## Miller, Diane M. (CDC/NIOSH/EID)

**From:** hondobear@aol.com
**Sent:** Friday, November 18, 2011 6:37 PM
**To:** NIOSH Docket Office (CDC)
**Subject:** Docket No. NIOSH-245
**Attachments:** FEMA NIOSH 111811.pdf

Dear Sir/Ms.:
Comments are attached to this email on the draft document "Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione" by The Flavor and Extract Manufacturers Association of the United States. Please include these comments in NIOSH Docket Number NIOSH-245.

Please acknowledge your receipt and filing of these comments. Thank you.

Sincerely,
John Hallagan

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18 November 2011

RE: "Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione." 76 *Fed. Reg.* 44338. 25 July 2011; 76 *Fed. Reg.* 64353. 18 October 23011. Docket Number NIOSH -245.

Dear Sir/Ms.:

The Flavor and Extract Manufacturers Association of the United States (FEMA) is pleased to respond to the request for comments on the document "Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione" ("Criteria Document") published by the National Institute of Occupational Safety and Health (NIOSH). 76 *Fed. Reg.* 44338. 25 July 2011; 76 *Fed. Reg.* 64353. 18 October 2011. FEMA presents these comments on the draft NIOSH Criteria Document in the spirit of its longstanding policy of collaboration and cooperation with NIOSH on this critically important matter.

**The Flavor and Extract Manufacturers Association of the United States**

FEMA, founded in 1909, is the Washington, D.C.-based national association of the U.S. flavor industry. FEMA's members include flavor manufacturers, flavor users, flavor ingredient suppliers, and others with an interest in the U.S. flavor industry. FEMA's flavor manufacturing members include all of the twenty-five largest flavor manufacturers in the U.S., and FEMA's flavor manufacturing members produce >95% of all flavors consumed in the U.S. FEMA and its members are committed to assisting flavor manufacturers in having the safest workplaces possible.

**FEMA's Program on Respiratory Health and Safety in Flavor Manufacturing**

FEMA has been very active in assisting flavor manufacturers on respiratory health and safety matters since the initiation of FEMA's efforts in 1997 (FEMA, 2004). Since 1997, FEMA has sponsored four workshops (1997, 2002, 2004, and 2007), with the 2004 and 2007 workshops including extensive training sessions for

flavor and food manufacturers on the safe handling of flavors, proper medical surveillance of workers, and hazard communication. In addition to the workshops, since 2001 FEMA has held numerous information sessions for its members and others in an effort to share relevant information in a timely manner.

Since 2001, FEMA has had extensive meetings and discussions with NIOSH, the Occupational Safety and Health Administration (OSHA), and the California Department of Industrial Relations, Division of Occupational Safety and Health (Cal/OSHA) on these matters and has shared extensive information with these agencies in cooperative and collaborative relationships. Representatives of NIOSH, OSHA, and Cal/OSHA have attended FEMA meetings and workshops, and have also made presentations at a number of these sessions. FEMA supported the regulatory efforts of Cal/OSHA which resulted in 2010 in the implementation of the first workplace safety regulation related specifically to flavor manufacturing.

**Flavoring Substances and Their Regulation and Use**

The inclusion of flavoring substances in food is an important part of food processing and manufacturing in the U.S. Many individual flavoring substances, such as diacetyl, are commonly present in food as natural constituents. For example, diacetyl is commonly found in butter, dairy products, and in many other foods often as a product of fermentation. Diacetyl is endogenous in humans and is the single substance most responsible for the human perception of the taste of butter.

The "compounding" of flavors and how they are used in food manufacturing was described by Hallagan and Hall (2009). Compounded flavors typically contain individual flavoring substances at levels well below 1.0% of the compounded flavor. Compounded flavors are in turn most often added to foods also at levels below 1.0%. So, the concentration of individual flavoring substances in food is most often in low ppm concentrations (i.e. 10-200 ppm).

Before they may be marketed and added to food, flavoring substances must comply with the requirements of the Federal Food, Drug, and Cosmetic Act (FFDCA) through the premarket approval requirements instituted by the Food and Drug Administration mandating that these substances be safe for ingestion. In most instances, flavoring substances permitted for use in the U.S. have regulatory status as substances determined by FDA to be approved food additives or substances determined to be "generally recognized as safe" (GRAS), or as flavoring substances determined to be GRAS by FEMA (Hallagan and Hall, 1995; 2009). About 600 flavoring substances, including diacetyl and 2,3-pentanedione, have both explicit FDA regulatory status and FEMA GRAS status.

Both diacetyl and 2,3-pentanedione are permitted for use in food by FDA (21 CFR 184.1278 as a GRAS substance and 21 CFR 172.515 as an approved food additive, respectively). Like the vast majority of flavoring substances, this

regulatory status means that they may be added to food consistent with good manufacturing practices (GMP). The use of flavoring substances and other food ingredients consistent with GMP means that the substances should be used in the minimum amount to achieve their desired technical effect in food.

## General Comments on the Criteria Document and Requests for Revisions

Much of the advice and many of the recommendations contained in the Criteria Document are consistent with the advice and recommendations that FEMA has provided to flavor and food manufacturers for many years through reports (e.g. FEMA, 2004) and workshops. Some of the general comments and requests for revisions below are elaborated in the following sections of these comments.

### Naturally Occurring Diacetyl and the Proposed RELs

Diacetyl occurs naturally in a wide variety of foods including some fruits and vegetables, dairy products such as milk, butter, cheese and yogurt, and fermented beverages such as beer, wine, and some distilled spirits (Nijssen et al., 2011). It is important that throughout the Criteria Document there is a clear recognition that there have been no reported health effects in workers in any industries where exposure to diacetyl is solely from the naturally occurring substance – there are no reports of illness among workers in the wine, dairy, beer, or distilled spirits production industries. It is also important to be clear on which foods may contain flavors and which may not. For example, while standard wine may contain naturally occurring diacetyl because of malolactic fermentation, it cannot by law contain added flavors.

FEMA requests that NIOSH make it clear throughout the Criteria Document that any recommended exposure limits (RELs) for diacetyl or 2,3-pentanedione do not apply to facilities where exposure to either of these substances may occur solely through exposure to naturally occurring diacetyl or 2,3-pentanedione in foods and beverages. Therefore, wine, beer, and distilled spirits production facilities, and dairy-related facilities not engaged in the production of flavoring materials such as butter starter distillate, would be subject to the RELs only if neat diacetyl or 2,3-pentanedione was present in these facilities, or compounded flavors are present containing these substances.

### NIOSH's Descriptions of the Relevant Illness

FEMA requests that the Criteria Document be carefully reviewed for accuracy and consistency when the illness at issue is described and make appropriate revisions to assure that the illness described is supported by the reported clinical findings. Sometimes the illness is referred to as bronchiolitis obliterans, sometimes as "fixed obstructive lung disease suggestive of bronchiolitis obliterans," "severe fixed obstructive lung disease consistent with bronchiolitis obliterans" and other descriptions. None of these terms, with the exception of "bronchiolitis obliterans," are defined in the glossary provided at Pages ix-xi of the Criteria Document.

If this wide variety of terms is to be used in the final version of the Criteria Document then FEMA requests that each term be fully defined to allow clear distinction among the descriptive terms. King and Kinder (2008) describe the difficulties in accurately classifying these illnesses and the Criteria Document could benefit significantly from a more thorough use of this reference on this subject.

There also are inconsistencies in the Criteria Document in other aspects of the illnesses observed. For example, in some instances, workers are described as having "restrictive lung disease" and in some instances workers are described as having their illness stabilize which is inconsistent with the progression of bronchiolitis obliterans. In a number of instances, individuals described as having "developed bronchiolitis obliterans" would be more correctly described as displaying "clinical symptoms consistent with bronchiolitis obliterans" or as noted by King and Kinder (2008), as having a "clinical syndrome(s) associated with bronchiolitis."

"Causation" and Diacetyl and 2.3-Pentanedione

FEMA has consistently advocated for the application of sound science in addressing respiratory health and safety issues in flavor manufacturing. Throughout the Criteria Document NIOSH has assumed that causation has been established with a high degree of scientific certainty – that exposure to diacetyl causes bronchiolitis obliterans. This assumption, in addition to not being scientifically appropriate, risks creating a false sense of certainty in what is an extremely complex situation.

In the face of significant uncertainty related to causation, which remains today, FEMA has recommended for more than ten years that flavor manufacturers focus on the key elements of exposure control for many flavoring substances including diacetyl, medical surveillance when appropriate, and hazard communication (e.g. FEMA, 2004). It is clear that the current scientific information on the toxic potential of diacetyl does not allow a conclusion that diacetyl causes bronchiolitis obliterans (or related illnesses) according to the well-recognized criteria established by Hill (1965). Consistent with Hill's conclusions, the relationship between diacetyl and bronchiolitis obliterans is most properly considered an association. Hill identified nine criteria to establish causation:

1. The existence of a temporal relationship
2. A strong statistical correlation
3. A dose-response relationship
4. Consistent replication of the observed effect
5. Plausibility of the connection between cause and effect
6. The consideration and rejection of alternate explanations
7. Appropriate experimental support for a causal relationship
8. Support for a causal relationship by the specificity of the cause and effect
9. The coherence of the causal relationship – compatibility of existing theory and knowledge

It is clear that the available information on diacetyl meets few, if any, of Hill's criteria for causation. The complexity of determining the causes of bronchiolitis obliterans and related respiratory illnesses was acknowledged by King and Kinder (2008) in the definitive reference on these illnesses in which they listed "volatile flavoring agents" as possibly resulting in "inhalation injury" and "clinical syndromes *associated* with bronchiolitis." (emphasis added).

A major issue in establishing that diacetyl causes bronchiolitis obliterans is the absence of an appropriate animal model for the illness because rodents are "obligate nose breathers" and therefore are not able to simulate human exposure to gases and vapors. The absence of an appropriate animal model for bronchiolitis obliterans (and related illnesses) has severely hindered research that could advance our understanding of the role that diacetyl may play in the development of these illnesses in workers in microwave popcorn and flavor manufacturing facilities.

Intra-tracheal instillation in rodents, a highly artificial route of exposure, has resulted in the production of some interesting data (e.g. Flake et al., 2010) that have yet to be verified as relevant to human exposure. It seems clear that the appropriate characterization of the relationship between diacetyl and bronchiolitis obliterans is that an association exists but that causation has not been established.

With respect to 2,3-pentanedione, we are unaware of any instances of human illness that have been associated with exposure to this substance. 2,3-Pentanedione shares similarities of chemical structure with diacetyl which indicates that appropriate precautions be taken with this substance as should be taken with diacetyl.

FEMA requests that NIOSH revise the Criteria Document to describe the relationship between diacetyl and respiratory illness, including bronchiolitis obliterans, as an association and not as a causative relationship. FEMA also requests that NIOSH revise the Criteria Document throughout to make it clear that there are no known cases of respiratory illness associated with exposure to 2,3-pentanedione. As noted previously, FEMA recognizes and fully supports sound workplace safety practices regarding potential exposure to these substances and has long called for an active workplace safety approach in the face of significant uncertainty (FEMA, 2004).

Priority Flavoring Chemicals

The term "priority flavoring chemicals" or "priority substances" appears in several places in the Criteria Document (e.g. Section 8.3.6) but is not defined. The concept of prioritizing flavoring substances to indicate suggested areas of focus for potential workplace exposures was developed by FEMA and first appeared in the NIOSH Industry Alert (NIOSH, 2003 – with attribution to FEMA) and the FEMA report "Respiratory Health and Safety in the Flavor Manufacturing Workplace" (FEMA, 2004). The Criteria Document also includes other terms such as "other flavoring chemicals," "chemicals with structural similarities," and "agents of

concern," none of which are defined or included in the glossary. FEMA requests that the Criteria Document provide definitions of these terms and assure consistency in their use.

**Specific Comments**

Cover of the Criteria Document

The cover photograph is inappropriate. It shows a worker pouring what appears to be a liquid butter flavor without the use of engineering controls. The fact that the worker is shown wearing a respirator compounds the problem by implying that personal respiratory protection is acceptable as the primary means of exposure control. The cover photograph contradicts the advice provided in the document. FEMA requests that the cover be revised to either include no photograph or a photograph showing appropriate exposure controls.

Chapter 1 – Introduction

In Section 1.5, the Criteria Document lists examples of "flavored food products" and includes beer and wine in this list. Standard wine is not permitted to contain added flavors nor is beer unless it is clearly labeled as containing flavors. Standard wine may contain naturally occurring diacetyl through the natural process of malolactic fermentation but it may not contain added flavors. FEMA requests that NIOSH clarify this sentence by deleting reference to wine and beer. FEMA also requests that NIOSH include information explaining the distinction between diacetyl which may be present in foods naturally (i.e. through natural occurrence or through natural fermentation processes and not through addition) and diacetyl present in foods through intentional addition to provide flavor. FEMA also notes that diacetyl is endogenous in humans through normal metabolism.

In Section 1.3 of this chapter, NIOSH states in the context of information on diacetyl that "Occupational exposures in the flavoring and food production industry (sic) have been *associated* (emphasis added) with respiratory disease . . ." Several sentences later in the same paragraph NIOSH states "Although a *causative relationship* between diacetyl and respiratory disease has been observed . . ." (emphasis added). With reference to FEMA's comments above on causation, FEMA requests that NIOSH revise this and all other statements in the Criteria Document to accurately reflect the current state of scientific knowledge that there is an association between inhalation exposure to diacetyl and respiratory illness but that causation consistent with the Hill criteria has not been established.

Chapter 3 – Effects of Exposures in Workers

We request that this chapter be carefully reviewed for consistency when the illness at issue is described consistent with FEMA's concerns expressed above. An example of the problems created by the use of varied, imprecise terms and descriptions is presented in Section 3.1.2.7 in the discussion of the Lockey et al. (2003) report. The Criteria Document states that "A cluster of cases of bronchiolitis obliterans (emphasis added) among production workers at a flavoring

manufacturing company was reported by Dr. James Lockey . . . After identification of an index case of bronchiolitis obliterans at this plant, a survey of the workforce identified an additional four workers with clinical findings consistent with bronchiloitis obliterans. All five workers with bronchiloitis obliterans (emphasis added) . . ." According to the Lockey abstract (Lockey et al., 2003), there was one "index" case of a worker with bronchiolitis obliterans and four workers with clinical findings "consistent with" bronchiolitis obliterans but without pathological confirmation. Lockey also stated "After removal from exposure for four to five years, these patients have no further loss in their lung function." Furthermore, as NIOSH is aware, Lockey attributed the illness observed to possible exposure to acetaldehyde, not diacetyl.

Cross-sectional data are briefly summarized in this chapter from workers from six microwave popcorn manufacturing plants, five flavor manufacturing plants, one baking mix plant, and three restaurants. FEMA requests that the available medical surveillance data from these workers be analyzed and reported together. The information presented in Table 3.1 (Page 47) is interesting but limited in usefulness because of the highly variable descriptions of the findings. This table would be much more valuable if the descriptions of the findings used standard terminology. This table would be the ideal place to describe the total number of workers examined, the total number with possible and confirmed lung disease, and if available, data on the presence of diacetyl in the facilities.

In Section 3.1.2.2 it appears that NIOSH used area samples to associate exposure to diacetyl with the development of illness in terms of workers' personal cumulative exposures. This is contrary to sound industrial hygiene practice (AIHA, 2006), is contrary to NIOSH's recommended sampling strategies (Leidel et al. 1977), and is inconsistent with NIOSH's recommendations in the Criteria Document regarding compliance with the NIOSH REL for diacetyl. It is a well-recognized industrial hygiene principle that area samples are not reliable representations of potential exposures that may be more accurately estimated by personal breathing zone samples. A misplaced reliance on area sample data can be a serious flaw and can call into question quantitative risk assessments. FEMA requests that NIOSH explain their use of area sample data and why the use of such data do not adversely affect the accuracy of the risk assessments described in the Criteria Document.

On Page 51 of Chapter 3, NIOSH states, "Because of concerns for patient welfare and the invasive nature and low sensitivity of lung biopsy for diagnosing constrictive bronchiolitis obliterans, most patients have been diagnosed upon clinical findings." FEMA requests that NIOSH explain this statement, with appropriate references, especially the statement regarding the "low sensitivity of lung biopsy" which most pulmonologists consider the gold standard for the diagnosis of constrictive bronchiolitis obliterans.

In Chapter 3, substantial information is provided regarding the symptoms and spirometric findings in several NIOSH investigations. However, there is inadequate reporting of smoking histories and other potential confounding factors for the evaluation of the existence of employment-related obstructive lung disease. Important factors that should be addressed include pre-existing asthma and whether pre-employment spirometric data are available. FEMA requests that NIOSH address these potential short-comings.

In the discussion in Chapter 3 on rapid lung function decline, how many workers were affected? On Page 73, Wang and Petsonk (2004) are cited for the statement "a yearly decline in FEV1 greater than 8% of 330 ml. should not be considered normal" but it is not clear if this is what NIOSH means by "rapid decline." Precision in this discussion is important because this seems to be the basis for recommendations that flavor workers undergo spirometry testing every 3-6 months. FEMA requests that NIOSH clarify its definition of "rapid decline."

In Chapter 3, Section 3.3, NIOSH does not explain the role that various factors such as body mass index may have in evaluating pulmonary restriction. FEMA requests that NIOSH include an explanation of the roles that such factors may play especially because the data presented are being used to support recommendations for medical surveillance.

Chapter 5 - Quantitative Risk Assessment Based on Worker Data

It appears that NIOSH has based many of its conclusions and recommendations on data from the "sentinel" microwave popcorn manufacturing facility in Jasper, Missouri (NIOSH, 2006). Such significant reliance on a single data set isn't scientifically appropriate.

It is a challenge to address the broad use of flavoring substances in manufacturing an extremely diverse set of flavors and foods together with the large number and diversity of facilities producing flavors and foods. However, limiting the quantitative risk assessment described in the Criteria Document to one facility, the sentinel plant, means that the risk assessment has limited relevance to flavor manufacturing. We request that NIOSH explain the relevance of the quantitative risk assessment presented in Chapter 5 to flavor manufacturing facilities.

Several years after completing its work at the Gilster Mary Lee facility (NIOSH, 2006), NIOSH recognized that the analytical method used to characterize breathing zone and area samples (NIOSH Method 2557) was subject to perturbation by ambient humidity (Cox-Ganser et al., 2011). NIOSH proposed a correction methodology for the published data noting that "underestimation of worker exposure may lead to overestimation of respiratory health risk in quantitative exposure-effect analyses." (Cox-Ganser et al., 2011). However, for reasons that are not clear, NIOSH chose not to apply its correction methodology to samples identified as being below the limit of detection (LOD) stating "It is not possible to know if the workplace diacetyl concentration was indeed below the LOD or if losses due to

humidity and days from sampling to extraction in the laboratory caused the sample value to be below the LOD." (Cox-Ganser et al., 2011).

Failure to correct and include the LOD samples in the overall collection of data points introduces a significant amount of uncertainty and affects the confidence to be placed on resulting exposure data. For example, 40 percent of the personal samples and 42 percent of the area samples collected at the Gilster Mary Lee facility were reported to be below the LOD. Furthermore, 251 sample results using the initial uncorrected method were below the LOD as noted by NIOSH in the exposure assessment in the Criteria Document. If the analytical results for these samples were corrected and used by NIOSH the risk assessment may have yielded a much different outcome resulting in a higher and more reasonably achievable REL for diacetyl – FEMA requests that NIOSH perform this analysis and report the results in the Criteria Document.

Chapter 6 – Quantitative Risk Assessment Based on Animal Data

In Section 6.1.4.1, "Comparison with other animal-based risk assessments," NIOSH discusses the work on the non-profit organization Toxicology Excellence for Risk Assessment (TERA) and cites a preliminary TERA analysis submitted to OSHA in 2008 as "IDFA, 2008." This preliminary analysis was expanded, completed, and published in 2010 (Maier et al., 2010). The Maier et al. publication is of critical importance to both the risk assessments in the Criteria Document based on animal and human data and is not discussed or cited in the Criteria Document.

An important aspect of the Maier et al. report is the report's thorough evaluation and consideration of the available information and especially its use of the information and analysis of the report by Lockey et al. (2009) who reported on findings from a microwave popcorn production facility other than the sentinel microwave popcorn plant (NIOSH, 2006) so heavily relied on by NIOSH for its risk assessments.

FEMA requests that NIOSH, in both Chapters 5 and 6 on its risk assessments, and in Chapter 7 on the basis of its REL for diacetyl compare the results of its risk assessments yielding an REL of 5 ppb (8hr. TWA) for diacetyl with the OEL of 0.2 ppm recommended by Maier et al (2010) and thoroughly explain its rationale for the substantial difference.

Chapter 7 – Basis of the Recommended Standards for Diacetyl and 2,3-Pentanedione

As noted previously, it is scientifically inappropriate to conclude that diacetyl causes bronchiolitis obliterans. FEMA has significant concerns related to the extremely low recommended exposure limits (RELs) proposed for diacetyl and 2,3-pentanedione and whether these RELs are reasonably achievable.

With respect to 2,3-pentanedione, we are unaware of any instances of human illness that have been associated with exposure to this substance. 2,3-Pentanedione shares similarities of chemical structure with diacetyl which indicate

that appropriate precautions should be taken with this substance. However, it appears premature to propose a REL for this substance.

With respect to diacetyl, the proposed REL of 5 ppb (8 hr. TWA) is exceedingly low and it is highly unlikely that the majority of flavor manufacturers will be able to comply with this limit without the use of respirators that, according to NIOSH, is the least desirable method of exposure control. The low proposed REL is unlikely to be reasonably achievable for the majority of flavor manufacturers.

The proposed REL of 5 ppb is approximately 10-fold lower than the estimated daily exposure to diacetyl from smoking about one-half of a pack of cigarettes per day. If converted to a daily dose the proposed REL of 5 ppb may be expressed as 0.005 mg/kg/day. The mean diacetyl content in cigarette smoke is 0.336 mg/cigarette (Fujioka and Shibamoto, 2006) meaning that smoking one-half of a pack of cigarettes per day for 15 years results in a daily dose of 0.048 mg/kg/day, more than ten times greater than the proposed REL for diacetyl. There is no evidence that cigarette smoking is associated with the development of bronchiolitis obliterans.

Maier et al. (2010) developed an occupational exposure limit (OEL) for diacetyl of 0.2 ppm (8 hr. TWA) based on many of the same data as used by NIOSH in developing its REL. It appears that the significant difference in the two proposed exposure limits is due to NIOSH's over-reliance on the data from a single microwave popcorn manufacturing facility, the Gilster Mary Lee facility (NIOSH, 2006). Maier et al. relied on a broader data set including significant information in Lockey et al. (2009).

As described above, it is important to note that the Maier et al. report is not referenced in the Criteria Document. The Criteria Document references only a preliminary report as "IDFA, 2008" suggesting that NIOSH did not evaluate or use information from Maier et al., 2010. FEMA requests, as explained above, that NIOSH review the information from Maier et al. (2010) and use it as requested in the Criteria Document.

FEMA also requests that NIOSH make it clear that the proposed RELs do not apply to facilities in which the only potential exposures are to naturally occurring diacetyl such as facilities involved in the production of wine and beer where no neat diacetyl or diacetyl-containing flavors are present. The RELs should also not apply to dairy-related facilities unless those facilities are engaged in the production of dairy-based concentrated flavoring products such as butter starter distillate.

Chapter 8 – Hazard Prevention and Control of Exposures to Diacetyl and 2,3-Pentanedione

Nearly all of the recommendations in this chapter are consistent with recommendations made by FEMA in training workshops conducted by FEMA for flavor and food manufacturers in 2005 and 2007. As noted by FEMA (FEMA, 2004), flavor manufacturing facilities are extremely diverse in size and number of employees, facility design and layout, and products manufactured. For flavor manufacturing, one size does not fit all. Furthermore, the large majority of flavor manufacturers in the U.S. qualify as small businesses under the definition of the Small Business Administration – businesses with less than 500 employees. In fact, the majority of flavor manufacturing companies in the U.S. have less than 100 employees. The use of the term "reasonably achievable" in the context of exposure controls to achieve the proposed REL for diacetyl of 5 ppb therefore clearly becomes a relative term.

"Reasonably achievable" to a large flavor manufacturer with corresponding financial resources will mean something far different to the majority of flavor manufacturers in the U.S. that are relatively small in size. A small flavor manufacturer seeking to comply with the exceedingly low RELs suggested for diacetyl and 2,3-pentanedione may seek to employ respirators routinely as an alternative to engineering controls which, as explained by NIOSH in Chapter 8, are the preferred option consistent with the hierarchy of controls.

Whether the recommended exposure limits are reasonably achievable for flavor manufacturers has not been demonstrated. FEMA requests that NIOSH review and revise its recommendations to address whether they are likely to be reasonably achievable in relation to the low proposed RELs by the majority of flavor manufacturers that are in fact small businesses.

NIOSH discusses engineering controls in Section 8.2. It is important to focus on engineering controls that are carefully considered and demonstrated to result in reductions in exposure because while some controls may appear to be likely to reduce exposure, they may in fact increase exposure. Of particular importance are engineering controls intended to capture or dilute vapors and powders. The installation and operation of engineering controls must be carefully and fully evaluated to assure that they result in reductions in potential exposure. One system that works well in one flavor manufacturing facility may not work in another because of differences in facility design and operation. It should be stressed in this chapter that controls must be validated by the operator for each specific facility. For example, one type of powder control may work in a facility that uses drums for shipping but may not work in another facility that uses a different transfer process or a different shipping container.

NIOSH discusses work practice controls in Section 8.3. It is important to focus on work practice controls that are carefully considered and that may result in reductions in exposure because while some actions may appear to be likely to

reduce exposure, they may in fact increase exposure. For example, NIOSH recommends the use of HEPA vacuums to clean up flavoring powders. However, this may actually increase exposure due to evaporation from the HEPA filter itself. NIOSH recommends the use of wet sweeping methods in areas where powdered encapsulated flavors are present that may actually increase exposure as water dissolves the encapsulation material releasing its contents.

NIOSH discusses hazard communication in Section 8.3.7. Hazard communication is not just a key part of any workplace safety program for flavor manufacturing, but it is a legal requirement as noted in the Criteria Document (Section 8.3.7). FEMA recommends that this section be expanded to remedy several deficiencies. In 2007, OSHA published hazard communication guidance for diacetyl (OSHA, 2007). This important document is not described or referenced in the Criteria Document and must be. FEMA provided specific information related to hazard communication for "high priority" flavoring substances (FEMA, 2004) that can also be referenced in this section of the Criteria Document.

Chapter 9 - Medical Monitoring and Surveillance of Exposed Workers

NIOSH's recommendations in this chapter are similar to recommendations made by FEMA for many years. However, unlike FEMA, NIOSH has not adequately addressed key facts about flavor manufacturing that make "one size fits all" proposed solutions unhelpful. Many flavor manufacturers are small businesses with limited resources. Some of the recommendations in this chapter suggest that individual manufacturers establish what amounts to sophisticated epidemiology study programs. For example, in Section 9.3, NIOSH describes the creation of individual company databases on workers' medical findings that would require substantial expertise and resources unlikely to be available to small businesses. Furthermore, NIOSH fails to describe the implications of significant worker privacy issues associated with individual's confidential medical histories. FEMA requests that NIOSH explain in Chapter 9 how it would address these concerns.

## Summary of Requests for Revisions and Responses

In summary, FEMA requests that NIOSH make the following revisions to the Criteria Document. If NIOSH decides not to make the revisions requested by FEMA then we request that NIOSH fully explain its reasons.

1. FEMA requests that the cover of the NIOSH Criteria Document be revised to either include no photograph or a photograph showing appropriate exposure controls.

2. FEMA requests that NIOSH clarify statements describing food and beverages that contain diacetyl by deleting reference to wine and beer. Standard wine is not permitted to contain added flavors. Beer may contain added flavors only if clearly labeled as such.

- FEMA also requests that NIOSH include information in the Criteria Document explaining the distinction between diacetyl which may be present in foods

naturally (i.e. through natural occurrence or through natural fermentation processes and not through addition) and diacetyl present in foods through intentional addition to provide flavor.

3. FEMA requests that NIOSH review and revise accordingly the recommended exposure limits (REL) proposed in the Criteria Document to address whether they are reasonably achievable by flavor manufacturers, especially in light of the fact that the majority of flavor manufacturers that are small businesses.

4. FEMA requests that NIOSH make it clear throughout the Criteria Document that any recommended exposure limits (RELs) for diacetyl or 2,3-pentanedione do not apply to facilities where exposure to either of these substances may occur solely through exposure to naturally occurring diacetyl or 2,3-pentanedione in foods and beverages.

5. FEMA requests that the Criteria Document be carefully reviewed for consistency when the illness at issue is described and make appropriate revisions to assure that the illness described is supported by the reported clinical findings.

- If the variety of terms currently used is to be used in the final version of the Criteria Document then FEMA requests that each term be fully defined to allow clear distinction among the descriptive terms.

6. FEMA requests that NIOSH revise the Criteria Document to describe the relationship between diacetyl and respiratory illness, including bronchiolitis obliterans, as an association and not as a causative relationship.

7. FEMA also requests that NIOSH revise the Criteria Document throughout to make it clear that there are no known cases of respiratory illness associated with exposure to 2,3-pentanedione.

8. FEMA requests that the NIOSH Criteria Document include definitions of terms such as "priority flavoring chemical," "priority substance," "other flavoring chemicals," "chemicals with structural similarities," and "agents of concern," none of which are defined or included in the glossary. FEMA requests that the Criteria Document provide definitions of these terms and assure consistency in their use.

9. FEMA requests that the available medical surveillance data from workers described in Table 3.1 on Page 47 of the NIOSH Criteria Document be analyzed and reported together with standard descriptions of the findings because as the information is currently reported it is limited in usefulness because of the highly variable descriptions of the findings. This table would also be the ideal place to describe the total number of workers examined, the total number with possible and confirmed lung disease, and if available, data on the presence of diacetyl in the facilities.

10. FEMA requests that NIOSH explain their use of area sample data in Chapter 3, Section 3.1.2.2 and why the use of such data does not adversely affect the accuracy of the risk assessments described in the Criteria Document.

11. FEMA requests that NIOSH explain the following statement on Page 51, Chapter 3: "Because of concerns for patient welfare and the invasive nature and low sensitivity of lung biopsy for diagnosing constrictive bronchiolitis obliterans, most patients have been diagnosed upon clinical findings." Please explain, with supporting references, the statement regarding the "low sensitivity of lung biopsy" which most pulmonologists consider the gold standard for the diagnosis of constrictive bronchiolitis obliterans.

12. FEMA requests that in Chapter 3 NIOSH explain the absence of a thorough discussion of smoking histories and other potential confounding factors for the evaluation of the existence of employment-related obstructive lung disease. Important factors that should be addressed include pre-existing asthma and whether pre-employment spirometric data are available.

13. FEMA request that NIOSH clarify its definition of "rapid decline" in lung function as used in Chapter 3 and elsewhere in the Criteria Document.

14. FEMA requests that NIOSH include in Chapter 3, Section 3.3 an explanation of the role that factors such as body mass index may play in evaluating pulmonary restriction.

15. Recognizing that the analysis presented in Chapter 5 of the NIOSH Criteria Document is almost exclusively based on data from the sentinel microwave popcorn manufacturing plant, FEMA requests that NIOSH explain the relevance of the quantitative risk assessment presented in this chapter to flavor manufacturing facilities.

16. FEMA requests that NIOSH revise Chapter 5 of the Criteria Document to report an analysis of the application of the Cox-Ganser et al. (2011) correction methodology to samples reported in this chapter to be below the limit of detection. If the analytical results for these samples were corrected and used by NIOSH the risk assessment may have yielded a much different outcome resulting in a higher and more reasonably achievable REL for diacetyl.

17. FEMA requests that NIOSH, in both Chapters 5 and 6 on its risk assessments, and in Chapter 7 on the basis of its REL for diacetyl compare the results of its risk assessments yielding an REL of 5 ppb (8hr. TWA) for diacetyl with the OEL of 0.2 ppm recommended by Maier et al (2010) and thoroughly explain its rationale for the substantial difference.

18. FEMA requests that Chapter 8, Section 8.3.7 on hazard communication be revised to include a description of OSHA's hazard communication guidance for diacetyl (OSHA, 2007).

19. FEMA requests that NIOSH explain in Chapter 9 how it would address concerns associated with individual small business company resources and worker privacy issues resulting from the implementation of medical monitoring programs.

We would be pleased to respond to any questions and comments, and requests for additional information that you may have. We look forward to continuing a productive relationship with NIOSH. My email address is Hondobear@aol.com and my direct telephone number is 202.331.2333.

Sincerely,

John B. Hallagan

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