A Bold New Direction for Environmental Health Research

The biotechnology revolution has opened new opportunities for addressing current inadequacies in decision making regarding environmental health. Strategic investments need to be made (1) to develop high-throughput technologies that could accelerate toxicity testing and generate a mechanistic understanding of toxicity, (2) to incorporate individual susceptibility into risk assessments, and (3) to establish a rational basis for testing and regulatory decision making. New initiatives of the National Institute of Environmental Health Sciences, including the Environmental Genome Project and the Toxicogenomics Center, are discussed. (*Am J Public Health.* 2001; 91:1964–1967)

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INFORMATION IS THE BASIS of decision making in our private lives. For example, when it is time for many of us to buy a car or a house, we take great pains to study the market, examining factors such as reliability, safety, and resale value before committing ourselves to such a major investment. As a nation, however, we frequently make decisions about regulation of the levels of exposure to chemical and physical agents in the environment to protect human health—moves that cost the public and private sectors hundreds of billions of dollars—without adequate information. Are these policy decisions that affect the lives of hundreds of millions of Americans less important than the routine family matters just described? This critical lack of information is becoming more evident as we move into an era in which the biggest threats we face are from exposures to low doses of chemical and physical agents, not the high doses we have traditionally faced and tried to control.

Formal risk assessments of environmental and occupational health standards place an awesome burden on regulatory agencies, requiring a period as long as 10 to 15 years for assessment and implementation of some standards. Risk assessment is so difficult because all stages of the process (hazard identification, dose–response analysis, exposure assessment, and risk characterization) are fraught with uncertainty. Uncertainties lead to acrimonious debates among scientists, industry leaders, and public interest groups about the risks and management strategies proposed. These debates become so intense at times that the public must be confused about what is known and what is assumed. Fundamentally, the problem relates to the quality and completeness of the information and the need to extrapolate from animals to humans and from high-dose to low-dose exposure levels.

THE PRECAUTIONARY APPROACH

The foundations of many risk assessments rest on rodent studies at high doses that elicit certain toxic endpoints, such as tumors or organ damage. These studies are sometimes augmented by epidemiologic observations that associate environmental exposures with certain health endpoints. With these data, risk assessors must develop a predictive schema that defines the level of environmental exposure that would lead to disease in a portion of the population. Ideally, regulators would have detailed toxicity information on a chemical, would understand by what mechanism it operates in both rodents and humans, would know the actual exposure uptake, and would be able to factor in how subgroups (children, the elderly, the impoverished) differ in regard to their susceptibility to an environmental agent.

Typically, however, regulators must operate in a less-than-perfect world in which they have much less information on which to base their decisions. To compensate for this lack of information and to ensure that standards protect human health, regulators resort to default assumptions and the precautionary principle in making risk assessment decisions. The debates in risk assessment revolve around levels of comfort with the default assumptions and the potential for standards to be set at needlessly low levels that offer no added benefit in protecting health. Even in instances in which extensive information has been generated, there are uncertainties in transforming toxicity and exposure data into suitable standards. That fact notwithstanding, one would certainly be more comfortable with decisions based on detailed toxicity, mechanistic, and exposure data in which many of the uncertainties have been eliminated.

DOES SUCCESS BREED NEW CHALLENGES?

In part, the current dilemma in human risk assessment has resulted from the success of environmental remediation and pollution control and reduction efforts over the past 30 years. These efforts have dramatically reduced the human health threats posed by the thousands of new chemicals and technologies introduced into our environment during the 20th century. In fact, we have been so successful in improving the quality of our environment that there are those who argue that the environment no longer represents a serious threat to human health. Although polls show that 60% to 70% of

Americans believe that environmental problems are still a concern, there is nonetheless a vocal minority that maintain the job is done. It is the contention of these groups that the low-dose exposures experienced by most Americans pose no significant health threat.

We have no idea what kinds of risks are posed by chronic low-dose exposures, however, because testing to this point has, out of necessity, focused on higher exposure levels. Also, some toxicants can accumulate in human tissue. Choices that are relatively easy when dealing with high-dose exposures become more difficult in the low-dose range of exposures. Poor decisions will levy huge burdens on society in the form of pain and suffering, health care costs, environmental degradation and loss of species diversity, and diminished competition of American industry. Thus, it is in the national interest that we make investments in science to generate the information needed to make these important decisions.

Traditional environmentalism has concerned itself with a narrow set of issues related to the development of a complex system of laws and policies. As a consequence, the "big picture" issues have not received the attention they deserve. One example of such a neglected area involves the paucity of information on susceptibility, exposure, toxicity, and the interactive nature of chemical mixtures. Solutions to environmental health problems require a more strategic, holistic approach that targets the significant information gaps in risk assessment.[1] The missing information is needed to develop the framework for accurately assessing human disease risk, and such information falls in 3 categories.

First, we must capitalize on recent advances in molecular biology to develop high-throughput technologies that can more quickly and reliably assess toxicity. Second, we must develop the knowledge base necessary to understand differences in susceptibility. Third, we must develop a more rational basis for testing and regulatory decision making based on knowledge of mechanisms of action, actual exposure, possible interactions between agents, and exposure–disease association studies.

TOXICOGENOMICS

Toxicologists are taking advantage of recent developments in human genomics to develop new carcinogenicity and toxicity test systems that are fast and efficient and involve the use of fewer animals than current approaches based on tissue pathology. The new toxicogenomics approach, based on gene-array technology, monitors precursor molecular events involved in the initiation of disease. Given that gene expression is continuously modulated by environmental cues, exposure to toxic agents can be expected to elicit unique patterns of gene expression. DNA microarray technology, which allows monitoring of the expression of thousands of genes simultaneously on small wafer-sized chips, may be useful as a highly sensitive tool to assess toxicity.[2] The assumption is that toxicity is likely to evoke quantitative or qualitative changes in gene expression.

Identifying the genes transcribed under different exposure conditions in various cells, tissues, and organisms could have both evaluative and predictive potential. For example, this technology may allow toxicologists to expose cells or tissues to chemicals whose toxicity is unknown and match the results against the "signature," or common set of changes in gene expression, produced by a known class of toxicants. Our expectation is that we will be able to use the toxicogenomic gene-array approach to survey the entire human genome and thus determine which genes are affected by specific chemicals. This approach will reduce the need for lengthy and expensive animal bioassays and could lend itself to testing for the effects of low-dose, chronic exposure and assessing the toxicity of mixtures. The approach should also be very useful for extrapolating from surrogate models to humans.

To promote the development and use of toxicogenomic approaches, the National Institute of Environmental Health Sciences (NIEHS) has developed a national Toxicogenomics Center consisting of the NIEHS Microarray Center and 5 university-based regional centers. The NIEHS center will coordinate the national effort and serve as the national repository for gene-expression data.[3] However, years of experience with the technology will be necessary to develop the confidence and appropriate databases to validate these approaches. Also, the signature patterns generated must be evaluated in population-based studies in terms of disease association. Without new, high-throughput technologies, however, we will not be able to assess the toxicity of the thousands of chemicals on which there are inadequate toxicity data.

GENETIC BASIS FOR DIFFERENCES IN SUSCEPTIBILITY

Genetic susceptibility, environmental exposure, age, sex, nutritional status, and behavior all determine an individual's unique risk for developing disease. However, we limit the brief discussion presented here to the contribution of genetics and environmental exposures. Because of the dramatic discoveries in human genetics over the past decade, many have come to believe that the problem of disease etiology will be solved with the decoding of the human genome. But, contrary to this view, a recent study showed what scientists have long recognized: that the environment—the chemical, physical, and biological agents to which we are exposed, along with our lifestyles—plays an important role in the development of most chronic diseases such as cancer.[4] The current view is that most chronic diseases arise from complex interactions of multiple genes and environmental exposures. Therefore, the prevention of most human diseases will require a more thorough understanding of both the genetic and the environmental contributions to their etiology.

Recent developments in human genetics now permit more definitive studies of gene–environment interactions in the development of disease. The recent publication of the "reference sequence" of the human genome provides an important resource to assess the role of genetic polymorphism in susceptibility to environmental exposure. Evidence that genetics plays a significant role in the development of disease has come from

studies of familial clusters identifying genes with 1 or several alleles that are associated with an increased risk for a specific disease. Inheritance of such alleles in the population is rare and probably accounts for fewer than 5% of known diseases. Thus, the contribution of monogenic disease genes to the overall incidence of disease is relatively small, although the risk for an individual with a specific disease allele is relatively high.

Most common human diseases appear to be polygenic, resulting from complex interactions of multiple genes. A variant of 1 gene may not be detrimental, but it might become detrimental in combination with specific alleles of 1 or more other genes. Such so-called susceptibility genes increase disease risk only a few-fold, yet they can have a major impact on the incidence of disease in the human population because of their frequency. Susceptibility genes are not sufficient to cause disease; they modify risk.

The Environmental Genome Project was initiated in 1997 to stimulate research into the role of genetic variation in the human body's response to environmental exposures.[5–8] The goal is to catalog information about human genetic polymorphism and to apply this information to understanding disease susceptibility and individual responses to environmental exposure. Among the genetic polymorphisms of interest would be those coding for the following: cytochrome P450 metabolizing enzymes, which influence risk of smoking-induced lung cancer; *N*-acetyltransferase-2, which influences risk of smoking-induced bladder and breast cancers; paraoxonase, which influences pesticide-induced nerve damage; and glutathione *S*-transferase M1, which influences toxicities and cancer risks.

The Environmental Genome Project is being carried out in 3 phases.[8] The first phase will identify polymorphisms in a set of genes that are likely to play important roles in environmentally associated diseases. The second phase will involve functional analysis of the various polymorphisms occurring in coding and regulatory regions of genes. This phase will require laboratory-based as well as population-based studies to establish that a specific polymorphism is associated with a specific disease. The third phase of the project will involve the development of animal models for use in studies of how environmental agents interact with specific polymorphisms to cause human illnesses. Throughout these phases, care is being taken to predict and manage the ethical risks implicit in any project that identifies individual risk of disease, particularly environmentally associated diseases. A full-time ethicist has been hired by NIEHS to oversee this aspect of the project and to stay current in this new and rapidly evolving field.

The mechanisms by which information on susceptibility can be used to reduce risk from exposure to environmental toxicants have not yet been determined. However, several possible approaches can be envisioned, including (1) screening using genetic variation as a biomarker, (2) eliminating or reducing exposure, (3) gene therapy, and (4) pharmacologic intervention.

RATIONAL BASIS FOR TESTING AND REGULATION

Again, information gaps limit rational decision making. For example, we typically have very little information about mechanism, actual exposure dose, and how environmental toxicants interact in a mixture. Therefore, investments in these areas are critically important.

Quantitative risk assessment relies on knowledge of mechanisms to predict dose–response relationships. Studies at both high- and low-dose exposures are needed to identify thresholds when they exist. Selection of the appropriate experimental models to assess toxicity and to understand differences in susceptibility due to genetics, age, sex, behavior, and nutritional status is also improved if mechanisms of action are known. Most important, however, knowledge of mechanisms is critical for the design of primary and secondary prevention strategies characteristic of the practice of public health. NIEHS-supported research has also served as the source of information for many of the regulatory standards put forward by the US environmental health regulatory agencies to protect human health.

In regard to lack of information that is important to human risk assessment, lack of information on exposure is probably the most serious problem. Estimation of exposure using indirect surrogates (e.g., toxic release and production inventories and environmental monitoring) is inadequate and limits our understanding of dose–response relationships. This area of environmental health is in need of development and application of innovative technologies for assessing exposure based on considerations of individual uptake, metabolism, and excretion as well as behavioral differences. We need tools designed to directly measure the amount of tissue deposition of environmental pollutants.

However, risks of exposure to environmental toxicants may be very different from current estimations and assumptions based on animal studies involving exposure to 1 agent at a time. In reality, humans are exposed to multiple agents simultaneously. Now that we have the capacity to develop technologies (e.g., DNA microarray) to assess the toxicity of mixtures, NIEHS has made this a top priority.

CONCLUSIONS

The new era of toxicogenomics, made possible by advances in human genomics, promises to revolutionize the practice of public health as it relates to environmental health protection. Understanding human genetic variation and genomic reactions to specific environmental exposures will have a significant impact on our ability to uncover the causes of variations in response to environmental exposures. The Environmental Genome Project will provide the foundation for the emerging fields of toxicogenomics and pharmacogenomics. These new disciplines hold the promise of reducing the costs and time lines associated with animal and human studies designed to assess the toxicity and efficacy of both environmental pollutants and therapeutic agents.

As with any nascent science, initial costs must be met before the promise can be fulfilled. NIEHS will this year alone commit more than $22 million to combined genomics efforts. These funds, however, are truly strategic investments that will lead to a revolution in our approach to the study of toxicity. It

will be through the genomics support of the NIEHS and others that the current ritualistic approach to toxicology and risk assessment can finally give way to a more rigorous, scientifically based approach involving cutting-edge technologies of genetics and molecular biology. ■

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This commentary was accepted May 23, 2001.

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Implications for Tobacco Control of the Multistate Tobacco Settlement

The 1998 master settlement agreement between major tobacco manufacturers and the US states will have a profound effect on many tobacco industry practices and will significantly influence future settlements with the tobacco industry. This article analyzes the settlement's key provisions pertaining to youth sales, advertising, marketing, and lobbying. It also examines the ways in which the settlement restricts industry practices as well as the many industry practices that remain unregulated. (*Am J Public Health.* 2001;91:1967–1971)

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IN THE WAKE OF THE $145 billion in punitive damages awarded by a Florida jury in July 2000, Philip Morris launched a nationwide television campaign extolling the virtues of the "master settlement agreement" (MSA). Implicit in the advertising is the claim that the MSA fundamentally changed the way cigarettes are sold, obviating the need for further reform or punishment. This commentary examines that claim by reviewing the effects of the MSA on tobacco control efforts.

On November 23, 1998, the attorneys general of 46 states and the major tobacco manufacturers entered into the MSA, resolving outstanding state lawsuits against the tobacco companies.[1] Under this settlement and previous settlements with the other 4 states, the tobacco companies are obligated to pay the states an average of $10 billion per year for the indefinite future. In addition, the companies have agreed to significant restrictions on their advertising, marketing, and lobbying practices. The companies have not accepted responsibility for their past misdeeds, however. Nor have they agreed to cease many troubling practices.

BACKGROUND

The MSA arose out of efforts by 41 states to sue tobacco manufacturers for state health care costs attributable to tobacco-related illnesses. These suits represented a major threat to the industry, which had previously avoided all liability.[2]

Faced with potentially bankrupting liability, on June 20, 1997, the industry agreed with a group of state attorneys general and private attorneys to enter into a so-called "global settlement"[3] that would have resolved all of the tobacco industry's domestic liability concerns.[4] Because this global settlement would have affected the Food and Drug Administration's authority over tobacco, as well as closed the door to private litigation, legislation was required.

Various versions of the proposed global settlement were introduced in Congress. In March 1998, the Senate Commerce Committee endorsed one version, the McCain bill, that was less favorable to the tobacco industry than the original settlement. As a result, industry representatives withdrew their support[5] and successfully campaigned to defeat the bill.[6]

Industry representatives then met with attorneys general to discuss a less comprehensive settlement. By then, 4 states had

reached individual agreements with the industry. In November 1998, the attorneys general of the remaining states and the participating manufacturers, including Brown & Williamson Tobacco Corp, Lorillard Tobacco Co, Philip Morris Inc, and RJ Reynolds Tobacco Co, agreed to the MSA.

Because the MSA had no direct impact on federal policies or private litigation, it did not require federal approval. Instead, it takes its effect from consent decrees approved by each relevant state court. The states that had not previously sued then did so solely to obtain such consent decrees. Enforcement is left primarily to the attorneys general, although the agreement calls for the National Association of Attorneys General to monitor the settlement and attempt to reconcile conflicting interpretations.

MONETARY TERMS

In their suits, the states sought billions of dollars for tobacco-related health care expenses. This amount might have been tripled if the states had prevailed on antitrust or racketeering grounds. In some states, punitive damages might also have been assessed. The MSA relieved the tobacco companies of these potentially crippling judgments.

In return, the industry agreed to pay each state each year an amount, set through a schedule and a series of adjustment formulas, designed as a reasonable estimate of each state's future tobacco-related health care costs. Including the 4 states that had settled previously, the industry will owe in total about $10 billion per year, adjusted for inflation, to be paid by the companies largely on the basis of their market shares.[7] The companies are expected to cover these costs by raising cigarette prices, with only modest adverse effects on their future profitability.[8]

The MSA provides each state, on average, a $200 million annual revenue enhancement. The settlement also relieved states of paying their outside counsel; the industry agreed to pay these lawyers through a complicated arrangement that reduced or eliminated the lawyers' claims on the states' receipts.[9]

From a public health perspective, however, the MSA's accomplishments are more modest. Perhaps the clearest benefit derives from the cigarette price increase imposed to cover the first year's payments. That increase has produced a decline of about 10% in cigarette sales.[10]

The settlement money could produce further public health benefits if it is spent on tobacco control. Experience with comprehensive programs in California and Massachusetts[11] indicates that such programs can yield significant declines in cigarette sales. The Centers for Disease Control and Prevention (CDC) therefore recommended a range of expenditures of MSA money for states to allocate to comprehensive tobacco control programs.[12] The MSA, however, did not require states to earmark their receipts for public health purposes.

Predictably, early results indicate that, contrary to widespread public opinion,[13] most states will spend little for public health, much less for tobacco control. As of August 4, 2000, for example, approximately 18 states had allocated $1 million or more of the settlement money for tobacco control, and of these states only 4 had allocated settlement funds for tobacco control in amounts that fell within the CDC's recommendations.[14]

The MSA also created an industry-funded foundation to run tobacco control programs and make grants to the states and their subdivisions.[15] The American Legacy Foundation is charged with supporting studies and programs designed to reduce use of tobacco products and substance abuse among young people and to prevent diseases associated with tobacco products (see www.americanlegacy.org).

The MSA describes more than 10 specific foundation activities, including a major national counteradvertising campaign. In addition, foundation grants will separately fund state and local advertising and educational programs to counter youth tobacco use and to educate consumers about tobacco-related diseases. However, the MSA imposes some significant limits on foundation funds. For example, the agreement prohibits use of foundation funds for personal attacks or vilification of any person, company, or government agency. This could censor hard-hitting advertising campaigns that put the spotlight on industry manipulation.

LIMITATIONS ON TOBACCO INDUSTRY PRACTICES

Youth Access Provisions

The MSA declares that tobacco manufacturers and settling states are "committed to reducing underage tobacco use by discouraging such use and by preventing Youth access to Tobacco Products."[16] The actual provisions, however, do little toward achieving that end.

Some reduction in youth access may be accomplished by the MSA's prohibition of gifts, credits, or coupons based on proof of purchase without documentation that the recipient is an adult.[17] However, a careful reading of how the MSA defines the critical terms *adult* and *underage* suggests that the restriction may apply only in states that have made the purchase or possession of tobacco products by minors illegal.

According to the MSA, an "underage" person is one who is "under the minimum age to purchase or possess (whichever minimum age is older) cigarettes applicable in the settling states."[18] Whereas all states prohibit the *sale* of tobacco products to minors, not all outlaw youth purchase or possession, and many public health advocates believe that "criminalizing" youth purchase and possession may be counterproductive.[19]

Another significant loophole permits redemption of proofs of purchase by mail. Although recipients must provide a copy of age identification, this requirement could be easily circumvented.

The MSA appears to restrict the distribution of free sample cigarettes. This provision also is more limited than initially evident, because manufacturers can distribute free samples at adult-only facilities.[20] Again, the definition of *adult-only facilities*[21] is tied to the problematic definition of *underage*. As a result, states that do not outlaw youth purchase or possession may not be able to enforce the ban. Manufacturers may also be able to continue to distribute free samples to college students in many venues.[22]

Another provision prohibits participating companies from

producing, selling, or distributing so-called kiddie packs, cigarette packs containing fewer than 20 cigarettes and packages of loose tobacco with fewer than 0.60 oz (16.80 g) of tobacco.[23] However, this prohibition expires in December 2001.

The MSA fails to include certain key tools for reducing youth access. For example, it does not limit self-service displays, vending machines, or point-of-sale advertising. And, unlike the proposed global settlement, the MSA does not establish any specific targets for reducing youth smoking. Nor does it impose any "look-back" financial penalties on tobacco manufacturers for failing to reduce youth smoking.

In short, the MSA advances only 3 very limited youth access measures. However, it does not expressly diminish the power of states and localities to adopt and enforce additional youth access laws.

Advertising Restrictions

The MSA's advertising restrictions[24] also involve many loopholes. They follow past industry concessions by allowing tobacco companies to shift advertising dollars to other media while restricting a carefully defined set of activities.[25] Indeed, in the first year of the MSA era, the industry increased tobacco advertising by 33% in magazines with high (15% or greater) youth readership.[26]

The MSA prohibits cartoon tobacco advertising,[27] but the definition of *cartoon* limits the ban's scope.[28] For example, although "Joe Camel" cartoons are banned, drawings of a camel are permitted unless they exaggerate or attribute human or superhuman qualities to the camel. Moreover, the "no cartoon" rule does not ban the use of the "Marlboro Man" or other human characters. The MSA also "grandfathers" existing cigarette logos.[28]

Under the MSA, tobacco product billboards, transit advertising, and certain other types of outdoor advertising (signs and placards in open-air or enclosed arenas, stadiums, shopping malls, and video game arcades) must be removed. However, tobacco retailers may continue to post any number of advertisements, each up to 14 sq ft (1.26 m^2) in size, on the windows of their establishments or anywhere else on their property.[29] Retailers are thus likely to remain an important venue for tobacco advertising.

The advertising restrictions are distinct from provisions applying to brand name sponsorships. These complex provisions ban 4 types of sponsorships: concerts, events at which "the intended audience" is composed of "a significant percentage of youth," events featuring paid youth contestants or participants, and "any athletic event between opposing teams in any football, basketball, baseball, soccer or hockey league."[30] Exceptions exist, however, for certain concerts, such as the Kool Jazz Festival.[31] And important questions remain as to how the ban will be interpreted. For example, it is unclear what percentage of an audience must consist of young people in order for the youth ban to apply.

The MSA also contains a complex series of restrictions on other types of brand name sponsorships, including a "one brand name sponsorship per year" rule.[32] These rules have many detailed exceptions that will permit tobacco companies to engage in a wide variety of brand name sponsorship activities and advertising.

Limitations on Endorsements and Other Marketing Restrictions

Under the MSA, tobacco manufacturers may not give anything of value to induce a person or entity to refer to, use, or display a tobacco product, package, or advertising "in any motion picture, television show, theatrical production or other live performance, live or recorded performance of music, commercial film or video, or video game."[33] However, media viewed in an adult-only facility, adult use of instructional media for nonconventional cigarettes, and media not intended for public distribution or display are excepted. In addition, the ban on endorsements and product placement does not apply to the permitted brand name sponsorships.[34]

The MSA also prohibits participating tobacco manufacturers from marketing, distributing, offering, selling, or licensing any merchandise or apparel bearing tobacco product brand names.[35] Once again, there are exceptions. For example, the ban does not apply to merchandise distributed in an adult-only facility.

Restrictions on Lobbying

Historically, tobacco industry lobbying, either directly or via proxy groups, has impeded the enactment of state and local tobacco control laws.[36] The MSA addresses this problem, but only to a limited extent. Rather than banning all industry efforts to derail tobacco control laws, the MSA prohibits lobbying against specific hypothetical state laws or regulations,[37] including laws limiting youth access to vending machines and laws enhancing preexisting prohibitions on youth tobacco sales. Participating manufacturers remain free to oppose other significant youth access restrictions such as limits on self-service displays.

The MSA makes clear as well that participating manufacturers may oppose all tobacco-related excise or income tax provisions.[37] The industry can also continue to oppose enforcement of existing legislation or rules. Given that enforcement is often key to the success of tobacco control measures, this limitation may undermine the efficacy of the lobbying restriction.

The status of industry lobbying in support of state laws that preempt local tobacco control initiatives is not entirely clear. Because such laws would forbid local legislation pertaining to the initiatives covered by the lobbying ban, tobacco control advocates may argue that preemption falls within the ban. However, manufacturers can counter that the MSA preserves their right to support statewide bills that are not explicitly included within the lobbying ban.

The MSA also restricts participating manufacturers from supporting any diversion of the settlement proceeds to any other than tobacco- or health-related uses. However, it leaves the industry free to seek the diversion of the funds to health-related uses other than those focusing on tobacco.

Finally, the MSA dissolves the Council for Tobacco Research—USA (CTR) and the Tobacco Institute, Inc, and includes the statement that the industry "may not reconstitute CTR or its function in any form."[38] Manufacturers may, however, create new tobacco-related trade associations.

EFFECT OF THE MSA ON OTHER TOBACCO LITIGATION

The MSA settled the states' claims for past, present, and future tobacco-caused health care expenses. Because localities are subdivisions of states, their claims are also resolved. However, the states are not prevented from enforcing the MSA or from seeking court orders to enjoin tobacco industry misbehavior.

Nor does the MSA impede individual or class action cases brought by smokers, families of smokers, or afflicted nonsmokers. Indeed, the millions of pages of documents released in the course of the state litigation,[39] many of which will be made publicly available under the MSA,[40] have been crucial in fueling additional successful litigation. In 1999 alone, 2 large punitive damage verdicts were handed down in individual actions against Philip Morris,[41,42] along with a detailed and damning verdict against all of the major cigarette manufacturers in the first phase of a Florida class action.[43]

Other third-party payers, such as BlueCross BlueShield plans, may also seek tobacco-related health care costs. The most dramatic such case was the one filed by the Justice Department in 1999, seeking recovery of tobacco-caused health care expenses. The costs at issue in the case were estimated to total more than $20 billion per year. However, these claims were recently dismissed by the court.[44]

The federal action still raises claims under the Racketeer Influenced and Corrupt Organizations Act. That action seeks the disgorgement of the tobacco industry's profits from its decades-long pattern of fraudulent behavior, as well as the cessation of future misbehavior and the funding of public information projects. A successful conclusion to the case could contribute substantially to public health goals by increasing the price of cigarettes, thereby discouraging consumption, and by plugging many of the MSA's loopholes.

LESSONS LEARNED

The MSA and the 4 individual state settlements that preceded it represent a watershed in regard to tobacco control efforts. For the first time, the industry has assumed a significant share of the costs related to the illnesses it causes. And, for the first time, the industry has agreed to many restrictions on advertising, marketing, and lobbying.

Still, the MSA has not fundamentally changed the way cigarettes are sold. Nor has it punished the industry for its misdeeds. Even the ban on billboard advertising, arguably the most significant MSA restriction, has been circumvented through redirecting tobacco advertising to youth-oriented magazines.[24] Tobacco company profits actually increased subsequent to the MSA.[45]

Several lessons seem to follow. First, bargains struck without substantial public health input may be less meaningful than they initially appear. Second, federal, state, and local regulations are as needed as ever. Finally, tobacco litigation remains an important public health tool. Litigation brought the industry to the bargaining table in the first place. Even after the MSA, it may be a potent tool for exposing industry misbehavior and weakening the industry's power to resist effective controls. ■

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This commentary was accepted December 13, 2000.

Note. Any opinions, findings, and conclusions expressed in this article are those of the authors and do not necessarily reflect the views of the prime sponsor.

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The authors worked together to plan and structure the paper. R.A. Daynard took primary responsibility for sections pertaining to the monetary implications of the settlement. W. Parmet was primarily responsible for discussion of the settlement's background and editing the paper. G. Kelder was the primary author of the section on lobbying provisions. P. Davidson was primarily responsible for sections pertaining to the youth access provisions and advertising restrictions.

Acknowledgments

This article is based on work supported by a National Institutes of Health/National Cancer Institute award (grant 1 R01 CA67805-01).

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