



EHSO | EXCELLENCE THROUGH
INTEGRITY, COOPERATION AND LEADERSHIP

EMERGING INFECTIOUS DISEASES IN ACADEMIC RESEARCH: BIOSAFETY LESSONS LEARNED FROM WORK WITH ZIKA VIRUS

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OBJECTIVES

1. To establish workflows for reviewing research proposals involving emerging infectious agents, both in vivo and in vitro
2. To identify stakeholders
3. To determine the role of the Biosafety Office in the implementation and maintenance of the Institutional Biosafety guidance

CASES IN THE US

US States

- Locally acquired mosquito-borne cases reported: 59
- Travel-associated cases reported: 3,565
- Laboratory acquired cases reported: 1
- Total: 3,625
 - Sexually transmitted: 30
 - Guillain-Barré syndrome: 12
- Pregnant women with any laboratory evidence of possible ZIKV infection
 - 808 (US States)

US Territories

<http://www.cdc.gov/zika/geo/united-states.html> - September 2016

CASE 1 – IN VITRO-PROPAGATION

1. Procedures

- i. Propagation of the ZIKV
- ii. Testing of potentially infected human samples

2. Personnel

1. Principal investigator had experience handling dengue virus

3. Facilities

- i. BSL3 facility was available to perform work
 - i. Autoclave
 - ii. Anteroom

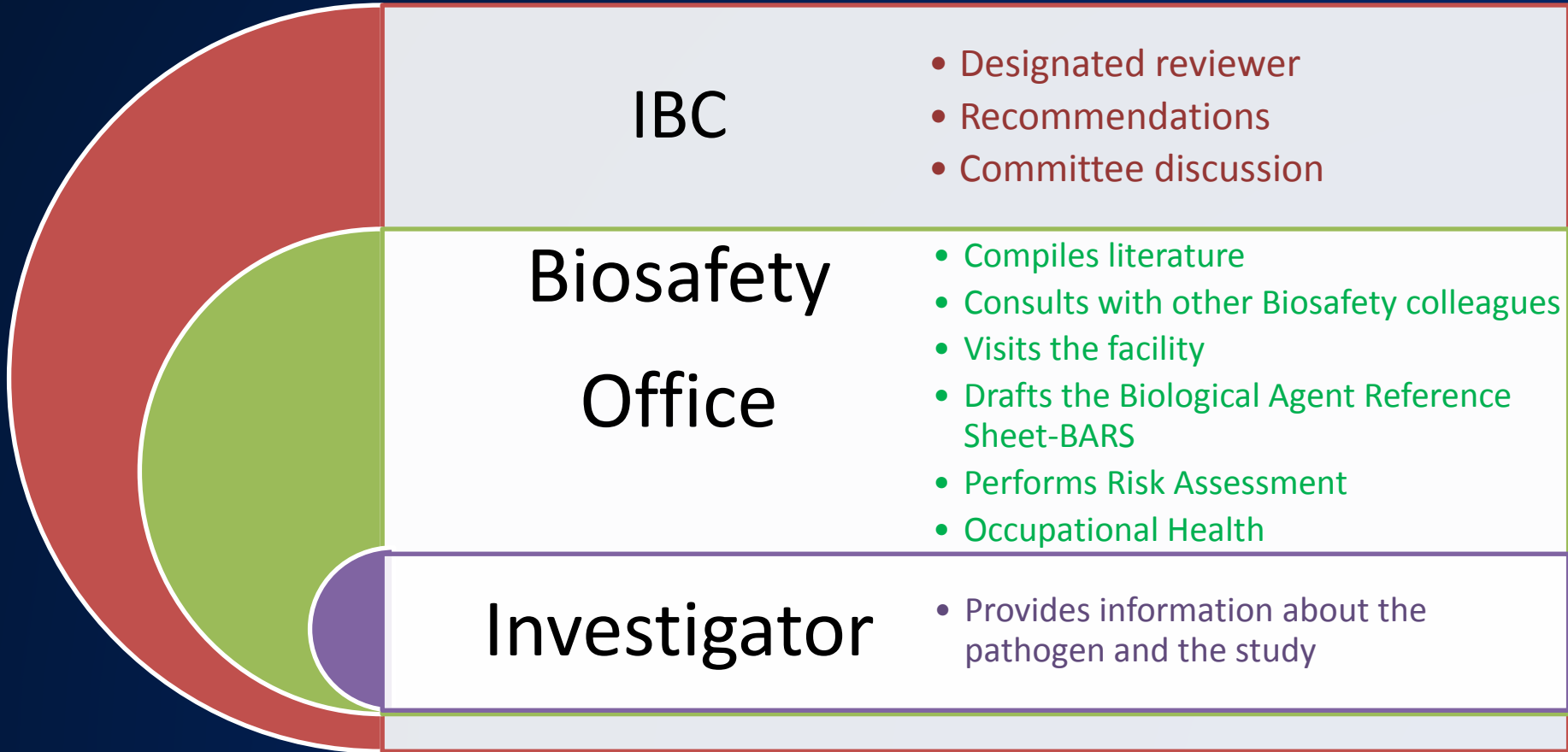
CASE 2 IN VITRO- VACCINE TRIAL

1. Procedures
 - i. Collection of human samples
 - ii. Recombinant vaccine including ZIKV genes
2. Personnel
 1. Principal investigator is a leading expert in vaccine trials
 2. Research nurses and laboratorians are familiar with handling potentially infectious materials
3. Facilities
 - i. BSL2 facility was available to perform work
 - ii. Autoclave was not available

CASE 3 IN VITRO & IN VIVO

1. Procedures
 1. Propagation
 2. Inoculation of large and small animals
2. Personnel
 1. Laboratorians
 2. Animal Care: Veterinarians, Research Resources
 3. Pathology
3. Facilities
 - i. In vitro work: BSL3
 - ii. In vivo work: ABSL2 (NHPs) and ABSL3 (rodents)

EVALUATION



IBC

- Designated reviewer
- Recommendations
- Committee discussion

Biosafety Office

- Compiles literature
- Consults with other Biosafety colleagues
- Visits the facility
- Drafts the Biological Agent Reference Sheet-BARS
- Performs Risk Assessment
- Occupational Health

Investigator

- Provides information about the pathogen and the study

REFERENCE DOCUMENT

<http://www.ehso.emory.edu/content-guidelines/BARS-Zika-Virus.pdf>

BIOLOGICAL AGENT REFERENCE SHEET

Zika Virus (ZIKV)

CHARACTERISTICS			
Morphology	Zika virus (ZIKV) is a single-stranded RNA virus of the Flaviviridae family, genus Flavivirus, Spondweni group. There are two ZIKV lineages: the African lineage and the Asian lineage which has recently emerged in the Pacific and the Americas.		
Growth Conditions	Inoculate intracerebrally into suckling mice. Resuspend 20% sMb (sucking mouse brain) with 7.5% BSA in PBS.		
Sources	-ATCC® VR84 – from MR766 (original strain) -Wild virus isolated from infected human diagnostic samples		
HEALTH HAZARDS			
Host Range	Humans and NHPs, non-pathogenic for hamster, guinea pig or rabbit.		
Modes of Transmission	ZIKV is transmitted by infected <i>Aedes</i> mosquitoes. Perinatal, in utero, sexual and transfusion transmission events have also been reported.		
Signs and Symptoms	About 1 in 5 people infected with ZIKV become ill. The most common symptoms of Zika are fever, rash, joint pain, or conjunctivitis (red eyes). Other common symptoms include muscle pain and headache. The illness is usually mild with symptoms lasting for several days to a week. There may be an association between ZIKV infection in pregnancy and microcephaly of the fetus.		
Infectious Dose	Unknown		
Incubation Period	The incubation period ranges between approximately three to 12 days after the bite of an infected mosquito. Most of the infections remain asymptomatic (between 60 to 80%).		
MEDICAL PRECAUTIONS / TREATMENT			
Prophylaxis	None		
Vaccines	None		
Diagnosis	ZIKV disease diagnostics is primarily based on detection of viral RNA from clinical specimens in acutely ill patients. The viremic period appears to be short, allowing for direct virus detection during the first 3–5 days after the onset of symptoms.		
Treatment	The treatment is symptomatic and mainly based on pain relief, fever reduction and anti-histamines for pruritic rash.		
Surveillance	People infected with ZIKV, chikungunya, or dengue virus should be protected from further mosquito exposure during the first few days of illness to prevent other mosquitoes from becoming infected and reduce the risk of local transmission		
Emory Requirements	Occupational Health Consultation prior to handling ZIKV. Report all incidents.		
LABORATORY HAZARDS			
Laboratory Acquired Infections (LAIs)	Accidental infection has occurred in laboratory personnel		
Sources	Unknown		
SUPPLEMENTAL REFERENCES			
European CDC	http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/factsheet-health-		
	http://www.cdc.gov/zika/prevention/index.html http://www.cdc.gov/biosafety/publications/bmbIS5/bmbIS5_sect_viii_1.pdf		
CDC			
ATTC	http://www.atcc.org/products/all/VR-84.aspx#documentation		
CONTAINMENT			
BSL2+/ABSL2+	Appropriate safety procedures should always be used with this material. See BMBL Section VIII. Biosafety containment requirements: BSL2+/ABSL2+ means BSL2 containment with BSL3 practices and or PPE. Lab specific procedures (SOPs) will outline specific containment and practices and PPE.		
SPILL PROCEDURES			
Small	Notify others working in the lab. Allow aerosols to settle. Don appropriate PPE. Cover area of the spill with paper towels and apply an EPA approved disinfectant, working from the perimeter towards the center. Allow 30 minutes of contact time before disposal and cleanup of spill materials.		
Large	For assistance, contact Emory's Spill Response Team 404-727-2888.		
EXPOSURE PROCEDURES			
Mucous membrane	Flush eyes, mouth or nose for 15 minutes at eyewash station.		
Other Exposure	Wash area with soap and water for 15 minutes.		
Reporting	Immediately report incident to supervisor, complete an employee incident report, and submit to Occupational Injury Management (OIM).		
Medical Follow up	<table border="1"> <tr> <td>7am–4pm (OIM): EUH (404-686-7941) EUHM (404-686-7106) WW (404-728-6431)</td> <td>After Hours: OIM NP On Call 404-686-5500 PIC# 50464 Yerkes: Maureen Thompson Office (404-727-8012) Cell (404-275-0963)</td> </tr> </table>	7am–4pm (OIM): EUH (404-686-7941) EUHM (404-686-7106) WW (404-728-6431)	After Hours: OIM NP On Call 404-686-5500 PIC# 50464 Yerkes: Maureen Thompson Office (404-727-8012) Cell (404-275-0963)
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VIABILITY			
Disinfection	Unknown. Other flaviviruses are susceptible to 70% ethanol, 10% bleach, and 2% glutaraldehyde		
Inactivation	Inactivated by heat and low pH.		
Survival Outside Host	Unknown.		
PERSONAL PROTECTIVE EQUIPMENT (PPE)			
Minimum PPE Requirements	At minimum, personnel are required to don gloves, closed toed shoes, lab coat, and appropriate face and eye protection when working with ZIKV. Additional PPE may be required depending on lab specific SOPs and containment.		
Additional Precautions	All procedures that may produce aerosols, or involve high concentrations or large volumes should be conducted in a biological safety cabinet (BSC). The use of needles, syringes, and other sharp objects should be strictly limited. Additional precautions should be considered with work involving animals or large scale activities.		

ACKNOWLEDGEMENT LETTER



AGREEMENT FOR WORK IN CONTAINMENT

SECTION A (to be completed by EHSO)

NAME: _____ DATE: 2/9/2016

DEPARTMENT: Pediatrics

EMPLOYEE NUMBER: _____ LABORATORY BIOSAFETY LEVEL: BSL2+

AGENTS: Zika Virus

The following *in vitro* work practices will be followed:

-BSL3 containment and practices per facility Standard Operating Procedures.

The following *in vivo* procedures will be performed: Not Applicable

The following special precautions will be adhered to: This person will not work directly with Zika Virus or its derivatives, however, this person shares the same work space where research with Zika virus will be performed.

SECTION B: This section will be reviewed by Emory University's Occupational Health Physician/Infectious Disease Physician with the Employee

I understand that due to my occupational exposure to _____ materials, I may be at risk. I have been provided information and offered a consultation on risks and hazards associated with the listed agent(s).

- I have accepted the consultation with the Occupational Health Physician.
- I have declined the consultation with the Occupational Health Physician but have received required training and information from EHSO and Occupational Health. If in the future I continue to have occupational exposure and want consultation, I can receive more information and/or a consultation from Occupational Health.

_____ has been made aware of the importance of adhering to all safety precautions and we will continue to monitor the employee's status regularly to ensure compliance.

We have been notified and consent to this agreement of work.

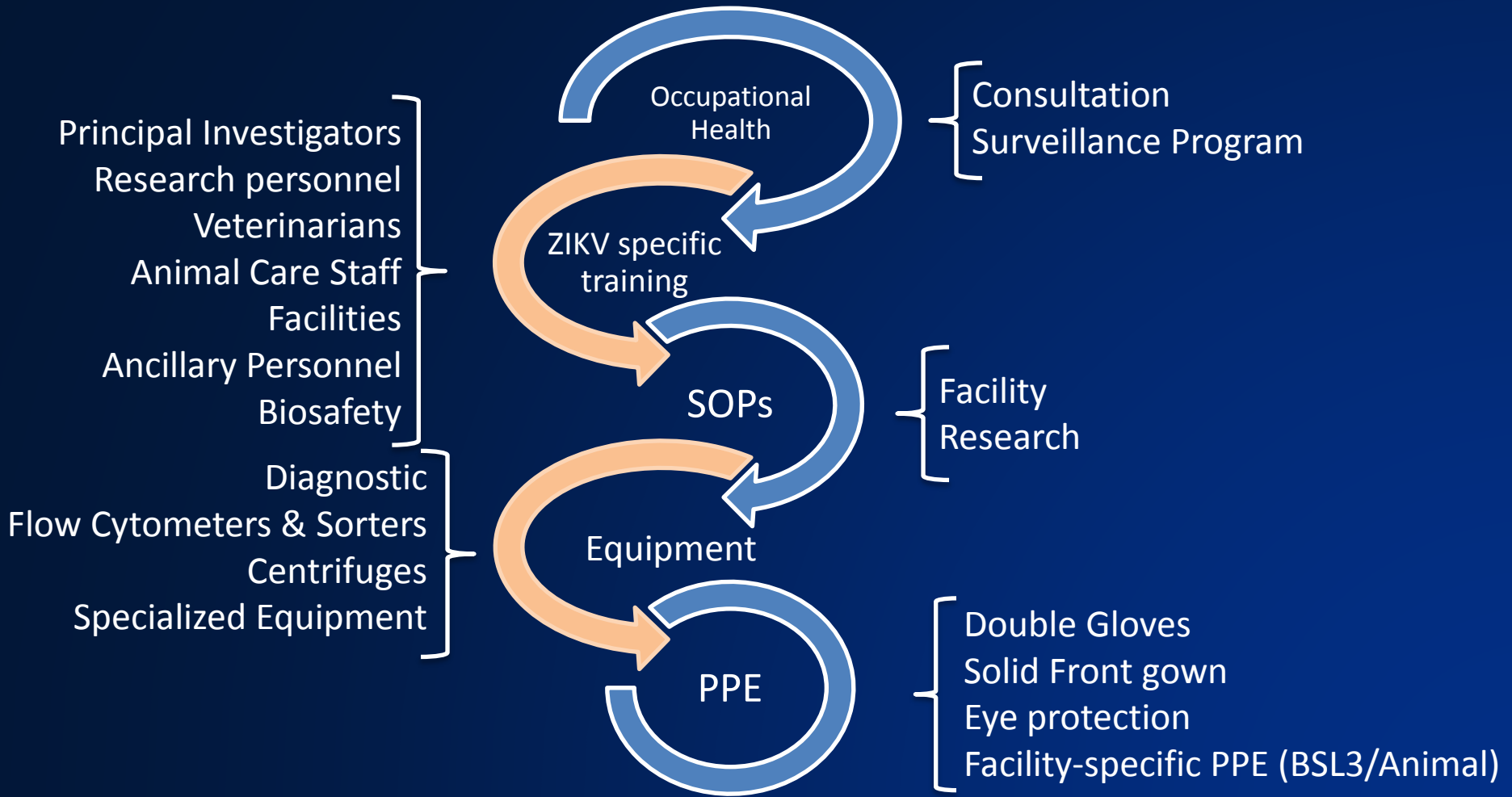
Employee Date: _____

Principal Investigator Date: _____

Occupational Health Physician Date: _____

Biosafety Officer Date: _____

WORKING WITH ZIKV



WORKING WITH ZIKV

- Transport of Samples
 - Inactivation of samples before leaving containment facility
 - Movement of samples between buildings- Chain of Custody
- Importing samples: domestic/abroad
 - Permits associated with the samples

POST EXPOSURE

1. Wash for 15 minutes
2. Report via PeopleSoft
3. Medical Follow Up

SPILLS

**SMALL SPILL
USE SPILL KIT AND FOLLOW SOP**



DECONTAMINATION

- **Disinfection: unknown**

- February 2016 - Other flaviviruses susceptible to 70% ethanol, 10% bleach, and 2% glutaraldehyde
- *ZIKV can be inactivated by 70% ethanol, 1% hypochlorite, 2% glutaraldehyde, 2% paraformaldehyde

- **Inactivation: unknown**

- February 2016 - Other flaviviruses inactivated by heat and low pH
- *ZIKV can be inactivated at 60C, pH < 4

* Muller JA et. al. Emerging Infectious Diseases September 2016

CDC INTERIM GUIDANCE

- Released 4/10/2016
- Contains special section for Healthcare and Laboratory Workers
 - Universal Precautions
 - Standard Precautions
 - Hand hygiene
 - PPE: ,gowns, gloves, masks, eye protection
 - Follow SOPs
 - Word about sharps
 - Reporting
 - Enhanced precautions according to activities
- Guidance for employer
- Guidance for travelers



https://www.cdc.gov/niosh/topics/outdoor/mosquito-borne/pdfs/osha-niosh_fs-3855_zika_virus_04-2016.pdf

RISK ASSESSMENT

Meyer E. *et. al.* Applied Biosafety 2016

Table 1. Risk Mitigation Implemented at Emory University for Work with ZIKV.

	In Vitro Work	In Vivo Work
Engineering controls	BSL-2 with restricted access and BSL-3 work practices ¹ All agent work to be conducted in a biosafety cabinet Use of centrifuge caps No use of sharps	ABSL-2 facility (nonhuman primate and rodent vivarium), with restricted access and BSL-3 work practices Open rodent cages inside biosafety cabinet Manipulation of virus or rodents inoculated with the virus is conducted in the biosafety cabinet Limited use of sharps and use of needle-safe devices
Personal protective equipment	Double gloves Solid-front gown Booties Respiratory protection if there is a risk for aerosol formation (ie, flow cytometry)	Double gloves Solid-front gown/fluid-resistant coveralls Booties/dedicated shoes + booties Respiratory protection with designated practices
Waste management	Autoclave waste before disposing If autoclave is not available, use of double bag after surface decontamination with approved chemical disinfectant Dispose of waste through approved vendor	Autoclave waste before disposing Disposal through approved vendor
Administrative Controls		
Occupational health	Consultation with occupational health physician to discuss the potential reproductive hazards Letter of acknowledgment	
ZIKV-specific training	Creation of ZIKV Biological Agent Reference Sheet (http://www.ehso.emory.edu). Biosafety office provided agent-specific training and reviewed work practices and personal protective equipment with involved workers.	
Documentation	The occupational health consultation letter of acknowledgment and the training documentation are filed with the investigators' biosafety approval. Protocol approval was contingent on completion of both the health consultation and training. The occupational health consultation was added to the individual's health card for future record.	
Procedures and practices	Agent-specific standard operating procedures Medical alert cards	

Abbreviations: ABSL, animal biosafety level; BSL, biosafety level; ZIKV, Zika virus.

THANK YOU