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NIOSH Comments to EPA

COMMENTS OF THE
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ON
THE ENVIRONMENTAL PROTECTION AGENCY'S
REQUEST FOR COMMENT
ON REGULATORY APPROACH OF BIOTECHNOLOGY

Docket Control No. OPTS-00049C

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

5/15/89

The National Institute for Occupational Safety and Health (NIOSH) offers the following comments in response to the issues raised by the Environmental Protection Agency (EPA) concerning the direction of its program under the Toxic Substances Control Act (TSCA) for regulation of biotechnology products [54 FR 7027].

Under the Occupational Safety and Health Act of 1970, NIOSH has been given a number of responsibilities including the identification of occupational safety and health hazards, evaluation of these hazards, and recommendation of standards to regulatory agencies to control the hazards. One of the methods by which NIOSH meets these mandates is to evaluate existing or new technologies to determine if there are any occupational safety or health hazards associated with the technologies. Particular attention is directed to new or existing technologies that have high growth potential, such as biotechnology.

To date, NIOSH has conducted a number of studies and developed several reports in the field of biotechnology that EPA may find relevant for developing regulations for microorganisms under TSCA. These reports are:

1. NIOSH Perspective on Commercial Recombinant DNA/Biotechnology Development [Pauker 1981]

2. Medical Surveillance of Biotechnology Workers: Report of the CDC/NIOSH Ad Hoc Working Group on Medical Surveillance For Industrial Applications of Recombinant DNA [Landrigan et al. 1982]

3. The Biotechnology Industry [Landrigan et al. 1983]

4. Industrial Hygiene Characterization of Commercial Applications of Genetic Engineering and Biotechnology [Elliott et al. 1983]

5. Perspectives on Opportunities Toward a Hazard Free Bio-processing Environment [Elliott et al. 1987]

6. Gypsy Moth Control Project [Health Hazard Evaluation Report No. 85-309-1739]

7. Occupational Biohazards: A Review [Dutkiewicz et al. 1988]

8. Control Technology Assessment of Enzyme Fermentation Processes [Martinez et al. 1988]

9. Quantification of Airborne Endotoxin Levels in Various Occupational Environments [Olenchock 1988]

10. An Exposure Characterization of a Large Scale Application of a Biological Insecticide, Bacillus Thuringiensis [Elliott et al. 1988]

This overview primarily concerns workers who may be exposed to microorganisms during environmental release; however, it should also be noted that workers may also be exposed prior to this phase. For example, microorganisms prepared for release in the environment will be grown utilizing fermentation techniques, and the potential for worker exposure during this phase also exists. In addition, workers may be exposed during the research and development phase where microorganisms are isolated from nature or developed using genetic engineering techniques. Although the types of hazards (i.e., pathogenicity, toxicity, and allergic reactions) probably are the same as those discussed below for environmental release, the risk and potential for exposure will vary from phase to phase.

Risk to Workers During Environmental Release

In the case of chemicals, hazard identification is based on observed endpoints such as undesirable acute or chronic effects. However, when considering the potential negative health effects to workers exposed during environmental release of microorganisms, the endpoints are not always that clear. In general, the potential occupational hazards related to environmental release of microorganisms can be divided into three categories based on the following criteria: (1) the pathogenicity of the microorganisms, (2) the potential sensitizing effect of the microorganisms or their cellular components and by-products, and (3) the toxic effects of any constituents that may be contained in the final formulated product that is dispersed such as endotoxins, stabilizing agents, or dispersing agents [Lisella and Herring 1988; Manufacturing Chemist 1986; Elliott et al. 1986; Dutkiewicz et al. 1988].

It is not anticipated that microorganisms that are known to be pathogenic to humans will be used to develop products for environmental release. However, the potential for microorganisms, especially genetically altered organisms, to cause disease should be examined before environmental release when workers may be exposed. Also, there are other endpoints that should be examined, such as immune diseases including hypersensitivity pneumonitis and asthma which result from individual immunologic sensitization to microorganisms, their cellular components, or metabolic products. In addition, the toxic properties that may be associated with components of the final formulated product, such as endotoxins, should be examined.

NIOSH recommends that workers who may be exposed to microorganisms during environmental release receive preemployment and periodic follow-up medical examinations. The basis for this recommendation is discussed in detail in the enclosed publication by Landrigan et al. on the Medical Surveillance of Biotechnology Workers: Report of the CDC/NIOSH Ad Hoc Working Group on Medical Surveillance for Industrial Applications of Recombinant DNA. In brief, the primary purpose of these examinations is to identify conditions which may place a worker at heightened risk of work-related illness. Fitness for employment must be established on an individual basis for each underlying medical condition.

Potential for Worker Exposure

The potential exposure of workers to microorganisms or formulations developed for environmental release will depend upon a number of factors. These factors include (1) the mechanisms used for delivery of the microorganisms, such as the use of hand sprayers or airplanes, (2) the composition of the final product (e.g., liquid, granule, or powder) and whether or not it must be mixed prior to application, (3) the size of the area to be treated as well as the intended use of the microorganisms, (4) the capability of the microorganisms to survive and multiply in the environment, and (5) the quantity of microorganisms released.

The greatest potential for exposure to large numbers of microorganisms appears to be during application of the product. Exposure will vary with the application method, composition of the formulated product, and use of the product. Microorganisms that are used as pesticides will be released into the soil or onto plant surfaces while those used for pollution control will be released into sewage and water [Johnson and Robinson 1984] or contaminated soil [Ghosal et al. 1986]. Microorganisms used for oil or metal recovery will be released into ore or oil fields [Moses and Springham 1982; Curtis 1983]. Once the microorganisms have been released, workers may still be exposed. For example, in agriculture, farmers and transporters of treated products may be exposed. The amount of exposure in this case will depend primarily on the ability of the microorganisms to survive and multiply following release.

RESPONSE TO SPECIFIC QUESTIONS IN NOTICE

1. **What should be the scope of the microorganisms subject to EPA's review?**

Exposure to microorganisms developed for release into the environment and their related toxins or antigens may result in an adverse health outcome for workers, including those involved in research, production,

application, and end-users, such as farmers. The potential detrimental exposures can occur with natural, as well as genitically manipulated, microorganisms. Therefore, NIOSH does not differentiate between the risks associated with naturally-occurring microorganisms, genetically selected or altered organisms, and inter-genetic organisms. Also, because of the potential differences in the phenotype of different strains of a microorganism, each strain should undergo risk evaluation.

From an occupational health standpoint, NIOSH recommends that all microorganisms should be evaluated by EPA for possible health effects prior to the potential exposure of workers. Also, additional risk analysis should be conducted if there is a change in the composition of the final formulated product, or if there is an alteration made in the genotype of the microorganism from that previously evaluated.

2. **What should be the scope of EPA's review of R&D activities involving release of microorganisms into the environment?**

NIOSH recommends that EPA maintain involvement in the approval, release, and subsequent monitoring of microorganisms which result from research and development activities.

3. **Since TSCA only allows EPA to review those microorganisms developed for "commercial purposes", how broadly or narrowly should EPA define "commercial purposes" in the context of research conducted at educational and research facilities?**

Researchers, technicians, and support staff may be exposed to levels of microorganisms and their toxins that could produce an adverse health response. Therefore, NIOSH recommends that EPA broadly interpret the term "commercial purposes" in order to provide regulatory oversight at educational and research facilities.

4. **If the definitions of "release to the environment" and "contained facility" are to be used to determine whether there is EPA review of specific uses of microorganisms, how should these terms be defined? To what extent should EPA rely on the definition of "contained facility" found in the guidelines of the National Institutes of Health (NIH)?**

The NIH guidelines represent a widely accepted benchmark for containment and NIOSH recommends that the definition be adopted by EPA. However, the following should also be noted:

   a. All microorganisms should be evaluated for potential occupational risk prior to large scale growth of the microorganisms. If there is a risk associated with a particular microorganism, it should be identified as early as possible in the development process. Also, by identifying the risks as early as possible, there may be

a considerable savings in investments of time and money if a microorganism is found unsuitable for environmental release.

b. Fermentation systems should be evaluated by EPA to ensure compliance with the guidelines even if the systems are "contained."

5. **To what extent should EPA establish independent expert review groups (i.e., Environmental Biosafety Committees [EBCs]), similar to the NIH Institutional Biosafety Committees (IBCs) , to assist in the review of potential environmental releases of microorganisms? What should be the scope of review by those groups?**

NIOSH commends EPA in its attempt to provide public input into the review process. However, the concept, as presented by EPA in the December 2, 1988, draft proposal to regulate products of biotechnology, to develop Environmental Biosafety Committees (EBCs) gives the appearance that EPA is delegating its regulatory responsibilities to the EBCs. Therefore, NIOSH recommends that EPA alter its proposal to ensure that accountability and oversight are maintained by EPA and that institutional, geographic, and public interests are properly addressed.

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16. Abstract (Limit: 200 words) This testimony concerned the work of (NIOSH) in the field of biotechnology that the Environmental Protection Agency may find useful in developing regulations for microorganisms under the Toxic Substances Control Act. The NIOSH activities mentioned included: perspectives on commercial recombinant DNA/biotechnology development, medical surveillance of biotechnology workers, the biotechnology industry, industrial hygiene characterization of commercial applications of genetic engineering and biotechnology, perspectives on opportunities toward a hazard free bioprocessing environment, gypsy-moth control project, occupational biohazards, control technology assessment of enzyme fermentation processes, quantification of airborne endotoxin levels in various occupational environments, and an exposure characterization of a large scale application of a biological insecticide, Bacillus-thuringiensis. This overview concerned the risks to workers during environmental release and indicated that the potential exposure of workers is related to such factors as the mechanisms used for delivery of the microorganisms, the composition of the final product, the size of the area to be treated, the ability of the microorganisms to survive and multiply in the environment, and the quantity of microorganisms released.

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