields. Across brands, the toxicant to nicotine ratios varied from 1.8 for tar/nicotine by either method, to 3.3 to 3.4 for acrolein/nicotine, for ISO and intensive methods respectively. Under ISO test conditions, HCN/nicotine and butadiene/nicotine varied four fold between brands, but under intensive test conditions both varied less—HCN/nicotine varied 2-fold and butadiene/nicotine 2.4-fold.

Comparing relative toxicity, low yield brands (relative average toxicity 1.17, SD 0.16) were 19% more potent overall than medium yield brands (relative average toxicity 0.98, SD 0.11), based on the toxicant to nicotine ratio ($p < 0.01$), standardised against Canadian medium-nicotine brands (relative toxicity 1.00).

Spreadsheet estimates show that if HEM nitrosamine (NNN) emissions were increased five-fold to the levels seen in the US Marlboro brands,²⁴ HEM's overall toxicity would have increased by (only) 0.1%.

Discussion

The main findings

- Holiday Extra-mild, New Zealand's most popular mild cigarette, was the most toxic of the 37 brands for which published toxicities were available, based on toxicant/nicotine ratios.
- The method described shows scope for down-regulating individual toxicant emissions, and total brand toxicity, to that of lower emission brands.
- Export A full flavor, the least toxic cigarette, was estimated at 39% less toxic than HEM. Export A's reduced toxicity was mostly due to its higher nicotine emission, and the correspondingly lower toxicant/nicotine ratio.
- Focusing on the 13 leading toxicants among the 4000 chemicals in tobacco smoke makes regulation feasible.⁹ The top three accounted for 65% of the cigarette's toxicity. The dominant toxicant for cancer was 1,3-butadiene for cancer; for cardiovascular disease, HCN; for respiratory disease, acrolein. The emissions of these toxicants varied considerably between brands, suggesting that much of the toxicity of a cigarette can be influenced by cigarette engineering or the tobacco blend used.
- Under intensive smoking conditions low nicotine brands tended to have higher toxicant emissions than medium nicotine brands, as judged by toxicant/nicotine ratios.

Strengths and weaknesses of this study

Strengths—For the first time, this study shows how cigarette brands can be scored by a summary measure of overall brand toxicity, based on leading toxicants and their target organs, assessed by toxicological risk assessment methods.

Test results includes all brands with published test results from the same independent laboratory, Labstat Inc, using Health Canada intensive smoking conditions; others were not considered.

Weaknesses and limitations—Reproductive and developmental toxicity effects were not considered. The two leading toxicants in this category, arsenic and 1,3-butadiene,¹⁶ were already given weight in Table 1, and so brand rankings would not greatly change if this extra toxicity effects category was included. Only British Columbia displayed chemical emissions under intense conditions for all or most brands sold. New Zealand, thus far, has tested only one New Zealand brand (HEM) under intense smoking conditions.²⁰ Holiday regular, the highest volume-selling New Zealand cigarette, was tested in 2002 by ISO method only.²⁰

The toxicant to nicotine ratio adjusts for compensatory over-smoking in low yield brands, and its usefulness for medium-nicotine brands may need reassessment once puff volume data is known for New Zealand smokers and brands. A lack of cigarette engineering information on filter ventilation, filter efficiency, or paper porosity precluded further elucidation of the reasons for brand to brand differences found in smoke emissions. The toxicity estimates are not absolute, but relative, and compare only the identifiable, measurable toxicants in mainstream smoke.

This study compares cigarettes and their machine-generated smoke, but does not allow for how smokers smoke their cigarette, and how much they inhale.

Table 1 gives the estimated cancer risk of smoking one cigarette daily over a lifetime. As estimated, the identified carcinogenic emissions account for 35% of cigarette cancer mortality. For non-cancer risk there is no method to link toxicity level to absolute levels of disease risk; we cannot estimate how much of the total cardiovascular and respiratory risk has been identified, or how much the estimated reduction in emissions will translate into reduced toxicant absorption and decreases in mortality.

The percentage differences between the toxicity of HEM and Export A full flavor in Table 3 may not reflect reductions in toxicity obtainable for the total market. HEM is the only brand fully tested to date, and its relative toxicity may be higher or lower than the New Zealand all-brand average.

Comparison of results with current knowledge

In a toxicity-regulated cigarette, unidentified or unmeasured toxicants in smoke, such as free radicals, may or may not reduce in parallel to the reductions anticipated for known toxicant emissions, may not do so immediately, and the time required for effective switching to reduced-toxicant brands is uncertain.²⁷

The risk assessment approach, using toxicological data largely from animal studies for toxicity, emphasises the vapour phase rather than tar or particulates (Table 1), and emphasises the vapour phase carcinogens 1,3-butadiene and benzene (Table 1) rather than the tar constituents nitrosamines, and benzo(alpha)pyrene. For cardiovascular toxicity, risk assessment emphasises HCN rather than CO (Table 2).

The test results for HEM only apply to the cigarettes sampled for testing. For tar and nicotine at least, the results were confirmed by almost identical results from cigarettes purchased 6 months later. The manufacturer (BAT) reported the HEM brand yielded 0.8 mg nicotine on ISO testing in 2002,³ but manufacturers' reports had not previously been checked by an independent laboratory.

What this study means

Overall smoke cancer risk indices can be estimated, and non-cancer indices also, but with less certainty. The overall toxicity of brands can be compared, based on each toxicant's potency per microgram and the amount of each in that brand's smoke. The relative toxicity scores for each brand allow comparison of brands across countries and time periods, if identical methods and, as in this study, the same laboratory is used. Potency factors may be revised by expert groups from time to time, and emissions will change also. Thus relative toxicity scores may need revision at least annually.

The toxicant to nicotine ratio—This ratio could only be used because all the cigarettes were of commercial design, so that tar and nicotine varied within narrow limits. Research cigarettes, if low in nicotine yield at 0.05 mg and with tar at 10 mg, have a tar/nicotine ratio of 200:1.²⁸

Cancer risk (Table 3)—As addicted smokers may tend to seize on any excuse to keep smoking, undue claims of lessened toxicity or disease prevention are unhelpful.

Conversely, unduly conservative estimates may discourage regulators from removing excess toxicants. This paper suggests that regulation based on exploiting existing brand differences (without using charcoal filters) could lower the *identifiable* cancer risk of HEM by 37%. As identifiable risk represents about 35% of total cigarette cancer risk, the overall total cigarette cancer risk reduction achievable (if, and only if, this brand's toxicity was representative of all brands) would be $(0.35 \times 37\%) = 13\%$ or 224 of the 1732 cigarette cancer deaths in 2000.²⁵

Non-cancer toxicity.(Table 2)—With respiratory disease, and particularly with cardiovascular disease, we lacked sufficient clinical or toxicological data to determine the total non-cancer fraction of total toxicity represented by the toxicants in Table 2.

Overall toxicity (Table 3)—If the cigarette with the highest overall toxicological risk estimate (HEM in this case) was re-engineered to achieve the toxicant/nicotine emission of the average of 15 Canadian medium nicotine brands, its identifiable toxicity would reduce 28%. If re-engineered to achieve those of the least toxic brand, Export A full flavor, HEM's identifiable toxicity could be reduced by 39%.

Nitrosamines—We confirm great variation in nitrosamine levels. Marlboro cigarettes sold in New Zealand were imported from the United States. HEM's NNN emission in Table 1 on intensive testing is eight times lower than for US Marlboro cigarettes machine smoked less intensively.²⁴ Regulation can force highly toxic brands off the market, but if regulation is confined to nitrosamines, it will do little for New Zealand smokers. Less than 0.1% of cigarette cancer deaths would be prevented (Table 1), and none of the 60% of cigarette deaths due to non-cancer causes.²⁵ Comprehensive regulation of all leading cigarette toxicants is required.

Lag times—After implementation of the regulations, the interval before death rates decreased would vary with the disease. Half of the achievable reduction in cardiovascular risk can be expected within a year of implementation, achieving full effect on cigarette mortality within 10 to 15 years, based on the known effects of stopping smoking.²⁹

Regulations to require regular monitoring, brand by brand disclosures of tobacco constituents and emissions, and reductions in leading emissions across all cigarettes, are now overdue. Though many toxicants remain unidentified or unmeasured this paper provides a framework for comparing and substantially reducing the identifiable toxicity of both manufactured and hand-rolled cigarettes.

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Potential conflict of interest: The authors are co-inventors for a patent *Apparatus and methods for testing toxicity of cigarette smoke*, NZP 537968, 28 January 2005.

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What this paper adds

This is the first published report comparing the overall toxicity of cigarette brands across countries using risk assessment and intensive machine smoking, and adjusting for smoke nicotine and the mortality distribution between disease groupings. The method provides a relative toxicity score as a rational basis for regulating cigarette emissions across all brands sold.

Holiday Extra-mild's overall estimated *identifiable* toxicant emission levels would reduce 39%, and its cancer risk by 37%, if this cigarette was required by regulation to have the same emissions as a certain Canadian regular brand, Export A full flavor. Regulation to reduce brand differences in emissions, without employing charcoal filters,³⁰ would reduce total cancer risk by 13% for Holiday Extra-mild, based on measurable toxicants. Any toxicity reduction from including a charcoal filter³⁰ would be additional.

Glossary

Yield or emission (mainstream smoke), or potential exposure The weight of toxicant or harmful constituent collected from the mouth end by smoking the cigarette by machine.

Low nicotine or low yield Nicotine less than 0.9 mg per cigarette on ISO test.

Medium nicotine or medium yield Nicotine 0.9 mg or more per cigarette on ISO test.

NNN N-Nitrosornicotine, a tobacco-specific nitrosamine.

NNK 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, a tobacco-specific nitrosamine.

Standard ISO or FTC machine smoking Machine takes a puff of 35 ml, puff lasts 2 seconds, 60 seconds between puffs. No taping of the filter.

Intensive machine smoking (Health Canada) Machine takes 55 ml puff, puff lasts 2 seconds, 30 seconds between puffs. Tape covers all of filter and tipping paper.

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