COST-EFFECTIVENESS OF LOWERING THE AFLATOXIN TOLERANCE LEVEL

C. R. DICHTER
Department of Nutrition*

and

M. C. WEINSTEIN
Department of Biostatistics, Harvard School of Public Health, 665–667 Huntington Avenue, Boston, MA 02115, USA

(Received 15 November 1983)

Abstract—The cost-effectiveness of adopting aflatoxin tolerance levels of 15, 10 and 5 ppb for peanuts and peanut products was assessed. Estimates of the annual cost to manufacturers of monitoring and controlling peanut aflatoxin levels at the current 20-ppb action level, and estimates of the projected increase in costs of establishing lower tolerances were elicited from producers by questionnaire. Exposures to peanut products were derived from the HANES I survey and from peanut production statistics. The risk of liver cancer at each tolerance level was estimated using both epidemiological and extrapolated experimental data assuming that exposure would be reduced in direct proportion to the decrease in the tolerance. It was found that the 15-ppb tolerance would cost $60,000 per cancer death averted (range $20,000–$1,700,000) and is therefore relatively cost-effective. The marginal costs per life saved for both the 10-ppb and 5-ppb levels were found to be $1.7 million (range $0.6 million–$11.4 million) and $1.6 million (range $0.6 million–$31.1 million), respectively. Conclusions on the optimal regulatory approach should be guided by comparisons of these figures with corresponding cost-effectiveness ratios for alternative regulatory uses of national resources in the interests of public health.

INTRODUCTION

Aflatoxin has been demonstrated to be the most potent of identified animal carcinogens. Chronic low-level ingestion of aflatoxin produces liver tumours in laboratory animals and has been found to be associated with primary liver cancer in certain populations living in the Third World. In the USA, where liver-cancer incidence and mortality are relatively low, the disease is often found to be associated with alcoholism and cirrhosis (Alpert & Isselbacher, 1974). It is not known to what extent, if any, aflatoxin is involved in its aetiology. However, since aflatoxin contamination of foodstuffs is known to exist in the USA, a basic tenet of regulatory policy has been to limit exposure to the lowest level possible (Federal Register, 1974).

The level of aflatoxin in peanuts has been regulated since 1965, prior to which the identity, occurrence and physiological effects of this substance had not been defined (Rodricks, 1977). Farmers' stock peanuts intended for human consumption in the USA are inspected for the presence of aflatoxin by the US Department of Agriculture (USDA) and cannot be placed in human food channels if they contain amounts that exceed a specific legal limit. In addition, the Food and Drug Administration (FDA) regulates the level of aflatoxin that is permissible in finished peanuts and peanut products. The FDA has been operating since 1969 under an action level of 20 ppb.

Since an action level is technically a temporary or interim tolerance, the establishment of a permanent level for aflatoxin in peanuts and peanut products remains a pending regulatory matter. Although the FDA proposed to establish a tolerance of 15 ppb (Federal Register, 1974), to date it has not instituted any formal action.

Since aflatoxin contamination of peanut products is deemed to be unavoidable, a trade-off must be made between the economic and health costs associated with various permissible levels. It becomes necessary to effect some compromise between costs and benefits, aiming, in principle, to maximize health benefits within resource limits.

Cost-benefit and cost-effectiveness analyses are tools that can be used to guide allocation of resources for establishing preventive health measures (Thompson, 1980; Weinstein & Stason, 1977). While both techniques evaluate the costs and benefits associated with a given health measure, cost-benefit analysis requires that all benefits and other outcomes be expressed in monetary terms, while cost-effectiveness analysis permits the expression of health benefits in terms of lives saved or quality-of-life effects. Thus cost-benefit analysis provides a basis for directly weighing health-related outcomes against purely economic outcomes, while cost-effectiveness analysis is best suited to determining the optimal allocation of resources in achieving health goals. Cost-effectiveness analysis gives the decision maker, rather than the analyst, the responsibility for the final weighting of outcomes. When used in conjunction with the technique of sensitivity analysis, it can accommodate

*Present address: Department of Nutrition, Simmons College, 300 The Fenway, Boston, MA 02115.
The primary purpose of this report is to describe the methods and results of economic and health effects associated with determining a tolerance for aflatoxin in peanuts and peanut products. It was hypothesized at the outset that this model can satisfactorily incorporate data on the uncertainty surrounding quantitative estimates of human health risk based on animal data. This in itself should not act as a barrier because, as noted above, uncertainty can be accommodated using this technique, and can be defined precisely through the use of sensitivity analysis.

A major practical problem for the regulator to overcome in order to utilize this approach in the food safety area, is the lack of a suitable economic data base. No published empirical data exist that would enable determination of the relation between the tolerance level for aflatoxin and the economic costs involved. Individual processors or manufacturers are reluctant to make public any information of this nature, lest they lose a competitive advantage. Furthermore, government agencies, such as the FDA, cannot require submission of this type of information and must rely upon voluntary testimony. In order to use the cost-effectiveness approach for food safety questions, the requisite economic data must be obtained from the industry involved.

The primary purpose of this report is to describe the use of a cost-effectiveness decision model for determining a tolerance for aflatoxin in peanuts and peanut products. It was hypothesized at the outset that this model can satisfactorily incorporate data on the relationships among economic and health effects associated with alternative tolerance levels and can provide a quantitative index for comparison. In order to test this approach, it was necessary to collect and analyze several distinct types of data.

One phase of the research was devoted to the collection of economic data. Another involved analyzing both food intake records obtained from the HANES I survey and peanut production statistics in order to generate estimates of population exposure to aflatoxin and dietary adequacy. The risk-assessment phase of the research involved the mathematical extrapolation of selected animal studies as well as the generation of estimates on the basis of epidemiological data.

This paper will describe the methods and results of the cost-effectiveness analysis derived from the data described above. The details of the risk assessment are reported elsewhere (Dichter, 1982 & 1984).

### METHODS

#### Economic effects

**Quality-control costs.** In order to determine the current costs of aflatoxin quality control in manufacturing and processing operations, a sample survey was conducted of companies of varying size involved in the manufacture or processing of peanut butter, salted peanuts and peanut candies. Since the data required could not be obtained directly from the individual companies contacted because of the confidential factors involved, it was arranged that the requisite information be collected through a trade group, The Peanut Butter and Nut Processors Association. Twelve companies completed the questionnaire, and one other supplied useful supplemental information. The respondents collectively accounted for 20% of the edible-grade peanuts used in primary products during the period covered by the survey.

In order to develop a means for determining how accurate the survey results were, one of the authors (C.D.) observed the operation of several peanut processing plants, consulted equipment manufacturers on the costs, capacity and durability of quality control devices, and visited USDA inspection stations, laboratories and research facilities.

Sufficient data were supplied by the manufacturers to estimate average quality control costs under the current 20-ppb action level. Since the quality control cost per unit processed is greater for small than for large manufacturing operations, an adjusted average industry cost was computed. This adjusted value was calculated by weighting the average costs determined for small and large companies from the survey according to their approximate market share (40 and 60%, respectively). This estimate was found to be in close agreement with an industry estimate generated privately for USDA.

When the survey results were reviewed with regard to the adequacy of the data provided for determining the incremental (marginal) costs of achieving future tolerances, it was determined that data from only

<table>
<thead>
<tr>
<th>Aflatoxin tolerance (ppb)</th>
<th>Predicted number of liver cancer cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Extrapolated Fischer Linsell</td>
</tr>
<tr>
<td></td>
<td>Modified Peers</td>
</tr>
<tr>
<td>20</td>
<td>151</td>
</tr>
<tr>
<td>15</td>
<td>113</td>
</tr>
<tr>
<td>10</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
</tr>
</tbody>
</table>

*Based on mean values obtained from combined extrapolation models (additive background).

The data are from Dichter (1982) and assume a US population of 220 million.
three of the respondent companies were sufficient. One of these was a small scale operation, handling fewer than 10 million lb shelled peanuts/yr. The other two companies are considered to be large-scale operations since each handles in excess of 40 million lb/yr. One of these large companies estimated costs that were markedly higher than the other two companies’ estimates. These have been interpreted to be maximal values and are treated separately in the analysis. The central (average) cost estimate has been calculated from the data supplied by the other two companies.

It has been assumed in all calculations that the increased cost of a proposed tolerance is equal to the incremental cost of the manufacturers’ quality control operations. This might involve such aspects as increased sorting and assaying, purchase of additional equipment and supplies, increased personnel, productivity losses and increased product discard.

Future value of costs. Although the health benefits of decreasing current aflatoxin exposure would theoretically not be observable until many years after permissible levels were reduced, because of the latency period associated with tumour development, the expenditures resulting from the establishment of decreased tolerances would begin immediately. This lack of synchrony affects the projectable dollar outlay and necessitates the use of a procedure that can compensate for the time gap, since money will increase in value with time through investment. (The rate at which this occurs is dependent upon both the rate of inflation and the prevailing real interest rate.)

One means of compensating for this time gap is to express present expenditures in terms of their real, inflation-adjusted, value at a time in the future when the health effects associated with them become observable (Stokey & Zeckhauser, 1978). The future value (FV) of the annual costs associated with each tolerance has been calculated using the formula:

\[ FV = S_0(1 + r)^n \]

where \( S_0 \) is the annual cost expressed in 1978 dollars that will be borne in the period beginning \( n \) years hence, \( n \) is the latency period and \( r \) is the inflation-adjusted interest rate. Future value analysis, in this instance, expresses all costs in terms of their values at the future time when benefits are first realized, but at 1978 price levels.

The future value of the costs calculated for each potential aflatoxin tolerance level has been determined assuming an inflation-corrected (i.e. real) discount rate of 5\% and an average latency period of 20 yr. Most economists advocate a real discount rate of between 2 and 10\% with the consensus centering around 4–6\%. Since the latency period is not known precisely, and the appropriate discount rate is a topic of some controversy (Stokey & Zeckhauser, 1978), similar calculations have been made using inflation-adjusted discount rates of 2 and 10\% and average latency periods of 15, 25 and 35 yr.

Health effects

Exposure estimation. In order to assess potential exposure to aflatoxin at each tolerance under consideration, average residue levels were estimated using FDA survey results. The average aflatoxin residue level in peanuts and peanut products, under the current 20 ppb action level, is estimated by the FDA to be 2 ppb (FDA, 1978). It is assumed that residue levels at lower tolerances would exhibit the same proportionality. Thus, tolerances of 15 and 10 ppb would give rise to residue levels of 1.5 and 1.0 ppb in finished products, respectively. However, such a proportional reduction represents an ideal situation and thus may lead to an upper bound estimate of the health benefit that can be expected.

Risk estimation. The estimated number of cases of liver cancer potentially attributable to peanut-product ingestion at each tolerance under consideration has been estimated using both an experimental and an epidemiological data base. In the former case, data collected by Wogan, Pagliaiunga & Newberne (1974) on the effects of aflatoxin B\(_1\) ingestion in the male Fischer rat were extrapolated (Dichter, 1984). In the latter, a modification of a relationship determined by Peers & Linsell (1977) was used (Dichter, 1984). These data are summarized in Table 1.

It has been assumed that the dose–response curve is approximately linear in the dose region under consideration and, therefore, that liver cancer incidence will be decreased by the same percentages as the average residue levels. This assumption will result in an over-estimate of the reduction in cancer incidence if the dose–response curve is convex.

Liver cancer mortality. The expected reduction in liver cancer incidence at each of the tolerances under consideration has been calculated from the above values. Two estimates of disease reduction at each tolerance level, derived using the modified Peers–Linsell relationship and the extrapolated animal data (Dichter, 1984), give, respectively, an expected reduction and a maximum reduction in liver cancer cases.

Nutritional status. Adverse health effects, which would be considered to be negative benefits, have also been considered for this analysis. Those that might result from a decreased consumption of peanut products in response to higher prices would be primarily energy or protein deficits. Peanut products are considered to be an inexpensive protein source in the US diet. Thus, a protein deficit was considered to be the more likely outcome, since low-cost foods are available that could provide substitute calories. The number of inexpensive, high-quality protein sources is considerably more limited. The protein deficit that would be predicted at each tolerance level was thus determined. This calculation took into account the consumption patterns of US consumers of various ages, living above and below poverty level, as well as the protein adequacy of their diets. All of these parameters were determined through an analysis of the food intake records of participants in the HANES I survey (Dichter, 1982). In addition, the price elasticity of demand for peanut butter was estimated on the basis of the altered consumption patterns that followed a precipitous increase in the retail price of peanut butter in 1981 (Dichter, 1982). This enabled calculation of the decrease in consumption that would be expected to occur in response to various price changes. Since it was found that, even at the 5-ppb level, the predicted protein deficit would be less than 1\% of the recommended daily allowance for the
youngest consumers as well as for those living below poverty level, it was concluded that no significant adverse nutritional effects would result from lower aflatoxin tolerances.

**Cost-effectiveness**

Effectiveness has been defined in this analysis as the reduction in the number of cases of liver cancer. Since death from this disease occurs relatively quickly after diagnosis, often within 6 months (Alpert & Isselbacher, 1974), effectiveness may also be interpreted as the number of lives saved.

Three different estimates of the cost-effectiveness ratios have been calculated at each tolerance level, because the estimates of both cost and risk could not be made with a high degree of certainty. These represent a likely, a worst-case and a best-case estimate. The likely and best-case ratios are both estimated on the basis of the average cost estimates but use epidemiological and experimental risk estimates, respectively; the worst-case estimate is calculated on the basis of maximum cost estimates and epidemiologically derived risk estimates.

Incremental, or marginal, cost-effectiveness ratios have been calculated, in order to determine whether or not adoption of a 15-, 10- or 5-ppb tolerance is a reasonable use of national resources. These ratios are calculated by determining the increase in cost and decrease in cases of liver cancer predicted for each tolerance, relative to the tolerance that is 5 ppb higher. Thus, the incremental or marginal cost-effectiveness ratio (change in cost/change in effect) calculated for 15 ppb is relative to the 20-ppb tolerance, that for 10 ppb is relative to the 15-ppb tolerance, and that for 5 ppb is relative to the 10-ppb tolerance.

**Sensitivity analysis**

The variation in the cost-effectiveness ratios due to uncertainty in the exposure and risk estimates was determined, as was the effect of selecting alternative discount rates and latency periods.

**RESULTS**

**Cost-effectiveness**

The data collected from industry on quality control costs for the current 20-ppb action level ranged in value from 0.2 to 1.4 cents/lb peanuts processed. When the average market share of large and small companies was considered an average adjusted (industry-wide) value of 0.9 cents/lb was computed from these estimates.

The information supplied by the manufacturers on the anticipated increased costs of complying with each of the lower tolerances under consideration has been summarized in Table 2. On the basis of the average values presented, it is apparent that adoption of a 15-ppb tolerance would result in a small increase (0.027/0.9 = 3%) in quality control costs, whereas adoption of a 10-ppb level would increase costs by 80% and a 5-ppb level would increase costs by 126%.

The greater increases at the two lower levels were due in large part to the anticipated costs of additional equipment. The maximum estimates, which were computed from the data supplied by a single, large manufacturer, reflect the heavy losses in productivity and the large increase in product discard that the company anticipated would result from the more stringent tolerances.

The peanut crop processed during the period from August, 1979 to July 1980 contained approximately 2 billion lb shelled edibles, of which 1.29 billion lb were used in primary food products (Crop Reporting Board, 1981). The increased total cost of implementing each tolerance under consideration was calculated by multiplying the estimated price increase per lb by 1.29 billion lb (Table 2). On the basis of the average estimated values, a 15-ppb tolerance would cost an additional $300,000/yr, a 10-ppb tolerance would cost approximately thirty times that amount and a 5-ppb tolerance would cost sixty times that anticipated at 15 ppb.

The future value of these costs was calculated assuming a 5% discount rate and a 20-yr latency period for liver cancer. The values are presented in Table 3 with the estimated decrease in liver cancer incidence. The incremental (marginal) costs, reductions in cancer mortality and cost-effectiveness ratios were calculated and the central, worst-case and best-case estimates of the marginal cost-effectiveness ratios were determined (Table 3). While the ratios based on maximum cost estimates indicate that the 10-ppb tolerance is approximately three times as cost-effective as the 5-ppb level, the central estimates indicate that the two are almost equivalent; that is, if it is considered cost-effective to reduce the tolerance to 10 ppb, it would also be cost-effective to reduce it to 5 ppb. It will also be noted that the spread of values estimated for the marginal ratios increases as the tolerance is decreased, owing to the increased divergence in estimates of the incremental cost of lower tolerances. (It should be recalled that the reduction in the number of cases of liver cancer was assumed to be equal for each decrement in the tolerance.)

**Sensitivity analysis**

The degree of uncertainty in the ratios computed above can be estimated by analysing the level of uncertainty that exists in (1) the cost estimates supplied by the manufacturers, (2) the computed values of future cost, (3) the exposure estimates and (4) the risk estimates.

The effect of uncertainty on the cost estimates has

<table>
<thead>
<tr>
<th>Tolerance (ppb)</th>
<th>Increased costs (cents/lb peanuts)</th>
<th>Total annual costs ($million)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Average</strong></td>
<td><strong>Maximum</strong></td>
</tr>
<tr>
<td>15</td>
<td>0.027</td>
<td>0.72</td>
</tr>
<tr>
<td>10</td>
<td>0.72</td>
<td>5.5</td>
</tr>
<tr>
<td>5</td>
<td>1.4</td>
<td>18.1</td>
</tr>
</tbody>
</table>
been taken into account explicitly by deriving cost estimates on the basis of maximum as well as average values. The possibility exists that the average values generated may be over-estimates; however there is no basis for assuming this to be the case. The computed values of future cost are dependent upon the discount rate and the duration of the latency period that have been assumed. The cost-effectiveness ratios could be approximately 11 times greater than those calculated, if both a longer latency period (35 yr) and a higher discount rate (10%o) are considered. A latency period of 35 yr whilst holding the discount rate constant would result in a doubling of the ratio. Similarly, if the appropriate discount rate were 10% and the latency period were held at 20 yr, a 2.5-fold increase would be observed.

The exposure levels for which the risk estimates are calculated have taken into account all domestically produced shelled peanuts used annually in primary food products. This procedure could therefore err in the direction of over-estimation since wastage has not been taken into account, and it is clear that not all food produced is consumed. If the actual exposure were 0.005 ppb, as estimated by the FDA (FDA, 1979), on the basis of its analysis of food-intake data and approximation methods to estimate food frequency, the actual risk would be half of the computed values. The risk reduction or effectiveness of each aflatoxin tolerance will be half the assumed value and the cost-effectiveness ratios twice as large. In the authors' view this is the maximum variation that might result from uncertainty in the exposure parameter, using a comparison of exposure estimates derived from various methods (Dichter, 1982).

A high degree of uncertainty is associated with the risk estimates. This is largely the result of scientific limitations relating to integrating varying exposures during the life cycle, extrapolating laboratory data and accounting for varying sensitivities to carcinogens in the human population. Since it is not known by what factor(s) the actual health risks will vary, calculations have been made assuming that the actual risk may be as low as one tenth the estimated value. The central values for the marginal ratios for the 15-, 10- and 5-ppb tolerances would then equal $0.6 million, $17 million and $16 million, respectively, for each life saved.

Since it is clear that uncertainty exists in both the exposure and risk estimation procedures, the effect of simultaneous variation is of interest. Because the effect is multiplicative, the largest ratio multiplier possible within the defined ranges of uncertainty for both the exposure and risk parameters is 20. For example, a multiplier of 4 would result if both the exposure and risk estimates were over-estimated by a factor of 2.

It should be recalled that by providing both worst-case and best-case estimates of the cost-effectiveness ratios, the increased susceptibility of the male Fischer rat as compared to the human populations studied, has been taken into account. Thus a much wider variation in risk than that revealed by the sensitivity analysis has been defined.

**DISCUSSION**

The data presented in this paper provide estimates of the cost-effectiveness of adopting aflatoxin tolerances of 15, 10 and 5 ppb. The values generated provide a comparison of each of the three levels under consideration as well as a basis for comparing these policy options with those for other preventive measures.

The analysis suggests that the 15-ppb tolerance is the most cost-effective level under consideration, in the sense that cancer mortality can be reduced at the lowest cost per death averted. This does not necessarily imply, however, that it should be recommended for adoption. It may be that even this cost per cancer averted is higher than can be justified in the face of more cost-effective uses of the resources. On the other hand, the higher costs per cancer averted by even more stringent tolerance levels may still compare favourably to alternative uses of resources in environ-
mental control. Before reaching such a decision, the policy maker should consider the incremental cost-effectiveness of each tolerance level in the context of other environmental measures aimed at preventing cancer. A recent analysis of the cost-effectiveness of two different types of cancer research (Weinstein, 1983) provides a case for establishing priorities using cost-effectiveness criteria. Using this same reasoning, it appears logical to develop priorities for regulations and policy decisions on the same basis (Zeckhauser & Shepard, 1976).

Graham & Vaupel (1981) analysed 35 studies dealing with the costs and benefits of preventive health policy options considered by five different federal regulatory agencies. They computed median values of the cost per life saved for each of the agencies for the policy options selected for analysis. The median costs computed for the Consumer Product Safety Commission and the National Highway and Traffic Safety Administration options were $50,000 and $64,000, respectively, per life saved. Both of these agencies had accident prevention as their objective. The options under consideration in the Department of Health and Human Services had a median cost of $102,000 per life saved, reflecting programmes in heart disease prevention, immunization and genetic screening. The measures under consideration by the Environmental Protection Agency (EPA) were projected to cost $2.6 million per life saved and those at the Occupational Safety and Health Administration (OSHA), $12.1 million. Both EPA and OSHA options had a major emphasis on reducing the levels of exposure to carcinogens.

When examined in the context of the median cost-effectiveness values calculated for EPA and OSHA, a 15-ppb tolerance for aflatoxin clearly has a favourable ratio. Even when one takes into account the ratio multipliers computed as part of the sensitivity analysis, this tolerance appears cost-effective in all but the worst-case estimate. Even assuming that exposure has been over-estimated by a factor of 1.25 (a value that seems reasonable in the light of the methodology used), and that risk has been over-estimated by a factor of 10, the marginal cost-effectiveness for 15-ppb level would be increased to $750,000 per life saved. If the discount rate were 10", and the latency period 25 yr, the ratio would increase to approximately $3 million. While these adjusted ratios are markedly inflated, the values are still within the range of those computed for other environmental measures aimed at reducing exposure to carcinogens. Exposure to aflatoxin, as with exposure to other environmental agents, is largely outside the individual's control. Graham & Vaupel (1981) point out that policy makers may decide to expend more resources in particular areas (for example those in which involuntary exposures are involved). Exposure to aflatoxin, in this regard, is similar to involuntary exposure to airborne or waterborne carcinogens, or carcinogens found in the workplace.

The incremental cost of eliminating each case of liver cancer by lowering the tolerance of aflatoxin from 20 ppb to 10 or 5 ppb in peanuts and peanut products appears to be extremely high. However, the increased cost to individual consumers of a 5-ppb tolerance, the lowest level considered, would prob-ably be less than 5 cents/jar (18 oz) of peanut butter (Dichter, 1982). What may be considered excessive as a governmental or public expenditure may be judged to be appropriate when paid for by the consumers who will be directly affected.

The cost estimates obtained from industry may be suspected of being over-estimates by those who may wish to avoid future regulations. No systematic study of the relation between pre-regulation predictions of cost by industry and actual post-regulation costs has, to our knowledge, been conducted. However, the regulation of exposure to vinyl chloride monomer actually resulted in profits to the industry (by virtue of materials recovery) rather than the high costs originally projected. Although it is difficult to imagine how additional processing of peanuts could result in profits, it may be that an innovative process will be discovered that will achieve the desired tolerances at much lower cost than anticipated.

The determination of a formal or legal tolerance for aflatoxin in peanuts and peanut products is a regulatory question that warrants attention for its own sake as well as for its value as a prototype. The use of cost-effectiveness analysis for determining an appropriate level for an unavoidable carcinogen in the food supply could potentially have important implications for arriving at other food safety decisions as well as for suggested legislative alteration of the Delaney clause of the Food Additives Amendment. It is also possible that the use of this approach for a food safety issue will stimulate interest in its broader applicability.

Acknowledgements—This research was supported by grants from the Interdisciplinary Programs in Health and the Department of Nutrition, Harvard School of Public Health. We would like to thank Drs James Austin, C. Peter Timmer and Peter Goldman for their encouragement and support of this work.

REFERENCES


