The SECRET and SOUL of Marlboro

Phillip Morris and the Origins, Spread, and Denial of Nicotine Freebasing

| Terrell Stevenson, BA, and Robert N. Proctor, PhD

Philip Morris and other tobacco companies have been using ammonia in their manufacturing for more than half a century, and for a variety of purposes: to highlight certain flavors, to expand or "puff up" the volume of tobacco, to prepare reconstituted tobacco sheet ("recon"), to denicotinize (reduce the amount of nicotine in) tobacco, and to remove carcinogens.

By the early 1960s, however, Philip Morris had also begun using ammonia to "freebase" the nicotine in cigarette smoke, creating low-yield (reduced-tar or -nicotine) cigarettes that still had the nicotine kick necessary to keep customers "satisfied" (i.e., addicted). We show that Philip Morris discovered the virtues of freebasing while analyzing the impact of the ammoniated recon used in Marlboro cigarettes.

We also show how Marlboro's commercial success catalyzed efforts by the rest of the tobacco industry to discover its "secret," eventually identified as ammonia technology, and how Philip Morris later exploited the myriad uses of ammonia (e.g., for flavoring and expanding tobacco volume) to defend itself against charges of manipulating the nicotine deliveries of its cigarettes. (Am J Public Health. 2008;98:1184—1194. doi:10.2105/AJPH.2007.121657)

AMMONIA OCCURS NATURALLY

in cured tobacco leaf, from close to 0% in some varieties up to about 1% (by weight) in the leaves used in some higher-quality cigars. The compound is also commonly used as a tobacco additive, either in its native form as a clear, pungent gas (NH₃, an ingredient in smelling salts) or as an aqueous or solid ammonium salt (NH_4^+) . Although toxic in large doses, ammonia is relatively easy to remove from processed tobacco leaves; the gaseous form is quite volatile, and the salt is easily neutralized by the addition of an acid.² The

tobacco industry has for many years used ammonia as a relatively innocuous additive to augment certain flavors, to economize on costs by expanding or "puffing" the cured leaf, to denicotinize (reduce the amount of nicotine in) tobacco, and even to reduce some of the carcinogens in tobacco smoke.

By the early 1960s, however, Philip Morris scientists had discovered that ammonia could also be used to increase the free nicotine in cigarette smoke, providing a more powerful nicotine kick than the milder low-pH tobaccos traditionally used in Americanblend cigarettes. The discovery seems to have come about by accident, in the course of exploring the properties of the ammoniated tobaccos used in the preparation of reconstituted tobacco sheet ("recon").

This freebased version of Marlboro cigarettes was one of the greatest triumphs in the history of modern drug design and one reason the brand became the world's most popular cigarette. Yet to this day, Philip Morris denies it has ever deliberately freebased tobacco to boost nicotine yields. The company recalls only the many innocuous uses of ammonia-as a "flavorant" or binder required for the manufacture of recon, for example. The industry reminds us that ammonia is naturally found in foods, fertilizers, and the very air we breathe.

We have analyzed internal documents of the tobacco industry to show that Philip Morris discovered ammonia's freebasing ability while attempting to understand

the impact of the ammoniated tobacco sheet used in its Marlboro cigarettes. The archival record shows that ammonia technology eventually spread throughout the industry, but only after diligent efforts to reverse engineer the chemistry of Marlboros to discover their "secret." Philip Morris later exploited the alternate uses of ammonia-in flavoring, expanding, reconstituting, and denicotinizing tobacco-to defend itself against charges of having manipulated the nicotine in cigarettes. The tobacco industry is notorious for having manipulated science; it is now in the process of renarrating the history of science to defend itself against charges of having deliberately taken paths that led to massive death and disease.3

THE OMNIPRESENT ADDITIVE

Ammonia's capacity to improve tobacco smoke flavor has been recognized at least since the early 1950s, when Claude E. Teague Jr, an RJ Reynolds chemist who later became the company's director of research, found that ammonia gave smoke a richer, smoother, "chocolate-like" taste reminiscent of a burley blend, the most alkaline of the common varieties of tobacco leaf.4 Philip Morris scientists also recognized this relationship between alkalinity and burley's rich taste, and in the late 1950s and early 1960s began using a range of bases, including ammonia, diammonium phosphate (DAP), and various ethanolamines and carbonates to "improve smoke flavor."5

In these early years, tobacco manufacturers were not sure why ammonia—most often regarded as an irritant—improved the taste of tobacco smoke. They eventually came to understand that there was a threshold level beyond which further additions of the compound would no longer improve flavor. In 1971, Philip Morris experimented on competitors' brands and found that ammonia added at 0.25% concentration created a taste that was "milder, more aromatic, sweeter, less harsh, and more like a Marlboro," whereas ammonia added at 0.50% concentration created an "off taste." RJ Reynolds scientists later hypothesized that ammonia might improve tobacco smoke flavor by reacting with sugars to produce heterocyclic ring compounds known as pyrazines. Because pyrazines were already known for their vibrant flavors, RJ Reynolds scientists hypothesized (in documents marked "secret") that amino-sugars such as pyrazines might be the key to ammonia's ability to improve tobacco.⁷

Ammonia has also been used in a number of cost-saving processes, including the production of expanded or "puffed" tobacco. Increasing tobacco's volume was a priority in the 1970s, when tobacco companies first recognized that expanding a given volume of tobacco could increase its "filling power," thereby reducing the mass of leaf required to fill a cigarette of some fixed length and circumference. The reduced mass of tobacco per cigarette encouraged customers to smoke more to get their desired amount of "satisfaction," the industry's euphemism for nicotine.

There are a number of ways to expand tobacco. The most common today is the dry ice expanded tobacco (DIET) process, which uses carbon dioxide (CO₂) in solid form to freeze-dry and "puff up" the tobacco. In 1973, however, Philip Morris patented a puffing procedure that used ammonia in conjunction with CO₂.

The cured leaf was treated with dry ice and ammonia—in liquid or gaseous form, as a hydroxide with CO₂ or as a carbonate or bicarbonate—followed by applications of heat.⁸ This method was soon discontinued in favor of the DIET process,⁹ apparently because of cost concerns. According to confidential Philip Morris records, it took 143 pounds of ammonia to make 2000 pounds of expanded tobacco¹⁰; dry-ice methods, by contrast, were relatively cheap.

Reconstituted tobacco has been a more enduring use of ammonia. Essentially a paper-making process, recon was developed in the 1930s and 1940s as part of an

This freebased version of Marlboro cigarettes was one of the greatest triumphs in the history of modern drug design and one reason the brand became the world's most popular cigarette. Yet to this day, Philip Morris denies it has ever deliberately freebased tobacco to boost nicotine yields.

effort to salvage more of the tobacco leaf, including the stems or mid-ribs formerly thrown away as waste. To make these waste parts smokable, however, and to increase sheet strength, required the addition of a substance "to release the pectins in tobacco stems so they may form a gel which becomes the binder in the blended leaf sheet."11 In the 1950s Philip Morris had begun exploring the use of diammonium phosphate (DAP) in recon and found it to be a successful pectin releaser and a potent flavor enhancer, masking the unpleasant taste of stem. 12 The company set up its first pilot plant for ammoniating tobacco (with DAP) in 1961, and 6 years later patented the "diammonium phosphateblended leaf" (DAP-BL) process after realizing diammonium

phosphate's ability to increase free nicotine "delivery" in cigarettes. 13 The patent, interestingly, contains nothing about DAP's ability to freebase nicotine, citing only its importance as a pectin releaser.14

The tobacco industry also uses ammonia to remove nicotine from tobacco. The procedure is simple: Tobacco leaves are exposed to gaseous ammonia, which replaces nicotine in the salts that bind the alkaloid to the leaf. The ammonia and resulting nicotine are then removed by steam. This method of nicotine reduction gives tobacco manufacturers a degree of control over the amount of nicotine in a given tobacco blend.15

CANCER PREVENTION?

In the 1990s, Philip Morris and the other tobacco companies often mentioned these relatively innocuous uses of ammonia-in flavoring, expanding, and denicotinizing tobacco and in making reconstituted tobacco sheet-when defending themselves against charges of having used ammonia to freebase tobacco. Essentially, their argument was, how could we have done something insidious and underhanded with a molecule like ammonia that is so commonplace, public, and patented for use in so many different kinds of manufacturing processes?16 Typical was a February 24, 1998, letter to the New York Times from Philip Morris's director of external relations that claimed that the company's use of ammonia in cigarette manufacturing "does not increase the amount of nicotine delivered to the smoker, does not increase the amount of nicotine absorbed in the lungs of the smoker, and does not affect the form of nicotine delivered to the smoker's brain."17 The company was responding to a New York

Times exposé on the industry's widespread use of ammonia technology. 18

Prior even to the discovery of ammonia's ability to increase nicotine availability, however, tobacco companies were using the reagent in confidential experiments to reduce carcinogens in cigarettes. Throughout the 1950s and 1960s, industry scientists were researching the idea that certain ammonium salts, such as ammonium sulfamate and ammonium chloride, could reduce the levels of benzpyrene,19 one of the forty carcinogens in cigarette smoke named by Helmut Wakeham, Philip Morris's director of research and development, in 1961.20 This research on reducing benzpyrene was part of Philip Morris's Project 0107, the purpose of which was to develop cigarettes with "less tendency to cause lung cancer in smokers."21 The Celanese Corporation in 1964 patented a tobacco substitute "in which ammonia salts are used to inhibit benz-a-pyrene formation,"22 and in 1967 British American Tobacco researchers reported similar reductions with potassium carbonate.²³

THE "SECRET" (AND **SOUL) OF MARLBORO**

Marlboro began in the 1920s as a women's cigarette. Advertisements called it "mild as May," and it was taken off the market during World War II because of a sales slump. In the mid-1950s, however, with growing public concerns about the link between smoking and lung cancer, Philip Morris decided to reintroduce the brand with a new and improved filter, a flip-top box, and a new masculine image.²⁴ This new version of Marlboro sold surprisingly well, and for an unanticipated reason.

Philip Morris researchers discovered that the reconstituted tobacco they were using to cut costs-the DAP-BL-had some fortunate side effects. Diammonium phosphate, which breaks down into ammonia when a cigarette is burned, improved the flavor of the smoke, giving it that smooth, "chocolate-like" taste, while also increasing the availability of nicotine in the smoke.²⁵ Soon thereafter Philip Morris began using diammonium phosphate and other forms of ammonia in its other cigarettes, including its healthconscious (low-tar) Merit brand. Merits were introduced in 1976 and within 3 years accounted for about 20% of Philip Morris's cigarette sales.26

How, though, did diammonium phosphate freebase the nicotine in cigarettes? Freebasing entered public consciousness in the mid-1980s, when a cheaper street version of cocaine known as "crack" came on the scene.27 In point of fact, however, a kind of folk freebasing has been widely used in different parts of the world for many centuries. Archaeologists have found evidence of the use of lime or wood ash to freebase botanicals such as pituri (Duboisia hopwoodii), a nicotine-containing plant used by Australian aborigines to help them endure the harsh desert climate. Folk freebasing can also be found among traditional chewers of coca leaves, betel nuts, and tobacco.²⁸

The chemistry of freebasing is not complex. A base, such as ammonia, accepts a proton from a positively charged nicotine carboxylic acid salt (e.g., a malate or a tartrate) found in tobacco. The ammonia (NH₃) is thereby transformed into a cation (NH₄+), and the positively charged nicotine acid salt is deprotonated to become neutral. This neutral, deprotonated

nicotine is "free" in that it is no longer bound to another molecule (or anion) in the form of a salt. Free nicotine is more volatile; James F. Pankow, of Oregon Health and Science University, stresses that "increasing the proportion of the particle-phase nicotine that is in the freebase form will . . . tend to drive more nicotine into the gas phase."29 Gasphase nicotine is able to deposit quickly and easily in the respiratory tract and, because of its freebase form, crosses the bloodbrain barrier more readily ("moves easily into fatty tissues"30), making the nicotine more "available" to the smoker and therefore more potent.

Ammoniation increases nicotine's volatility. There is not universal agreement on whether ammoniation also increases the rate of nicotine delivery, but freebasing is widely thought to increase the impact of nicotine by increasing its efficiency of extraction during the smoking process.31 Many tobacco industry documents mention augmentation of nicotine impact, and many of those also reveal a conviction that ammoniation was increasing the rate of nicotine delivery, causing a more immediate and profound "kick" to a smoker's central nervous system (Figure 1). Philip Morris admitted the increased rate of nicotine delivery in a 1989 interoffice memo, noting that "the CNS [central nervous system] effects obtained using the NC [nicotine citrate] cigarettes were approximately half the magnitude of those obtained with FB [freebase nicotine] and unextracted cigarettes."33

Many different terms have been used within the tobacco industry to describe this augmented impact, including volatile nicotine, pH effect, amelioration, extractable nicotine, burley impact, and increased satisfaction or augmentation.34

Channing Robertson, a Stanford chemical engineer, was barred from using the term freebase nicotine in his 1998 testimony for the plaintiffs in Minnesota v. Philip Morris, so he testified instead

about what he called "crack nicotine."35 Crucial for the tobacco industry, however, was that this augmented "kick" provided by ammoniation could offset declining levels of tar and nicotine in

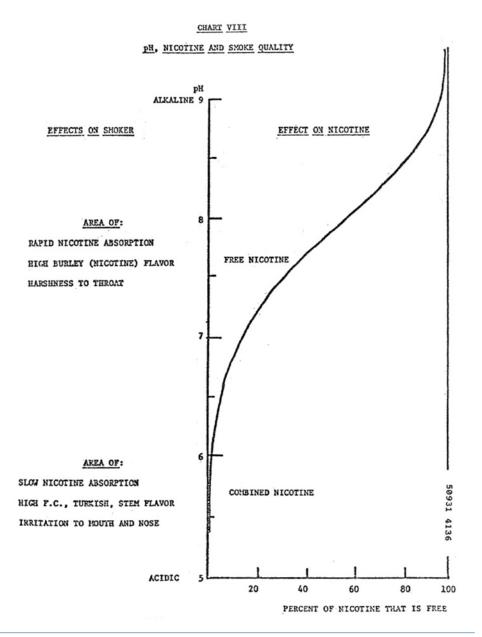


FIGURE 1-The chemistry of freebasing. The tobacco industry has long appreciated the importance of smoke pH for boosting nicotine's impact. This page, from a 1973 report by Claude E. Teague Jr of RJ Reynolds (Implications and Activities Arising From Correlation of Smoke pH With Nicotine Impact), shows how the freebase form of nicotine in smoke increases with increasing alkalinity. Although pH is a good indicator of relative freebase availability, it tends to underestimate the actual amount available. Other industry methods for measuring free nicotine—such as oil versus water partitioning or studies of nicotine volatility—reveal free nicotine levels much higher than those predicted from pH alone.³²

Summery of Progress in 1971 on Project TE-5001

DEVELOPMENT OF A CIGARETTE WITH INCREASED SMOKE OH

Robert E. Villiams

Section: Organic

te: December 16, 1971

Checked by:

CHRONOLOGY

May-June - Tobaccos treated with Ca (OH) to increase smoke pH showed increased tobacco of but no increase in smoke pH in handmade L+M

July-August - Tobacco treated with Ca(OH) showed an increase in amoke pH if the digarette was of the unfiltered type.

September-October - Sample elgerattes were made in the factory adding three levels of Ca(OH)a. The project was turned over to Physical Section.

Increasing the pH of a medium in which micotine is delivered increases the physiological effect of the nicotine by increasing the ratio of free base to said sait form, the free base form being more readily transported across physiological membranes. We are pursuing this project with the eventual goal of lowering the total migotime present in smoke while increasing the physiological effect of the micotine which is present, so that no physiological effect to lost on micotine reduction.

Source. Reference 36.

)

FIGURE 2-The Industry's Rationale for Freebasing. Liggett and Myers in 1971 explained the rationale behind the company's experiments to increase the proportion of "freebase" nicotine as part of its multiyear "Project TE-5001."

> cigarettes, which fell by more than half from the 1950s through the 1980s as the industry sought to reassure worried smokers. Freebasing meant you could maintain a high nicotine impact while lowering reported tar and nicotine levels. As one 1971 Liggett document states, "there could be a reduction in total nicotine in the smoke without a reduction in the physiological satisfaction associated with nicotine"36 (Figure 2).

THE ORIGINS AND **SPREAD OF AMMONIA TECHNOLOGY**

Long before the widespread use of freebasing, tobacco industry scientists knew that nicotine deliveries were sensitive to pH manipulation (by adding acids or bases). Several documents from the 1930s and 1940s discuss how to reduce the amount of free nicotine in tobacco by adding an organic acid, which would combine

with the free nicotine base to form a (bound) nicotine salt.³⁷ Free (vs "combined") nicotine in those early years was often characterized as "toxic,"38 which made sense at a time prior to the push to reduce tar and nicotine in the "filter wars" and "tar derby" of the 1950s and 1960s. Many other industry documents from this earlier period describe the well-known art of denicotinization, which often used a base (such as ammonia) and steam to remove the offending alkaloid from tobacco. Denicotinization involves some of the same processes as freebasing, although the desired outcomes are different. Denicotinization involves the application of gaseous ammonia so that, upon addition of steam, the nicotine can be removed; freebasing impregnates tobacco with a salt (such as DAP) so that ammonia is released when the cigarette is lit, making nicotine more available to the smoker.

Tobacco chemists knew enough to freebase nicotine as early as the 1930s and 1940s,39 but there was little reason then to manipulate cigarettes in this manner. Smoking was not yet widely accepted as a cause of lung and heart disease, 40 and most people still smoked cigarettes yielding very high levels of tar and nicotine. Only beginning with the "health scare" of the 1950s, and with increasing urgency in the 1960s and 1970s, did Philip Morris and the other manufacturers scramble to appease a rattled public by marketing cigarettes with lower levels of tar and nicotine, which is where the value of ammoniation came in.

It is difficult to say whether Philip Morris scientists expected diammonium phosphate to increase the availability of free nicotine in its new version of Marlboro, introduced in the mid-1950s. After all, the compound was largely being used as a pectin releaser and flavorant in reconstituted tobacco. Philip Morris chemists were, however, experts in pH manipulation, as were chemists more generally. Freebasing was not an unknown phenomenon, but there was not yet a practical need for it in the cigarette business.

In 1962, a Philip Morris study found diammonium phosphate products delivering 0.57 mg of nicotine per cigarette versus 0.44 mg in untreated tobaccos. 41 Keenly aware of the increasing demand for cigarettes low in nicotine, 42 Philip Morris later used its patented DAP-BL process to give its "low-yield" Merit brand an edge over its competitors. Merit cigarettes boasted a total nicotine yield (measured by Federal Trade Commission machines) only half of that found in Marlboros, but still managed to make available the same amount of free nicotine to smokers (about 0.33 mg in both instances). Brown and Williamson scientists reflected on this in 1980, commenting that "in theory a person smoking these cigarettes [Merit and Marlboro] would not find an appreciable difference in the physiological satisfaction from either based on the amount of free nicotine delivered."43

This was not the first time Brown and Williamson had pondered the value of freebasing. Its parent company, British American Tobacco, in the mid-1960s had recognized along with Philip Morris that the "strength" or "impact" of a cigarette was related not to the total nicotine content of the smoke but rather to the amount of "extractable" or "free" nicotine, which varied significantly with smoke pH.44 Brown and Williamson in

1971 had given the code name UKELON to urea, an ammonia source that the company recognized as "a way of achieving normal impact from low tar cigarettes."45 The same company's "Project LTS" (low "tar" satisfaction) acknowledged that free (unprotonated) nicotine was "more readily absorbed and thus has a decidedly satisfying effect on the smokers' taste receptors." The goal of LTS was a cigarette containing "greater levels of 'free' nicotine" in "an enhanced alkaline environment."46 By 1980, the company had concluded that "we have sufficient expertise available to 'build' a lowered mg tar cigarette which will deliver as much 'free nicotine' as a Marlboro, Winston or Kent without increasing the total nicotine delivery above that of a 'Light' product."47

Apart from DAP-BL recon, Philip Morris experimented with other kinds of ammonia technology. As early as 1957, for example, the company came up with the economically unfeasible "New Idea No. 46"48 to "soak stems in liquid ammonia," imparting to them greater "proteinlike" material and "those properties now being produced by the aqueous NaOH, by virtue of its basic nature."49 The ammonia was difficult to recycle, however, and the idea was quickly abandoned. A 1966 progress report on "nicotine and smoke pH" discussed the results of adding ammonium carbonate and oxalic acid to tobacco and concluded that nicotine deliveries could be "controlled via filler or smoke pH adjustment."50 Throughout this time, from the mid-1960s through the 1970s and 1980s, the company kept a close eye on the pH levels of its major brands.51

THE STAMPEDE TO KEEP **UP WITH THE MARLBORO MAN**

Although some historians maintain that Philip Morris's rise to the top of the tobacco industry in the mid-1970s was because of its ingenious Marlboro ad campaign, featuring a ruggedly handsome cowboy in the beautiful and equally rugged West⁵²-"Marlboro Country"-the makers of competitor brands could justifiably disagree. In the 1960s, with Philip Morris brands streaking ahead of the pack, RJ Reynolds, American Tobacco, Lorillard, Liggett, and Brown and Williamson all began investigations into what would later be called "the secret" 53 and eventually "the soul" of Marlboro.54 All discovered the virtues of freebasing, but this didn't happen overnight.

Brown and Williamson and its parent, British American Tobacco, were apparently the first (after Philip Morris) to realize the importance of ammonia in increasing nicotine availability, but American Tobacco⁵⁵ and the other companies were not far behind. RJ Reynolds incorporated ammoniated sheet into Camel filters in 1974, allowing them to deliver 36 mg of ammonia per cigarette in the mainstream smoke.⁵⁶ Five years later, the company began using ammoniated sheet in its popular Winston brand.⁵⁷ Teague, in a 1973 report marked "secret," noted that Marlboro, in comparison with RJ Reynolds's own Winston, showed

> 1) higher smoke pH (higher alkalinity), hence increased amounts of "free" nicotine in smoke, and higher immediate nicotine "kick", 2) less mouth irritation, less stemmy taste and less Turkish and flue-cured flavor, and 4) [sic] increased burley flavor and character.

Teague then went on to point out that cigarettes with rising sales, especially Philip Morris brands, all showed evidence of pH manipulation. Another RJ Reynolds document from 1973 (aimed at targeting the youth market) stated that "for public relations reasons it would be impossible to go back all the way to the 1955 type cigarettes"-high in tar and nicotine-but took comfort from the fact that "still, with an old style filter, any desired additional nicotine 'kick' could be easily obtained through pH regulation."59

Sometime during the 1980s, Lorillard caught up with Philip Morris and began using ammonia technology in its own cigarettes, by which time British American Tobacco had initiated Project AMTECH to investigate "the potential benefits of ammonia technology."60 By the end of the 1980s, five of the "big six" of the industry (all but Liggett, which had researched but apparently never commercialized a freebase concept using calcium hydroxide)61 were using a total of 10 million pounds of ammonia per annum, amounting to about 10 mg per cigarette. RJ Reynolds alone released 900 000 pounds of ammonia in 1989 from its factory in North Carolina.62

British American Tobacco and Brown and Williamson held the first of several ammonia technology conferences in the spring of 1989 to enhance "rapid commercial application" of ammonia technologies and to provide a forum to discuss "research strategies and priorities." Here we find an acknowledgment that ammonia technology was "the key to competing in smoke quality with [Philip Morris] worldwide" we also find a discussion of the

different ways ammonia was being used to achieve the freebasing effect. Philip Morris was using DAP recon and urea; RJ Reynolds was using ammonia gas; American and Lorillard were using DAP recon; and Brown and Williamson itself was using DAP recon and urea, code-named QUELAR and UKELON.64 At the second Annual Ammonia Technology Conference one year later, the opening statement affirmed that "ammonia technologies have been developed in the group to the stage where US blended products can be manufactured with comparable smoking quality to Marlboro."65 A Brown and Williamson strategy document from 1991 concluded that ammonia technology was "the key factor" and "critical to the taste, character and delivery of Marlboro."66

Of course, the joy felt by Brown and Williamson and the other tobacco companies after uncovering "the secret of Malrboro" was matched by disappointment at Philip Morris, which had enjoyed this advantage over its competitors for years. William A. Farone, director of Applied Research at Philip Morris from 1976 to 1984, recalls that "when Winston started increasing their level of ammonia we had, you knowthe roof fall down on us from [corporate headquarters in] New York City."67

THE OUTSIDE WORLD LEARNS THE TRUTH

Philip Morris's use of ammonia to freebase nicotine remained essentially a company secret until the 1970s and an industry secret until the 1990s. With access to documents produced in litigation, however, groups outside the industry began to catch on. Alix M. Freedman broke the story in a

Pulitzer Prize-winning article for the Wall Street Journal in 1995,68 based partly on documents unearthed through Commissioner David Kessler's investigations at the FDA. In 1996, in its regulations restricting the sale and distribution of cigarettes, the FDA noted that "compounds in free or unbound forms are vaporized more readily than compounds bound together in salts," giving both nicotine and cocaine as examples. The FDA went on to note that cigarette manufacturers had provided no evidence to rebut charges that "the conversion of nicotine from its bound form to its free form increases the transfer of nicotine to smoke."69 One year later, James F. Pankow published a paper describing how ammonia increased nicotine volatility and availability in cigarette smoke, comparing this to the "immediate and intense high" produced by the freebasing involved in the making of crack cocaine.⁷⁰

The industry's response was quick and characteristically dismissive. In 1998, Philip Morris lawyers deposed Pankow, questioning not just the details of his experimental design but also his professional ethics.71 The company also criticized his assertion of a similarity between the tobacco industry's use of ammonia and the freebasing of cocaine.⁷² Philip Morris lawyers also used the 1979 surgeon general's report to help them debunk the charge of freebasing. According to this report, produced under Surgeon General Julius B. Richmond, "the percentage of nicotine present as the free base is .40 at pH 5.35, 1.7 at pH 6, 15 at pH 7, 64 at pH 8, and 85 at pH 8.6."73 Philip Morris maintained that because its cigarettes had a pH of about 6, nearly 99% of its nicotine was in the form of a protonated salt. So

whatever effect ammonia might be having on the percentage of freebase nicotine, and thus the rate of nicotine "delivery," would be trivial.

From experiments performed by other companies, however, we know that even very slight increases in pH can have a significant effect on the availability of freebase nicotine in smoke. Recall Brown and Williamson's 1980s demonstration that Merit cigarettes had only half the total nicotine of Marlboro cigarettes while still delivering the same amount of free nicotine, thanks to only a 0.5 increase in pH. The companies were also aware that pH provides only an imperfect estimate of free nicotine availability.⁷⁴ Wayne, Connolly, and Henningfield have reviewed the industry's internal documents on freebasing and shown that free nicotine levels of Philip Morris's and other companies' cigarettes were significantly higher than those predicted from pH values alone.³²

Company officials also argued that while ammonia might well increase the rate of nicotine delivery, the same total amount of nicotine was delivered nonetheless. Rate of nicotine delivery, though, is a key aspect of addiction. That is one reason nicotine gums and patches usually cannot deliver the same "satisfaction" as smoking: lung deliveries are far more intense, and freebasing only heightens this effect. A 1994 draft report on experiments conducted at Philip Morris's secret research center (INBIFO) in Cologne, Germany, conceded that when subjects inhaled the same amount of nicotine at different pH levels, those who inhaled at higher alkalinity experienced faster rates of entry of nicotine into the bloodstream.⁷⁵

DISGUISING THE USE OF AMMONIA AS A FREEBASING AGENT

In their attempts to defend against charges of freebasing, Philip Morris and the other companies took advantage of ammonia's innocuous uses to draw attention away from its freebasing ability. Tobacco executives argued: how could ammonia, a natural compound found in tobacco, food, fertilizer, pesticides, and many other everyday products, have this secret ability to control nicotine levels? In a 1994 Tobacco Institute response to FDA Commissioner David Kessler we find such arguments, along with the claim that ammonia's most important use was in reconstituted tobacco, "so the blended leaf sticks together."76 This same document suggests that the idea of the FDA regulating tobacco was ludicrous, making no more sense than the FDA regulating coffee or beer. (Philip Morris has since reversed course and now argues in favor of FDA regulation, hoping this regulation will help preserve its position as the nation's number one cigarette maker.)

There are many other industry pronouncements from the 1990s that attempt to draw attention away from ammonia's freebasing function. A 1994 Brown and Williamson document (prepared for use in public relations or litigation) points out that ammonia and its many derivatives are found in everyday foods: ammonium bicarbonate in baked goods; ammonium hydroxide in cured pork; diammonium phosphate in dough, ice cream, and gelatin; and ammonium sulfide in baked goods and meats. And ammonia itself is found in human breath.77 An RJ Reynolds document insists that

the industry's uses of ammonia "are similar to many of the applications commonly used in the food industry."78

Philip Morris has also tried to exonerate ammonia by emphasizing its roles as a flavorant and pectin-releaser.⁷⁹ In Iron Workers v. Philip Morris, Harold G. Burnley Jr, the company's former vice president of operations, was asked, "Is it true that Philip Morris uses ammonia for the purpose of increasing a nicotine kick?" He answered, "No, sir . . . it was used really initially in BL [blended leaf] to hold the sheet together, and it was used as a flavorant in RL [reconstituted leaf]."80 In 1997, Philip Morris lawyers interrogated their company's former director of applied research about his claim that ammonia was used to increase nicotine availability, asking, in so many words: how do you know it's not just a flavor thing?81 Pankow was questioned along similar lines in Washington v. American Tobacco Co, with lawyers for the defense asking how he could be sure that the increase in nicotine delivery was from the ammonia added and not the ammonia already present in the tobacco.82 Similar rationalizations were put forward at the industry's second Annual Ammonia Technology Conference, where we hear that ammonia simply "enhances processes that occur naturally during tobacco and cigarette aging and during combustion."83

Philip Morris and the other tobacco companies also split chemical hairs by denying they had ever used gaseous ammonia to achieve any kind of freebasing effect.84 A small truth here hides a larger deception, because it is true that the freebasing effect is not ordinarily achieved by using ammonia in gaseous form. The more usual practice is to use

nitrogen-containing compounds such as proteins and amino acids (e.g., lysine) and ammonium salts such as DAP and ammonium tartrate, carbonate, and citrate along with ammonium hydroxide and urea, all of which readily transform into ammonia upon the addition of heat (as when a cigarette is lit). Tobacco manufacturers have also freebased using weakly basic substances that, when heated, convert into more-alkaline compounds (sodium carbonate produces sodium oxide, for example, which turns into sodium hydroxide in the presence of water).85 Philip Morris in 1994 claimed that even if it had been adding ammonia (in a volatile gaseous form) to cigarettes the compound would simply evaporate away, reducing the pH to its normal level before the cigarette was even shipped.86 That, however, is why most companies use nonvolatile ammonium salts such as DAP as their freebasing reagents: ammonium salts break down into ammonia, increasing the pH of the tobacco and deprotonating the nicotine in the process, but only after the cigarette has been lit.

CRACK NICOTINE?

In the mid-1990s, FDA Commissioner Kessler was using the tobacco companies' recently discovered manipulation of nicotine to argue for the regulation of tobacco.87 The industry knew that any admission of using ammonia to increase the availability of nicotine would be an admission that nicotine is the addictive sine qua non of smoking, and tobacco manufacturers did not want to have cigarettes compared to crack cocaine. (According to Farone, the industry made a conscious effort in the 1980s and 1990s to avoid

the term freebasing in any documents or statements because it didn't want to be associated with cocaine.⁸⁸) With so much at stake, it is not surprising that the industry attempted to cover up its use of ammonia as a freebasing reagent.

It is important to keep in mind that the ammonia cover-up is only one of dozens of similar coverups, part of the industry's calculated disregard for human health.89 The industry has tried to efface the truth in depositions and even in internal documents, but the facts are clear: Philip Morris by the early 1960s had realized ammonia's ability to augment the potency of nicotine and then used this knowledge to develop cigarettes that were nominally low in tar and nicotine while still having a powerful nicotine kick. Sales of Philip Morris products skyrocketed as a result, spiking the company to the top of the market charts. And the other manufacturers took notice: RJ Reynolds, American Tobacco, Brown and Williamson, Liggett, and Lorillard all worked hard to figure out Marlboro's secret and by the 1970s and 1980s had developed their own versions of ammonia technology, which all but Liggett implemented commercially.

It should also be noted that freebasing represented a reversal of a decades-old effort to make cigarettes "milder." The first major US cigarette brand, Camel, introduced in 1913, succeeded on the basis of its use of a flavored blend of oriental, burley, and flue-cured Virginia tobaccos, producing a milder and more inhalable smoke than previous generations of tobacco products. Flue-cured "bright" tobacco blends were less alkaline and therefore easier to inhale than traditional varieties, notably those used in the pipe and

cigar trade, where tobaccos were typically high in pH (circa 8) but generally too harsh to inhale. Cigarette makers modified the chemistry of tobacco throughout the 1930s and 1940s, seeking to produce an ever-milder smoke that could be inhaled without stimulating coughing. When demand for lower-tar and lower-nicotine cigarettes arose in the 1950s and 1960s, however, the industry realized there were limits to how low nicotine levels could go without "weaning"90 smokers from their habit. Cigarette manufacturers worried about producing an "emasculated"91 cigarette devoid of flavor and missing the grip of addiction. Freebasing solved a big part of this problem, because tar and nicotine levels could now be lowered-up to a point-without the risk of losing customers. Teague at Reynolds in 1973 summarized the achievement: "As a result of its higher smoke pH, the current Marlboro, despite a two-thirds reduction in smoke 'tar' and nicotine over the years, calculates to have essentially the same amount of 'free' nicotine in its smoke as did the early WINSTON."92

It is not yet clear to what extent manufacturers in other parts of the world-for example, China and Japan-use ammonia in the manufacture of their cigarettes; this topic deserves further study. Diammonium phosphate is not legal for use in cigarettes in Austria, Germany, or Spain:93 does this mean that freebasing is achieved by other means? Nicotine yields of American cigarettes have risen steadily over the past few years94: could this mean a retreat from the practice of ammoniation in favor of other methods of nicotine manipulation?

What is not in doubt is that the continued pull of nicotine has

generated a global epidemic of lung and heart disease. Tobacco has become the world's single largest preventable cause of premature death, accounting for about 5 million fatalities per annum, a number expected to grow to about 10 million per year over the next couple of decades.⁹⁵ There is also tragedy, though, in the fact that so many scholars have helped to perfect and enhance this terrible technology of mortality. Tens of billions of dollars have been spent by the industry on tobacco chemistry⁹⁶ in the decades since British and American scientists followed the Germans in proving that smoking could cause lung cancer and heart disease.97 Cigarettes are among the most carefully (and craftily) designed small objects on the planet, but they also cause more death and disease than any other invention since humans first learned how to spark fire from stone and metal. We should not be so surprised that the industry has manipulated cigarette chemistry to keep people smoking; what is surprising, though, is how easily they have gotten away with it.

About the Authors

Terrell Stevenson is with the School of Medicine, University of California, San Francisco. Robert N. Proctor is with the Department of History, Stanford University, Stanford, CA.

Requests for reprints should be sent to Robert N. Proctor, Department of History, Stanford University, Stanford, CA 94305-2024 (e-mail: rproctor@stanford.edu).

This article was accepted August 31, 2007

Contributors

R.N. Proctor suggested the topic, and T. Stevenson did most of the research and writing.

Acknowledgments

T. Stevenson presented an early version of this article in R.N.P.'s "Tobacco and Health in World History" class at Stanford University, Stanford, CA. R.N. Proctor has worked as an expert witness in litigation against the tobacco industry.

The authors would like to thank Jan Logemann and Peder Roberts for help locating certain documents.

ENDNOTES

- 1. "Ammonia," RJ Reynolds, 1982, Bates no. 500990999-1004, http://legacy.library.ucsf.edu/tid/agk59 d00 (accessed February 26, 2007).
- 2. "Tower Processes. Process 3: Expansion with Mixtures of Gaseous Ammonia and Carbon Dioxide," Philip Morris, May 1, 1970, Bates no. 2022232496-2498, http://tobac-codocuments.org/pm/2022232496-2498.html (accessed February 26, 2007).
- 3. Robert N. Proctor, "Everyone Knew But No One Had Proof': Tobacco Industry Use of Medical History Expertise in US Courts, 1990–2002," *Tobacco Control*, 15 (2006): iv117–iv125.
- 4. Claude E. Teague Jr, "Modification of Tobacco Stem Materials by Treatment with Ammonia and Other Substances," RJ Reynolds, August 3, 1954, Bates no. 504175083-5084, http://legacy.library.ucsf.edu/tid/gpt58d 00 (accessed February 26, 2008); trial testimony of David Eugene Townsend, Engle v. RJR Co, March 2, 1999, Bates no. townsendD030299PM, http://legacy.library.ucsf.edu/tid/vny75 a00 (accessed February 26, 2007), 25749–50.
- 5. R.B. Seligman, "The Use of Alkalis to Improve Smoke Flavor," Philip Morris, 1965, Bates no. 2026351158-1163, http://legacy.library.ucsf.edu/tid/klk15e 00 (accessed February 26, 2007).
- 6. F.H. Crayton and H.L. Spielberg, "Flavor Development: Effects of Ammonia—Odor and Smoke," Philip Morris, November 8, 1971, Bates no. 2028660823-0831, http://legacy.library.ucsf.edu/tid/cuq74e00 (accessed February 26, 2007), 5.
- 7. William J. Casey and Thomas A. Perfetti, "Method to Improve Quality of Tobacco via Sugar-Ammonia Reactions," RJ Reynolds, March 19, 1980, Bates no. 504168866-8868, http://legacy.library.ucsf.edu/tid/yrt58d00 (accessed February 26, 2007).
- 8. R.G. Armstrong et al., "U.S. Patent 3,771,533, Process for Puffing Tobacco," Philip Morris, November 13, 1977, Bates no. 2056171184-1196, http://legacy.library.ucsf.edu/tid/prk36e 00 (accessed February 26, 2007).
- 9. Trial testimony of Harold George Burnley Jr, Local No. 17 Bridge and Iron Workers Insurance Fund v. Philip Morris Inc, March 9, 1999, Bates no.

- burnleyH030999, http://legacy.library. ucsf.edu/tid/hka85a00 (accessed February 26, 2007), 17.
- 10. Frank Friedman, "The Availability of Ammonia," Philip Morris, July 10, 1974, Bates no. 2022236810-6850, http://legacy.library.ucsf.edu/tid/hrp45e 00 (accessed February 26, 2007), 6.
- 11. Helmut Wakeham to Hugh Cullman, "The Question of Deleterious Substances in DAP-BL," Philip Morris, June 23, 1962, Bates no. 1000862896-2897, http://legacy.library.ucsf. edu/tid/xct28e00 (accessed February 26, 2007), 1.
- 12. G.E. Inskeep, "Improvement of Flavor of Rolled Tobacco Stems with Diammonium Phosphate," Philip Morris, July 15, 1966, Bates no. 2026363161-3165, http://legacy.library.ucsf. edu/tid/dez04e00 (accessed February 26, 2007).
- 13. H.O. Trimmer Jr to R.B. Seligman, "Analysis of TPM and Nicotine Delivery of Production DAP," Philip Morris, June 29, 1962, Bates no. 2050872548, http://legacy.library.ucsf.edu/tid/haq45 e00 (accessed February 26, 2007).
- 14. J.D. Hind and R.B. Seligman, "3,353,541, Tobacco Sheet Material," Philip Morris, November 21, 1967, Bates no. 2056136774-6783, http://legacy.library.ucsf.edu/tid/itg26e 00 (accessed February 26, 2007).
- 15. Glenn P. Moser, "Patent Specification 969,144: Process for Removing Nicotine from Tobacco Material," Philip Morris, September 9, 1964, Bates no. 2026535674-5678, http://legacy.library.ucsf.edu/tid/jqe25e00 (accessed February 26, 2007).
- 16. "Issue Module Product Integrity," Philip Morris International, 1964 (est.), Bates no. 2501100284-0502, http://to-baccodocuments.org/pm/2501100284-0502.html (accessed February 26, 2007), 37–47.
- 17. Peggy Roberts to Barry Meier, Philip Morris, February 24, 1998, Bates no. 2076733606-3607, http://legacy.library.ucsf.edu/tid/bbh85 c00 (accessed February 26, 2007), 1.
- 18. Barry Meier, "Cigarette Maker Manipulated Nicotine, Its Records Suggest," *New York Times*, February 23, 1998.
- 19. H.J. Rand Cigarette Co., "An Investigation of Possible Cancer Producing Agents in Cigarette Smoke and their Elimination," Brown and Williamson, May 3, 1955, Bates no. 650340722-0759, http://legacy.library.ucsf.edu/tid/pfw14f00 (accessed February 26, 2007).
- 20. Helmut Wakeham, "Tobacco and Health—R&D Approach," Philip Morris, November 15, 1961, Bates no.

- 1005069026-9050, http://legacy.library.ucsf.edu/tid/fot38e00 (accessed February 26, 2007).
- 21. T.S. Osdene and E.W. Robb, "Smoke Chemistry Control," Philip Morris, November 19, 1965, Bates no. 1001897059-7208, http://legacy.library.ucsf.edu/tid/sbi54e00 (accessed February 26, 2007), 4.
- 22. See W.C. Hopkins, "Special Report: Project 33-1502 Designed Filler Cigarettes," Philip Morris, March 17, 1967, Bates no. 1000341549-1573, referencing French patent 1379831 from October 19, 1964, http://legacy.library.ucsf. edu/tid/fnu64e00 (accessed February 26, 2007), 1.
- 23. R.R. Johnson to E.P. Finch, "Current Chemistry Research at Southampton," Brown & Williamson, July 14, 1967, Bates no. 500012128-2142, http://legacy.library.ucsf.edu/tid/usv24f 00 (accessed February 26, 2007), 2.
- 24. Richard Kluger, Ashes to Ashes: America's Hundred Year Cigarette War, the Public Health, and the Unabashed Triumph of Philip Morris (New York: Knopf,
- 25. James F. Pankow et al., "Conversion of Nicotine in Tobacco Smoke to Its Volatile and Available Free-Base Form through the Action of Gaseous Ammonia," Environmental Science and Technology, 31(1997): 2428-33.
- 26. Kluger, Ashes to Ashes, 397.
- 27. Dorothy K. Hatsukami and Marian W. Fischman, "Crack Cocaine and Cocaine Hydrochloride: Are the Differences Myth or Reality?" JAMA, 276 (1996): 1580-88.
- 28. R.J. Sullivan and E.H. Hagen, "Psychotropic Substance-Seeking: Evolutionary Pathology or Adaptation?" Addiction, 97 (2002): 389-400.
- 29. Pankow et al., "Conversion of Nicotine," 2428.
- 30. "Nicotine Toxicity," RJ Reynolds, 1977, Bates no. 511194087-4114 (page 9), http://legacy.library.ucsf.edu/tid/ggg53 d00 (accessed February 26, 2007).
- 31. Peter P. Rowell and Lawrence A. Carr, "Historical Review of Nicotine's Actions," University of Louisville for Philip Morris, February 19, 1997, Bates no. 2505486601-6749, http://legacy. library.ucsf.edu/tid/ceb05c00 (accessed February 26, 2007).
- 32. G. Ferris Wayne, G.N. Connolly, and J.E. Henningfield, "Brand Differences of Free-base Nicotine Delivery in Cigarette Smoke: The View of the Tobacco Industry Documents." Tobacco Control, 15 (2006): 189-98.
- 33. F.P. Gullotta et al. to H.L. Spielberg, "When Nicotine Is Not Nicotine,"

- Philip Morris, August 2, 1989, Bates no. 2025986931-6935, http://legacy. library.ucsf.edu/tid/jcz74e00 (accessed February 26, 2007), 1.
- 34. H.J. Minnemeyer, "Continuation of Nicotine Augmentation Project (Conap)," Lorillard, February 9, 1977, Bates no. 00982446-2453, http://legacy.library. ucsf.edu/tid/aut71e00 (accessed February 26, 2007).
- 35. Channing Robertson, in discussion with R.N. Proctor, April 2, 2007.
- 36. Robert K. Williams, "Progress During May-June on Project No. TE-5001: Development of a Cigarette with Increased Smoke pH," Liggett and Myers, July 13, 1971, Bates no. LG0295596-5600, http://legacy.library.ucsf.edu/ tid/fqf67a00 (accessed February 26, 2007), 1.
- 37. "Basic Data 1939-1945. 'The Bible," American Tobacco, n.d., Bates no. MNAT00887648-7930, http://legacy.library.ucsf.edu/tid/kho31 a00 (accessed February 26, 2008), 136; compare S. Pawlowski and S. Woytowicz, "Method for the Refining of Smoking Tobacco," German Reich Patent No. 634104 (translation), August 18, 1936, Bates no. 85670246-0250, http://legacy.library.ucsf.edu/tid/vxl31e 00 (accessed February 26, 2007).
- 38. H.B. Parmele to A. Riefner, Lorillard, August 30, 1930, Bates no. 80690651-0654, http://legacy.library. ucsf.edu/tid/ocz21e00 (accessed February 26, 2007), 2.
- 39. See, for example, Aleksandr A. Shmuk, The Chemistry and Technology of Tobacco, ed. N. I. Gavrilov, trans. J. Lengy (Moscow: Pishchepromizdat, 1953), 7-12.
- 40. Allan M. Brandt, The Cigarette Century: The Rise, Fall, and Deadly Persistence of the Product That Defined America (New York: Basic Books, 2007).
- 41. Trimmer to Seligman, "Analysis of TPM and Nicotine Delivery of Production DAP," Philip Morris, Bates no. 2050872548, http://tobaccodocuments.org/pm/2050872548.html (accessed February 26, 2007).
- 42. "Nicotine Delivery of Cigarettes Based on Total Sales," Philip Morris, 1963, Bates no. 2022242304, http://legacy.library.ucsf.edu/tid/kpo53 e00 (accessed February 26, 2007).
- 43. C.F. Gregory, "Observation of Free Nicotine Changes in Tobacco Smoke/ #528," Brown and Williamson, January 4, 1980, Bates no. 510000667-0670, http://legacy.library.ucsf.edu/tid/zds24f 00 (accessed February 26, 2007), 2.
- 44. I.D. Backhurst, "A Relation between the 'Strength' of a Cigarette and the 'Extractable Nicotine' in the Smoke,"

- British American Tobacco, November 16, 1965, Bates no. 508102918-2941, http://tobaccodocuments.org/ product_design/NcSmBAT19651116.Rg. html (accessed February 26, 2007).
- 45. R.P. Newton and E.F. Litzinger, "Further Evaluations of UKELON Treated Cigarettes," Brown and Williamson, January 17, 1972, Bates no. 650105652-5663, http://legacy.library.ucsf.edu/tid/bqq00f00 (accessed February 26, 2007), 5.
- 46. Hawkins, McCain & Blumenthal, Inc., "Project LTS," Brown and Williamson, June 20, 1977, Bates no. 660094371-4451, http://legacy.library.ucsf.edu/tid/wnj14f00 (accessed February 26, 2007), 10.
- 47. Gregory, "Observation of Free Nicotine Changes," 3.
- 48. R.C. Sproull, "New Idea No. 46," Philip Morris, January 14, 1957, Bates no. 2021627611, http://legacy.library. ucsf.edu/tid/orj44e00 (accessed February 26, 2007).
- 49. H.B. Merritt and R.B. Seligman, "Idea No. 46: Tobacco Stems Soaked in Liquid Ammonia," Philip Morris, February 1961, Bates no. 2021627171, http://legacy.library.ucsf.edu/tid/vcu58 e00 (accessed February 26, 2007).
- 50. Leo F. Meyer to R.N. Thomson, "Progress Report-Nicotine and Smoke pH," Philip Morris, March 31, 1966, Bates no. 2076733778-3783, http://tobaccodocuments.org/pm/2076733778-3783.html (accessed February 26, 2007), 1.
- 51. "Chart Listing Ammonia and pH Levels by Brand," Philip Morris, 1998, Bates no. 2063130886-0889, http://legacy.library.ucsf.edu/tid/yhy04 c00 (accessed February 26, 2007).
- 52. Kluger, Ashes to Ashes, 292-97.
- 53. R.R. Johnson, "Ammonia Technology Conference Minutes, Louisville, Kentucky, May 18-19," Brown and Williamson, June 12, 1989, Bates no. 583106691-6725, http://tobaccodocuments.org/bw/1442608.html (accessed February 26, 2007), 8.
- 54. J.H. Lauterbach and R.R. Johnson, "The Project Adverb Study of Marlboro KS," Brown and Williamson, October 10, 1989, Bates no. 570244005-4027, http://legacy.library.ucsf.edu/tid/lvs20f 00 (accessed February 26, 2007).
- 55. Trial testimony of Channing R. Robertson, Minnesota v. Philip Morris, Inc, February 4, 1998, Bates no. ROBERTSONC020498, http://legacy. library.ucsf.edu/tid/mkn05a00 (accessed February 26, 2007).
- 56. "Ammonia," RJ Reynolds, 4; compare the deposition of William Anthony Farone, September 22, 1999, for NERI v. RJR

- Tobacco, Bates no. FARONEW092299, http://legacy.library.ucsf.edu/tid/nxz75a00 (accessed February 26, 2007), 26.
- 57. "Technology: Ammoniation," RJ Reynolds, 1981, Bates no. 509018864-8865A, http://tobaccodocuments.org/ rjr/509018864-8865A.html (accessed February 26, 2007).
- 58. Claude E. Teague Jr, "Implications and Activities Arising from Correlation of Smoke pH with Nicotine Impact, Other Smoke Qualities, and Cigarette Sales," October 2, 1973, Bates no. 509314122-4154, http://tobaccodocuments.org/rjr/ 509314122-4154 D1.html (accessed February 26, 2007), 509314126.
- 59. Frank G. Colby to R.A. Blevins Jr, "Cigarette Concept to Assure RJR a Larger Segment of the Youth Market," December 4, 1973, Bates no. 500529772-9773, http://tobaccodocuments.org/rjr/5005 29772-9773.html (accessed February 26, 2007), 1 (emphasis in original).
- 60. Ian Brown and Chris Jenkins, "Optimizing Ammonia at BAT: Project Amtech," n.d., Bates no. 582104744-4748, http://tobaccodocuments.org/ bw/960067.html (accessed February 26, 2007), 582104746.
- 61. Williams, "Progress During May-June."
- 62. Johnson, "Ammonia Technology Conference."
- 63. "Second Annual Ammonia Technology Conference: Commercialization of Ammonia Technology, Louisville, Kentucky," Brown and Williamson, June 11-13, 1990, Bates no. 570353434-3770, http://legacy.library.ucsf.edu/ tid/rys20f00 (accessed February 26,
- 64. Johnson, "Ammonia Technology Conference."
- 65. "Second Annual Ammonia Technology Conference," 3.
- 66. E.E. Kornhurst, "PM's Global Strategy: Marlboro Product Technology," Brown and Williamson, October 26, 1992, Bates no. 569203392-3628, http://legacy.library.ucsf.edu/tid/ hus20f00 (accessed February 26, 2007), 45.
- 67. Deposition of William Anthony Farone, Ph.D., Labelle v. Philip Morris Inc, July 20, 2000, Bates no. faronew072000, http://tobaccodocuments.org/datta/FARONEW072000.ht ml (accessed February 26, 2007), 230.
- 68. Alix M. Freedman, "Impact Booster': Tobacco Firm Shows How Ammonia Spurs Delivery of Nicotine," Wall Street Journal, December 28, 1995.
- 69. U.S. Food and Drug Administration, "Nicotine in Cigarettes and Smokeless Tobacco Is a Drug and These Products

- Are Nicotine Delivery Devices under the Federal Food, Drug, and Cosmetic Act: Jurisdictional Determination 61," Federal Register, August 28, 1996, 44970–75.
- 70. Pankow et al., "Conversion of Nicotine," 2429.
- 71. Deposition of James F. Pankow, Ph.D., Washington v. American Tobacco Co, April 2, 1998, Bates no. pankowj040298, http://legacy.library.ucsf.edu/tid/yyy75 a00 (accessed February 26, 2007); "Possible Questions to Pose to Professor William H. Glaze, ed. of the Journal of Environmental Science and Technology," Philip Morris, November 1996, Bates no. 2065349638-9639, http://legacy.library.ucsf.edu/tid/qpu63 c00 (accessed February 26, 2007).
- 72. Jeffrey I. Seeman, Jay A. Fournier, and John B. Paine III, "Thermal Properties of Nonprotonated and Protonated Nicotine. The Contrast of Nicotine's Transfer to Smoke with the Mechanism of Cocaine 'Freebasing," Philip Morris, November 1998, Bates no. 2063664635-4657, http://tobaccodocuments.org/product_design/2063664635-4657.html (accessed February 26, 2007).
- 73. Smoking and Health: A Report of the Surgeon General (Washington, D.C: U.S. Department of Health and Human Services, 1979), 14–85.
- 74. Meyer to Thomson, "Progress Report," 1.
- 75. "The Effects of Cigarette Smoke pH' on Nicotine Delivery and Subjective Evaluations," Philip Morris, June 1994, Bates no. 2025986551-6553, http://legacy.library.ucsf.edu/tid/osq74e 00 (accessed February 26, 2007).
- 76. Tobacco Institute, "Tobacco Institute Statement in Response to FDA Commissioner, David Kessler," June 21, 1994, Bates no. TIMN0327789-7791, http://legacy.library.ucsf.edu/tid/tvr52f00 (accessed February 26, 2007), 2.
- 77. "Ingredients Added to Tobacco in the Manufacture of Cigarettes by the Six Major American Cigarette Companies," Brown and Williamson, April 12, 1994, Bates no. 606000841-0889, http://legacy.library.ucsf.edu/tid/aii93f00 (accessed February 26, 2007).
- 78. RJ Reynolds, "Ammonia," 5.
- 79. Seeman, Fournier, and Paine, "Thermal Properties," 14–15.
- Testimony of Harold George Burnley Jr, 17.
- 81. Deposition of William Anthony Farone, Ph.D., ARCH [BARNES] v. American Tobacco Co, August 28, 1997, Bates no. faronew082897, http://tobaccodocuments.org/datta/FARONEW 082897.html (accessed February 26, 2007), 34.

- 82. Deposition of James F. Pankow, 217
- 83. "Second Annual Ammonia Technology Conference," 3 (emphasis in original).
- 84. William A. Farone, e-mail and telephone communication with Terrell Stevenson, November 17, 2005.
- 85. Jeffrey Wigand, e-mail communication with Terrell Stevenson, November 8, 2005.
- 86. "Effects of Cigarette Smoke 'pH."
- 87. David A. Kessler, A Question of Intent: A Great American Battle with a Deadly Industry (New York: Public Affairs, 2001).
- 88. Farone, e-mail and telephone communication, November 17, 2005.
- 89. Gladys Kessler, "Final Opinion," *USA v. Philip Morris USA et al.*, August 17, 2006, https://ecf.dcd.uscourts.gov/cgi-bin/show_public_doc?1999cv2496-5732 (accessed February 26, 2007).
- 90. Claude Teague, "Proposal of a New, Consumer-Oriented Business Strategy for RJR Tobacco Company," RJ Reynolds, September 19, 1969, Bates no. 500915701-5719, http://legacy.library.ucsf.edu/tid/drr59d00 (accessed February 26, 2007), 9.
- 91. Hiram R. Hanmer to Mrs. Keith Shipley Sutton III, American Tobacco, October 14, 1955, Bates no. 950738681-8682, http://legacy.library.ucsf.edu/tid/fbv51a00 (accessed February 26, 2007), 2.
- 92. Teague, "Implications and Activities," 2.
- 93. Johnson, "Ammonia Technology Conference," 11.
- 94. Gregory N. Connolly et al., "Trends in Smoke Nicotine Yield and Relationship to Design Characteristics Among Popular U.S. Cigarette Brands," Harvard School of Public Health, 2007, http://www.hsph.harvard.edu/nicotine/t rends.pdf (accessed January 1, 2007).
- 95. R.N. Proctor, "Tobacco and the Global Lung Cancer Epidemic," *Nature Reviews Cancer*, 1 (2001): 82–87.
- 96. Charles R. Green and Alan Rodgman, "The Tobacco Chemists' Research Conference: A Half Century Forum for Advances in Analytical Methodology of Tobacco and Its Products," RJ Reynolds, June 26, 1996, Bates no. 525445600-5772, http://legacy.library.ucsf.edu/tid/qzt82a00/pdf (accessed February 26, 2007). 7
- 97. Robert N. Proctor, *The Nazi War on Cancer* (Princeton, NJ: Princeton University Press, 1999).