The Relative Risk Reduction Continuum

It's the smoke stupid!

–anonymous

- A Changing Environment
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- Summary and Conclusion

We began this paper noting that not all tobacco and tobacco products carry 'equal harm' and that as technologies and science continue to develop there will be an ever-increasing number of tobacco products and tobacco like products appearing on the market (as well as nicotine containing products and other types of cessation products). We also noted that while we will need to continue to keep an active and careful watch on the tobacco industry to ensure that past abuses do not reoccur and to demand greater transparency of all stakeholders, we must also begin to look at how we can effectively modify tobacco products to reduce health risks associated with their use and to assess these products in terms of the level of relative risk.

Tobacco product modification, however, cannot be done in a vacuum and it must be considered in light of other important factors addressed in this paper, such as, public health, the need for governmental oversight, greater transparency of all stakeholders, technological advances, consumer and individual rights, agricultural production, economics and competition, etc.

We must also have a better system for assessing product risks. Many consumer products in our society carry risks—some more than others. And in various categories there are products that have differing relative risks. All automobiles require safety standards to minimize risks and yet we know that driving an automobile not only presents risks to ourselves but to others around us as well. And not all automobiles–in spite of mandated safety standards–carry the same risks. Some provide greater risk protection than others.

We know that unsafe sex not only increases the potential for HIV infection and other sexually transmitted disease but also unwanted pregnancies as well, both having significant ramifications on not only the individuals involved but on society as a whole. The foods we eat and the pharmaceuticals we use all have relative risks associated with their use and how much they are used. One only has to see the types of pharmaceutical advertising on television these days to realize that products that are promoted as 'life saving' also often carry significant risks, sometimes life threatening risks, associated with them. 100% safe, while commendable is not something that is feasible in a free society. Agencies like the FDA, the EPA, the CPSC, USDA, establish standards and requirements for the risks and relative risks of the products under their regulatory authorities, ensuring that there is a level playing field.

And so the case should also be for tobacco and tobacco products. Unless we ban tobacco there are certain tradeoffs that have to be considered in our efforts to reduce risks from the use of tobacco.

There are significant health risk differences between a combustible and noncombustible tobacco product. And there are relative risks for various products in each of these respective categories. Even with respect to products designed for cessation (whether tobacco or nicotine) there is a tremendous spectrum of products appearing on the market each having their own risks and benefits profile.

As a longer term goal, I believe that we need to try and move away from focusing on and attempting to classify a tobacco product as a PREP and begin to talk in terms of the risks and relative risks of products on the market and to label them based upon clearly established sound scientific standards and principles.

The concept of risks and relative risks allows one to compare products not only between categories (cigarettes, versus, smokeless, versus, pharmaceuticals) but also to compare the risks of products within categories. Consumers of tobacco need to be given a better picture as to what products are available and which products present what levels of comparative risks.

What might be considered a PREP today may not be a PREP in five years and in fact may even become one of the

relatively higher risk products on the market. There may be tobacco-based products, particularly in the noncombustible area whose risk may be commensurate with some of the pharmaceutical products on the market today. Swedish snus and the tobacco 'lozenge', as some like to call it, may be such products already on the market. And there may be cessation products (both tobacco and nicotine) that are yet to be developed and brought to the market that will be more effective than the cessation products currently on the market today. The nicotine vaccine is a good example. Assessing the risk and determining the extent of how the product should be labeled etc, cannot be left in the hands of the tobacco industry although it will be critical that they actively and openly participate in the process.

The prospects for an expanding 'continuum' of products starting with those having higher risk and moving down the continuum to total elimination of both tobacco and nicotine will, as pointed out elsewhere in this paper, require a governmental agency with the scientific, medical, and enforcement authorities necessary to ensure that the regulatory playing field is level and that consumers have full, complete and accurate information about the risks and relative risks of products-choosing products that are best suited to their personal preferences and health goals. But that will require Congressional action and the prospects for quick enactment of legislation is not good at this time. I have been working on the need for FDA oversight of tobacco products for over 15 years and I sometimes feel like I am 'waiting for Godot'. However, I still believe that governmental oversight of tobacco, is both necessary and inevitable. But we need to move forward even as we push for a more level and playing field.

A changing environment

We have noted two critical elements that will be necessary to sort through the complex scientific and marketing questions that will arise as new products enter current market place. We will need:

- Transparency and ongoing engagement of various stakeholders and experts to address a spectrum of inter-related issues, challenges and opportunities.

- A regulatory agency that can establish a meaningful and workable process and standards that establish a set of 'rules of the road' and which can provide validation by which any new products or claims will be made.

There are an increasing number of technologies that have either been developed or are soon to be introduced. These include new filter technologies, curing methods for tobacco leaf, the removal of pesticides and the elimination of chemicals that might cause harm. They also include the use of genetically modified tobacco, which according to many researchers holds great and significant potential for changing both the tobacco used in a tobacco product as well as the product itself. Such technologies may be a gateway to reducing toxicity, improving leaf qualities, reducing the use of pesticides and other potentially harmful components. Such technologies also hold promise for the development of pharmaceutical products and industrial enzymes of potentially great value to society.

We need to get beyond the rhetoric and the posturing that has so dominated tobacco control. Those who think that perpetuating current strategies of attacking the industry are the **only** way to affect change should consider that Wall Street analysts are today saying that given recent decisions in some of the tobacco litigation the industry is in a stronger position than it has been in since 1994. As David Adelman of Morgan Stanley noted in December 2005:

> *On the back of the Miles/Price decision, it is increasingly clear that the US Tobacco industry is in its strongest overall legal position since the 1994 emergence of the state health care cost recovery claims. Dynamics include: an increasingly conservative US Supreme Court; State Farm's limitations on punitive damages; the enactment of the Class Action Fairness Act; the increased prevalence of state appeal bond caps, the Illinois Supreme Courts extremely favorable ruling in Miles/Price; the Eight Circuit's unanimous favorable ruling in the Watson Lights class action, the US Supreme Court's denial of Certioari regarding the availability of disgorgement under Civil RICO; the Second Circuit's rejection of class certification in Simon II, a smoking and health class action claim of interest to the Florida Supreme Court (e.g., Engle; the industry low public profile; the absence of the emergence of any new large –scale legal risk; the filing of a few new claims; the continuation of defense verdicts in the few claims that survive trial; the passage of time, which because of the 1969 warning label preemption makes claims incrementally more difficult –over time—for plaintiffs.*

(Email assessment from David Adelman, Morgan Stanley – Tobacco: January US Tobacco Litigation Timeline, December 29, 2005

This may not only embolden the larger companies (particularly those opposed to regulation and transparency) but give smaller companies a green light to push the envelope in marketing cigarettes and other tobacco products free from any kind of controls, responsibility or accountability.

As has noted by N Gray, J Henningfield, N Benowitz et al in a recent edition of **Tobacco Control**,

The epidemiology tells us that tobacco products delivering nicotine vary considerably in harmfulness. Within each product category there is a (sometimes wide) variation of dose and manner of use, but the extreme ends of the spectrum differ in harmfulness by orders of magnitude.

("Towards a Comprehensive long term nicotine policy," N Gray, J E Henningfield, N L Benowitz, G N Connolly, C Dresler, K Fagersrom, M J Jarvis, ***Tobacco Control****/ 2005;14:161-165)*

O'Connor, Hyland, Giovino et al, have noted :

Future research should focus on methods of communicating relative risk information to smokers, so that smokers are not misled by comparative claims for either modified cigarettes or cigarette-like products or SLT products.

There is little doubt that the tobacco industry, especially the cigarette industry, will continue to develop and market supposedly less-harmful products with claims –explicit or implied – that such products will reduce the health risks of smoking. In an environment in which tobacco products – and the advertising and marketing that accompany them – are only loosely regulated or unregulated, these claims will continue to lull smokers into a false sense of security concerning health risks. The findings presented in this paper clearly demonstrate that smokers are confused about relative safety claims of reduced exposure tobacco products. More smokers believe that so-called reduced exposure cigarette products were safer than standard cigarettes than believed SLT was safer, even when awareness of products was controlled for. These data suggest that smokers are confused and mislead by cigarette marketing , even when such marketing does not include overt health messages. Companies looking to market reduced-exposure tobacco products should be required to demonstrate convincingly that smokers will not be confused or mislead by marketing claims.

(American Journal of Preventive Medicine, " Smoker Awareness of and Beliefs About Supposedly Less-Harmful Tobacco Products", Am.J.Med. 2005,29(2), page 89.)

For several years I have believed that there would be a *convergence of interests* between the tobacco industry and the pharmaceutical industry. I believe that such convergence is already taking place. I believe that some of the larger tobacco companies will devote more and more resources to the development of products using both pharmaceutical and food type technologies and science. One only has to realize that some of the largest of the tobacco manufacturers are in the food business and also have pharmaceutical interests to understand that they not only have the resources, but also the scientific capabilities to change their products. I cannot predict, however, the pace at which this will occur, but I believe that the market place of tobacco and nicotine products will be a dramatically different one ten years from now. In 2005, Altria/ Philip Morris, announced that:

We have chosen an adjacency growth strategy, looking at potential moves into complimentary tobacco and tobacco related products or processes that would allow PM to use its existing core infrastructure elements (Emphasis added)

(Statement made at the Prudential Back to School Consumer Conference, 2005)

In April and May of 2006, both Philip Morris and Reynolds American announced that they were moving into the noncombustible smokeless tobacco market with Reynolds purchasing the second largest smokeless tobacco manufacturer, Conwood. With these actions the two largest cigarette manufacturers virtually erased a line over night that had clearly divided cigarette manufacturers from the smokeless industry for decades.

Other signs and indicators that the industry is undergoing and will continue undergo change include the fact that:

- Vector Tobacco has used genetically modified tobacco in its Quest products.
- Reynolds acquired a pharmaceutical company some years back (Targacet).
- Star Scientific has developed a curing process for significantly reducing the TSNA's in tobacco leaf.
- Filligent, a biotech company out of Hong Kong has developed new filter technologies that are considered to be significantly different than anything currently on the market.
- There is research being conducted on the use of genetically modified tobacco for a spectrum of purposes.

And one has to ask, will pharmaceutical companies and other biotech companies one day develop tobacco-based products (particularly noncombustible products to start with) using food and pharmaceutical technologies that would be marketed and sold, not through their pharmaceutical divisions, but through their consumer product divisions?

The point of all this is that nothing would or will surprise me as to how the environment and the market place will continue to change over the next 5-10 years.

Combustible Tobacco Products Versus Non-Combustible Tobacco Products

We have noted in several places in this paper that there are wide differences between the relative risks of tobacco which is burned and tobacco which is used in a noncombusted form. A great deal of discussion and dialogue between the risks and relative risks of combustible and noncombustible tobacco products has taken place as well on whether noncombustible tobacco products in particular have a role to play in harm reduction strategies. If in fact they are lower in risk, the next question is what should harm reduction strategies using noncombustible tobacco products entail and how should they be implemented. How as noted above 'do we develop methods of communicating relative risk information to smokers so that smokers are not misled by comparative claims?'

Combustible Tobacco Products

Cigarette smoking remains this nation's leading preventable cause of death and disease – accounting for over 400,000 premature deaths each year.

When a cigarette burns, there are over 4,000 chemical constituents produced in the smoke that are inhaled into the lungs. As many as 60 such constituents are known carcinogens and many others (such as carbon monoxide) contribute significantly to other diseases such as cardiovascular disease, stroke and other pulmonary diseases.

In addition to the tobacco (for which there are different types and which contain varying degrees of toxins,) there are pesticides and chemicals used in both the tobacco leaf as well as the manufactured product. Little is known about the effects of such chemicals and pesticides when burned, either alone or in combination with other ingredients and pesticides.

Hundreds of additives and flavorings are used in the manufacture of cigarettes. According to the Department of Health and Human Services (HHS) while many of these additives and flavoring may be viewed as GRAS (generally recognized as safe) when used in their raw (non-combusted) state, such additives and flavorings may in fact pose additional toxic harms when burned.

Because of the complexity of a burning tobacco product coupled with a mix of chemicals, additives and ingredients that are burned, it will be a challenge to begin to logically, rationally and responsibly sort through not only the products that are currently on the market but also those that will be appearing on the market in the coming months and years.

There are, however, technologies (filters, curing methods, reduction of additives and the potential use of genetically modified tobacco) that are being employed that are demonstrating that it is possible to remove some but not all of the toxins contained in cigarette smoke. But does the reduction or elimination of one ore more toxins in a cigarette justify the allowance of any type of health claim (direct or implied)? At the moment, probably not.

A number of products which have already appeared on the market include:

- Elclipse -- a cigarette like tobacco product that heats rather than burns.
- Advance –- a cigarette that uses low TSNA tobacco and uses what is called the 'trionic filter'
- Accord
- Omni
- Quest
- Fact
- EHCCS –- This is an electronically heated cigarette system developed by Philip Morris USA

A company called XXII Century Tobacco, Inc. has indicated that it plans to develop and potentially bring to market tobacco products that are infused with higher levels of nicotine, thereby giving the smoker a 'satisfactory' dose of nicotine sooner thereby (theoretically) cutting down on the inhalations of toxins.

But as Ken Warner cautions as we look at the combustible market place in particular,

> *.....cigarette smoke contains thousands of chemicals with possibly hundreds of them hazardous to health. No one knows which chemicals, or which combinations, pose the greatest danger. Further, the novel products achieve their exposure through a variety of techniques that may themselves pose risks, possibly new risks to the health of the consumer. For example, one reduced brand of cigarette uses palladium to achieve its objective. Is inhaling combusted palladium dangerous? No one knows.*

If toxicity information and other information about ingredients, flavors, etc is to be made available in factual terms (not as direct health claim) what other information should be required to provide the necessary information to ensure that consumers fully understand the risks and relative risks for the product.

Many health groups have advocated that 'if the technologies exist then toxins should be removed'. As noted in the report Hope or Hazard? , "Although the extent of reduction in exposure to tobacco toxins may not necessarily lead to a proportional reduction in disease, if the technological capacity currently exists, all marketed tobacco products should meet performance standards that would reduce or eliminate toxins in tobacco products. Such an effort toward maximum risk reduction has not been pursued heretofore with respect to toxin exposure from cigarettes" (Hope Or Hazard? ,What research tell us about potentially reduced-exposure tobacco products, Transdisciplinary Tobacco Use Research Center, April 2005, p.8)

In addition, how does one provide incentives to the tobacco industry to remove such toxins? How do you encourage and acknowledge those companies willing and able to remove the toxins, as opposed to those manufacturers who will not use the technologies? How do you keep companies from using the tactics employed in the marketing of low tar and low nicotine cigarettes, that may ' potentially produce public health harm if these claims increase smoking initiation, maintenance, or relapse'? For me the answers lie in a variety of short term and long term efforts that must be undertaken and which will be dealt with in more detail later in this paper.

Noncombustible Tobacco Products

While still complex, the scientific issues surrounding noncombustible tobacco are far less complicated than when assessing combustible tobacco products. Because these products are not burned the number of hazardous constituents and toxins are significantly reduced.

It is a misstatement to suggest that smokeless tobacco products are as harmful as cigarettes as has often been the case. It is also a misstatement to suggest that all products within the smokeless tobacco category carry the same level of risk. The public health community has had to confront and begin to deal with the scientific realities that there are significant differences between products that are burned and those that are not. The idea that noncombustible tobacco products are not lower in risk neither stands up to common sense nor science. But does that mean such products are safe? No. While many have suggested that claims that smokeless tobacco are as hazardous as cigarettes are for the public good and 'well intentioned' to counter the industry's efforts to mislead the public, such tactics are contrary to the precept of 'truthful' disclosure. When the Surgeon General of the United States, no matter how well intentioned, goes before Congress and makes statements that are not an accurate reflection of science, it damages the credibility and role of the government as well as the public health community.

In reviewing the literature on smokeless tobacco, there seems to be a long overdue acknowledgment (and in many of cases an acceptance) of the fact that noncombustible forms of tobacco are significantly lower in risk than combustible products and that some forms of smokeless tobacco lower in risk than others.

As Hoffman, Hoffman and El-Bayoumy noted in a paper in 2001,

> *TSNA's are the major carcinogens in chewing tobacco and snuff and are associated with cancer in the oral cavity of snuff dippers.*
>
> *On the basis of our current knowledge, a drastic reduction of TSNA levels in chewing tobacco and snuff is expected to lower the risk for oral cancer; in fact such low levels of TSNA's may be below the threshold level for the induction of tumors in snuff dippers. However it will be of importance to investigate the possible endogenous formation of the carcinogenic TSNA in consumers of the snuff brands that contain only traces of TSNA.*
>
> *("The Less Harmful Cigarette: A Controversial Issue. A Tribute to Ernst L. Wynder," D Hoffman, I Hoffman, K El-Baypumy,* **Chemical Research in Toxicology** *(published by the American Chemical Society), Volume 14, Number 7, July 2001, page 784.*

Ken Warner who has been in the forefront in the discussion of harm reduction noted in a paper published on the subject of noncombustible smokeless products that:

> *Driving interest in low-nitrosamine smokeless products are two basic facts. First they are clearly dramatically less hazardous to health than cigarette smoking. Second, to many observers, the first of their bread, snus, a product used by 30% of Swedish males, serves as the worlds only major natural experiment in tobacco harm reduction. Thanks primarily to substantial tax-driven price differentials (ie cigarettes are heavily taxed; snus is not) snus has come to dominate smoking in male tobacco use in Sweden. As a consequence, Sweden has the lowest rate of male smoking in Europe, and the lowest rate of male lung cancer.*

An expert panel, asked to provide their opinions on the mortality risks associated with the use of low nitrosamine smokeless tobacco concluded:

> *On the narrow question of the relative risk of LN-SLT products, these results clearly indicate that experts perceive these products to be far less dangerous than conventional cigarettes. Based on the available published scientific literature as of 2003, there seems to be consensus that LN-SLT products pose a substantially lower risk to users than do conventional cigarettes. This finding raises ethical questions concerning whether it is inappropriate or misleading for government officials or public health experts to characterize smokeless tobacco products as comparatively dangerous with cigarette smoking.*
>
> *In comparison with smoking, experts perceive at least a 90% reduction in the relative risk of LN-SLT. The risks of using LN-SLT products therefore should not be portrayed as comparable with those smoking cigarettes as has been the practice of some government and public health authorities in the past. Importantly, the overall public health impact of LN-SLT will reflect use patterns, its marketing, and governmental regulation of tobacco products.*

Note: While reaching what is a strong consensus on the relative risk of LN-SLT with cigarettes, the study also found:

> *The results from this study should not be interpreted to mean that there is a consensus that smokeless products are an acceptable harm reduction alternative to conventional cigarettes. In addition to toxicity, an evaluation of the harm reduction potential of LN-SLT should consider who uses the product and how much they use it. Attention should be given as to whether it substitutes for smoking, is used in conjunction with or as a gateway to smoking, or substitutes for complete nonuse of tobacco products*

The panel additionally cautioned that :

> *The results from this study also should not be interpreted to mean that all smokeless tobacco products are less hazardous or less risky by the same margin than conventional cigarettes because our panel members only considered a handful of unique LN-SLT products.*

D Levy,E Mumford, KM Cummings, E Gilpin, G Giovino, A Hyland, D Sweanor, K Warner, The Realtive Risks of a Low-Nitrosamine Smokeless Tobacco Product Compared with Smoking Cigarettes: Estimates of a Panel of Experts, **Cancer Epidemiology ,Biomarkers & Prevention**, *December 2004.*

A position statement entitled **European Union Policy on Smokeless Tobacco – a statement in favour of evidence-based regulation for public health**, concluded that:

We support the replacement of the ban on oral tobacco with an approach that regulates the toxicity of all smokeless (and smoking) products. Our approach has the following advantages:

a) *It would create a legally defensible, fair and rational policy – in which public health is given primacy consistent within the framework of EU law.*
b) *It would create public health benefits through smoking cessation and smoking substitution.*
c) *It gives smokers an extra strategy for controlling their risks and eliminating ETS risk, and thereby respects their consumer and human rights.*
d) *It would apply toxicity controls to the currently unregulated chewing products such as gutka and paan available in the EU and currently unregulated.*
e) *It would have benefits beyond Europe if a good regulatory model is developed for controlling toxicity of smokeless tobacco – for example, establishing regulatory norms in the WHO Framework Convention on Tobacco Control*
f) *It opens the dominant cigarette makers to competition from tobacco products do far less harm.*

(European Union policy on smokeless tobacco – a statement in favour of evidence-based regulation for public health, C Bates,, K Fagerstrom M Jarvis, M Kuntz, A McNeil, L Ramstrom, February 2203, p. 10)

While it seems that there is now a consensus on the significant comparative risks between combustible and non-combustible products (especially those having very low levels of TSNAs), there are a number of issues (see above) that are being raised by some concerning whether noncombustible products can play a role in harm reduction efforts in the United States. See for example " The United States Isn't Sweden – Why UST's Efforts to Make Comparative claims is Wrong and Threatens Public Health", May 2003.

In that fact sheet, the CFTK argues that:

UST should not be allowed to make comparative claims about its products in the absence of an appropriate regulatory scheme that can provide review and approval of the claim. The government not the manufacturer, should decide what claims are appropriate and how and under what circumstances they can be made. Effective tobacco product regulation by the US Food and Drug Administration must include the ability to set product performance standards for toxins and carcinogens in smokeless tobacco products and must regulate the ability and circumstances under which a health claim can be made in association with a specific product.

The above statement raises the additional important question, challenge, and opportunity of being able to also determine differing levels of risk between the spectrum of noncombustible products on the market. There are many different products currently on the market and there will undoubtedly be more. Even products that are currently used in other countries (Gutkha, Zarda, Tombak etc.) may find their way into the American market place as more and more diverse populations become a part of American society. An interesting study from the UK looked at various forms of smokeless tobacco, including products from India, Sweden, Asia and the US, some of which are used in the UK and others which are currently prohibited. The study found wide differences of various toxins in the products concluding that:

Toxin standards should be set for all the smokeless tobacco products available on the UK market, with a reasonable timescale for compliance. The toxin standards set by parts of the industry – for example, the Gothiatek Standard used by Swedish Match – could be used as a starting point, but it should be possible over a short time frame to reduce key toxins and carcinogens to the lowest levels which are technically feasible which in most cases would be non-detectable levels.

(A McNeil, R Bedi, S Islam, MN Alkhatib, R West, "Levels of toxins in oral tobacco in the UK, **Tobacco Control** *2006;15:64-67, page 65)*

In the US, we continue to have a more divisive debate and discussion over smokeless tobacco with some still making the argument that smokeless tobacco is not a 'safe' alternative to smoking even though there is agreement that these products are significantly lower in risk than cigarette smoking. As was reported in the press:

Dr Stephen Hecht and colleagues from the University of Minnesota Cancer Center in Minneapolis compared the levels of cancer-causing nitrosamines in popular smokeless tobacco products and medicinal nicotine products such as the nicotine patch, nicotine gum, and nicotine lozenges. The results' clearly show that the levels of cancer causing nitrosamines are far higher in smokeless tobacco products that they are in medicinal nicotine products" Hecht said during a press briefing.

Nitrosamine levels were highest in oral snuff tobacco products made in the US, followed by Swedish 'snus(another type of smokeless tobacco) where as the 'lowest levels were found in hard snuff lozenges. The snuff lozenges actually did "quite well in our study" - it does appear to have lower levels of carcinogenic nitrosamines" than most of the other smokeless tobacco products, Hecht said.

Yet, while recognizing that there some products that 'did quite' well, Hecht goes on to conclude that "smokeless products are dangerous".

These findings were recently elaborated on in an April 2006 article in the journal Nicotine and Tobacco Research which looked at the range of tobacco specific nitrosamines (TSNA's) in new tobacco products. The study noted:

A number of new brands (alternative smokeless tobacco products) are being test marketed in the United States. These products are targeted to smokers and smokeless tobacco users who wish to reduce or quit tobacco use or who want to use 'safer 'products. Manufacturers' claims include statements of reduced toxin content and implied reduced risk, but it may take years before the real health effects of these new tobacco products are known. TSNA's are among the most important carcinogens in tobacco, and it is imperative that objective data on levels of these compounds be available.

The lowest TSNA levels in the tobacco-containing products we analyzed were found in the compressed tobacco lozenges Ariva and Stonewall. Levels of strongly carcinogenic NNN and NNK were only 56-99/ng/g with most of the TSNA content comprised of NAT, which is apparently noncarcinogenic. These products use Star Scientific specially cured tobacco known to be low in TSNA's. The emergence of these new products with relatively low levels of carcinogenic TSNA's is an encouraging sign.

The Swedish snus General, which is manufactured using the GothiaTek process and quality standard designed to minimize nitrosamine contamination, contained relatively low levels of TSNA's, compared with conventional smokeless tobacco products. The variation in TSNA content observed in General in 2002 and 2003 is consistent with a study done by the Swedish National Food Aministration that demonstrated a noticiable decrease in TSNA content in moist snuff on the Swedish market. However, TSNA levels in Exalt, which is supposedly produced by the same technology, were comparable with those in the same conventional commercial brands of smokeless tobacco such as Copenhagen and Kodiak, which have had relatively high amounts of these compounds for many years. (Hecht & Hoffman, 1988; Hoffman et al. 1995; Radu et al 2004). Lower levels were found in Revel;howver, these levels were still considerably higher than nitrosamine levels in other products such as food and beer.

(I Stepanov,J Jenson, D Hatsukami, S Hecht (2006). "Tobacco-specific nitrosamines in new tobacco products", **Nicotine and Tobacco Research**, *Vol.8,No 2)*

All of the above points out the urgent need for us to devise a way in which we can have transparent discussions and consider options that can or should be taken. If as both the UK studies and the US studies indicate – that it is possible to reduce the TSNA levels to virtually non-detectable levels (as well as other possible toxins), and if there is a consensus on the fact that L-TSNA smokeless tobacco products are clearly and substantially lower in risk than cigarettes, shouldn't we be talking about how to implement standards and technologies within the smokeless category to achieve that goal?

As we have indicated throughout this paper, the question in my mind is not so much if but rather how and under what

conditions and parameters we can move forward in testing products and determining how any claims or statements can be made. The last section of this paper will outline what I believe may be a process for discussing and dealing with some of those outstanding issues and questions now, even as we work towards governmental oversight by an agency like the FDA. Several of these issues and questions might include:

- How such products can and should be labeled and marketed, including how and under what circumstances comparative claims should be allowed?
- What kind of regulatory system needs to be in place to ensure a level playing field (and what can be done in the interim without FDA oversight).
- How can current scientific studies be assessed and 'ranked' to guide efforts and activities?
- At what levels do TSNA's in smokeless tobacco constitute a health threat?
- Can a system similar to the Swedish 'Gothiatek' system be devised to establish quality standards for ingredients, TSNs and other toxins?
- What is the role of competition and what 'incentives' can be provided to force changes on the industry?
- What kind of monitoring and surveillance systems should be developed and implemented?

In assessing the risks and relative of cigarettes, and smokeless tobacco, what should those risks be compared with?

Consumers of tobacco and nicotine products should be able to make an across-the-board assessment of the risks and relative risks of products that are available to them. As we noted at the beginning of this paper, harm reduction entails trying to meet users 'where they are'. There are no silver bullets and what might work for one person in reducing their risks or quitting might not work for another person. In order for consumers to fully and completely understand the spectrum of products available to them we need to bring some order to the existing chaos that currently exists in the market place. This will be even more critical as more and more products and players enter into the stream of commerce.

I have been somewhat baffled as to why a few in the public health community have taken the position that smokeless tobacco products should only be compared with the risks associated with medicinal nicotine and cessation products, rather than looking across at a spectrum of products including cigarettes. Is this because many find it difficult to bring themselves to make scientific and medical distinctions that might require them to acknowledge that there are differing degrees of risks between tobacco products?

I would argue that it is equally important for users and consumers of tobacco to understand the spectrum and relative risks of different types of tobacco products as it is for them to understand the risks and relative risks of using different forms on tobacco and using different nicotine replacement therapies. Such factual, fair and balanced information will need to come from and/or be verified by government in the form of improved labeling and disclosure and regulatory oversight of the industry; from educational initiatives by the public health sector, and even from industry itself.

Thus a goal should be for users of tobacco products (and NRT) to be able to understand and compare:

Between Categories

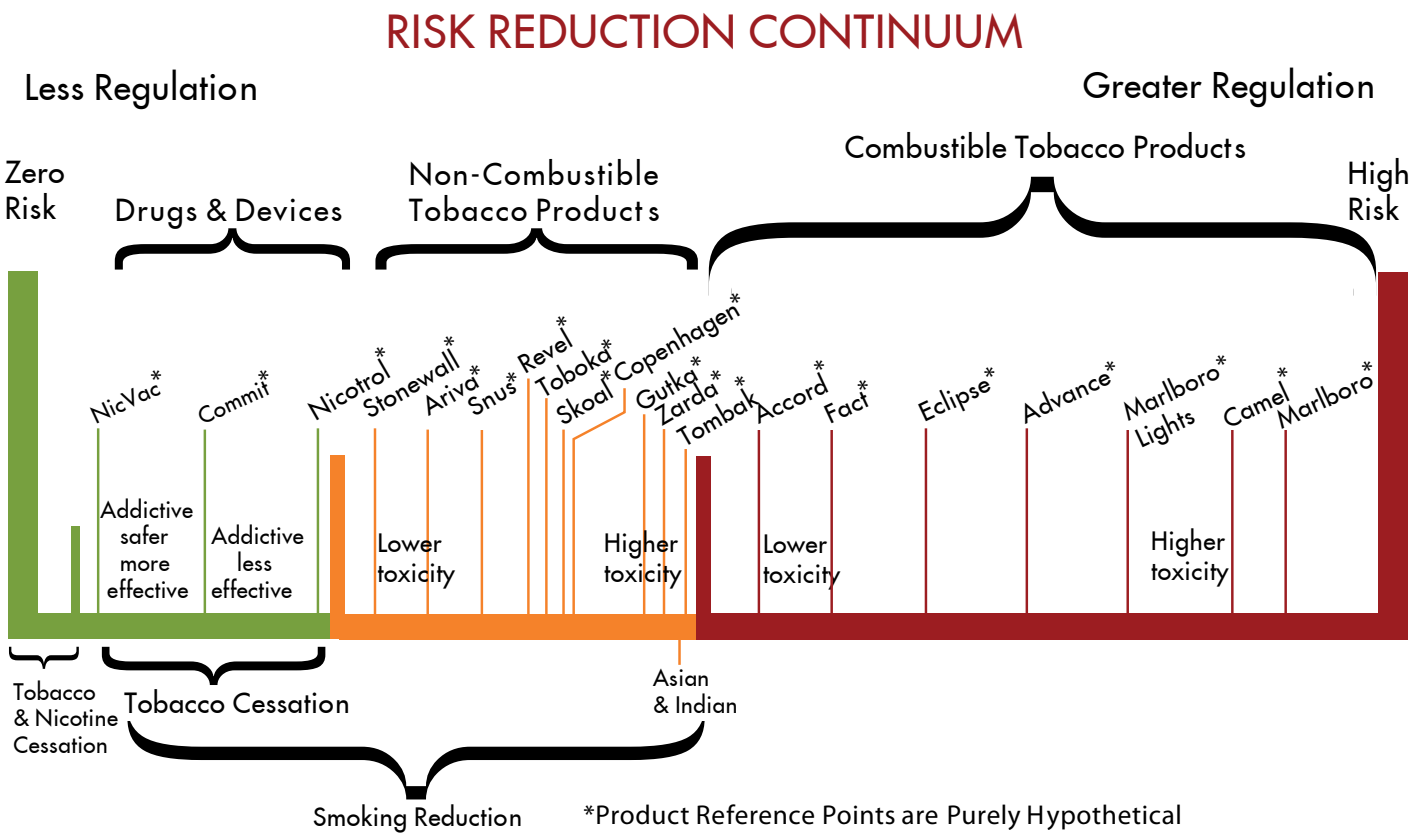
- Cigarettes with smokeless and NRT products
- Smokeless with cigarettes and NRT Products
- NRT products with smokeless and cigarettes

Within Categories

- Cigarettes with cigarettes
- Smokeless with smokeless
- NRT with NRT

The Comparative Risk Reduction Continuum Chart

The following chart is a hypothetical representation of the relative risks that are presented by spectrum of products–from those that are highly toxic and in the form of combusted tobacco to those that are at the other end of the spectrum, where risks are very small or even negligible. In each case, the regulation of the product should be based on risk. The higher the risk the more the more regulation (labeling, warnings, marketing restrictions, taxation etc.) The lower the risk the less regulation. I believe that if we begin to develop better and more consistent methods for testing tobacco products (and NRT), we can in fact plot where we would expect products to fall on the continuum.



POPULATION RISK V. INDIVIDUAL RISK
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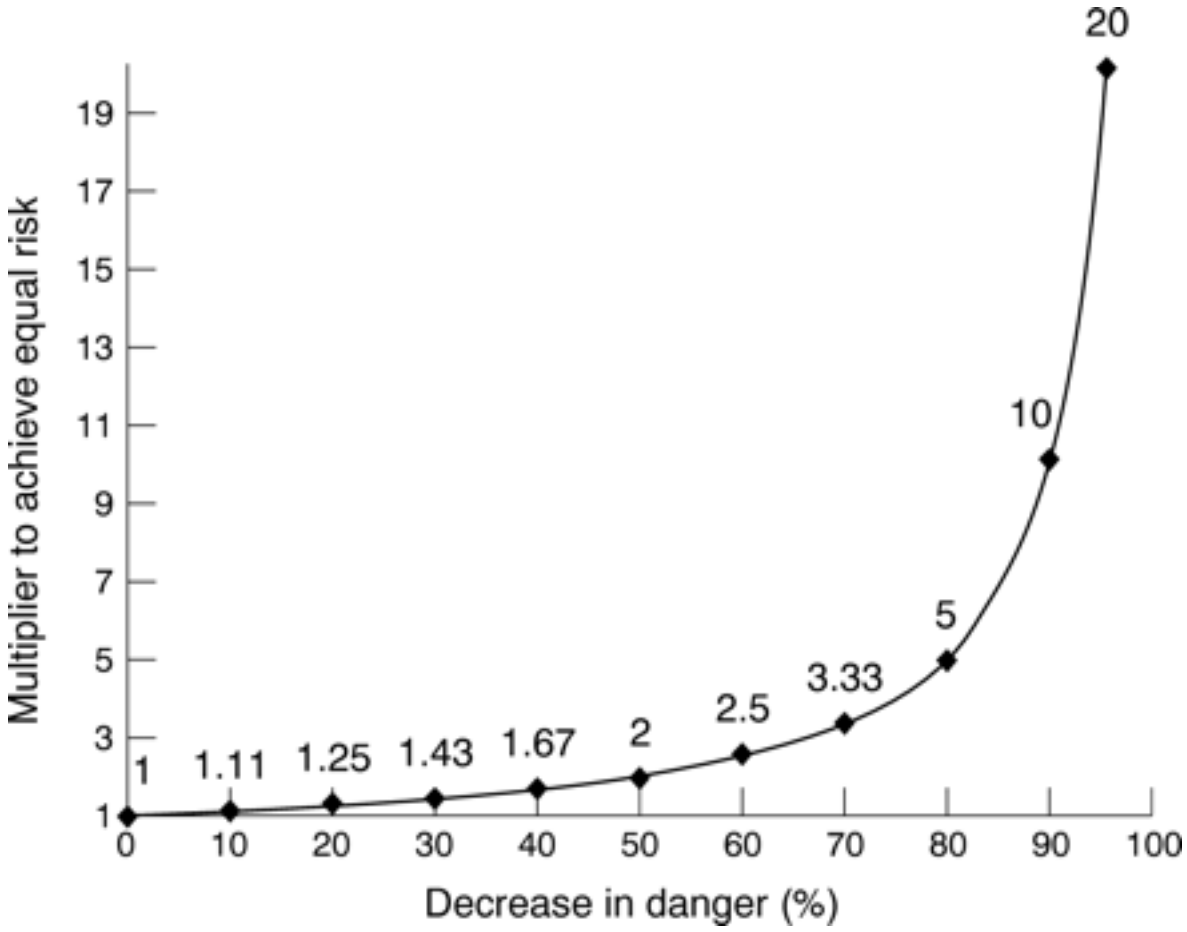

Kozlowski LT, et al. Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. *Tobacco Control* 2001; 10: 201-203

The Risk Reduction Equilibrium

In addition to getting a better idea of the risks and relative risks of various products, it is also useful to use the Risk Reduction Equilibrium", that was devised by Professor Lynn T. Kozlowski but also employed and referenced by others (Gionno, Warner, Cummings, Sweanor)

The risk/use equilibrium allows for the evaluation of possible problems (and benefits) caused by increased use of a less dangerous product-an equilibrium achieved by increasing use as risk decreases.

Both the Relative Risk Assessment Continuum and the Risk Reduction Equilibrium analysis could be further refined and allow for a more organized evaluation of products in the future. Such refinement would help in labeling and marketing efforts as well as surveillance, two critical components of an effective harm reduction effort. How we might proceed will be addressed in the last sections of this paper.

Regulation of Products on the Continuum Should be Commensurate with Risk

As we suggested on the Risk Reduction Continuum Chart, the degree of regulation of a product should be commensurate with level of harm caused by the product. This includes the labeling and marketing allowances for each product category and for each product within that category. A highly toxic combustible product for example should carry the most stringent warnings, labeling and marketing restrictions, while a noncombustible tobacco product would have less stringent labeling and marketing restrictions and requirements. Pharmaceutical would have even less restrictions. Products in each of these two (three) categories could be further differentiated based upon the level of scientific evidence available on each product. Such might be the case for making distinctions between smokeless tobacco products that have varying (and meaningful differences) levels of tobacco specific nitrosamines. Such might be the case for combustible products that have demonstrated (through agreed upon testing methods) that certain significant toxins have either been reduced or eliminated. This type of product differentiation based on the level of risk is not unique to tobacco but is applied to other products such as pharmaceuticals, and foods. The FDA already has extensive experience with labeling and disease claims. The FTC has extensive experience with unfair and deceptive marketing practices, the CDC with surveillance issues as well as a state of the art laboratory testing facility. There is also a great deal of experience and models on labeling and marketing (including assurances of operating within the parameters of the First Amendment) that can be drawn on.

The IOM Report contains a set of regulatory principles that should be used for mapping out potential short term and long term goals and objectives, including such things as disclosure of product ingredients; assessing yields and testing of various toxicants; pre-marketing approval of products making health claims; criteria and methods for the labeling and marketing of products; conducting post-marketing surveillance; and establishing performance standards. (For a complete listing of the regulatory principles and a more thorough discussion, see IOM report, Clearing the Smoke, pages 206-229)

Surveillance of Products is Critical

There is little disagreement that if we go down the harm reduction path we will need to be able to monitor use of such products both within the broad categories under which they are marketed and as individual products. This will require a cooperative effort of the government, the public health community, industry, retailers and wholesalers, and consumers.

The IOM report **Clearing the Smoke** (page 180) noted that:

> *The goal of surveillance systems in epidemiology and public health is to provide timely information from populations on the occurrence of disease and conditions of interest, the presence of risk factors for those conditions, and the impact of disease control programs.*
>
> *The Centers for Disease Control and Prevention (CDC) offers the following definition of surveillance (Thacker and Berkelman, 1988):*
>
> > *Public health surveillance is the ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link in the surveillance chain is the application of these data to prevention and control. A surveillance system includes a capacity for data collection, analysis, and dissemination linked to public health programs.*

It is unfortunate, however, that when it comes to tobacco, effective and comprehensive surveillance systems have not been instituted. The IOM report goes on:

> *One important issue is who would conduct surveillance on conventional tobacco products and PREPs. The types of data recommended above (see report pages 183-195) would almost preclude all surveillance being*

conducted by one organization or agency. It is likely that the elements of surveillance will come from many sources, and a coordinated effort will be needed to plan, assimilate, and interpret information for reasons of efficiency and standardization. As noted elsewhere, it will be important to include all conventional tobacco products, since they become one critical reference for health outcome studies, and to monitor changes in these products themselves. A part of the surveillance system would be to validate manufacturer claims of product distribution, content and biological and clinical effects.

The report concludes with the following recommendations (page 197):

1. *There is an urgent need for a national and comprehensive surveillance system that collects information on a broad range of elements necessary to understand the population impact of tobacco products and PREPs, including attitude, beliefs, product characteristics, product distribution and usage patterns, markets messages such as harm reduction claims and advertising, the incidence of initiation and quitting and non-tobacco risk factors for tobacco related conditions. There should be surveillance of major smoking-related diseases as well as construction of aggregate population health measures of the net impact of conventional products and PREPs.*
2. *The surveillance system should consist of mandatory, industry-furnished data on tobacco product constituents, additives, and population distribution and sales.*
3. *Resources should be made available for a program of epidemiological studies that specifically address the health outcomes of PREPs and conventional tobacco products, built on a robust surveillance system and using available basic and clinical scientific findings.*

Scientific Standards for Allowing or Disallowing Claims and the Disclosure of Information

The scientific methods by which the risks of the spectrum of products are assessed that will allow or disallow claims and other information will be critical. There must be agreed upon standards. This is particularly important if we are to avoid the problems of the low tar and low nicotine fiascos of the recent past. Currently there are no uniform specific standards or rules for tobacco relating to misleading and deceptive claims and marketing (and other information) which is broadly governed under the authorities of the Federal Trade Commission. The FTC reviews claims and labeling for misleading and deceptive statements on a case by case basis, falling far short of what will be needed in an ever- more complex and expanding market place. The development of scientific standards will be critical if we are going to establish a process and a yardstick by which all products on the market can be measured both for validation of the product itself and any claims that may be made.

I believe that given the Supreme Courts decision preventing FDA from regulating tobacco products and putting the burden back in the hands of Congress, there will be efforts by many in the industry to push the envelope in making claims. The provisions of the MSA can continue to be used to prevent false and misleading claims but this is not a system that in my view will serve the long term interests of the parties if harm reduction is going to continue to move forward.

In addition, the First amendment cases on commercial speech have increasingly given commercial speech greater protection. Several cases concerning the allowance or disallowance of health claims on foods are very instructive as to how the courts might deal with tobacco and how health claims and other information is made available to the public. We need to consider the case law and to develop labeling and marketing systems that will meet First amendment requirements.

Summary and Conclusion

Not all tobacco products carry the same level of risks. Whether in combustible or noncombustible form, the level of risk associated with a particular tobacco product can vary substantially. Combustible forms of tobacco carry the highest level of risks because of the number of harmful constituents produced in the smoke. Noncombustible forms of tobacco, because they are not burned generally carry a significantly lower level of risk. And within each of these two categories there can also be very different degrees of risk associated with the product. Each product, in effect, carries its own 'risk profile'. The challenge to the scientific community, the public health community, the tobacco industry, biotech companies, growers, government and others is to work towards the development of

standards and testing methods by which tobacco products can be evaluated so that we can understand the risks and relative risks of such products not only between categories but within those as categories as well. Models and regulatory standards that the FDA uses for both food and pharmaceutical products (prescription and OTC) could be very useful in developing a similar a system for tobacco products.

The manner in which products are labeled and marketed would therefore be commensurate with the risks they pose-based on their 'risk profile'. The higher toxic products would have greater labeling and marketing requirements and restrictions, while those products deemed to be lower in risk would have fewer and different requirements. All products, including NRT products can, with the use of agreed upon testing and evaluation methods be placed on the 'relative risk continuum,' allowing consumers and the public to better understand the products that are in the market place and the level of risk they produce. Competition would be stimulated under this system rewarding companies who are true innovators and pushing those who wish to circumvent science and health out of the market place.

This process of being able to evaluate products based on relative risks will be critical if we are going to be able to meet the individual 'health needs' of users of both tobacco products as well as NRT.