February 6, 2003

Minh Thomas
Select Agents Program
Centers for Disease Control and Prevention
1600 Clinton Road, E-79
Atlanta, Georgia 30333

Dear Ms. Thomas:

The University of Wisconsin-Madison is committed to national efforts to restrict access to research materials included on the CDC Select Agent list, the USDA list of High Consequence Livestock Pathogens or Toxins and the APHIS plant pathogen list to individuals having legitimate research needs. In considering the national interest it is also important to note that research conducted by university faculty, staff and students using these materials will ultimately aid in the war on terrorism by contributing to advances in the detection, tracking, diagnosis and treatment of the harmful effects that might result from exposure to these agents. Hence, the regulatory process must be attentive to the benefits of legitimate research efforts as well as the risks associated with research access to select agents and toxins. We offer the following comments on the provisions of 42 CFR Part 73, 7 CFR Part 31 and 9 CFR Part 121 in the interest of defining an appropriate balance between the need to restrict the availability of research materials that may be subverted for purposes of acts of bioterrorism and the benefits to be realized from the application of these same materials in legitimate research settings.

In defining this critical fulcrum point we are guided by the following perspectives:

- Cutting edge research conducted at American universities contributes significantly to the health and well-being of U.S. citizens, fuels the nation's economic growth and will provide the fundamental science and technology required to develop and deploy effective bioterrorism counter-measures;
- Research conducted at American universities may involve the use of materials which can be subverted for use as weapons;
- Enhanced control of such materials is responsible, desirable and feasible;
- Potential for restrictions should be commensurate with risks posed;
- Universities should take a leadership role in efforts to inventory and control material with potential for use in terrorist attacks, reducing existing inventories where possible and restricting access where appropriate.

In general, our comments refer to specific sections of 42 CFR 73. However, considering the compatibility of the majority of provisions in 42 CFR 73, 7 CFR 31 and 9 CFR 121 our comments to 42 CFR 73 are intended to equally apply to the corresponding sections of 7 CFR 31 and 9 CFR 121. In addition, a recommendation to exclude *Ralstonia solancacerum* race3, biovar2 from the APHIS plant pathogen list enumerated at 7 CFR 331.2(a) is provided at the conclusion of our comments to 42 CFR 73. Our comments are offered in this format with the

understanding that comments will be shared between the CDC and APHIS personnel.

GENERAL COMMENTS:

Consistency among the related rules. We are extremely grateful to the rule makers for the high degree of consistency among the Interim Final Rules promulgated by CDC and APHIS. Nevertheless, some troublesome differences exist (detailed in individual sections below). Our ability to comply with the regulations would be enhanced and associated costs reduced if uniformity among the regulations were improved by addressing residual differences.

Costs and federal cost sharing. The cost estimates for compliance with the regulations are grossly understated. Our estimates suggest that one-time costs to retrofit existing facilities to satisfy the regulations will easily exceed a million dollars and recurring annual costs could top $100,000. We support the Council on Governmental Relations' recommendation that select agent infrastructure grants be made available to assist universities with the added expenses associated with implementing the regulations.

Lack of detail about the process and information required for DOJ review and approval of personnel. With the deadline for submission of information for approval of the Responsible Official looming and the submission date for individuals not far behind, it is extremely disappointing that the Interim Final Rules fail to provide any details about the scope or nature of the approval process. Even more frustrating is the fact that nearly two months after publication of the Interim Final Rules the Department of Justice has still not issued any specific information or guidance. Disclosure of personal information is a sensitive issue that can be expected to evoke considerable anxiety among university personnel subject to the regulations. The most effective means to alleviate these concerns is to fully inform individuals subject to the regulations of the personal information that will be required and how that information will be handled.

COMMENTS ON SPECIFIC SECTIONS:

§73.0 Applicability:

We appreciate the fact that the Interim Final Rules provides for phase-in periods for certain requirements that allow entities to comply with the regulations without disrupting on-going research programs. However, effective implementation dates for APHIS and CDC regulations differ. Furthermore even within the individual Interim Final Rules some deadlines and filing requirements generate confusion. For example, §73.7 indicates that the minimum information that will be required at the time of entity registration will include identification numbers assigned by the Attorney General for compliance with §73.8. The deadline for submission of registration material (§73.7) is March 12, 2003, but the anticipated completion date for DOJ review of the RO and entity (§73.8) is April 12, 2003. Similarly confusing is the requirement in §73.7 to provide details addressing safety (§73.10), security (§73.11), emergency response plans (§73.12), and training (§73.13) as part of the registration process even though the deadline for compliance with some of those provisions is much later in calendar year 2003.

We recommend that both the APHIS and CDC regulations share an effective date of February 11, 2003. In addition to making the effective dates consistent, this modification would make implementation of the regulations coincide with, rather than precede, the conclusion of the published deadline for comments and would provide the full 60 day period between promulgation (December 13, 2002) and implementation (February 12, 2003).

We also recommend that CDC and APHIS establish consistent effective dates for all sections in the Final Rules and provide clarification as to what material (e.g. identification numbers) is expected in the original registration application.

§73.1 Definitions:

"Responsible Official"

The definition of "Responsible Official" provided in the proposed APHIS Interim Final Rules ("The individual designated by an entity to act on its behalf. This individual must have the authority and control to ensure compliance with the regulations in this Part." 7 CFR 331.1) clearly describes the scope and nature of the authority of the Responsible Official. **We recommend that this definition be included in 42 CFR 73.1.**

"Access"

Much of 42 CFR 73 seeks to restrict "access" to select agents. However, the term is not defined in the proposed language, and is in fact used to describe two distinct situations: 1) access to select agents and toxins by individuals who are authorized to handle and use them and 2) approved entry to an area where select agents and toxins are present by individuals who are not authorized to handle or use select agents and toxins. **We recommend inclusion of a definition of "access" in 42 CFR 73.1. Furthermore, we support use of the definition proposed by the Howard Hughes Medical Institute: "The ability to gain physical control of select agents and toxins."** "Access" would therefore apply to those individuals who are authorized to handle and use select agents and toxins. "Entry" (rather than "access") would refer to admission of unapproved individuals into an area where select agents and toxins are present.

§73.7 Registration:

§73.7(b)(2)(viii)

We recommend elimination of §73.7(b)(2)(viii) as this provision is redundant. The need for further inquiry or inspection is adequately addressed in the last sentence of §73.7(e).

§73.7(f)

Specification of the covered location needs clarification. Currently the proposed language states that registration will cover activities at only one general physical location, further defined as a building or complex of buildings at a single mailing address. As such, individual universities

might be expected to complete and submit multiple registrations since research activity involving covered agents or toxins may be distributed across campus even though administrative responsibility for all is administered centrally. **We recommend that for purposes of registration the entity be defined as "a single administrative organization under a single Responsible Official."**

§73.7(g)

§73.7(g) sets a 3 year expiration time for the entity certificate, while §73.8(f) sets a 5 year expiration on the security risk assessment. **We recommend that the certificate of registration also be valid for 5 years to simplify paperwork logistics for the entity.**

<u>§73.8 Security Risk Assessment:</u>

§73.8(c) stipulates that an entity must "submit to the Attorney General the information requested for the entity, the Responsible Official, any individual who owns of controls the entity, and any other individuals required to obtain approval under this section." §73.8(d) further states "The Attorney General will conduct a security assessment on entities and individuals whose identifying information is properly submitted." Unfortunately neither the "information requested" nor the process for "properly" submitting the information have been provided, even two months after issuance of the proposed Interim Final Rules. We would like to have had an opportunity to comment on those aspects of the Interim Final Rules as well, but considering the implementation timetable outlined in the document it is hard to imagine that such a review will be possible.

Submission of personal information and criminal backgrounds checks of university personnel represents one of the larger challenges facing universities attempting to comply with the proposed rules.

We recommend that the Attorney General's Office provide:

- **a description of the information that must be submitted for assessment of individuals (§73.8(c));**
- **a description of the process that will be employed to assess an individual's eligibility for access to select agents and toxins (§73.8(d)); and**
- **a description of a process by which an individual or the registered entity can appeal a decision to deny access (§ 73.8(e)).**

<u>§73.9 Responsible Official:</u>

§73.9(b)

§73.9(b) implies that only the Responsible Official (RO) or Alternate Responsible Official (ARO) may perform the actions detailed in §73.9(c). It would be impractical, even inappropriate, to require these officials to participate, for example, in the mechanical aspects of transferring a select agent/toxin or to perform data entry to maintain records. **We recommend the following addition to §73.9(b): "This does not preclude the assignment of activities in §73.9(c)(1) -**

§73.9(c)(7) to other individuals, provided the activities are performed or supervised by a person approved under §73.8 and the results are reviewed and approved by the RO or the ARO acting in the absence of the RO."

Similarly, per §73.15, the Responsible Official is expected to maintain complete records relating to activities covered by this Part. Rather than requiring the RO to maintain records, or to "provide appropriate training in safety" (§73.13(c)), or to fulfill any other specific functional requirements stipulated in other sections of the rule, it would be best to alter the language to stipulate that the RO will be responsible for ensuring that the various obligations stipulated in the regulations are satisfied. Assignment of responsibility for ensuring compliance rather than performance of specific functions would be more compatible with the administrative organization and operations of large research universities. This principle is incorporated in 7 CFR 331 and 9 CFR 121, each of which defines the RO in terms of having "the authority and control *to ensure compliance* with the regulations…" rather than in terms of having the responsibility for performing required functions.

We recommend adoption of the definition of RO proposed above (see §73.1 Definitions) and revision of the language throughout 42 CFR 73 to reflect the change in emphasis from responsibility for performance to responsibility for ensuring compliance.

§73.10 Safety:

We are grateful that the Interim Final Rule provides for performance-based programs for handling and containing select agents and toxins. This approach is appropriate because the Interim Final Rules direct entities to institute programs consistent with the guidance provided in Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines). These publications are recognized as authoritative codes of practice that reflect the best judgment of experienced and knowledgeable scientists, clinical microbiologists, and health and safety professionals on how to protect the safety of laboratory workers and the public health. They are updated regularly to reflect changes in science, technology and best laboratory practices. Incorporating these guidelines as prescriptive requirements in the Final Rule would compromise their value and intent and weaken the concept of a code of practice embraced by scientists, and health and safety professionals. Furthermore, the guidelines would soon lose current relevance because revisions would require rulemaking, which is a time-consuming and costly process.

We therefore join the Howard Hughes Medical Institute in recommending that the HHS Secretary not incorporate the Biosafety in Microbiological and Biomedical Laboratories and the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) as requirements in the Final Rule. We recommend that the Final Rule recognize these guidelines as authoritative codes of practice that entities should consider in developing and implementing a performance-based safety plan for the safe possession and use of select agents.

§73.10(d)

We recommend that prior to listing new experiments in §73.10(d) the CDC seek broad scientific review and guidance.

§73.11 Security:

The requirement to "develop and implement a security plan" based on "a systematic approach in which threats are defined, vulnerabilities are examined, and risks associated with those vulnerabilities are mitigated with a security systems approach" is a reasonable expectation considering the nature of some of the agents and toxins that will covered by the Final Rules. This language, abstracted from §73.11(a), implies that registered entities will be afforded some degree of flexibility in devising security systems that recognize differences in the risks involved with differing agents and that they will be permitted to exercise professional judgment in developing security plans tailored to the specifics of individual laboratory situations or the needs of collaborative research operations. Such a performance-based approach to security is much appreciated. However, many of the specific expectations noted in §73.11(b)-(f) appear to be inconsistent with this preferred strategy, amounting in some cases to prescriptive implementation of uniform security measures regardless of risks posed. **We recommend that the Final Rules allow individual entities to implement security measures that take into account specific risks and unique features of individual laboratory situations as stated in §73.11(a).**

We further recommend that the operational definition of "area" as used in §73.11(b),(d),(e) and other sections of the rules be left to the judgment of registered entities. In our opinion this latitude will actually enhance the security that can be provided while preserving maximal research productivity.

§73.11(d)(2) should be revised to allow persons not approved under §73.8 to enter an area where select agents or toxins are stored without escort provided that 1) all select agents and toxins have been secured in locked cabinets, rooms or other containers, 2) the containers cannot be forced open without tools and without visible signs of damage; 3) rooms are secure against entry by unauthorized personnel; 4) keys, combinations, etc. are controlled as presently required; and 5) entry to the area is limited to employees of the entity.

This approach to security is consistent with requirements for handling classified documents under which persons without clearance may enter rooms without escort provided the documents are secured in cabinets (see for example 10CFR95.25). It will also reduce the burden on the Attorney General's office, allowing it to perform more extensive checks on a smaller number of individuals.

§73.11(d)(3) requires select agents and toxins to be in direct view at all times. The requirement is unnecessarily stringent and is not feasible in many laboratories because of alcoves or intermediate partitions. **We recommend that §73.11(d)(3) be revised to require that materials be under *direct control*, but not necessarily in direct view. Direct control should mean that an unauthorized person cannot approach the select agent or toxin without coming into the view of approved staff.**

Many laboratories at major research universities serve multiple purposes and are used by multiple users. Furthermore, many expensive items of equipment are shared among research groups. Revision of §73.11(d)(2) and §73.11(d)(3) as proposed above would allow localized secure storage and constant *control* of target agents and toxins when in use as alternatives to indiscriminate "area" control. These changes will also reduce the need for expensive renovations that would otherwise be required to bring many facilities into compliance with the proposed rules.

§73.11(d)(4) is at once ambiguous and impractical. For example, will it be necessary to have all supply packages delivered from commercial venders opened and searched before they are allowed to enter restricted areas? Does the "package" inspection expectation extend to searches of briefcases, backpacks or purses whenever anyone enters or exits an area? If this provision is intended to apply only to packages in which select agents or toxins are shipped or received the provisions of the EA101 Select Agent Transfer requirement should suffice.

We recommend that this section be clarified or eliminated from the final rules.

Finally, **we recommend that §73.11(f) be made consistent with §73.7(h) by requiring prior notification before destruction of select agents or toxins that may be of interest to others, constitute valuable collections or which represent important archival material.**

<u>§73.13 Training:</u>

§73.13 (a)

We support the revision to this section as recommended by the Howard Hughes Medical Institute. Specifically, **we recommend revising this provision in its entirety to read, "An entity required to register under this Part must provide information and training on safety and security for working with select agents and toxins to each individual approved for access under § 73.8 and each unapproved individual working in or visiting areas where select agents and toxins are handled or stored. An entity may modify the training according to the needs of the individual, the work they will do and their potential exposure. The training need not duplicate training provided under the OSHA Bloodborne Pathogen Standard 29 CFR Part 1910, §1910.1030."**

COMMENT ON 7 CFR 331.3 LIST OF BIOLOGICAL AGENTS AND TOXINS:

The following comment questions the inclusion of *Ralstonia solanacearum* race 3 (Rs race 3), biovar 2 on the APHIS list of plant pathogens.

The scientific data on Rs race 3, biovar 2 and the disease that it causes indicate that it does not "have the potential to pose a severe threat to plant health or plant products" in the context of U.S. agriculture. Rs race 3, biovar 2 is an important pathogen of potatoes in the tropics and semi-tropics, but has never caused an economically serious level of disease in a cold-temperate climate. Specifically:

- The temperature requirement of Rs race 3, biovar 2 does not correspond with the climate characteristics of the major U.S. potato growing regions (Maine, Wisconsin, Minnesota, North Dakota, Idaho). Rs race 3, biovar 2 is intolerant of freezing and does not generally survive winters in regions with sustained temperatures below 20 F. Thus, the bacterium is unlikely to become established in the northern U.S. where potatoes are commercially grown.
- Even if it does become established, Rs race 3, biovar 2 is unlikely to cause an economically damaging disease outbreak in climatic conditions characteristic of North America. This race was recently introduced into Europe. Evidence indicates that the bacterium was present in potato fields in the Netherlands as early as 1988, but only during an unusually hot summer in 1995 were a few symptomatic potatoes observed. Since then, symptoms have been very rarely observed despite the presence of the bacterium in latently infected potatoes, soil, and waterways.
- This bacterium has been repeatedly introduced into the United States without impact. Over the past 20 years, researchers have documented the repeated introduction of Rs race 3, biovar 2 into the United States on ornamental plants from Central America. However, to our knowledge no case of potato brown rot caused by Rs race 3 biovar 2 has ever occurred in the U.S. or Canada.
- RS race 3, biovar 2 is a serious pathogen of potatoes in the developing world. Vigorous research on this pathogen is therefore vitally important for global food security. The restrictions that would be imposed by the proposed new regulations should Rs race 3 remain on the list of restricted plant pathogens will pose an inappropriate constraint on research progress.

We recommend that *Ralstonia solanacearum* race 3, biovar 2 be removed from the APHIS list of plant pathogens.

We thank you for the opportunity to comment on the Interim Final Rules and hope that the recommendations we have offered will assist CDC and APHIS in crafting balanced Final Rules that will ensure the protection of the public from potential harm that could result from misuse of research material without needlessly impeding the benefits that are sure to accrue from research conducted by responsible university faculty, staff and students.

Sincerely,

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