

Select Agent Restricted Experiments: Authorizations and Regulatory Compliance

Institutional Biosafety Committees: Promoting Optimal
Practice Now and in the Future

Robbin S. Weyant, PhD, Director
Division of Select Agents & Toxins
Coordinating Office for Terrorism Preparedness and Emergency
Response



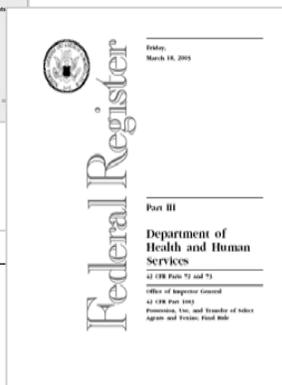
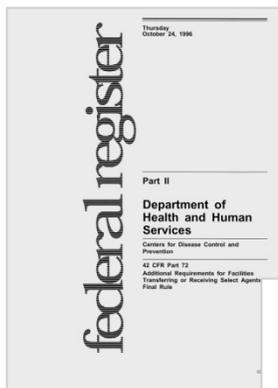
Select Agent Program Legislative Mandates

- **Antiterrorism and Effective Death Penalty Act of 1996 (Signed April 24, 1996)**

- **Public Health Security and Bioterrorism Preparedness and Response Act 2002, Title II (Signed June 12, 2002)**



Current Select Agent Regulations



- Interim Final Rule: “Possession Use, and Transfer of Select Agents and Toxins” (42 C.F.R. 73, 9 C.F.R. 121, and 7 C.F.R. 331)
 - Effective February 7, 2003
- Final Rule: “Possession, Use, and Transfer of Select Agents and Toxins” (42 C.F.R. 73, 9 C.F.R. 121, and 7 C.F.R. 331)
 - Effective April 18, 2005
- Interim Final Rule: “Reconstructed Replication Competent Forms of the 1918 Pandemic Influenza Virus Containing Any Portion of the Coding Regions of All Eight Gene Segments” (42 C.F.R. 73)
 - Effective October 20, 2005



42 CFR Part 73.13: Restricted Experiments

- Prior approval from HHS Secretary for restricted experiments with HHS SAs.
- Prior approval from APHIS Administrator for restricted experiments with USDA SAs.
- Prior approval from HHS Secretary after consultation with APHIS Administrator for Overlap SAs



Restricted Experiment Definition from 42 CFR Part 73.13(b)(2)

- “Experiments Involving the deliberate formation of recombinant DNA containing genes for the biosynthesis of select toxins lethal for vertebrates at an LD(50) of <100 ng/Kg body weight”



Restricted Experiment Definition from 42 CFR Part 73.13(b)(1)

- “Experiments utilizing recombinant DNA that involve the deliberate transfer of a drug resistance trait to select agents that are not known to acquire the trait naturally, if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture.”



Select Agent Program Guidance Regarding Experiments Using Antibiotic Resistance Markers...

- **Obtain Select Agent Program Pre-Approval**



How Do I Obtain Approval to Perform a Restricted Experiment?

- Have a valid registration with CDC or APHIS for the possession of the SA of interest
- Have your RO contact your CDC or APHIS liaison with a written request for authorization



Information Required in Authorization Requests

- Synopsis/Objectives of proposed work
- Description of insert (complete sequence not required)
- Description of cloning/expression vector
- Description of host organism(s) for cloning
- Methods used for selection (including all antibiotic markers)
- Discussion of availability/applicability of non antibiotic resistance markers
- Discussion of the specificity of the antibiotic resistance marker/potential for cross-resistance
- Description of any planned animal work
- Applicable scientific references
- IBC minutes relevant to the project



Intragovernmental Select Agent & Toxin Technical Advisory Committee (ISATTAC)

- Chartered May 2005
- Federal membership, representatives from HHS (CDC,NIH,FDA), USDA (ARS, APHIS, CVB), DOD, DHS.
- Advises national Select Agent Programs on:
 - SA Exclusions
 - Restricted Experiment Approvals
 - Review of Select Agent Lists



ISATTAC Activity Since 2005 on Restricted Experiments

- Reviewed 335 protocols involving antibiotic resistance markers
- Reviewed 40 protocols involving cloning of SA toxin genes
- Requests received from 110 SA entities
- Current turn-around time for a request: 1-2 months



Select Agent Compliance Issues: Restricted Experiments

- Failure of Entity RO to obtain Pre-Approval from Select Agent program
 - Failure of Principal Investigator to inform Entity RO of restricted experiments
 - Failure of lab worker (junior staff member, post-doc, student) to inform Principal Investigator of restricted experiments
- Assumption that local IBC approval is a substitute for Select Agent program approval



Thank you

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