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RISK ESTIMATES OF LIVER CANCER DUE TO AFLATOXIN EXPOSURE FROM PEANUTS AND PEANUT PRODUCTS

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Abstract—An assessment was undertaken of the risk of liver cancer in the USA associated with aflatoxin ingestion from peanuts. Both laboratory-animal data and epidemiological data collected from the scientific literature and several prominent mathematical extrapolation techniques were used. Risk estimates differed by a factor of >1000 when the extrapolated results of three selected animal studies were analysed. Dose-response data for the male Fischer rat, the most sensitive mammalian species studied, produced an estimate of 158 cases of liver cancer per year in the USA at current levels of aflatoxin exposure. An estimate of 58 annual cases was predicted on the basis of epidemiological data of populations in Africa and Thailand.

INTRODUCTION

Aflatoxin is one of the most potent carcinogens found in our food supply. It is considered to be an unavoidable naturally occurring contaminant of peanuts in particular and efforts to restrict exposure to this substance have been made by governmental agencies and the peanut industry since an awareness of the toxin's existence and hazard developed (Rodricks, 1977). The Food and Drug Administration (FDA) estimates that the average concentration of aflatoxin found in consumer peanuts and peanut products in the USA is 2 ppb (FDA, 1978). The current action level (highest permissible level) for aflatoxin in finished peanut products sold for human consumption is 20 ppb, a technically 'temporary' tolerance level which has been in effect since 1969.

In 1974, the FDA proposed a tolerance level for aflatoxin of 15 ppb in peanut products, a level that the agency believed could be easily met by a high percentage of the industry (*Federal Register*, 1974). At the present time the 20-ppb level remains in effect and it is not clear why the 15-ppb level was not made into a formal rule. An analysis of both the actual tolerance level to be set for aflatoxin and the process to be used to arrive at such a policy decision seems particularly relevant. In the USA, at the present time, serious discussion of a possible modification of the food safety provisions of the Food, Drug, and Cosmetics Act are underway in the US Congress (*Food Chemical News*, 1983). If enacted into law, one such change under consideration would grant the FDA broader responsibility for defining health risk, particularly with regard to potential carcinogens. Careful analysis of the 'aflatoxin situation' can reveal a great deal about our current ability to quantify risk and can also help to determine whether new techniques, such as cost-effectiveness analysis, can be used to formulate policy decisions in the food safety area (Dichter, 1982).

The analysis reported in this paper was undertaken in order to estimate the health risk associated with current and projected levels of exposure to aflatoxin through consumption of peanuts and peanut products. Although the ultimate goal was to utilize the results for determining the cost-effectiveness of alternative aflatoxin tolerances (Dichter & Weinstein, 1984), it was also performed with the objective of further elucidating both the strengths and limitations of using laboratory animal studies for quantitative assessments of human health risk.

Experimental evidence indicates that there is a wide spectrum of sensitivity to the carcinogenic effects of aflatoxin feeding. The two most highly sensitive species, studied, the male Fischer rat and the rainbow trout, exist at one end of this spectrum, while the mouse, the most resistant species studied, occupies the other extreme (WHO Task Group, 1979). Human sensitivity is presumably bounded by these two endpoints, but the question of selection of a single species upon which to base risk predictions remains unresolved. The same ambiguity prevails with regard to the selection of an appropriate mathematical extrapolation model (Krewski & Van Ryzin, 1980). Thus, all risk projections derived for man using experimental animal data will be a function of both the animal species and the extrapolation model chosen.

Estimates of aflatoxin carcinogenicity can also be derived from human epidemiological data, collected in various parts of Africa and Thailand. Peers & Linsell (1977) have analysed and summarized several studies and have determined that they can be collectively represented by the linear equation:

$$y = 0.106x + 2.2$$

where y represents the crude liver cancer incidence rate, the number of cases per 100,000 persons per year, x is the quantity of aflatoxin ingested from food

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(ng/body weight/day) and 2.2 represents the background incidence rate.

A direct equivalency does not exist however between the US population and the Third World populations that were studied owing to differences in exposure to both infectious and non-infectious agents. Hepatitis B virus is one specific factor that is believed to be associated with liver cancer (Ziegler, Adamson, Barker *et al.* 1978) and is endemic in many of the Third World countries in which liver cancer incidence is high (Alpert & Isselbacher, 1983). Its interactive or synergistic effects with aflatoxin in the aetiology of liver cancer have not been quantified. Third World and US populations also differ in their overall health and nutritional status, and have significant differences in dietary and occupational exposures and lifestyle, which could affect disease incidence. Despite the lack of direct comparability, however, risk estimates based on epidemiological studies can provide additional comparative data which can be used to define the potential health risk for the US population.

Both Carlborg (1979a & unpublished manuscript, 1979) and the FDA (1978) have previously undertaken assessments of the health risk associated with aflatoxin ingestion, using both animal and epidemiological data. Carlborg explored the use of various mathematical models for this purpose while the FDA used only the Mantel–Bryan procedure. The latter is widely accepted as 'conservative' insofar as it defines the upper bound of risk, the 99% confidence limit. The choice of animal studies and treatment of epidemiological data also differed in the two analyses. The analysis reported below has attempted to extend these previous efforts by using multiple extrapolation models and data from species of varying sensitivity. Risk estimates have also been generated for a wider range of possible exposure levels than those previously reported to provide sufficient data for analysis of the models utilized.

METHODS

The risk analysis described below is based upon the following assumptions: (1) it is appropriate to use dose-response data obtained from experimental animals to predict risk in man; (2) average daily exposure (assumed to be constant and continuous throughout life) can be used to predict risk in place of a distribution function of exposures that vary over time; (3) mathematical extrapolation procedures can be used to determine a dose-response relationship at doses lower than those studied experimentally; (4) with regard to aflatoxin carcinogenicity, the liver will be the site of tumour formation in man.

Estimated current exposure to aflatoxin through consumption of peanuts and peanut products has been determined using several methods (Dichter, 1982). On the basis of a reported average residue level for aflatoxin of 2 ppb in peanuts and peanut butter (FDA, 1978), and accounting for all domestically produced shelled peanuts used in primary food products, the estimated current average daily exposure in the USA was found to be 0.01 ppb (Dichter, 1982). The FDA estimated exposure at 0.005 ppb (FDA, 1978) from peanuts and peanut products, relying exclusively upon 24-hr intake data and an indirect method to estimate frequency.

For the purpose of risk estimation, dose-response data from three experimental studies have been used for low-dose extrapolation and the pertinent data from each are given in Table 1. The most recent study (Wogan, Paglialunga & Newberne, 1974) is clearly superior for this purpose because of the large number of doses (five) that were tested. The study by Ayres, Lee, Wales & Sinnhuber (1971), using the rainbow trout, involved fewer doses but has been selected because it provides results in the low-dose region and represents a very sensitive species. In this study two different observation periods of 12- and 16-months duration have been treated as two separate experiments for the purpose of extrapolation. The study by Epstein, Bartus & Farber (1969) was selected because a somewhat less sensitive species, the male Wistar rat, was used and consequently higher doses of aflatoxin were administered than in the other studies. According to the experimental feeding protocol used in this study, aflatoxin was only administered during the first 21 weeks of life, rather than throughout the

Table 1. Summary of experimental studies used for risk estimation

Animal species	Dietary aflatoxin level (ppb)	Tumour rate	Duration of feeding (wk)	Time to first tumour (wk)
Male Fischer rat	0	0/18	74 109	
(Wogan *et al.* 1974)	1	2/22	78 105	104
	5	1/22	65 93	93
	15	4/21	69 96	96
	50	20/25	71 97	82
	100	28/28	54 88	54
Rainbow trout	0	0/20	52	Not
(Ayres *et al.* 1971)	4	10/40		known
	8	40/57		
	20	62/80		
	0	0/40	69	Not
	4	14/40		known
	8	32/40		
Male Wistar rat	0	0/24	21	
(Epstein *et al.* 1969)	250	8/13		66 (87)
	500	13/18		74 (89)
	1000	12/14		72 (106)

Parentheses indicate a mean value.

duration of the experiment, as was the case in the other studies selected. It should also be noted that the authors reported kidney tumours in some animals in addition to the liver tumours expected, but only the liver tumour incidence has been considered for the purpose of this analysis.

The procedure used to estimate the health risk associated with current and projected levels of aflatoxin ingestion is outlined below:

Step 1: Risk estimates were obtained for doses relevant to human exposure using the probit, logit, Weibull, multi-hit and multi-stage models. Calculations were made for both the additive background and independent background cases for all but the multi-stage model, which was only used for the independent background case. The extrapolations were performed by special arrangement by the Environmental Protection Agency using DORES 81 (a computer program developed by J. Kovar and D. Krewski, Health and Welfare Canada, 1981) for all but the multi-stage model. GLOBAL 79 (developed by K. S. Crump, H. A. Guess and K. L. Deal, revised August 1979) was used for the multi-stage model.

Step 2: The range of values of lifetime risk calculated from the extrapolated results of each experiment using the above-mentioned extrapolation procedures, was estimated for an average daily aflatoxin exposure level of 0.01 ppb of the diet.

Step 3: The range of values of lifetime risk of liver cancer was estimated using the combined results of all animal studies (Table 1) and the male Fischer rat study alone (Wogan *et al.* 1974).

Step 4: (a) The estimated lifetime cases of liver cancer were obtained by multiplying the calculated risk by 220 million (the estimated size of the US population). (b) The annual number of cases of liver cancer was computed by dividing the number of lifetime cases by 70 (the estimated average lifespan (yr) in the USA).

Step 5: The predicted annual incidence rate of liver cancer resulting from aflatoxin ingestion was estimated from epidemiological data using a modification of the Peers–Linsell relationship (Peers & Linsell, 1977).

(a) The annual incidence rate (cases per 100,000 persons) above background (y′) was estimated from the equation $y' = 0.106x$, where x represents ng aflatoxin ingested/kg body weight/day.

(b) Average daily exposure, expressed as ppb of diet, was converted to ng/kg body weight by assuming an average body weight of 60 kg and an average dietary intake of 1500 g moist solid food/day. Accordingly, an average intake of 0.01 ppb is equal to 0.25 ng/kg body weight.

(c) From the annual incidence rate of liver cancer corresponding to an average daily aflatoxin exposure of 0.01 ppb, the annual number of cases has been calculated by dividing the incidence rate by 100,000 and multiplying this number by 220 million. These results were compared with those obtained from the animal-study extrapolations.

RESULTS

The results of the five extrapolations for the four selected animal studies, expressed as lifetime risks or probabilities, for exposures ranging from 0.001 ppb to 0.100 ppb are presented in Tables 2 and 3. The estimates in Table 2 represent the risk when additive background is assumed, and in Table 3 they represent the independent background case. (The multi-stage model is not described under the additive background assumption because of the lack of availability of a suitable computer program for such calculations.)

The extrapolated risk data presented in Table 2 indicate that there is considerable variation among the animal studies at each exposure level for any given extrapolation model. The difference in risk estimates is greatest when the probit model is used, varying by up to 10^7. When the risks obtained from a specific experiment using different extrapolation models are compared, a great deal of variation is seen in all but the Wogan *et al.* (1974) experiment. Only in the latter case are the results at each exposure level of the same order of magnitude. The extrapolated results from the Epstein *et al.* (1969) and Ayres *et al.* (1971) 12-month study, on the other hand, show an internal variation of 10^6 or more at 0.001 ppb, 10^4 at 0.010 ppb and 10^3 at 0.100 ppb.

An analysis of the data in Table 3 also reveals widely divergent values of risk in addition to several other points of interest. The striking consistency of results seen earlier with the Wogan *et al.* (1974) data no longer exists. Also noteworthy is the finding that the probit model yields a risk of zero at all the dose levels tested for this data set. (At 0.250 ppb, however, a risk of 10^{-16} is obtained (data not shown).) Zero risk levels are also obtained at all but one dose level for the Ayres *et al.* (1971) 16-month study using this model. These results can be attributed to the mathematical formulation of the probit distribution for the independent background case. The excess risk over background approaches zero very rapidly in the low-dose region in this case, and to a greater extent than any other of the 'independent' models (Krewski & Van Ryzin, 1980).

It should be noted that the logit and Weibull independent background models produce results for all but the Wogen *et al.* (1974) study that are exactly or nearly identical with those produced by the additive models. However, this is not true for the gamma multi-hit model, where the results differ by 1–7 orders of magnitude. Among all the extrapolation models used, only the multi-stage model, using Abbott's correction, yields results for all of the studies that differ by a factor of less than 100 at all dose levels.

Due to the wide variation in the results obtained by extrapolation, it seems useful to describe the risk estimates as a range of values at each exposure level. This appears to have more intrinsic value for the purpose of risk estimation than a calculated mean. For the additive background case, the range of values of annual incidence of liver cancer that would be

Table 2. Estimated risk of liver cancer due to dietary aflatoxin based on extrapolated animal studies using additive background models

Study	Mathematical model...	Risk estimates: Probit	Logit	Weibull	Multi-hit
		0.001 ppb			
Wogan*		0.47×10^{-5}	0.40×10^{-5}	0.53×10^{-5}	0.53×10^{-5}
Epstein†		0.71×10^{-8}	0.16×10^{-4}	0.15×10^{-2}	0.90×10^{-6}
Ayres‡		0.44×10^{-11}	0.12×10^{-4}	0.90×10^{-3}	0.49×10^{-4}
Ayres§		0.37×10^{-12}	0.24×10^{-10}	0.61×10^{-7}	0.10×10^{-10}
		0.005 ppb			
Wogan*		0.24×10^{-4}	0.20×10^{-4}	0.26×10^{-4}	0.27×10^{-4}
Epstein†		0.63×10^{-7}	0.69×10^{-4}	0.35×10^{-2}	0.45×10^{-3}
Ayres‡		0.13×10^{-7}	0.97×10^{-4}	0.30×10^{-2}	0.24×10^{-3}
Ayres§		0.23×10^{-11}	0.22×10^{-8}	0.13×10^{-5}	0.13×10^{-8}
		0.010 ppb			
Wogan*		0.47×10^{-4}	0.40×10^{-4}	0.53×10^{-4}	0.53×10^{-4}
Epstein†		0.21×10^{-6}	0.13×10^{-3}	0.50×10^{-2}	0.90×10^{-5}
Ayres‡		0.24×10^{-6}	0.24×10^{-3}	0.51×10^{-2}	0.49×10^{-3}
Ayres§		0.59×10^{-11}	0.16×10^{-7}	0.49×10^{-5}	0.11×10^{-7}
		0.050 ppb			
Wogan*		0.24×10^{-3}	0.20×10^{-3}	0.26×10^{-3}	0.27×10^{-3}
Epstein†		0.65×10^{-5}	0.58×10^{-3}	0.11×10^{-1}	0.45×10^{-4}
Ayres‡		0.79×10^{-4}	0.19×10^{-2}	0.17×10^{-1}	0.24×10^{-2}
Ayres§		0.26×10^{-9}	0.17×10^{-5}	0.10×10^{-3}	0.17×10^{-5}
		0.100 ppb			
Wogan*		0.48×10^{-3}	0.41×10^{-3}	0.53×10^{-3}	0.53×10^{-3}
Epstein†		0.30×10^{-4}	0.11×10^{-2}	0.16×10^{-1}	0.90×10^{-4}
Ayres‡		0.60×10^{-3}	0.46×10^{-2}	0.29×10^{-1}	0.49×10^{-2}
Ayres§		0.50×10^{-8}	0.13×10^{-4}	0.39×10^{-3}	0.14×10^{-4}

*Wogan *et al.* 1974.
†Epstein *et al.* 1969.
‡Ayres *et al.* 1971; 12-month study.
§Ayres *et al.* 1971; 16-month study.

predicted in the US population at each exposure level are presented in Table 4. No species conversion factor has been used to derive these estimates. Accordingly, they represent the number of cases of liver cancer that would occur if man had the same sensitivity to aflatoxin as the experimental animals tested. Due to the wide variation in the risk estimates, the annual incidence predictions at dietary aflatoxin concen-

Table 3. Risk of liver cancer attributable to dietary aflatoxin based on extrapolated animal studies using independent background models

Study	Mathematical model...	Risk estimates: Probit	Logit	Weibull	Multi-hit	Multi-stage
				0.001 ppb		
Wogan*		0	0.44×10^{-13}	0.63×10^{-9}	0.14×10^{-13}	0.50×10^{-5}
Epstein†		0.24×10^{-10}	0.16×10^{-4}	0.15×10^{-2}	0.16×10^{-1}	0.26×10^{-5}
Ayres‡		0.44×10^{-11}	0.12×10^{-4}	0.90×10^{-3}	0.66×10^{-2}	0.93×10^{-4}
Ayres§		0	0.24×10^{-10}	0.61×10^{-7}	0.72×10^{-11}	0.14×10^{-4}
				0.005 ppb		
Wogan*		0	0.54×10^{-11}	0.16×10^{-11}	0.24×10^{-11}	0.25×10^{-4}
Epstein†		0.64×10^{-8}	0.69×10^{-4}	0.35×10^{-2}	0.26×10^{-1}	0.13×10^{-4}
Ayres‡		0.13×10^{-7}	0.97×10^{-4}	0.30×10^{-2}	0.15×10^{-1}	0.46×10^{-3}
Ayres§		0	0.21×10^{-8}	0.13×10^{-5}	0.12×10^{-8}	0.72×10^{-4}
				0.010 ppb		
Wogan*		0	0.43×10^{-10}	0.63×10^{-7}	0.22×10^{-10}	0.50×10^{-4}
Epstein†		0.55×10^{-7}	0.13×10^{-3}	0.50×10^{-2}	0.32×10^{-1}	0.26×10^{-4}
Ayres‡		0.24×10^{-6}	0.24×10^{-3}	0.51×10^{-2}	0.21×10^{-1}	0.93×10^{-3}
Ayres§		0	0.16×10^{-7}	0.49×10^{-5}	0.10×10^{-7}	0.14×10^{-3}
				0.050 ppb		
Wogan*		0	0.52×10^{-8}	0.16×10^{-5}	0.39×10^{-8}	0.25×10^{-3}
Epstein†		0.49×10^{-5}	0.58×10^{-3}	0.11×10^{-1}	0.52×10^{-1}	0.13×10^{-3}
Ayres‡		0.79×10^{-4}	0.19×10^{-2}	0.17×10^{-2}	0.48×10^{-1}	0.46×10^{-2}
Ayres§		0.22×10^{-15}	0.17×10^{-5}	0.10×10^{-3}	0.16×10^{-5}	0.77×10^{-3}
				0.100 ppb		
Wogan*		0	0.41×10^{-7}	0.62×10^{-5}	0.36×10^{-7}	0.50×10^{-3}
Epstein†		0.27×10^{-4}	0.11×10^{-2}	0.16×10^{-1}	0.63×10^{-1}	0.26×10^{-3}
Ayres‡		0.60×10^{-3}	0.46×10^{-2}	0.29×10^{-1}	0.68×10^{-1}	0.92×10^{-2}
Ayres§		0.23×10^{-11}	0.12×10^{-4}	0.39×10^{-3}	0.14×10^{-4}	0.17×10^{-2}

*Wogan *et al.* 1974.
†Epstein *et al.* 1969.
‡Ayres *et al.*, 1971; 12-month study.
§Ayres *et al.* 1971; 16-month study.

Table 4. Predictions for total annual incidence of liver cancer in the USA due to dietary aflatoxin

Aflatoxin level (ppb)	Predictive annual incidence of liver cancer cases		
	Combined extrapolation models (additive background)		Multistage model (independent background)
	Combined animal studies*†	Male Fischer rat study†	Combined animal studies*†
0.001	0–4714	15 (0.48×10^{-5})	8–292
0.005	0–1414	75 (0.24×10^{-4})	41–1446
0.010	1–16,029	151 (0.48×10^{-4})	82–2923
0.050	20–75,429	754 (0.24×10^{-3})	409–14,457
0.100	44–91,143	1540 (0.49×10^{-3})	817–28,914

*Epstein *et al.* 1969; Ayres *et al.* 1971, 12- and 16-month studies.
†Wogan *et al.* 1974.
Nos in parentheses are mean lifetime risk values.

trations of 0.005 ppb and above differ by several thousand cases.

For comparative purposes, the extrapolated data based only on the Wogan *et al.* (1974) Fischer rat study were used for incidence predictions and the arithmetic mean of lifetime risk at each exposure level has been determined from the results of the extrapolations using the four additive background models (Table 4). Since the male Fischer rat has been found to be the most sensitive mammalian species tested, these data can be construed to represent the maximum number of cases that would be predicted on the basis of the probit, logit, Weibul and gamma multi-hit models. However these estimates are lower than the upper bounds of the estimates obtained when the results of all of the studies were combined because data from the rainbow trout were included with the latter. This non-mammalian species has been found to be more sensitive to the effects of aflatoxin than the male Fischer rat.

All of the above risk predictions are based on additive background models. The range of values of annual incidence of liver cancer that would be predicted using the multi-stage (indendent background) model and all the animal studies has been calculated separately and is also presented in Table 4. The multi-stage procedure was chosen because the logit and Weibull were very similar for both additive and independent backgrounds; the probit indicated zero risk at low doses and the multi-hit model produced divergent values for the various studies under independent background conditions.

The results of the risk estimation procedure based on the epidemiological studies, using a modification of the Peers–Linsell relationship are presented in Table 5. At the 0.01 ppb exposure level, the predicted incidence from the epidemiological data is approximately one third that predicted from the male Fischer rat study (Table 4) and is also lower than the lowest estimate based on the multi-stage model for all the studies.

The estimated annual liver cancer incidences for an average daily exposure of 0.01 ppb dietary aflatoxin using the studies and extrapolation models described above are summarized in Table 6. Also included in this table are the risk estimates obtained from extrapolated animal data from the FDA (1978) and Carlborg (1979a). There is a 'rough' agreement of predicted incidence, with the exception of the values calculated from a combination of the animal studies selected for this analysis. It should be noted that there is also a reasonable agreement between the risk predicted by the animal studies and the epidemiological data.

DISCUSSION

The range of estimates displayed in Table 6 emphasizes the sensitivity of the risk estimates to both the extrapolation model and the study or combination of studies used for the analysis. The wide variation in risk estimates obtained using the combined animal studies, as contrasted with those based only on the male Fischer rat study is noteworthy. Since this animal model represents the most sensitive mammalian species tested, the incidence of liver cancer that is predicted can be construed as representing a maximal value for mammals. A comparison of the

Table 5. Risk estimates of liver cancer at various aflatoxin exposures based on a modified Peers–Linsell relationship*

Dietary aflatoxin level (ppb)	Crude incidence rate of liver cancer†	Predicted no. of liver-cancer cases/yr
0.001	0.00265	5.8
0.005	0.01325	29.2
0.010	0.0265	58.3
0.050	0.1325	292
0.100	0.265	583
0.250	0.6625	1415
0.50	1.325	2915
1.0	2.65	5830

*Peers & Linsell, 1977.
†Rate above background/100,000 persons/yr.
Estimated USA population = 220 million.
A dietary aflatoxin level of 1.0 ppb is considered to be equivalent to 25 ng aflatoxin/kg body weight.

Table 6. Summary of estimated annual liver cancer incidence for 0.01 ppb dietary aflatoxin

Mathematical model and experimental data used	Estimated annual incidence of liver-cancer cases
Combined extrapolation models (additive background); combined animal studies*†	1–16,029
Multi-stage model (independent background); combined animal studies*†	82–2923
Combined extrapolation models (additive background); male Fischer rat study†	126–167 (151)
Multi-stage model; male Fischer rat study†	157
Modified Peers Linsell‡	58
Mantel–Bryan; 'pooled' rat studies (Bureau of Foods, 1978)	220
Mantel–Bryan; male Fisher rat study (Carlborg, 1979a)	160§

*Epstein *et al.* 1969; Ayres *et al.* 1971, 12- and 16-month studies.
†Wogan *et al.* 1974.
‡Peers & Linsell, 1977.
§For males only.
Parentheses indicate a mean value.

results obtained from epidemiological (Peers & Linsell, 1977) and experimental data reveals that the estimates of liver cancer incidence based on male Fischer rat data are almost three times higher than those based on human data. It thus seems reasonable to conclude that man's sensitivity to aflatoxin and, consequently, the health risk associated with its ingestion will be over-estimated by the Fischer rat data. It also suggests that the much higher estimates obtained from the combined animal studies and the combined extrapolations should not be used for the risk assessment. It should be recalled that the human data utilized for risk estimation were derived from populations that may be highly susceptible to the effects of aflatoxin and the risk may thus be considered a maximum estimate.

In the USA the incidence of liver cancer that is associated with present levels of ingestion of aflatoxin from peanuts and peanut products appears to be very low. The estimated risk of liver cancer, based on epidemiological projections, at the current action level of 20 ppb is equal to approximately 0.026 cases per 100,000 persons. This represents a small fraction (less than 2%) of the total incidence of this disease.

If average residue levels of aflatoxin in peanut products would decrease in proportion to reductions in the permissible levels, establishing a tolerance of 15 ppb would reduce the current risk by 25%, 10 ppb by 50% and 5 ppb by 75%. It is beyond the scope of this paper to make value judgements regarding what an acceptable level of risk for a contaminant such as aflatoxin should be. Such a decision can only be made by the policy maker. It does appear important, however, for the analyst to estimate or measure the relative health risks posed by various substances in the food supply, as well as the health benefits that would be expected to result from various policy alternatives. This information coupled with a knowledge of the costs that would be associated with proposed regulations should serve to promote the most cost-effective alternatives when funds and resources are constrained.

There is considerable dialogue in both scientific and legislative circles regarding our current ability to quantify health risk using animal models (Food Safety Council, 1982). The analysis described here clearly demonstrates the limitations of using laboratory studies for predictions of human risk. Uncertainty in the selection of both a suitable animal study and mathematical extrapolation model produces uncertainty of varying degrees in defining point estimates. Variations of several orders of magnitude resulted when studies that involved a limited number of doses were extrapolated. It should also be clear, however, that the divergence of such estimates decreases as the number of data points in a study increases. The data presented also indicate that a well constructed scientific experiment can produce meaningful estimates. In instances when the regulator must be concerned with relative or competing risks, laboratory experiments can provide this useful information.

The aflatoxin example is unusual insofar as there exist both human and laboratory data for use in risk analysis. The estimates that emerge from each of these sources are within reasonable range, and are clearly of the same order of magnitude. If appropriately performed animal studies had been relied upon exclusively, the fundamental conclusions of this research would probably not have been significantly altered. These results emphasize that well designed laboratory animal feeding studies coupled with the appropriate extrapolation procedure(s) can provide reliable information about the potential risks of carcinogens from food contaminants or additives. Such data can then be used in further analyses, in conjunction with cost estimates, to help determine regulatory policy in the food safety area.

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