Application of the AVMA Guidelines for the Depopulation of Animals to Biomedical Research

OLAW Online Seminar
September 26, 2019

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Axel Wolff, MS, DVM, NIH, Office of Laboratory Animal Welfare
PHS Policy and Euthanasia

PHS Policy on Humane Care and Use of Laboratory Animals (IV.C.1.g.)

“Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association (AVMA) Panel on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator.” *


• Guides veterinarians in making humane decisions when large numbers of animals must be killed quickly in response to a disease outbreak or natural disaster.

• Depopulation refers to the rapid destruction of a population of animals in response to urgent circumstances with as much consideration given to the welfare of the animals as practicable.
It is recommended that the disaster plan include contingencies for applying the AVMA Depopulation Guidelines in an emergency.
Depopulation of Laboratory Animals

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September 26, 2019
Humane Endings Guidance: What is it?

A method of killing that minimizes pain, distress, and anxiety experienced by the animal prior to loss of consciousness, and causes rapid loss of consciousness followed by cardiac or respiratory arrest and death.

AVMA Guidelines on...

Euthanasia (2013)
Humane Slaughter (2016)
Depopulation (2019)
Humane Endings Guidance: Depopulation

What is Depopulation?

• Refers to the rapid destruction of a population of animals in response to urgent circumstances with as much consideration given to the welfare of the animals as practicable.

• May employ euthanasia techniques, but not all depopulation methods meet the [AVMA] criteria for euthanasia.

• Balances rapid response with prevention of further devastation and suffering with the most humane method possible.

• Occurs when doing nothing can result in greater animal suffering and endanger responders.
Humane Endings Guidance: Depopulation

Classifying Methods

Preferred

• These methods are given highest priority and should be utilized preferentially when developing emergency response plans and when circumstances allow reasonable implementation during emergencies.

• They may correspond to AVMA Guidelines for the Euthanasia of Animals or the AVMA Guidelines for the Humane Slaughter of Animals techniques but adjusted for situational considerations.
Humane Endings Guidance: Depopulation

Classifying Methods

Permitted in Constrained Circumstances

- These methods are permitted only when the circumstances of the emergency are deemed to constrain the ability to reasonably implement a preferred method.

- Examples include zoonotic disease risk, response time, human safety, depopulation efficiency, deployable resources, equipment, animal access, disruption of infrastructure, and disease transmission risk.
Humane Endings Guidance: Depopulation

Classifying Methods

Not Recommended

• These methods should be considered ONLY when circumstances preclude the reasonable implementation of any of the “preferred or permitted in constrained circumstances” methods, AND when the risk of doing nothing is deemed likely to have a reasonable chance of resulting in significantly more animal suffering than that associated with the proposed depopulation technique.

• Examples of such situations include, but are not limited to, structural collapse or compromise of buildings housing animals, complete inability to safely access animals for prolonged period of time or any circumstance that poses a severe threat to human life.

• Not Recommended ≠ Unacceptable
Depopulation: Examples

Low-medium expansion foam for poultry

- Involves covering birds with blanket of foam, to a depth of 15-30 cm
- May be used in a variety of housing types (e.g., open sided, naturally ventilated; damaged structures that are unsafe to enter)
- Birds must be contained to the floor

Photo: Thornber PM, Rubira RJ, Styles DK. Humane killing of animals for disease control purposes. Rev. sci. tech. Off. int. Epiz., 2014;33(1):303-310. Available at: https://pdfs.semanticscholar.org/a897/4bbf1be6178312f0a7d2863409767980d20e.pdf
Planning for Emergency Killing in Research Settings

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2018 Humane Endings Symposium
November 4, 2018
Chicago, IL
Acknowledgments

Panel on Depopulation

• Laboratory Animal Working Group
  – Dr. Sam Cartner, Chair (UAB, Birmingham, AL)
  – Dr. Bob Adams (Johns Hopkins, Baltimore, MD)
  – Dr. Emily Patterson-Kane (AVMA, Schaumburg, IL)
  – Dr. Kate Pritchett-Corning (Harvard, Cambridge, MA)
  – Dr. Jennifer Pullium (NYU Langone Med Ctr, NY, NY)
  – Dr. Helen Valentine (U of Illinois, Urbana-Champaign, IL)
  – Dr. Michael Huerkamp (Emory, Atlanta, GA)

• AVMA: Dr. Cia Johnson, Lindsey McKinney

Images: Dr. Ryan Curtis, Dr. Bob Livingston
Depopulation
Small laboratory and wild-caught rodents

**Preferred**: Euthanasia techniques
- Carbon Dioxide (CO₂)
- Isoflurane overdose
- Intraperitoneal (IP) euthanasia solution
- Physical methods

**Permitted in Constrained Circumstances**
- Compatible: confluent monolayer + CO₂
- Incompatible: CO₂ in home cage
- Pre-charged chamber + high-flow
Depopulation
Laboratory dogs, cats, ferrets, rabbits, sheep, goats, and swine

Preferred: Injectable anesthetic overdose or injectable euthanasia solutions

• Two-step method:
  1. anesthesia followed by
  2. physical or adjunctive method or injection of Potassium chloride (KCl) or Magnesium sulfate (MgSO₄)

Permitted in Constrained Circumstances

• Use of effective compounded or non-pharmaceutical-grade, expired anesthetic or euthanasia agent
• Reuse of needles (5x)
Depopulation
Nonhuman Primates

Preferred: Euthanasia or slaughter techniques

- Two-step method:
  1. anesthesia followed by
  2. physical or adjunctive method or injection of KCl or MgSO₄

Permitted in Constrained Circumstances

- Use of effective compounded or non-pharmaceutical-grade (NPG), expired anesthetic, or euthanasia agent
- Gunshot by trained operator in appropriate outdoor environment
Depopulation
Aquatic Vertebtrates

Preferred: Euthanasia or slaughter techniques
  • Rapid chilling of small tropical fish
  • Anesthesia followed by adjunctive method
  • Pithing, blunt force followed by adjunctive method

Permitted in Constrained Circumstances
  • Use of effective compounded or non-pharmaceutical-grade, expired anesthetic, euthanasia, or toxic agent
Depopulation
Avian and Poultry

Preferred: Euthanasia or slaughter techniques
• Inhaled or injectable agents
• Anesthesia followed by adjunctive method

Permitted in Constrained Circumstances
• Use of effective compounded or non-pharmaceutical-grade, expired anesthetic, or euthanasia agent
Depopulation

Special Considerations

Dangerous animals
- Keep nets, snake hooks, darting apparatus on hand

Animals exposed to hazardous agents (e.g., BSL3 or 4)
- Should not require responders to enter primary containment

Fetal or neonatal animals
- Altricial: physical methods (e.g., cervical dislocation, decapitation)
- Precocial: euthanized as adults of the same species

Embryonated poultry eggs
- Cooling or freezing
Agricultural vs. Laboratory Settings
Facility & Program Attributes
Research Facilities

• Physical plant
• Protective distances
• High value, sometimes irreplaceable animals
• High population density
• Epizootic approach
• Extensive experience
• Mandatory emergency preparedness plans
• Attending Veterinarian
Facility & Program Attributes

Physical Plant

• Indoors containment, resilient construction, system redundancy
• Utilities: hardened supply with or without self-generation, emergency power
Facility & Program Attributes
Distance Matters

• Biosecurity: isolated from different institutional animals
• Minimal fomites such as service vehicles between institutions
Facility & Program Attributes
High Value Census

• Irreplaceable attributes and high value of many research models
  – Novel founder mice: $7,500 each
  – Cryopreservation of genetics
Facility & Program Attributes
Dense, Mobile Populations

• High concentration of large numbers
  – Mice: ~30-40/Net Square Foot (NSF), 100K+/institution
  – Broilers: 1-2/NSF (National Chicken Council)

• Mobility of some housing systems: racks and pens on wheels
Facility & Program Attributes

Epizootics

• Different impact
• Usually managed in-place
• Isolate, test, and cull by cage, room or greater scale
Emergency Planning
Regulations and Requirements

- “Facilities must ...have a disaster plan” (p. 35)
- “Animals that cannot be relocated or protected...must be humanely euthanized.” (p. 35)

- May involve ranking of species
- Defined decision tree
- Communication most likely disrupted
Emergency Planning
Attending Veterinarian

• Required by the *Guide for the Care and Use of Laboratory Animals (Guide)*
  – Responsible for the health and well-being of all laboratory animals (p. 14)
  – Facilities *must* have a disaster plan (p. 35)

• Allowed to deviate from conventional practices, AVMA guidelines
  – Professional judgement

• Depopulation guidelines
  – IP injection of 70% ethanol to mice, immature rats
  – Use of compounded or non-pharmaceutical-grade injectable anesthetics, euthanasia agents
  – Expired drug deployment
  – Needle reuse
Disaster Response Plan

- Prevention/Mitigation
- Preparedness
- Response
- Recovery

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### Natural Hazards

#### HAZARD AND VULNERABILITY ASSESSMENT TOOL

**NATURALLY OCCURRING EVENTS**

<table>
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<th>EVENT</th>
<th>PROBABILITY</th>
<th>HUMAN IMPACT</th>
<th>PROPERTY IMPACT</th>
<th>BUSINESS IMPACT</th>
<th>PREPAREDNESS</th>
<th>INTERNAL RESPONSE</th>
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*Score: 0 = N/A, 1 = Low, 2 = Moderate, 3 = High

**Severity = (Magnitude - Mitigation)**

**Risk: Relative threat**

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Research Institution Census
(approximate rank order by head-count)

1. Mice
2. Zebra fish
3. Rats
4. Guinea pig
5. Rabbit
6. Hamster
7. NHP
8. Livestock
9. Dog
10. Cat
11. Amphibian
12. Ferret
13. Gerbil
14. Other species of birds, amphibians, fish and rodents

Sources: USDA annual report & ACLAM test template
“Big Academe” Scenario
Mass Euthanasia / Total Depopulation

• Pandemic flu
  • Flu: state quarantined, animal food milled out-of-state and depleted
• 20,000 mouse cage depopulation

• Euthanex SmartBox™ chambers x 7
  • 16 cages + 400 L CO₂ per cycle
  • 12,310 L per 50-lb CO₂ tank
  • Mass depopulation requires 21 **FULL** 50-lb tanks,
  • 45 hrs x 14 people

• 35 gallon waste containers x 20 stations x 40 people = 20 hrs and 20 50-lb CO₂ tanks
Sizable Populations of Large Animals

To anesthetize 3,000 NHPs requires ~240 bottles of Telazol or Ketamine HCl
Conclusions

• Complete pre-emptive depopulation event is unlikely
  – Hardened facilities/programs + unpredictable, fast-moving event

• Adapt and apply the Panel on Euthanasia & Panel on Humane Slaughter guidelines
  – AV can assess effectiveness of non-pharmaceutical-grade and expired drugs

• Include in disaster planning & practice table top exercises
• Inventory anesthesia and euthanasia agents
• Advocate for cryo storage
Disaster Response and Recovery

Jennifer K. Pullium, MVB, DACLAM
Senior Director, Division of Comparative Medicine
NYU School of Medicine
Topics Covered

• Disaster response
  – Incident command
  – Vivarium
    • Animals
    • Staffing

• Disaster recovery
  – Short-term measures
  – Other considerations and innovative planning
Incident Command

• Integrated institutional disaster response
• Participants:
  – Animal Resources Director/AV
  – Facilities and environmental health and safety
  – Information technology
  – Institutional senior leadership
  – Public relations
  – Purchasing
  – Human resources and labor relations
Responsibilities

• Everyone in the institution has their area of focus
  – Don’t assume everyone will (or is able) to drop everything and assist you

• Need to ensure multiple people are capable of leading the vivarium disaster response
  – Don’t assume the Director or AV will be onsite
Responsibilities

- Issues that previously would have required multiple meetings and much hand wringing – now just require decisions
- Remember – indecision is a decision
- Differences between clinical and research staff become more apparent
Vivarium

• Personnel safety comes first
  – May be working in an unfamiliar site
  – Need to know the emergency egress(es)

• Began by rounding all animal facilities and satellites for: animal health, food, water, +/- bedding, temp, relative humidity
  – Had already stockpiled food, bedding, etc.
  – Bottled water (water cooler) for everything
Vivarium

- Consider a stash of cash (few thousand)
- Relocated satellite animals for easier care
- Store emergency supplies in multiple locations
Vivarium

- To what point do you allow environmental parameters outside the Guide or Animal Welfare Act before euthanasia?
  - Days? Week(s)?
  - Assuming the animals are clinically normal…
  - Are you going to euthanize everything because there are no air exchanges but temp and relative humidity are OK?
Vivarium

• Just because the storm/earthquake/event has passed…doesn’t mean the disaster is over
  – Couple weeks after the storm, another building was not going to resume utilities
  – ~4,000 cages; 8 different species; 50 PIs
  – Winter is coming…

• Recommend local institutions determine what housing can be offered in a disaster
Smilow rescue
Staffing

• Don’t assume people will come to work just because they are “essential personnel”
• Effective disciplinary program
• Have people staying onsite in advance
• Make it as comfortable as possible
  – Hotel room(s), food (before, during, after)
• Satellite phones
Press
• Myths from my residency training:
  – Lab animal vets don’t speak to the press
  – Your Public Relations (PR) people will take care of everything
  – Just give them a briefing about animal research

• Realities I learned the hard way:
  – No one knows your operation as well as you
  – A briefing to PR folks is not enough
  – If you want something done right, do it yourself
Press

• News cycle isn’t aware that you’ve been working almost 48 hrs with no sleep
• “Not available for comment” = “Not sitting by the phone with nothing to do but answer endless questions”
• Encourage staff not to read internet comments
• And if you still think briefing PR folks is enough…
Personnel

• Now members of an “exclusive club”
  – Find a way to communicate this fact to outsiders

• Mandatory Post Traumatic Stress Disorder (PTSD) counseling

• Look for hidden opportunities with previously difficult staff members

• Look after each other
  – Make sure people are eating, sleeping, home OK
Recovery: Short-term Measures

- Replacement animals
  - Cryo makes it much easier
  - Takes time to bring back and need housing

- Replacement facilities
  - Temporary and permanent
  - Better hope you’ve been nice to people
What can we do to really plan?

- Tabletop exercises are **not** enough
  - Reading comprehension test of disaster plan
  - Doesn’t tell you how anyone would perform in an actual emergency
- Tactical Decision Games (TDGs)
  - Developed by the military
  - Civilian use by industrial psychologists
  - Can’t simulate a disaster, but failure is not an option
What can we do to really plan?

• What really matters are the human factors (non-technical skills)

• Participants are given an emergency scenario and asked to make decisions under stress
  – Distractions, time limits, role play
  – Recommended for ALL levels of employees
  – Pullium et al., Nature 2014, Oct 23

• Leadership for Disaster Response (LeDR)
  – Conducted TDGs throughout the US, as well as UK, Ireland, Australia (academia and industry)
Depopulation guidelines

• We were fortunate in not having to depopulate for Hurricane Sandy

• Useful guidelines if we had to depopulate:
  – Combining cages of mice for euthanasia (perhaps in large containers)
  – Using all available pentobarbital (possibly expired)
  – Re-using needles until dull
References


Questions

Submit to the chat box in the GoToMeeting control panel
Question 1

How can depopulation be accomplished to minimize compassion fatigue?
Question 2

Who should be included in the decision to depopulate?
Question 3

Please talk more about networking with other nearby Institutions during an emergency. How do you initiate and maintain arrangements so that they are in place when a disaster occurs?
Question 4

Can you share some strategies for developing talking points on depopulation for media communications?
Questions

Submit to the chat box in the GoToMeeting control panel
21st Century Cures Act: Next Steps

OLAW Online Seminar
December 5, 2019