

# National Select Agent Workshop

**Dr. Freeda Isaac**

**Dr. Rob Weyant**

Directors, National Select Agent Program



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# National Select Agent Program Workshop

## Future Directions

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- Inspections
  - More coordination with CDC
  - Inspectors better informed about facility
  - Increased training
- Regular
  - Increased frequency allows more interaction with entity
  - More rigorous evaluation will address issues early
- Compliance
  - Unannounced in order to observe daily operations
  - More security focused

**OVERALL GOAL: Prevention of problems**



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## Future Directions

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- Reauthorization Bill “Select Agent Program and Biosafety Improvement Act of 2008” has been introduced into committee, not final or passed
- Reauthorized through 2013
- National Academy of Sciences review of SAP
  - Affects on international scientific collaboration
  - Affects on scientific advances
- Additional criteria for listing SA
  - Endemic
  - Biological Risk Assessments by DHS
  - Agents genetically modified or created synthetically



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## Future Directions

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- Increased information sharing with states
  - Emergency preparedness
  - Some States have regulations in place to protect release of information
- Guidance on inventories
- Guidance on surge work
- BSL-3 Laboratories capacity and construction
- Biosafety Training for BSL-3/4
- External incident reporting system



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# Synthetic Biology

**Dr. Rob Weyant**

Division of Select Agents and Toxins



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# Synthetic Biology

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*“Synthetic biology is the engineering of biology: the synthesis of complex, biologically based (or inspired) systems which display functions that do not exist in nature. This engineering prospective may be applied at all levels of the heirarchy of biological structures – from individual molecules to whole cells, tissues and organisms. In essence synthetic biology will enable the design of ‘biological systems’ in a rational and systematic way”*

The European Commission 2005



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# Landmarks in Synthetic Biology

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- 1970: First synthetic gene (207 bp)
- 1995: First synthetic plasmid (2700 bp)
- 2002: First synthetic infectious virus (polio, 7400 bp, 1 year to complete)
- 2003: First synthetic bacteriophage (phiX174, 5400 bp, 2 weeks to complete)
- 2008: First synthetic bacterial genome (*M. genitalium*, 582,970 bp)



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# The Promise of Synthetic Biology

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- New vaccines and therapeutics
- Environmental remediation
- Improved agriculture
- New energy sources



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# Synthetic Biology Concerns: the National Science Board for Biosecurity

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- Chartered March 2004
- Federal Advisory Committee including 25 leaders in biology, microbiology, genetics, infectious disease
- Provides advice to HHS Secretary on Issues of Dual Use in research
- December 2006 Report “Addressing Biosecurity Concerns Related to the Synthesis of Select Agents”



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# NSABB Recommendations

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- **HHS/USDA develop harmonized guidance for what is currently regulated**
- USG should assist providers of synthetic nucleic acids in the screening of orders for regulated materials
- USG should repeal 18 U.S.C. 175c (smallpox clause)
- USG should review taxonomic classification of select agents in light of synthetic biology



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# Developing a Harmonized Guidance Document for Synthetic Genomics Providers

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- Joint effort involving CDC and USDA APHIS
- Efforts coordinated through White House NSC Policy Coordination Committee on synthetic biology
- Input solicited from private industry/academic subject matter expert group
- Outreach to Department of Commerce to include interpretation of export regulations



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# Currently Regulated Genetic Elements

(Section 3c of 42 CFR 73, 9 CFR 121, and 7 CFR 331)

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- Nucleic Acids that can produce infectious forms of any of the select agent viruses
- Recombinant nucleic acids that encode for the functional form(s) of select agent toxins if the nucleic acids:
  - Can be expressed *in vivo* or *in vitro* or,
  - Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro*
- Select agents and toxins that have been genetically modified



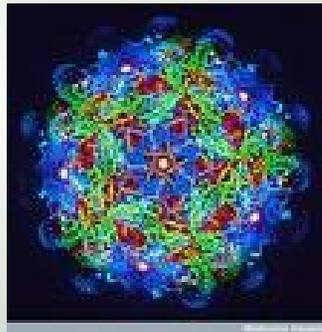
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# Which Select Agents have Regulated Genomes?

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- Single stranded (positive strand) RNA viruses
- Double stranded DNA viruses that utilize host polymerases



# Current Select Agent Viruses with Regulated Genomes

- Tickborne encephalitis complex (flavi) viruses:
  - Central European Tick-borne encephalitis
  - Far Eastern Tickborne encephalitis
  - Russian Spring and Summer encephalitis
  - Kyasanur forest disease virus
  - Omsk Hemorrhagic Fever virus
- Eastern Equine Encephalitis virus
- Venezuelan Equine Encephalitis Virus
- Classical Swine Fever virus
- Foot-And-Mouth Disease virus
- Japanese Encephalitis virus
- Swine Vesicular Disease virus
- Cercopithecine Herpesvirus 1 (Herpes B virus)
- Malignant Catarrhal Fever virus (Alcelaphine Herpesvirus Type 1)



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# Synthetic Genomics: Regulatory Issues

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- Producer screening of sequence orders
- Producer screening of customers
- Reference sequences
- ?Rulemaking?
- ANPR (Advance Notice of Proposed Rulemaking) to be published in the Federal Register in 2009



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# Select Agent List

**Dr. Charles Divan**

Agriculture Select Agent Program



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# USDA

## Plant Select Agents and Toxins List 7 CFR 331.3

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- *Peronosclerospora philippinensis* (*Peronosclerospora sacchari*)\*
- *Phoma glycinicola* (*Pyrenochaeta glycines*)\*
- *Ralstonia solanacearum*, race 3, biovar 2
- *Rathayibacter toxicus*\*
- *Sclerophthora rayssiae* var. *zeae*
- *Synchytrium endobioticum*
- *Xanthomonas oryzae*\*
- *Xylella fastidiosa* (citrus variegated chlorosis strain)
- \* New Addition as of November 17, 2008



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# HHS/USDA

## Over-lap Select Agents and Toxins List 9 CFR 121.4 and 42 CFR 73.4

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- *Bacillus anthracis*
- *Brucella abortus*
- *Brucella melitensis*
- *Brucella suis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus



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# HHS

## Human Select Agent and Toxin List

### 42 CFR 73.3

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- Abrin
- Botulinum neurotoxins\*
- Botulinum producing species of *Clostridium*\*
- Cercopitheceine herpesvirus 1
- *Clostridium perfringens* epsilon toxin\*
- *Coccidioides immitis*\*
- *Coccidioides posadasii*
- Conotoxins
- *Coxiella burnetii*\*
- \* New addition as of November 17, 2008



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# HHS

## Human Select Agent and Toxin List

### 42 CFR 73.3 Cont'd

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- Crimean-Congo haemorrhagic fever virus
- Diacetoxyscirpenol
- Eastern equine encephalitis virus\*
- Ebola virus
- *Francisella tularensis*\*
- Lassa fever virus
- Marburg virus
- Monkeypox virus
- Reconstructed replication competent forms of 1918 pandemic influenza virus containing any portion of the coding regions of all 8 gene segments\*
- \* New addition as of November 17, 2008



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# HHS

## Human Select Agent and Toxin List

### 42 CFR 73.3 Cont'd

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- Ricin
- *Rickettsia prowazekii*
- *Rickettsia rickettsii*
- Saxitoxin
- Shigatoxin\*
- Shiga-like ribosome inactivating proteins
- South American haemorrhagic fever viruses
  - Flexal
  - Guanarito
  - Junin
  - Machupo
  - Sabia
- \*New addition as of November 17, 2008



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# HHS

## Human Select Agent and Toxin List

### 42 CFR 73.3 Cont'd

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- Staphylococcal enterotoxins\*
- T-2 toxin\*
- Tetrodotoxin
- Tick-borne encephalitis complex (flavi) virus
  - Central European tick-borne encephalitis
  - Far Eastern tick-borne encephalitis
  - Kyasanur Forest disease
  - Omsk hemorrhagic fever
  - Russian Spring and Summer encephalitis
- \* New addition as of November 17, 2008



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# HHS

## Human Select Agent and Toxin List 42 CFR 73.3 Cont'd

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- Variola major virus (Smallpox virus)
- Variola minor virus (Alastrim)
- *Yersinia pestis*



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# USDA

## Animal Select Agent and Toxin List

### 9 CFR 121.3

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- African horse sickness virus
- African swine fever virus
- Akabane Virus
- Avian influenza virus (highly pathogenic)
- Bluetongue virus (exotic)
- Bovine spongiform encephalopathy agent (BSE)
- Camel pox virus
- Classic swine fever virus
- *Ehrlichia ruminantium* (Heartwater)
- Foot-and-mouth disease virus
- Goat pox virus
- Japanese encephalitis virus
- Lumpy skin disease virus



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# USDA

## Animal Select Agent and Toxin List 9 CFR 121.3 Cont'd

- Malignant catarrhal fever virus (Alcelaphine herpesvirus type 1)
- Menangle virus
- *Mycoplasma capricolum* subsp. *capripneumoniae* (contagious caprine pleuropneumonia)
- *Mycoplasma mycoides* subsp. *mycoides* (contagious bovine pleuropneumonia)
- *Peste des petits ruminant* virus
- Rinderpest virus
- Sheep pox virus
- Swine vesicular disease virus
- Vesicular stomatitis virus (exotic)
  - Indiana subtypes VSV-IN2, VSV-IN3\*
- Virulent Newcastle disease virus\*
- \* New addition as of November 17, 2008



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Questions?



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