Dragon, Karen E. (CDC/NIOSH/EID)

From: Gary Whitmyre <Gary.Whitmyre@toxcel.com>
Sent: Thursday, November 17, 2011 6:47 PM
To: NIOSH Docket Office (CDC)
Cc: Alan Katz
Subject: Docket No. NIOSH-245
Attachments: SKMBT_C45011111718320.pdf

Attached is a duplicate comment document (as a .pdf file) for Docket No. NIOSH-245 regarding the criteria for a recommended standard for occupational exposure to diacetyl and 2,3-pentanedione, as prepared by ***toXcel, LLC*** of Gainesville, Virginia. This is the identical document as that submitted minutes ago, but this accompanying email this time contains the checked option for a return receipt.

Please feel free to contact us if you have any questions.

Sincerely,

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November 17, 2011

NIOSH Docket Office
Robert A. Taft Laboratories
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NIOSH Mailstop: C-34
Cincinnati, Ohio 45226

RE: *Submission of Comments to Docket No. NIOSH-245 on Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione*

toxcel, LLC is pleased to provide the following comments on the August 12, 2011, external review draft document "*Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-Pentanedione.*" Please feel free to contact us if you have any questions.

Sincerely,

Gary K. Whitmyre, M.A., D.A.B.T.
Senior Director of Exposure and Risk Assessment

COMMENTS ON THE NIOSH PROPOSED RULE REGARDING THE CRITERIA FOR A RECOMMENDED STANDARD FOR OCCUPATIONAL EXPOSURE TO DIACETYL AND 2,3-PENTANEDIONE

toXcel, LLC is pleased to submit the following comments on the proposed rule relating to the establishment of recommended worker exposure standards for the chemicals diacetyl and 2,3-pentanedione. These chemicals are of considerable economic importance in the U.S. food and food flavorings industry. According to NIOSH, there is a literature accumulating that would paint a presumably compelling picture of severe irreversible lung effects resulting from worker exposures to diacetyl and/or 2,3-pentanedione primarily in the food and food flavoring industries. NIOSH asserts that diacetyl exposure is associated with severe obstructive lung disease, morphological changes known as Bronchiolitis Obliterans (BO), and decreases in lung function. NIOSH has also raised concern regarding 2,3-pentanedione because it is an alpha-diketone, and because inhalation studies in laboratory animals indicate similar morphological effects on the respiratory tract. This literature, which is often inconsistent and conflicting, consists of anecdotal evidence, experiments in laboratory animals, epidemiological studies involving relatively small populations of workers, and industrial hygiene surveys of affected sites. The proposed rule sets recommended 8-hour time-weighted-averages (TWAs) of 5 ppb for diacetyl and 9.3 ppb for 2,3-pentanedione. The latter is based in part on the lowest reliable quantification limit for 2,3-pentanedione. In addition, NIOSH is proposing to set short-term-exposure-limits (STELs) of 25 ppb for diacetyl and 31 ppb for 2,3-pentanedione. STELs are not-to-exceed maximum allowable air concentrations in the workplace for a 15-minute period. NIOSH is also proposing an action level of 2.6 ppb for diacetyl to proactively protect worker health. No action level is being proposed by NIOSH for 2,3-pentanedione.

Our comments focus on the following primary issues:

- Whether the recommended exposure limits (RELs) for diacetyl and 2,3-pentanedione are supported by available science;
- The extent to which the recommended exposure limits (including TWA, STEL, and action levels) are feasible;
- The role of multiple chemical exposures in confounding the attribution of effects to diacetyl and 2,3-pentanedione;
- Whether the current lack of full understanding of the role of diacetyl and 2,3-pentanedione in the development of obstructive respiratory disease in the workplace permits defensible promulgation of standards at this time;
- The complications of older workers who contracted obstructive lung disease in previously uncontrolled job environments, in terms of estimating the actual impacts of contemporary exposure;

- Available dose-response information;
- The appropriateness of the benchmark dose approach used by NIOSH;
- The expansive scope of the rule; and
- Whether the role of NIOSH in promoting substitutes at this time is appropriate.

Comment 1: NIOSH's recommended TWA of 5 ppb for diacetyl is not justified. The NIOSH recommended exposure limit of 5 ppb for diacetyl as an 8-hour time-weighted-average (TWA) is based in part on an inappropriate interpretation of exposure data. NIOSH's claim that diacetyl is a threat to workers' health at levels just above 5 ppb is justified neither by exposure data or precedent in toxicology. The upper end of the measured range of airborne concentrations of diacetyl at which some workers are reported to show adverse respiratory changes appear to be approximately 50 ppm, or 50,000 ppb. The four orders of magnitude (i.e., 10,000-fold) difference between what NIOSH suggests as nonhazardous to human health (i.e., 5 ppb) and a point where adverse respiratory changes occur in some workers (i.e. 50 ppm) appears to be an arbitrary, unconventional and unexpectedly wide range. A TWA of 5 ppb with an action level of 2.5 ppb would likely be experienced by every short-order cook and baker in the country who uses real butter, margarine, or butter flavoring. The Rosati data suggest that a 5-ppb REL and 2.5 ppb action level would include those millions of workers who make popcorn at the office. At the very least, they would have to be included in a worker monitoring program to determine their exposure under this proposed rule. Further, the NIOSH proposed RELs and action levels are near or below the odor threshold for diacetyl and 2,3-pentanedione. If the proposed rule is finalized in its current form, anyone who can smell the odor of butter in their workplace would need to be included in a compliance program because, by this rule, they would be overexposed. The odor threshold of diacetyl, which is incorrectly reported in the Criteria Document (NIOSH 2011b, pp. 16-17), is correctly reported at 4.37 ppb (Devos et al. 1990) and 1.42-7.39 ppb (Rychlik et al. 1998). The implication of this simple analysis is that millions of Americans are at or above the proposed REL when they smell butter odor.

Comment 2: The NIOSH proposed STEL of 25 ppb for diacetyl is unjustified.
There is no evidence that short-term exposures to diacetyl in the low ppm range can cause harm to humans. NIOSH's rationale that without a STEL a worker might be exposed to diacetyl for 2400 ppb for one minute and to zero for the remainder of the day is neither a realistic scenario nor an intrinsic problem. NIOSH asserts that a STEL would limit this scenario to a peak exposure of 375 ppb, without any basis for determining that exposure to 2400 ppb for one minute is hazardous and to 375 ppb for one minute is nonhazardous. While NIOSH may have a concern that peak exposures may have greater toxicity than the same total dose spread out over a longer period of time (Ubbink and Schoonman 2002), no evidence supporting the decision to act on this concern has been presented in the criteria document (NIOSH 2011b).

Comment 3: The action Level of 2.6 ppb for diacetyl is burdensome and not feasibile. NIOSH acknowledges that"*...Employers in the food manufacturing sector are generally small business owners with 89% in establishments employing fewer than 100 workers and nearly 53% in establishments employing fewer than 10 workers....*" (NIOSH 2011b, p. 214). Diacetyl is used as an additive in a range of prepared food products, and is served in many places where fresh foods are prepared due to its natural occurrence in wine, beer, butter, cheese, coffee, fruit and other foods (NIOSH 2011b, p. 21). In fact, diacetyl is formed endogenously in small amounts in humans (Kawano 1959; Zlatkis and Sivetz 1960; Gabriel et al. 1972). With an action level that is barely twice the quantitation limit, it is difficult to imagine a food or beverage processing or preparation area that would not exceed this proposed action level. The requirements that are triggered by the proposed action level for diacetyl, therefore, render the requirement to measure down to 2.6 ppb unreasonable and not technologically feasible. A comprehensive health and safety program that includes exposure monitoring (i.e., industrial hygiene sampling) is required if there is a possibility that an employer might be at the action level. Given the near ubiquity of diacetyl in our society, there would not be enough industrial hygienists to meet this demand. Measurements of airborne concentrations of diacetyl at the action level would also trigger a requirement for medical surveillance, including spirometry. NIOSH acknowledged the paucity of spirometric services that can deliver quality spirometry for reliably pinpointing subtle changes that would be required. For example, NIOSH diacetyl researchers found that:

> *"...In California public health surveillance, only one of 13 commercial providers of surveillance spirometry for flavoring workers who reported results to the California Department of Public Health met a minimum quality criterion of 80% of test sessions with FEV1 of good quality...."* (Cai et a. 2006)

Thus, NIOSH's requirement for spirometry and medical surveillance for the large population group that would be "captured" by this proposed rule is simply not feasible.

Comment 4: NIOSH's proposed 2,3-pentanedione REL of 9.3 ppb is unjustified by the science. As part of its HHEs for flavoring compounds, NIOSH did not develop an exposure profile or hazard analysis for 2,3-pentanedione. In fact, NIOSH has only measured 2,3-pentanedione in one flavoring HHE that we were able to identify. At a bakery mix producer, NIOSH found extremely low detectable air concentrations of 2,3-pentanedione, which was introduced to the facility as a substitute for diacetyl a few months before NIOSH's evaluation; hence, no association could be found between 2,3-pentanedione and adverse respiratory changes. Lacking any data, NIOSH has set the REL at the reliable quantitation limit for the analytical method. Similarly, NIOSH's proposed 2,3-pentanedione STEL of 31 ppb is unjustified by the science. Lacking any data, NIOSH has set the STEL at the reliable quantitation limit for the shorter sampling period.

Comment 5: Consumer and office worker exposure levels provide a reality check on the RELs.
In the matter of Newkirk v Conagra Foods, the Plaintiff claimed that his BO was the result of airborne exposures to diacetyl from making and eating large quantities of diacetyl-containing microwave popcorn. Judge Rosanna Peterson found this to be an unbelievable stretch of logic. Judge Peterson excluded the plaintiff's expert witness, writing:

> *"....There is simply too great an analytical gap between the existing data, indicating that exposure to butter flavoring vapors in the occupational setting can cause bronchiolitis obliterans, and Dr. Egilman's opinion that a consumer of microwave popcorn is exposed to a vaporized substance equivalent to production plant butter flavoring vapors at levels sufficient to cause bronchiolitis obliterans...."*[i] (Detroit Legal News 2010).

In fact, a person's exposure to diacetyl when eating butter-flavored popcorn as Mr. Newkirk did, may exceed NIOSH's proposed TWA of 5 ppb for diacetyl. Rosati, Krebs and Liu, scientists at the USEPA, measured diacetyl in air when bags of fresh microwave popcorn were opened. Although not an exposure study, they found that an average of 779 ug of diacetyl were emitted from each bag of popcorn, mostly in the first few minutes of opening the bag. If a person were a frequent popcorn eater and inhaled diacetyl while standing in a small 15 m^3 kitchen, they would experience a potential concentration of (779 ug)/(15 m^3) = 52 ug/m^3, or 15 ppb. This is an airborne level 3 times higher than a worker exposed at the NIOSH proposed level of 5 ppb. Therefore, it is unlikely that ppb levels of diacetyl actually cause BO, for if that assumption were valid, the incidence of BO would have reached epidemic proportions in the general population by this time from the frequent popping of popcorn in home and office microwave ovens.

Comment 6: Many of the industrial hygiene studies involve multiple chemical exposures.
All of the industrial hygiene monitoring studies used to justify the proposed rule for diacetyl and 2,3-pentanedione involve workers who were also simultaneously exposed to other toxic chemicals that cause damage to the respiratory tract. These include exposures to acetic acid, acrolein, and acetaldehyde. These chemicals cause irritation in the airways, but acrolein itself can cause cumulative damage. It is likely that the bronchiolar damage attributed to exposure to diacetyl reflects the combined effect of damage to the respiratory tract from multiple chemicals. The recommended occupational standards for a chemical should represent the effect of the chemical of interest alone, rather than the aggregate effects of a chemical mixture. It is our contention that the proposed standards, while targeted at diacetyl and 2,3-pentanedione, are based on effects and worker exposure settings in which it is difficult to unravel the individual effects of one chemical from another. While some of these additional chemicals may not necessarily cause BO, they may exacerbate the effects of diacetyl and 2,3-pentanedione. For example, exposure to a chemical that inhibits the enzyme pathway that metabolizes diacetyl or 2,3-pentanedione, may become the chemical that actually causes the

damage to the airway. Accordingly, the proposed rule would effectively regulate a single chemical based on data gathered in a mixed chemical environment. Animal testing data show a NOAEC for obstructive lung disease from inhalation exposure to diacetyl near 200 ppm for short-term exposures (Hubbs 2008; Morgan et al. 2008) and 50 ppm subchronic inhalation exposures 6 or 12 weeks in duration. It is difficult to accept that there would be such disparity with worker medical surveillance data to support a proposed TWA four orders of magnitude below this latter NOAEC. A likely explanation would be the combined effects of other chemicals in expressing BO and prior unmeasured exposures of workers to higher levels before PPE and engineering controls were implemented in the workplace. As described in the NIOSH criteria document, every study to date has found exposures to multiple chemicals in the workplace such that the respiratory conditions identified could not be tied to exposure to a single chemical.

Comment 7: Some of the studies include older workers who were "historically-exposed." Some workers who display or were observed to have respiratory symptoms in recent years from exposure to flavoring agents worked before 2001 when work conditions were more adverse and exposures were less controlled. Thus, their symptoms probably reflect higher long-term levels that may have permanently damaged their respiratory tract in the past. Current functional measurements would not be able to separately account for previous long-term exposures. This would lead to *underestimation* of the concentrations of diacetyl or 2,3-pentanedione that would need to be present to cause the currently-observed functional deficits in respiratory function. Because the respiratory tract changes from these two chemicals are permanent (i.e., irreversible), currently observed functional deficits may reflect primarily long-term damage in workers with exposure experience before 2001. There is a lack of baseline spirometry measurements for workers in some studies. Measurements of airborne levels and lung function measurements would not be able to discern between pre-existing permanent obstructive lung disease and effects caused by contemporary exposure conditions. For example, in the quantitative human health risk assessment section of the draft criteria document (NIOSH 2011b), the risk assessment relies on an analysis of the index study recently published as Kanwal et al. (2011). In the study a total of sixty-six percent of mixers, maintenance workers and quality control workers who were hired after exposure controls were put into place reported respiratory symptoms suggests that pre-existing respiratory impairment already existed. If true, this group may not represent the typical newly hired employee working under current industry practices.

Comment 8: Worker exposure monitoring data do not suggest a clear dose-response curve. In the index study, the mean length of employment for workers hired after exposure controls were implemented is 6 months. The affected workers with suspected pre-existing obstructive lung disease had an average length of employment of six years, indicating a work period before exposure controls were implemented, most likely associated with significantly higher airborne concentrations of diacetyl and other chemicals. These two groups of workers also vary significantly in age. Workers hired after exposure controls were implemented were on average 10 years younger than the older workers with pre-existing lung disease. Per the testimony of Dr. Kathleen Kriess of NIOSH at the August 26, 2011 public hearing (p.59) in Washington, DC, four companies that used at least 800 lbs. of diacetyl per year employed workers with moderate to severe obstructive lung disease who had worked for 9 years, compared to 1.5 years for those with only mild degrees of obstruction. **Eighteen of the 467 individuals employed and exposed at these "heavy-use" facilities showed spirometric obstruction. A few individuals of these 18 exhibited "severe" obstruction based on the spirometric measurements.** These factors make it difficult to compare or combine the health outcomes of these groups. Further, in this study and others, the general expectation that job categories or locations that would normally be associated with the highest concentrations of diacetyl would be associated with the highest incidences of obstructive lung disease was not consistently the case. In the index study, and in other studies, job categories with the highest airborne levels of diacetyl and other flavoring chemicals are not necessarily the jobs associated with the highest incidence of obstructive lung disease. Thus, the basis of NIOSH's dose-response and quantitative risk assessment is a set of skewed data that likely does not represent the effects of current exposures with contemporary PPE and engineering controls in place. It is difficult to understand how NIOSH could propose a numerical value for a recommended standard for occupational exposure when a clear dose-response is lacking in workers.

Comment 9: Available animal data provide a more understandable dose-response curve.
Based on available inhalation studies in animals, the lowest observed adverse effect concentration (LOAEC) in rats for bronchial damage from a single 6-hour inhalation exposure to either diacetyl appears to be approximately 300 ppm, with a no-observed-adverse-effect concentration (NOAEC) near 200 ppm (Morgan et al. 2008; Hubbs et al. 2010; Hubbs et al. 2008). The NOAEC for subchronic inhalation studies in mice administered diacetyl for 6 hours/day, 5 days/week for 6 or 12 weeks was 50 ppm (Morgan et al. 2008). NIOSH stated that it believes the bronchiolar region for humans is 10-fold more sensitive to damage from diacetyl than in rats or mice (NIOSH 2011a). This is supported by a study by Gloede et al. (2011) in which estimated airway concentrations in humans exposed to 1 ppm diacetyl were 3 to 7 fold higher than those in rats exposed to the same level of diacetyl. If, for example, this 10-fold adjustment was applied to the subchronic NOAEC, this would produce a "point of departure" of (50 ppm)/(10) = 5 ppm, or 5,000 ppb for development of an allowable TWA.

Comment 10: The exposure parameters used by NIOSH in its deliberations are incorrect. Per the testimony of Dr. Ann Hubbs at the August 26, 2011 public hearing (p. 85) in Washington, DC, it is cited that by light exercising, workers can absorb a 40-fold greater dose to the bronchiolar epithelium than experimentally-exposed rats. NIOSH should consider what portion of the day the worker is involved in light exercise and what portion at more sedentary or standing inhalation rates. It is likely that most of the work day is spent at lower inhalation rates, and that calculation of a time-averaged inhalation rate across an 8-hour work day would reflect this. Thus, arbitrarily inferring that workers would obtain a 40-fold greater dose than rats is unfounded and unlikely. NIOSH needs to reconsider and update its exposure parameter data from more recent sources, such as the newly-released Exposure Factors Handbook from the U.S. Environmental Protection Agency.

Comment 11: The benchmark dose approach used by NIOSH is not appropriate.
In its proposed rule, NIOSH has utilized a benchmark dose approach for setting the recommended worker exposure standard for diacetyl. The benchmark dose model develops for a given response rate a central value benchmark dose (BMD) and a benchmark dose limit (MBDL), which is an equivalent dose value at the 95% lower confidence limit *below* the central value for the dose equivalent to the given benchmark response rate. This method provides much more restrictive benchmarks for conducting a quantitative risk assessment as opposed to using the more conventional NOAELs and LOAELs as the point of departure for the risk assessment. In its benchmark dose technical guidance document (USEPA 2000), the U.S. Environmental Protection Agency states that:

> *"...However, it is likely that there will continue to be endpoints that are not amenable to modeling [by the benchmark dose procedure] and for which a NOAEL/LOAEL approach must be used ..."*

Furthermore, a requirement for the BMD approach (USEPA 2000) is:

> *"...the minimum data set for calculating a BMD should at least show a significant [and monotonic] dose-related trend in the selected endpoint(s)..."*

It is important to note that the data sets used by NIOSH for their benchmark dose modeling do not adequately meet this basic and fundamental requirement. Further, the data sets for each of the four sites combine older workers with historical exposures and younger workers exposed only after PPE and engineering controls have been in place. This complexity of confounding factors makes it difficult to combine the response rates and severities of these two cohorts in a meaningful way, and ultimately makes a combined statistical analysis meaningless.

While benchmark dose modeling may be useful for individual risk assessments, it is unclear whether this is an advisable method for establishing recommended standards in this case. Using a BMD approach for developing recommended occupational exposure standards for diacetyl and 2,3-pentanedione drives the proposed standards to overly-conservative levels and puts these recommended standards at odds with those developed by NIOSH for similar chemicals. The statistical analysis and adjustments used by NIOSH makes for a rigorous (but flawed) statistical analysis that yields a benchmark dose that is so skewed that it has no real meaning in terms of toxicologically-significant levels. For these reasons, and due to the limitations, complexities, confounding factors, and inconsistent dose-response curves from the existing data sets available for worker exposures to diacetyl, it is recommended that a more traditional NOAEL/LOAEL approach be used in establishing recommended occupational exposure standards for diacetyl and 2,3-pentanedione.

Comment 12: The proposed RELs for diacetyl and 2, 3-pentanedione are premature. Attempts have failed to separate the hazards posed by diacetyl and 2, 3-pentanedione from those of other chemicals with which diacetyl and 2, 3-pentanedione are found in the workplace. NIOSH has conducted numerous Health Hazard Evaluations (HHEs) of manufacturing facilities with likely cases of BO and/or likely exposures to butter flavoring diacetyl. Despite air sampling for a wide range of volatile and potentially hazardous ingredients in these facilities, NIOSH has been unable to identify the relative hazard posed by each ingredient or combination of ingredients. The following explanation, from NIOSH's 2004 HHE Report on American Pop Corn plant, presents a frank discussion of this issue (Kanwal et al. 2004):

> *"....NIOSH measured the air levels of diacetyl and acetoin, two common ingredients in butter flavoring, as indicators of exposure to butter flavoring vapors. Animal experiments at NIOSH indicate that diacetyl is one of the chemicals in butter flavoring that can lead to airway injury. The other chemical components that may contribute to toxicity, and the levels of exposure that are considered safe, are still not known. Recommended air exposure limits have not been established for most chemicals used in flavorings...."*

There is no doubt that occupational illness has been linked to certain food manufacturing operations; however, the key question of "what chemical component(s) is/are causing disease?" remains unanswered. NIOSH cites a series of studies by van Rooy and Frits (e.g., Frits et al. 2007) as important in establishing a causal link between diacetyl exposure and BO. Their investigation of workers at a chemical plant in the Netherlands that produced diacetyl found BO in only three of 102 workers. Air concentrations ranged from 1.8 to 351 mg/m^3 (0.51 to 100 ppm) for diacetyl and from 0.4 to 29 mg/m^3 (0.22 to 16 ppm) for acetaldehyde. As NIOSH points out:

> *"...During production of diacetyl, workers were also potentially exposed to acetoin, acetaldehyde, and acetic acid.... the investigators were not able to demonstrate an exposure-response relationship between relative cumulative exposure to diacetyl and FEV1...."*

The study authors were careful not to overstate the findings of their study by noting that:

> *"...Our study suggests a causal role of diacetyl. However, we cannot rule out a possible contribution of acetoin or even acetaldehyde, either as causative or contributing agents..."*

In the criteria document, NIOSH states (NIOSH 2011b, p.23) that:

> *"...Many work environments have mixed exposures, with multiple chemical agents present. Although the primary focus of this criteria document is diacetyl and 2,3-pentanedione, other compounds can also be of concern. Depending upon the processes employed in a workplace, sampling should be conducted for agents of concern to maintain safe work environments..."*

The fact that NIOSH has collected hundreds of samples showing the presence of diacetyl in workplaces where workers have contracted lung disease does not prove a causal relationship. NIOSH has sampled for diacetyl as a surrogate for the dozens of other chemicals in butter and other flavorings. In one plant (Kreiss et al. 2011), NIOSH discovered that workers were exposed to 24 of the 34 food additives listed by Flavor and Extract Manufacturers Association (FEMA) as "high priority" substances; that is, "flavoring substances that may have the potential to pose respiratory hazards in flavoring-manufacturing workplaces (OSHA 2010)." In a popcorn plant, NIOSH found more than 100 different volatile organic compounds in the air of the mixing room (Kreiss et al. 2002). Until epidemiology studies can confirm the theory that occupational exposure to diacetyl by itself causes BO, the promulgation of the proposed recommended exposure limits (RELs) for diacetyl and 2,3-pentanedione is premature.

Comment 13: NIOSH's expansion of the scope to include all flavoring agents is not justified.
Per review of NIOSH's Criteria Document's requirements for employers to implement exposure monitoring, medical monitoring, respiratory protection programs, engineering controls and other administrative controls, NIOSH's intent in the document is to regulate exposure to ALL flavoring agents that may pose a health hazard. For example:

- *"....A safety and health program designed to protect workers from the adverse effects of exposure to diacetyl, 2,3-pentanedione, and other flavoring chemicals should include mechanisms to identify all risk factors for exposure to flavoring substances...."* (NIOSH 2011b, p. 281)

- *"....Because flavorings can consist of many chemicals in addition to diacetyl and 2,3-pentanedione, deciding what to sample often requires preliminary knowledge of the specific flavoring chemicals being produced or used, or that are present in flavorings or other food ingredients used in the workplace, and the known exposure hazards posed by each...."* (NIOSH 2011b, p. 284)

- *"....All workers (permanent, temporary and contract workers) who regularly work in or enter areas where diacetyl and similar flavor ingredients (or products that contain these ingredients) may benefit by being included in the medical monitoring program...."* (NIOSH 2011b, p. 260)

- *"....An analysis should be performed on each operation involving diacetyl, 2,3-pentanedione, or other food flavoring compounds to assess the potential exposures and to establish specific guidance about when to use skin, eye, and face protection...."* (NIOSH 2011b, p. 244).

This vast expansion in scope is not supported by the title of the Criteria Document or data presented therein. NIOSH has not even attempted to establish a scope, justification or scientific basis for such an expansion. This regulatory short-cut is clearly not warranted and would have vast repercussions throughout the entire food production and service industry. Literally thousands of flavoring chemicals are in use currently. Of these, only 46 have OSHA PELs (NIOSH 2011b, p.14). Meaningful implementation of any new requirements on flavorings would require that NIOSH identify each chemical of interest, and develop a recommended exposure limit (REL) for each chemical that NIOSH would wish to include. Justification is clearly lacking with regard to why exposures to flavoring agents in general, and diacetyl and 2,3-pentanedione specifically, would be elevated to priority status above other workplace chemical exposures.

Comment 14: NIOSH's call for development of substitutes at this time is ill-advised. The recommendation by NIOSH that substitutes be developed for diacetyl and 2,3-pentanedione is unwarranted because the available science as selectively presented by NIOSH does not provide adequate justification for regulating the current worker population's exposures to diacetyl and 2,3-pentanedione, per the above comments. Further, the encouragement of substitutes at this time may result in chemicals entering the flavoring marketplace that may be associated with poorer performance and perhaps even greater toxicity. In fact, we know even less about the hazards of some of the proposed substitutes for diacetyl than we do about diacetyl and 2,3-pentanedione. It may be decades before any proposed substitutes can be adequately tested to provide a level of assurance of safety.

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