BEFORE THE

UNITED STATES FOOD AND DRUG ADMINISTRATION

DOCKET NOS. 95N-0253, 95N-0253J

COMMENTS OF PHILIP MORRIS INCORPORATED
ON STATEMENTS FILED BY FDA ON MARCH 18, 1996

The Agency has reopened the comment period on its analysis regarding purported FDA jurisdiction over "nicotine-containing" cigarettes to permit comments on "declarations" from three former Philip Morris employees that "FDA might rely on . . . in support of any final decision it might make on its jurisdiction." 61 Fed. Reg. 11,419 (March 20, 1996).[1] According to the Agency, these declarations describe "the industry's understanding of nicotine and industry practice with respect to the control of nicotine levels in cigarette manufacture." Id.

As described below, in the accompanying comments of the industry as a whole, and in the comments previously filed on January 2, 1996, a great many of the factual propositions

[1] Philip Morris contends that FDA's assertion of jurisdiction over cigarettes and the initiation of this rulemaking are an unlawful usurpation of authority that Congress has reserved to itself or delegated to other state and federal agencies. Philip Morris, along with other manufacturers, has filed a legal action against this proceeding. By submitting these comments, Philip Morris does not waive its objection to FDA's authority to proceed with this rulemaking.

Perhaps most importantly for present purposes, Dr. Uydess had no role in the formulation of any brand of Philip Morris cigarettes, much less with Philip Morris' marketing of those products. Nor, of course, can Dr. Uydess say anything about what has transpired at the company over the last seven years -- and thus his "understandings" are outdated at best.

Quite apart from all of these problems, Dr. Uydess' speculative charges are simply not true. In the pages that follow, we respond to his allegations, more or less in the order in which they were presented.

A. Nicotine And The Design Of Commercial Cigarettes

At various points in his declaration (Paragraphs 7-15, 21), Dr. Uydess states that "to the best of [his] knowledge" "nicotine has always been an important consideration to Philip Morris in the design, development and manufacturing of cigarettes." This overt hedging by Dr. Uydess -- which occurs at the beginning, middle, and end of his declaration -- is significant because, in fact, he was not involved in the design of Philip Morris' commercial cigarettes. Nor was he involved in any research that focused on nicotine, except, as described below, to the extent he reviewed work on the possible development of a low nicotine species of tobacco.

It is thus quite telling that at no point in his declaration does Dr. Uydess ever identify any specific Philip

Morris cigarette that was "targeted" or "manipulated" to achieve some preordained nicotine yield. To be sure, he speculates that "[w]henever nicotine, or any other major component (such as sugars, tars, etc.) had to be adjusted by Philip Morris in a new or existing product, it was frequently a matter of knowing which tobaccos to use in the blend to make the necessary (targeted) adjustments." Uydess Declaration at 8. But in making such a vague and general statement, Dr. Uydess fails to provide any specifics that would demonstrate that Philip Morris ever attempted to maintain (much less increase) nicotine levels independently of those other well-known natural constituents of tobacco. Rather, he confuses the issue by recounting snippets of what he claims to have overheard during coffee breaks and then leaves the reader to draw some illicit conclusion. The facts, however, show just how invalid his generalized speculations are.[6]

For example, in Paragraph 12 of his declaration, Dr. Uydess notes that Philip Morris scientists understood that nicotine had something to do with a cigarette's "impact". Dr. Uydess concedes that the term "impact" relates to "the feeling that the smoker experiences at in [sic] the back of the throat immediately upon inhaling a nicotine-containing cigarette." Uydess Declaration at 12. Philip Morris agrees with that definition and with the well-known fact that nicotine, in addition to imparting a taste

[6] Tobacco blending -- the only "technique" cited by Dr. Uydess to support his general claim of "nicotine targetting" -- is addressed at length in the Industry Comments at IV-65 to IV-72.

sensation on the tongue and an aroma sensation in the nose, has such an effect on the back of a smoker's throat -- a sensation that many smokers desire (just as many consumers enjoy the throat "impact" of hot peppers or carbonated soft drinks).[7]

Philip Morris, however, disputes Dr. Uydess' alternative contention that the term "impact" is also "used by the tobacco industry" to describe a second "somewhat more complicated (and delayed) physiological effect which apparently results from the interaction of nicotine with receptor sites in the brain." Uydess Declaration at 12. It is significant that Dr. Uydess does not provide any specifics to support his very different alternative interpretation of the term.

In Paragraph 13 of his declaration, Dr. Uydess similarly obscures the issue of nicotine's contribution to the acceptability of a cigarette in describing an internal meeting at which disappointing test market results of a low-yield cigarette were discussed. He notes that some consumers had reported that the new product was "missing something." Uydess Declaration at 12. Yet, even Dr. Uydess must acknowledge that the particular product under discussion was a low-"tar", as well as a low-nicotine, cigarette -- and that "tar", as well as "tar"-to-nicotine ratios, "were also discussed" at the meeting he apparently attended. Id. at 12-13.

---

[7] See Industry Comments at III-112 to III-121.

The fact that Philip Morris employees may have noted the lower yields of "tar" and nicotine in connection with the commercial failure of a low-yield product is, of course, hardly surprising. As described in greater detail in the Industry Comments, those inside (as well as outside) the industry have long known that both "tar" and nicotine contribute to the flavor of a cigarette and that, as a general rule, a low-"tar"/low-nicotine product will have less flavor. Industry Comments at III-112 to III-121. But such a general discussion can hardly be extrapolated, even by Dr. Uydess, to argue that people smoke "nearly exclusively" for the pharmacological effect of nicotine, that the contribution of "tar" and other flavors to the smoking experience is irrelevant, or that those at Philip Morris who discussed this particular low-"tar"/low-nicotine product accepted either of those extreme propositions.

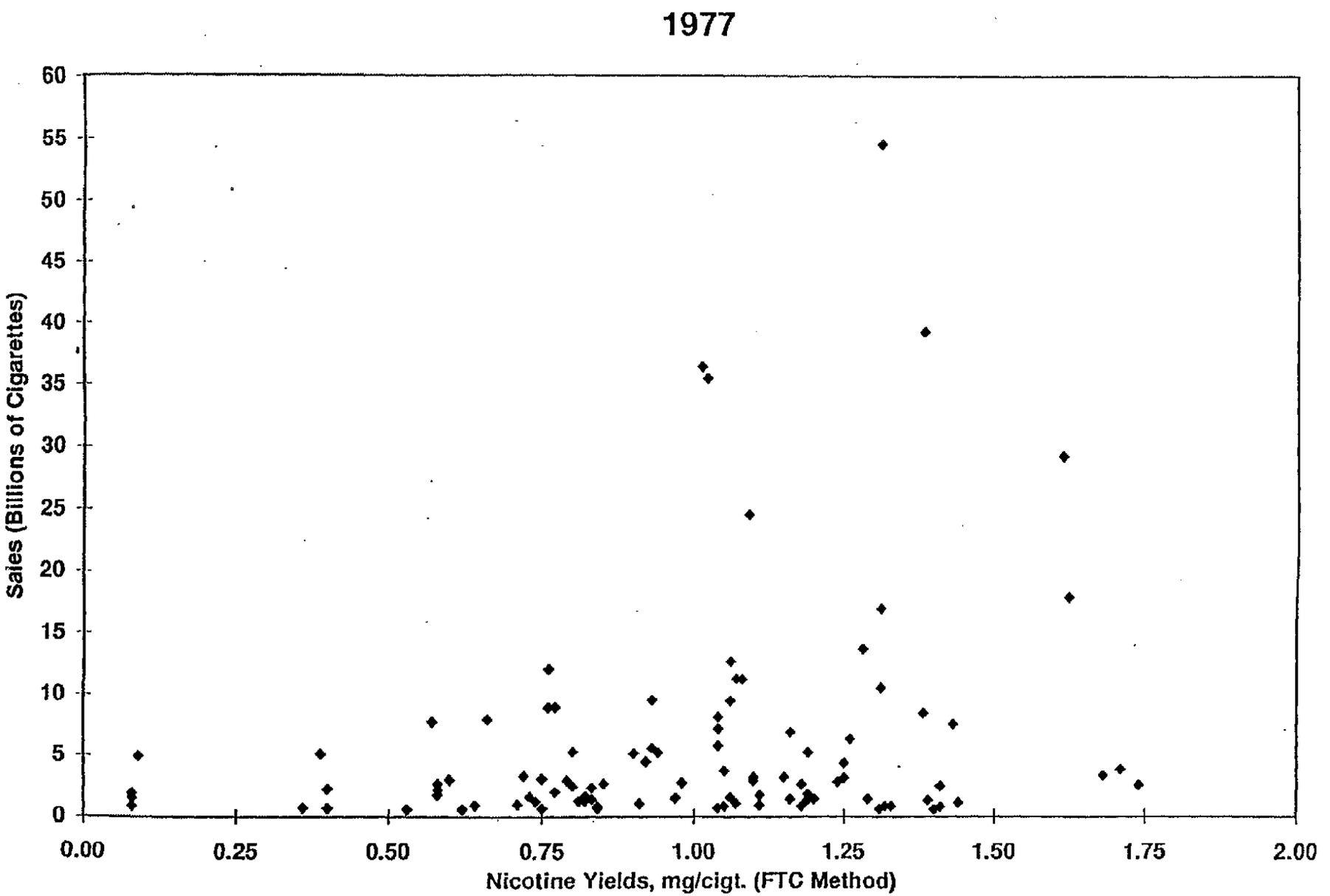
At various points Dr. Uydess does suggest that he is generally aware of some relationship between nicotine yields and consumer acceptance of particular cigarettes. But here too his vague recollections and speculations simply cannot withstand scrutiny.

For example, in Paragraph 14 of his declaration, Dr. Uydess refers to a graph he apparently saw "during an informal discussion at Philip Morris that generally correlated nicotine level to product acceptability." Uydess Declaration at 13. He concedes that this graph did not (as some anti-tobacco critics have suggested) predict a direct relationship between nicotine yield

and sales, such that sales continue to increase as nicotine yields increase -- as one would predict if people truly "smoke for nicotine." Rather, Dr. Uydess recalls that the informal graph showed that there was a "high" as well as a "low" limit which indicated "at least in a general manner, the range of nicotine levels over which adequate product acceptability (market share) was believed to occur." Uydess Declaration at 13.[8]

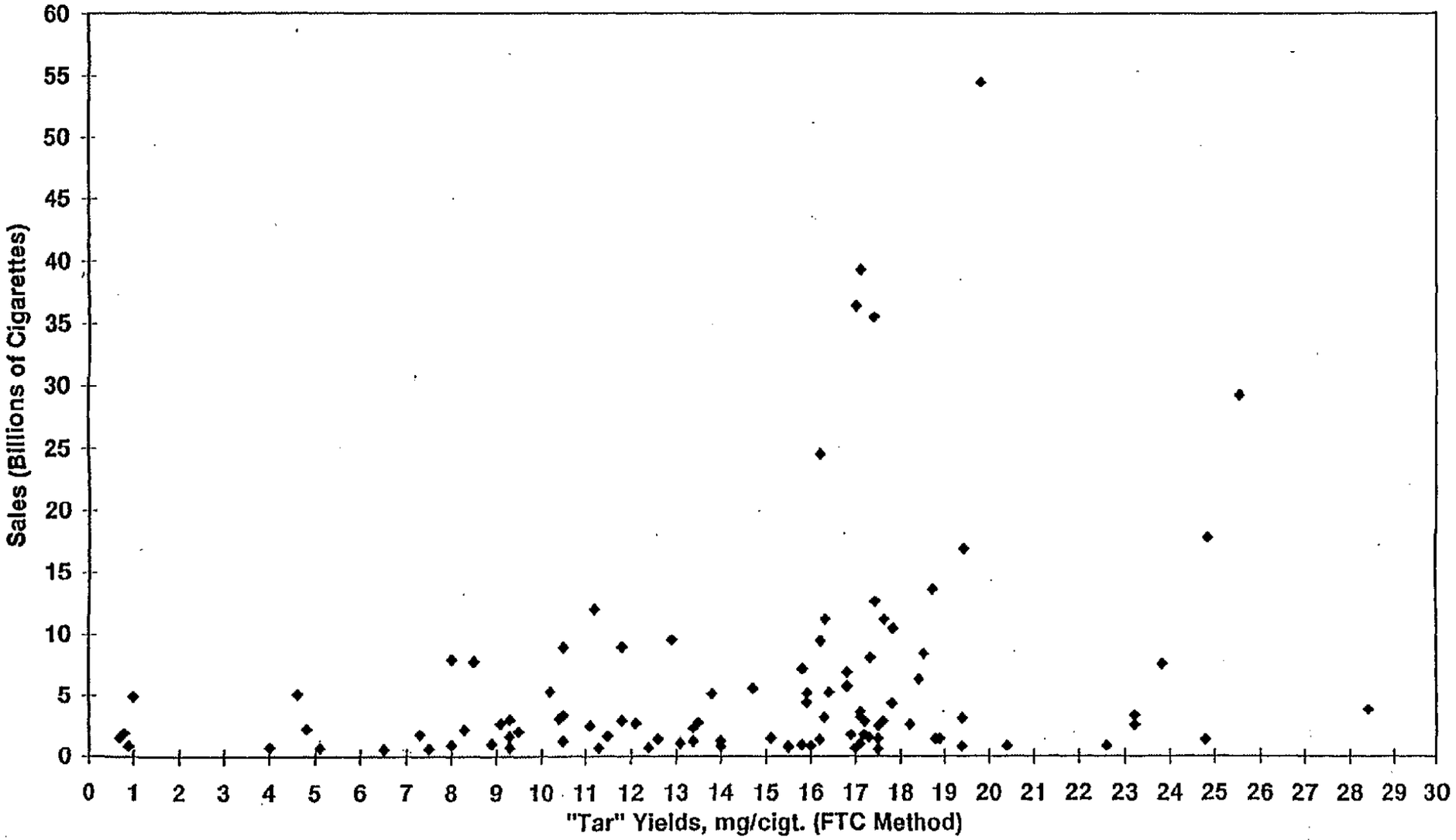
Yet actual market share data -- rather than some "informal" graph Dr. Uydess may have seen ten or fifteen years ago -- do not support the notion that, even within some "general" middle range, a cigarette's sales can be predicted by its nicotine yield. As the following charts demonstrate, whether one selects 1977 (the year Dr. Uydess came to Philip Morris), 1989 (the year he left), or 1995 (the last year for which FTC test data are available), one cannot predict a cigarette's sales failure or success based on nicotine yields.

[8] Although Dr. Uydess then drops any further reference to the upper limit on nicotine yields and smoker acceptance, his recollection is that a cigarette which yields too much nicotine was also likely to be unacceptable to smokers. The Agency's jurisdictional theory, by contrast, would suggest that a "nicotine delivery device" would be all the more acceptable to consumers as nicotine levels increased -- or, at least, that all products would be equally acceptable above a certain "minimum threshold." As even Dr. Uydess recognizes, that is simply not the case.



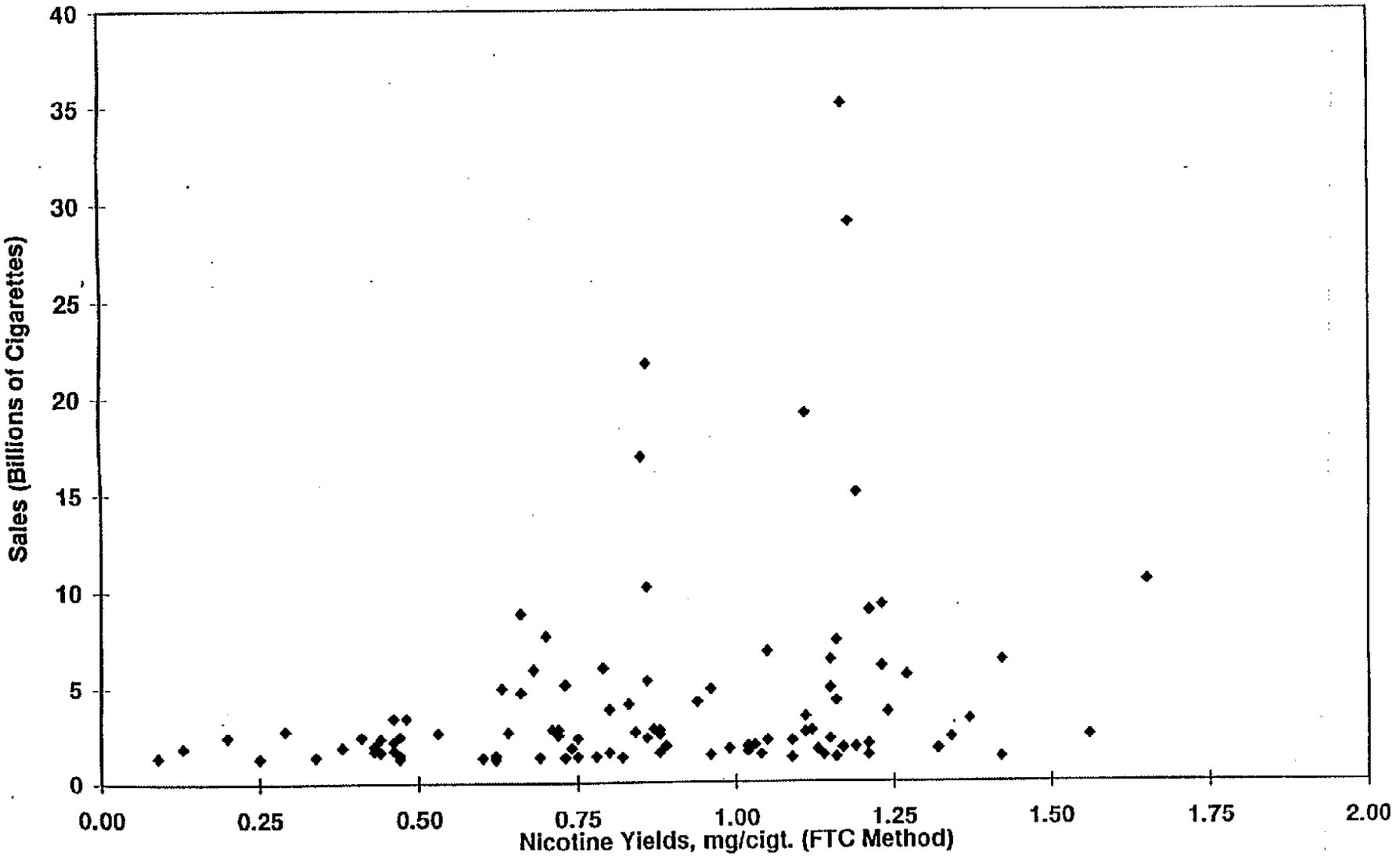
2078124101

1977



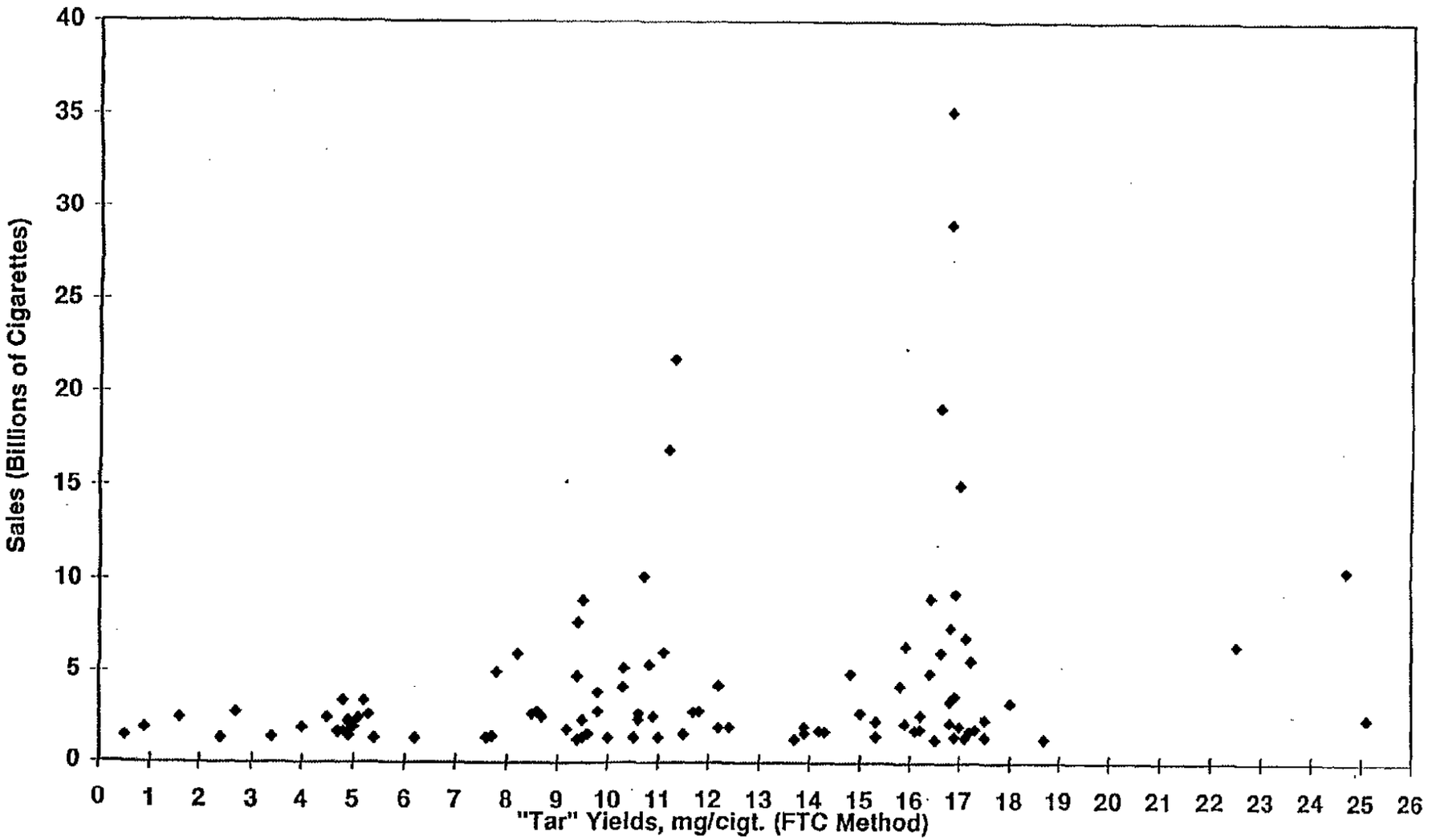
2078124102

1989



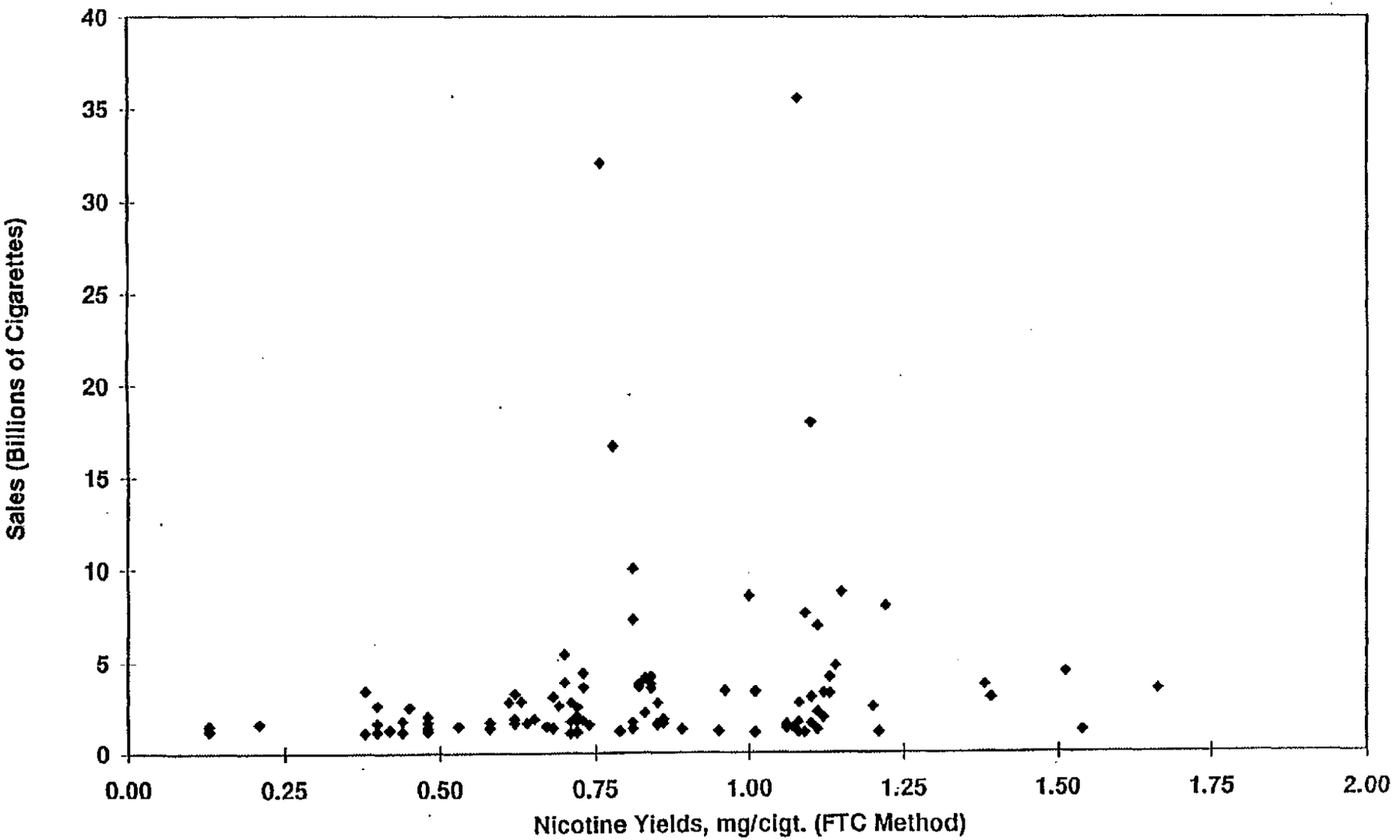
2078124103

1989



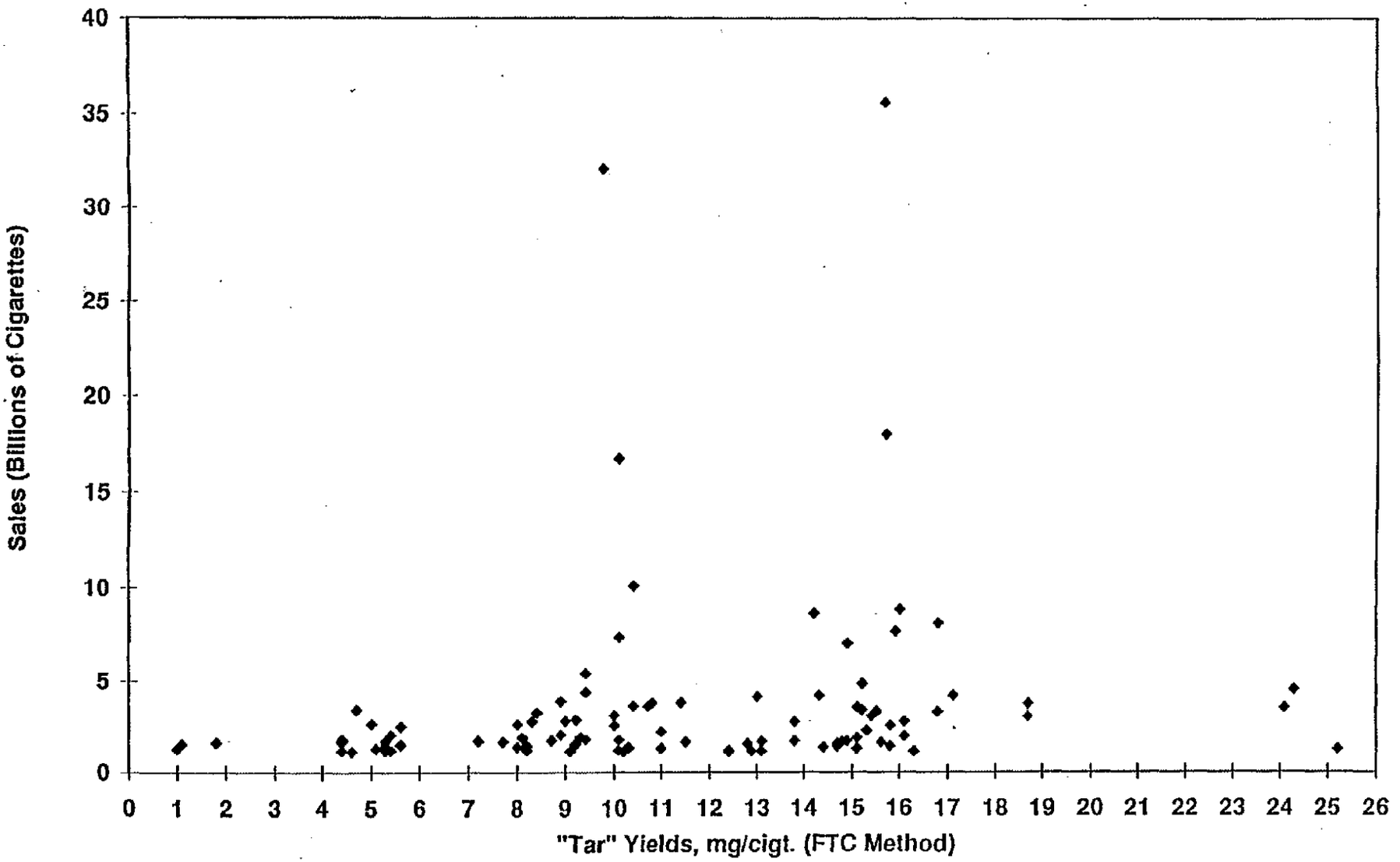
2078124104

1995



2078124105

1995



2078124106

As these scatter-plots plainly show, while there are successful brands in the middle nicotine ranges, other products with exactly the same nicotine yields fare very poorly in the marketplace. Clearly, cigarette consumers make their purchasing decisions on the basis of attributes other than nicotine yields.

Conversely, the success of a number of brands with far lower nicotine yields -- brands which, in many cases, are far more successful than brands with higher, supposedly "optimal" nicotine yields -- confounds any attempt to predict sales on the basis of nicotine yields. For example, as early as 1977, TRUE, a cigarette manufactured by Lorillard, had achieved the rank of 32nd among the 152 packages for which data was available, even though it yielded only .39 mg of nicotine.[9] TRUE thus substantially outsold more than 100 other brand-packages that had higher nicotine yields -- including many with the "magic" level in the middle range suggested by Dr. Uydess. Similarly, in 1989 Reynolds sold substantial numbers of a version of its NOW cigarette (48th on the list of 293 brand-packages) despite the fact that those cigarettes yielded only .2 mg of nicotine. That same year American's ultra-low yield Carlton 100s (.13 mg nicotine yield) ranked 64th out of 293 brand-packages for which data was available.

---

[9] The sales information -- and brand rankings -- are taken from the Management Science Associates ("MSA") database. That database provides sales figures as reported to MSA by each manufacturer. Each different package (e.g., soft-pack, hard-pack, king-size) for each different brand name (e.g., Marlboro) is given a separate ranking.

The success of low, and even ultra-low, cigarettes is even more true today. For example, in 1995, Doral Ultra Lights 100 ranked 27th among 457 brands for which data was available -- that is, it outsold more than 90% of the brands on the market -- even though it yielded only .38 mg of nicotine per cigarette. Philip Morris' own Merit Ultra Lights, which yields only .44 mg of nicotine per cigarette, similarly ranked 54th and outsold Philip Morris' regular Merit brand-package (58th) which yielded more nicotine (as well as more "tar"). And the continued sales of such ultra-low brands as Carlton (ranking 67th among the 457 brand-packages), with barely detectable nicotine yields, continue to confirm that cigarettes are sold across the whole spectrum of nicotine yields.

The point, of course, is not to dispute the fact that most cigarettes, including the most popular brands, fall within a broad "middle range" in terms of their "flavor" or "strength" -- just as most people prefer peppers that are neither too spicy, nor too bland, and apples that are neither too tart, nor too sweet. But, as these scatter-plots clearly demonstrate, the same cigarettes fall within a similar middle range in terms of their "tar" yields as well, because "tar" and nicotine are so closely linked. Neither the Agency nor Dr. Uydess has any evidence to suggest that consumers are preferring those products because they are in some broad mid-range in terms of their nicotine yields as opposed to the fact that they are equally in the mid-range of "tar" and hence overall flavor or "strength".

Moreover, as a result of changing tastes of American consumers and the response of manufacturers to those changing tastes, both the overall sales-weighted yields of "tar" and nicotine, and the specific profiles of the most successful brands, have declined over time. Compare charts for 1977, 1989, and 1995 which show a shift to lower "tar" and nicotine yields. This undeniable fact is further evidence that the cigarette manufacturers are not increasing (or even assiduously maintaining) nicotine yields, as one would expect if they truly accepted the proposition that higher nicotine yields mean higher sales.

Indeed, even Dr. Uydess does not suggest that his views, which he may have gleaned from an informal graph shown at a coffee break, on the relationship between nicotine yields and sales was somehow Philip Morris corporate policy. As he acknowledges, "[s]ome participants at this meeting forwarded the idea that the flavor group could overcome these 'problems', while others held fast to their belief that the data 'spoke for themselves.'" Uydess Declaration at 13. In this respect, Dr. Uydess' declaration is thus entirely consistent with the statements previously made by Philip Morris that various individuals at the company believed that people smoke for many reasons, not solely for nicotine; that others at Philip Morris who, unlike Dr. Uydess, actually develop new cigarettes, therefore work very hard on flavor substitutes to create acceptable low-"tar" and low-nicotine products; and that Philip Morris has not "manipulated" the nicotine yields of its commercial cigarettes.

Finally, Dr. Uydess has failed to put Philip Morris' nicotine-related research, especially with respect to the theoretical possibility of cigarettes with altered nicotine yields, into a proper historical context. He forgets (or perhaps never knew) that a number of government officials and non-industry scientists in the 1970s advocated the development of a cigarette with higher-than-average nicotine-to-"tar" ratios. These proponents of a low-"tar"/high-nicotine cigarette suggested that the American manufacturers investigate the possibility of such a cigarette.

For example, in 1977 the National Institutes of Health, through the Smoking and Health Program of the National Cancer Institute, reported that NCI would study experimental low-"tar" cigarettes with "relatively high" nicotine yields:

> "Consideration is being given to the design of experimental low tar cigarettes yielding relatively high nicotine. . . . Designs being considered involve cigarettes with tar/nicotine ratios less than 10. Several problems are being considered; e.g., the source and nature of the nicotine to be used, the role of extenders to influence nicotine delivery, safety of extenders and the type of tests that should be conducted."[10]

Similarly, in 1976 researchers funded by the American Cancer Society recommended that smokers be "encourage[d] to switch to cigarettes with a high yield of nicotine relative to tar and

---

[10] *Smoking and Health -- Status Report December 1977.* National Cancer Institute, National Heart, Lung and Blood Institute, National Institutes of Health 33 (1978). (This article and all other articles cited in these comments are provided in the accompanying Appendices.)

carbon monoxide."[11] The ACS researchers publicly thanked Philip Morris for providing experimental cigarettes used in their study.[12] As described by the ACS researchers, these were "special cigarettes yielding amounts of nicotine and tar that are not correlated."[13] Clearly, Philip Morris did not try to hide the fact that it had assisted the ACS researchers in such an investigation of the theoretical possibility of creating experimental cigarettes with altered nicotine-to-"tar" ratios.

Last, but certainly not least, the Surgeon General himself in 1981 advocated research into the development of a low-"tar"/ medium-nicotine cigarette:

> "It is necessary to evaluate cigarettes with lower tar to nicotine ratios than are currently found in the market place. . . . A low ratio might be a desirable strategy for lower risk cigarettes."[14]

The Surgeon General elaborated that

> "Variations in 'tar' to nicotine ratios should be of special concern. It is important to determine the lowest ratios that still produce a satisfying cigarette. Obviously, identical tar and nicotine ratios can occur in cigarettes that have very different standard nicotine yields. Research could show if there is an optimum combination of

---

[11] Goldfarb T., Gritz E., Jarvik M.E., et al. *Reactions to Cigarettes as a Function of Nicotine and "Tar."* Clinical Pharmacology and Therapeutics 19(6): 767-772, 771 (1976).

[12] Id.

[13] Id. at 767.

[14] U.S. Department of Health and Human Services. The Health Consequences of Smoking: The Changing Cigarette, A Report of the Surgeon General. U.S. Gov't Printing Office, 1-252, 58 (1981) (emphasis added).

> standard yield and ratio that leads to maximum satisfaction and minimal exposure to toxic products. Cigarettes that vary systematically in tar to nicotine ratios are needed for this research."[15]

It is thus hardly surprising that Philip Morris conducted basic research relating to nicotine, including varying nicotine-to-"tar" ratios, when the Surgeon General, NIH, and many others called for such work. But the even more important point for purposes of this rulemaking is that the unsupported speculation in Dr. Uydess' declaration that this and other nicotine-related research was used to increase the nicotine yields of commercial cigarettes is simply not true. None of this basic research was ever used by Philip Morris to increase nicotine yields in a commercial cigarette. And, for that reason alone, all of this speculation is simply irrelevant to these proceedings.

B. Philip Morris' Knowledge About Tobacco and Agricultural Technology

Dr. Uydess devotes considerable space in his declaration to Philip Morris' knowledge of, and research on, the tobacco plant. For example, Dr. Uydess reports that Philip Morris maintained information about the "various chemical, mechanical and agronomic properties of the tobaccos it used in its products." Uydess Declaration at 9.

This is true -- but hardly surprising. Like FDA in some of its prior remarks on such agricultural research, Dr. Uydess

---

[15] Id. at 184-185 (emphasis added).

official wrote some 16 years ago:

> "The tobacco plant has been the object of extensive basic research and much is known of its genetics, culture, physiology, biochemistry, and post-harvest metabolism."[18]

Indeed, as discussed below, the specific types of research and expertise noted by Dr. Uydess were all the subject of published articles well before Philip Morris conducted its studies.

Finally, and most importantly, Philip Morris' "chemical, biological and engineering" expertise on the basic tobacco plant has never been used to increase artificially the nicotine yield of its commercial cigarettes. Again, for all of its sound and fury, Dr. Uydess' review of this Philip Morris "expertise" proves nothing about the cigarettes the company actually sells (much less the claims it makes for those cigarettes -- the only relevant basis for any assertion of FDA jurisdiction).

1. Ratooning

Dr. Uydess' revisionist history is evident in his account of Philip Morris' limited research on the agricultural process

---

[Footnote continued from previous page]
we conducted a simple search of just one well-known database -- Biosis Previews. We have provided in the accompanying Appendices a list of over 200 articles on tobacco biology and chemistry in that one database that were published at, or before, the time Dr. Uydess worked at Philip Morris. A full search of similar publication lists by the various state extension services, public and private universities, and the research community at large would, of course, show many more publications.

[18] Tso T.C. *Modification Through Agricultural Techniques for Developing a Safer Tobacco.* In: Gori G.B., Bock F.G. (eds.) Banbury Report: A Safe Cigarette? 181-190, 188 (1980).

known as "ratooning." In Paragraph 17 of his declaration, Dr. Uydess claims that Philip Morris used "ratooning" to develop "nicotine-enriched" tobacco. That charge is false.

"Ratooning" was not used by Philip Morris with any intent to increase nicotine content in tobacco; the process in fact did not result in "nicotine-enriched" tobacco; and Philip Morris never used this technique (or any other) to grow high-nicotine tobacco for use in any commercial product. Indeed, as Dr. Uydess and FDA so often seem to forget, it is tens of thousands of individual tobacco farmers, not Philip Morris, who grow the tobacco used in Philip Morris cigarettes.

First, as a general matter, ratooning is not used to increase the nicotine content of tobacco, but rather is simply a process that can be employed, under unusual circumstances, to obtain a second crop from many types of plants. As described by one source, "ratooning is the severing of the stem of each tobacco plant at 5-15 cm above ground level, and the fostering of growth of one remaining axillary bud by the removal of others that develop."[19] Thus, a "new" plant is grown from the original root system. The procedure is sometimes used in tropical areas to achieve a second tobacco crop; it may also be used to salvage a

---

[19] Whitfield D.M. *Effects of Simulated Hail Damage on Yield and Quality of Flue-Cured Tobacco.* Aust. J. Exp. Agric. Husb. 22:244-248, 244 (1982).

crop that has been cut down prematurely following significant hail damage.[20]

Ratooning is not a viable commercial process for tobacco farmers in most of the tobacco-growing areas of the United States where the overall growing season is not long enough to permit two successive crops. On average, tobacco in the United States takes about three to four months to mature. Yet, the available growing season in the tobacco states is only about four to five months long. To use "ratooning" on a commercial basis, American farmers would therefore need to harvest their first crop of tobacco leaves before the leaves were fully matured -- which would result in a valueless crop.[21] Any suggestion that Philip Morris (or anyone else) could have convinced the tens of thousands of independent tobacco farmers to follow such an uneconomic practice is ludicrous.

Indeed, for the past 30 years, ratooning to obtain two full crops would run afoul of the tobacco support program administered by the United States Department of Agriculture ("USDA"). The USDA closely regulates the production of tobacco and since 1965 has

---

[20] As one publication noted 40 years before Dr. Uydess "revealed" ratooning to FDA, after significant hail damage, "[i]t is generally better to grow a sucker from a strong root system than to plow up and plant later." Pointer J.P., Woltz W.G., McCants Co. *When Hail Hits Tobacco*. North Carolina Agricultural Extension Service Circular No. 398, 9 (1956).

[21] As noted in one publication, ratooning tobacco before the first crop's leaves have "ripened sufficiently to be cured" is potentially disastrous: "The fresh leaf therefore has no potential value and crops may have to be abandoned." Whitfield D.M. at 244.

limited the quantity that may be sold. Burley tobacco is controlled by a strict poundage quota, 7 U.S.C. § 1314e, while flue-cured tobacco is controlled by an acreage-poundage quota. 7 U.S.C. § 1314c. The use of ratooning under such weight-based quota systems would make no economic sense because a farmer would need to expend additional labor to harvest two "crops" and yet would still be limited in the amount that he could produce for market.

Second, ratooned tobacco simply does not have higher nicotine content than non-ratooned tobacco. As shown by documents that were reviewed by Dr. Uydess, among others, the very Philip Morris research he notes found that ratooned tobacco was generally lower in total alkaloid content than non-ratooned tobacco.

Philip Morris' ratooning experiments were conducted to determine whether the ratooned tobacco had different characteristics than those of tobacco grown under normal conditions. In addition to examining physical characteristics, routine chemical analyses were conducted on the ratooned tobacco. These analyses measured many constituents -- both "desirable" and "undesirable" -- including, among other things, nitrates, sugars, starch, hot water solubles and alkaloids.[22] The chemical analyses were not conducted for the purpose of determining whether the

[22] *Project 1720 - Tobacco Microstructure "Trends in Greenhouse and Field Tobacco Surface Morphology and Field Tobacco Chemistry"* at 9-10 (Nov. 22, 1982) (distributed to Ian Uydess, among others). (The relevant portion of this and other Philip Morris documents cited herein are provided in the accompanying Appendices.)

ratooned tobacco was "nicotine enriched"; they merely reported nicotine as one of many variables.

Dr. Uydess states that these ratooning experiments "produced tobacco leaves that had higher nicotine levels than the leaves of non-ratooned plants." Uydess Declaration at 15. This is one of the few statements in his declaration which Dr. Uydess does not hedge with a string of qualifiers. It is therefore quite telling that this statement is refuted by the very documents Dr. Uydess received. In fact, the alkaloid levels of the ratooned tobacco were generally lower than those of the non-ratooned "control" tobacco:

Measured Alkaloids[23]

	Control	Ratooned #1	Ratooned #2
1979			
Bottom stalk	2.33%	1.27%	1.86%
Middle stalk	3.28%	2.22%	2.54%
Top stalk	4.51%	1.87%	2.68%
1980			
Bottom stalk	2.15%	2.56%	2.64%
Middle stalk	4.47%	3.74%	3.91%
Top stalk	5.33%	3.50%	3.58%

For some stalk positions, the reduction in alkaloids was substantial -- as shown above, in the 1979 study the reductions ranged between 20% and 50%. The only increase in total alkaloids was seen in the bottom stalk position in the 1980 experiment. The overall figures from the two 1980 experiments for all three stalk

[23] Id.

positions showed a reduction by about 10% and 20%. This is hardly "nicotine-enriched" tobacco.

Finally, Dr. Uydess does not cite any instance of the use of ratooned tobacco -- or any other "nicotine-enriched" tobacco -- in any Philip Morris commercial cigarette. Indeed, he admits that he "do[es] not know if any nicotine-rich leaves that were produced through ratooning ever got into production." Uydess Declaration at 15. Dr. Uydess does not "know" because the fact is that the ratooned tobacco was never used by Philip Morris in commercial production.

As the Industry Comments previously explained, higher-nicotine content tobacco has been rejected by the tobacco companies, including Philip Morris.[24] An article quoted in the Industry Comments provides a few well-known examples:

> "During unusually dry seasons, the nitrogen content in U.S. grown tobaccos surges above desirable levels because total nitrogen and alkaloid values, even in normal years, are at the extreme upper end of the range. Buyers are apt to reject the drought-affected crops on a massive scale, as occurred in 1977 with flue-cured and in 1983 with Burley tobacco. Nicotine levels for much of the 1983 Burley Crop were reported to be well above 5 percent. Nearly half of the Burley tobacco grown that year is still stored in stabilization warehouses unsold."[25]

Why, if high-nicotine content tobacco was the "optimal" kind of tobacco, were tobacco farmers unable to sell high-nicotine

---

[24] Industry Comments at IV-64.

[25] DeJong D.W. *The Role of American Tobacco Leaf Chemistry in Low-Yield Cigarettes: An Agricultural Viewpoint.* Tabak J. Int'l. 376-83, 383 (1985) (emphasis added).

cultures can biosynthesize the alkaloids nicotine and anabasine."[36] Indeed, even the National Institutes of Health funded studies involving the somaclonal variation of nicotine in tissue cultures.[37]

Second, and more importantly, the goal of Philip Morris' tissue culture work was not the maximization of nicotine in tobacco plants. Early tissue culture research investigated the development in vitro of tobacco cells that had both high and low levels of nicotine. But, as Dr. Uydess should recall, this initial work was done solely to determine whether the process of somaclonal variation seen in cells was expressed in plants regenerated from those cells. It never led to the development of a high-nicotine content tobacco for commercial purposes. To the contrary, one goal of the nicotine-related tissue culture project was to develop a reduced nicotine plant.

Dr. Uydess misleadingly states that "[a] variety of cultural techniques (including variations in growth conditions, nutrients, plant hormones, etc.)" were used to "maximize" the production of "targeted materials," which he defines as nicotine.

---

[36] Staba E.J. *The Biosynthetic Potential of Plant Tissue Cultures.* Developments in Industrial Microbiology 4:193-198, 193 (1963).

[37] Kinnersley A.M., Dougall D.K. *Correlation Between the Nicotine Content of Tobacco Plants and Callas Cultures.* Planta 149:205-206, 206 (1980) (thanking NIH "for supporting this work through Grant No. GM 25994").

Kinnersley A.M., Dougall D.K. *Variation in Nicotine Content of Tobacco Callus Cultures.* Planta 154:447-453, 452 (1982) (thanking NIH "for supporting this work through Grant No. GM 25994").

Uydess Declaration at 16. What Dr. Uydess is presumably referencing are the attempts to "grow" cells that expressed nicotine in measurable amounts in cultures. As reported in the published scientific literature, nicotine, like other secondary metabolites, is not readily produced by tobacco cells in vitro.[38] To measure any variation or difference among the cells' nicotine production -- whether to develop a somaclone which is more or less efficient at expressing nicotine -- it is necessary that the cells generate measurable amounts of nicotine in vitro. Philip Morris researchers therefore used a variety of cultural techniques -- such as the use of hormones and nutrients -- to encourage (or, as Dr. Uydess puts it, "maximize") the production of nicotine in vitro. But those techniques were nothing more than standard procedures to encourage cell growth in cultures.[39]

Dr. Uydess' suggestion that the "overall goal" of the tissue cultures was the "optimization" of nicotine in tobacco plants is wrong. In fact, just the opposite was true. As the

---

[38] See Lockwood G.B., Essa A.K. *The Effect of Varying Hormonal and Precursor Supplementations on Levels of Nicotine and Related Alkaloids in Cell Cultures of Nicotiana Tabacum*. Plant Cell Reports 3:109-111, 109 (1984).

Pinol M.T., Palazon J., Serrano M. *Growth and Nicotine Content of Tobacco Callus Cultures Without Organogenesis*. Plant Science Letters 35:219-223 (1984).

[39] Hutchins E.M. *Micropropagation of Tobacco*, Carolina Tips 47(9):34 (Sept. 1, 1984) (recommending the use of "macronutrients" and "hormones" to encourage the growth of tobacco cells in vitro).

final report on this project states, the goal was to produce tobacco with reduced levels of nicotine:

> "The goal of producing a burley tobacco plant with reduced green leaf nicotine levels was pursued through the techniques of somaclonal variation.
>
> * * * *
>
> "Reducing the nicotine level in green tobacco leaf has been a continuing challenge. Other than classical breeding techniques, which are very time consuming, or chemical manipulation of the cured leaf, no method is known which might accomplish this goal. The plant tissue culture laboratory took on this challenge with the goal of producing a burley (Kentucky 10) tobacco plant with reduced green leaf nicotine levels and acceptable subjectives through somaclonal variation."[40]

Dr. Uydess' description of the related work conducted for Philip Morris on a contract basis by Crop Genetics International is equally misleading on this fundamental point. Dr. Uydess correctly states that Crop Genetics entered into a joint venture with Philip Morris "to explore the application of plant tissue culture and cloning techniques to the selection/regeneration of tobacco plants with 'most desirable' characteristics (characteristics selected/targeted by Philip Morris)." Uydess Declaration at 16. But Dr. Uydess does not identify the specific characteristics that were "targeted" by Philip Morris. To be sure, he implies that Philip Morris was looking to maximize nicotine content; but even he does not say that per se.

---

[40] *Report Project 1730 - Plant Tissue Research* (Jan. 9, 1987) (emphasis added).

The truth is that while Philip Morris identified a number of desirable characteristics that it hoped Crop Genetics could develop in tobacco plants through somaclonal variation, none of those characteristics was high-nicotine content. Indeed, at one point, Philip Morris suggested that one desirable characteristic that might be pursued by Crop Genetics was a "low-alkaloid" tobacco plant.[41]

Last, but by no means least, even Dr. Uydess again admits that "[w]hile Philip Morris explored the potential (future) use of this and related technologies, they did not at that time employ it in the manufacture of any of their products." Uydess Declaration at 16 (emphasis added). In fact, Philip Morris has never used biotechnology to increase the nicotine levels in tobacco plants that were then used in commercial cigarettes. Once again, this basic research is thus entirely irrelevant to any assertion of FDA jurisdiction.

C. Research On Nicotine Analogs And The Research of Dr. DeNoble

In Paragraphs 19 and 20 of his declaration, Dr. Uydess alludes to Philip Morris research projects in which he was not involved to try to suggest that the company had concluded that nicotine is "addictive." Uydess Declaration at 16-17. In fact,

---

[41] Letter from W. Farone to Crop Genetics International, attaching list of projects of interest to Philip Morris (July 18, 1983).

jurisdiction over cigarettes would itself be arbitrary and capricious.

III. THE RIVERS DECLARATION

Because the issues presented by the declaration of Jerome Rivers, a former supervisor in Philip Morris' Blended Leaf Plant, are so clear-cut and capable of objective refutation, our comments on that document will be quite brief.

Mr. Rivers' declaration makes three essential allegations: first, that while he was working at Philip Morris' Blended Leaf Plant, that facility was monitoring or measuring for alkaloids or nicotine on a daily basis as part of the blended leaf manufacturing process and was using a gas chromatograph in the laboratory in the Blended Leaf Plant to do so (Rivers Declaration at 2-3); second, that Philip Morris had alkaloid or nicotine "standards or 'specs'" for the blended leaf product (Rivers Declaration at 3); and third, that Philip Morris' other reconstituted tobacco plant, the Park 500 facility at which a product commonly referred to as "reconstituted leaf" was made, also used a gas chromatograph to monitor or measure for alkaloids or nicotine in that process. Rivers Declaration at 4.

These allegations are false. As set forth in the accompanying affidavits of Jerry Bazemore and John Whitman, which address the specific practices at the Blended Leaf and Park 500 reconstituted tobacco manufacturing facilities:

1. At no point in the manufacture of blended leaf does the Blended Leaf Plant or its laboratory monitor or measure for alkaloids or nicotine -- whether by gas chromatograph or by any other instrument or device. Bazemore Affidavit ¶ 4; Whitman Affidavit ¶ 3.

2. Nor does Philip Morris have a "standard or 'spec'" for the alkaloid or nicotine content of the blended leaf product. Bazemore Affidavit ¶ 5; Whitman Affidavit ¶ 3. Mr. Rivers is thus flatly wrong when he charges that the Blended Leaf Plant conducted such nicotine testing, that there was a "standard or 'spec'" for nicotine, or that finished product was reprocessed when it was "out-of-spec" for nicotine. Bazemore Affidavit ¶ 5. Because there was no "spec" for alkaloids or nicotine, there was no "out-of-spec" for alkaloids or nicotine.

3. Mr. Rivers' hearsay account that Philip Morris was using a gas chromatograph at the Park 500 Plant "to measure the alkaloid content of the reconstituted leaf" is likewise untrue. The Park 500 facility did not, and does not, monitor or measure for alkaloids or nicotine in connection with the reconstituted leaf process -- whether by gas chromatograph or by any other instrument or device. Whitman Affidavit ¶ 3.

Contrary to Mr. Rivers' declaration, and as Philip Morris has previously stated publicly, nicotine in the tobacco used in Philip Morris' products is measured at only two points in the

cigarette manufacturing process -- before the tobacco materials are blended into cigarettes, and then after the tobacco materials have been made into finished cigarettes. Representative periodic sampling is done with respect to all tobacco materials that go into the cigarette manufacturing process -- natural leaf tobacco, expanded tobacco, as well as blended and reconstituted leaf. Such periodic sampling includes measurements of as many as 16 different characteristics of the tobacco materials, including alkaloids or nicotine. Subsequent to manufacture, representative samples of finished cigarettes are tested using the FTC-prescribed method for measuring "tar" and nicotine yields from smoke. None of these periodic sampling tests bears the remotest resemblance to Mr. Rivers' allegations of regular -- indeed, hourly -- monitoring of nicotine at the Blended Leaf Plant in order to manage the nicotine levels in the blended leaf process or product.

In short, Mr. Rivers is either grievously mistaken or deliberately stating something he knows to be untrue. In either case, as the accompanying affidavits demonstrate, it would be arbitrary and capricious -- if not outright irresponsible -- for the Agency to place any reliance at all on Mr. Rivers' statements.

IV. THE FARONE "REPORT"

The "report" by Dr. William Farone, a former Philip Morris employee who was discharged by the company in 1984, is essentially a rehash of prior charges made by various anti-tobacco critics. Philip Morris has already refuted most of these allegations and

speculations in its prior individual and joint industry submissions. In fact, most of Dr. Farone's more significant assertions are entirely undocumented. And where he does provide some citation, the documents and published literature he cites do not support his charges.

In the pages that follow, we will address a few points Dr. Farone asserts on the basis of certain specific Philip Morris documents.[79]

A. Dr. Farone's Contention that Nicotine Is a Principal Reason People Smoke

Dr. Farone makes repeated statements to the effect that the "cigarette industry" recognized or understood that consumers smoke solely because of the pharmacological properties of nicotine. Farone Statement at 1-3, 6-7. These statements are not supported by the documents Dr. Farone cites; and they are simply not true. As explained at greater length in the Industry Comments, consumers do not smoke cigarettes "nearly exclusively" for the pharmacological effects of nicotine. Rather, they smoke for many reasons, ranging from the flavor of tobacco smoke, to oral

[79] The other leading cigarette producers are joining with Philip Morris in responding jointly to certain statements by Dr. Farone about the "industry" as a whole. In other instances, Dr. Farone has referred to documents of manufacturers other than Philip Morris -- and indeed to statements made by companies which do not produce cigarettes at all -- and has attempted to relate them to every company in "the industry." We again remind the Agency that any decision on FDA jurisdiction must be made on an individual product-by-product basis -- and then only on the basis of statements made to the public in connection with the marketing of that specific product.

B. Low-Yield Cigarettes

Dr. Farone suggests that a key objective of cigarette manufacturers was to design a cigarette with reduced "tar" levels while maintaining an unidentified "acceptable" level of nicotine. In so doing, Dr. Farone attempts to give credibility to speculation and innuendo previously set forth by FDA by packaging it as the thoughts of an industry "insider." Yet Dr. Farone, like FDA, provides no specific basis for his claims and ignores the historical and scientific facts refuting his theories as previously set forth in the January 1996 Industry Comments. We will not belabor them here. But a few points merit specific comment.

Dr. Farone repeatedly suggests that manufacturers use various tobacco technologies to produce cigarettes with unnaturally high levels of nicotine. In most cases, however, Dr. Farone does not provide any specifics, much less any sources, to support this charge. And in the few cases where he does cite some source, the facts -- as recorded in that very document -- undercut his "nicotine theory".

For example, Dr. Farone recycles FDA's theory that cigarette manufacturers use the very design features that have indisputably resulted in dramatic reductions in "tar" and nicotine yields over the last 40 years to "manipulate" the ratio of nicotine to "tar" in marketed cigarettes. Like FDA, Dr. Farone ignores the scientific fact that the physics of these advances in cigarette design do not reduce "tar" and nicotine yields to

precisely the same degree -- a fact recognized in some of the very documents cited by Dr. Farone.[88]

Dr. Farone also recycles the allegation made almost a year ago by Congressman Waxman that one of Philip Morris' cigarettes, Merit Ultra Light, "was introduced in 1981 with an elevated tar-to-nicotine ratio of 0.11" -- a ratio Dr. Farone apparently believes shows some manipulative intent. Dr. Farone, however, does not provide any further information on this brand; rather, he simply cites Congressman Waxman's remarks.

By relying entirely on Mr. Waxman, Dr. Farone thus ignores the facts previously set forth by Philip Morris that (a) Merit Ultra Light was an ultra-low yield product; (b) according to the FTC, the nicotine yield of a Merit Ultra Light in 1981 was only .3 mg; (c) the .3 mg nicotine yield of Merit Ultra Light was the 20th lowest among the 206 cigarette brands tested by the FTC that year; and (d) the .11 "nicotine-to-tar" ratio of the Merit Ultra Light likewise was equal to, or lower than, every one of the 50 other low-yield products on the market that year.

Dr. Farone's blind acceptance of Mr. Waxman's charge likewise ignores the fact, described in detail in the industry's prior comments, that slightly elevated "nicotine-to-tar" ratios are a natural consequence of the substantial reductions in both "tar" and nicotine achieved by modern filters. As the industry

---

[88] See, e.g., "*Filter Material Reduces CO/Tar Ratio Without Pressure Drop*," Tobacco Reporter, 112(4):30-31 (April 1985). See also Industry Comments at IV-112 to IV-117; Philip Morris Comments at 40-44.

explained -- quoting published literature -- the more efficient filters and ventilation used on ultra-low yield products reduce "tar" to a somewhat greater degree than nicotine -- and hence increase slightly the "nicotine-to-tar" ratios of those ultra-low products.[89] Dr. Farone does not discuss or refute any of these facts; and his mere repetition of Mr. Waxman's unfounded charge does not give it any greater credibility.

Dr. Farone likewise fails to substantiate his contention that cigarette manufacturers have used flavors to "mask" enhanced nicotine deliveries. To "support" this contention, Dr. Farone cites only a single Philip Morris document which mentions that Philip Morris has used various flavors in its regular Merit brand.[90] But that document nowhere states that the purpose of those flavors was to mask higher nicotine yields. To the contrary, the document states that the purpose of the flavors was to provide an acceptable level of taste in a cigarette that had reduced tar and nicotine yields.[91]

Again, the facts undermine Dr. Farone's speculations. First, the regular Merit brand was, and still is, a low-yield cigarette. Using the same 1981 reference year, Merit, with a "tar" yield of 7 mg per cigarette and a nicotine yield of .5 mg per cigarette, was squarely in the low yield category (ranking

---

89 Industry Comments at IV-98 to IV-117.

90 Farone Statement at 10-11.

91 "Third Speaker, Merit Team" Remarks, Philip Morris, 2-3 (January 14, 1976).

50th lowest out of the 206 brands tested by the FTC that year in terms of its nicotine yield). The "nicotine-to-tar" ratio of Merit was thus .07 -- the level which FDA seems to believe is "natural".[92]

Indeed, that internal Philip Morris presentation further states that those at Philip Morris who developed Merit did not believe that it was a mere "nicotine delivery device" -- but rather that the explanations for the smoking habit were much more complex:

> "But what do smokers get out of cigarettes? We know it is a mistake to look for one source of the satisfaction of smoking. For example, the nicotine in tobacco smoke is often singled out, and it does act as a mild stimulant and a mild relaxant. In some way its moderate effects can be similar to those of coffee, tea, or cocoa.
>
> "But nicotine is an inexpensive tasteless constituent that can easily be consumed as a pill or in chewing gum and candy. In fact, those methods have been tested and they haven't been satisfying to smokers.
>
> "Obviously other satisfactions are also involved. They include -- to a greater or lesser degree depending on the individual smoker -- the oral satisfaction of puffing on a cigarette and the tactile sensations of handling it.
>
> "The original smokers, Indians, and more recently a number of poets expressed the belief that cigarette smoke offers passive satisfaction to people such as they may get from watching a sunset or a crackling fireplace.

---

92 Another way of looking at this undeniable fact is that, unlike the Merit Ultra Light which had the greater degree of filtration and ventilation of an ultra-low product which naturally increases a "nicotine-to-tar" ratio, the regular Merit had a less dense filter which allowed more of both "tar" and nicotine to come through.

> "But basically cigarettes provide a fundamental pleasure -- the simple enjoyment of the flavor of tobacco smoke.
>
> "Since the earliest days in the history of tobacco, flavor has been a critical factor.
>
> "Europeans first enjoyed tobacco in cigars and pipes. Because of flavor, cigar leaf from certain climates became preferred to others, and to this day tobacconists and pipe smokers constantly experiment with blends to achieve different flavors.
>
> "Cigarettes started to gain popularity in England in the latter half of the last century, and again flavor was significant.
>
> "Through the years, the flavor of cigarettes has been improved with the development of new strains of tobacco and, more recently, filtration and new blends. And the taste preferences of smokers have become much more refined as our cigarettes have become better. . . .
>
> "To a few, like the social smokers who light up cigarettes only at parties, the tactile sensation of holding and handling something seems to be the primary satisfaction they derive.
>
> "But the common denominator among the overwhelming majority of smokers is the enjoyment of flavor. This knowledge guided Philip Morris scientists as they achieved a great flavor breakthrough."[93]

Significantly, while the document goes on to discuss the fact that these flavor packages could compensate to some extent for the fact that the "tar" yield of the regular Merit was relatively low, there is not one word about the nicotine yield of that cigarette. The whole thrust of the document was that nicotine, while perhaps one component to some of the satisfaction

[93] Merit Team Second Speaker (Jan. 14, 1976) at 1003288908-910.