

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 765

[OPTS-62033; FRL 2581-5]

Formaldehyde; Determination of Significant Risk

AGENCY: Environmental Protection Agency (EPA).

ACTION: Advanced notice of proposed rulemaking (ANPR).

SUMMARY: On November 18, 1983, EPA announced in the *Federal Register* its decision to rescind its previous decision that section 4(f) of the Toxic Substances Control Act (TSCA) did not apply to formaldehyde and to reconsider the issue. The public was asked to comment on whether formaldehyde should be given priority consideration under section 4(f). After reviewing the public comments and the health and exposure data relevant to formaldehyde, EPA has determined that section 4(f) does apply to two formaldehyde exposure categories. The exposures which led to this so-called "trigger" decision are those associated with manufacture of apparel from fabrics treated with formaldehyde-based resin are used. In addition, EPA is simultaneously announcing a second decision, which fulfills the statutory requirement to "initiate appropriate action," be made at the same time as the "trigger" decision, nor has EPA done so in previous cases where the Agency has found section 4(f) to be applicable to a chemical. However, the Agency believes that initiation of an investigation at this time is appropriate for formaldehyde because of the length of time that this chemical has been under Agency review and because of the particular circumstance surrounding this substance. EPA expects that on future section 4(f) decisions, the decision to conduct a regulatory investigation will not be made until after the "trigger" decision. The Agency invites interested parties to submit data and comments relevant to the control of exposure to formaldehyde in the areas on which its regulatory investigation will be focused.

DATE: All comments must be received by July 23, 1984.

ADDRESS: Since some comments may contain Confidential Business Information (CBI), all comments should be sent in triplicate to: Document Control Office (TS-793), Office of Toxic Substances, Environmental Protection Agency, Rm. E-409, 401 M St., SW., Washington, D.C. 20460.

Comments should include the docket control number OPTS 62033. Comments

received on this ANPR, except those containing CBI, will be available for review and copying from 8 a.m. to 4 p.m., Monday through Friday, excluding legal holidays, in Rm. E-107 at the address given above.

FOR FURTHER INFORMATION CONTACT: Edward A. Klein, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Environmental Protection Agency, Rm. E-543, 401 M St., SW., Washington, D.C. 20460, toll-free: (800-424-9065), in Washington, D.C.: (554-1404), outside the U.S.A.: (Operator-202-554-1404).

SUPPLEMENTARY INFORMATION: As published in the *Federal Register* of November 18, 1983 (48 FR 52507), EPA rescinded its previous decision that section 4(f) did not apply to formaldehyde. EPA stated that it would determine by May 18, 1984, whether section 4(f) does apply to formaldehyde. Comments were solicited from the public. This notice announces EPA's decision and explains the basis for the decision.

I. Notice Outline

This notice is organized as follows: Unit II. TSCA Section 4(f) summarizes the legislative language of this statutory provision and how EPA views that language. Unit III. Summary of EPA's Section 4(f) Decision summarizes EPA's decision on formaldehyde. Unit IV. Background describes: (1) The history of EPA's section 4(f) decision on formaldehyde, (2) the Consensus Workshop on Formaldehyde, (3) the process established for the present determination, and (4) addresses comments on EPA's decision to reconsider. Unit V. Basis for EPA's Determination presents a discussion of the major factors considered in EPA's determination such as EPA's cancer policy, animal tests, epidemiology data exposure data, quantitative risk analysis calculations, and EPA's reasons for the decision. Unit VI. Regulatory investigation discusses EPA's planned regulatory action and related activities of other Federal agencies. Unit VII. Confidential business information discusses how EPA will handle this kind of information. Unit VIII. Public Record and Unit IX. References are self-explanatory. EPA's responses to the principal comments received in response to EPA's November 18, 1983, *Federal Register* notice can be found in the pertinent Units.

II. TSCA Section 4(f)

A. Legislative Language

Under section 4(f) of TSCA, if EPA receives test data or other information—

*** which indicates to the Administrator that there may be a reasonable basis to conclude that a chemical substance or mixture presents or will present a significant risk of serious or widespread harm to human beings from cancer, gene mutations, or birth defects, the Administrator shall, within the 180-day period beginning on the date of the receipt of such data or information, initiate appropriate action under section 5, 6, or 7 [of TSCA] to prevent or reduce to a sufficient extent such risk or publish in the *Federal Register* a finding that such risk is not unreasonable.

Thus, there are two decisions to make under section 4(f) before a chemical is to be afforded priority regulatory attention. First, EPA must make the section 4(f) threshold determination that available information on a chemical indicates there "may be a reasonable basis to conclude" that the chemical presents a "significant risk of serious or widespread harm to humans from cancer, gene mutations, or birth defects." Second, if the threshold determination is made, the Agency is obligated to decide quickly whether to initiate regulatory action.

B. How EPA Views Section 4(f)

The purpose of section 4(f) is to focus the Agency's attention on chemicals that pose potentially high risks to people from cancer, gene mutations, or birth defects, by setting a 180-day deadline, the statute ensures that Agency resources will be immediately devoted to assessing whether action should be initiated to prevent or control the risks.

Section 4(f) applies to only a limited set of human health effects. Health effects other than cancer, gene mutations, or birth defects, as well as environmental effects, are not included under section 4(f). In addition, this priority review is not for all chemicals with the three biological effects of concern, but rather only for those which the available information indicates may cause "significant risk of serious or widespread harm." To decide whether this test is met for any particular chemical, EPA must analyze factors which permit predictions of risk, namely: (1) The chemical's hazardous properties, and (2) the questions of how many people are or will be exposed to how much of the chemical for how long. Once a determination of the risk posed by a chemical is made, it is necessary to determine if this represents a "significant risk of serious or widespread harm." While the terms "significant risk of serious harm" and "significant risk of widespread harm" are not defined by TSCA, the language of the statute indicates that both standards reflect attempts to define

situations of apparent gravity. The "significant risk of serious harm" standard covers situations in which persons are exposed to particularly high risks. The "significant risk of widespread harm" standard covers situations in which the risks to exposed individuals are somewhat lower, but the number of persons exposed is very large. This is borne out by the legislative history of section 7(f) of TSCA which utilizes the terms "serious or widespread injury" as part of the definition of "imminently hazardous chemical substances" against which EPA may seek injunctive relief. Congress indicated [H.R. Rep. No. 1679, 94th Cong., 2d Sess. 78 (1976) (Conference Report)] that "widespread injury" was intended to refer to a "risk affecting a substantial number of people." The term "serious" was distinguished from "widespread" by the fact that if a risk is "serious" it need not be "widespread" to meet the criteria for action under section 7(f). Within these relatively broad statutory boundaries, the application of these standards involves the exercise of discretion informed by policy.

Thus, the determination that a chemical problem meets the section 4(f) threshold and should receive section 4(f) priority involves an examination of the chemical's potential to cause any of the three designated effects, the likelihood of harmful exposure levels, and the number of persons exposed.

If EPA does not find section 4(f) applicable in a given case, this does not necessarily indicate a decision by the Agency not to pursue regulatory consideration. It means only that based on currently available information EPA does not consider the risk to meet the statutory standards for triggering expedited consideration under section 4(f) of TSCA. Likewise, a section 4(f) determination does not presuppose regulation.

A draft document containing EPA's working interpretation of section 4(f) and the criteria for applying it, will be available to the public in the near future.

III. Summary of EPA's Section 4(f) Decision

After review of the scientific data and public comments relevant to formaldehyde, EPA has determined that there may be a reasonable basis to conclude that certain exposures to formaldehyde present or will present a significant risk of widespread harm to human beings from cancer. The exposures which triggered this decision are those associated with manufacture of apparel from fabrics treated with formaldehyde resins and residence in

conventional and manufactured (mobile) homes containing construction materials in which certain formaldehyde resins are used. It is with respect to these two exposures that EPA believes the criteria of section 4(f) are met. The basis for this determination can be found in Unit V of this notice. This determination is based on EPA's evaluation of the hazard and exposure data and the risks estimated by mathematical models. The use of these models is discussed in Unit V.C.1. Calculation of Risk. EPA is also using this Federal Register notice to announce the start of a regulatory review of the exposure categories of concern. EPA will work with other Federal agencies, such as the Consumer Product Safety Commission (CPSC), the Occupational Safety and Health Administration (OSHA), and the Department of Housing and Urban Development (HUD) in this investigation.

As explained in Unit II.B above, a chemical risk will be found subject to section 4(f) if EPA decides that there may be a reasonable basis to conclude that a "significant risk of serious harm" or a "significant risk of widespread harm" is or will be presented. Applying these standards involves the exercise of discretion informed by policy. The following paragraphs will explain how EPA has applied these statutory standards to decide that certain exposures to formaldehyde are subject to section 4(f).

In the case of formaldehyde, and as will be the case for many chemicals evaluated by EPA, the Agency has started with data showing that formaldehyde causes cancer in animals at particular dose levels and has applied mathematical models to extrapolate from the animal dose levels to those levels to which humans would likely be exposed. These mathematical models give EPA an objective measurement of the relative risks of different chemicals and, thus, provide a mechanism to allow the Agency to set priorities. Because section 4(f) is a priority-setting provision, EPA believes it is appropriate to use these models to decide whether section 4(f) is triggered by a given chemical.

The application of the mathematical models to the animal data and the extrapolation to human dose levels results in a determination of the potential risk to individuals over their lifetimes. This is generally expressed as a probability. For example, the model extrapolations may show that certain categories of individuals exposed to formaldehyde at a given level over a given period of time could contract cancer with a probability of 1×10^{-4} which is a chance of 1 in 10,000.

The individual risk number derived from the model may then be multiplied by the number of exposed persons believed to be exposed to that dose level. That product provides an indication of how many of these persons could contract cancer.

Because of substantial variability in the doses different individuals may receive, uncertainties in the relationship between dose and risk at low doses, and variability in sensitivity to the effects of a chemical among the human population, EPA generally uses for its priority-setting decisions models which provide an "upper bound" of the risk, i.e., the models provide the upper 95 percent confidence limit. This is a statistical method for estimating the range in which the true risk may lie. The true risk is not likely to be higher than the "upper bound" estimate, but it could be lower. This has been done in the case of EPA's evaluations of formaldehyde's cancer risks. Thus, the calculations performed using those models should not be interpreted as predictions of the actual number of cancer cases that may occur.

In determining whether a chemical risk may meet either statutory test—"significant risk of serious harm," or "significant risk of widespread harm"—EPA applies the models as described. Under the "significant risk of serious harm" test, the individual risk would be high for a population of significant size. Under the "significant risk of widespread harm" test, the individual risk calculation may be lower, but the large number of persons exposed would lead to a potential for a significant number of persons in the population to be injured by the effect under consideration.

IV. Background

A. History of the Section 4(f) Decision

In November 1979, EPA received information that the interim results of a 24-month rat bioassay conducted by the Chemical Industry Institute of Toxicology (CIIT) showed that a number of the rats had developed nasal cancer after inhalation of formaldehyde.

In November of 1980, the Federal Panel on Formaldehyde, formed by several Federal agencies under the aegis of the National Toxicology Program, published a report finding that CIIT's bioassay methodology was consistent with accepted testing standards. Using the data available through the 18-month point of the CIIT study, the Federal Panel concluded that "formaldehyde should be presumed to pose a risk of cancer to humans." Also in November

significant risk of serious or widespread harm before invoking section 4(f).

EPA's view of section 4(f) is between these two extremes. EPA believes that section 4(f) applies to those chemical risks that have the potential to cause grave injury even though the evidence allows formation of only a preliminary viewpoint. Thus, while section 4(f) applies to high priority chemical risks, EPA does not need to show that concern by a high level of evidence.

EPA's interpretation focuses on the statutory language as a whole. The requirement that there "may be a reasonable basis to conclude" indicates that the level of evidence is not as high as that needed for regulation. Under TSCA, regulation is warranted if there "is" a reasonable basis to conclude. The requirement that EPA find a "significant risk of serious or widespread harm" indicates that the Agency is to examine only those risks of high concern under section 4(f). Because section 4(f) is a priority-setting mechanism, EPA must rank chemical risks according to the relative levels of concern they present to public health. Accordingly, it is within EPA's discretion to use mathematical models to assist in this ranking and it is an appropriate application of section 4(f) to focus on different exposure scenarios among different groups of people. Thus, EPA may apply the section 4(f) designation to specific formaldehyde uses which result in risks to specifically-designated populations.

To adopt either the views of NRDC or the industry groups could seriously defeat EPA's ability to adequately protect public health. The low threshold view of section 4(f) would result in placing chemicals on a regulatory priority that do not present a "significant risk of serious or widespread harm," thus restricting EPA's ability to focus attention on the truly serious risks for which section 4(f) was intended. The industry view, which would have the Agency delay action until evidence shows clear risk, would defeat the remedial nature of TSCA. TSCA is meant to allow EPA to act to prevent risks from occurring. If EPA had to wait for clear evidence before setting priorities under section 4(f), much damage could be done before the Agency could act.

EPA's view of section 4(f) also avoids some of the more extreme consequences of the NRDC and industry views. Under the NRDC view, numerous regulatory actions would be initiated for chemicals that may not present actual risks. Under the industry view, a declaration that a chemical triggers section 4(f) would be a sign of a dire emergency and may send incorrect signals to the public. EPA

wishes to make it clear that today's decision on formaldehyde does not mean that the Agency believes the chemical presents short-term emergency risks. Rather, there is a cause for concern and EPA intends to investigate seriously the problem on a priority basis. Information available to the Agency does not indicate that people should substantially change their habits if they are being exposed to some level of formaldehyde.

A number of commenters disagreed with EPA's decision to reconsider its previous formaldehyde section 4(f) determination for a number of reasons. They have argued that EPA's first decision was correct and that, unless new medical evidence is presented that formaldehyde presents a carcinogenic risk to humans, EPA should not reconsider. Public controversy, according to these commenters, should not be a basis for rescinding an Agency decision. To the extent that new evidence may be uncovered by the Workshop, EPA should wait until the final reports are in and properly assessed before it decides to reconsider its formaldehyde decision. Finally, commenters argue that a decision by the United States Court of Appeals for the Fifth Circuit overturning regulation of urea-formaldehyde foam insulation (UFFI) (701 F.2d 1137) by the Consumer Product Safety Commission shows that there is no substantial basis to consider formaldehyde under section 4(f).

EPA disagrees with these comments. Reconsideration of EPA's formaldehyde section 4(f) decision was dictated by public controversy that called into question the objectivity of EPA's scientific analysis and policy decisions. A number of questions were raised regarding EPA's adherence to its own cancer policy guidelines. Meetings were held with selected members of the public, which appeared to some persons to be inappropriate. When such questions are raised about EPA's procedures and policies, it is incumbent on the Agency to rectify the situation. Rather than contribute further to the public controversy, EPA decided to remove any appearance to taint in its decision and submit the entire formaldehyde section 4(f) process to a public administrative forum. Thus, EPA believes that its decision to revoke the earlier section 4(f) decision and reconsider it was justified.

Since the reasons stated above adequately justify EPA's decision to reconsider its formaldehyde decision, new medical evidence on formaldehyde is not a prerequisite to such reconsideration. Nor is new evidence ever a prerequisite to any decision to

reconsider EPA policy decisions on chemicals subject to its regulatory jurisdiction. EPA may reconsider decisions as long as it presents its reasons and adequately justifies the change. For example, changes in the interpretation of evidence already in EPA's possession also could support modification of Agency decisions.

Further, EPA does not believe it needs to wait for final assessment of Workshop results before it makes its formaldehyde section 4(f) decision. This argument is, in EPA's view, another aspect of the argument that the Agency should wait for clear evidence before it makes decisions under section 4(f). As stated above, such a delay could defeat the remedial intent of TSCA. In any event, EPA has had access to all draft Workshop reports and is confident that the Workshop's position on topics critical to EPA's decision would change only in the face of substantial new data, new data to which the Agency would have access.

EPA also disagrees with the comments that argue that the Fifth Circuit decision in the UFFI case affects EPA's ability to consider formaldehyde under section 4(f). That decision applied only to one product, which apparently is no longer manufactured. EPA's decision today affects entirely different products. Furthermore, the section 4(f) decision is far more preliminary than the final regulatory action considered by the Court in the UFFI case. Thus, the reasoning applied does not affect today's decision under any interpretation of the Court's opinion. It is important to note, moreover, that the UFFI opinion did not reject CPSC's determination that formaldehyde presents a risk of cancer to humans. Rather, the Court found that CPSC's exposure analysis did not support the regulatory action.

Finally, commenters stated that EPA should not consider formaldehyde under section 4(f) because TSCA is not the appropriate mechanism to regulate any of the significant risks that formaldehyde may present. These commenters argue that EPA should defer to other Federal agencies capable of regulating formaldehyde risks, such as the Occupational Safety and Health Administration and the Department of Housing and Urban Development. Also, they note that, since formaldehyde is ubiquitous in the environment and occurs naturally in the atmosphere and in human cells, there is no regulatory option under TSCA.

EPA believes that these comments are not applicable to today's decision. This decision relates to the toxicity and

morphological evidence that polypoid adenomas progress to squamous cell carcinomas (Ref. 2). This was the recommendation of the Carcinogenicity Panel also. However, consideration will be given to the benign tumors in further assessing formaldehyde's risks as part of the Agency's regulatory investigation.

Other studies support the results of the CIIT study. In two studies carried out by Albert et al. (Ref. 3), rats were exposed for life by inhalation to formaldehyde alone, mixtures of hydrochloric acid (HCl) and formaldehyde, or HCl alone.

In the first study, 99 male rats were exposed to a mixture of HCl and formaldehyde (premixed at high concentrations before introduction into the exposure chamber to maximize the production of bis(chloromethyl) ether (BCME)). This was done because the investigators were studying the hazard associated with the use of HCl and formaldehyde in close proximity in the workplace. A report had linked the production of BCME from mixing HCl and formaldehyde gas. The average concentrations were 10 ppm HCl 14 ppm formaldehyde, and about 1.0 part per billion (ppb) BCME. Of the 99 animals exposed to the test mixture, 25 developed squamous cell carcinomas of the nose. The contribution by the BCME was thought to be minimal because the expected response to 1.0 ppb was estimated to be less than 1.5 percent and there was a 25 percent incidence of nasal tumors in the study.

The second Albert study, in which male rats (100 per group) were exposed to HCl alone (10.2 ppm), premixed HCl-formaldehyde mixture (14.3 ppm formaldehyde/10.0 ppm HCl), nonpremixed formaldehyde-HCl mixture (14.1 ppm formaldehyde/9.5 ppm HCl), or formaldehyde alone (14.2 ppm), showed statistically significant numbers of squamous cell carcinomas of the nasal cavity in the rats exposed to formaldehyde alone and the HCl-formaldehyde mixtures. A control group of 100 rats was used. No nasal cancers were seen in the HCl-only exposed rats or in the controls. Also, it appeared that the irritant HCl gas did not enhance the carcinogenic response because the frequency of tumors was similar in the formaldehyde alone and formaldehyde-HCl groups.

Other studies, such as Dalbey (Ref. 4); and Kusch et al. (Ref. 5) have not shown a significant carcinogenic response to formaldehyde in the hamster. However, these studies suffer from certain weaknesses such as inadequate pathology (only two microscopic sections of the nose were examined in the Dalbey study) and short duration

(six months for the Rusch study), which makes it difficult to rely upon the negative results as being reliable for the endpoint in question.

EPA concludes that there is credible evidence to show that formaldehyde is carcinogenic in rats, and that there is suggestive evidence in mice.

4. *Epidemiology.* The body of epidemiologic data cannot be used to support the hypothesis that formaldehyde is not a human carcinogen and, thus, cannot be used to negate the animal data. Although several studies show significant increases in leukemia and brain cancer among individuals potentially exposed to formaldehyde, the data do not demonstrate that formaldehyde exposure is a cause of human cancer. EPA's evaluation of the epidemiology is summarized in this section and explained in greater detail in the administrative record for this proceeding.

a. *EPA's analysis.* Formaldehyde has been and is the subject of many epidemiologic studies. Fourteen major studies and several minor studies were reviewed by EPA. To reach a decision regarding whether a particular study showed any association with specific cancers, EPA evaluated the conclusions reached by the investigators and the power of the study to detect specific cancer outcomes. The power of a study is its ability to detect true association of the exposure and disease. If a study is likely to conclude that the exposure to a particular chemical is not associated with a disease, when in fact an association exists, the study has a low power to detect that association. The ability of a well-conducted study to detect an increased risk depends upon such factors as sample size, years of follow-up, magnitude of the increased risk, background incidence of the disease among the population, desired statistical significance of the conclusion, and the type of statistical analyses used by the study investigators.

The completed epidemiologic studies of these populations have reported excess cancer risks among textile workers, garment workers, brickmasons, shoemakers, leather workers, film processors, paint-lacquer-glue workers, chemical workers, and certain medically related professions—pathologists, morticians, embalmers, and anatomists.

Although the studies considered by EPA are of cohort or case-control design—designs essential for inferring causality from epidemiologic studies—inferences regarding specific chemicals cannot be drawn at this time. A major limitation of the studies is their inability to separate the contributions of formaldehyde from the contributions of

other occupational exposures. Other limitations include small sample sizes and inadequate control for confounding variables such as smoking in the analyses. Last, a working population is generally healthier than the total population and will tend to show lower mortality when compared to the general population.

One outcome of the limitations has been low power in each study to detect small relative risks for the rarer forms of cancer. For specific cancers, the completed epidemiologic studies do not have sufficient power to detect, at the formaldehyde levels to which the medically related professions may be exposed, increased risks of 100 percent or less (these risks were calculated from the coefficients obtained from the 3-stage multistage model using the animal data).

While the individual studies lack adequate power to detect specific cancer outcomes, acceptable statistical methods may be employed in order to obtain a general perspective on the total evidence available and to increase power. The Epidemiology Panel combined observed and expected numbers of cancer deaths for specific sites from both standard mortality ratio (SMR) and proportionate mortality ratio (PMR) studies. EPA combined the results of several studies according to Fisher's method for combining probabilities. As a result of their analyses the Epidemiology Panel concluded that the medically related professions have a significantly increased mortality from leukemia and brain cancer. EPA concluded that: (1) For SMR studies, brain cancer mortality is significantly elevated among the medically related professions and among the medically related professions and chemical workers together, and (2) for PMR studies, leukemia and brain cancer mortality is significantly elevated among the medically related professions.

These analyses by EPA and the Epidemiology Panel, however, do not causally link formaldehyde exposure with cancer. Formaldehyde exposure is a major exposure among the medically related professions, but exposures to dyes, solvents and other organic chemicals as well as pathogenic organisms also occur. Indications that formaldehyde may not be the causal agent comes from epidemiologic studies of other occupational groups who may be exposed to similar agents, these studies also report excesses in leukemia and brain cancer.

In summary the epidemiologic studies of the medically related professions are

upon inhalation. This is supported by the Structure Activity Panel of the Workshop which stated:

Despite its rapid removal, the possibility exists that transient increases in formaldehyde may occur in the intact animal. The Panel could not exclude the possibility that formaldehyde may be transported to, and exert toxic effects at, distant sites following inhalation, but definitive evidence for effects of formaldehyde *per se* at distant sites is lacking.

7. Structure-activity relationships.

Formaldehyde is structurally similar to other aldehydes such as acetaldehyde, acrolein, crotonaldehyde, malondialdehyde and glycidaldehyde. These aldehydes have been shown to have oncogenic effects. For instance acetaldehyde has produced tumors of the nose and larynx in hamsters by inhalation and glycidaldehyde has produced skin tumors in mice in skin painting tests. The conclusion that formaldehyde is carcinogenic is consistent with this association between structure and effects.

8. Comments about human risk.

Commenters have suggested several reasons for EPA to find that formaldehyde does not present a cancer risk to humans at present exposures. These reasons include: hypotheses that there is a threshold level of exposure at which formaldehyde will cause cancer and that this threshold is above current levels of exposure; a suggested role of the respiratory mucous layer in acting as a barrier to formaldehyde; and a suggestion that low amounts of formaldehyde can be handled normally by cells without carcinogenic results. In addition, some have suggested that EPA use the least sensitive species of animal in which formaldehyde has been tested, rather than the rat, in predicting the human response.

EPA's decision is based on currently available data. Both EPA and the Consensus Workshop Panels view the weight of this evidence as suggesting potential human carcinogenicity at low doses. Both EPA and the Panels have acknowledged that factors such as cytotoxicity and the mucous layer may play a role; however, neither has concluded that the weight of evidence presently supports using these factors as a basis for finding low dose exposures to be free from risk. Further consideration of these factors is appropriate.

a. *Threshold—in general.* EPA's Cancer Policy explains that the evidence for a no-threshold concept of cancer induction emerged in the debate over the health effects of radioactive fallout from atomic weapons in the 1950's. This concept supports the idea that any

exposure, however small, will confer some risk of cancer on the exposed population. The Cancer Policy further states that evidence has accumulated that the no-threshold concept can also be applied to chemical carcinogens (41 FR 21401).

Accordingly, EPA as a matter of policy generally assumes that there is no threshold to cancer induction unless there is clear evidence for a threshold in the case of a particular chemical. In the case of formaldehyde, EPA has reviewed the available data, including information submitted by commenters, and has concluded that the available evidence does not demonstrate a threshold for formaldehyde carcinogenesis. This determination is consistent with that of the Risk Estimation Panel of the Workshop which stated:

With regard to the possibility of a threshold dose for a tumor response, in the absence of any clear evidence for a threshold, it is misleading to assume that one exists, and the assumption of a non-threshold dose-response is more prudent (Ehrenberg et al., 1983; Lyon et al., 1983). The Panel concludes, therefore, that it is inappropriate at this time to consider a threshold model for formaldehyde carcinogenesis.

Commenters have presented three general arguments supporting a threshold for formaldehyde's carcinogenicity. These are discussed below.

b. *Threshold-cytotoxicity.* In the CIIT study there was a very steep dose-response curve, approximately a 50-fold increase in response from 5.6 ppm to 14.3 ppm, with less than a 3-fold increase in dose. This rapid increase in the response at 14.3 ppm has been attributed by some to formaldehyde's cytotoxic effects, which caused massive irritation, breakdown of mucociliary clearance function, and subsequent cell death and restorative cellular repair.

These observations have led to an hypothesis that formaldehyde's cytotoxicity has a threshold and that this threshold is also a threshold for carcinogenicity. A related hypothesis has been suggested that the cytotoxic and carcinogenic effects occur only when the protective mucous layer is broken down and that this break-down is a threshold for both effects. (The role of the mucous layer is discussed further below.) The reasoning for a cytotoxicity-related threshold is that cytotoxicity, by causing increased cell division, would increase the opportunity for carcinogenic events to be expressed. Thus, at exposure levels that do not cause cytotoxicity, the carcinogenic risk would be greatly reduced.

EPA does not believe that the available evidence demonstrates that the absence of cytotoxicity represents a practical threshold to formaldehyde's carcinogenic potential. Although EPA and the Carcinogenicity Panel acknowledge that cytotoxicity may play a role in formaldehyde's carcinogenicity, its relative contribution is unknown. Consequently, EPA cannot infer that the absence of cytotoxicity equates with a practical threshold.

c. *Threshold—observations from data.*

Commenters have argued that the absence of malignant tumors at low doses in the available studies indicates a "no-effect level", or threshold, for formaldehyde carcinogenicity. Commenters specifically cite the CIIT study, which showed no malignancies at the lowest dose, and a study by Rusch, et al (Ref. 5). According to the commenters, the Rusch study showed "no adverse effects whatsoever on rats, monkeys, and hamsters exposed to 0.2 ppm, or even to 1.0 ppm of formaldehyde, 22 hours a day, seven days a week, over a period of six months * * *. The CIIT and Bio/dynamics (Rusch study) results thus indicate a practical threshold below which there is no effect even in the rat."

EPA disagrees with the conclusion expressed in these comments.

With respect to the CIIT study, it is not uncommon to see marginal or no response at the lower doses employed in a chemical bioassay. This does not mean that no effect would occur at that dose, only that studies are necessarily limited in the response that can be detected at low doses (there were groups of approximately 120 male and female rats for each dose level).

With respect to the Rusch study (Ref. 5), a number of factors prevent it from being used to support a threshold hypothesis. The study contained small test populations (groups of 6 monkeys, 40 rats, and 20 hamsters) and was of short duration (6 months). Although the total exposure time was approximately 5 times longer per week than in the CIIT study and the rats at 1 ppm in the Rusch study received 2.5 times the cumulative dose received by rats at 2.0 ppm in the 2-year CIIT study, the animals were sacrificed after 6 months and a carcinogenic response would not be likely to be observed in such a short duration. In addition, the small study populations also decreased the sensitivity of the study.

d. *Threshold—mucous layer.* The third threshold hypothesis of some commenters is that at low levels (in the current human exposure range and below the OSHA standard) the mucous

categories: nonconsumptive uses, pseudo-consumptive uses, and consumptive uses. In nonconsumptive uses, the chemical identity of the formaldehyde does not change. In pseudo-consumptive uses, the chemical identity of formaldehyde does change, but it is not irreversibly altered. Under appropriate conditions, some or all of the original formaldehyde may be regenerated. Consumptive uses, on the other hand, are those uses in which formaldehyde serves as a feedstock for the preparation of other chemicals. The derivatives are irreversibly formed and usually contain only residual levels of unreacted formaldehyde. Under extreme conditions, such as very high temperatures or highly acidic conditions, some of the derivatives may degrade and release formaldehyde.

Formaldehyde's major nonconsumptive uses are: (1) disinfectant, (2) preservative, (3) deodorant, and (4) textile and paper uses.

The major pseudo-consumptive uses

are: (1) Urea-formaldehyde resins which are used in fiberboard, particleboard, plywood, laminates, urea-formaldehyde foams, molding compounds, and paper, textiles, and protective coatings; (2) urea-formaldehyde concentrates which are used to produce time-release fertilizers, and (3) hexamethylenetetramine which is used as a special anhydrous form of formaldehyde to cure resins and to treat textiles and rubber.

The major consumptive uses are: (1) Melamine-formaldehyde resins which are used for molding compounds, fiberboard, particleboard, plywood, laminates, paper and textiles, (2) phenol-formaldehyde resins which are used in fiberboard, particleboard, plywood molding compounds, and insulation; (3) pentaerythritol which is used to produce alkyd resins, (4) 1,4-butanediol which is used to produce tetrahydrofuran, (5) acetal resins which are used in the manufacture of engineering plastics, and (6) trimethylolpropane which is used in the production of urethanes.

2. *Estimates of current human*

exposure. To obtain estimates of human exposure to formaldehyde and its products, the Agency commissioned a contractor study (Ref. 11). This study integrated the existing monitoring data, engineering or modeling estimates, use data, population estimates, and assessment of the likelihood of exposure from formaldehyde-related activities into an exposure assessment detailing those activities having a high formaldehyde exposure potential. The summary results of that assessment are presented in Table 1. EPA has updated some portions of Table 1 to reflect new data received in response to the Federal Register Notice of November 18, 1983. The data from Table 1 were used as the basis for the risk assessment. It should be noted that only the nonpesticidal uses of formaldehyde were used in the section 4(f) determination because, under section 3(2)(b)(ii) of TSCA, pesticides are not defined as chemical substances under TSCA and do not fall under the purview of section 4(f).

BILLING CODE 6560-50-M

Exposed Population	Number Persons Exposed	Exposure Duration (Hrs./Wk.) (Wks/Yr)	Exposure Level Personal Area (ppm)
Installers of U-F foam insulation	<1,000 ³ /	34.7 50	A 0.52 A 0.49
Manufacturers of metal molds and castings	60,000	39.3 50	A 0.33 B 1.55 A 0.66
Manufacturers of plastic products	16,575	39.8 50	No Data B 0.26 A 0.13
Manufacturers of paper & paperboard	>9,730	44.4 50	A 0.15 A 0.42
Manufacturers of textiles	17,800	40.1 50	A 0.70 B 0.42
Manufacturers of apparel	777,000	36.0 50	A 0.64 A 0.23
Wholesale trade of apparel	66,400	36.8 50	A 0.38 A 0.12
Manufacturers of building paper and coatings	3,800	44.9 50	C 0.33 ² / C 0.31

Exposed Population	Number Persons Exposed	Exposure Duration (Hrs./Wk.) (Wks./Yr)	Exposure Level Personal Area (ppm)
College students	2,903,000	5 36	A $\frac{0.434}{0.14}$
Medical students	74,900	5 36	A $\frac{0.434}{0.14}$
Nursing students	245,000	5 36	A $\frac{0.434}{0.14}$
Dental students	21,500	5 36	A $\frac{0.434}{0.14}$
Funeral service workers	55,000	16 50	A $\frac{1.70}{1.37}$
New mobile home ⁵ / residents	4,200,000	112 52	A $\frac{0.256}{0.25}$
Conventional home residents (UFFI)	1,750,000	112 52	A $\frac{0.073}{0.073}$
Conventional home residents	>100,000,000	112 50	0.0307/

As Table 1 shows, most exposures are below 0.5 ppm. For occupational groups, about one-fourth of the exposures are between 0.5 ppm and 1 ppm. Students and teachers are exposed to low levels for short durations from the use of preserved biological specimens, generally less than 0.5 ppm. This level can be reduced in the future as more schools purchase specimens that have been washed free of formaldehyde and then shipped in a non-formaldehyde-based medium (ethylene glycol). Based on available monitoring data, use of specimens processed in this manner can significantly reduce formaldehyde exposures to students and teachers. The proportion of specimens packed in glycol solutions has been growing since the early 1970's and will likely continue to grow in the future. With the exception of a few small firms, most firms offer routinely (or on request) specimens washed and packed in glycols (Ref. 12).

Also, many industrial users of formaldehyde and formaldehyde resins are attempting to reduce formaldehyde levels by changing resin formulations to decrease the amount of excess formaldehyde. This is especially true for particleboard and other "formed" wood products. Textile producers and manufacturers of products for the textile industry are attempting to reduce formaldehyde levels through processing techniques, fiber blend changes, and new resin products.

The apparent trend is for efforts by industry to reduce formaldehyde levels in their products through relatively inexpensive methods. Such action may lead to significant reductions in formaldehyde levels. However, these mitigations of exposure are difficult to quantify at this time, except for students and teachers where formaldehyde monitoring data show the difference between old and new methods of processing biological specimens.

Because of limitations in the monitoring data, two fairly typical assumptions for exposure assessments were made in assembling Table 1. First, since specific monitoring data for all types of potentially exposed worker classifications or operational settings within an industry were generally not available, all workers in a given industry were assumed to be exposed to the exposure levels reported in Table 1. All worker exposure, however, is not in fact identical; worker exposure can vary because of the physical characteristics of the work site and the employee's work station for example. However, in the absence of data EPA must make reasonable assumptions regarding exposure levels to protect public health.

Workers were assumed to be exposed 5 days per week for 40 years. General population exposures were assumed to be for 70 years. Manufactured home residents were assumed to be exposed 112 hours per week for 10 years (see Quantitative Risk Assessment on Formaldehyde in the record of this decision).

Second, the reported exposure levels are assumed to be representative of the actual exposure levels for a given population. The limitation that this assumption presents is that the estimated exposure levels for some populations may differ, in some cases widely, from the actual situation. This is especially true for those populations for which little or no monitoring data are available and also for those populations for which the monitoring data were collected as a result of complaint investigations.

Despite these limitations, however, the monitoring data are fairly extensive and usually contain at least two studies for each exposure setting where significant formaldehyde exposure levels can reasonably be expected. These data, therefore, can be considered as an example of the exposure levels experienced by the identified populations. In addition, confidence in the data concerning the number of persons exposed to some level of formaldehyde and daily or weekly duration of exposure is high because the data are based on Census of Manufactures data and other Federal labor statistics. For a section 4(f) decision, the data are adequate for determining whether "there may be a reasonable basis to conclude" that there is a "significant risk * * *"

Finally, the limited monitoring data submitted by the public in response to the notice published in the *Federal Register* of November 18, 1983 are in good agreement with the corresponding exposure level estimates contained in EPA's exposure assessment (Ref. 13). Some of these data were used in Table 1 to fill data gaps as noted in the table.

C. Significant Risk of Serious or Widespread Harm

In Units V.A and V.B, EPA has explained its view of the evidence on the toxicity of formaldehyde and the available exposure information. These are the elements necessary to make the decision whether section 4(f) applies.

A chemical may not be subject to section 4(f), however, until EPA decides that it may present a "significant risk of serious or widespread harm." Thus, the mere determination that a chemical is a potential carcinogen in humans and that substantial numbers of persons may be

exposed to it, does not trigger section 4(f). Rather, section 4(f) is triggered only after EPA determines the magnitude of the risk based upon consideration of the estimated individual risks and the number of persons exposed to those risks at given levels over given periods of time. These analyses are explained below.

1. *Calculation of risk.* The determination of individual risk can be made through the use of epidemiologic or animal studies. Epidemiologic data will show human effects at dose levels generally experienced by humans. Epidemiologic studies suitable for risk extrapolations are rarely available, however, and are not available in the case of formaldehyde. Thus human cancer risk from formaldehyde must be estimated through use of animal studies. This necessitates extrapolation from high to low doses because, typically, test animals are exposed to concentrations much higher than those expected to be experienced by humans. These extrapolations are carried out by fitting mathematical models to the observed animal data.

a. *Dosage data used in models.* Of the animal studies showing a statistically significant increase in malignancies (Refs. 1 and 3), the CIIT rat study was selected for the application of models because it was a well conducted multi-dose study that showed a dose-response relationship suitable for extrapolating to human risk at expected human doses.

A number of adjustments to the CIIT and the human exposure data were necessary before the models could be run. First, the number of rats at risk in the CIIT study had to be determined. An animal was considered at risk if it was sacrificed or died after the first squamous cell carcinoma was observed. All rats were assumed to have a lifetime of 24 months, even though some rats were permitted to live beyond 24 months. The first occurrence of squamous cell carcinoma was at 11 months. Thus, rats sacrificed at six months or those dying prior to 11 months were not considered to be at risk. Rats sacrificed at 12 and 18 months were considered to be at risk for the equivalent of one-half or three-quarters of their lifetime, respectively. Because the 20 rats sacrificed at 12 months were only at risk for one-half of their lifetimes, these rats collectively contributed 10 rat lifetimes to the study. Similarly, the 40 rats sacrificed at 18 months were at risk for three-fourths of their lifetimes and contributed 30 rat lifetimes to the study. This, in effect, reduces the total number of rats at risk during the study and was done to aid in

TABLE 3--INDIVIDUAL LIFETIME RISKS AND LIFETIME ADDITIONAL OCCURRENCES PER POPULATION

Exposed Population	Number Persons Exposed	Additive Weibull	Weibull Upper 95	Multistage (3-Stage)	Multistage Upper 95
Manufacturers of CH ₂ O	1,400	1.58 X 10 ⁻⁵ a/<1	1.63 X 10 ⁻⁴ <1	8.8 X 10 ⁻⁶ <1	4.0 X 10 ⁻⁴ <1
Manufacturers of resins (U-F, P-F, M-F, acetal)	5,025	8.91 X 10 ⁻⁵ <1	7.02 X 10 ⁻⁴ 4.3	2.81 X 10 ⁻⁴ 1.7	1.53 X 10 ⁻³ 9.2
Manufacturers of hardwood plywood	6,700	2.70 X 10 ⁻⁵ <1	2.64 X 10 ⁻⁴ 1.8	2.99 X 10 ⁻⁵ <1	6.28 X 10 ⁻⁴ 4.2
Manufacturers of particleboard	4,000	9.64 X 10 ⁻⁶ <1	1.03 X 10 ⁻⁴ <1	2.62 X 10 ⁻⁶ <1	2.08 X 10 ⁻⁴ <1
Manufacturers of wood furniture	59,000	2.11 X 10 ⁻⁶ - 6.57 X 10 ⁻⁵ <1-4	2.40 X 10 ⁻⁵ - 5.53 X 10 ⁻⁴ 1.8-33	4.10 X 10 ⁻⁶ - 1.68 X 10 ⁻⁴ <1-10	6.66 X 10 ⁻⁵ - 1.22 X 10 ⁻³ 4.1-72
Manufacturers of mobile homes and related structures	31,500	1.26 X 10 ⁻⁵ <1	1.33 X 10 ⁻⁴ 4.4	5.12 X 10 ⁻⁶ <1	3.38 X 10 ⁻⁴ 10.7
Manufacturers of U-F foam chemicals	<50	1.58 X 10 ⁻⁵ <1	1.63 X 10 ⁻⁴ <1	8.8 X 10 ⁻⁶ <1	4.08 X 10 ⁻⁴ <1
Installers of U-F foam insulation	<1,000	1.58 X 10 ⁻⁵ <1	1.63 X 10 ⁻⁴ <1	8.8 X 10 ⁻⁶ <1	4.08 X 10 ⁻⁴ <1

Exposed Population	Number Persons Exposed	Additive Weibull	Weibull Upper 95	Multistage (3-Stage)	Multistage Upper 95
Manufacturers of U-F concentrates	40	1.58×10^{-5} <1	1.63×10^{-4} <1	8.8×10^{-6} <1	4.08×10^{-4} <1
Manufacturers of nitrogenous fertilizers	1,600- 2,850	4.12×10^{-5} <1	3.78×10^{-4} 1.1	7.08×10^{-5} <1	8.68×10^{-4} 2.5
Manufacturers of large volume CH ₂ O derivatives	>210	1.58×10^{-5} <1	1.63×10^{-4} <1	8.8×10^{-6} <1	4.08×10^{-4} <1
High school teacher	38,600	1.03×10^{-6} <1	1.19×10^{-5} 1.2	5.13×10^{-9} <1	3.33×10^{-5} 2.7
High school students	3,834,000	1.01×10^{-8} <1	1.17×10^{-7} <1	5.12×10^{-15} <1	3.33×10^{-7} 1
College/university teachers	108,600	2.11×10^{-6} <1	2.4×10^{-5} 3	4.10×10^{-8} <1	6.66×10^{-5} 7.6
College students	2,903,000	1.01×10^{-7} <1	1.17×10^{-6} 3	5.12×10^{-12} <1	3.33×10^{-6} 9.6
Medical students	74,900	1.01×10^{-7} <1	1.17×10^{-6} <1	5.12×10^{-12} <1	3.33×10^{-6} <1
Dental students	21,500	1.01×10^{-7} <1	1.17×10^{-6} <1	5.12×10^{-12} <1	3.33×10^{-6} <1

2. EPA's section 4(f) determination.

The mathematical models were used to estimate the risks associated with the exposures shown in Table 1. The exposure categories identify populations. The basic inquiries under section 4(f) are: Is there any population at very high risk (significant risk of serious harm) or a large population at lower, but still considerable risk (significant risk of widespread harm)? The exposure categories allow us to ask these questions in a meaningful way because they show the populations associated with particular exposure conditions. For instance, each occupational category identifies a population of workers associated with a particular kind of production for which data are available to estimate exposure levels. Each category was constructed to be as large as possible and still be a meaningful association of persons with similar activities and exposure levels. Thus, EPA has tailored its use of section 4(f) and has designated only those specific formaldehyde uses which result in significant risks of widespread harm to specifically-designated populations.

Table 3 shows that the populations exposed to formaldehyde are at a wide range of risks, from approximately 1 in 1,000 to 1 in 10 million (multistage upper 95). The table also shows the excess tumors expected in the lifetime of each population. For many of the populations, less than one excess tumor is estimated for the lifetime of the entire population; there is very little risk to be addressed in these populations. Estimates for the remainder, by the linearized multistage model (multistage upper 95), range from 1 to over 11,000.

None of the risks for the populations in Table 3 meet EPA's criterion for "significant risk of serious harm; there is no population at sufficiently high risk. EPA's two previous section 4(f) determinations under the serious harm criterion involved populations in which available exposure data indicated that persons were exposed at levels associated with individual lifetime risks of one per 100 or more in a group of several thousand persons or at levels comparable to those producing a significant incidence of cancer in laboratory animals (see 48 FR 19078 and 49 FR 845). There is no population in Table 3 which is at this high an individual risk level.

The second inquiry is whether there is a large population at a high, although less serious, risk—significant risk of widespread harm. The populations in Table 3 for which more than one excess tumor is estimated in the lifetime of the population are large populations. Table

3 shows that, of these, the populations estimated to have by far the greatest lifetime numbers of excess tumors are occupants of new mobile homes, conventional home residents (non-UFFI), apparel workers, and rural and urban populations exposed via ambient air.

EPA has concluded that the risks to conventional and mobile home residents and apparel workers should receive priority attention as significant risk of widespread harm.

EPA does not believe the exposure or risk estimates for ambient exposure situations are sufficiently reliable to indicate that there may be a reasonable basis to conclude that a section 4(f) priority risk is presented from ambient exposure. The contribution to human risk from ambient levels of formaldehyde is difficult to quantify for a number of reasons. First, ambient levels of formaldehyde are determined by three sources: (1) Production of formaldehyde from photochemical conversion of hydrocarbons emitted from biota and natural combustion sources; (2) combustion of fossil fuels and photochemical conversion of hydrocarbons released from anthropogenic sources; and (3) the release of formaldehyde from the direct production and use of formaldehyde and formaldehyde-based products. Second, ambient levels are influenced by seasonal and climatic condition which contribute to local and regional variations. Third, measured levels have been reported to differ significantly from year to year and from month to month. However, the potential risks from formaldehyde in ambient air warrant investigation and consequently EPA's Air and Radiation Office will accelerate its assessment of formaldehyde.

The populations triggering section 4(f) represent a significant proportion of all formaldehyde exposures. Apparel workers represent nearly 70 percent of non-teaching occupational exposures, and home residents exposed to formaldehyde from off-gassing construction materials number in the tens of millions. EPA's decision gives priority to the most important of the risks identified. This is consistent with the purpose of section 4(f) which is to give priority to some risks over others, even when—as in this case—the other risk are due to the same chemical. The smaller population risks in other categories may require attention, but not the priority of section 4(f).

More detailed explanations of those exposures that trigger section 4(f) appear below.

a. *Apparel workers.* EPA has estimated that 777,000 persons are exposed to formaldehyde during apparel manufacture. Available data indicate that 8-hour average mean exposure levels are less than 1 ppm, with levels measured in the work area averaging about 0.23 ppm and levels measured using personal monitors of about 0.64 ppm. A recent industrial hygiene survey of an apparel plant conducted by NIOSH supports the area levels (Ref. 14). One important finding of the study was the fact that formaldehyde exposures were ubiquitous in the plant and were not limited to a small category of workers.

The source of the formaldehyde in apparel plants is from the formaldehyde-based resins that are used to treat textiles to impart stain and crease resistance (permanent press garments). All resin systems used in the United States to treat textiles are formaldehyde-based and release formaldehyde during textile processing and apparel manufacture. Consequently, every worker handling treated textile is potentially exposed to formaldehyde.

b. *Home residents.* EPA is concerned that significant numbers of persons are exposed to formaldehyde in their homes, principally from building materials that contain formaldehyde-based resins, such as particleboard and plywood. The problem is particularly troublesome in manufactured homes, where large amounts of particleboard and hardwood plywood are used. Also, reduced ventilation in newer homes, especially manufactured homes, resulting from measures instituted to reduce heating costs by reducing outside/inside air exchanges, results in elevated formaldehyde levels. Increasing numbers of persons have complained about acute reactions to formaldehyde in their homes, especially manufactured homes. Consequently, HUD has recently proposed changes in HUD's manufactured housing regulations that would limit indoor ambient levels to 0.4 ppm of formaldehyde. The limit would be achieved by setting product emission standards for particleboard (0.3 ppm) and plywood (0.2 ppm) as published in the Federal Register of August 16, 1983 (see 48 FR 37136). HUD believes that if the product standards are met, ambient levels will not exceed 0.4 ppm under certain temperature and humidity conditions. The proposed HUD regulation, however, was designed to reduce acute reactions to formaldehyde and is not based on formaldehyde's potential carcinogenicity in humans.

i. *Conventional homes.* The information available to EPA indicates

chemical, the genetic makeup of the strain of animal, or a background level of the toxic substance present in the environment. The method of incorporating the spontaneous background response into the model effects the shape of the dose-response curve at low doses, and hence affects estimates of the risk.

If the background response is assumed to be totally independent of the response to the experimental dose, then the shape of the dose-response curve remains qualitatively the same as when no background response is included. However, if the background response is assumed to be additive in the sense that the effective dose is construed to be the background dose plus the experimental dose, then in many cases the dose-response curve becomes linear at low doses, and would reflect higher risks than a non-linear curve. This is true for most of the commonly used models, including the probit, logit, Weibull, one-hit, gammamultihit, and multistage models. In this case, although no squamous cell carcinomas were observed in control animals, the models employed by EPA assume an additive background response and estimate higher risks than models assuming an independent response.

It is often difficult to decide from experimental data whether background responses are independent, additive, or both. Therefore, it has been suggested that models incorporating additive background be used unless there is good evidence to assume otherwise (Ref. 17). Consequently, lacking data to the contrary and believing that formaldehyde can interact with other carcinogenic agents thus producing a dose-response relationship that is linear at low doses (see below), models incorporating additive background were used by EPA for the formaldehyde risk assessment.

Because our understanding of the carcinogenic process is incomplete, it is difficult to determine the true nature of the dose-response relationship at low levels of exposure. However, a number of arguments have been put forth that suggest that the dose-response relationship should be essentially linear at low doses and support the use of the "linearized" multistage model. The biological basis for low dose linearity emerged in the 1950's in connection with investigation of the carcinogenic risk from ionizing radiation. This work was extended to chemical carcinogenesis in the 1970's. As the Risk Estimation Panel of the Workshop stated, other arguments have been advanced for low dose linearity:

Ehrenberg et al. (1983) have pointed out that the kinetics of the various chemical processes involved in the uptake and metabolism of chemicals, and their reactions with target molecules, become first order at low concentrations, leading to low dose linearity. It has been suggested that when the action of a given carcinogen adds to those of other causes of cancer in a given target tissue, the incremental effect of small delivered doses of the given carcinogen is virtually linear regardless of the observed shape of the dose-response relationship at the tested doses (Crump et al., 1976; Guess et al., 1977; Peto, 1978; and Hoel, 1980). The rationale is that the carcinogen is augmenting some background component in causing a carcinogenic event. Formaldehyde shares with other chemical carcinogens the properties of genotoxicity and an ability to react directly with DNA (as concluded by the panels on Structure Activity/Biochemistry/Metabolism and Carcinogenicity/Histopathology/Genotoxicity). Further, the latter panel found that formaldehyde can transform, as well as mutate, various cultured cell lines and enhance the transformation of Syrian hamster embryo cells harboring adenovirus. Research at the CIIT has shown additionally, that formaldehyde can initiate and promote the actions of other promoters and initiators in *in vitro* mammalian cultured cell transformation assays (Frazell et al., 1983; Ragan et al., 1981). These data suggest that formaldehyde can interact with a wide range of carcinogenic agents or processes.

Consequently, EPA has not considered in section 4(f) determination risk estimates from models that are highly nonlinear at low doses.

As previously stated, EPA (supported by the Risk Estimation Panel) has no current basis to assume that a threshold exists for formaldehyde's carcinogenic effects, and therefore, no adjustments to the models were made concerning the amount of formaldehyde reaching target cells, because EPA believes that available data do not demonstrate such a reduction. In other words, the models assume that the same percentage of the formaldehyde contained in inhaled air reaches the target tissues of rats and humans at all concentrations considered. However, EPA is not ruling out the possibility that a non-linear relationship between air concentration and the effective dose to target tissues may exist and may be demonstrated through further experimentation.

The Agency recognizes that there is uncertainty in quantitative carcinogenic risk assessments, but it believes models do provide a means of considering the possible risks presented by chemicals and can be useful tools, particularly in section 4(f) decisions. Also, it is not true that models have no biological basis. The problem arises when the carcinogenic process of a particular chemical is unknown and the Agency must assume, lacking better data, that

the process operates by a mechanism postulated by a particular model. As a matter of policy, agencies generally choose the more conservative models, and rely on the upper 95 percent confidence limit since it is better to err on the side of too much protection than not enough.

VI. Regulatory investigation

This Federal Register notice is also an Advance Notice of Proposed Rulemaking (ANPR), in which EPA is announcing initiation of a full regulatory investigation concerning formaldehyde exposure to workers in apparel manufacture and to residents of manufactured and conventionally constructed housing. This ANPR fulfills the statutory requirement that, within 180 days of obtaining information that warrants designating a substance under 4(f), EPA shall either initiate appropriate action to reduce the risk from that substance or issue a finding in the Federal Register that the risk giving rise to the 4(f) designation does not constitute an unreasonable risk.

EPA cannot, at this time say that the designated formaldehyde exposures do not present an unreasonable risk. In order to make such a determination EPA would have to find that the economic impacts of regulation outweigh the risks that may be reduced. Preliminary information indicates, however, that there may be reasonable ways to reduce the risks from formaldehyde.

Accordingly, EPA is announcing the initiation of appropriate action in this ANPR. Issuing the 4(f) designation simultaneously with the decision to initiate appropriate action is at variance with EPA's normal practice in 4(f) actions, but is justified in this situation. In past section 4(f) actions EPA followed a two-stage process. In the first stage, EPA decided that section 4(f) was applicable to a chemical and announced that decision in a Federal Register notice which also solicited public comment on how EPA should proceed to the second 4(f) decision whether to initiate appropriate action or declare that the chemical does not present an unreasonable risk. See 48 FR 19078 (1983) (decision on 4,4'-Methylenedianiline (MDA)); 49 FR 845 (1984) (decision on 1,3-Butadiene). After reviewing the public comments, EPA made the second 4(f) decision. See 48 FR 42898 (1983) (MDA); 49 FR 20524 (1984) (1,3-Butadiene). In the case of formaldehyde, however, EPA is making the second 4(f) decision simultaneously with the 4(f) designation because the Agency has been able to conduct the type of review it typically would

40 homes (including conventional homes) conducted for CPSC by the Oak Ridge National Laboratory.

3. Control options. EPA will analyze the cost and effectiveness of several options for reducing formaldehyde exposure for the two exposed populations of apparel workers and housing residents. EPA's intention is initially to focus the investigation on these populations. However, if the investigation makes it apparent that the most appropriate control measure is one that would also reduce the exposures of other populations, EPA would expand its investigation and consider in its analysis the benefits resulting from reducing the risk to these other populations as well.

C. Potential Control Options

EPA has preliminarily identified a number of technical control options for reducing residential exposure to formaldehyde from plywood and particleboard used in construction and for reducing the exposure of apparel workers to formaldehyde from treated textiles.

1. *Plywood and particleboard.* One way to reduce formaldehyde exposures from pressedwood products is to ban the use of certain urea-formaldehyde resins in plywood and particleboard used in residential construction. It appears to be feasible to substitute phenol-formaldehyde resins in these products. It may also be possible to develop urea-formaldehyde resins that emit less formaldehyde when used in plywood or particleboard.

There appear to be other ways to reduce the formaldehyde emissions from particleboard and plywood while still using the same or similar urea-formaldehyde resins. Three such options are: (1) Treating pressed-wood products with scavenging solutions (chemical solutions to reduce the amount of free formaldehyde in finished products), (2) aging pressed-wood products prior to distribution, and (3) coating or laminating the wood products with materials that act as vapor barriers.

2. *Garment manufacture.* There are a number of possible ways to reduce the exposure of garment workers to formaldehyde. One is to reduce the amount of formaldehyde emitted by the fabrics. The predominant formaldehyde-releasing textile treatment is dimethylol dihydroxyethylene urea (DMDHEU). A preliminary study, done for EPA in 1981, identified some substitutes that were then available (although these were more expensive than DMDHEU). It may also be possible to reduce formaldehyde emissions from textiles by washing or otherwise processing the textiles prior to

their use in apparel manufacture. Another approach would be to require better ventilation in garment factories.

D. Referral to Another Agency

As mentioned earlier, if EPA finds that these uses of formaldehyde constitute an unreasonable risk under TSCA, EPA may either promulgate a regulation under section 6 of TSCA or, if appropriate, refer some, or all, aspect of regulation of such risks to other Federal agencies.

The statutory provisions for such a referral is in section 9 of TSCA. Under TSCA section 9, EPA may make such referral if it determines that there is an unreasonable risk and determines, in the Administrator's discretion, that the risk can be eliminated or adequately reduced under the authorities available to another agency. EPA may establish a date by which the other agency must reply with a finding regarding the risk and the agency's intention whether to initiate rulemaking. If the other agency finds that the risk is not unreasonable or if it initiates action to regulate, EPA may not regulate. If the other agency does neither of these, EPA may exercise its authority under section 6. As part of taking appropriate regulatory action on formaldehyde, EPA will determine whether referral to other Federal agencies is appropriate.

E. Actions Being Taken by Other Agencies

Several Federal agencies have conducted or initiated regulatory investigations into some aspect of formaldehyde exposure. EPA will coordinate with those agencies and, as explained above, EPA may eventually refer some, or all, aspects of the regulation of formaldehyde exposure to other Federal agencies.

In 1982, the CPSC banned the use of UFFI in residential and school construction. This ban was set aside by the Fifth Circuit of the U.S. Court of Appeals on April 7, 1983 because, in the opinion of the court, CPSC's rulemaking record did not contain sufficient evidence to estimate the risk of cancer resulting from UFFI.

CPSC recently initiated the creation of a Chronic Hazard Advisory Panel to advise CPSC on the risks of formaldehyde from urea-formaldehyde foam insulation and from other sources of consumer exposures. CPSC has been studying the emissions of pressed-wood products, has studied other possible sources of formaldehyde in conventional homes, and is studying dermal exposure from wearing garments made with fabrics which release formaldehyde. (This last exposure is of concern to

CPSC because dermal contact with formaldehyde can cause allergic reactions. CPSC does not believe dermal contact with treated garments causes cancer.)

The Department of Housing and Urban Development has proposed standards for pressed-wood construction materials used in manufactured housing and is proceeding with the development of final standards. The proposed HUD standards are designed to reduce the acute effects of formaldehyde exposures in manufactured housing and do not consider whether further reductions would be justified because of the potential for carcinogenicity.

The Occupational Safety and Health Administration has not initiated any recent regulatory investigation on formaldehyde. In 1981, OSHA was petitioned to establish an emergency temporary standard reducing the allowable workplace exposure to formaldehyde. OSHA denied that petition in 1982 and that decision is currently under litigation.

F. Relationship to Recent Test Rule Announcement

In a separate action, signed May 11, 1984, EPA announced a tentative decision to initiate rulemaking to require toxicity testing of urea-formaldehyde resins (either the syrupy liquid oligomeric mixture or its dried or reconstituted equivalent).

This tentative decision is distinct from EPA's investigation of regulatory options to reduce exposure to formaldehyde. The decision to initiate rulemaking to test the UF resins is not based on the toxicity of formaldehyde. It is based on the potential toxicity of the monomeric and oligomeric reaction products of urea combined with formaldehyde. EPA cannot at this time conclude that the investigation of regulatory options to reduce formaldehyde exposures to apparel workers and housing residents will lead to reduction in the occupational exposures to the uncured UF resins which was the exposure of primary concern in initiating rulemaking to require toxicity testing.

G. Request for Comments

EPA solicits information and comments relevant to its further investigation for formaldehyde exposures to apparel workers and housing residents. Below is a summary of the principal areas in which EPA seeks information.

1. *Carcinogenicity of formaldehyde.* The issues involved in assessing the

Binding in the Labeling of Macromolecules in the Rat Nasal Mucosa and Bone Marrow by Inhaled [¹⁴C]-[³H] Formaldehyde Republication Copy (1984).

11. USEPA. Exposure Assessment for Formaldehyde: Prepared by Versar Inc. (1982).

12. CPSC. Briefing Package: Exposure to Formaldehyde from Preserved Biological Specimens. 1982.

13. USEPA. Occupational Exposures to Formaldehyde. Memorandum from Greg Schweer to Richard Hefter. 1984.

14. NIOSH. In-Depth Industrial Hygiene Survey Report of the Arrow Shirt Company. Atlanta, Georgia. October 26, 1983.

15. CPSC. Status Report on Indoor Air Quality Monitoring in 40 Homes. 1984.

16. Anderson, H. A., Dally, K. A., Hanrahan, L. P., Echmann, A. D., Kanarek, M. S., and Rankin, J. The Epidemiology of Mobile Home Formaldehyde Vapor Concentration and Residents' Health Status. TSCA Section 28 Cooperative Agreement with State of Wisconsin. Report Number CS806859-01-3 (1983).

17. State of California. Health and Welfare Agency. Carcinogen Identification Policy: A Statement of Science as a Basis of Policy. Section Z: Methods for Estimating Cancer Risks from Exposure to Carcinogens. 1982.

18. National Research Council. Formaldehyde and Other Aldehydes.

National Academy Press: Washington, D.C., 1981.

[Sec. 6, Pub. L. 94-469, 90 Stat. 2020 (15 U.S.C. 2605)]

List of Subjects in 40 CFR Part 765

Environmental protection. Hazardous materials. Recordkeeping and reporting requirements. Formaldehyde.

Dated: May 18, 1984.

Alvin L. Alm.

Deputy Administrator.

[FR Doc. 84-13428 Filed 5-21-84; 8:45 AM]

BILLING CODE 6560-50-M