



University of Pittsburgh

Looking Beyond the Risk Group: Risk Assessment Challenges in Models of Emerging and Zoonotic Disease

University of Pittsburgh
Department of Environmental Health & Safety

Molly S. Stitt-Fischer, PhD, CPH, CBSP, (SM)NRCM





Risk Groups, Biosafety Levels, and Research

Risk Group	Infectious Agent – Severity of Disease	Treatment
1	Typically does not cause disease in healthy adults	Yes
2	Can cause disease; Not airborne	Yes
3	Can cause serious disease; Airborne transmission	Sometimes
4	Serious, and often potentially fatal disease	No



Risk Groups, Biosafety Levels, and Research

Risk Group	BSL	Infectious Agent – Severity of Disease	Treatment
1	1	Typically does not cause disease in healthy adults	Yes
2	2	Can cause disease; Not airborne	Yes
3	3	Can cause serious disease; Airborne transmission	Sometimes
4	4	Serious, and often potentially fatal disease	No



Risk Group



BSL



Risk Group \approx BSL



Risk Group



BSL



Human pathogen?

Animal pathogen?

Transmission route?

Risk Group

BSL

Aerobiology, imaging, etc.?

Animal research? Species?

Available facilities?

Personnel performing work?

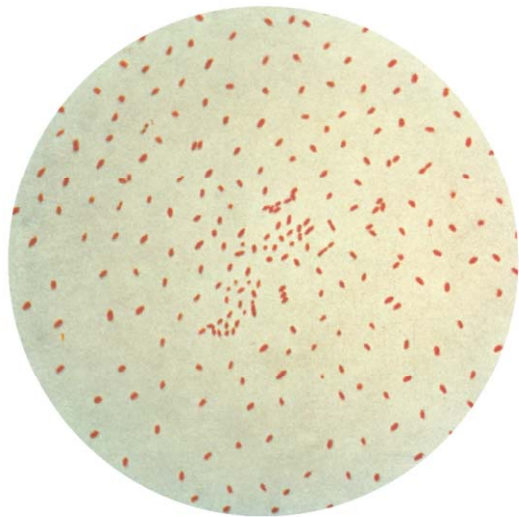


Case Studies: Process and Potential Stumbling Blocks

- Juvenile baboon model of reemerging disease
 - *Bordetella pertussis* (pertussis; whooping cough)
- Host-pathogen interactions
 - *Batrachochytrium dendrobatidis* (Bd)



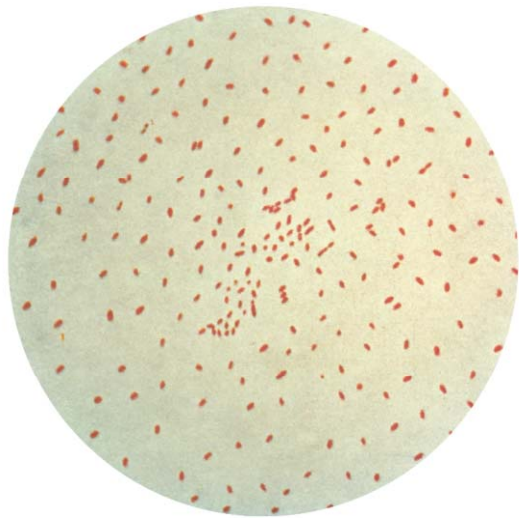
Pertussis: A Reemerging Disease



- Agent mainly causes disease in children and infants, but adults may develop symptoms as well.



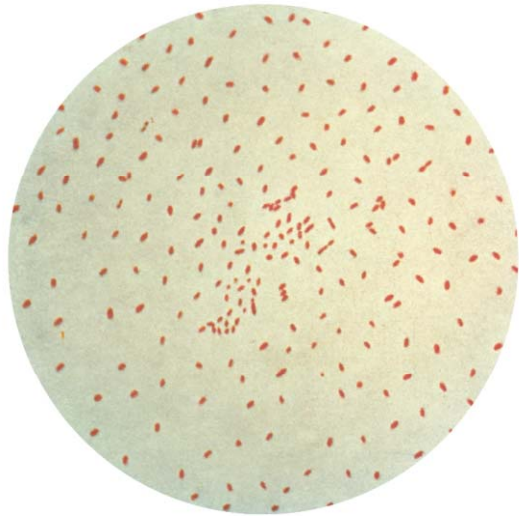
Pertussis: A Reemerging Disease



- Agent mainly causes disease in children and infants, but adults may develop symptoms as well.
- Exposure of infants to agent can lead to severe disease and high mortality.



Pertussis: A Reemerging Disease



- Agent mainly causes disease in children and infants, but adults may develop symptoms as well.
- Exposure of infants to agent can lead to severe disease and high mortality.
- Agent is contagious and spreads from person-to-person through direct contact and/or inhalation of respiratory droplets



Pertussis: A Reemerging Disease



GRANDMA, WHAT A BIG WHOOPING COUGH YOU HAVE.

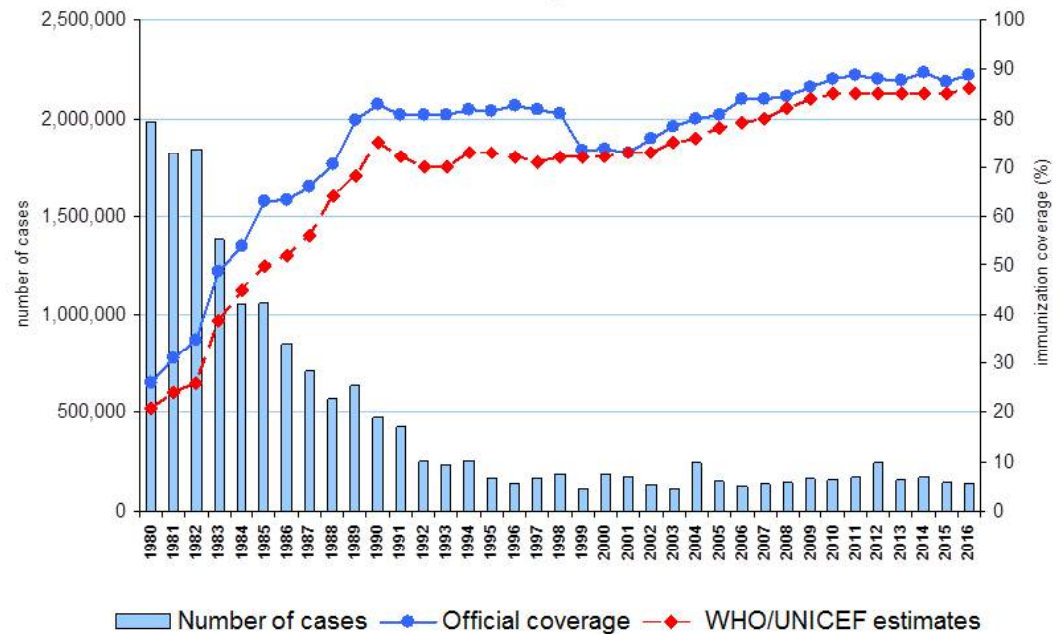
Understand the danger your grandchild faces from whooping cough. It's a highly contagious disease that can be especially serious—even fatal—for infants. Unfortunately, many people who spread it may not know they have it. If you have a new grandchild or one on the way, talk to your doctor or pharmacist about ways you can help protect yourself and your family from whooping cough, including getting vaccinated.

The Centers for Disease Control and Prevention (CDC) recommends everyone, including those around babies, make sure their whooping cough vaccination is up to date.

Ask your doctor or pharmacist if a whooping cough vaccination is right for you and your family.

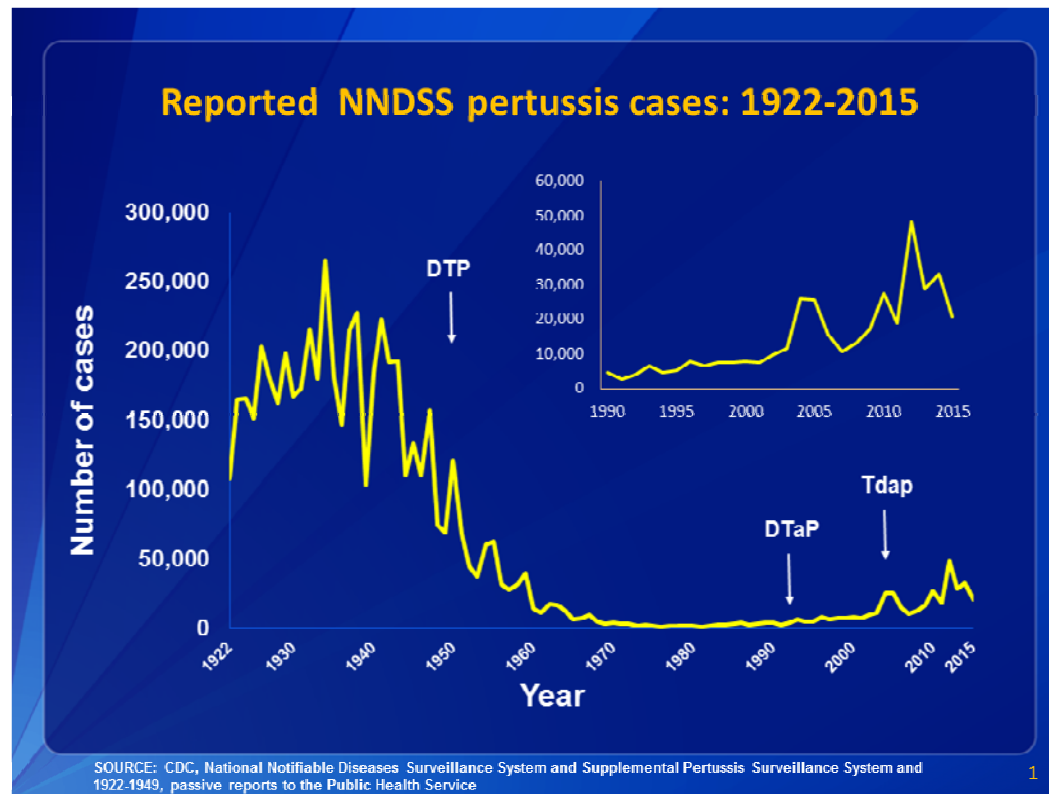
©2011 GSK group of companies. All rights reserved. Printed in U.S.A. 2/201108 February 2011 Visit BigBadCough.com/yfnet to learn more.

Pertussis global annual reported cases and DTP3 coverage, 1980-2016





Pertussis: A Reemerging Disease





2016 Provisional Pertussis Surveillance Report

Reported Pertussis Incidence and Cases

	Incidence (per 100,000)	No. of Cases
ALABAMA	3.3	160
ALASKA	19.5	144
ARIZONA	4.1	278
ARKANSAS	1.4	42
CALIFORNIA	2.8	1098
COLORADO	14.1	771
CONNECTICUT	2.3	81
DELAWARE	1.6	15
D.C.	1.3	9
FLORIDA	1.7	339

OKLAHOMA	3.1	121
OREGON	4.5	180
PENNSYLVANIA	11.4	1454
RHODE ISLAND	6.7	71
SOUTH CAROLINA	3.7	180
SOUTH DAKOTA	1.6	14
TENNESSEE	2	131
TEXAS	4.1	1119
UTAH	6.9	206
VERMONT	43.5	272
VIRGINIA	2.2	181
WASHINGTON	7.1	512
WEST VIRGINIA	1.3	23
WISCONSIN	21	1212
WYOMING	3.1	18
TOTAL	4.9	15737

<https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2016-provisional.pdf>

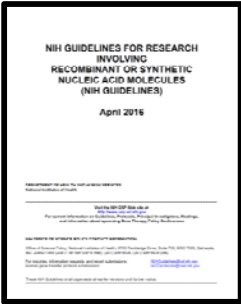


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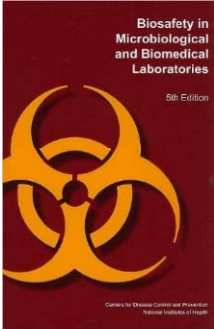
Risk Assessment: Infectious Agent

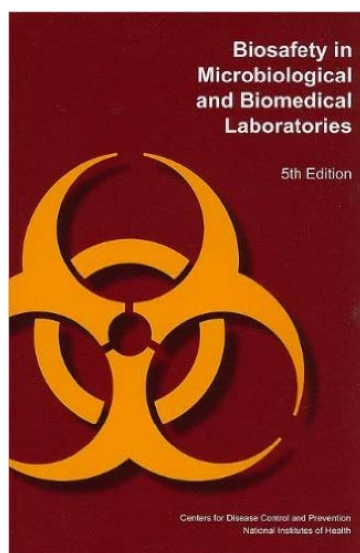


Bacteria	Genus	Species
	Bordetella	pertussis
NIH: 2		
BMBL*: 2		
Australia/New Zealand: 2		
Belgium: 2		
Germany: 2 notes: AR		
EU: 2 notes: V		
Singapore: 2		
Singapor Schedule:		
Switzerland: 2		
UK: 2 notes: Vaccine available		
Human Pathogen: y Animal Pathogen: n Plant Pathogen: n		
Select Agent CDC: n Select Agent USDA: n		



<https://my.absa.org/tiki-index.php?page=Riskgroups&default%5bcontent%5d=bordetella>





Containment Recommendations

BSL-2 practices, containment equipment, and facilities are recommended for all activities involving the use or manipulation of known or potentially infectious clinical material and cultures. **BSL-2 practices and containment equipment should be employed for housing experimentally infected animals.** Primary containment devices and equipment, including biological safety cabinets, safety centrifuge cups or safety centrifuges should be used for activities likely to generate potentially infectious aerosols. BSL-3 practices, containment equipment, and facilities are appropriate for production operations.



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Risk Assessment: Animal Model



What will our research entail?



Journal of Infection (2017) 74, S114–S119



BIAM
British Infection Association

www.elsevierhealth.com/journals/jinf

Pertussis disease and transmission and host responses: insights from the baboon model of pertussis

BRIEF REPORT

Marta V. Pinto ^a, Tod J. Merkel ^{b,*}
Journal of Infection (2017) 74, S114–S119

*Airborne Transmission of
Bordetella pertussis*

Jason M. Warfel,¹ Joel Beren,² and Tod J. Merkel¹

¹Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, and ²Division of Veterinary Services, Center for Biologics Evaluation and Research, FDA, Bethesda, Maryland

The Journal of Infectious Diseases 2012;206:902–6



Risk Assessment: Treatments or Vaccines Available?



Vaccines and Work Practices: What should we recommend?

- An FDA-approved vaccination is available for *Bordetella pertussis*
 - The University has a required vaccine program for other high risk pathogens
 - Should we require personnel to be boosted? Recommend?
 - Is vaccination enough given baboons develop severe disease?



Vaccines and Work Practices: What should we recommend?

- Is there a possibility that fomites or worker exposure could lead to family and/or community risk?
 - High impact to infants and children
 - Work with baboons infected with *Bordetella pertussis* at ABSL-3



Are we being too conservative?

- Ask a peer review committee for their feedback on recommendations



<http://www.safar.pitt.edu/sites/default/files/pictures/rangosresearch.jpg>

http://www.upmc.com/media/NewsReleases/2009/PublishingImages/CHP_New_Facade_large.jpg



Are we being too conservative?

No.



<http://bioethics.pitt.edu/sites/default/files/person-images/bioethics-inside-image%20%281%29.jpg>



<https://i.pinimg.com/736x/a7/9f/1c/a79f1cd0cf6cbc9056de53ba92a025ab--children-s-hospital-encouragement.jpg>



Case Study #2: What are factors to consider for work with an agent that is not infectious to humans?



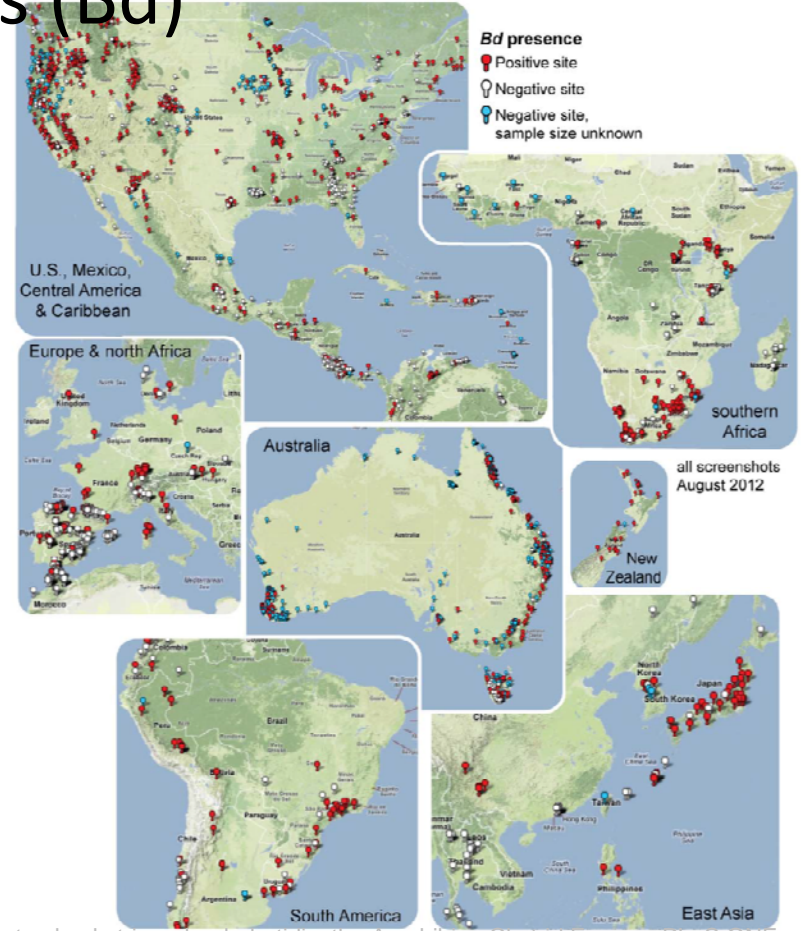
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Risk Assessment: Biological Agent Information



Batrachochytrium dendrobatidis (Bd)

- Chytrid fungus severely affecting amphibian species worldwide
 - Over 700 species have shown decline

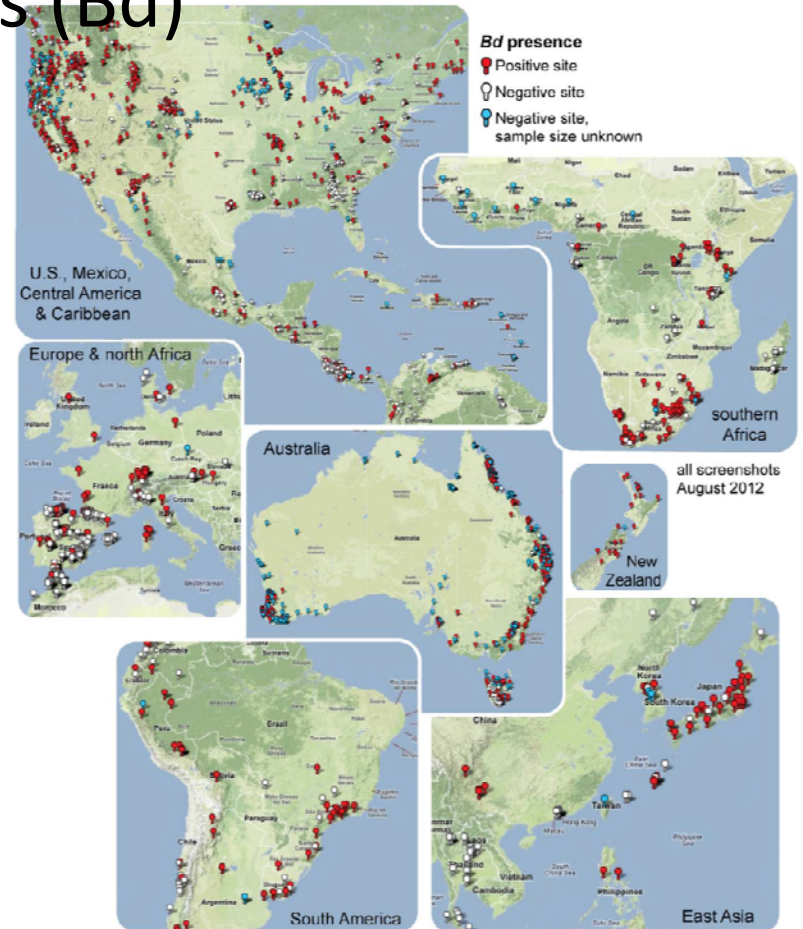


Olson DH, Aanensen DM, Ronnenberg KL, Powell CI, Walker SF, et al. (2013) Mapping the Global Emergence of Batrachochytrium dendrobatidis, the Amphibian Chytrid Fungus. PLoS ONE 8(2): e56802. doi:10.1371/journal.pone.0056802



Batrachochytrium dendrobatidis (Bd)

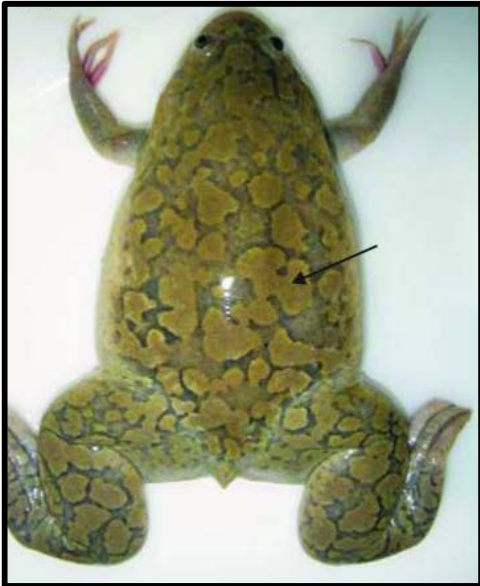
- Chytrid fungus severely affecting amphibian species worldwide
 - Over 700 species have shown decline
- More species extinct than any other infectious disease known
 - At least 200





Batrachochytrium dendrobatidis (Bd)

- Spread via pet trade/research/testing



African clawed frog
Xenopus laevis



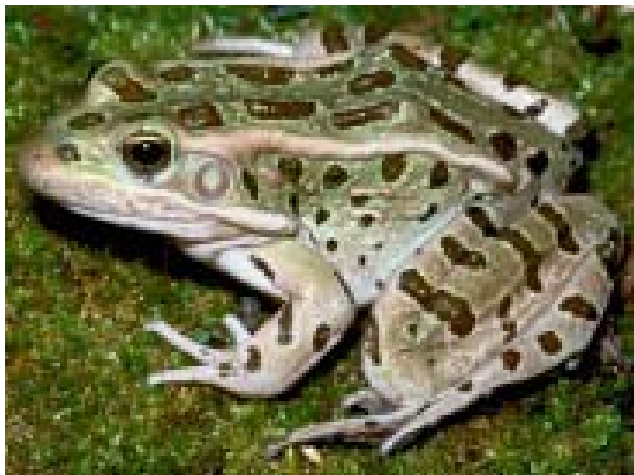
North American bullfrog
Lithobates catesbeianus

http://www.nationalgeographic.com/content/dam/animals/pictures/amphibians/a/american-bullfrog/american-bullfrog_01.adapt.1900.1.JPG

<https://www.ncbi.nlm.nih.gov/corecgi/tileshop/tileshop.fcgi?p=PMC3&id=347300&s=24&r=1&c=1>



Batrachochytrium dendrobatidis (Bd): Natural Hosts



Northern leopard frog
Lithobates pipiens



Aquatic salamander
Cryptobranchus alleganiensis



Louisiana crayfish
Procambarus clarkii



Everglades crayfish
Procambarus alleni



Risk Assessment: Research Planned



https://toxics.usgs.gov/photo_gallery/photos/armi/ARMI_b_boreas_SpruceLK_CWA_1.jpg
<https://ecos.fws.gov/ServCat/DownloadFile/15727?Reference=16196>

[Lab Anim \(NY\)](#), 2010 Sep;39(9):267-8.



Research Plan: Field studies

- Field studies
 - Established SOPs to avoid cross contamination during sample collection
 - New nitrile gloves, separate sterile container for each animal or sample collected





Research Plan: Field studies

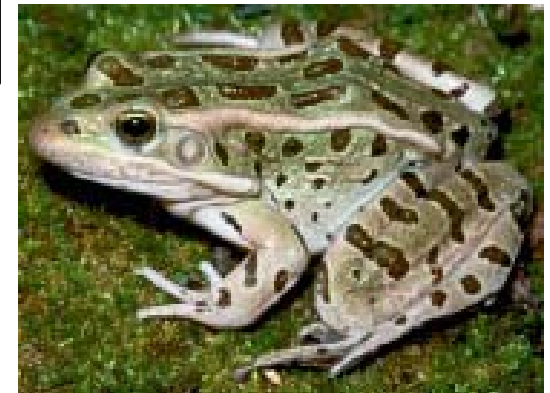
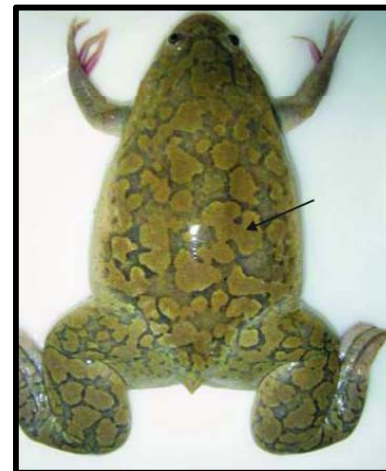
- Field studies
 - Established SOPs to avoid cross contamination during sample collection
 - New nitrile gloves, separate sterile container for each animal or sample collected
 - Does this translate to the lab?





Research Plans: In the lab

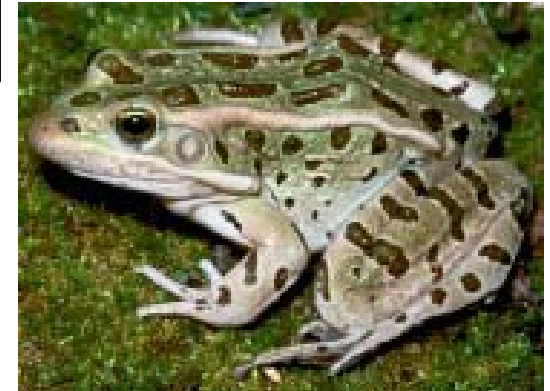
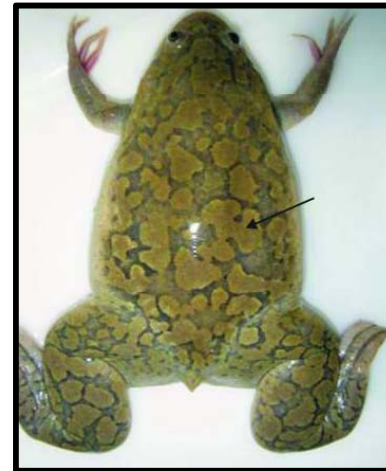
- Culture *Bd* and intentionally infect animals





Research Plans: In the lab

- Culture *Bd* and intentionally infect animals
- Maintain research colonies of uninfected animals in common facility





Risk Assessment: Research Plans

- Do we have capacity to house infected animals in shared facility?





Risk Assessment: Research Plans

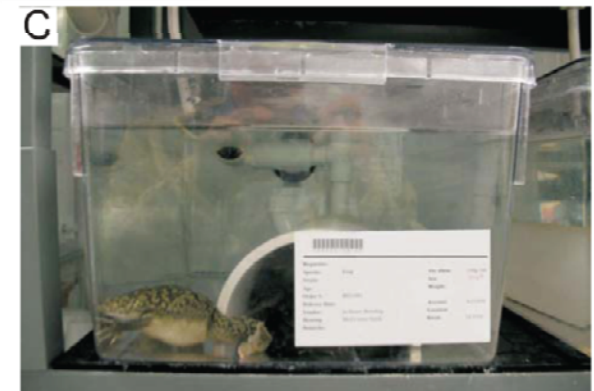
- Do we have capacity to house infected animals in shared facility?
- How would our other researchers feel about that?





Risk Assessment: Logistics

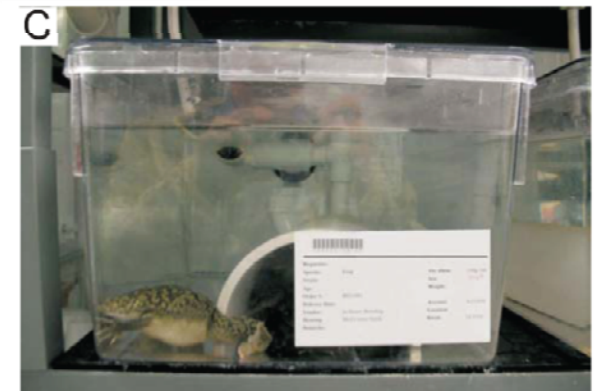
- Can we renovate or otherwise modify existing research space to accommodate housing of infected animals?





Risk Assessment: Logistics

- We will still need to house uninfected animals in the common housing area





Risk Assessment: Logistics

- We will still need to house uninfected animals in the common housing area
 - Emphasize strict traffic patterns
 - Uninfected animals first
 - No re-entry to common housing area after work in laboratory space





Risk Assessment: Logistics

- Use engineering controls and standard microbiological practices and PPE for culture of pathogen and handling of infected animals





Risk Assessment: Logistics

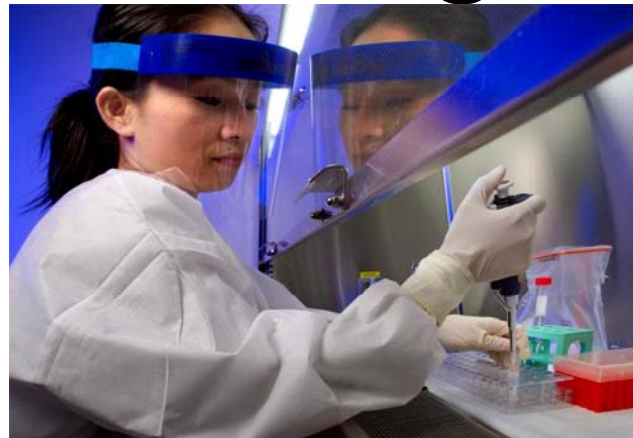
- Already familiar with use of BSCs for cultures





Risk Assessment: Logistics

- Already familiar with use of BSCs for cultures
- Lab coats?? Why would we need those?



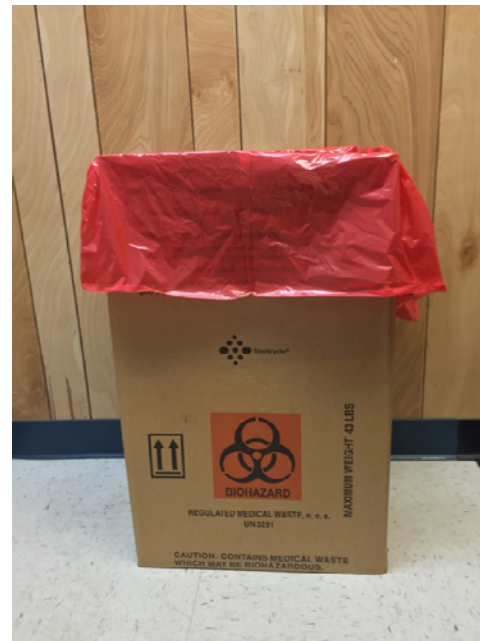
<https://www.cdc.gov/about/facts/cdcfastfacts/cdcfacts.html>

<https://ecos.fws.gov/ServCat/DownloadFile/15727?Reference=16196>



Risk Assessment: Logistics

- Waste disposal, transport, and storage of cultures
 - Biological waste storage and -80 freezers require personnel to walk past clean *Xenopus* facility



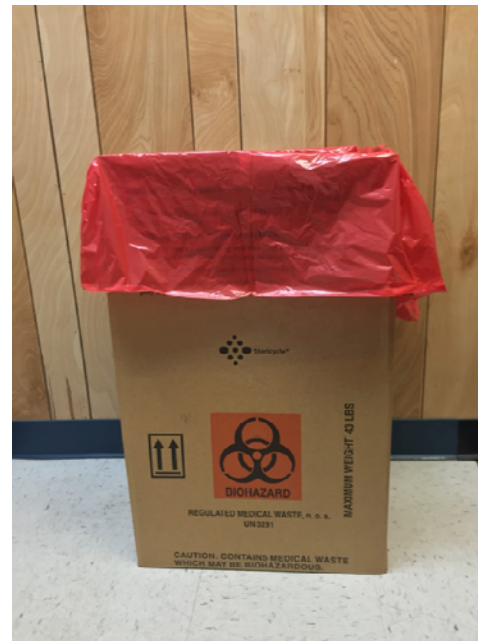
http://www.utsa.edu/safety/images/bio_pickup_procedure/3.png

http://mms.businesswire.com/media/20150412005035/en/462185/5/TSX_front.jpg



Risk Assessment: Logistics

- Waste disposal, transport, and storage of cultures
 - Secondary containers and surface disinfection



http://www.utsa.edu/safety/images/bio_pickup_procedure/3.png

http://mms.businesswire.com/media/20150412005035/en/462185/5/TSX_front.jpg



Risk Assessment: Personnel

- Undergraduate student researchers
 - Lack of research experience
 - Participation in laboratory and/or field work as part of courses





Risk Assessment: Personnel

- Undergraduate student researchers
 - Can they recognize the importance of adhering to strict SOPs?
 - Required, documented training by PI





University of Pittsburgh Department of Environmental Health and Safety

Lessons Learned: What is a Risk Assessment?



University of Pittsburgh Department of Environmental Health & Safety Risk Assessment for IACUC Protocol

Section 1: Hazard Assessment Overview		Protocol Date	/ /	Assessment Completion Date	
Project Title: Mechanisms of Telomere Mediated Lung Disease					
PI Name	Jonathan Alder	Office	MUH NW620	Phone	412 602 2118
PI E-Mail	jaldar@pitt.edu	Lab Locations	TRC; MUH W1200		
IACUC #	1600011202	IBC #	201700209	Location Animals Transported To	MUH W1200
Animal Species Used	Mouse. For species specific occupational health info, please visit shs.uodavis.edu/animal/ris/index.htm				
Implementation Review Required	<input checked="" type="checkbox"/>	Required Participants	N/A		
NOTE: If an Implementation Review is indicated for this protocol, the PI must notify the appropriate departments (DUAR, EH&S, Radiation Safety) prior to animal ordering to determine if a further meeting or plan is required. Failure to perform this notification may cause delays or other setbacks in project commencement and/or completion.					
Hazard Summary	Surgical and research injectables, anesthetic gases				
Use of Agents in Animals	<p>Surgical and research injectable</p> <ul style="list-style-type: none"> Care must be exercised when manipulating (weighing, solubilizing) powder or crystalline forms of this agent to decrease the risk of inhalation exposure. Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects. <p>Anesthetic gases</p> <ul style="list-style-type: none"> Specific engineering controls should be utilized to scavenge or remove agent from the air surrounding any operations (if not scavenging or not possible, usage should occur in a chemical fume hood) 				
Section 2: Use of Biological Agents		Total # of Bio Agents	0		
Bio Agents:	None	Biosafety Level	N/A		
Section 3: Use of Chemical Agents		Total # of Chem Agents	0		
Chem Agents:	5-Ethynyl-2-deoxyuridine (EdU)	CAG #	01100-00-9		
Chem Agent Administered to Animals?	Yes				
Hazard and Use Info	<ul style="list-style-type: none"> The agent is a novel alternative for BrdU (5-Bromo-2'-deoxyuridine) assay to directly measure active DNA synthesis or G₁-S phase synthesis of the cell cycle. Agent has a suspect reproductive hazard and mutagen. Any protocol involving the use agent should be performed in a chemical fume hood. The agent will be administered once before sacrifice. All used cages/bedding should be cleaned/disposed in a controlled manner (junk station). All used bedding should be incinerated. Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects. Gloves should be worn at all times, double gloving (latex over nitrile) is recommended. Other personal protective equipment (PPE), including lab coat and eye protection should also be utilized. 				
Chem Agents:	Casprofen (Rimadyl)	CAG #	02710-49-7		
Chem Agent Administered to Animals?	Yes				
Hazard and Use Info	<ul style="list-style-type: none"> Agent is an anti-inflammatory analgesic; acute exposure may produce nausea, vomiting, ringing sounds in ears, and altered mental function. Acute overexposure to agent may produce disorders of heart rate or rhythm, increased blood pressure, kidney and liver toxicity, altered skin reflexes and conductivity to light. Care must be exercised when manipulating (weighing, solubilizing) powder or crystalline forms of this agent to decrease the risk of inhalation exposure. Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects. 				



Lessons Learned: What is a Risk Assessment?

University of Pittsburgh
Department of Environmental Health & Safety
Risk Assessment for IACUC Protocol

Section 1: Hazard Assessment Overview	Protocol Date	/2017	Assessment Completion Date	
Project Title: Mechanisms of Tobacco Mediated Lung Disease				
PI Name: Jonathan Alder	Office: MUH N1620	Phone: 412-602-2118		
PI E-Mail: jald@pitt.edu	Lab Location: TRC: MUH N1200			
IACUC #: 1600011202	IBC #: 201700208	Location Animals Transported To: MUH N1200		
Animal Species Used: Mouse	For species specific occupational health info, please visit sis.usdhs.edu/animal/196/index.htm			
Implementation Review Required: No	Required Participants: NA			
NOTE: If an Implementation Review is indicated for this protocol, the PI must notify the appropriate departments (DUAR, DHS, Radiation Safety) prior to animal ordering to determine if a further meeting or plan is required. Failure to perform this notification may cause delays or other setbacks in project commencement and/or completion.				
Hazard Summary:	Surgical and research injectables, anesthetic gases			
Use of Agents in Animals:	Surgical and research injectable • Care must be exercised when manipulating (weighing, solubilizing) powder or crystalline forms of this agent to decrease the risk of inhalation exposure. • Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects. Anesthetic gases • Specific engineering controls should be utilized to scavenge or remove agent from the air surrounding any operations (if scavenging is not possible, usage should occur in a chemical fume hood)			
Section 2: Use of Biological Agents	Total # of Bio Agents:	0		
Bio Agents: None	Biosafety Level:	N/A		
Section 3: Use of Chemical Agents	Total # of Chem Agents:	0		
Chem Agents: 2-Ethynyl-2-Desoxyuridine (EdU)	CAG #:	01100-00-9		
Chem Agent Administered to Animals?:	Yes			
Hazard and Use Info:	• The agent is a novel alternative for BrdU (5-Bromo-2'-deoxyuridine) assay to directly measure active DNA synthesis or S-phase synthesis of the cell cycle. • Agent has a suspected reproductive hazard and mutagen. • Any protocol involving the use of agent should be performed in a chemical fume hood. • The agent will be administered once before sacrifice. • All used cages/handling should be clean/disposed in a controlled manner (pump station). All used handling should be non-pressured. • Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects. • Gloves should be worn at all times, double gloving (latex over nitrile) is recommended. Other personal protective equipment (PPE), including lab coat and eye protection should also be utilized.			
Chem Agents: Casprofen (Piroxicam?)	CAG #:	02710-49-7		
Chem Agent Administered to Animals?:	Yes			
Hazard and Use Info:	• Agent is an anti-inflammatory analgesic; acute exposure may produce nausea, vomiting, ringing sounds in ears, and altered mental function. • Acute intraperitoneal injection may produce disorders of heart rate or rhythm, increased blood pressure, kidney and liver toxicity, uterine pain, hypoxemia and convulsions to light. • Care must be exercised when manipulating (weighing, solubilizing) powder or crystalline forms of this agent to decrease the risk of inhalation exposure. • Routine laboratory handling using appropriate chemical hygiene practices should not pose significant exposure risk. However, accidental ingestion or injection may produce significant adverse effects.			





Lessons Learned: A good investment

- Conversations with researchers and peer review committees are worth the time in the long run
 - Demonstrate that you are a resource



Lessons Learned: A good investment

- Conversations with researchers and peer review committees are worth the time in the long run
 - Demonstrate that you are a resource



http://www.biology.pitt.edu/sites/default/files/facilities-images/PLE/IMG_1956.JPG

<http://www.biology.pitt.edu/sites/default/files/facilities-images/Facilities1.jpg>



Lessons Learned: What other risks should be considered?

- Take time to evaluate and communicate non-traditional risks

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<http://old.post-gazette.com/images5/thursday.pdf>

<https://www.gannett-cdn.com/sites/usatoday/images/site-masthead-logo-dark@2x.png>



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Acknowledgements

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Jay Frerotte, MBA, Director and RO

