18 August 2009

MDA Environmental Stewardship Division
PO Box 30017
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Attn: Lisa Lipsey, via email to lipseyl@michigan.gov, with copy to Review Committees

RE: Sierra Club Comments on the: 2010 DRAFT GAAMPs for Site Selection and Odor Control for New and Expanding Livestock Production Facilities, and for Manure Management and Utilization

Dear Ms. Lipsey,

Thank you for this opportunity to share our expertise and to provide comments on the 2010 DRAFT GAAMPs. The Sierra Club Michigan Chapter has worked for clean air, clean water, and safe healthy communities since 1967. Since before 2000, our Chapter has worked for stronger regulation of large-scale livestock operations known as concentrated animal feeding operations (CAFOs), because communities were being harmed by discharges and emissions of manure-contaminated water and air from them. As you know, scientific knowledge of better management practices for large-scale animal agriculture has advanced tremendously since then. Therefore we urge the Michigan Department of Agriculture and the GAAMPs Review Committees to consult with other experts, in addition to those you've cited in the 2010 DRAFT GAAMPs, and to read additional information about scientific and peer-reviewed studies. These comments, which are primarily in regards to GAAMPs used at CAFOs, will also provide some new reference materials for Review Committee consideration.

## General Remarks

### Lack of Clear Definitions Creates Ambiguity and Confusion

In order to be fair and predictable in the application of GAAMPs, the MDA must have clear and definite guidelines with no ambiguity about the provisions that can imbue substantial financial benefits (lawsuit protection) for some while taking away substantial economic benefits and quality of life from others. For example, the Site Selection GAAMPs provide significant wiggle room by using terms such as "can" and "should" in place of clear, unambiguous terms like "shall" and "must." The Manure Management and Utilization GAAMP uses the word "should" more than 100 times, most of those in contexts without clarity about what exactly is required. For example, the GAAMP says that leachate and runoff "should" be controlled, when in fact these "must" be controlled to prevent contamination of surface and groundwater. A determination that a facility is not verified is virtually impossible in the face of such language.

In each case the ambiguity in the GAAMP language makes it harder for MDA and MSUE and Conservation District staff, and others, to be clear on the specifics of the GAAMPs, and harder for Michigan citizens to know if compliance is achieved or not achieved. This means decisions that can permanently affect the health and prosperity and quality of life of neighbors of CAFOs in particular are prone to an increasingly subjective process in the hands solely of MDA field staff.

**2010 DRAFT GAAMP for Manure Management and Utilization**

**Human Welfare and Animal Welfare**

In the last sentence of the first paragraph of the Introduction to the 2010 DRAFT GAAMP for Manure Management and Utilization, the words "animal welfare" were changed to "animal care" and "human welfare" was changed to "neighbor relations", signaling MDA's and the Review Committee's encouragement of livestock producers' shifting away from caring about deleterious health impacts to CAFO neighbors and instead trying to improve CAFO's public image, so that neighbors may be less willing to file complaints in order to avoid looking like the "bad guy".

**Why Changing Human Welfare to Neighbor Relations Matters**

Because large-scale animal agriculture has such an enormous capacity to negatively impact the health of nearby neighbors, we cite here an article from the *Environmental Health Perspectives Online Journal*, specifically ***Health Effects of Airborne Exposures from Concentrated Animal Feeding Operations***, located at http://www.ehponline.org/members/20068835/8835.html. (Environ Health Perspect 115:298–302 (2007) . doi:10.1289/ehp.8835 available via http://dx.doi.org/ [Online 14 November 2006]) (A printed copy is included with these comments as Appendix A.) **From the Article Abstract:** "Toxic gases, vapors, and particles are emitted from concentrated animal feeding operations (CAFOs) into the general environment. These include ammonia, hydrogen sulfide, carbon dioxide, malodorous vapors, and particles contaminated with a wide range of microorganisms. Little is known about the health risks of exposure to these agents for people living in the surrounding areas."

Therefore, we urge MDA and the GAAMPs Review Committees to encourage producers' diligence in avoiding causing the situations where neighbors feel trapped in their own homes to avoid not only the nauseating odors, but also to avoid exposure to toxic emissions that accompany the odors.

For example, throughout the manure management GAAMP, the phrase "immediate incorporation" is used – and then defined as within 48 hours. Forty-eight hours is **not** immediate. Same-day incorporation of manure on a field would be much more meaningful a good-neighbor policy than holding farm tours and hosting athletic teams.

**GAAMPs Benefits to Producers**

A determination of compliance with GAAMPs means the state of Michigan confers a substantial benefit to a livestock agriculture operation, far too often at substantial cost to their neighbors. In short, if an agriculture industry representative determines that the operation is following GAAMPs - then that operation cannot be sued by neighbors under any nuisance claim. No other industry in Michigan is granted such protection.

In return for this boon, it is incumbent upon MDA and the GAAMPs Review Committees to provide equal protection for CAFO neighbors by assuring that the GAAMPs actually provide the benefits associated with them.

For example, the practice of "temporarily stockpiling manure" is allowed within 50 feet of a residence, for up to 6 months, or up to 12 months, "if covered with an impermeable cover".

This image, dated August 7, 2009, shows a stockpile of manure that was dumped within 100 to 150 feet of a home (not visible here), which is double the distance recommended in the GAAMPs. Yet - the homeowners still had to close all windows and stuff towels under the doors to lessen the odors and emissions coming into their home, and had to deal with nuisance numbers of flies that came in the doors every time someone came in or went out. It's obvious the fly outbreak occurred because of the manure – and it's disgusting and worrisome to know the same flies that were landing on and walking on manure get into homes in large numbers where they land on counter tops and tables where food is prepared. Stockpiling of manure shouldn't be allowed within a half-mile of homes, especially if it's going to be left there for any length of time.

**Stacked Solid Manure GAAMP #15, Setback to Surface Water, pages 13-14**

The setback distance of 150 feet from a surface water is meaningless if there are field tiles present, and most of Michigan's fields do have field drainage tiles. The MDA and MDEQ should require the removal of field tiles from fields where stockpiling is to be done, or where application of liquid manure is to be done.

**Land Application GAAMP #6, page 9, top paragraph:**

The last sentence says "…can be utilized if applied at rates that supply 75% or less of the annual phosphorus removal for the <u>current crop</u> or next crop to be harvested." Is this sentence suggesting that adding manure to a field with growing food crops is still an acceptable practice? With all the recent media coverage of *E. coli* making its way into tomatoes and lettuce, it is clearly time to end this practice. MDA and MDEQ and the Michigan Department of Community Health should ban the application of manure to growing food crops.

**Method of Manure Application GAAMP #36, top page 27:**

This last sentence was struck: "An application that results in manure flow in a field tile line is an unacceptable practice." This doesn't seem right, as to strike the sentence would indicate that MDA and the Review Committees feel that a field-tile line discharge is acceptable, when clearly any discharge of manure or animal waste is unacceptable. Also – the same sentence was not struck from the Quick Reference page 7.

The second paragraph on page 27 describes several suggestions for reducing risk of runoff and erosion losses of manure nutrients, and states that a "vegetative buffer should be maintained between the application area and any surface water." However, a vegetation buffer cannot help if there are field tiles draining the field, since the buffer strips are completely bypassed.

**Timing of Manure Application, GAAMP #38, page 28:**
"Ideally, manure (or fertilizer/other source) nutrients should be applied as close as possible to, or during, periods of maximum crop nutrient uptake to minimize nutrient loss from the soil-plant system." Does this recommendation also suggest that it is permissible and advisable to apply manure to growing crops? MDA and MDEQ and the Michigan Department of Community Health should ban manure application to growing food crops.

**GAAMP #39, page 28:**
Last sentence page 28 states "In either situation, provisions must be made to control runoff and erosion with soil and water conservation practices, such as vegetative buffer strips between surface waters and soils where manure is applied."
This doesn't make sense -- vegetative buffer strips wouldn't work in the winter because there is no uptake of nutrients by dead plants.

**2010 DRAFT GAAMP for Site Selection and Odor Control for New and Expanding Livestock Production Facilities**

**Part III Determining Acceptable Locations for Livestock Production Facilities, page 4:**
The three categories make sense, except that neither of the first two mention environmental concerns, only Category 3 states that the environment is of concern in locating a livestock production facility, in addition to too many non-farm residences. If it matters in Category 3, it also matters in Categories 1 and 2, and it should state so. The process of determining acceptable locations for livestock production should also include the process of assuring enough near-by land-base for manure application that also isn't too close to neighbors to cause problems. It should also assure that the manure application sites do not have streams or drains cutting across them, or adjacent to them.

In other words, the entire "Siting Process" should include scrutiny of the location of surface water and application of appropriate setbacks from surface water, steep land slope, location of drainage tiles from both production areas and from fields – because the presence of any or all these sets the operation up for a future discharge. GAAMPs are not just about neighbor relations and possibilities of odor, they're also intended to protect the environment.

**Siting Selection GAAMPS Pick Winners and Losers**
The Site Selection GAAMP fails to protect a significant number of neighbors from air pollution problems. The fundamental idea of this GAAMP that a certain number of residential units <u>can be</u> located within a half mile or quarter mile distance of a CAFO means that MDA and the GAAMPs Review Committees have decided that a significant number of rural residents will simply have to live with and put up with the pollution problems caused by the CAFO with no recourse and no recompense. There is no scientific basis for deciding that the five homeowners within ½ mile of an AFO with 750-999 animal units will somehow suffer less harm than if there were 10 homes within that distance, yet one group will be prohibited by law from bringing nuisance actions – and so their quality of life and health will be sacrificed, while the others will be protected by state law.

**Siting Needs to Include Production Area and Fields**
The Siting of CAFOs must address not only the buildings and production area but the location of fields onto which wastes are to be spread. Location of facilities in 100 year flood plains should be prohibited entirely because the danger of contamination of surface waters with large amounts of toxic and pathogenic waste is so significant that the state must not allow it.

In addition, setback from all wells must be applied not only to buildings but to the land application of manure, and, depending on soil types, may be required to be much larger than provided currently. The history of the Walkerton, Ontario, tragedy, the study of the Hartford Dairy CAFO (and subsequent development of a TMDL for *E. coli* in two nearby streams), increasing evidence of the residence time of pathogens in the soil, and evidence of contaminated drinking water wells near CAFOs raises the increasing concern that field application of wastes are posing serious threats to public health even in situations where the waste is apparently applied at agronomic rates. Yet the GAAMPS do not address this at all.

Site Plans must include all fields that may be used for manure application and all wells or groundwater recharge areas beyond the borders of the property managed by the CAFO. The requirement that CAFOs with more than 5,000 animal units must obtain a groundwater permit and that any discharge to groundwater requires the operator to obtain a permit must be included in the GAAMP as well.

Page 6: In development of an Odor Management Plan, MDA should strongly consider the use of the USEPA's AERMOD Modeling System, instead of the OFFSET odor model. From USEPA website: http://www.epa.gov/scram001/dispersion_prefrec.htm "These refined dispersion models are listed in Appendix W and are required to be used for State Implementation Plan (SIP) revisions for existing sources and for New Source Review (NSR) and Prevention of Significant Deterioration (PSD) programs. The models in this section include the following: **AERMOD Modeling System** - A steady-state plume model that incorporates air dispersion based on planetary boundary layer turbulence structure and scaling concepts, including treatment of both surface and elevated sources, and both simple and complex terrain."

**Site Suitability Approval: page 15**
The process of asking for review of an MDA Site Determination seems subjective in the extreme, with all the benefits and assumptions to be afforded to the would-be livestock producer and none to the neighbor. If a neighbor asks that a Site Determination be reviewed, MDA calling in 3 Recognized Professionals, (selected from a short-list that includes only one potentially objective third party), makes it seem impossible that a decision would ever be found in favor of the neighbor.

**Appendix A Michigan Odor Management Plan, page 17**
The last sentence in the first paragraph states "Because of the subjective nature of human responses to certain odors, recommending appropriate technology and management practices is not an exact science." **This sentence is a cop-out** and completely ignores recent scientific findings about impacts of both malodors and toxic emissions of gases from CAFOs. Again, we urge MDA and the GAAMPS Review Committees to refer to the Environmental Health Perspective peer-reviewed articles on these topics, attached to these comments. Studies have identified hundreds of gases, including volatile organic compounds in samples of air around CAFOs.

**Example Dairy Odor Tracking and Response Plan, page 21**
The first item states that farm employees will be asked to keep track of odors, and to notify management if the odors become offensive. This won't work over time, because people become desensitized to odors. Unfortunately, people do not become desensitized to toxic emissions, the deleterious effects still occur. The second paragraph of item #3 under the same section states that outside observers, such as MSUE or MDA staff, will be asked to provide an objective analysis. Unfortunately, neither MSUE nor MDA staff can be truthfully described as objective outside observers. It would be more useful and helpful to call in staff from the Michigan Department of Community Health, or staff from the Local Health Department, whose mission is to protect the health and wellbeing of Michigan residents.

**Request for a Responsiveness Summary to All Comments Submitted**
We respectfully request that MDA provide a responsiveness summary for all of the comments submitted in the public comment period, identifying the questions or comments raised and responding specifically to each issue.

Again, thank you for the opportunity to provide comments on these new revisions of the GAAMPs. We hope you will consider and follow each recommendation. Please contact us if you have questions at 517.484.2372.

Sincerely,

Rita Jack, Clean Water Program Director
Lynn Henning, CAFO Water Sentinel
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# Health Effects of Airborne Exposures from Concentrated Animal Feeding Operations

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**Toxic gases, vapors, and particles are emitted from concentrated animal feeding operations (CAFOs) into the general environment. These include ammonia, hydrogen sulfide, carbon dioxide, malodorous vapors, and particles contaminated with a wide range of microorganisms. Little is known about the health risks of exposure to these agents for people living in the surrounding areas. Malodor is one of the predominant concerns, and there is evidence that psychophysiologic changes may occur as a result of exposure to malodorous compounds. There is a paucity of data regarding community adverse health effects related to low-level gas and particulate emissions. Most information comes from studies among workers in CAFO installations. Research over the last decades has shown that microbial exposures, especially endotoxin exposure, are related to deleterious respiratory health effects, of which cross-shift lung function decline and accelerated decline over time are the most pronounced effects. Studies in naïve subjects and workers have shown respiratory inflammatory responses related to the microbial load. This working group, which was part of the Conference on Environmental Health Impacts of Concentrated Animal Feeding Operations: Anticipating Hazards—Searching for Solutions, concluded that there is a great need to evaluate health effects from exposures to the toxic gases, vapors, and particles emitted into the general environment by CAFOs. Research should focus not only on nuisance and odors but also on potential health effects from microbial exposures, concentrating on susceptible subgroups, especially asthmatic children and the elderly, since these exposures have been shown to be related to respiratory health effects among workers in CAFOs. *Key words:* air quality, asthma, biological agents, endotoxin, inflammation, odor, poultry, swine. *Environ Health Perspect* 115:298–302 (2007). doi:10.1289/ehp.8835 available via *http://dx.doi.org/* [Online 14 November 2006]**

## Background and Recent Developments

*Gases and vapors.* A number of toxic gases and vapors are emitted by concentrated animal feeding operations (CAFOs) into the work and general environments. In particular, occupational studies have yielded information about exposure levels of ammonia ($NH_3$), hydrogen sulfide ($H_2S$), and carbon dioxide ($CO_2$). The characteristic odor of a CAFO is the result of a complex mixture of these gases and many volatile and semivolatile organic compounds. Odor emissions are especially associated with quality of life issues for exposed populations. Specific gases such as $H_2S$ are being used as proxies to estimate or regulate exposure to the whole complex mixture. Although this approach has the advantage of simplicity and exposure estimates can be compared with guideline exposure values, it also has several limitations. Situations may arise where the surrogate compound does not co-vary with other toxicants in the mixture. The issue of which specific community health effects may result from CAFO emissions is open and controversial. There is limited evidence that symptom patterns may be the result of CAFO exposures in individuals living in their vicinity. Changes in immunoglobulin A responses have been observed in individuals and associated with exposure to odor, suggesting that psychophysiologic responses can occur (Avery et al. 2004). The underlying mechanistic explanation is that these physiologic changes are most likely stress related; however, other mechanisms including sensitization may also contribute.

Very little information exists about lung function changes among populations living in the vicinity of CAFOs. Emission studies, in combination with modeling approaches, are helpful but not sufficient to relate exposures to health effects because the exposure depends on personal activity patterns and time spent near different sources. A recent report from Germany found that people residing in proximity to many CAFOs (> 12 within a 500-m radius) experienced significantly increased prevalence of self-reported wheezing and decreased forced expiratory volume in 1 sec ($FEV_1$) indicative of inflammatory effects of CAFO emissions in the lungs (Radon et al. 2005). However, a problem with the interpretation is that clear differences existed in sensitization rates between rural participants and the urban comparison population. In addition, it can be expected that differences existed within the rural population associated with childhood exposure patterns to animals on these farms compared with those experienced with CAFOs. This raises methodologic issues regarding appropriate comparison populations and confounders or effect-modifying variables that need to be included in multiple regression models to make accurate comparisons. Nevertheless, the results from this study are of interest and similar studies need to be undertaken in other populations with more subjects living in proximity to CAFOs.

Most information on potential health effects comes from working populations. Gases seem to play a limited role in the explanation of work-related respiratory symptoms in CAFO workers, but this may not be true for humans living in the surrounding areas. The distribution of adverse effects by age is different, and susceptibility may be an important issue, with children and elderly individuals belonging to the most vulnerable populations. Also, socioeconomic relationships between workers and companies, as opposed to neighbors and companies, are different, and this will have an impact on the willingness to tolerate hazardous exposures, and bear an increased burden of ill health.

***Exposure inside CAFOs.*** In early studies on respiratory health of CAFO workers, several constituents of dust have been considered. Exposure to allergens from pigs and storage mites has received some attention, but most studies have shown that sensitization rates to swine urine proteins among farmers are relatively low and cannot explain the high symptom rates in CAFO workers (Brouwer et al. 1990; Cormier et al. 1991; Crook et al. 1991;

This article is part of the mini-monograph "Environmental Health Impacts of Concentrated Animal Feeding Operations: Anticipating Hazards—Searching for Solutions."

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Harries and Cromwell 1982; Katila et al. 1981). Similarly, responses against storage mites seem to be explained mainly by cross-reactivity to house dust mites.

Early studies have shown that the CAFO industry environment is rich in microbial life. Kiekhaefer et al. (1995) made detailed microbial characterizations of the environment in various types of CAFOs across seasons and showed that moderately elevated culturable mold levels exist with an overall mean concentration of $5.3 \times 10^3$ colony-forming units/m$^3$ and mean total organisms (orgs) concentrations of $1.1 \times 10^8$ orgs/m$^3$. The predominant fungal types were *Cladosporium* and *Alternaria* in the summer and fall and yeasts *Penicillium* and *Fusarium* in the winter and spring. Mainly gram-positive bacteria are found in CAFOs, but gram negatives play an important role as well. As a result, endotoxin levels are clearly elevated. Although microbial markers other than endotoxin have been associated with respiratory health and specific respiratory inflammation (Zhiping et al. 1996), endotoxin has been most extensively studied in experimental studies with naïve subjects and epidemiologic studies using a range of study designs.

***Endotoxin exposure.*** Particulate exposure in the environs surrounding CAFOs occurs but has not received much attention to date. Considerable information exists about workplace exposure to dust from CAFOs (Schenker et al. 1998), and since the 1980s, endotoxins have been identified as important causal and toxic agents (Attwood et al. 1987; Donham et al. 1984).

Endotoxin is composed of lipopolysaccharides (LPS) and is a nonallergenic cell-wall component of gram-negative bacteria with strong proinflammatory properties. Endotoxins are ubiquitous and commonly present inside CAFOs, the general environment, and house dust (Douwes et al. 1998, 2000; Michel et al. 1991; Peterson et al. 1964; Schenker et al. 1998; Thorne et al. 2005). Very high endotoxin exposure occurs in farming, particularly livestock farming (Kullman et al. 1998; Schenker et al. 1998). Elevated endotoxin levels are present in homes where children have regular contact with farm animals and in homes where pets are present (Douwes et al. 2000; Thorne et al. 2003; von Mutius et al. 2000). Larger numbers of family members, poverty, and roach infestation are also associated with higher endotoxin in homes (Thorne et al. 2003, 2005). Inhalatory endotoxin exposure has been associated with a range of respiratory health effects in both the work and the domestic environment (Douwes and Heederik 1997; Douwes et al. 2002). Because results of research on respiratory health effects of endotoxin exposure were focused on different aspects for the occupational and domestic environments, overall results are reviewed briefly here for both environments.

***Work environment exposures and adult onset allergy and asthma.*** Early studies on endotoxin exposure and farming activities began in about 1982. Swine production facilities have especially been studied since that period. Endotoxin exposure is high for workers in these industries, and several large-scale studies suggest that the mean exposure varies between a few hundred up to 15,000 endotoxin units (EU)/m$^3$ of air in situations where ventilation is limited because of extreme climatic conditions (Douwes and Heederik 1997). These exposures have been associated with increased symptoms, both respiratory and systemic (Rylander et al. 1989), across-shift lung function changes (Donham et al. 2000), reduced lung function in cross-sectional studies and accelerated decline in lung function in longitudinal studies (Vogelzang et al. 1998). Neutrophil-mediated inflammation has been observed in naïve subjects and swine confinement workers after exposure that is limited to periods of a few hours (Jagielo et al. 1996; Sandström et al. 1992; Von Essen and Romberger 2003). The exact pathophysiology is not clear, but it is well established that it is mediated by an acute inflammatory response involving a variety of cytokines, including interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor (TNF)-$\alpha$, and the subsequent massive recruitment and activation of neutrophils in the lower and upper airways. The inflammatory reactions are orchestrated by alveolar macrophages that carry specific endotoxin binding receptors [LPS binding protein, CD14, MD2, toll-like receptor (TLR) 4], which play a crucial role in the activation of these cells and the subsequent inflammatory processes (Gioannini et al. 2003). Considerable interindividual variability in response to endotoxin has been observed in endotoxin provocation experiments with naïve subjects (Kline et al. 1999).

Recent studies suggest that environmental endotoxin exposure might protect against the development of atopy and possibly allergic asthma (Gereda et al. 2000a, 2000b; Liu and Leung 2000; Martinez and Holt 1999; von Mutius et al. 2000). A low prevalence for atopy, hay fever, and to a lesser extent, asthma has been observed in the children and adolescents of farming families and first-year university students with a farming background (Braun-Fahrländer et al. 1999; Ernst and Cormier 2000; Kilpelaïnen et al. 2000; Portengen et al. 2002; Riedler et al. 2000; von Ehrenstein et al. 2000). Contact with livestock in the first year of life appeared to be one underlying determinant of this reduced risk. These observations are usually referred to as the "hygiene hypothesis." Hence, exposure to endotoxin may reflect two sides of a coin: *a*) producing a protective effect with regard to atopy, and *b*) inducing inflammation that leads to nonallergic asthma. Two recent studies of adult farmers are in agreement with this hypothesis (Douwes et al. 2002). In the European Community Respiratory Health Survey, which investigates occupational asthma in 15,637 randomly selected people 20–44 years of age, the highest risk of asthma was shown for farmers [odds ratio (OR) = 2.6; 95% confidence interval (CI), 1.3–5.4] and agricultural workers (OR = 1.8; 95% CI, 1.0–3.2) (Kogevinas et al. 1999). An increased risk of asthma morbidity and mortality for farmers has been reported in several other studies as well (Fishwick et al. 1997; Neijari et al. 1996; Toren et al. 1991). Farmers involved in animal production seem to have the highest risk for asthma compared with subjects not involved in animal production (Melbostad et al. 1998). In the same study population, asthma in the absence of atopic sensitization to common allergens was associated with an increased exposure to endotoxin (Eduard et al. 2004). Other studies have reported conflicting results for the association of endotoxin exposure and asthma in farmers (Kimpbell-Dunn et al. 1999; Omland et al. 1999; Vogelzang et al. 1999). A study among Dutch pig farmers showed that the prevalence of atopic sensitization decreased sharply with increasing occupational endotoxin exposure, with the lowest prevalence at levels above 750 EU/m$^3$ (Portengen et al. 2005). A study from Iowa showed an increased prevalence of childhood asthma on farms with increasing numbers of swine (Merchant et al. 2005). This raises the question as to whether exposures that begin in adulthood may lead to lowered risk for atopic sensitization as well, as opposed to the prevailing belief that a healthy worker selection is responsible for this phenomenon.

***Domestic endotoxin exposure and allergy and asthma in children.*** Most research on domestic endotoxin exposures has focused on the question of whether this exposure can explain the observations made in several studies describing a protective effect related to the development of atopy and allergic asthma in children who have grown up on small, traditional farms (Braun-Fahrländer et al. 1999; Klintberg et al. 2001; Portengen et al. 2002; Riedler et al. 2000; von Ehrenstein et al. 2000). It was indicated that contact with livestock reduced the risk of atopic asthma in children (von Ehrenstein et al. 2000) and young adolescents (Portengen et al. 2002). Although no specific protective factors were determined in these studies, it has been suggested that respiratory exposure to endotoxin may play an important role (Klintberg et al. 2001; von Ehrenstein et al. 2000), as it is well known, especially from occupational studies, that animal husbandry is associated with high exposures to bacterial endotoxin. However, exposures to other bioaerosol components such as fungi, gram-positive and gram-negative bacteria, bacterial DNA motifs, storage mites, and allergens from crops and animals are expected to be higher on farms and could also play a role.

The immune system is known to be skewed toward a proatopic direction during fetal and perinatal life. It has been proposed that proinflammatory microbial products, such as bacterial endotoxin, prokaryotic DNA, and glucans, markedly modulate the response of the immune system away from its tendency to develop atopic immune responses (Liu and Leung 2000; Martinez and Holt 1999). This may be a dose-dependent phenomenon, with low doses of these compounds providing some protective effects (as accounted for in the hygiene hypothesis of allergic asthma and atopy) and higher doses leading to a skewed and harmful response. Bacterial endotoxin and prokaryotic DNA can strongly induce IL-12 production by antigen-presenting cells, leading to the elaboration of interferon (IFN)-γ, IL-18, and other mediators. These mediators, many of which are transduced through one of the conserved TLR, are well recognized as promoting T helper (Th)1 (counter to Th2) responses. It has also been shown that the protective effect of farming exposure is regulated by a TLR2 response, as only children with the wild type of this gene were protected from allergy, given they were born on a farm (Eder et al. 2004). More recently, however, the promotion of "regulatory" responses (e.g., regulatory CD4$^+$ T-cells and antigen-presenting cells such as dendritic cells and macrophages) has received prominent attention. These cells, when activated by microbial products referred to as pathogen-association molecular patterns (PAMPs) use IL-10 and TGF-β to mediate their attenuation effects; regulatory responses can downregulate both Th1 and Th2 immune responses. This category of inflammation may account for the observations that both Th1-mediated diseases (e.g., diabetes mellitus) and Th2-mediated diseases (asthma and atopic disorders) have been rising in industrialized countries over the past several decades where children are exposed to lower levels of microbial products and infections than in the past or in preindustrialized or agricultural societies. Further infections associated with eosinophilia (e.g., helminth infestations), that promote both Th2 and regulatory responses, can protect against asthma and atopy (Kline et al. 1998; Shirakawa, 1997; Yazdanbakhsh et al. 2002).

To date few studies have produced direct *in vivo* evidence that endotoxin exposure may protect against the development of atopy by enhancing Th1 responses. A U.S. study of infants with documented wheezing episodes showed that endotoxin levels were correlated with IFN-γ–producing T cells (Th1) but not with IL-4–, IL-5–, or IL-13–producing cell proportions (Th2) (Gereda et al. 2000b). A Swiss–German study of farm children showed a decreased capacity to release IFN-γ, TNF-α, IL-10, and IL-12 in peripheral blood leucocytes upon stimulation with LPS, with increasing endotoxin load in the beds (Braun-Fahrländer et al. 2002), which could be a consequence of "exhaustion" of the atopic immune system as proposed in association to atopy by Kruger et al. (2004). Animal experimental studies with ovalbumin and endotoxin have not yielded consistent results.

Studies that found a consistent protective effect of farming exposure against atopy (Braun-Fahrländer et al. 2002; von Mutius et al. 2000) have shown only a weak protective effect against asthma itself, or they have shown a dual response in children with atopic asthma and allergy to be lower with increasing LPS exposure, and contrary to this, an increased prevalence of nonatopic wheeze with increasing LPS exposure (Braun-Fahrländer et al. 1999). There is considerable evidence that endotoxin exposure may both exacerbate preexisting asthma and induce new asthma. Several studies have also shown that endotoxin in house dust is associated with exacerbations of preexisting asthma in children and adults (Michel et al. 1991, 1996, 1997). A cohort study in 499 infants with a familial predisposition to asthma or allergy showed that early indoor endotoxin exposure was associated with an increased risk of repeated wheeze during the first year of life rather than a decreased risk (relative risk = 1.6; 95% CI, 1.03–2.38) (Shirakawa et al. 1997). A recent study of endotoxin in 831 homes across the United States demonstrated that indoor endotoxin was a significant risk factor for asthma symptoms, medication use, and wheezing. The adjusted OR for households with both bedding and bedroom floor endotoxin exceeding 19.6 EU/mg compared with those below was 2.83 (95% CI, 1.01–7.87). This effect was seen regardless of allergy status (Thorne et al. 2005).

Thus, for asthma alone, there is consistent evidence that endotoxin is both a secondary and primary cause of asthma, and that this occurs through nonatopic (i.e., nonimmunoglobulin E–mediated) mechanisms.

Because of the health effects related to environmental exposures, exposure standards have been suggested (Rylander 1997). The Health Council of the Netherlands proposed a health-based occupational exposure limit of 50 EU/m$^3$ over 8 hr for the working environment, which has been modified to 200 EU/m$^3$ because of feasibility issues. The introduction of this standard has been postponed because agricultural industries cannot meet this level, but exposure reduction action plans are being implemented so that this level can be met in a few years.

## Workshop Recommendations

***Priority research needs.***

- Candidate agents: Most research has been focused on specific gases, organic dust, or on bioaerosols containing endotoxins. Occupational studies indicate that exposures occur to other agents, such as antibiotics and disinfectants, and that these agents may be related to increased risks for respiratory disease.
- Odor: There is a need to investigate in greater detail psychophysiologic responses related to malodor exposures in people living in proximity to swine CAFOs, exploring different potential mechanisms. The influence of factors such as mood and coping styles on perceived responses to odors and physiologic responses has been minimally investigated in relation to CAFO exposures.
- CAFO mixed exposures: CAFO exposures involve, by definition, exposure to complex mixtures. These include pulmonary irritants, inflammatory agents, odoriferous compounds, allergens, and antibiotics. Problems of the interaction in mixtures need to be addressed.
- Environmental particulate matter exposures: Studies of particulate-matter exposure in rural areas are needed because of the huge gap in knowledge. Exposure mechanisms for particulates are expected to be different than those for gases because particulates from CAFOs are biologically active and are known to be relatively large. Therefore, sedimentation out of the air is expected to be considerable at short distances. Resuspension in the air, walk-in, and take-home exposures are important candidate mechanisms of transfer leading to exposure indoors. Finally, exposures arising from the handling and distribution of manure to the fields as primary aerosol and secondary re-suspension need to be addressed.
- Analytical techniques: International harmonization of methods for bioaerosol exposure assessment is needed. In the case of harmonization of endotoxin assay, the United States should give serious consideration to adoption of the existing European Committee for Standardization protocol.
- Susceptibility and genetics: Only scarce information is available for evaluating the susceptibility of groups to the effects of organic dust exposure. The candidate genes responsible for changes in the reactions to specific agents have been only sporadically investigated.
- Susceptibility and gender: Recent studies from Canada suggest that women are more prone than men to develop asthma from

working in CAFOs. This points to the need for renewed investigations regarding gender effects in workers exposed to high concentrations of organic dust.

- Outcome assessment: There is a need to collect information regarding respiratory health in people living in proximity to CAFOs. Respiratory symptom status and lung function should be measured, as has been done in confinement workers in the last decades. Information on sensitization rates to common allergens and presence of allergic responses is crucial, as clear differences exist with nonrural populations and within rural populations, depending on early childhood exposure to animals. Recent developments in outcome assessment include more sensitive markers of inflammation, for example, IL-1β, IL-8, TNFα, C-reactive protein, and new sources to be studied by noninvasive approaches such as tear fluid, nasal lavage, exhaled breath condensate, and whole blood. These markers can elucidate the nature of the inflammatory response and facilitate a more detailed interpretation of the available information.
- Design: Panel studies have been shown to be powerful tools in air pollution research and should be pursued in studies of communities exposed to organic dust and CAFO emissions. They enroll sensitive individuals as a starting point and consider exacerbations of disease over time as the end point of interest. Exposure assessment in these studies requires combinations of exposure modeling, use of time-activity patterns and personal exposure assessment to calibrate the modelling. Alternatively, large-scale studies using hospital admission data in combination with spatial analysis to map the patients' homes and schools to CAFOs may be a cost effective and useful additional approach.

***Translation of science to policy.***

- Surveillance studies of workers in agricultural industries and panel studies in communities are warranted.
- The livestock industry should promote good housekeeping practices locally and worldwide and develop hygienic strategies to reduce exposure in the workplace and emissions to the general environment. Occupational health and hygiene expertise is scarce in these industries and should be improved. The cost effectiveness of various technological solutions should be established.
- Exposure standards should be promulgated for some key agents, including endotoxin, and where they exist, exposure levels should be maintained below the current standards. International guidelines for occupational and community health are needed for specific toxicants.

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