

## **Appendix 7**

**Statement by David A. Kessler, M.D.  
Commissioner of Food and Drugs, on Nicotine-Containing Cigarettes  
Before the Subcommittee on Health and the Environment,  
Committee on Energy and Commerce,  
U.S. House of Representatives,  
March 25, 1994**

**Statement on Nicotine-Containing Cigarettes**

by

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Commissioner of Food and Drugs**

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Mr. Chairman, the cigarette industry has attempted to frame the debate on smoking as the right of each American to choose. The question we must ask is whether smokers really have that choice.

Consider these facts:

- o Two-thirds of adults who smoke say they wish they could quit<sup>1</sup>.
- o Seventeen million try to quit each year, but fewer than one out of ten succeed<sup>2</sup>. For every smoker who quits, nine try and fail.
- o Three out of four adult smokers say that they are addicted<sup>3</sup>. By some estimates, as many as 74 to 90 percent are addicted<sup>4</sup>.
- o Eight out of ten smokers say they wish they had never started smoking<sup>5</sup>.

Accumulating evidence suggests that cigarette manufacturers may intend this result -- that they may be controlling smokers' choice by controlling the levels of nicotine in their products in a manner that creates and sustains an addiction in the vast majority of smokers.

That is the issue I am here to address. Whether it is a choice by cigarette companies to maintain addictive levels of nicotine in their cigarettes, rather than a choice by consumers to continue smoking, that in the end is driving the demand for cigarettes in this country.

Although FDA has long recognized that the nicotine in

tobacco produces drug-like effects, we never stepped in to regulate most tobacco products as drugs. One of the obstacles has been a legal one. A product is subject to regulation as a drug based primarily on its intended use. Generally, there must be an intent that the product be used either in relation to a disease or to affect the structure or function of the body. With certain exceptions<sup>6</sup>, we have not had sufficient evidence of such intent with regard to nicotine in tobacco products. Most people assume that the nicotine in cigarettes is present solely because it is a natural and unavoidable component of tobacco.

Mr. Chairman, we now have cause to reconsider this historical view. The question now before us all is whether nicotine-containing cigarettes should be regulated as drugs. We seek guidance from the Congress on the public health and social issues that arise once the question is posed. This question arises today because of an accumulation of information in recent months and years. In my testimony today, I will describe some of that information.

The first body of information concerns the highly addictive nature of nicotine. The second body of information I will be talking about -- in some detail -- concerns the apparent ability of cigarette companies to control nicotine levels in cigarettes. We have information strongly suggesting that the amount of nicotine in a cigarette is there by design. Cigarette companies must answer the question: what is the real intent of this design?

## I. NICOTINE IS A HIGHLY ADDICTIVE SUBSTANCE

Let me turn then to my first point about the addictive nature of nicotine.

The nicotine delivered by tobacco products is highly addictive. This was carefully documented in the 1988 Surgeon General's report. You can find nicotine's addictive properties described in numerous scientific papers<sup>7</sup>.

As with any addictive substance, some people can break their addiction to nicotine. But I doubt there is a person in this room who hasn't either gone to great pains to quit smoking, or watched a friend or relative struggle to extricate himself or herself from a dependence on cigarettes.

Remarkably, we see the grip of nicotine even among patients for whom the dangers of smoking could not be starker. After surgery for lung cancer, almost half of smokers resume smoking<sup>8</sup>. Among smokers who suffer a heart attack, 38 percent resume smoking while they are still in the hospital<sup>9</sup>. Even when a smoker has his or her larynx removed, 40 percent try smoking again<sup>10</sup>.

When a smoker sleeps, blood levels of nicotine decrease significantly. But the smoker doesn't need to be an expert on the concept of nicotine blood levels to know full well what that means. More than one-third of smokers reach for their first cigarette within 10 minutes of awakening<sup>11</sup>; nearly two-thirds smoke within the first half hour<sup>12</sup>. Experts in the field tell us that smoking the first cigarette of the day within 30 minutes

of waking is a meaningful measure of addiction<sup>13</sup>.

I am struck especially by the statistics about our young people. A majority of adult smokers begin smoking as teenagers<sup>14</sup>. Unfortunately, 70 percent of young people ages 12-18 who smoke say that they believe that they are already dependent on cigarettes<sup>15</sup>. About 40 percent of high school seniors who smoke regularly have tried to quit and failed<sup>16</sup>.

It is fair to argue that the decision to start smoking may be a matter of choice. But once they have started smoking regularly, most smokers are in effect deprived of the choice to stop smoking. Recall one of the statistics I recited earlier. Seventeen million Americans try to quit smoking each year. But more than 15,000,000 individuals are unable to exercise that choice because they cannot break their addiction to cigarettes. My concern is that the choice that they are making at a young age quickly becomes little or no choice at all and will be very difficult to undo for the rest of their lives.

Mr. Chairman, nicotine is recognized as an addictive substance by such major medical organizations as the Office of U.S. Surgeon General, the World Health Organization<sup>17</sup>, the American Medical Association<sup>18</sup>, the American Psychiatric Association<sup>19</sup>, the American Psychological Association<sup>20</sup>, the American Society of Addiction Medicine<sup>21</sup>, and the Medical Research Council in the United Kingdom<sup>22</sup>. All of these organizations acknowledge tobacco use as a form of drug dependence or addiction with severe adverse health consequences.

Definitions of an addictive substance may vary slightly, but they all embody some key criteria: first, compulsive use, often despite knowing the substance is harmful; second, a psychoactive effect -- that is, a direct chemical effect in the brain; third, what researchers call reinforcing behavior that conditions continued use<sup>27</sup>. (Chart A) In addition, withdrawal symptoms occur with many drugs and occur in many cigarette smokers who try to quit. These are hallmarks of an addictive substance and nicotine meets them all.

When a smoker inhales, once absorbed in the bloodstream, nicotine is carried to the brain in only 7-9 seconds<sup>23</sup>, setting off a biological chain reaction that is critical in establishing and reinforcing addiction.

Over the past few years, scientists have generated a tremendous amount of information on the similarities among different addictive substances. Some crucial information has come from the fact that, in a laboratory setting, animals will self-administer addictive substances. This self-administration may involve the animal pushing a lever or engaging in other actions to get repeated doses of the addictive substance. With very few exceptions, animals will self-administer those drugs that are considered highly addictive in humans, including morphine and cocaine, and will not self-administer those drugs that are not considered addictive<sup>24, 25</sup>.

Understanding that animals will self-administer addictive substances has fundamentally changed the way that scientists view

addiction in humans<sup>24</sup>. It has turned attention away from the concept of an "addictive personality" to a realization that addictive drugs share common chemical effects in the brain<sup>24</sup>.

Despite the wide chemical diversity among different addictive substances, a property that most of them share is the ability to affect the regulation of a chemical called dopamine in parts of the brain that are important to emotion and motivation<sup>26</sup>. It is now believed that it is the effect of addictive substances on dopamine that is responsible for driving animals to self-administer these substances and for causing humans to develop addictions<sup>24</sup>.

Regulation of dopamine, rewards the activity, and causes the animal or person to repeat the activity that produced that reward<sup>24</sup>,<sup>26</sup>. The process by which the regulation of dopamine leads an animal or a human to repeat the behavior is known as "reinforcement<sup>24</sup>." Drugs that have the ability to directly modify dopamine levels can produce powerfully ingrained addictive behavior<sup>24</sup>."

One of the ways that researchers now test the addictive properties of drugs is to determine whether animals will self-administer that substance and then to determine whether the animals will stop self-administering if the chemical action of the substance is blocked by the simultaneous administration of another drug that prevents the first substance from acting in the brain. Data gathered over the past 15 years have documented that



laboratory animals will voluntarily self-administer nicotine<sup>25</sup>,<sup>27</sup>; that nicotine does stimulate the release of dopamine<sup>28</sup>; and that laboratory animals will decrease self-administration of nicotine if the action of nicotine, or the release of dopamine, in the brain is blocked<sup>29,30</sup>.

A number of top tobacco industry officials have stated that they do not believe that tobacco is addictive<sup>31</sup>. They may tell you that smokers smoke for "pleasure," not to satisfy a nicotine craving. Experts tell us that their patients report that only a small minority of the cigarettes they smoke in a day are highly pleasurable<sup>32</sup>. Experts believe that the remainder are smoked to primarily sustain nicotine blood levels and to avoid withdrawal symptoms<sup>32</sup>.

The industry couches nicotine's effects in euphemisms such as "satisfaction" or "impact" or "strength." Listen to what they say in one company's patent:

It also has been generally recognized that the smoker's perception of the "strength" of the cigarette is directly related to the amount of nicotine contained in the cigarette smoke during each puff<sup>33</sup>.

-patent no. 4,595,024 C1:33-36

But these terms only sidestep the fact that the companies are marketing a powerfully addictive agent. Despite the buzzwords used by industry, what smokers are addicted to is not "rich aroma" or "pleasure" or "satisfaction." What they are addicted to is nicotine, pure and simple, because of its psychoactive effects and its drug dependence qualities.

To smokers who know that they are addicted, to those who

have buried a loved one who was addicted, it is simply no longer credible to deny the highly addictive nature of nicotine.

## II. CONTROLLING THE LEVEL OF NICOTINE IN CIGARETTES

My second point today involves a growing body of information about the control of nicotine levels exercised by the tobacco industry. Mr. Chairman, I do not have all the facts or all the answers today. The picture is still incomplete. But from a number of pieces of information, from a number of sources, a picture of tobacco company practices is beginning to emerge.

The public thinks of cigarettes as simply blended tobacco rolled in paper. But they are much more than that. Some of today's cigarettes may, in fact, qualify as high technology nicotine delivery systems that deliver nicotine in precisely calculated quantities -- quantities that are more than sufficient to create and to sustain addiction in the vast majority of individuals who smoke regularly.

But you don't have to take it from me. Consider how people in the tobacco industry itself view cigarettes.

Just take a moment to look at the excerpts from an internal memorandum written by a supervisor of research that circulated in the Philip Morris Company in 1972:

Think of the cigarette pack as a storage container for a day's supply of nicotine. . . . Think of the cigarette as a dispenser for a dose unit of nicotine. . . . Think of a puff of smoke as the vehicle for nicotine. . . . Smoke is beyond question the most optimized vehicle of nicotine and the cigarette the most optimized dispenser of smoke.

"Dispensers of smoke . . . which is a vehicle for delivering nicotine." This quote is a revealing self-portrait.

Or listen to the words in one tobacco company patent:

Medical research has established that nicotine is the active ingredient in tobacco. Small doses of nicotine provide the user with certain pleasurable effects resulting in the desire for additional doses<sup>34</sup>.

-patent no. 4,676,259 C1:21-24

### The Design of Cigarettes

How does this industry design cigarettes?

The history of the tobacco industry is a story of how a product that may at one time have been a simple agricultural commodity appears to have become a nicotine delivery system. Prior to the 1940's, the waste products from cigarettes -- the stems, the scraps, and the dust -- were discarded. The tobacco industry had identified no use for these materials in the cigarette manufacturing process.

Then, in the 1940s and '50s, the industry created reconstituted tobacco from the previously unusable tobacco stems, scraps, and dust. This gave cigarette makers the ability to reduce the cost of producing cigarettes by using fewer tobacco leaves and making up the difference by using reconstituted tobacco. While the motive appeared to be purely economic, the reconstitution process was nevertheless a critical development that started the industry down the path toward controlling and manipulating nicotine levels. The ability to control and manipulate nicotine levels becomes important in light of another key realization. Industry patents show that the industry

recognized that nicotine is the active ingredient in tobacco smoke. It is what produces the psychoactive effects that lead smokers to crave cigarettes.

Numerous patents illustrate how the industry has been working to sustain the psychoactive effects of nicotine in cigarettes. These charts show samples from several categories of patents: eight patents to increase nicotine content by adding nicotine to the tobacco rod (Chart B); five patents to increase nicotine content by adding nicotine to filters, wrappers and other parts of the cigarette (Chart C); three patents that use advanced technology to manipulate the levels of nicotine in tobacco (Chart D); eight patents on extraction of nicotine from tobacco (Chart E); and nine patents to develop new chemical variants of nicotine (Chart F).

Patents not only describe a specific invention. They also speak to the industry's capabilities, to its research, and provide insight into what it may be attempting to achieve with its products.

It is prudent to keep in mind that patents do not necessarily tell us what processes are currently being used in manufacturing cigarettes. Nevertheless, the number and pattern of these patents leaves little doubt that the cigarette industry has developed enormously sophisticated methods for manipulating nicotine levels in cigarettes. Today, a cigarette company can add or subtract nicotine from tobacco. It can set nicotine levels. In many cigarettes today, the amount of nicotine present

is a result of choice, not chance.

Let me show you the language in some of these patents. This is in the industry's own words.

Listen to what industry says it wants to be able to do with nicotine.

First, the industry wants precise control of the amount of nicotine in cigarettes to provide desired physiological effects:

Maintaining the nicotine content at a sufficiently high level to provide the desired physiological activity, taste, and odor...can thus be seen to be a significant problem in the tobacco art<sup>35</sup>.

-patent no. 3,280,823 C1:43-48

Second, the industry wants to increase the amount of nicotine in some cigarettes.

...the perceived taste or strength of the cigarettes classified as having lower levels of "tar" and nicotine are progressively less than that of the cigarettes which are classified as approaching the characteristics of the "full flavor" cigarettes. It has been proposed to add nicotine and other flavorants to the cut filler of the lower "tar" cigarettes to enhance the taste, strength, and satisfaction of such cigarettes<sup>36</sup>.

-patent no. 4,830,028 C1:40-47

This invention...concerns the problem of maintaining or increasing the nicotine content of the smoke whilst avoiding an undesirable level of particulate matter in the smoke....<sup>37</sup>

-patent no. 3,861,400 C1:1-10

Now listen to what the industry says it can do, right now, at least for patent purposes, with the nicotine in cigarettes:

It can precisely manipulate nicotine levels in cigarettes:

This invention permits the release into tobacco smoke, in controlled amounts, of desirable flavorants, as well as the release, in controlled

amounts and when desired, of nicotine into tobacco smoke<sup>38</sup>.

-patent no. 3,280,823 C2:37-40

It is another object of the invention to provide an agent for the treatment of tobacco smoke whereby nicotine is easily released thereinto in controlled amounts<sup>39</sup>.

-patent no. 3,584,630 C2:69-71

[I]t can be seen that the process...enables the manipulation of the nicotine content of tobacco material, such as cut leaf and reconstituted leaf, by removal of nicotine from a suitable nicotine tobacco source or by the addition of nicotine to a low nicotine tobacco material<sup>40</sup>.

-patent no. 4,215,706 C3:61-66

...processed tobaccos can be manufactured under conditions suitable to provide products having various nicotine levels<sup>41</sup>.

-patent no. 5,031,646 C5:63-65

Examples of suitable tobacco materials include...processed tobacco materials such as expanded tobaccos, processed tobacco stems, reconstituted tobacco materials or reconstituted tobacco materials having varying levels of endogenous and exogenous nicotine....<sup>42</sup>

-patent no. 5,031,646 C5:21-27

...the present invention...is particularly useful for the maintenance of the proper amount of nicotine in tobacco smoke.

...previous efforts have been made to add nicotine to tobacco products wherein the nicotine level in the tobacco was undesirably low<sup>43</sup>.

-patent no. 3,584,630 C2:5-15

It can precisely manipulate the rate at which the nicotine is delivered in the cigarette:

It is a further object of this invention to provide a cigarette which delivers a larger amount of nicotine in the first few puffs of the cigarette than in the last few puffs<sup>44</sup>.

-patent no. 4,595,024 C2:23-26

It can transfer nicotine from one material to another at will:

Moreover, the process is useful for transferring naturally occurring nicotine from tobacco having a generally high nicotine content to a nicotine deficient tobacco, tobacco filler materials, or RL (reconstituted leaf) which are used in the production of cigarettes and other smoking products... [A] low nicotine tobacco ...can also be used as the nicotine donor...<sup>45</sup>

-patent no. 4,215,706 C1:40-48

It is another object of this invention to provide a process for the migration of nicotine from one tobacco substrate (leaf material or reconstituted leaf) to a second tobacco substrate (leaf material, reconstituted leaf material or tobacco stems) or to a non-tobacco substrate<sup>46</sup>.

-patent no. 5,018,540 C2:39-43

It can increase the amount of nicotine in cigarettes:

If desired, nicotine can be incorporated into the expansion solvents used to provide a volume expanded processed tobacco material having a high nicotine content<sup>47</sup>.

-patent no. 5,031,646 C5:65-68

The present invention provides a nicotine-enhanced smoking device with a high nicotine release efficiency....Thus, the smoker is provided with more nicotine from the nicotine-enhanced device than from a similar smoking device which does not contain the nicotine solution or from a comparable cigarette<sup>48</sup>.

-patent no. 4,676,259 C2:30-33, 53-56

The present invention is concerned with the application of additives, such as... physiologically active agents such as nicotine components to the smoking rod, in order to improve or help to improve the satisfaction provided to the smoker<sup>49</sup>.

-patent no. 4,236,532 C1:35-40

It can add nicotine to any part of the cigarette:

The salts [nicotine levulinate] can be incorporated into the smoking article in a variety of places or sites. For example, the salt can be applied to the filler material,

incorporated within some or all of the filler material, applied to the wrapper of the tobacco rod, applied within the glue line of the wrapper of the tobacco rod, applied within a region (e.g., a cavity)....<sup>30</sup>

-patent no. 4,830,028 C5:59-65

It can use a variety of methods to add nicotine to tobacco:

...[T]he additive [nicotine levulinate] can be applied using syringes or techniques such as spraying, electrostatic deposition, impregnation, garniture injection, spray drying, inclusion and encapsulation technologies, and the like.<sup>31</sup>

-patent no. 4,830,028 C6:4-7

Let me describe in some detail how some of the technologies can be used to increase or control the nicotine level of tobacco.

The industry had to tackle a new problem beginning in the 1960s as public concern about the health consequences of smoking intensified. The industry began to market cigarettes it described as low yield. It faced a major challenge, however, because in the words of patent no. 4,830,028, "the perceived taste or strength of the cigarettes classified as having lower levels of 'tar' and nicotine are progressively less than that of the cigarettes which are classified as approaching the characteristics of the "full flavor" cigarettes."

The patent then describes a way to add nicotine to the "low yield" cigarettes. If nicotine alone is sprayed on a blend of tobacco, the patent states that the smoke that results will be unacceptably harsh or irritating to the user. So, instead of just spraying nicotine on the tobacco blend, the patent combines nicotine with another compound, an organic acid called levulinic acid, to form a salt that masks the irritating qualities of



nicotine. (Chart G and H) The patent demonstrates that different percentages of the nicotine salt can be added to blends of tobacco to produce different nicotine concentrations. The control cigarette, the one without any added nicotine, contains 1.66 percent nicotine. Adding one percent nicotine salt results in a cigarette with 2.05 percent nicotine. As one increases the amount of nicotine salt sprayed on the tobacco blend, the nicotine content of the tobacco increases.

In this process, great care is paid to the pH of the smoke because pH affects the bioavailability of nicotine -- that is, how much the body absorbs. The patent demonstrates the technology to increase nicotine content in tobacco by up to 76 percent.

U.S. patent no. 5,065,775 (Chart I) describes another technology that can control the nicotine content of tobacco filler. This involves a process for "modifying the alkaloid content of a tobacco material and, in particular, for providing a processed tobacco material having a controlled nicotine content." (C2:57-60) In the words of the patent "[t]he process of the present invention provides a skilled artisan with an efficient and effective method for changing the character of a tobacco material (e.g., rearranging components of a tobacco material or altering the chemical nature or composition of a tobacco material) in a controlled manner. That is, the process...can be employed in a way such that changes in the chemical composition of tobacco can be monitored as to occur to a desired degree."

(C3:55-63)

The patent allows for the removal of selected substances from tobacco, and incorporating controlled amounts of substances into tobacco. Example 4 within this patent shows how a tobacco blend that starts off with a 2.3 percent nicotine content can end up with a 5.2 percent nicotine content. A highly concentrated nicotine solution is created by subjecting a tobacco blend to a series of chemical steps, including adding water, removing solids, increasing the pH, and mixing this substance with chlorofluorocarbon (CFC) 11 and then evaporating off that CFC 11. This concentrate is then added to water-washed tobacco to increase its nicotine content. This patent demonstrates the technology to increase the nicotine content in tobacco by more than 100 percent.

A third example of sophisticated technology involves the direct transfer of nicotine from one type of tobacco to another type of tobacco. (Chart J) U.S. patent no. 4,898,188 utilizes supercritical fluid extraction. In example 2 in the patent, liquid carbon dioxide is used to transfer nicotine from Burley cut tobacco filler to flue-cured cut tobacco. The flue-cured cut filler starts off with a nicotine content of 2.59 percent and ends up with a nicotine content of 4.83 percent. The Burley cut filler starts off with a nicotine content of 3.56 percent and ends with a nicotine content of 0.88 percent. This patent demonstrates that nicotine can be transferred in significant amounts from one type of tobacco filler to another.

Additional information about the ability to set nicotine content at varying levels comes from the following ad, headlined "More Nicotine or Less," which appeared in an international tobacco trade publication: (Chart K)

Nicotine levels are becoming a growing concern to the designers of modern cigarettes, particularly those with lower "tar" deliveries. The Kimberly-Clark tobacco reconstitution process used by LTR INDUSTRIES permits adjustments of nicotine to your exact requirements. These adjustments will not affect the other important properties of customized reconstituted tobacco produced at LTR Industries: low tar delivery, high filling power, high yield, and the flexibility to convey organoleptic modifications. We can help you control your tobacco.

In fact the process described in this advertisement can raise the level of nicotine beyond what is naturally found in tobacco materials, especially the stems and scraps. A 1985 tobacco journal article describing the LTR process states

Though standard reconstituted tobacco products contain 0.7 - 1.0 percent nicotine, LTR Industries offers the possibility of increasing the nicotine content of the final sheet to a maximum of 3.5 percent...

A dramatic increase in tobacco taste and smoke body is noted in the nicotine-fortified reconstituted tobacco.<sup>52</sup>

All of this apparent technology for manipulating nicotine in tobacco products raises the question of how the industry determines how much nicotine should be in various products. More importantly, since the technology apparently exists to reduce nicotine in cigarettes to insignificant levels,<sup>53</sup> <sup>54</sup> why, one is led to ask, does the industry keep nicotine in cigarettes at all?

The tobacco industry would like you to believe that all it is doing is returning the nicotine that is removed during the process of producing reconstituted tobacco. It should be clear from what I have described thus far that the technology the industry may have available goes beyond such modest efforts.

The industry may also tell you that it is adjusting nicotine levels to be consistent with established "FTC yields" -- these are the amounts of tar, nicotine, and carbon monoxide that are measured for each cigarette product by smoking machines, and disclosed under a voluntary agreement with the Federal Trade Commission. In fact, the control of nicotine levels in cigarettes, dating back at least to patents granted in 1966 for adjusting nicotine levels, preceded the first rules adopted by the FTC on disclosing tar and nicotine yields. Moreover, there is nothing about the FTC yields that would require tobacco companies to increase nicotine in low tar cigarettes, as the industry patents suggest they do. There are no FTC restrictions on nicotine levels, and the FTC guidelines take into account crop variability by sampling completed cigarettes from 50 retail outlets across the country. Indeed, there is no FTC restriction that would prevent the industry from reducing nicotine below addicting levels or eliminating it altogether.

In fact, the technology reflected in the cigarette industry's patents appears to be intended to allow the industry to set the nicotine content of tobacco products at defined levels that have little to do with either the amount of nicotine that

was removed during the processing of the tobacco, or with the simple goal of maintaining consistency with established FTC yields. The technology may exist to allow the industry to set nicotine levels wherever it want, or, in fact to remove nicotine entirely. With all the apparent advances in technology, why do the nicotine levels found in the vast majority of cigarettes remain at addictive levels?

Nicotine levels may be dictated in part by marketing strategies and demographics. A blatant example comes from information on the marketing of smokeless tobacco. There is evidence that smokeless tobacco products with lower amounts of nicotine are marketed as "starter" products for new users, and that advertising is used to encourage users to "graduate" to products with higher levels of nicotine. (Chart L) The evidence was developed in lawsuits brought against one manufacturer of smokeless tobacco.

The tobacco industry may tell you that nicotine is important in cigarettes solely for "flavor." There is a great deal of information that suggests otherwise. Some of the patents specifically distinguish nicotine from flavorants.<sup>55</sup> An RJR book on flavoring tobacco, while listing around a thousand flavorants, fails to list nicotine as a flavoring agent.<sup>56</sup> Even research scientists from the same company acknowledge that the nicotine in cigarettes provides pharmacological and psychological effects to smokers in addition to any mere sensory effects<sup>57</sup>.

Moreover, the available information shows that the industry

has gone to significant lengths to develop technologies to mask the flavor of increased levels in cigarettes. As I have already noted, the industry's own patents reveal that increasing nicotine in fact usually produces an unacceptably harsh and irritating product, and that the industry has had to take special steps to mask the flavor of increased nicotine in low tar cigarettes.

This should not come as a surprise. The Merck Index, the authoritative encyclopedia of chemicals, describes nicotine as having "an acrid, burning taste." Webster's 7th New Collegiate Dictionary defines acrid as "sharp and harsh or unpleasantly pungent in taste or odor; irritating, corrosive." In fact, U.S. patent 4,620,554 uses the word "hazardous" to describe the taste of nicotine.

What appears to be true is that smokers become accustomed to, and associate, the sensory impact of nicotine (burning in the throat) with the resulting psychoactive effects of nicotine, and thus look for those sensory signals in a cigarette; this is called "conditioned reinforcement."<sup>58</sup>

Moreover, if nicotine is just another flavorant in tobacco, why not use a substitute ingredient with comparable flavor, but without the addictive potential? For example, it has been repeatedly shown that substitute ingredients, such as hot pepper (capsaicin)<sup>59</sup> and citric acid<sup>60</sup>, have similar irritating sensory effects.

### Similarities to the Pharmaceutical Industry

Mr. Chairman, this kind of sophistication in setting levels of a physiologically active substance suggests that what we are seeing in the cigarette industry more and more resembles the actions of a pharmaceutical manufacturer. Besides controlling the amount of a physiologically active ingredient, there are a number of other similarities.

One similarity between the cigarette industry and the pharmaceutical industry is the focus on bioavailability. Bioavailability is the rate and extent that pharmacologically active substances get into the bloodstream. For example, the pH of tobacco smoke affects the bioavailability of nicotine<sup>61</sup>. The tobacco industry has conducted research on the pH of smoke<sup>62</sup> and has undertaken to control the pH in tobacco smoke. In patent examples, chemicals have been added to tobacco to affect the pH of tobacco smoke<sup>63</sup>. The industry has even performed bioavailability and pharmacokinetic studies on conventional and novel cigarettes<sup>64</sup>.

The cigarette industry has undertaken research to look at the specific activity of added versus naturally occurring nicotine<sup>65</sup>. Additional research looked at the differences between spiking, spraying and blending compounds into cigarettes<sup>66</sup>.

Development of an "express" cigarette, a shorter, faster burning cigarette with the same amount of tar and nicotine, has been reported in the lay press recently. This is another example

of how cigarette companies appear to be controlling the amounts of nicotine to deliver set levels<sup>67</sup>.

The cigarette industry has also undertaken a significant amount of research looking at the potential "beneficial" effects of nicotine. It has studied the effects of nicotine on anxiety, heart rate, electroencephalographs (EEG's), and behavioral performance tasks. Such research on the physiological effects of an active ingredient is a common part of pharmaceutical drug development<sup>68, 69, 70, 71, 72, 73, 74, 75</sup>.

Perhaps the most striking aspect of the research undertaken by the tobacco industry is its search for, and its patenting of, new nicotine-like chemicals that exhibit pharmacological properties which, in their own words, "are indicated for utility as potential psychotherapeutic agents"<sup>76</sup>. One patent describes nicotine-like chemicals which

exhibit tranquilizing and muscle-relaxing properties when administered to mammals. The nicotine analogs do not exhibit nicotine-like properties, such as tachycardia, hypertension, gastrointestinal effects, emesis in dogs, and the like.

Example XXIX in the patent

illustrates the pharmacological properties of nicotine analogs....

The tranquilizing effects of invention nicotine compounds are measured after intraperitoneal (IP) and intraventricular (IVC) administration in the form of hydrochloride salts.

Sedation is determined by measuring locomotion in an open field maze, and the response to noxious (air blast) stimuli. Body tone is estimated by handling rats and by the ability to hang from a rotating rod.

Tranquilization after intraventricular (IVC injection) is estimated from muscle weakness in all four limbs, body tone and general activity".



Chart M illustrates the results.

### The Problem of the Low-yield Cigarette

We, at the Food and Drug Administration, are concerned not only about the control over nicotine levels exercised by the cigarette industry, we are also concerned that the problems associated with nicotine are aggravated by significant limitations in consumer's ability to reduce their exposure to nicotine by selecting "low" nicotine cigarettes.

Most people who smoke low yield or "light" cigarettes believe that they are getting less nicotine and tar by smoking these cigarettes. For the last 25 years the American public has relied on FTC ratings of tar and nicotine in advertising to tell them what they will be consuming. The "FTC method" utilizes a machine that tests cigarettes in a process involving a two-second, 35 milliliter puff each minute until a predetermined butt length is reached<sup>78</sup>.

Most people don't realize that low yield cigarettes, as determined by the FTC method, do not usually result in proportionally less nicotine being absorbed when compared to high yield cigarettes<sup>79</sup>. Furthermore, there is little correlation between low yield FTC ratings and the total amount of nicotine in cigarettes<sup>80</sup>.

It is a myth that people who smoke low nicotine cigarettes are necessarily going to get less nicotine than people who smoke high nicotine cigarettes. There are several reasons for this.

One reason is that there are differences between the smoking habits of a machine and a human. The way in which a cigarette is smoked is probably the most important determinant of how much tar and nicotine is inhaled. Humans can compensate -- and do compensate -- when smoking low yield cigarettes, by altering puff volume, puff duration, inhalation frequency, depth of inhalation, and the number of cigarettes smoked<sup>81, 82, 83, 84, 85, 86, 87</sup>. As a result of these compensatory mechanisms, a low yield cigarette can actually result in a relatively high intake of nicotine<sup>88</sup>.

Beyond the human compensatory mechanisms, several other factors under manufacturers' control contribute to a lowering of machine ratings. These factors include the positioning of ventilation holes, how fast the cigarette paper burns, and the length of the filter paper overwrap<sup>91</sup>.

To understand how the position of ventilation holes in a cigarette can confound the FTC ratings, it is important to recognize that the main determinants of whether a cigarette has a high or low yield in machine testing are the cigarette's ventilation and burning characteristics<sup>89</sup>. Most low yield cigarettes achieve their low ratings because of filter characteristics and also because the smoke is diluted with air. The air dilution is accomplished in part by placing ventilation holes in the filter. What scientists have demonstrated is that "although smoking machines which measure tar and nicotine do not occlude the perforations," 32-69 percent of low tar smokers have blocked the holes with their fingers or lips, resulting in larger

nicotine yields<sup>90</sup>. The ventilation holes are sometimes laser generated and can be hard for the smoker to see. Not all smokers are aware of the existence of these holes or that the smoker may be blocking them. (Chart N)

Two other factors that are under manufacturers' control can also confound the usefulness of the FTC ratings. The FTC method smokes a cigarette down to within 3 millimeters of the tipping paper overwrap. According to one study, "between 1967 and 1978, 18 brands of filter cigarettes underwent increases in overwrap width that reduced the amount of tobacco smoked in the cigarettes on the machine, even though the remaining tobacco is still smokeable<sup>91</sup>." (Chart O) Another way that the FTC numbers can be confounded is by "increasing the rate at which cigarettes burn." A faster burning cigarette lowers the puff count. Manufacturers can increase the rate at which a cigarette burns by controlling the porosity of the cigarette paper. The machine takes a puff every minute, but humans can adjust their smoking rate<sup>91</sup>.

Because of all these confounding factors we are concerned that consumers may assume that low yield cigarettes in fact deliver low tar and nicotine when in reality they do not.

#### Actual Nicotine Levels in Cigarettes

To assess the levels of nicotine in cigarettes, we did two things. First, FDA laboratories measured the amount of nicotine actually in several types of cigarettes. We analyzed three varieties of one brand family of cigarettes; one that is regular,

one that is low tar, and one that is ultra low. What surprised us was that the variety advertised as having the lowest yield in fact had the highest concentration of nicotine in the cigarette. (Chart P)

Second, we formally requested from our colleagues at the Federal Trade Commission summary information derived from their data base on the levels of nicotine in cigarettes. What we found was that since 1982 (the earliest year for which the computer data base is available), the sales weighted levels of FTC nicotine in cigarettes appear to increase. (Charts Q,R,S, and T) What was equally striking was that when we segmented sales into high tar, low tar, and ultra low tar cigarettes, the nicotine/tar ratio was higher in the ultra low tar group. (Chart U) We would not have expected to see these differences because high tar has usually been associated with high nicotine, low tar has usually been associated with low nicotine. It has often been said that tar and nicotine travel together in the cigarette smoke. The disparities in the nicotine/tar ratios among these varieties raise the question as to how this can occur.

### III. FDA REGULATION OF NICOTINE IN CIGARETTES

The next task facing the FDA is to determine whether nicotine-containing cigarettes are "drugs" within the meaning of the Federal Food, Drug, and Cosmetic Act.

Our inquiry is necessarily shaped by the definition of "drug" in the Act. It is a definition that focuses on "vendor

intent." More specifically, it focuses primarily on whether the vendor intends the product to, "affect the structure or any function of the body."

Mr. Chairman, the evidence we have presented today suggests that cigarette manufacturers may intend that most smokers buy cigarettes to satisfy their nicotine addiction.

We do not yet have all the evidence necessary to establish cigarette manufacturers' intent. It should be clear, however, that in determining intent what cigarette manufacturers say can be less important than what they do. The fact that the technology may be available to reduce the nicotine to less than addictive levels is relevant in determining manufacturer intent.

It is important to note that the possibility of FDA exerting jurisdiction over cigarettes raises many broader public health and social issues for Congress to contemplate. There is the possibility that regulation of the nicotine in cigarettes as drugs would result in the removal of nicotine-containing cigarettes from the market, limiting the amount of nicotine in cigarettes to levels that are not addictive, or otherwise restricting access to them, unless the industry could show that nicotine containing cigarettes are safe and effective. If nicotine were removed, the nation would face a host of issues involving the withdrawal from addiction that would be experienced by millions of Americans who smoke.

There is, of course, the issue of black market cigarettes. With nicotine, as with other powerfully addicting substances, a

black market could develop.

In these issues, we seek guidance from Congress.

The one thing that I think is certain is that it is time for all of us -- for the FDA, for the Congress, for the American public -- to learn more about the way cigarettes are designed today and the results of the tobacco industry's own research on the addictive properties of nicotine.

Thank you.

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# Criteria for Drug Dependence

## Primary Criteria

- highly controlled or compulsive use
- psychoactive effects
- drug-reinforced behavior

## Additional Criteria

### *Addictive behavior often involves:*

- stereotypic patterns of use
- use despite harmful effects
- relapse following abstinence
- recurrent drug cravings

### *Dependence-producing drugs often produce:*

- tolerance
- physical dependence
- pleasant (euphoric) effects

**(Source: U.S. Surgeon General's Report, 1988)**

## Increase Nicotine Content by Adding Nicotine to Tobacco Rod

PATENT # DATE	DESCRIPTION	ASSIGNEE
3,109,436 11/05/63	Increase nicotine content of smoke tobacco by adding a composition of nicotine-ion exchange resin directly to tobacco.	Abraham Bavley and Frank E. Resnik
4,215,706 8/05/80	Process to transfer nicotine from a tobacco source to a nicotine-deficient tobacco, reconstituted tobacco or tobacco filler material.	Loew's Theatres, Inc.
4,830,028 5/16/89	Increase nicotine content of smoke by adding nicotine and an organic acid (nicotine levulinate salt) to the cigarette.	R.J. Reynolds Tobacco Company
4,836,224 6/06/89	Make high nicotine smoke less harsh by adding an organic acid additive to tobacco.	R.J. Reynolds Tobacco Company
5,031,646 7/16/91	Make high nicotine smoke less harsh by adding an organic acid additive to tobacco.	R.J. Reynolds Tobacco Company
3,861,400 1/21/75	Increase nicotine content of smoke by adding complexes of nicotine and galacturonic acid or polymannuronic acid to tobacco	Imperial Tobacco Group Limited
4,715,389 12/29/87	Lowers ratio of particulate matter to nicotine in smoke using internal heat sinks and special nicotine-containing adsorbent.	R.J. Reynolds Tobacco Company
4,595,024 6/17/86	Segmented cigarette that delivers a larger amount of nicotine in the first few puffs of the cigarette than in the last few puffs.	R.J. Reynolds Tobacco Company

## Increase Nicotine Content by Adding Nicotine to Filters, Wrappers, etc.

PATENT # DATE	DESCRIPTION	ASSIGNEE
3,280,823 10/25/66	Increase nicotine content in the tobacco smoke by use of a nicotine-ion exchange placed in the filter.	Phillip Morris Incorporated
3,584,630 6/15/71	Increase nicotine content in the smoke of a tobacco product by adding nicotine to carbon black in filter.	Phillip Morris Incorporated
5,105,834 4/21/92	Add tobacco extract containing nicotine to the filter of cigarettes.	R.J. Reynolds Tobacco Company
4,676,259 6/30/87	Device to deliver increased nicotine by applying nicotine solution to the filter.	Advanced Tobacco Products Inc.
4,236,532 12/02/80	Method of producing a wrapper for a smoking rod which has screen printed on it, among other things, a "physiologically active agent" such as nicotine.	Gallaher Limited



## Highly Selective Manipulation of Nicotine

PATENT # DATE	DESCRIPTION	ASSIGNEE
0,280,817 1989	Supercritical extraction process using CO <sub>2</sub> and/or water to move nicotine from tobacco leaf or reconstituted tobacco to different leaves or reconstituted tobacco, thereby selectively increasing or decreasing nicotine content.	Philip Morris Incorporated
4,898,188 2/06/90	Supercritical extraction of nicotine and other flavors from tobacco. Extracted materials can be transferred to other products.	R.J. Reynolds Tobacco Company
5,018,540 5/28/91	Supercritical extraction of nicotine from tobacco and process for migration of nicotine from one tobacco substrate to another substrate.	Philip Morris Incorporated

# Extraction of Nicotine

PATENT # DATE	DESCRIPTION	ASSIGNEE
3,046,997 7/31/62	Method of removing nicotine from tobacco using organic solvent.	Philip Morris Incorporated
4,068,671 1/17/78	Denicotinize tobacco by rapid drying of an alkaline aqueous dispersion of tobacco.	AMF Incorporated
4,557,280 12/10/85	Reduces nicotine and nitrate content of tobacco by use of microorganisms to produce mild smoke.	Brown & Williamson Tobacco Corporation
3,139,435 6/30/64	Method of extracting nicotine from tobacco.	Philip Morris Incorporated
4,150,677 4/24/79	Distillation of nicotine and flavorants from tobacco by hot gas extraction to make a flavor that enhances the organoleptic properties of smoke.	Philip Morris Incorporated
5,065,775 11/19/91	Process to provide a "denicotinized" tobacco extract and remove nicotine from tobacco.	R.J. Reynolds Tobacco Company
4,967,771 11/6/90	Process for providing tobacco extracts having certain components removed.	R.J. Reynolds Tobacco Company
5,018,540 5/28/91	Process for the selective removal of basic materials from plant products, in particular, for removing nicotine from tobacco without materially affecting the other components of tobacco.	Philip Morris Incorporated

## Development of New Nicotine-Like Molecules

PATENT # DATE	DESCRIPTION	ASSIGNEE
5,138,062 8/11/92	Nicotine analogs with tranquilizing effects.	Philip Morris Incorporated
5,015,741 5/14/91	Nicotine analogs exhibiting tranquilizing effects in mammals	Philip Morris Incorporated
4,590,278 5/20/86	Preparation of cotinine and nicotine analogs.	Philip Morris Incorporated
4,155,909 5/22/79	Improved manufacture of 2-alkylnicotinoids.	Philip Morris Incorporated
4,321,387 3/23/82	Preparation of nicotine analogs, particularly, enantiomerically pure nicotine analogs containing alkyl substituents on the pyridine ring at 4, 5, and/or 6 positions.	Philip Morris Incorporated
4,220,781 9/02/80	Improved methods for producing 2-alkyl nicotinoids.	Philip Morris Incorporated
4,442,292 4/10/84	Preparations of cotinine and nicotine analogs.	Philip Morris Incorporated
4,452,984 6/05/84	Preparations of cotinine and nicotine analogs.	Philip Morris Incorporated
4,332,945 6/01/82	Preparations of cotinine and nicotine analogs.	Philip Morris Incorporated

# US Patent 4,830,028

(assignee: R.J. Reynolds Tobacco Company)

	Control 1	Sample 1 1% nicotine salt added	Sample 2 3% nicotine salt added	Sample 3 5% nicotine salt added
<p><b>Burley 9%</b> <b>Flue-cured 41%</b> <b>Reconstituted 32%</b> <b>Oriental 18%</b></p> <p><b>SPRAY ON</b></p> <p><b>L-nicotine levulinate (32% nicotine) as 1:1 with water</b></p> <p><b>BLEND IN</b></p> <p><b>Expanded Burley 75%</b> <b>Expanded Flue-cured 25%</b></p>	1520 g	1520 g	1520 g	1520 g
	0 g	20 g	60 g	100 g
	480 g	480 g	480 g	480 g
<b>Total nicotine</b>	1.66% (12.3 mg)	2.05% (15.2 mg)	2.51% (18.6 mg)	2.91% (21.6 mg)
<b>FTC nicotine</b>	0.38 mg	0.56 mg	0.69 mg	0.81 mg
<b>Smoke pH</b>	5.98	5.88	5.84	5.83
<b>Organoleptic compared to control</b>		Not Reported	"Not Significantly Different"	"Greater impact and smoothness ... less harshness"

**Example 2:**  
Tobacco weight: 0.742 g; Air dilution 50%

# US Patent 4,830,028

(assignee: R.J. Reynolds Tobacco Company)

	Control 2	Sample 4 3% nicotine salt added	Sample 5 7% nicotine salt added	Sample 6 10% nicotine salt added
<p><b>Burley 43%</b> <b>Flue-cured 6%</b> <b>Reconstituted 19%</b> <b>Turkish 32%</b></p> <p><b>SPRAY ON</b></p> <p><b>L-nicotine levulinate (32% nicotine) as 1:1 with water</b></p> <p><b>BLEND IN</b></p> <p><b>Expanded Burley 75%</b> <b>Expanded Flue-cured 25%</b></p>	940 g	940 g	940 g	940 g
	0 g	60 g	140 g	200 g
	1060 g	1060 g	1060 g	1060 g
<b>Total nicotine</b>	2.08% (10.1 mg)	2.64% (12.9 mg)	3.22% (15.7 mg)	3.92% (19.1 mg)
<b>FTC nicotine</b>	0.18 mg	0.29 mg	0.39 mg	0.51 mg
<b>Smoke pH</b>	6.28	6.09	6.03	6.11

Organoleptic compared to control

Not Reported

“Not Significantly Different”

“Greater impact and smoothness ... less harshness”

**Example 3:**

**Tobacco weight:** 0.4875 g; **Air dilution** 75%

**Control 3:** Add nicotine (not as salt) to make total nicotine 3.92% (19.1 mg). Organoleptic “is extremely harsh and is not palatable.”

**Sample 7:** Add nicotine (not as salt) to make total nicotine 4.53% (22.1 mg). Organoleptic “exhibits a smooth smoking character and is palatable.”

**U.S. Patent No. 5,065,775****Example 4****Increases nicotine in a tobacco blend**

**Start with a:** **2.3% Nicotine-Containing Tobacco Blend**

•  
•

**Mix with water**

•  
•

**Collect water**

•  
•

**Adjust pH to 10**

•  
•

**Mix with Chlorofluorohydrocarbon #11**

•  
•

**Evaporate Chlorofluorohydrocarbon #11 and water**

•  
•

**Results in:**

- 1. a liquid containing about 60% nicotine**
- 2. a solid containing about .01% nicotine**

•  
•

**Mix 1+2 with water**

•  
•

**Add to another batch of 2.3%  
nicotine-containing tobacco blend**

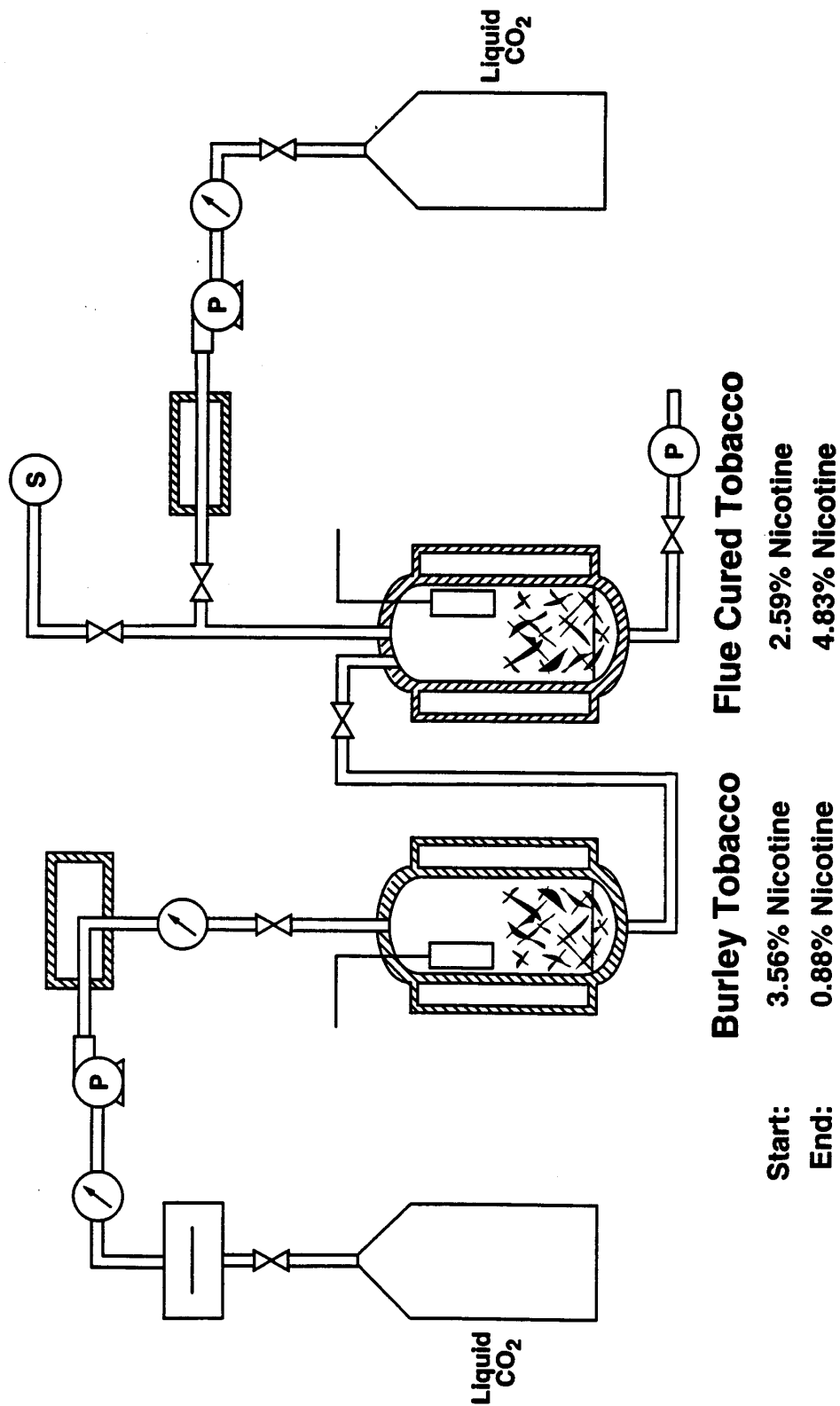
•  
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**End with a:** **5.2% Nicotine-Containing Tobacco Blend**

# US PATENT 4,898,188

## Example 2

### Transfer of Nicotine from One Tobacco to Another





*A likeness of Jean Nicot, French diplomat, after whom "nicotine" and "Nicotiana Tabacum" were named.*

## MORE OR LESS NICOTINE

Nicotine levels are becoming a growing concern to the designers of modern cigarettes, particularly those with lower "tar" deliveries. The Kimberly-Clark tobacco reconstitution process used by LTR INDUSTRIES permits adjustments of nicotine to your exact requirements. These adjustments will not affect the other important properties of customized reconstituted tobacco produced at LTR INDUSTRIES: low tar delivery, high filling power, high yield and the flexibility to convey organoleptic modifications. We can help you control your tobacco.



**INDUSTRIES**

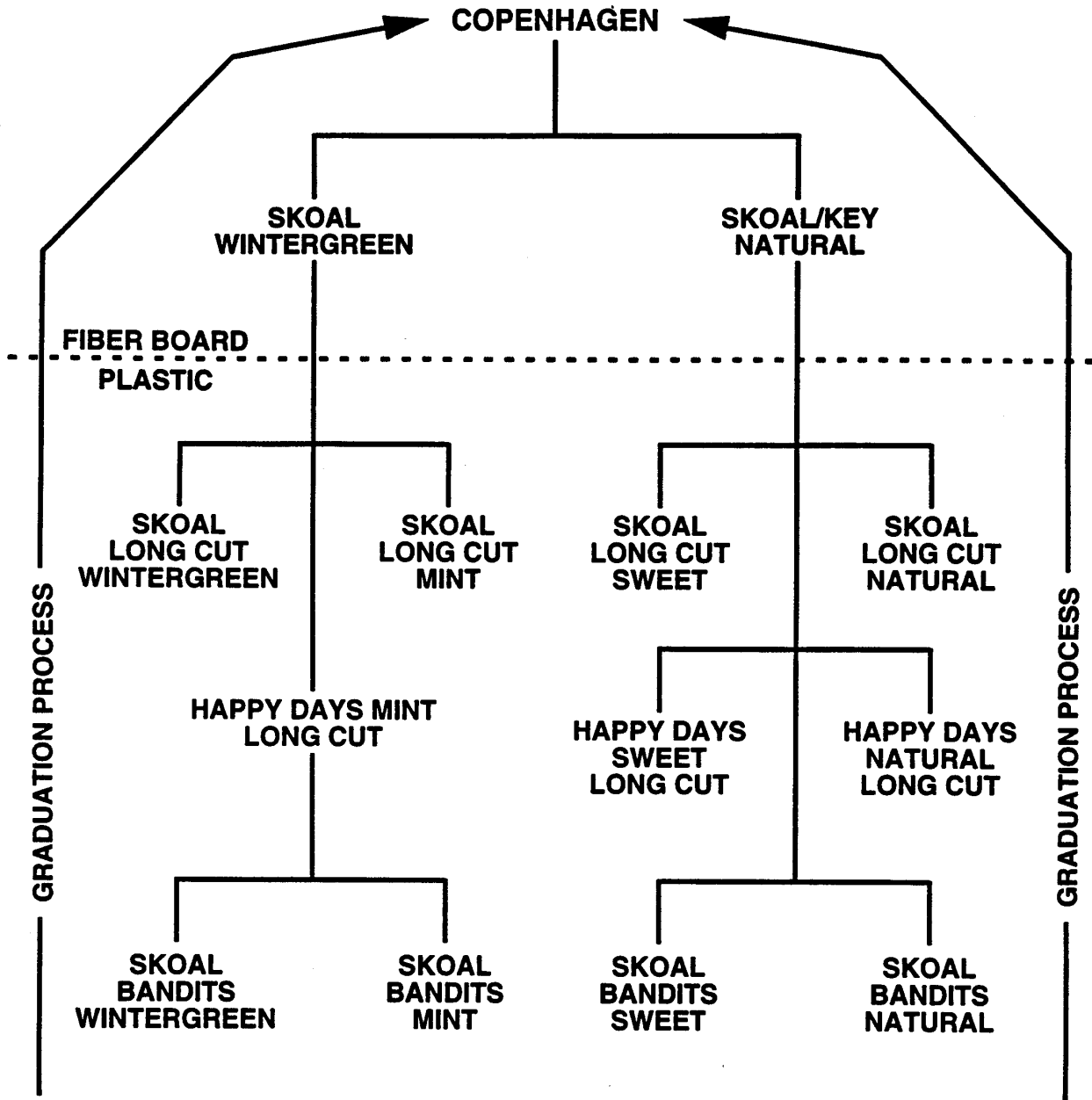
7 AVENUE INGRES, 75016 PARIS, FRANCE  
PHONE (33-1) 4414 32 00 • TELEX 640 314 TABREC F  
TELEFAX (33-1) 44 14 32 49

Get more tobacco from all your tobacco

LTR INDUSTRIES, a subsidiary in France of  
 KIMBERLY-CLARK Corporation



TABLE 1

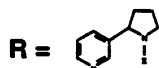


Source: Marsee v. US Tobacco Co., Plaintiff's Exhibit 100 (Provided by Plaintiff's Attorney)

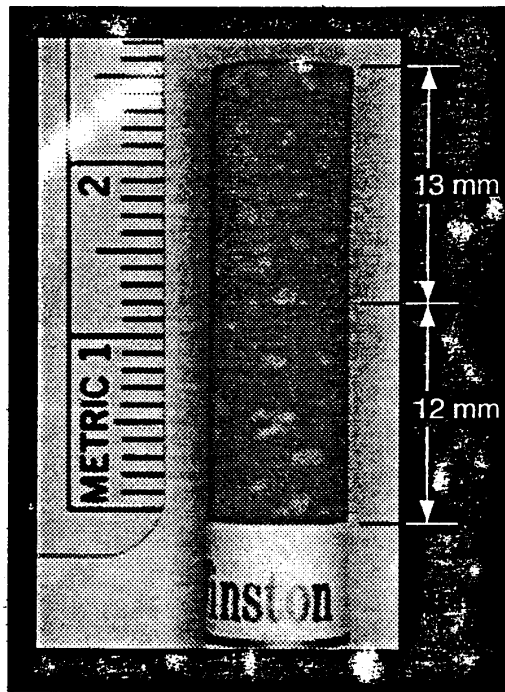
# Psychotherapeutic Agents

(Patent 5,138,062)

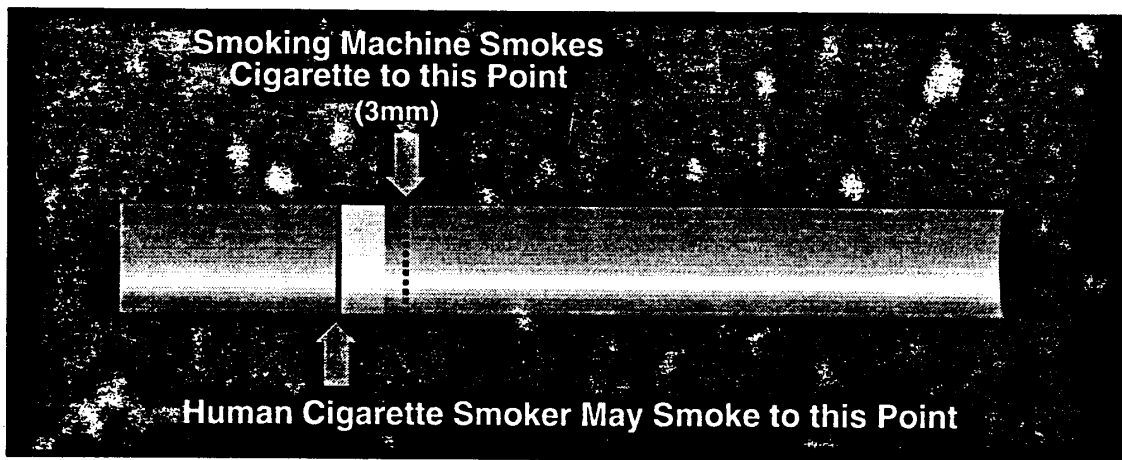
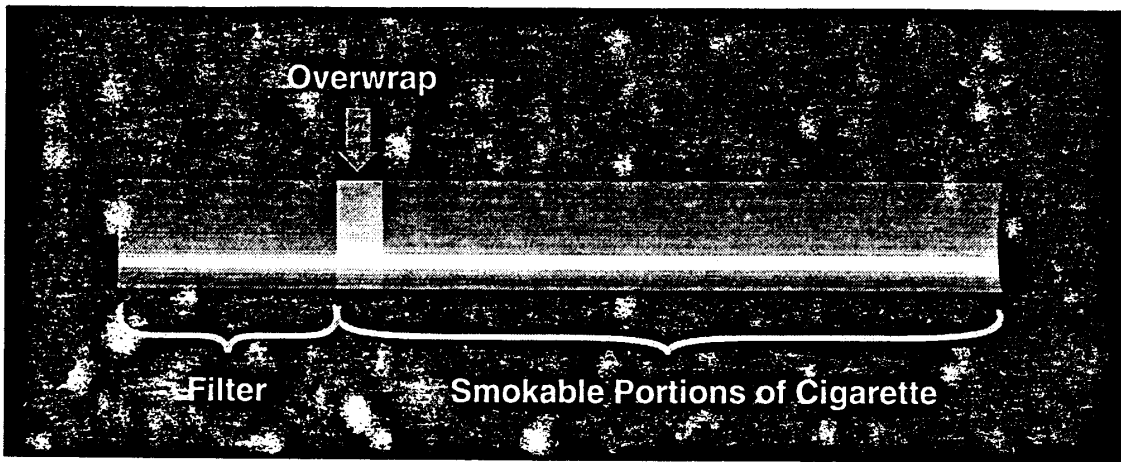
Nicotine Analogues	Dose (IP) mg/kg	Sedation	Body Tone	Tranquilization (IVC) 50 ug
① $R-(CH_2)_2-N(CH_3)_2$	10	+	+	++++
	20	++	++	
② $R-(CH_2)_3-N(CH_3)_2$	5	+	+	++++
	10	++	+	
	20	+++	++	
③ $R-(CH_2)_4-N(CH_3)_2$	10	+	+	+++
	20	+	+	
④ $R-(CH_2)_5-N(CH_3)_2$	40	++	++	+++
⑥ $R-(CH_2)_3-NH_2$	10	0	0	+++
	20	+	0	
⑦ $R-(CH_2)_4-NH_2$	10	0	0	+++
	20	+	0	
⑧ $R-(CH_2)_3-N$ (pyrrolidine)	10	+	0	+++
	20	++	++	
⑨ $R-(CH_2)_3-N$ (piperidine)	10	0	0	++
	20	++	+	
⑩ $R-(CH_2)_2-N$ (piperazine)	10	0	0	+
	20	+	+	
⑪ $R-(CH_2)_2-N(CH_3)-N(CH_3)$ (N,N'-dimethylpiperazine)	20	++	+	++++
	40	+++	++	



(Data from Rats)



# Cross Sectional Diagram of A Filter Cigarette Demonstrating Overwrap

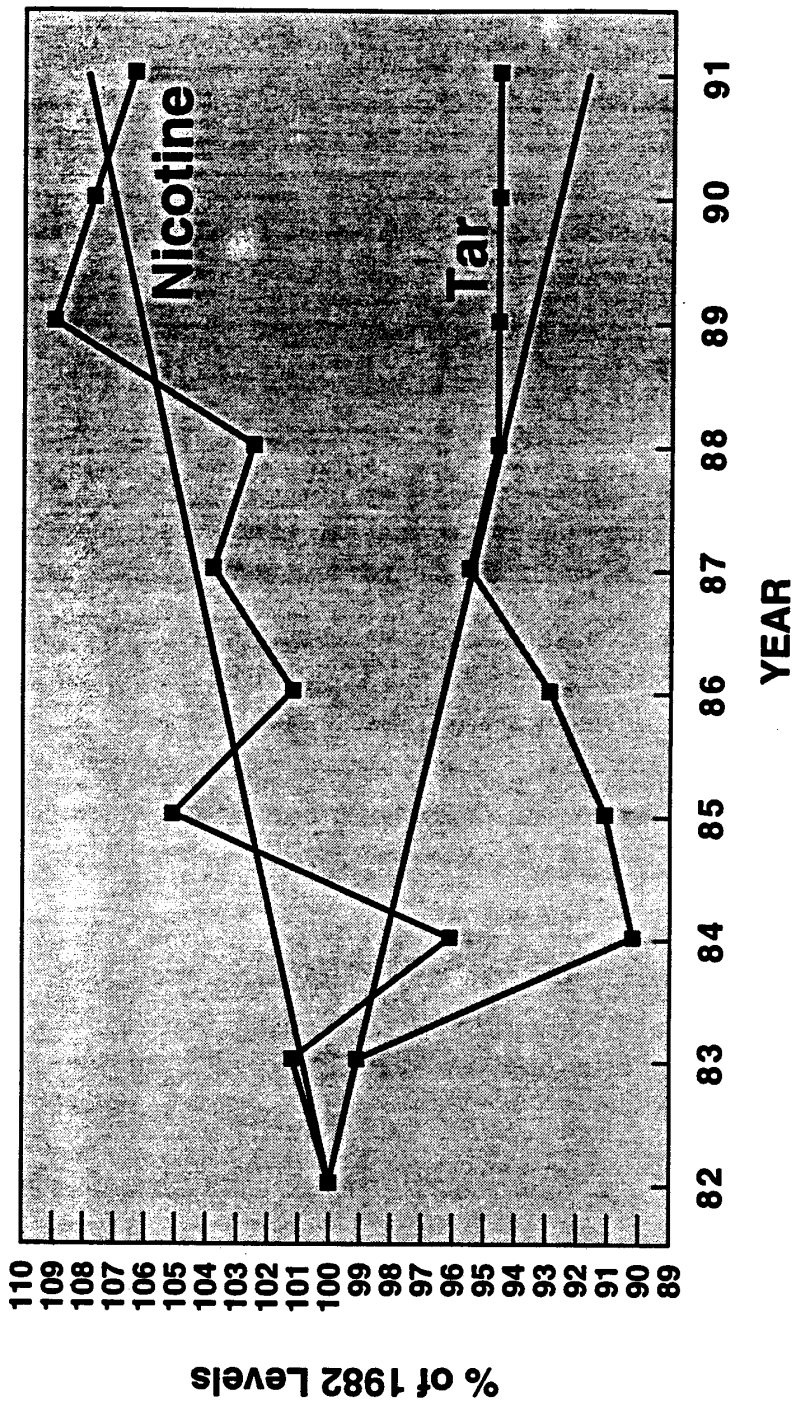


(Source: Grunberg, 1985)

# % Nicotine in One Brand Family

Variety	% Nicotine (mg/grams)
Regular 100's	1.46
Low Tar 100's	1.67
Ultra Low Tar 100's	1.99

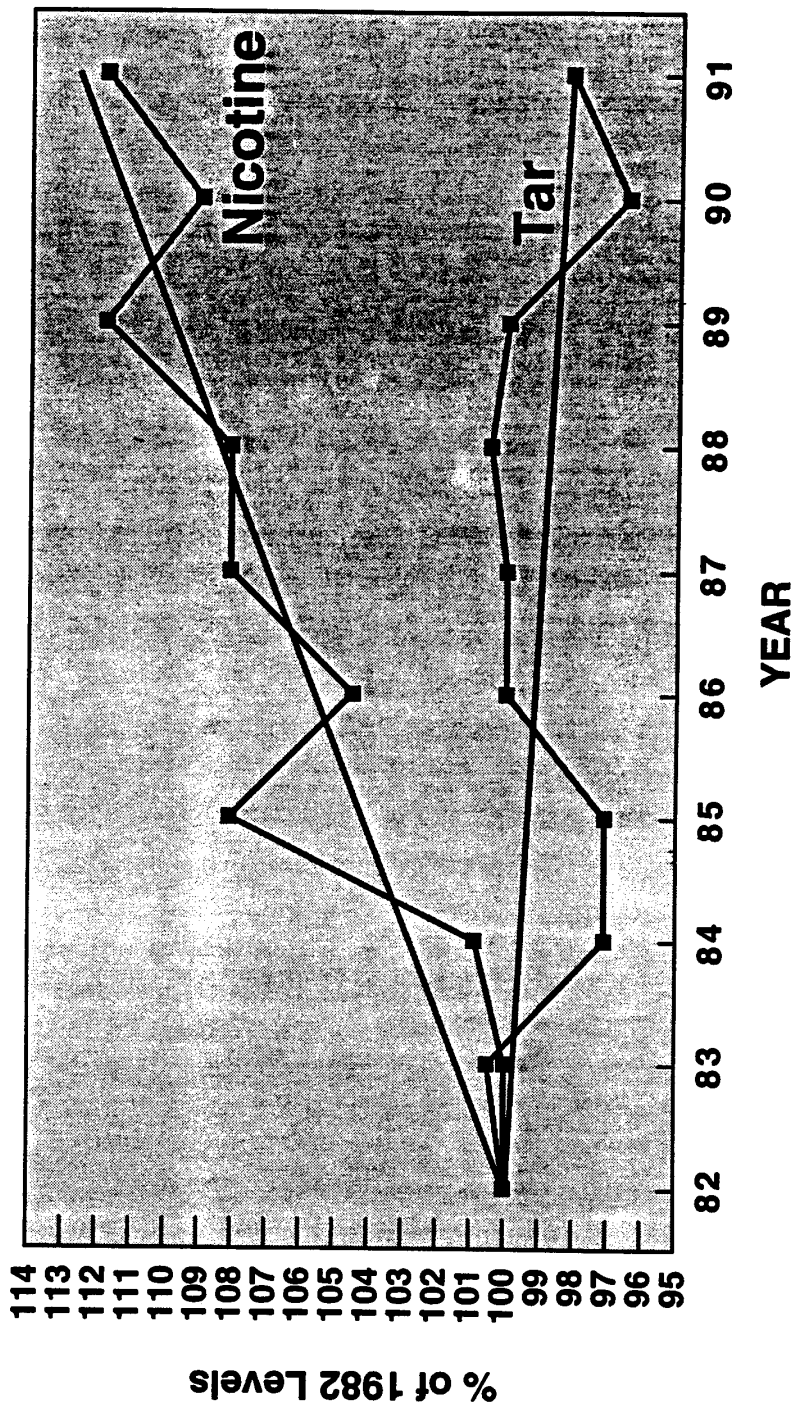
# Sales-Weighted Nicotine and Tar Levels in Smoke As % of 1982 Levels Low Tar Category\*



\*Low Tar Category = 6-15 mg tar  
by FTC method

(Source: FTC Annual Data)

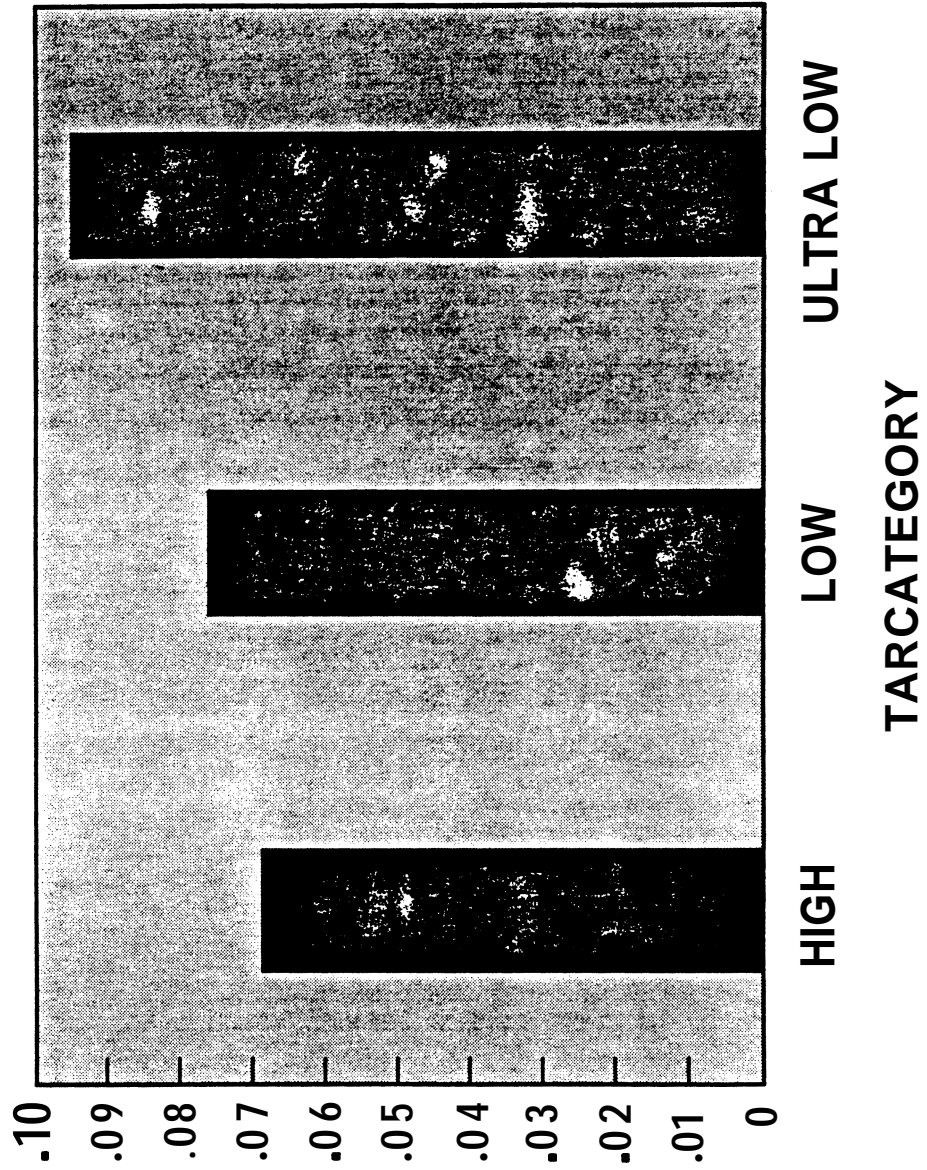
# Sales-Weighted Nicotine and Tar Levels in Smoke As % of 1982 Levels High Tar Category\*



\*High Tar Category = greater than 15 mg tar by FTC method

(Source: FTC Annual Data)

# Sales-Weighted Nicotine/Tar Ratios 10 Year Average 1982-1991



(Source: FTC Annual Data Weighted by Sales)