CEEZAD UPDATE
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Kansas State University
To conduct research, develop technology and train a specialized workforce to help DHS to defend US pre-harvest agricultural systems against agro-terrorism and other catastrophic events caused by high-threat foreign, emerging and zoonotic animal pathogens.
Overview

• CEEZAD was established June 2010 as a Center of Excellence by DHS Science and Technology Directorate (S&T) Office of University Programs (OUP)

• Co-leads were established for Center of Excellence for Zoonotic and Animal Disease Defense (ZADD)
  • Texas A&M University – National Center for Foreign and Zoonotic Diseases (FAZD)-established in 2004
  • Kansas State University – Center of Excellence for Emerging and Zoonotic Animal Disease (CEEZAD)-established in 2010

• DHS Funding
  • Total ZADD funding: Approximately $40M in financial assistance funding from DHS OUP (2004-2011)
  • CEEZAD funding from DHS approximately $4M since 2010
CEEZAD Research Partners

- CEEZAD research program has 16 projects (8 DHS & 8 KBA funded)
- CEEZAD project teams include:
  - 9 Universities in the U.S., plus University of Berlin, Germany
  - Government Agencies: USDA/ARS - Arthropod-Borne Animal Disease Research Unit (ABADRU), Manhattan, KS; Center for Medical, Agricultural & Veterinary Entomology, Gainesville, FL; Plum Island Animal Disease Center, NY.
- Industrial Partners: Pfizer, BI Vetmedica, Ceva Biomune, NewLink Genetics, Orion Biosciences Inc., Avimex Animal Health and others...
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<th>Research Area</th>
<th>Approaches</th>
<th>Expected Uses</th>
<th>Customers</th>
<th>COE Partners</th>
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</table>
| **Research Area 1:** Vaccines | • Vaccine platforms:  
  • Modified live Vaccines (RG-based)  
  • Vectored Vaccines  
  • Subunit vaccines  
  • Computational biology guiding vaccine design | ▪ Mitigate and/or prevent FAD/Zoonotic disease outbreaks  
  ▪ RVFV, Influenza, FMDV, Schmallenberg virus  
  ▪ Novel pathogens | ▪ Small businesses  
  ▪ Biologics industry  
  ▪ National Veterinary Stockpile  
  ▪ US Agricultural Systems | • Mount Sinai School of Medicine  
• Kansas State University  
• South Dakota State University  
• University of Texas Medical Branch  
• Bioprotection Systems Corp.  
• Orion Integrated Biosciences, Inc. |
| **Research Area 2:** Detection | • Antibody, antigen and nucleic acid-based tests  
  • MassTag PCR  
  • DIVA Companion tests  
  • Computational biology guiding diagnostics design/Bioinformatics  
  • Whole genome sequence analysis (NGS) | ▪ Detect FAD/Zoonotic disease outbreaks  
  ▪ Pathogen discovery  
  ▪ Unbiased pathogen detection  
  ▪ Microbial forensics | ▪ Veterinary Diagnostic Laboratories  
  ▪ NAHLN  
  ▪ Small businesses  
  ▪ Biologics Industry | • Columbia University  
• Kansas State University  
• Orion Integrated Biosciences, Inc.  
• South Dakota State University  
• Arthropod-Borne Animal Disease Research Unit (USDA) |
| **Research Area 3:** Epidemiology/Modeling | • International Epidemiological Studies  
  • Wildlife Studies  
  • Risk Assessment Models | ▪ Mitigate and Prevent FAD/Zoonotic disease outbreaks  
  ▪ Decision tools/ risk models | ▪ USDA  
  ▪ Business Continuity, Researchers, Planners and Responders | • University of Florida  
• University of Georgia  
• St. Jude’s Children’s Research Hospital  
• University of Washington |
# CEEZAD Education and Outreach Overlay

<table>
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<tr>
<th>Research Area</th>
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| Education / Outreach | ▪ Online Educational Resources related to emerging, foreign and zoonotic diseases  
▪ Increase knowledge of emerging and zoonotic diseases for students studying journalism  
▪ Diagnostic Lab Training  
▪ Fellowship support for DVM or DVM/PhD students | ▪ Formal education, continuing education (web-based), outreach and training                      | ▪ Graduate Students  
▪ Veterinarians  
▪ Medical and Public health professionals | ▪ Kansas State University  
▪ Center of Food Safety and Public Health  
▪ Iowa State University  
▪ 28 US Colleges as a required course or veterinarians that want to be accredited through the National Veterinary Accreditation Program  
▪ National Animal Health Laboratory Network (NAHLN) |
<table>
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<tr>
<th>Accomplishment</th>
<th>Impact</th>
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<tr>
<td>Rift Valley Fever Virus-Like Particles (VLP) as a potential subunit vaccine</td>
<td>Selected prototype subunit vaccine and tested in lab animals. Preparation of final trials in natural host animals and negotiations with industrial partners are in progress to provide US with safe and efficacious RVFV vaccine.</td>
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<td>(proof of concept in ruminants)</td>
<td></td>
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<tr>
<td>Newcastle Disease Virus as mammalian vaccine vector platform</td>
<td>Tested NDV-based influenza vaccine in pigs and shown to be protective against swine influenza. Further studies are planned to evaluate efficacy of NDV-based vectored vaccines in mammals.</td>
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<td>Mass-Tag PCR for Veterinary Use</td>
<td>Allows high through put detection of multiple pathogens in a single sample with simultaneous monitoring of FAD, zoonotic and endemic diseases</td>
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<td>Unbiased Detection of Pathogens in veterinary samples</td>
<td>Characterization by Next Generation Sequencing are done to samples showing unique clinical presentations (novel/emerging/re-emerging/zoonotic disease).</td>
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<td>BSL3-Select Agent Import Permits</td>
<td>Establishment of animal models for FAD/zoonotic diseases: AIV - select agent permit was granted; RVFV – select agent application in final stages of approval</td>
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<td>Web-based educational courses for FAD/Zoonotic disease</td>
<td>The Emerging and Exotic Diseases of Animals Course (EEDA) is part of the curriculum in all 28 US Veterinary Colleges and a mandatory part of the National Veterinary Accreditation Program.</td>
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Rift Valley Fever Vaccine

Family Bunyaviridae, genus Phlebovirus, RNA virus
Vector = mosquitoes
BSL3 Ag
Incubation 2-6 days
Zoonosis
**Case Fatality Ratio 1-20%**
Treatment symptomatic and specific: Red cells, platelets, rehydratation, electrolytic balance, intensive care
On the top of the NVS priority list
In U.S. only experimental vaccine available to humans in limited amount, no vaccine available for agricultural use
Rift Valley Fever distribution and outbreaks

Major Outbreaks

- **Saudi Arabia**: 2000
- **Mauritania**: 1987, 1998-99, 2002
- **Egypt**: 1977-78, 1997-98, 2003
- **Kenya**: 1931…1997-98, 2006-07
- **Somalia**: 1997-98, 2006-07
- **Mozambique**: 1969
- **Namibia**: 1955, 1974-75
- **Sudan**: 1973, 2007
- **Senegal**: 1999, 2002
- **Gambia**: 1999, 2002
- **Yemen**: 2000
- **Tanzania**: 1997-98, 2007

Countries at risk

- **Saudi Arabia**: 2000
- **Mauritania**: 1987, 1998-99, 2002
- **Egypt**: 1977-78, 1997-98, 2003
- **Kenya**: 1931…1997-98, 2006-07
- **Somalia**: 1997-98, 2006-07
- **Mozambique**: 1969
- **Namibia**: 1955, 1974-75
- **Sudan**: 1973, 2007
- **Senegal**: 1999, 2002
- **Gambia**: 1999, 2002
- **Yemen**: 2000
- **Tanzania**: 1997-98, 2007
- **Saudi Arabia**: 2000

Legend:
- ⭐ Major Outbreaks
- Yellow Countries at risk
Development of Efficacious DIVA-Compatible Vaccines for RVFV

**Overall Project Goal:**
Develop efficacious live and subunit vaccines for RVFV and accompanied immunoassays for DIVA

**Key Investigators and Institutions:**

- Juergen Richt, Wenjun Ma, Diagnostic Medicine/Pathobiology, Kansas State University
- Adolfo Garcia-Sastre, Mount Sinai School of Medicine
- Tetsuro Ikegami, Department of Pathology, University of Texas Medical Branch
- Alan Young, Biology and Microbiology, South Dakota State University
- William Wilson, ARS, Arthropod-Borne Animal Disease Research Unit, Manhattan, KS
Project Objectives

Virus Like Particles (VLP) Subunit Vaccine

• Baculovirus-expressed Gn/Gc/N VLP and/or Gn/Gc VLP
• NSs as differentiating antigen for DIVA (Gn/Gc/N VLP)
• N and/or NSs as differentiating antigen for DIVA (Gn/Gc VLP)

NDV-Based Vectored Recombinant RVFV Vaccine

• NDV LaSota as vector to express Gn&Gc of RVFV
• N protein of RVFV (or NDV proteins) for DIVA
Vaccines and Diagnostics for Transboundary Animal Diseases

Sep. 17-19, 2012 in Ames, IA

Sponsor: DHS S&T

Co-Hosts:
CFSPH, Director Jim Roth
CEEZAD, Director Juergen Richt
Participants of the Workshop

More than 180 participants from the U.S. and abroad (Canada, Germany, UK, Holland, South Korea, Nigeria, Australia, Caribbean region), including:

• Government agencies: DHS S&T, USDA-ARS/APHIS, CDC, NIH, CFIA (Canada) ...

• Academia: ISU, KSU, UMN, TAMU, UC Davis ...

• Industry: Elanco, Merial, Ceva Biomune, BI Vetmedica, Merck, Pfizer, IDEXX, Qiagen, NewLink ...
The primary objective of the workshop was to discuss state of the art measures related to vaccine and diagnostic tool development for significant transboundary animal diseases (TADs).

The workshop had four goals:
• Sharing progress on cutting-edge research and providing updates on the current status on vaccines and diagnostics for high priority TADs to help inform the decision making process;
• Presenting information to academic scientists to help them better understand the regulatory process and how to translate research into licensed novel vaccines and diagnostics for TADs;
• Providing the opportunity for government officials from each agency working in this area to convey their roles and responsibilities to a broad audience;
• Bringing together scientists from academia, industry and government in order to stimulate cross-talk.
Major Select Agents

Rift Valley Fever
Highly Pathogenic Avian Influenza
Exotic Newcastle Disease
Foot and Mouth Disease
Nipah and Hendra
African Swine Fever
Classical Swine Fever
Schmallenberg Virus
Q Fever
Heartwater
Ebola
Conclusions and Recommendations

Major Challenges:

• Restrictions on conducting research (incl. production) on BSL3 Ag and BSL4 pathogens and Select Agents
• Validation of field efficacy of vaccines and sensitivity/specificity of diagnostic tests for diseases not present in the US
• Field Application of vaccines/diagnostics
• Concurrent development of DIVA vaccines with diagnostics
• Endemic versus non-endemic situations demands for different vaccines and diagnostics
• Motivation for industry to develop vaccines and diagnostics for diseases with no US market
• Funding to develop and stockpile vaccines and diagnostics for TADs
• Rapid development of vaccines and diagnostics for unknown pathogens which may rapidly emerge in the future
Conclusions and Recommendations

Opportunities:

• Rapid advances in science provide promising avenues for development of novel approaches to vaccine and diagnostic test development (e.g. RVFV, CSF, Henipa, Schmallenberg, etc).

• Presence of transboundary animal diseases in endemic countries provides motivation for development of novel vaccines and diagnostics, the opportunity to evaluate them under field conditions, and potential markets for new products.

• International collaborations between government agencies, NGOs, industry and academia to rapidly develop countermeasures for emerging and transboundary animal diseases

• Concerns regarding global food security and emerging animal and zoonotic diseases have generated interest in international cooperation to address these issues.
Increased Food Supply Demands

**WORLD MEAT AND EGG PRODUCTION 1961 TO 2007**

- **1961**
  - Chicken: 75,826,354 tonnes
  - Egg: 7,555,887 tonnes
  - 14,409,313 tonnes
- **2007**
  - Chicken: 58,961,474 tonnes
  - Egg: 59,851,860 tonnes
  - 27,684,560 tonnes

- **1961**
  - 75,826,354 (tonnes)
  - 7,555,887 (tonnes)
  - 14,409,313 (tonnes)
- **2007**
  - 58,961,474 (tonnes)
  - 59,851,860 (tonnes)
  - 27,684,560 (tonnes)

**99,211,931 (tonnes)**

**24,748,082 (tonnes)**

**Increased Food Animal Production**

Veterinarians must play a major role in finding the balance between the needs for efficient food production, conservation of the environment, and animal welfare.

Source: FAO STAT
Conclusions and Recommendations

Next Steps:

• Prepare draft Gap analysis and recommendations for R&D priorities for vaccines and diagnostics for each disease by summarizing input from presentations and from participant questionnaires (submit to DHS within 30 days);

• Revise draft Gap analysis and recommendations into final consensus report to DHS (within 90 days);

• Edit manuscripts from meeting and submit to IABS for publication in “Developments in Biologicals”. 
Thank you!

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