

**Novel Tobacco Products:
Health Risk Implications
and International Concerns**

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By

Jeff Fowles, Ph.D.

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David Phillips
Science Programme Manager

Jeff Fowles, PhD
Project Leader

Kylie Gilmore, BSc (Hons)
Peer Reviewer

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SUMMARY

An increasing number of tobacco products are being marketed internationally (in the U.S., Japan, and parts of Europe) that claim or imply reduced harmfulness to their users. Tobacco companies and related industries are producing highly engineered nicotine-delivery devices, with varying resemblance to conventional tobacco products. These devices are marketed as less harmful to active and passive smokers and less offensive to passive smokers. As a result, concerns have arisen about the objective evaluation of harmfulness of these products, the potential for the claims of reduced harm to interfere with addicted smokers' efforts to quit, and the potential for these products to induce more youth to become addicted to nicotine.

Alterations to conventional tobacco products are mainly carried out through designs that cause a reduction in combustion products, or through a reduction of specific carcinogenic agents (e.g. nitrosamines) in the tobacco or tobacco smoke. Some of the products appear similar to cigarettes, but involve little in the way of combustion, so that many of the harmful smoke constituents are reduced. Because the health risks from smoking are generally related to the amount of exposure to cigarette smoke, the health impacts on a given individual smoker from such products would be viewed as generally positive if they were otherwise unable to quit smoking. Several products reviewed contain little or no actual tobacco, but rather pure nicotine or tobacco extracts. Some of these products may not be classified as tobacco products, even though the principle addictive component and the types of health risks involved are similar.

The departure from conventional design leaves the question open as to what types of testing requirements should be implemented for these products in order to compare delivered doses of chemicals and toxicants. At least one device, Eclipse, shows a much reduced nicotine "yield" on standardised smoking machine tests, but results in the same amount of nicotine in blood tests in smokers, compared with conventional cigarettes. This implies that the standardised method for constituent yield testing may be misleading for these products.

There is currently no regulatory framework that enables such products to be adequately and impartially evaluated. The array of different products available on overseas markets creates a blur in the distinction between nicotine delivery devices such as nicotine replacement therapies, and conventional tobacco products. Because the public health concerns over smoking are intertwined with concerns about nicotine addiction, a regulatory framework would ideally consider all such products in this spectrum and treat them with equal scrutiny.

1. PURPOSE OF THIS REPORT

A variety of new generation tobacco products and nicotine delivery devices have been developed in recent years and are now appearing in test market trials in other countries. It is unclear whether the existing regulatory frameworks for cigarettes and tobacco products would also cover these unconventional products should they become available in New Zealand. This report reviews these various products, and highlights the health implications of each product, in relation to factors that may influence their potential toxicity and/or addictiveness.

2. INTRODUCTION

Over the past decade, tobacco companies have been increasing efforts to produce tobacco products that can be sold as having claims of reduced harm compared with conventional tobacco products, while still meeting the physiological needs of the addicted consumer population. These products are also being developed to be less objectionable to non-smokers exposed to environmental tobacco smoke (ETS). The resulting products sometimes only distantly resemble conventional cigarettes. This has resulted in the term “nicotine-delivery device” being used, as the products may behave uniquely from a toxicological perspective, and pose a different set of health risks and public health concerns in comparison to conventional cigarettes.

Currently, no international regulatory frameworks exist to evaluate the potential harm from toxicity or addiction that these novel products might cause. Because tobacco products are responsible for enormous health tolls from cancer, respiratory and cardiovascular diseases, this is cause for concern. One result is that claims of harm reduction are being made by manufacturers without an objective process by which to measure whether or not this is actually the case.

3. PRODUCTS THAT ARE MARKETED AS CARRYING REDUCED HEALTH RISKS

3.1 Cigarettes that manufacturers claim “heats rather than burns tobacco”

A number of products being test marketed (discussed below) have a heating element that the manufacturing industries claim does not “burn” the tobacco. In these products, at least some tobacco is burned as per conventional cigarettes, but the amount is much less, and the amount of combustion products generated is reportedly reduced.

3.1.1 “Premier”

The first tobacco product that burns less tobacco and uses a heating element to volatilise nicotine was introduced by RJ Reynolds in 1988 as “Premier”. This product was not acceptable to smokers due to unpleasant taste and low nicotine intake (Stapleton et al., 1998).

3.1.2 “Eclipse”

The R.J. Reynolds tobacco company in the U.S. has been and is currently still test-marketing “Eclipse”, which is a novel tobacco product that is advertised to “primarily heat, rather than burn, tobacco”. This trial began in 1996, and has been marketed in Germany, under the name “HI-Q”, and in Sweden, under the name “Inside”. The product is under current scrutiny by tobacco and regulatory scientists, and some details regarding smoke constituents are now known (Borgerding et al., 1998; Higuchi et al., 1998).

The design of an Eclipse cigarette includes a carbon-based heating element connected to tobacco wrapped in aluminium foil core and surrounded by a fibreglass insulator, and ultimately connected to a cellulose acetate filter. The distal end of the cigarette apparently has a small piece of paper, made of tobacco, that serves to mimic the initial taste of a cigarette for the smoker. Once lit, the heated carbon element transfers heat along the wrapped core through two parts containing tobacco. The first is a light reconstituted tobacco that is high in glycerin, and the second (toward the mouth of the smoker) is a dark tobacco with a higher nicotine content. Nicotine volatilises as the core is heated and continues until the heat source is exhausted (about 15 puffs later) (ASAM, 1996).

The product ingredients and their quantities in Eclipse, like those of conventional cigarettes, are undisclosed by RJR. There is a report that this information has been supplied to the German Ministry of Health (ASAM, 1996).

Eclipse is an extension of the Vantage brand, which was previously advertised as the company’s “low tar” cigarette product. With Eclipse, however, a nicotine-containing aerosol is generated from burning only 25 mg or less of tobacco. The concentration of most of the toxic constituents, which are primarily products of combustion, in the aerosol is therefore greatly reduced. Borgerding et al. (1998) found that the deliveries of 24 target compounds were drastically reduced (84-99% lower than conventional cigarettes). The concentration of one compound tested in smoke from an Eclipse, furfural, was increased, and the amounts of nicotine and carbon monoxide remain at or above the deliveries of conventional cigarettes (ASAM, 1996; Borgerding et al., 1998). Therefore, on the basis of this evidence, it seems that the reduction in health risk from this product would be more significant in terms of cancer risk as compared to any reduction in cardiovascular disease. The significance of the increase in furfural is unknown, but this compound is a known respiratory irritant, and causes bronchospasm in high concentrations (Hazardous Substances DataBase, 2001).

A study was conducted to determine the *in-vivo* mutagenicity of smoke condensates from Eclipse using skin painting tests on mice (Brown et al., 1998). In this study, cigarette smoke condensate from Eclipse or Kentucky reference cigarettes was applied dermally to Sencar mice three times per week for 30 weeks. No increase in DNA adducts were seen for the Eclipse cigarette smoke condensate (CSC) compared to mice treated with acetone as the negative control. Significant adduct formation was observed with the CSC of the Kentucky reference cigarette, as expected. The authors, from RJR, concluded that cigarette smoke from Eclipse is much less genotoxic than that of conventional cigarettes.

The yields of constituents and the mutagenicity test results indicate that Eclipse would be expected to have a significantly reduced DNA-damaging potential and carry a correspondingly decreased cancer risk. The same cannot be said for cardiovascular disease risks, as both nicotine and carbon monoxide are known cardiovascular toxicants, and these compounds are not decreased in Eclipse. The reduction in harm with Eclipse is thus based on cancer risk only.

One piece of information needed to more fully characterise the health risk from Eclipse-types of products is the formation of dioxins. Dioxins are formed from pyrolysis and incomplete combustion of organic matter in the presence of chlorine and are known to be formed and measured in cigarette smoke, but none of the references available for review contained information on yields of polychlorinated dibenzodioxins or polychlorinated dibenzofurans.

In a study of the availability of nicotine from Eclipse, four volunteers smoking Eclipse cigarettes exhibited average blood nicotine peaks of 23.7 and 17.8 ng/mL for a first and second Eclipse, respectively (Stapleton et al., 1998). This is higher than that previously seen with the Premier cigarette (13 ng/mL), and also higher than that observed with conventional brands (range of approximately 12-15 ng/mL). These measurements are not consistent with the reported yields of nicotine from Eclipse. The Federal Consumer Trade Commission (FCTC) “yields” of Eclipse from two laboratories (RJRTC, and Labstat Inc., Canada) are 2.9 and 3.4 mg tar per cigarette, and 0.19 and 0.15 mg nicotine, with 7.5 - 8.8 mg carbon monoxide per cigarette (ASAM 1996). These nicotine yields contrast with the analysis of urine of human volunteers that showed cotinine levels in people smoking Eclipse were the same as when they were smoking their regular brand (Benowitz, 1997). Why this apparent conflict in the data is occurring is unknown, but this highlights the potentially misleading nature of relying on machine-derived yield information (Benowitz, 1997).

Table 1 shows the reported yield information from an Eclipse cigarette, and compares these values with yields from a typical cigarette. An additional column is provided in Table 1 that shows the adjusted yield of constituents if they were made to be proportional to a constant nicotine delivery. This is done because it is not clear whether smoking machines are able to approximate the way a smoker would use Eclipse, and because the nicotine deliveries to the bloodstream are similar between Eclipse and conventional cigarettes whereas the yields are markedly different, as previously discussed. It is possible that even this normalisation may result in an underestimate of the yields of various toxicants if the intensity of puffing an Eclipse differs significantly from conventional cigarettes.

Table 1. Reported yields and corresponding cancer risks from Eclipse (Adapted from Borgerding et al., 1997, and Fowles and Bates, 2000).

Chemical	ug/cigarette - Eclipse	ug/cigarette conventional cigarette	Normalised yield for Eclipse ¹	CPF	ca risk ² conventional cigarette	ca risk Eclipse	Adjusted ca risk Eclipse
Acetaldehyde	70	680	298.42	0.01	4.86E-05	5.00E-06	2.13E-05
Isoprene	9	264	38.37				
Nitrogen oxides	35	350	149.21				
Acetone	22	287	93.79				
Hydrogen cyanide	5.1	118.4	21.74				
Toluene	6.8	72.8	28.99				
Acrolein	20	68.8	85.26				
1,3-Butadiene	1.6	35.5	6.82	3.4	8.62E-04	3.89E-05	1.66E-04
Benzene	6.2	46.3	26.43	0.1	3.31E-05	4.43E-06	1.89E-05
Ammonia	5.5	12.2	23.45				
Acrylonitrile	1.3	8.9	5.54	1.0	6.36E-05	9.29E-06	3.96E-05
Formaldehyde	1.2	33	5.12	0.021	4.95E-06	1.80E-07	7.67E-07
Furfural	1.7	1.2	7.25				
Quinoline	nd	0.356					
NAT	0.015	1.9	0.06				
NNN	0.011	1.9	0.05	1.4	1.90E-05	1.10E-07	4.69E-07
NNK	0.014	0.39	0.06	1.4	3.90E-06	1.40E-07	5.97E-07
Catechol	0.4	88.2	1.71				
Hydroquinone	0.7	72.2	2.98				
Phenol	0.1	26.1	0.43				
Cresols	0.1	14	0.43				
Benzo[a]pyrene	0.0006	0.035	0.001	3.9	9.75E-07	1.67E-08	7.13E-08
2-Aminonaphthalene	0.0019	0.007	0.01	1.8	9.00E-08	2.44E-08	1.04E-07
4-Aminobiphenyl	nd	0.0012		21			
Carbon monoxide	7,500	13,609	31,973				
Nicotine	190	810	810.00				
					1.04E-03	5.80E-05	2.47E-04
						5.6%	23.9%

¹ yield estimates were obtained by normalising all Eclipse values by the difference in nicotine yields between Eclipse and conventional cigarettes.

² cancer risk estimates are derived from multiplying cancer potency factors (CPF) from California Environmental Protection Agency (www.oehha.ca.gov) that represent slope terms from the linearised multistage model (mg/kg/day)⁻¹, by yields (mg/cigarette) and assuming a 70 kg body weight and a smoking time frame of 35 years out of a 70 year lifespan.

3.1.2.1 The significance of reduced carcinogens in Eclipse

Table 1 shows that adjustment for yield discrepancies, using nicotine as the normalising factor, brings the Eclipse cancer risk up to almost 25% (from about 5%) for those potentially carcinogenic constituents that have been reported for Eclipse. The constituents listed for Eclipse are reported by tobacco industry funded studies, and do not cover all suspected carcinogens (see Table 2). However, they do represent chemical constituents that accounted

for 87% of the cancer risk from all reported constituents from conventional cigarettes in a previous assessment (Fowles and Bates, 2000).

Translating these reductions into health statistics can be done using some general assumptions. For example, the contributions of the individual chemical cancer risks can be compared with cancer mortality statistics. A 70 kg person smoking (and at risk) for 35 years out of a 70 year lifespan, would have a cancer risk estimate of between 1.2×10^{-3} and 2.8×10^{-4} per cigarette per day, if one sums all the individual cancer potency values from smoke carcinogens. The range represents the assumption of whether dioxins and 1,3-butadiene (the two most influential and controversial carcinogens) are included in the risk estimate (Fowles and Bates, 2000). This becomes a lifetime risk of 1.8×10^{-2} to 4.2×10^{-3} for a smoker that smokes an average of 15 cigarettes per day (Dr Murray Laugesen, personal communication). This result can be compared with reports of observed cancer incidence in the following way:

The expected male and female deaths from cancer in the USA in 1995 totalled 547,000, of which 168,057 (or 30.7%) are thought to have been due to cigarette smoking (Shopland, 1995). If one assumes that the cancer death rate in the American smoker population roughly corresponds to a similar rate for New Zealand smokers, a comparison of expected cancer risks can be constructed. For the total New Zealand population of 3,618,303 people in 1996 (Statistics New Zealand 1997), 24.9% or 900,957 people were current smokers (MOH, 1997). In 1996, there were also 16,057 cancer registrations and 7,461 cancer deaths (NZHIS, 2000). Assuming similar smoking-attributable cancer rates from the U.S., this would mean that 2,291 cancer deaths and up to 4,929 new cancers were attributable to smoking in 1996. This may be an overestimate since NZ smokers reportedly consume fewer cigarettes, on average, than American smokers (Dr Murray Laugesen, personal communication). An upper end lifetime cancer risk estimate for smokers would therefore be:

$[2,291 \text{ (cancer deaths from smoking in 1996)} \div 900,957 \text{ (number of smokers in 1996 @ 24.9\% prevalence)}] \times 35 \text{ years out of 70 year lifespan} = 0.089$ (or one in 11.2 chance of a smoker dying from a smoking-related cancer during 35 years of susceptibility).

Compared with cancers not attributable to smoking:

$7,461 - 2,291 \text{ (cancer deaths not attributable to smoking)} \div 3,618,303 \text{ (total resident population including smokers)} \times 35 \text{ years out of a 70 year lifespan} = 0.05$ (or one in 20 chance of a person dying from a non-smoking-related cancer). Note: – sidestream smoke cancers are included in this estimate, so this is an overestimate of the true cancer rates not attributable to cigarettes.

The excess cancer risk from smoking is therefore estimated at approximately $0.089 - 0.05 = 0.039$ or 3.9×10^{-2} . This value is about double that predicted by summing individual contributions to cancer risk of chemicals in smoke using cancer potency factors and including dioxins and 1,3-butadiene in the estimate (1.8×10^{-2}).

In conclusion, summing individual cancer potency values to form a cancer risk estimate for cigarettes provides an estimate that is 2.2-fold lower than what is observed using published

U.S. estimates for attributable cancer deaths from smoking. This is generally a close agreement considering the various assumptions and unknowns (e.g. the risks of cancer to ex-smokers, the variability in the number of cigarettes smoked per day, variations in the constituent yields, etc.). This probably indicates that NZ smokers are exposed to fewer carcinogens because they tend to smoke fewer cigarettes, on average, than American smokers. Alternatively, the cancer potency values may incompletely account for all of the carcinogenic potency of the smoke constituents. There are many compounds in cigarette smoke that have not been toxicologically evaluated, and there is a possibility that exposure to some compounds would increase the carcinogenicity of others.

The reduction in carcinogenicity of smoke in an Eclipse device means that the cancer burden for 1996, if all smokers had used Eclipse instead of conventional cigarettes, would have been closer to 5.6% - 23.9% of the 2,291 estimated deaths, or between 128 and 548 cancer deaths. This estimate is theoretical, but is consistent with the limited data that exist for the Eclipse device. A more precise estimate would be possible given more comprehensive smoke yield information for the device smoked under a range of conditions.

A similar estimate for cardiovascular disease is not feasible since the precise contribution of specific constituents to the cardiovascular toxicity and cardiovascular disease risk is not known.

3.1.2.2 Unequal reduction of smoke constituents in Eclipse

Of note are the disproportionately high ammonia and acrolein levels in Eclipse, in comparison with those from conventional cigarettes (Table 1). One explanation for the increase in acrolein, is that acrolein is formed as a combustion product from glycerin, which is added in high quantities to the reconstituted tobacco in Eclipse. The reason for the high ammonia content is not known, but presumably this would enhance the absorption and uptake of nicotine from this product. The pH of the smoke from Eclipse was not found in the literature. In addition to ammonia and acrolein, carbon monoxide intake is apparently greater with Eclipse if the intakes are normalised for nicotine yield.

It is unknown if further discrepancies exist in the yields of Eclipse. Further constituent testing, specifically from an independent laboratory and under conditions specified by regulatory authorities would be much more credible in this regard.

A previous report identified the compounds in cigarette smoke of greatest toxicological cancer risk. These are listed below (Table 2) in descending order of contribution to cancer risk.

Table 2. List of carcinogens, in descending order by risk estimate, in cigarette smoke (Fowles and Bates, 2000).

Rank	Carcinogenic constituent in smoke	Rank	Carcinogenic constituent in smoke
1	1,3 – Butadiene*	20	Nitrosodiethanolamine
2	Chlorinated dioxins	21	Benzo(a)pyrene*
3	Acrylonitrile*	22	Dibenz(a,h)anthracene
4	Arsenic	23	Urethane
5	Acetaldehyde*	24	4-aminobiphenyl*
6	Benzene*	25	o-toluidine
7	N-nitrosoornicotine*	26	Nickel
8	N-nitrosopyrrolidine	27	Benzo(j)fluoranthene
9	Cadmium	28	Benzo(b)fluoranthene
10	Formaldehyde*	29	Indeno(1,2,3-c,d)pyrene
11	Hydrazine	30	Benzo(k)fluoranthene
12	NNK*	31	Dibenz(c,g)carbazole
13	N-nitrosodimethylamine	32	5-methylchrysene
14	N-nitrosodiethylamine	33	Vinyl chloride
15	Chromium	34	Beryllium
16	N-nitrosoethylmethylamine	35	Benz(a)anthracene
17	N-nitrosobutylamine	36	Dibenz(a,j)acridine
18	2-Aminonaphthalene*	37	Lead
19	Dibenzo(a,i)pyrene	38	Chrysene

* indicates the compound has been quantified and reported for Eclipse devices

The above list shows the known or suspected carcinogens in conventional cigarettes. Only those with an asterisk have been reported in Eclipse, and these are at much lower yields than conventional cigarettes. The remaining compounds are likely to follow this trend, as most are products of combustion.

It appears, therefore, that Eclipse and similar products that heat, rather than burn, tobacco represent a reduced cancer risk for smokers and also to those exposed to passive smoke. In vitro and animal toxicity tests for DNA damaging potential are reported to be negative or just marginally positive for the smoke from these products (<http://ehpnet1.niehs.nih.gov/docs/1999/107-4/forum.html>). However, the cardiovascular risks may be as great or greater, depending on how one interprets the yield information from these devices. The chemical analyses from these products are incomplete in comparison with conventional constituent yields, however, the major combustion product levels are present, and it is unlikely that those combustion products or nitrosamines not listed would behave differently.

3.1.3 “Accord”

According to officials in the US Food and Drug Administration (USFDA), Philip Morris is test marketing a battery operated product in the U.S. called Accord that uses a cell-phone-like charger, and another device with computer chips and heating blades. The goal of this product is similar to that of Eclipse, which is to greatly reduce cancer risk to smokers and also reduce the amount of environmental tobacco smoke so that non-smokers will be less annoyed by those who smoke (Zeller, 2000). Accord works by electronically lighting the tobacco only when the smoker inhales, thus reducing the continuous burning nature of the cigarette and the

corresponding amount of environmental tobacco smoke (<http://ehpnet1.niehs.nih.gov/docs/1999/107-4/forum.html>). There is no lit end of the Accord device and temperatures in the device do not exceed 500 C (Philip Morris, 2001). Smoke constituent yields were not available for the Accord device, but there has been speculation that the exposures and risks from Accord are less than that for Eclipse (<http://ehpnet1.niehs.nih.gov/docs/1999/107-4/forum.html>).

The same product is apparently marketed in Japan under the name “Oasis”.

3.2 Low Nitrosamine Cigarettes

3.2.1 “Advance”

Marketed by Star Scientific, Inc., Advance cigarettes claim to be greatly reduced in nitrosamines. Nitrosamines are DNA-damaging, carcinogenic compounds found in cigarette smoke. Nitrosamines are formed largely from chemical reactions, under heat, between nitrates and nitrogen-containing alkaloids that are naturally present in tobacco. Nitrosamines are widely discussed in relation to cigarette smoke because many of the NAs are specific to tobacco (i.e. tobacco-specific nitrosamines, or TSNA).

A previous report from ESR (Fowles and Bates 2000) has shown that collectively, NA account for between 4% and 17% of the cancer risk associated with smoking. A removal or reduction in these compounds would be expected to result in reduced probability of getting cancer for smokers, provided that the concentrations of other known carcinogens or the overall intake of smoke did not increase.

Star Scientific, Inc. (“Star”), is a company based in the United States (US) that is marketing reduced NA cigarettes. This company has declared its support for the USFDA to regulate tobacco products and it appears to be dedicated to educating consumers about the toxic constituents of cigarette smoke and producing less harmful tobacco products (Star Scientific, Inc. 2001). Star has developed a technology called “StarCure”™ that effectively reduces the amount of NA and other constituents in cigarette smoke. This is accomplished through the addition of a charcoal activated filter to their test marketed cigarette, “Advance”. It is not specified and probably a closely guarded commercial secret, if there are additional technologies that lead to the reduced NA level.

The Advance cigarette is currently being test-marketed in Virginia and Kentucky in the U.S.

One way to reduce TSNA in cigarette smoke is to use “flue-cured” tobacco, which is apparently lower in nitrates and contains fewer TSNA or their precursors. R.J. Reynolds indicate that no-, or low-TSNA cigarettes will be available this year (presumably this refers to the U.S. market) (RJ Reynolds, 2001). RJR also claims reduced harm to the smoker will result from this modification, and cites sensitive in vitro tests as providing evidence.

3.2.2 Genetically modified tobacco

Another development in the novel tobacco product area is “virtually nicotine-free”, low-nitrosamine tobacco from a genetically modified tobacco plant, made by Vector Group of Miami (www.staugustine.com/cgi-bin/printme.pl). The claim that the product is “nicotine-free” requires careful examination, as a cigarette without nicotine would not be expected to produce or maintain the level of addiction required to keep people smoking. It would be important to test the tobacco nicotine alkaloid content and the smoke condensate of this product to measure any biological ‘nicotinic’ effects it may have, through interaction of non-nicotine compounds at the nicotine receptor. A separate, but important issue, would be the genetically modified nature of the product and whether the modification would meet the acceptance of the Environmental Risk Management Authority in New Zealand.

3.3 Low Polyaromatic Hydrocarbon (PAH) content cigarettes

3.3.1 “Omni”

Polyaromatic hydrocarbons (PAHs) are DNA-damaging compounds formed during combustion of organic material. PAHs are present in tobacco smoke and the Vector company in Miami, USA, have developed a product called “Omni” which is a cigarette that uses a palladium metal catalyst to break down and remove PAHs from mainstream smoke (www.staugustine.com/cgi-bin/printme.pl). It is unclear what the breakdown products are likely to be from this reaction, and no emission data could be found to evaluate the product’s toxicity. The company claims to have removed one of the most serious cancer causing agents in tobacco smoke (PAHs), but a previous risk assessment revealed that PAHs accounted for less than 1% of the total cancer risk from mainstream smoke (Fowles and Bates, 2000). A comparison of results of bioassays for mutagenic activity of Omni vs conventional cigarettes would help to better understand the health significance of the removal of PAHs.

Omni would purportedly combine the technology for removing PAHs, use genetically modified, low nitrosamine tobacco, and have little or no nicotine. The company that makes Omni is reported to have made claims that this product will save millions of lives and be a much safer cigarette. They are reportedly attempting to obtain US FDA approval or to reach an agreement so that health claims can be made about this tobacco product (www.nandotimes.com/noframes/story).

PAHs and nitrosamines combine for about 5-18% of the estimated cancer risk of mainstream cigarette smoke using standard FTC yield data (Fowles and Bates, 2000). If all nitrosamines were removed from the smoke as this device attempts to accomplish, and assuming that the absolute level of other carcinogens did not increase, this would appear to reduce cancer risk to some degree. However, a bioassay of mutagenic activity would still be useful in the evaluation of the toxicity of the smoke from Omni.

One report indicated that very few of the 60 people who volunteered to use “nicotine-free” Omni as a way to help stop smoking were actually able to quit (www.staugustine.com/cgi-bin/printme.pl). However, the study size was too small to draw firm conclusions.

3.4 De-nicotinised cigarettes

3.4.1 “Next”

In the late 1980’s, Philip Morris developed a cigarette, “Next”, that had undergone a high-pressure carbon dioxide treatment to remove nicotine from tobacco in a method adapted from a process used to remove caffeine from coffee (www.newstimes.com/archive98/apr2298/nah.htm). Next was a commercial failure, probably due to unsatisfactory taste or localised nerve sensations in absence of nicotine.

Experimental tobacco-derived de-nicotinised cigarettes are being studied currently and appear to satisfy cravings and withdrawal symptoms but lack a range of pharmacodynamic properties, including elevated heart rate and changes in EEG (Pickworth et al., 1999). These cigarettes deliver carbon monoxide and tar in levels comparable to conventional cigarettes, but only 0.06 mg nicotine. Smokers said these cigarettes had the same taste as regular cigarettes, and the authors expressed hope that these cigarettes could serve to help wean addicted smokers away from nicotine and eventually from smoking.

4. PRODUCTS MARKETED AS ALTERNATIVES TO CONVENTIONAL CIGARETTES

4.1 Kreteks

Kreteks are also known as clove cigarettes, as they typically contain 40% cloves and 60% tobacco. These cigarettes are the dominant form found in Indonesia and are now able to be sold in the U.S. and over the internet (www.gimonca.com/kretek/). The smoking machine yields for these devices were not found in the literature. The cloves would serve to provide aroma while also contributing eugenol, a natural component of cloves and a sensory deadening agent to numb the airways while smoking. The kretek cigarettes are densely packed and do not continue to burn when unattended. There is no reason to suppose that the inhaled smoke from these products is any less harmful or addictive than conventional cigarettes.

4.2 Bidis

Bidis are small, brown, hand-rolled cigarettes made typically in India and other southeast Asian countries. They are tobacco wrapped in a tendu or temburni leaf (*Diospyros melanoxylon*). In the U.S., these products are sold in different flavours (eg, mango, cherry, and chocolate). These products began to appear in the U.S. in the mid 1990’s and are now widespread in certain areas among youth and racial/ethnic minority adolescents. One survey in Massachussettes found that of 642 youth, 40% had tried bidis, and 16% were current bidi smokers (www.cdc.gov/mmwr/preview/mmwrhtml/mm4836a2.htm).

There was a common perception among the youth surveyed in the above study that these tobacco products were a less hazardous alternative to cigarettes. However, results from smoking machine tests show that bidis yield more nicotine, tar, and carbon monoxide than

cigarettes (www.cdc.gov/mmwr/preview/mmwrhtml/mm4836a2.htm). The low combustibility and permeability of the tendu leaf wrapper means that the intakes of constituents of the smoke from these products are relatively concentrated in comparison with conventional cigarettes.

The U.S. Center for Disease Prevention and Control (CDC) has indicated a need to research factors affecting the use of novel tobacco products, such as bidis, including how restrictions on access and advertising are being enforced, how pricing affects the use of these products, and how taxes and labelling are being used to reduce consumption and raise awareness of the risks of these products (www.cdc.gov/mmwr/preview/mmwrhtml/mm4836a2.htm).

5. NON-COMBUSTED TOBACCO PRODUCTS

Several non-cigarette tobacco products or nicotine-delivery devices have been recently developed and are now appearing on markets internationally.

5.1 “Cigarettes”

Cigarette is a nicotine-containing mint sweet produced by Star Scientific in the U.S. The product is comprised of about 60% crushed tobacco and sold under the name “Ariva” (Sunday Times, UK, 6 May, 2001). The stated market for this product is smokers who face increasing bans on smoking in public places, but concerns raised in the UK are also that the sweet may be attractive to children and lead to nicotine addiction and unknown health risks.

This product apparently releases approximately the amount of nicotine contained in a cigarette within a few seconds of oral contact, whereas nicotine replacement therapies, such as nicotine chewing gum, release nicotine slowly, up to the amount of a conventional cigarette.

While the argument that these products are not combusted and inhaled and therefore are less hazardous than cigarettes is correct, the health risks, particularly for heart disease, are unknown from ingesting tobacco and nicotine in this form. Additionally, it is not clear if and how such products would be regulated and the sale controlled to prevent people becoming addicted to nicotine.

5.2 “Nicotine water”

One product found on an internet search was Nicotine Water. This product, self-categorised as a dietary supplement, and advertised as a healthier alternative to smoking, appears to be in the form of bottled water with an advertised 2 cigarettes worth of nicotine per 2 litres water. The site strongly recommends not drinking more than 2 litres of nicotine water per hour. No company location is apparent on the website – only an email address (sales@nicotinewater.com) and telephone number (305-847-7946), which indicates that this product originates in the U.S.

5.3 “Nicotrol”

Nicotine inhalers are also available in the U.S., including one product, marketed by McNeil Consumer Products Company, called Nicotrol. This product replaces the nicotine exposures while also mimicking the hand-to-mouth motion of a smoker (Portyansky, 1997).

6. A REGULATORY FRAMEWORK FOR NOVEL TOBACCO PRODUCTS

Some scientists and public health advocates support the concept of replacing current tobacco products with “cleaner” nicotine delivery systems, essentially maintaining current levels of nicotine addiction in the population but doing so with a reduced toxic chemical exposure and a reduced risk of disease. In June 2000 the UK House of Commons Health Committee concluded, “Current regulation applying to tobacco products is entirely inadequate.” Areas of particular concern recognised by the Committee included marketing, advertising, sponsorship, packaging, labelling, health claims, brand stretching, harm reduction, product development, and the use of additives (Britton, 2001).

6.1 *Conclusions of the American Society for Addiction Medicine (ASAM)*

The following points by Dr John Slade, of the ASAM, have been raised regarding a possible regulatory framework for all nicotine delivery devices, including novel tobacco products, following the ASAM review of the Eclipse device (ASAM, 1996) (<http://www.asam.org/Frames.htm>).

1. The safety and toxicity of these products should be assessed by an independent body which can determine if the data are sufficient to warrant offering the device to the public, and can decide the conditions for sale.
2. Marketing of a nicotine delivery system could have unintended consequences. For example, while a product less harmful than cigarettes might be advantageous if its use were limited to persons who would not otherwise stop using tobacco, it could be detrimental, since it is not completely safe, if it were used by persons who would otherwise quit smoking or who had not previously used nicotine. A regulatory agency like USFDA would be able to set limits and monitor usage in ways that assured that good intentions led to good results.
3. Although initial advertising for these devices may be largely explanatory, marketing campaigns are likely to revert to image-based advertising of the kind now used to sell conventional cigarettes, unless there is regulation.
4. A regulatory structure is needed to provide a consistent approach to the marketing of the many different nicotine delivery devices expected on the market from diverse sources in coming years.

5. Because nicotine is addictive and Eclipse in particular is designed to deliver nicotine like a conventional cigarette, consumers will not be able to easily choose when to stop. This abridgement of free will means the government has a special interest in intervening actively to assure the greatest flow of information about these devices and the least amount of disease and death from their use.

6.2 U.S. National Academy of Sciences Evaluation

The United States National Academy of Sciences (NAS) has reviewed the implications of novel tobacco products on harm reduction (NAS, 2000; http://books.nap.edu/catalog/10029.html?onpi_webextra1). The document reviews what are termed potential reduced-exposure products (PREPs), which includes modified tobacco products and nicotine pharmaceuticals (e.g. nicotine replacement therapy). The principal conclusions of the reviewing committee are largely supportive of those given by the ASAM. In their principal conclusions (shown below in bullet points), the NAS concluded that there could be a successful, scientifically based harm reduction programme, if carefully implemented, and if:

- Manufacturers have the necessary incentive to develop and market products that reduce exposure to tobacco toxicants and that have a reasonable prospect of reducing the risk of tobacco-related disease
- Consumers are fully and accurately informed of all of the known, unknown, likely, and potential consequences of using these products
- Promotion, advertising and labelling of these products are firmly regulated to prevent false or misleading claims, explicit or implicit
- Health effects of using PREPs are monitored on a continuing basis
- Basic, clinical, and epidemiological research is conducted to establish the potential use of PREPs for reducing risks for disease in individuals and for reducing harm to the population as a whole, and
- Harm reduction is implemented as a component of a comprehensive national tobacco control programme that emphasises abstinence-oriented prevention and treatment

7. CONCLUSIONS

Tobacco products are presently diversifying and the tobacco industry is displaying the use of technologies that have the potential to significantly reduce the exposure to toxicants from their products. Some of these modifications may also serve to reduce objectionable reactions to exposure to ETS from non-smokers. Much of the focus on harm reduction of these products is on carcinogenicity, but modifications were not found that specifically reduced risk of cardiovascular disease. The U.S. NAS has concluded: “...*reducing risk of disease by reducing exposure to tobacco toxicants is feasible.*” However, the NAS also concluded: “*These products have not been evaluated comprehensively enough (including for a sufficient time) to*

provide a scientific basis for concluding that they are associated with a reduced risk of disease compared to conventional tobacco use” (NAS, 2000).

In addition to the “reduced harm” products, there are products such as sweets and aerosols being marketed and sold by other companies seeking to provide a “healthier” alternative to smoking while still maintaining an addiction to nicotine, through delivery of the drug in alternate forms. Finally, there are cigarettes of different composition and design that have been commonly used in some Asian countries, that are gaining popularity among youth and are often portrayed as healthier alternatives to conventional cigarettes, despite the lack of evidence to support this belief.

Aside from FTC smoking machine yields, which are unlikely to provide a sound basis for comparison of actual exposure, there are no objective, standardised scientific methods to evaluate the hazard potential of these products. In addition, the public, especially youth, are vulnerable to misleading messages and images about these products. All of the products reviewed in this report, with the exception of the de-nicotinised cigarettes, would be expected to exert a degree of addiction to nicotine. It is quite possible that some products, though comparatively benign toxicologically, could become gateway products for smoking conventional cigarettes due to the initiation of a dependence on nicotine, especially if conventional tobacco products were less expensive and easier to obtain.

A harm reduction programme for all tobacco products and nicotine delivery devices is potentially beneficial for public health if viewed as a tool to be used in the context of a broad strategy for reducing tobacco-related morbidity and mortality. Careful steps and monitoring are necessary to ensure that any such policy does not become counterproductive by creating false messages about the reduction of risks of smoking or dependence on nicotine.

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