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Report to Congressional Requesters

May 2022

DOD ANIMAL USE

Objectives and Performance Measures Needed to Monitor Use of Alternatives for Trauma Training

Accessible Version

GAO-22-103992

GAO Highlight

Highlights of GAO-22-103992, a report to congressional requesters

May 2022

DOD ANIMAL USE

Objectives and Performance Measures Needed to Monitor Use of Alternatives for Trauma Training

Why GAO Did This Study

DOD uses live animals, in addition to alternatives such as training videos, mannequins and cadavers, for trauma training–that is, training for military personnel to treat acute battlefield injuries. However, the use of animals in medical education has faced long-standing scrutiny due to a continuing focus on animal welfare and continued improvement in other training methods. Various laws have addressed how animals can be used in government testing, research, and training programs and have sought to reduce this use where possible. DOD has, among other things, established a two-level review process for documents justifying animal use for trauma training, called "protocols".

GAO was asked to review DOD's use of animals for trauma training. GAO evaluated the extent to which DOD has (1) made progress in its efforts to refine, reduce, and replace the use of animals for trauma training and (2) consistently applied guidance for reviewing and approving animal use protocols for trauma training. GAO analyzed DOD guidance and reviewed 21 fiscal year 2018–2020 animal use protocols for trauma training from the DOD component oversight offices included in GAO's review.

What GAO Recommends

GAO makes three recommendations including that DOD develop measurable objectives, develop and use performance measures, and clarify guidance pertaining to DOD efforts to refine, reduce, and replace the use of animals in trauma training. In written comments, DOD concurred with all three of the recommendations.

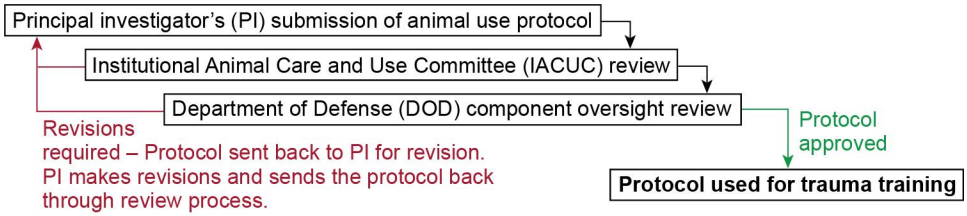
View GAO-22-103992. For more information, contact Cary B. Russell at (202) 512-5431 or russellc@gao.gov.

What GAO Found

The Department of Defense (DOD) has undertaken department-wide efforts to refine, reduce, and replace the use of animals for trauma training, in accordance with DOD policy, but cannot fully demonstrate the extent to which DOD has made progress in minimizing animal use. DOD has, for example, developed an incremental approach to limit the use of animals in trauma training curricula and coordinated among DOD entities and industry partners to develop training alternatives (e.g., mannequins). DOD officials told GAO that it is difficult to establish measurable objectives because they cannot predict how effective alternatives will be in the future. However, DOD does not have performance measures upon which to rely when assessing DOD's progress in reducing its use of animals. This lack of predictability does not preclude DOD from defining measurable objectives and then developing and using performance measures to monitor and evaluate its efforts. By developing specific and measurable objectives and performance measures for monitoring progress, DOD could provide greater assurance that it could assess progress in increasing its use of alternatives to live animals during trauma training.

DOD has inconsistently applied guidance for reviewing and approving trauma training protocols (see fig.).

DOD Review Process for Animal Use Protocols for Trauma Training



Source: GAO analysis of DOD documentation and interviews with DOD officials. | GAO-22-103992

That is, DOD component oversight offices have taken actions that they indicated are not needed (such as conducting certain literature searches) or implemented steps that may not be applicable to trauma training (such as obtaining statistician signatures). GAO found that the component oversight offices have done so because DOD had not clarified which provisions in its guidance specifically apply to animal use protocols for trauma training or what elements should be included in trauma training protocol documentation, as distinguished from protocol documentation for other contexts. By clarifying which guidance and data elements apply to animal use protocols for trauma training, DOD will be better positioned to ensure it is consistently applying its animal use policies for trauma training, such as considering alternatives to the use of animals whenever possible.

Contents

Abbreviations

DASD(HRP&O)	Deputy Assistant Secretary of Defense for Health Readiness Policy & Oversight
DOD	Department of Defense
IACUC	Institutional Animal Care and Use Committee
OUSD(R&E)	Office of the Under Secretary of Defense for Research and Engineering

RDT&E	research, development, test, and evaluation
USSOCOM	U.S. Special Operations Command

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May 3, 2022

Congressional Requesters

In order to minimize loss of life and disability resulting from combat injuries, the Department of Defense (DOD) provides military personnel with "trauma training"—intended to prepare them to treat acute battlefield wounds and injuries. Military personnel must be able to quickly perform life-saving procedures in battlefield environments and care for the wounded from the initial point of injury until evacuation. According to the U.S. Army Medical Research and Development Command, since mid-World War II, nearly 50 percent of combat deaths have been due to hemorrhage (i.e., blood loss). Of those, about half could have been saved if timely, appropriate care had been available. The difficulty in treating battlefield casualties is exacerbated by the long evacuation times often found in military operations. This requires military first responders, including combat medics, to stabilize patients for extended periods and distinguishes military from civilian trauma care. Because approximately 86 percent of all battlefield deaths occur within the first 30 minutes after wounding, the ability to rapidly locate, diagnose, and render appropriate initial treatments is vital to reversing the historical outcomes of battlefield injuries.[1]

DOD uses live animals and alternatives, such as training videos, mannequins and cadavers, among others, for trauma training. However, use of animals in medical education has faced long-standing scrutiny due to a continuing focus on animal welfare and continued improvement in other training methods. Statutes have addressed how animals can be used in government testing, research, and training programs and have

[1]A 2012 study published by the U.S. Army Institute of Surgical Research found that nearly a quarter of the 4,596 combat deaths in Iraq and Afghanistan from 2001 through 2011 were "potentially survivable" and that nearly 90 percent of deaths occurred before the injured reached a medical facility. According to the study, with better medical care and equipment, nearly one in every four troops who died of their wounds in the Afghanistan and Iraq wars could have been saved, according to the study. *See* Brian J. Eastridge et al., "Death on the Battlefield (2001–2011): Implications for the Future of Combat Casualty Care," *The Journal of Trauma and Acute Care Surgery*, vol. 73, no. 6, supp. 5 (December 2012): pp. S431-S437.

sought to reduce animal use where possible.[2] For example, the National Defense Authorization Act for Fiscal Year 2013 required DOD to submit a report that outlined a strategy, including a detailed timeline, to refine and, when appropriate, transition to human-based training methods for trauma training.[3] In 2018, a statute required the Secretary of Defense to use medical simulation technology, to the maximum extent practicable, before using live tissue, including live animals for training DOD medical professionals and combat medics, except where live tissue training is determined necessary by the medical chain of command.[4]

You asked us to review DOD's practices and oversight regarding the use of animals in trauma training. In this report, we evaluate the extent to which (1) DOD has made progress in its efforts to refine, reduce, and replace the use of animals for trauma training and (2) DOD has consistently applied guidance for reviewing and approving animal use protocols for trauma training. We include a list of our prior work examining DOD's efforts to reduce or replace animal use on the Related GAO Products section of this report page at the end of this report.

To address our first objective, we evaluated DOD efforts to monitor its progress in refining, reducing, and replacing the use of animals for trauma

[2]The Animal Welfare Act of 1966, for example, contains a congressional statement of policy that the regulation of animals and activities was, among other things, to ensure that animals intended for use in research facilities are provided humane care and treatment. Pub. L. No. 89-544, § 1 (1966) (act codified, as amended, at 7 U.S.C. §§ 2131-2159). The act defines animals as dogs, cats, nonhuman primates, guinea pigs, hamsters, rabbits, and other warm-blooded animals, with certain exceptions, which the Secretary of Agriculture may determine are being used, or are intended for use, for research, testing, experimentation, or exhibition purposes. Horses not used for research purposes and other farm animals used or intended for use as food or fiber are among those not covered by the act. 7 U.S.C. § 2132(g).

The act and its implementing regulations require, for example, that all research institutions report annually to the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) on any use of live animals covered by the act that may or may not involve painful procedures. 7 U.S.C. §§ 2144, 2143(a)(7)(A); 9 C.F.R. § 2.36 (2021). The Administrator of APHIS, under the Under Secretary for Marketing and Regulatory Programs, exercises the functions of the Secretary of Agriculture related to animal and plant health inspection, including under the Animal Welfare Act. 7 C.F.R. §§ 2.22(a)(2)(vi), 2.80(a)(6) (2021).

[3]National Defense Authorization Act for Fiscal Year 2013, Pub. L. No. 112-239, § 736(a) (2013).

[4]John S. McCain National Defense Authorization Act for Fiscal Year 2019, Pub. L. No. 115-232, § 718(a) (2018).

training by comparing the department's efforts with DOD guidance and federal standards for internal control characteristics pertaining to defining objectives, the use of quality information, and the establishment and operation of monitoring activities.[5] We also reviewed DOD documentation pertaining to efforts to research, develop, consider, and use alternatives in place of animals for trauma training. For example, we collected documentation and interviewed officials on

- efforts to develop alternatives to animals for research, development, test, and evaluation (RDT&E) and training, including trauma training;
- trauma training curricula for military first responders, including combat medics; and,
- the extent to which DOD had efforts underway to demonstrate that it had considered and used alternatives to refine, reduce, and replace the use of animals for trauma training.

To address our second objective, we reviewed DOD's instruction and other guidance governing animal use protocols for trauma training.[6] We also reviewed the two-level protocol review process used by Institutional Animal Care and Use Committees (IACUCs) and DOD component oversight offices to approve trauma training protocols, as well as the final layer of oversight provided by Office of the Under Secretary of Defense for Research and Engineering (OUSD(R&E)) in overseeing components'

[5]*See* DOD Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019). In this instruction, DOD states (1) it is DOD policy that alternatives to animal use will be considered and used whenever possible to attain the objectives of DOD-sponsored research, development, testing, and evaluation (RDT&E) or training if such methods produce scientifically or educationally valid or equivalent results; (2) it is DOD policy that procedures will cause the least pain or distress to the minimum number of animals and be consistent with the scientific or training needs; and (3) that alternatives to animal use are characterized by refinement, reduction, and replacement. For purposes of this report, we use "DOD-sponsored" to refer to RDT&E or training conducted by DOD entities or non-DOD entities with a contractual or other relationship with DOD for that RDT&E or training. GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

[6]DOD Instruction 3216.01; Director, Human Performance, Training, and BioSystems Directorate Memorandum, *Formats for Animal Use Protocol Submissions* (July 20, 2017); Army Regulation 40-33, Secretary of the Navy Instruction 3900.38C, Air Force Manual 40-401, Defense Advanced Research Projects Agency Instruction 18, Uniformed Services University of Health Sciences Instruction 3203, *The Care and Use of Laboratory Animals in DOD Programs* (Feb. 16, 2005). For the purposes of this report, we will refer to this last guidance document as Army Regulation 40-33.

implementation and execution of DOD guidance.[7] Under DOD Instruction 3216.01, lead researchers (called principal investigators) from DOD institutions will submit all proposed RDT&E and training (including trauma training) to the DOD institution's IACUC using the DOD Standard Animal Use Protocol Format (Standard Format) or in a pre-approved alternative format with comparable detail.[8] After DOD IACUC approval, the component oversight office must conduct an administrative review of certain RDT&E involving animals, including for all training using animals to teach human medical or surgical care. Principal investigators from non-DOD institutions submit documentation to DOD component oversight offices with all pertinent information and level of detail regarding animal care contained in the Standard Format, although they are not required to use the Standard Format itself. See appendix II for the DOD Standard Animal Use Protocol Format.

We compared DOD's instruction and Army Regulation 40-33 with the OUSD(R&E) and the DOD component oversight office review process. We conducted interviews about this process with officials from the OUSD(R&E) and the following DOD component oversight offices: the Army's Animal Care and Use Review Office, the Navy's Bureau of Medicine and Surgery, the Air Force's Medical Readiness Agency, and the U.S. Army's Special Operations Command.[9] Further, we compared the guidance and our interviews with those component oversight offices' evaluation of 21 fiscal year 2018–2020 animal use protocols for trauma training that we selected for our review—protocols from each of these

[7]Specifically, OUSD(R&E) officials told us that, although OUSD(R&E) does not review specific proposals for trauma training, it provides direction to the component oversight offices on appropriate implementation of DOD Instruction 3216.01, federal regulations, and guidelines and is available to advise and assist when components have questions on particular matters.

[8]The DOD Standard Animal Use Protocol Format (Standard Format) is designed to be used as a "fill-in-the-blank" type of document. Within this format, principal investigators provide specific information on their proposed use of animals such as the species and number of animals, surgical procedures, and alleviation of pain and distress. For the purposes of this report, the DOD Standard Animal Use Protocol Format will be referred to as the Standard Format.

[9]We selected these component oversight offices because their components conduct trauma training using animals. For the purposes of this report, the U.S. Army's Special Operations Command officials will be referred to as U.S. Special Operations Command (USSOCOM) officials. U.S Army Special Operations Command serves as the executive agent for USSOCOM to facilitate development, coordination, and implementation of the Joint Special Operations Medical Training Center.

offices and that remain current.[10] Finally, we compared the guidance, our interviews, and the component oversight offices' implementation of the 21 animal use protocols with *Standards for Internal Control in the Federal Government* principles that call for federal program managers to obtain relevant data from reliable internal and external sources in a timely manner based on the identified information requirements and that relevant data have a logical connection with, or bearing upon, the identified information requirements.[11] See appendix I for a more complete explanation of our objectives, scope, and methodology, including a discussion of how we selected the protocols that we reviewed, and the DOD and non-DOD organizations that we contacted.

We conducted this performance audit from December 2019 to May 2022 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

Trauma Training Involving Animal Use at DOD

Tactical Combat Casualty Care, or trauma training, reflects the realities of combat casualty care such as the nature of the injuries (e.g., penetrating vs. blunt trauma) and the conditions of practice on the battlefield (e.g., enemies, austerity, and inclement weather). Combat trauma differs from civilian trauma. For instance, blunt trauma predominates in civilian casualties, whereas most combat wounds are caused by penetration. Physicians and non-physicians without a medical background or experience participate in trauma training to gain proficiency to provide

[10]We selected 21 of the 40 current fiscal year 2018–2020 animal use protocols for trauma training: five from the Army, five from the Navy, six from the Air Force, and five from U.S. Special Operations Command (USSOCOM). We selected the protocols to represent each DOD component and because they constituted the most current ones as identified by DOD, considering that we began our audit work in fiscal year 2020 and that protocols remain active for 3 years.

[11]GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

lifesaving treatment under adverse and less-than-optimal conditions.[12] For example, these personnel must demonstrate proficiency in controlling major blood loss caused by wound to a major vein or artery.

Trauma training at DOD involves the use of live animals as well as alternatives and simulators. Live animals such as pigs and goats are used in trauma training because their organs and tissues are similar to humans, they have biological variation that can complicate treatment and provide opportunities to control medical conditions, and they provide immediate negative or positive feedback on interventions. During the training, they are injured in such a way as to simulate specific battlefield injuries, and then are treated by military personnel. According to DOD officials, animals that are used for this training are maintained under anesthesia to minimize pain and distress and are then humanely euthanized at the conclusion of the procedure.

DOD Policy on the Use of Animals in Research and Testing

It is DOD policy that RDT&E or training conducted or sponsored by DOD will comply with applicable federal and DOD policies and guidance that provide national standards for, among other thing, the acquisition, treatment, care, and use of animals. Specifically, according to DOD Instruction 3216.01, it is DOD policy that (1) alternatives to animal use will be considered and used whenever possible to attain the objectives of DOD-sponsored RDT&E or training if such methods produce scientifically or educationally valid or equivalent results and (2) procedures will cause the least pain or distress to the minimum number of animals and be consistent with the scientific or training needs. The instruction also states that alternatives to animal use are characterized by refinement, reduction, and replacement. “Reduction” refers to the use of fewer animals, existing procedures may be “refined” so that animals are subject to less pain and distress, and investigators may “replace” animals with less complex (i.e.,

[12]For example, Special Operations Surgical Team Members (e.g. critical care nurses and surgical technicians), Special Tactics Medical Personnel (e.g., physicians and physician assistants), and all combatants that include non-medical combat first-responders participate in trauma training.

sentient) models or use non-animal methods.[13] Finally, according to the instruction, DOD component oversight offices including those within the Army, the Navy, the Air Force, and the U.S. Special Operations Command (USSOCOM) must conduct an administrative review of certain RDT&E involving animals, including for all training using animals to teach human medical or surgical care.[14] For example, DOD and non-DOD institutions must submit proposals, known as protocols, that justify using animals for trauma training.[15] These protocols then must undergo two levels of review to obtain approval to use animals for trauma training.

DOD Entities Responsible for the Care and Use of Animals for RDT&E and Training

A number of DOD organizations are responsible for overseeing the department's care for, and use of, animals in research and training and in implementing DOD policy on the use of alternatives to animals where possible. These organizations include:

- **Under Secretary of Defense for Research and Engineering (OUSD(R&E))**, is the principal staff assistant and advisor to the Secretary and Deputy Secretary of Defense for all matters regarding, among other things, the DOD Research and Engineering Enterprise, technology development, and developmental testing activities and

[13]*See* DOD Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019). The instruction defines "animal" as any living or dead vertebrate animal, including birds, cold-blooded animals, rats of the genus *rattus* and mice of the genus *mus*.

[14]DOD component oversight offices include those of the military departments (Army, Air Force, and Navy). According to OUSD(R&E) officials, during the timeframe of our review, the Army's component oversight office, the Army's Animal Care and Use Oversight Office, oversaw the animal care and use activities of another DOD component, the Uniformed Services University for the Health Sciences. *See* Army Regulation 40-33, *The Care and Use of Laboratory Animals in DOD Programs* (Feb. 16, 2005). This guidance delineates the Secretary of the Army as the DOD Executive Agent for Veterinary Services to develop and issue service regulations to implement DOD Instruction 3216.01. DOD component oversight offices include the Army's Animal Care and Use Review Office, the Navy's Bureau of Medicine and Surgery, the Air Force's Medical Readiness Agency, and the U.S. Special Operations Command (USSOCOM).

[15]For the purposes of this report, we refer to universities, research laboratories, and research facilities conducting DOD-sponsored RDT&E and training as non-DOD institutions.

programs.[16] The Under Secretary develops policies, guidance, and direction for the protection of animal subjects in research, such as DOD Instruction 3216.01, Use of Animals in DOD Conducted and Supported Research and Training, and is the DOD point of contact for all matters related to DOD compliance with the Animal Welfare Act and the principal liaison with agencies outside DOD on matters pertaining to animal care and use for RDT&E, education, and training.

- **Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight (DASD(HRP&O))**, serves under the authority, direction, and control of the Assistant Secretary of Defense for Health Affairs.[17] In coordination with the OUSD(R&E), this office monitors and evaluates DOD component policy compliance with DOD Instruction 3216.01 and other federal regulations on the use of live animals in medical readiness training.
- **The Defense Health Agency**, enables the Army, Navy, and Air Force medical services to provide a medically ready force to combatant commands in peacetime and wartime.[18] The Director, Defense Health Agency, under the authority, direction, and control of the Under Secretary of Defense for Personnel and Readiness, in consultation with DOD components that have an animal use program, develops and issues supporting guidance for DOD Instruction 3216.01.[19]
- **Institutional Animal Care and Use Committees (IACUC)**, for DOD institutions, comprise a minimum of five members, including a primary

[16]DOD Directive 5137.02, *Under Secretary of Defense for Research and Engineering (USD(R&E))* (July 15, 2020).

[17]DOD Instruction 1322.24, *Medical Readiness Training* (Mar. 16, 2018) (incorporating change 1, effective Feb. 15, 2022).

[18]DOD has seven combatant commands that generally manage military operations in designated areas of responsibility: U.S. Africa Command, U.S. Central Command, U.S. European Command, U.S. Northern Command, U.S. Indo-Pacific Command, U.S. Space Command, and U.S. Southern Command.

[19]DOD Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019).

nonaffiliated member and at least one non-scientific member.[20] The IACUC is the first level of review for animal use protocols for trauma training. DOD IACUCs are established within each institution that uses animals for RDT&E, including trauma training. IACUCs are responsible for reviewing trauma training protocols submitted by principal investigators (i.e., lead researchers) for animal use programs conducted or sponsored by DOD components, organizations, or institutions.

- **The DOD component oversight offices** include the U.S. Army's Animal Care and Use Review Office, the Navy's Bureau of Medicine and Surgery, the Air Force Medical Readiness Agency, and the U.S. Army Special Operations Command's Veterinarian Review Office. These offices perform the second, administrative-level review for animal use protocols for trauma training.[21]

Protocol Review Process

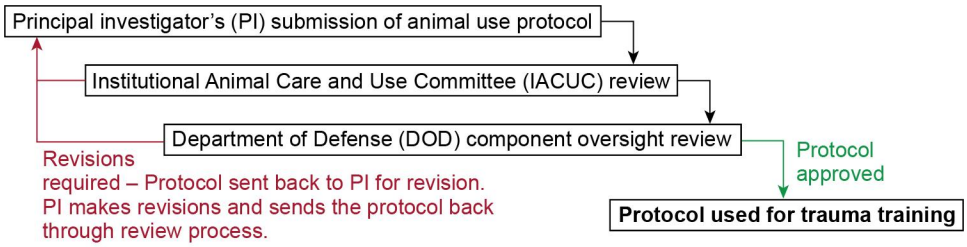
DOD has established a two-level protocol review process that is used to justify animal use for trauma training. Under the Standard Format detailed in Army Regulation 40-33, principal investigators at both DOD and DOD-

[20]DOD Instruction 3216.01. DOD Instruction 3216.01 states that DOD IACUCs should designate an alternate member or members for the nonaffiliated member to facilitate community representation in the IACUC's activities but OUSD(R&E) officials clarified that having such an alternate member is not required. Under the Animal Welfare Act and its implementing regulations, institutions using or intending to use live animals in research, tests, or experiments, including non-DOD institutions, are generally required to appoint an IACUC, although non-DOD institution IACUCs are not required to have the same membership as detailed above for DOD IACUCs. Among other things, IACUCs review RDT&E and training proposals to determine whether the proposed activities are in accordance with the act and its implementing regulations. In particular, the committees are to determine whether researchers have considered alternatives to procedures that may cause more than momentary or slight pain or distress to animals and have provided a written narrative description of the methods and sources used to determine that alternatives were not available. *See* 7 U.S.C. § 2143(b); 9 C.F.R. § 2.31 (2021).

[21]DOD Instruction 3216.01. These reviews are overseen by a component-level veterinarian, but are not intended to be another IACUC review. The purpose of these reviews is to ensure that the institution performing the RDT&E or training has met the requirements in all applicable regulations and policies and meets acceptable standards of animal care and welfare. DOD component oversight offices also require DOD and DOD-sponsored institutions to report, in a timely manner on, among other things, any significant deficiencies, noncompliance with DOD Instruction 3216.01, and reports of adverse events regarding RDT&E or training. Additionally, for DOD institutions, the DOD component oversight offices are responsible for regularly reviewing reports of the institutional program review conducted by the IACUC to ensure that corrective actions are completed in a timely manner.

sponsored institutions are to include in the protocols (1) justification for using animals for trauma training; (2) documentation of the consideration and use of alternatives to animal use through refining, reducing, and replacing animals; and (3) a pain and distress assessment and a description of any pain relief and prevention methods used, among other things.[22] Animal use protocols for trauma training are reviewed first by an IACUC and then by the component oversight office. Figure 1 illustrates that the review process is iterative, possibly involving a back-and-forth between the component oversight office and the principal investigator to clarify information written in the protocols and, in some cases, discrepancies that would require a principal investigator to revise a protocol. According to officials, all revised protocols require IACUC approval before being resubmitted to the respective component veterinary oversight office for approval.

Figure 1: Department of Defense (DOD) Animal Use Protocol Review Process for Trauma Training



Source: GAO analysis of DOD documentation and interviews with DOD officials. | GAO-22-103992

DOD Cannot Fully Demonstrate Extent to Which It Has Made Progress in Refining, Reducing, and Replacing the Use of Animals for Trauma Training

DOD has undertaken department-wide efforts to consider and use alternatives to refine, reduce, and replace the use of animals for trauma training. However, DOD was unable to fully demonstrate the extent to which it has made progress in doing so, and there are opportunities to

[22]Army Regulation 40-33. Although non-DOD institutions are not required to use the Standard Format, documents submitted to the component oversight office will provide all pertinent information and level of detail regarding animal care contained in the Standard Format. DOD Instruction 3216.01.

improve its processes to monitor and measure progress in refining, reducing, and replacing the use of animals for trauma training.

DOD Has Undertaken Department-wide Efforts to Consider and Use Alternatives to Refine, Reduce, and Replace the Use of Animals for Trauma Training

DOD has limited the use of animals through applying an incremental approach to trauma training curricula, sponsored studies that resulted in some procedures that no longer use animals, and established entities to coordinate and support the development of simulations department-wide.

An incremental approach to limit the use of animals. OUSD(R&E) officials told us that trauma training uses an incremental approach to limit the use of animals. Under such an approach, training uses simulators and culminates with an animal capstone event.

During trauma training, students may use simulators such as mannequins and perfused cadavers for the practical application of trauma training skills.[23] However, according to OUSD(R&E) officials, these simulators lack biological variation and immediate feedback, and cannot adequately simulate realistic experience in surgical procedures. Students will then participate in a capstone event, where they will perform treatment procedures on a live animal simulating realistic combat injuries.[24] According to DOD, the live animal model presents the most realistic training simulation model for a human combat casualty because a living animal creates a realistic sense of urgency and stress that cannot be emulated with simulators.

For example, USSOCOM provides a 36-week course primarily attended by selected Special Operations Forces, including combat medics. In the first three phases of the course, participants develop skills such as

[23]A mannequin can be used to practice skills such as cardiopulmonary resuscitation, according to a USSOCOM official. A “cadaver” is a deceased person’s body or body parts—for example, organs, tissue, eyes, bones, arteries or other specimens. In a “perfused” cadaver, a pump is used to simulate bleeding, pulsation, or liquid filling the arteries.

[24]It is DOD policy that the use of live animals in medical readiness training is minimized in accordance with DOD Instruction 3216.01 and only used when alternatives such as commercial training simulations, mannequins, moulaged actors, and cadavers are not appropriate to attain the training objective. DOD Instruction 1322.24, *Medical Readiness Training* (March 16. 2018) (incorporating change 1, effective Feb. 15, 2022)..

providing basic life support. The fourth phase of this training sets the foundation to learning trauma practical skills in which medics have to demonstrate proficiency in order to move on to the fifth phase, or Trauma II – a block that involves live tissue training (LTT) or the use of live animals, according to officials. According to USSOCOM officials, their curriculum uses approximately 81 simulations for the first three phases of trauma training prior to using animals for trauma training. USSOCOM's trauma training curriculum also limits animal use by maximizing the students to animals-used ratio.

DOD studies resulted in some procedures no longer using animals. In fiscal year 2010, DOD initiated a $20 million research effort that followed a systematic approach to quantify combat medic skill acquisition and to measure the effect of the animal model in trauma training.[25] This effort culminated in three studies that addressed the benefits of using simulations and live animals for trauma training. The studies concluded that there are instances where simulations may be more useful than using live animals, including the following findings:

- The combined use of simulations and animals allowed trainers to incorporate the parts of live tissue (i.e., live animals) or simulation that were most effective for a training objective. In 2019, DOD reported that DOD will continue to enhance the use of simulation technologies while retaining the use of live animals to address the gaps and limitations of simulation technology.[26]
- When training on some procedures, such as neonatal intubation, students retained more information when using simulations. In a 2016

[25]Office of the Under Secretary of Defense for Acquisition, Technology and Logistics, *Report to Congress on the Strategy to Transition to Use of Human-Based Methods for Certain Medical Training* (April 2013). These three studies were described in this report, which DOD submitted to the congressional defense committees in response to a provision in the National Defense Authorization Act for Fiscal Year 2013. Pub. L. No. 112-239, § 736(a) (2013).

[26]DOD reported this information in a briefing to the House and Senate Armed Services Committees in response to a provision in the John S. McCain National Defense Authorization Act for Fiscal Year 2019. Pub. L. No. 115–232, § 718(b) (2018); Office of the Under Secretary of Defense for Research and Engineering Human Systems Directorate, *FY 2019 NDAA Section 718 Medical Simulation Technology and Live Tissue Training within the Department of Defense* (Feb. 13, 2019).

briefing, DOD stated that it no longer uses animals for trauma training that involves neonatal/pediatric intubation.[27]

- Seven procedures demonstrated some added benefit from simulation training, suggesting simulation may be superior to using live tissue for introducing a new procedure to the novice learner.

Coordination among DOD entities and industry partners to develop simulations. The Army Central Simulation Committee, the Air Force Medical Modeling and Simulation Training Program, and the Navy Medical Modeling and Simulation Training managed simulation requirements and capabilities and medical simulation training needs, and also developed curricula that incorporate the use of alternatives such as simulation technologies. Each military department conducted separate efforts in medical modeling and simulation until DOD established the Defense Medical Modeling and Simulation Office in 2016. The Defense Medical Modeling and Simulation Office centralized the Army, Navy, and Air Force offices into one location where they could coordinate and share information such as resources and simulation technologies.

The Joint Program Committee-1 comprises both DOD and non-DoD medical and military technical experts. This committee plans, coordinates, and oversees a science and technology program focused on improving military training and education through medical simulation systems. The committee works with the military services and joint agencies to address requirement gaps. According to DOD officials, this joint program committee is also working with industry partners to develop an advanced modular mannequin—renamed the Modular Healthcare Simulation and Education System—that features interchangeable parts and an internal computer that can change vital signs and respond to human actions.

DOD Was Unable to Fully Demonstrate the Extent to Which It Has Made Progress in Refining, Reducing, and Replacing the Use of Animals for Trauma Training

DOD has not monitored or evaluated its progress towards achieving its objective of refining, reducing, and replacing the use of animals in RDT&E

[27]Office of the Under Secretary of Defense for Acquisition, Technology and Logistics, *Combat Casualty Care Training: An Information Brief on Three Studies Funded by the Department of Defense* (Mar. 22, 2016).

training.[28] OUSD(R&E) and DASD (HRP&O) officials told us there is no guidance or dashboard on measurable objectives or goals to monitor or evaluate DOD's progress in considering and using alternatives to refine, reduce, and replace use of animals for trauma training. DASD(HRP&O) officials told us that their office holds quarterly meetings with the Live Animal Use in Medical Education and Training working group to determine whether and why the use of animals has increased or decreased so that they can inform their leadership for informed decision making.[29] The officials said the working group is exploring why the use of animals has increased or decreased as a way to monitor and evaluate progress towards DOD's objective to reduce the use of animals in training. Officials further provided us with draft documentation from this effort. However, the draft documentation did not contain any evidence of measurable objectives or performance measures to monitor or evaluate DOD's progress.

DOD Instruction 3216.01 indicates that the department's objective is to use alternatives to animals whenever possible, if such methods produce scientifically or educationally valid or equivalent results, and cause the least pain or distress to the minimum number of animals when they must be used. Further, OUSD(R&E) is to establish a working group on animal use in DOD programs to ensure that DOD has a continued focus on refining, reducing, and replacing animal use in RDT&E and training.[30] Federal standards for internal control state that agency management should use ongoing monitoring and evaluation to have reasonable assurance that programs are operating as intended.[31] DOD has made limited attempts to put monitoring and evaluation measures in place, but

[28]In DOD Instruction 3216.01, DOD states (1) it is DOD policy that alternatives to animal use will be considered and used whenever possible to attain the objectives of DOD-sponsored RDT&E or training if such methods produce scientifically or educationally valid or equivalent results; (2) it is DOD policy that procedures will cause the least pain or distress to the minimum number of animals and be consistent with the scientific or training needs; and (3) alternatives to animal use are characterized by refinement, reduction, and replacement.

[29]According to DASD(HRP&O) officials, the working group consists of service representatives and subject matter experts from across DOD who facilitate exchange of information, needs, and requirements within their organization. The working group also looks for areas of opportunity to refine, reduce, or appropriately replace live animal use through medical modeling and simulation.

[30]DOD Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019).

[31]GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

its efforts to date have been unsuccessful because it has neither developed measurable objectives for refining, reducing and replacing animals in trauma training nor has it developed performance measures to gauge progress towards meeting those objectives.

Measurable Objectives

Federal internal control standards state that agency management should define objectives in measurable terms so that it can measure progress toward meeting those objectives. OUSD(R&E) officials told us that they are aware that the department's current efforts to evaluate progress are limited by the department not having established measurable objectives. They said that it is difficult to establish measurable objectives when they cannot predict what level of advancement simulations will achieve in the future. For example, officials said that current simulations such as mannequins, cadavers, or augmented and virtual reality lack realism to duplicate the needed senses of urgency and empathy. Because of these issues, neither can replicate the empathy and sense of urgency that results from using a live animal, according to DOD officials.

We recognize that the unpredictability of technological progress can make it difficult to develop timelines for phasing out live animals in training. However, the lack of predictability does not preclude DOD from being able to define measurable objectives for its animal use in policy, although we understand that DOD may need to revisit those objectives as technologies progress and change. By developing specific and measurable objectives, DOD could better assure Congress and other stakeholders that the department has established a baseline for making progress in refining, reducing, and replacing the use of animals for trauma training. Measurable objectives could also better enable DOD officials to target resources and make adjustments to training in response to technological developments–such as new technologies and techniques to better control bleeding.

Performance Measures

In addition to the absence of defined measurable objectives, which hampered DOD's efforts to monitor and evaluate its progress toward reducing the use of animals in trauma training, these efforts are also limited by DOD not adopting effective performance measures. Officials told us that they have used qualitative measures such as investing and developing alternative technologies to show the department's progress. However, these measures do not compare outcomes with expected

results and do not exhibit key attributes of effective performance measures that we have identified in our prior work. Specifically:

- OUSD(R&E) officials told us that they do not have defined performance measures to rely on when assessing DOD's progress in reducing the use of animals. Instead, officials said that they gauge progress by relying on qualitative measures, such as efforts to research and develop alternative technologies.[32] However, they were unable to link these inputs to expected or actual outcomes, such as incremental improvements in simulator fidelity.
- DASD(HRP&O) officials told us that the military services, including the medical training schools and training courses, provide animal and simulation use data to the office of the Assistant Secretary of Defense for Health Affairs through an annual data call. This annual data call is used to generate internal DOD reports that contain information on the component, the type of training, whether the training was approved by the IACUC, the type of animal used for training, and whether this training could be conducted without live animal use. While the data call might yield performance measures, DASD(HRP&O) officials told us that they could not demonstrate that it had been deployed and that there is no consensus within the department that it is an appropriate means of measuring progress.

Standards for Internal Control in the Federal Government call for federal program managers to use quality information to achieve program objectives and make informed decisions.[33] Our prior work has shown that performance measures provide critical information on whether a program

[32]Prior to 2007, in response to committee report direction, the Office of the Director, Defense Research and Engineering compiled and submitted fiscal year reports on the Department of Defense (DOD) Animal Care and Use Programs to the House and Senate Armed Services Committees including data by DOD component, species, types of use, and whether research or training caused the animal pain or distress. See H.R. Rep. No. 102-527, at 151-52 (1992). DOD officials said that, after submitting a final report for fiscal year 2006-2007 in fiscal year 2013, they no longer compile and report these data because doing so was overly burdensome and that animal counts can be misleading. Specifically, the officials said that demand for animal use can vary within different activities and each institution can have a different definition of what counts as "animal use."

[33]GAO-14-704G.

is succeeding in obtaining its objectives by comparing outcomes with expected results.[34]

The working group discussed capturing simulation hours and types of simulators being used in curricula, and reducing the number of hours of using live animals in training. However, they have not finalized any measures. Without clearly defined performance measures–whether qualitative, quantitative, or some combination–the department will be limited in its ability to assess the extent to which it is making progress increasing its use of alternatives to live animals in trauma training.

DOD Has Inconsistently Reviewed and Approved Animal Use Protocols for Trauma Training

DOD Component Oversight Offices Have Reviewed and Approved Protocols Inconsistently

DOD component oversight offices have inconsistently reviewed and approved trauma training protocols. Specifically, OUSD(R&E) officials and DOD component oversight offices have inconsistently taken certain actions that they also identified as not needed (such as including certain literature searches) or implemented steps that they indicated may not be applicable to trauma training (such as including statistician signatures).[35]

- **Literature search for duplication.** This literature search is performed to prevent the unnecessary duplication of previous experiments.[36] In

[34]GAO, *Social Security Disability: Additional Performance Measures and Better Cost Estimates Could Help Improve SSA's Efforts to Eliminate Its Hearings Backlog*, GAO-09-398 (Washington, D.C.: Sept. 9, 2009).

[35]The DOD component oversight offices include the U.S. Army's Animal Care and Use Review Office, the Navy's Bureau of Medicine and Surgery, the Air Force Medical Readiness Agency, and the U.S. Army Special Operations Command's Veterinarian Review Office. For the purposes of this report we refer to them as the Army, the Navy, the Air Force, and USSOCOM.

[36]The Standard Format requires that a literature search for duplication and a literature search for alternatives to painful or distressful procedures to each cite the sources searched, the date and period of search, key words used in the search, and a narrative summary of results.

general, OUSD(R&E) and the DOD component oversight offices from the Army, the Navy, the Air Force, and USSOCOM indicated that literature searches for duplication do not apply to trauma training protocols because trauma training is repetitive in nature. That is, the procedures are largely routine (e.g., for stopping hemorrhaging and for other standard trauma procedures). Nevertheless, the DOD component oversight offices included elements of literature searches for duplication in 19 of the 21 selected animal use protocols for trauma training that we reviewed.

- **Literature search for alternatives.** This literature search is performed to determine that alternatives to painful or distressful procedures were not available and discuss alternatives that were considered but not chosen.[37] DOD component oversight offices had inconsistent views on whether literature searches for alternatives to painful or distressful procedures were required for trauma training protocols. According to Army and Air Force officials, their services required literature searches for alternatives for DOD and non-DOD institutions.[38] Additionally, Navy officials stated that the Navy uses a protocol review checklist as an internal aid helpful in the component oversight office review process, although the checklists are not necessarily all-inclusive but highlight various elements within the review process, do not supersede approved protocols, and are not required by law or DOD guidance. We found the Navy checklist to be inconsistent with, and less comprehensive than, the Standard Format. For example, the checklist does not call for a narrative summary on the consideration of alternatives. All 21 animal use protocols for trauma training that we reviewed included a literature search for alternatives, including two Navy protocols for non-DOD institutions that the Navy told us were not required to be included. The Standard Format includes literature searches for alternatives as an element of an animal use protocol, but DOD guidance does not clarify whether these searches are required in trauma training protocols. Further, although OUSD(R&E) officials told us that non-DOD institutions' protocols are not required to use the Standard Format, but are required to provide the information that alternatives to painful and distressful procedures were considered, DOD guidance does not

[37]The Standard Format requires that a literature search for alternatives to painful or distressful procedures cite the sources searched, the date and period of the search, key words used in the search, and a narrative summary of results.

[38]According to USSOCOM officials, the DOD Standard Animal Use Protocol Format is used to review trauma training protocols under their purview.

expressly state this or whether such information is required in trauma training protocols.

- **Verification Signatures.** The Standard Format includes at least three signatures on the protocol cover sheet as required elements of an animal use protocol: principal investigator, either the department or division chief or the scientific review committee chairperson, and the individual performing the statistical review. All four DOD component oversight offices require signatures from a principal investigator, according to DOD component oversight offices officials. However, Army officials told us that a scientific review signature is not required as long as the principal investigator provides assurance that they consulted with a scientific reviewer. Officials from all four DOD component oversight offices told us that statisticians' signatures were not needed because statistician review was not applicable to trauma training protocols. Air Force officials told us that statisticians provide expertise in mathematical comparisons between groups and analyze experimental outcomes using statistical techniques–none of which is applicable to trauma training protocols. According to Army, Navy, and USSOCOM officials, trauma training does not involve statistical work. Instead, the Army allows the principal investigator to provide assurance in place of a statistician. However, the Standard Format includes scientific reviewer and statistician verification signatures as elements of an animal use protocol, and DOD guidance does not clarify whether these searches are required in trauma training protocols, leading to inconsistent results in how signatures were included in protocols across the military services. For the 21 animal use protocols for trauma training that we selected for review, most did not include all three verification signatures included as elements in the Standard Format (principal investigator, scientific review, statistician) on the cover sheet. However, we found that 18 of the 21 protocols we reviewed included a principal investigator signature on either the cover sheet or the assurance statement, 18 protocols included a scientific review signature, and seven included a statistician signature.

Standards for Internal Control in the Federal Government state that management should obtain relevant data from reliable internal and external sources in a timely manner based on the identified information requirements and that relevant data should have a logical connection with, or bearing upon, the identified information requirements. In this instance, OUSD(R&E) officials told us that DOD Instruction 3216.01 is the governing guidance for reviewing and approving protocols, including for trauma training. It states that DOD components will submit all proposed RDT&E or training to the IACUC using either the Standard Format

prescribed in the Army Regulation 40-33 or in a pre-approved alternative format with comparable detail approved by OUSD(R&E).[39]

The Standard Format includes literature searches for duplication and for alternatives to painful or distressful procedures as elements of an animal use protocol, with fields that include the literature sources searched, the date and period of the search, key words used in the search, and a narrative summary of the results. The Standard Format includes at least three signatures on the protocol cover sheet as required elements of an animal use protocol: that is, signatures from the principal investigator, either the department or division chief or the scientific review committee chairperson, and the individual performing the statistical review.[40] For example, the scientific reviewer signature verifies that the animal use proposal received appropriate scientific peer-review and is consistent with good scientific practice.[41]

OUSD(R&E) and DOD component oversight officials have applied the Standard Format's elements inconsistently because DOD had not clarified which provisions in its guidance specifically apply to animal use protocols for trauma training or what elements should be included in protocol documentation. In addition, neither DOD Instruction 3216.01 nor

[39]DOD Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019); Army Regulation 40-33, *The Care and Use of Laboratory Animals in DOD Programs*, Appx. C, "DOD Animal Use Protocol Format" (Feb. 16, 2005). The instruction also states, as previously noted, that although non-DOD institutions are not required to use the Standard Format, documents submitted to the component oversight office will provide all pertinent information and level of detail regarding animal care contained in the Standard Format.

[40]Army Regulation 40-33, *The Care and Use of Laboratory Animals in DOD Programs*, Appx. C, "DOD Animal Use Protocol Format" (Feb. 16, 2005). Additionally, an attending veterinarian signature is listed as one of four signatures on the Standard Format cover sheet, but the signature is not one of the three signatures the Standard Format states are required. The Standard Format states that the Animal Welfare Act's implementing regulations require that an attending veterinarian must be consulted in the planning of procedures/manipulations that may cause more than slight or momentary pain or distress, even if relieved by anesthetics or analgesics.

[41]In addition, at the end of the Standard Format protocol, the principal investigator makes several written assurances that alternatives to painful procedures were considered, among other things. For instance, the principal investigator assures that the proposed animal use protocol has received appropriate scientific peer review and is consistent with good scientific practice. The principal investigator also assures that they have consulted with a qualified individual who evaluated the experimental design with respect to the statistical analysis, and that the minimum number of animals needed for scientific validity will be used. See Army Regulation 40-33.

Army Regulation 40-33 provides any specific language or differentiations on trauma training.

- **Applicable guidance.** In June 2019 the Defense Health Agency publicly released a multi-service regulation that stated it canceled and replaced Army Regulation 40-33. Although OUSD(R&E) officials told us this regulation was rescinded because not all changes were reviewed and several component oversight offices did not fully agree to the regulation, we found that five USSOCOM trauma training protocols and three Navy memorandums approving trauma training protocols cited the multi-service regulation as applicable instead of Army Regulation 40-33. OUSD(R&E) officials told us that they plan to update the Standard Format as a separate document from a new or updated multi-service regulation, but they did not provide a date by which the regulation or updated Standard Format would be released.
- **Elements in protocol documentation.** OUSD(R&E) officials told us that they issued a memorandum in 2017 clarifying guidance regarding the implementation of DOD Instruction 3216.01.[42] In this memorandum, OUSD(R&E) officials approved an alternative format for protocol submission called the Electronic Institutional Review Board Animal Module. However, OUSD(R&E) officials told us that this module is no longer used and OUSD(R&E) holds no data records of it. According to OUSD(R&E) officials, the 2017 memorandum, in conjunction with DOD guidance, also provided flexibility for each DOD IACUC and component oversight office to determine what information is required in animal use protocols, including through checklists each component oversight office develops. However, we determined that DOD Instruction 3216.01, Army Regulation 40-33, the memorandum, and the component oversight office checklists do not specify what types of information are required for trauma training protocols or any other type of training. OUSD(R&E) officials told us that because of the flexibility of the 2017 memorandum, signatures were not present in some cases because they were not required in the protocol documentation for trauma training. They noted that this was appropriate because the IACUC would not approve a protocol without having seen signatures somewhere in the protocol documentation.

OUSD(R&E) and other officials acknowledged that there was some inconsistent use of the animal use protocol guidance and different application of which Standard Format elements need to be included in

[42]Director, Human Performance, Training, and BioSystems Directorate Memorandum, *Formats for Animal Use Protocol Submissions* (July 20, 2017).

guidance, such as those pertaining to statistician's signatures or literature search elements. However, they told us that these would not negatively affect animal welfare or well-being because, for example, the objective and goals of trauma training activities did not depend on statistical reviews to determine the minimum number of animals needed to achieve training objectives. Moreover, they stated that the staff developing protocols are trustworthy and have expertise in animal care. Also, OUSD(R&E) officials said that the flexibility authorized by DOD's guidance is preferred, so that each IACUC can make its own decisions when reviewing and approving protocols. Officials further stated that any clarification of guidance would be a documentation exercise that would not result in improvements to animal welfare or training.

We recognize that DOD benefits from an expert and professional workforce that strives to develop sound training protocols. However, this workforce has, at times, based its development of training protocols on guidance that was not fully reviewed within DOD, and it lacks clarity on the required elements for proposed animal use protocols for trauma training, as demonstrated by the inconsistent application in the protocols we reviewed. The Standard Format contains these elements because they help ensure DOD's use of animals in research and training is as minimal as possible. For example, the literature searches for alternatives to painful or distressful procedures element ensures that the principal investigator provides a narrative description of the methods and sources they used to determine that alternatives to a painful procedure were not available. Similarly, the signature and assurance statement elements provide assurances that the protocol was reviewed by subject matter experts and help ensure that the protocol is consistent with good scientific practice, has considered alternatives, and addresses animal welfare, among other things.

By clarifying which (1) current guidance governs animal use protocols for trauma training; and (2) elements in that guidance, such as for literature searches and verification signatures, apply or do not apply to animal use protocols for trauma training, OUSD(R&E) and the DOD component oversight offices can help ensure that all required provisions for animal use and care are being followed. Such clarification in guidance would provide IACUCs and the component oversight offices clear direction on what protocol elements should be included in trauma training protocols. Moreover, although OUSD(R&E) officials stressed that flexibility is important, clarifying which guidance governs animal use and which elements apply to trauma training protocols could help to forestall situations where components inadvertently rely on draft or outdated

guidance, or inconsistently review and approve trauma training protocols, as happened previously.

Conclusions

Through DOD trauma training, military first responders, including combat medics learn complex combat trauma care procedures to develop the skills to treat wounded personnel from initial point of injury through evacuation in chaotic and hostile battlefield environments.

This important training relies on an incremental approach that involves the use of live animals in some instances. DOD seeks to minimize the use of animals to the extent possible, but is limited in its ability to oversee this effort due to vaguely defined objectives and a lack of performance measures.

By developing objectives in specific and measurable terms, and establishing and using performance measures, DOD could better assure Congress and other stakeholders that the department is making progress in refining, reducing, and replacing the use of animals for trauma training. DOD could also better target training resources so that they are expended on the tools that most effectively teach military personnel trauma response skills and ensure that DOD is taking advantage of the most current training technologies.

Moreover, while DOD has a process in place to review the justification and appropriate use of animals for trauma training, DOD component oversight offices have sometimes inconsistently reviewed and approved trauma training protocols. The lack of clarity regarding which guidance governs animal use protocols for trauma training and the elements that protocol packages need to include increases the risk that DOD's policies and procedures may not be consistently applied across the department as intended. By clarifying the guidance and the data elements that apply to trauma training protocols, DOD will be better positioned to ensure that it is consistently applying its animal use policies for trauma training, such as considering alternatives to the use of animals whenever possible.

Recommendations for Executive Action

The Secretary of Defense should ensure that the Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and

Oversight, in coordination with the Under Secretary of Defense for Research and Engineering and the military services, develops objectives, in specific and measurable terms, for monitoring the department's progress in refining, reducing, and replacing animal use in trauma training. (Recommendation 1)

Once DOD has developed measurable objectives, the Secretary of Defense should ensure that the Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight, in coordination with the Under Secretary of Defense for Research and Engineering and the military services, develops and uses performance measures—including determining which data need to be collected to monitor the department's progress in refining, reducing, and replacing animal use in trauma training. (Recommendation 2)

The Secretary of Defense should ensure that the Under Secretary of Defense for Research and Engineering ensures that the components use fully approved guidance for animal use protocols for trauma training and clarifies which protocol elements, such as literature searches and verification signatures, apply to animal use protocols for trauma training. (Recommendation 3)

Agency Comments and Our Evaluation

We provided a draft of this report to DOD for review and comment. In written comments, DOD concurred with all three recommendations. In addition, DOD provided technical comments, which we incorporated as appropriate. DOD's comments are reprinted in their entirety in appendix III.

We are sending copies of this report to the appropriate congressional committees, the Secretary of Defense, and other interested parties. In addition, the report is available at no charge on the GAO website at https://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-5431 or russellc@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found at the end of this report. GAO staff who made key contributions to this report are listed in appendix IV.

Cary B. Russell
Director, Defense Capabilities and Management

List of Requesters

The Honorable Jack Reed
Chairman
Committee on Armed Services
United States Senate

The Honorable Richard Blumenthal
United States Senate

The Honorable Cory A. Booker
United States Senate

The Honorable Sherrod Brown
United States Senate

The Honorable Maria Cantwell
United States Senate

The Honorable Tammy Duckworth
United States Senate

The Honorable Mazie K. Hirono
United States Senate

The Honorable Patrick Leahy
United States Senate

The Honorable Robert Menendez
United States Senate

The Honorable Gary C. Peters
United States Senate

The Honorable Jacky Rosen
United States Senate

The Honorable Jeanne Shaheen
United States Senate

The Honorable Chris Van Hollen
United States Senate

The Honorable Sheldon Whitehouse
United States Senate

The Honorable Ron Wyden
United States Senate

Appendix I: Objectives, Scope, and Methodology

In this report, we evaluate the extent to which the Department of Defense (DOD) has (1) made progress in its efforts to refine, reduce, and replace the use of animals for trauma training and (2) consistently applied guidance for reviewing and approving trauma training protocols. For both objectives, we obtained documentation from and conducted interviews with cognizant officials and subject matter experts both within and outside DOD. Specifically:

- Office of the Assistant Secretary of Defense for Health Affairs
  - Deputy Assistant Secretary of Defense (DASD) for Health Readiness Policy and Oversight (HRP&O)
- Office of the Under Secretary of Defense for Research and Engineering (OUSD(R&E))
- Defense Health Agency
  - Defense Medical Modeling and Simulation Office
  - Joint Program Committee–1
- U.S. Department of the Army
  - Animal Care and Use Review Office
  - Walter Reed Army Institute of Research
  - U.S. Army Medical Research Institute of Infectious Diseases
  - Strategic Trauma Readiness Center of San Antonio
  - Central Simulation Committee
  - Army Contracting Command
- U.S. Department of the Navy
  - Bureau of Medicine and Surgery
  - Navy Medical Modeling and Simulation Training
- U.S. Department of the Air Force
  - Air Force Medical Readiness Agency
  - Air Force 59th Medical Wing

    - Air Force 355th Contracting Squadron
    - Air Force Medical Modeling and Simulation Training Program
- U.S. Special Operations Command (USSOCOM)
- U.S. Department of Agriculture
    - Animal and Plant Health Inspection Service
- Association for Assessment and Accreditation of Laboratory Animal Care International

For objective one, we reviewed DOD documentation, including DOD Instruction 3216.01 on the care and use of animals for research, testing, and training.[1] We also reviewed DOD documentation pertaining to efforts to research, develop, consider, and use alternatives in place of animals for trauma training. In completing this analysis we collected documentation and interviewed officials on

- the structure and role of DOD entities that oversee and support efforts to develop alternatives to animals for research, development, testing, and evaluation (RDT&E) and training, including trauma training;
- the military departments' and USSOCOM's trauma training curricula for military first responders, including combat medics; and
- OUSD(R&E) and DASD Health Readiness Policy and Oversight (HRP&O) official determinations on the extent to which DOD had efforts underway to demonstrate that it had considered and used alternatives to refine, reduce, and replace the use of animals for trauma training.

We compared the efforts described with DOD guidance and determined that the control activities, quality information and monitoring components of *Standards for Internal Control in the Federal Government* were significant to this objective, along with the associated underlying principles that management should

- define objectives in measurable terms so that progress toward those objectives can be assessed;

[1]Department of Defense Instruction 3216.01, *Use of Animals in DOD Conducted and Supported Research and Training* (March 20, 2019) establishes policy and assigns responsibilities for the use of animals in DOD conducted and supported research and training. This includes continuing efforts to refine, reduce, and replace the use of animals in RDT&E and training, including for trauma training.

- design a process that uses the entity's objectives to identify the information requirements and relevant data needed to achieve the objectives;
- use quality information to achieve the entity's objectives; and
- establish and operate monitoring activities as it seeks to achieve its objectives.[2]

We assessed DOD's efforts to monitor progress in refining, reducing, and replacing the use of animals for trauma training against these internal control standards. We also assessed DOD's efforts to consider and use alternatives in trauma training against DOD guidance.[3]

For objective two, we reviewed the two-level protocol review process used by DOD component oversight offices to approve animal use protocols for trauma training. We also analyzed DOD's guidance for animal use protocols. We did this by comparing the requirements established in multiple documents including DOD Instruction 3216.01, Army Regulation 40-33, and a 2017 Office of the Assistant Secretary of Defense for Research and Engineering memorandum.[4] We compared the DOD instruction and Army Regulation guidance with the OUSD(R&E) and DOD component oversight offices' approval and review process. Regarding the DOD component oversight office processes, we conducted interviews with officials from the Army's Animal Care and Use Review Office, the Navy's Bureau of Medicine and Surgery, the Air Force Medical Readiness Agency, and the U.S. Army's Special Operations Command. We also assessed the military departments' and U.S. Special Operations Command's protocol and review process against DOD guidance. We determined that the quality information component of the *Standards for Internal Control in the Federal Government* was significant to this objective, along with the associated underlying principle that management should obtain relevant data from reliable internal and external sources in

[2]GAO, *Standards for Internal Control in the Federal Government*, GAO-14-704G (Washington, D.C.: September 2014).

[3]DOD Instruction 3216.01; Army Regulation 40-33, Secretary of the Navy Instruction 3900.38C, Air Force Manual 40-401, Defense Advanced Research Projects Agency Instruction 18, Uniformed Services University of Health Sciences Instruction 3203, *The Care and Use of Laboratory Animals in DOD Programs* (Feb. 16, 2005) ("Army Regulation").

[4]DOD Instruction 3216.01; Army Regulation 40-33; Director, Human Performance, Training, and BioSystems Directorate Memorandum, *Formats for Animal Use Protocol Submissions* (July 20, 2017).

a timely manner based on the identified information requirements and that relevant data have a logical connection with, or bearing upon, the identified information requirements.

Finally, we compared the guidance with those component oversight offices' implementation of 21 animal use protocols for trauma training that we selected for our review. We selected 21 of the 40 current fiscal year 2018–2020 animal use protocols for trauma training: five from the Army, five from the Navy, six from the Air Force, and five from USSOCOM.[5] We selected the protocols to represent each DOD component and because they constituted the most current ones as identified by DOD, considering that we began our audit work in fiscal year 2020 and that protocols remain active for 3 years. We excluded all protocols that pertained to graduate medical education as that does not directly relate to trauma and combat training for the battlefield.

To understand DOD's process for contracting for trauma training with non-DOD institutions, we requested and received a sample of contracts from the Army, the Navy, and the Air Force related to the protocols we reviewed. In some cases, the military departments contract with non-federal institutions to carry out trauma training for DOD service members. DOD officials told us that they contract for this training because qualified contractors can provide cost-effective and beneficial training requiring live animals or teach methods with simulation and other alternatives. According to OUSD(R&E) officials, contractors provide IACUC-approved animal use protocols to DOD in order to become qualified to compete for DOD contracts to provide training (and other) services requiring live animals to be used.[6] DOD Instruction 3216.01 and DOD acquisition regulations require that contracts for DOD-sponsored RDT&E or training contain Defense Federal Acquisition Regulation Supplement clause 252.235-7002, "Animal Welfare," which prescribes certain rules such

[5]According to DOD animal use oversight officials, protocols using animals for trauma training account for a small number of the overall number of animal use protocols. For example, Navy officials told us that in fiscal year 2020 their component oversight office managed hundreds of active protocols, eight of which were related to trauma training using animals.

[6]According to the OUSD(R&E) officials, these contractors are solicited, evaluated, and selected to provide trauma training involving animals in the same manner as DOD solicits and competes its other requirements, with the exception that, to be eligible to compete for an award, contractors must demonstrate that they already (1) have an IACUC-approved protocol and (2) have been approved by a component oversight office to perform these types of services.

contractors must adhere to.[7] For instance, non-DOD institutions conducting trauma training must be registered with the U.S. Department of Agriculture's Animal and Plant Health Inspection Service.[8]

[7]DOD Instruction 3216.01; Defense Federal Acquisition Regulation Supplement, 48 C.F.R. § 235.072(a) (2021). Additionally, clause 252.235-7002 requires a contractor to agree that its care and use of animals will conform with the pertinent laws, APHIS regulations, and DOD policies and procedures including DOD Instruction 3216.01 and Army Regulation 40-33, including having its proposed animal use approved by a DOD component oversight office.

[8]Defense Federal Acquisition Regulation Supplement, 48 C.F.R. § 252.235-7002(a)(1) (2021); *see* 7 U.S.C. § 2136; 9 C.F.R. § 2.30(a)(1) (2021); DOD Instruction 3216.01.

Appendix II: The DOD Standard Animal Use Protocol Format

DOD Animal Use Protocol Format

C–1. Requirements

All DOD animal use protocols must use the format shown in this appendix. This protocol format includes requirements of the Animal Welfare Act Regulations, the Guide, and other applicable Federal regulations and DOD directives.

C–2. Protocol cover sheet

Before the protocol is submitted for IACUC review, at least three signatures are required on the protocol cover sheet (fig C–1). They must include those of the Principal Investigator (P.I.); either the department or division chief or the scientific review committee chairperson; and the individual performing the statistical review.

I. Name of Facility

II. Proposal Number

III. Title

IV. Principal Investigator(s)/Division/Phone/E-mail

a. Printed Name (First Name, MI, Last Name); Title; Division

b. Signature; Date (YYYYMMDD); Phone, Fax

V. Scientific/Division Review/Phone/E-mail

a. Printed Name (First Name, MI, Last Name); Title; Division

b. Signature; Date (YYYYMMDD); Phone, Fax

VI. Statistical Review/Division/Phone/E-mail

a. Printed Name (First Name, MI, Last Name); Title; Division

b. Signature; Date (YYYYMMDD); Phone, Fax

VII. Attending Veterinarian/Division/Phone/E-mail

a. Printed Name (First Name, MI, Last Name); Title; Division

b. Signature; Date (YYYYMMDD); Phone, Fax

Figure C–1. DOD animal use protocol cover sheet

a. Scientific/division review. This signature verifies that the animal use proposal received appropriate scientific peer review and is consistent with good scientific practice.

b. Attending veterinarian. The Animal Welfare Act Regulations require that an attending veterinarian must be consulted in the planning of procedures/manipulations that may cause more than slight or momentary pain or distress, even if relieved by anesthetics or analgesics.

c. Statistical review. A person knowledgeable in biostatistics is required to review all proposals to ensure that the number of animals used is appropriate to obtain sufficient data and/or is not excessive, and the statistical design is appropriate for the intent of the study.

C–3. DOD animal use protocol format

a. The format shown in figure C–2 is designed to be used with several word-processing programs on a personal computer as a "fill-in-the-blank" type of document. It is available electronically through the appropriate DOD component oversight office listed in appendix B. Each paragraph and subparagraph in the format must have a response. Title headings do not require a response. Portions of the protocol format that are not applicable will be marked "N/A." There are no space limitations for the responses. Pertinent standing operating procedures or similar documents that are readily available to the IACUC may be referenced to assist in the description of specific procedures.

PROTOCOL TITLE
PRINCIPAL INVESTIGATOR(S)
CO-INVESTIGATOR(S)
I. NON-TECHNICAL SYNOPSIS
II. BACKGROUND
II.1. Background
II.2. Literature Search for Duplication
II.2.1. Literature Source(s) Searched
II.2.2. Date of Search
II.2.3. Period of Search
II.2.4. Key Words of Search
II.2.5. Results of Search
III. OBJECTIVE/HYPOTHESIS
IV. MILITARY RELEVANCE
V. MATERIALS AND METHODS
V.1. Experimental Design and General Procedures
V.1.1. Experiment 1
V.1.2. Experiment 2
V.2. Data Analysis
V.3. Laboratory Animals Required and Justification
V.3.1. Non-animal Alternatives Considered
V.3.2. Animal Model and Species Justification
V.3.3. Laboratory Animals
V.3.3.1. Genus and Species
V.3.3.2. Strain/Stock
V.3.3.3. Source/Vendor
V.3.3.4. Age
V.3.3.5. Weight
V.3.3.6. Sex
V.3.3.7. Special Considerations
V.3.4. Number of Animals Required (By Species)
V.3.5. Refinement, Reduction, Replacement
V.3.5.1. Refinement
V.3.5.2. Reduction
V.3.5.3. Replacement
V.4. Technical Methods
V.4.1. Pain/Distress Assessment
V.4.1.1. APHIS Form 7023 Information (See attending veterinarian for assistance)
V.4.1.1.1. Number of animals
V.4.1.1.1.1. Column C: ___(Animal #)
V.4.1.1.1.2. Column D: ___(Animal #)
V.4.1.1.1.3. Column E: ___(Animal #)
V.4.1.2. Pain Relief/Prevention
V.4.1.2.1. Anesthesia/Analgesia/Tranquilization
V.4.1.2.2. Pre- and Post-procedural Provisions
V.4.1.2.3. Paralytics
V.4.1.3. Literature Search for Alternatives to Painful or Distressful Procedures
V.4.1.3.1. Sources Searched
V.4.1.3.2. Date of Search
V.4.1.3.3. Period of Search
V.4.1.3.4. Key Words of Search
V.4.1.3.5. Results of Search
V.4.1.4. Unalleviated Painful/Distressful Procedure Justification
V.4.2. Prolonged Restraint
V.4.3. Surgery

Figure C–2. DOD animal use protocol format

V.4.3.1. Pre-surgical Provisions
V.4.3.2. Procedure
V.4.3.3. Post-surgical Provisions
V.4.3.4. Location
V.4.3.5. Surgeon
V.4.3.6. Multiple Major Survival Operative Procedures
V.4.3.6.1. Procedures
V.4.3.6.2. Scientific Justification
V.4.4. Animal Manipulations
V.4.4.1. Injections
V.4.4.2. Biosamples
V.4.4.3. Adjuvants
V.4.4.4. Monoclonal Antibody (MAbs) Production
V.4.4.5. Animal Identification
V.4.4.6. Behavioral Studies
V.4.4.7. Other Procedures
V.4.4.8. Tissue Sharing
V.4.5. Study Endpoint
V.4.6. Euthanasia
V.5. Veterinary Care
V.5.1. Husbandry Considerations
V.5.1.1. Study Room
V.5.1.2. Special Husbandry Provisions
V.5.1.3. Exceptions
V.5.2. Veterinary Medical Care
V.5.2.1. Routine Veterinary Medical Care
V.5.2.2. Emergency Veterinary Medical Care
V.5.3. Environmental Enrichment
V.5.3.1. Enrichment Strategy
V.5.3.2. Enrichment Restriction
VI. STUDY PERSONNEL QUALIFICATIONS AND TRAINING
VII. BIOHAZARD/SAFETY:
VIII. ENCLOSURES: Enclosures such as IACUC policies on adjuvants, monoclonal antibody production, tissue sharing, food and/or water restriction, prolonged restraint, pathology addenda, and pain assessment criteria may be included at the discretion of the P.I. unless directed by the IACUC.

IX. ASSURANCES: The law specifically requires several written assurances from the Principal Investigator. Please read and sign the assurances as indicated.

As the Principal Investigator on this protocol, I acknowledge my responsibilities and provide assurances for the following:

A. Animal Use: The animals authorized for use in this protocol will be used only in the activities and in the manner described herein, unless a modification is specifically approved by the IACUC prior to its implementation.

B. Duplication of Effort: I have made every effort to ensure that this protocol is not an unnecessary duplication of previous experiments.

C. Statistical Assurance: I assure that I have consulted with a qualified individual who evaluated the experimental design with respect to the statistical analysis, and that the minimum number of animals needed for scientific validity will be used.

D. Biohazard/Safety: I have taken into consideration and made the proper coordinations regarding all applicable rules and regulations concerning radiation protection, biosafety, recombinant issues, and so forth, in the preparation of this protocol.

Figure C–2. DOD animal use protocol format—Continued

E. Training: I verify that the personnel performing the animal procedures/manipulations/observations described in this protocol are technically competent and have been properly trained to ensure that no unnecessary pain or distress will be caused to the animals as a result of the procedures/manipulations.

F. Responsibility: I acknowledge the inherent moral, ethical and administrative obligations associated with the performance of this animal use protocol, and I assure that all individuals associated with this project will demonstrate a concern for the health, comfort, welfare, and well-being of the research animals. Additionally, I pledge to conduct this study in the spirit of the fourth "R," namely "Responsibility," which the DOD has embraced for implementing animal use alternatives where feasible and conducting humane and lawful research.

G. Scientific Review: This proposed animal use protocol has received appropriate peer scientific review and is consistent with good scientific research practice.

H. Painful Procedures: (A signature for this assurance is required by the Principal Investigator if the research being conducted has the potential to cause more than momentary or slight pain or distress even if an anesthetic or analgesic is used to relieve the pain and/or distress.)

I am conducting biomedical experiments, which may potentially cause more than momentary or slight pain or distress to animals. This potential pain and/or distress WILL or WILL NOT (circle one or both, if applicable) be relieved with the use of anesthetics, analgesics, and/or tranquilizers. I have considered alternatives to such procedures; however, I have determined that alternative procedures are not available to accomplish the objectives of this proposed experiment.

(PRINT) First Name, MI, Last Name of Principal Investigator

Signature Date (YYYYMMMDD)

Figure C–2. DOD animal use protocol format—Continued

b. Some information may be added to the format to meet local needs. However, all labeled paragraphs and subparagraphs will remain in the same relative order. The added information will be similar or complementary to the information requested. Other types of requirements specific to a given Service, command, or locale (such as budgeting information, local coordinating requirements, or specific scientific review requirements, and so forth) can be added by placing them in front or behind the standard format.

C–4. Protocol format with completion aids

The format shown in figure C–3 is the same protocol format as in figure C–2. Explanations have been added to aid in completing the protocol proposal.

PROTOCOL TITLE: Title must include species of animal(s) used in research.

PRINCIPAL INVESTIGATOR(S)
CO-INVESTIGATOR(S)

I. NON-TECHNICAL SYNOPSIS: Provide a brief, narrative description of the proposal that is easily understood by a high school graduate. Include animal use in your description. (NOTE: This information may be used to complete the DOD Annual Report to Congress.)

II. BACKGROUND

II.1. Background: Include a brief statement of the requirement or need for the information being sought. Lengthy explanations are not required. Typically, the literature or the experience that led to the proposal will be briefly reviewed, references cited, and a description of the general approach will be provided.

II.2. Literature Search for Duplication: This search must be performed to prevent unnecessary duplication of previous experiments. A search of the Biomedical Research Database (BRD) is required. In addition, a search of EITHER the Federal Research in Progress (FEDRIP) OR the Computer Retrieval of Information of Scientific Projects (CRISP) database is required. Requirements for additional searches are at the discretion of the IACUC.

II.2.1. Literature Source(s) Searched

II.2.2. Date of Search

II.2.3. Period of Search

II.2.4. Key Words of Search

II.2.5. Results of Search: Provide a narrative description of the results of the literature search.

III. OBJECTIVE/HYPOTHESIS: State the objective of this protocol or the hypothesis to be accepted or rejected. (NOTE: This information will be used to complete the DOD Annual Report to Congress.)

IV. MILITARY RELEVANCE: Provide a brief and succinct military justification for the research with regard to military needs and mission requirements. If applicable, state the Science and Technology Objective (STO) that this work supports.

V. MATERIALS AND METHODS

V.1. Experimental Design and General Procedures: This section includes an explanation of experimental design. Technical methodology need not be described in this section, rather, it should be described under paragraph V.4, Technical Methods. Provide a complete description of the proposed use of animals to include a summary table of the experimental groups. Succinctly outline the formal scientific plan and direction of experimentation. If several experiments or sequential studies are to be included in the protocol, describe the experimental design of each separate experiment in sub-parts to this section. The length and detail required in this section depends largely on the complexity of the study. A clearly understandable description of the numbers of animals and their distribution into experimental groups is essential. The number requested must equal the minimum number required to complete the study yet be sufficient to yield meaningful results. The minimum number includes animals necessary for controls or technique development, and so forth. Inclusion of a summary table or flow chart showing the distribution of animals by experimental group is highly recommended. The total number of animals required for the study is listed in section V.3.4.

V.1.1. Experiment 1

Figure C–3. DOD animal use protocol format with completion aids

V.1.2. Experiment 2

V.2. Data Analysis: List the statistical test(s) planned or describe the strategy intended to evaluate the data. Describe the statistical methodology used to determine group size and total number of animals. A power-based assessment of the sample size is the preferable method of determining the minimum number that is likely to yield significant results with given alpha and beta errors, estimated effect size and expected variability. Be certain to include animals necessary for controls or technique development, and so forth.

V.3. Laboratory Animals Required and Justification

V.3.1. Non-animal Alternatives Considered: State all non-animal alternatives (for example, computer modeling, in vitro cell culture work) that were considered. Explain why animals are needed.

V.3.2. Animal Model and Species Justification: Provide a scientific justification for the choice of animal model(s). What physiological and morphological characteristics does this animal possess that make it the best possible model? If less sentient (invertebrate versus vertebrate) animal models were considered but not chosen, explain why.

V.3.3. Laboratory Animals

V.3.3.1. Genus and Species

V.3.3.2. Strain/Stock: If inbred or specialized animals are required, use proper terminology. (See the attending veterinarian for assistance.)

V.3.3.3. Source/Vendor: Provide a preferred source for the animals. Animals will be legally obtained from suppliers licensed by the U.S. Department of Agriculture (USDA) in accordance with Code of Federal Regulations, Title 9, Animals and Animal Products, Chapter 1, Subchapter A, Animal Welfare, Parts 1, 2, and 3. (See the attending veterinarian for assistance.)

V.3.3.4. Age

V.3.3.5. Weight

V.3.3.6. Sex

V.3.3.7. Special Considerations: List specialized requirements for animals here (for example, simian immunodeficiency virus or herpes antibody free, Pasteurella free, and so forth).

V.3.4. Number of Animals Required (By Species): The number of animals stated here must correspond exactly to that described in section V.1. If, during the completion of the protocol, additional animals are needed owing to technical or unavoidable circumstances, or to exploit a serendipitous finding, follow IACUC procedures for requesting approval of additional animals.

V.3.5. Refinement, Reduction, Replacement (3 Rs): Investigators are required to consider the 3 Rs when preparing an animal use research protocol. In the paragraphs below, describe all provisions in this protocol that refine, reduce, or replace the use of animals. Discuss what provisions were considered and why they were not chosen. If N/A is used, explain why.

V.3.5.1. Refinement: Procedures or measures taken to eliminate or minimize pain or distress in the animal(s) or enhance animal well-being. Examples of refinement include but are not limited to the use of analgesia to decrease pain or distress, the use of remote telemetry, which decreases the distress of restraint, or the use of adjusted early experimental endpoints. In addition to listing refinements, list

Figure C–3. DOD animal use protocol format with completion aids—Continued

refinement alternatives that would allow you to meet your scientific objectives and were considered but not adopted. Explain why they were not adopted.

V.3.5.2. Reduction: Procedures or measures taken to reduce the number of animals used. Examples of reduction include but are not limited to the use of shared or historical control groups, preliminary screening in non-animal systems, and innovative statistical packages. In addition to listing reductions that will be used, list reduction alternatives that would allow you to meet your scientific objectives and were considered but not adopted. Explain why they were not adopted.

V.3.5.3. Replacement: Procedures or measures that eliminate the use of animals. Examples of replacements include but are not limited to the use of non-animal models or less sentient animal species. In addition to listing replacements that will be used, also list replacement alternatives that would allow you to meet your scientific objectives and were considered but not adopted. Explain why they were not adopted.

V.4. Technical Methods: This information must be presented in sufficient detail, documented or referenced, so that the IACUC can adequately review the procedure, obtain a clear understanding of what is to be done and how the animals will be handled, and make a reasonable determination as to whether this proposed use of laboratory animals is in compliance with DOD regulations, guidelines, and Federal law.

V.4.1. Pain/Distress Assessment: The law defines a painful procedure as one that would "reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied; that is, pain in excess of that caused by injections or other minor procedures." If a procedure may involve pain or distress, even if relieved by anesthetics or analgesics, the P.I. must consult with the attending veterinarian.

V.4.1.1. APHIS Form 7023 Information: (See your attending veterinarian for assistance.) The protocol must contain an estimate of the number of animals that will be counted in columns C, D, and E of the APHIS Form 7023, Annual Report of Research Facility. Columns C, D and E represent specific pain categories. (See below paragraphs, V.4.1.1.1.1.-3.) The animal should be listed in the column corresponding to the most painful or distressful procedure experienced by the animal. It is possible for one protocol to have animals listed in several columns. For instance, control animals may be placed in Column C while experimental animals may be placed in Column D, depending upon the nature of the protocol. Reflect use of more than one species of animals in a duplicate table. The total numbers reflected in these three columns will add up to the number of animals requested for the entire protocol in paragraph V.3.4.

V.4.1.1.1. Number of Animals

V.4.1.1.1.1. Column C: _(animal #)
Examples of research procedures/manipulations that would require an animal to be placed in Column C are studies involving not more than slight or momentary pain and/or distress in a human being to which that procedure is applied.

V.4.1.1.1.2. Column D: _(animal #)
Examples of procedures/manipulations that would require an animal to be placed in Column D are procedures where anesthesia or analgesia will be administered to avoid or effectively relieve pain or distress. General anesthesia given for surgical procedures, or the use of analgesia or anti-inflammatory agents are examples of this category.

V.4.1.1.1.3. Column E: _(animal #)
Examples of procedures/manipulations that would require an animal to be placed in Column E are procedures in which alleviation of pain or distress are contraindicated for a scientifically justifiable reason such as the experimental results are likely to be confounded if drugs relieving pain or distress were

Figure C–3. DOD animal use protocol format with completion aids—Continued

administered. Detailed justification for putting animals into this category is required below in paragraph V.4.1.4.

V.4.1.2. Pain Relief/Prevention

V.4.1.2.1. Anesthesia/Analgesia/Tranquilization: Describe the methods or strategies planned to effectively relieve or prevent pain or distress if the study will cause more than slight or momentary pain or distress. If pain/distress relief/prevention is planned, specify agents to be used and when these agents will be given (pre-emptive or post-procedural). Provide agent, dosage, and frequency of administration.

V.4.1.2.2. Pre- and Post-procedural Provisions: Describe the provisions for both pre- and post-procedural care, including provisions for post-procedural observations and frequency of observations. (Information concerning pre- and post-surgical care should be listed in paragraphs V.4.3.1 and V.4.3.3). If analgesics are used for pain/distress relief, provide the frequency of administration, observational criteria utilized to determine if animals are experiencing pain or distress, and the location for the post–procedural care.

V.4.1.2.3. Paralytics: The use of paralytic agents without anesthesia is prohibited. Describe the monitoring method that will be used to ensure adequate depth of anesthesia while the animal is under the influence of the paralytic agent.

V.4.1.3. Literature Search for Alternatives to Painful or Distressful Procedures: Respond N/A if the animals will experience not more than momentary or slight pain or distress and are placed in column C of APHIS Form 7023. (See paragraph V.4.1.1.)

V.4.1.3.1. Source(s) Searched: Examples are AGRICOLA, MEDLINE, BIOSIS, Altweb, and so forth.

V.4.1.3.2. Date of Search

V.4.1.3.3. Period of Search

V.4.1.3.4. Key Words of Search: Examples are pain, surgery, alternatives, LD 50, analgesia, anesthesia, death as an endpoint, distress, species of animal(s) to be used, name of painful or distressful experimental procedure, and so forth.

V.4.1.3.5. Results of Search: Provide a narrative summary of the results of the literature search for alternatives. The Animal Welfare Act specifically states that the P.I. must provide a narrative description of the methods and sources, e.g., the Altweb (Johns Hopkins Center for Alternatives to Animal Testing), MEDLINE, Life Sciences Abstracts, AGRICOLA, and BIOSIS) that he/she used to determine that alternatives to the painful procedure were not available. Discuss alternatives (those that would meet your scientific objectives) considered but not chosen. The alternatives literature search MUST be performed even when animals are placed in Column D and the pain or distress is alleviated through the use of analgesics or anesthetics.

V.4.1.4. Unalleviated Painful/Distressful Procedure Justification: Procedures that cause more than slight or momentary pain or distress that is not alleviated through the effective use of anesthetics or analgesics must be justified on a scientific basis in writing by the P.I. This paragraph must be completed if there are ANY animals in this protocol that will experience unalleviated pain or distress.

V.4.2. Prolonged Restraint: Describe (period of restraint, method, and timing of animal observations, habituation/training of animal to restraint device) and justify in detail any prolonged restraint greater than 12 hours for nonhuman primates or in accordance with IACUC policy for other species. Examples of restraint methods are primate chairs, restraint boards, metabolism cages, and so forth. This section is not intended for short-term actions such as rabbit restraint for bleeding, and so forth.

V.4.3. Surgery: Major survival operative procedures on non-rodent species will be conducted only in dedicated facilities intended for that purpose, and operated and maintained under aseptic conditions.

Figure C–3. DOD animal use protocol format with completion aids—Continued

Non-survival operative procedures do not require a dedicated facility, but they should be performed using surgical gloves, mask, and clean instruments. Additionally, the surgical site should be clipped and cleaned prior to surgery. Major survival rodent surgery does not require a dedicated facility but it must be performed using aseptic technique; that is, aseptic patient preparation, surgical gloves, mask, and sterile instruments. A major operative procedure is defined as a procedure that penetrates and exposes a body cavity, or causes substantial or permanent impairment of physical or physiological function.

V.4.3.1. Pre-Surgical Provisions: Describe the provisions for pre-surgical care, including provisions for pre-surgical observations and frequency of pre-surgical observations. If analgesics are utilized for pain or distress relief, provide the time schedule for administration, observational criteria utilized to determine if animals are experiencing pain/distress, and the location for the pre-surgical care.

V.4.3.2. Procedure: Describe in detail any surgical procedures planned.

V.4.3.3. Post-Surgical Provisions: Describe the provisions for post-surgical care, including provisions for post-surgical observations, frequency of post-surgical observations and criteria for early euthanasia owing to surgical complications or pain that cannot be relieved. If analgesics are utilized for pain or distress relief, provide the time schedule for administration, observational criteria utilized to determine if animals are experiencing pain/distress, and the location for the post-surgical care.

V.4.3.4. Location: Give the location/room number for the proposed surgical procedure.

V.4.3.5. Surgeon

V.4.3.6. Multiple Major Survival Operative Procedures: The principal investigator must scientifically justify multiple major survival operative procedures performed on the same animal.

V.4.3.6.1. Procedures

V.4.3.6.2. Scientific Justification

V.4.4. Animal Manipulations: Describe any injections, sampling procedures, or other manipulations of the animals necessary for the study. A reference or SOP may be furnished to the IACUC to document a particular procedure in lieu of a detailed description.

V.4.4.1. Injections: Information must include route of injection, dosage, frequency, volume injected, needle size, and anatomic injection site.

V.4.4.2. Biosamples: Examples include cerebrospinal fluid taps, blood sampling, and biopsies. List volumes taken, sampling site, frequency of sampling, needle size, and method of sampling. Procedures performed or biosamples obtained during a necropsy need not be described here.

V.4.4.3. Adjuvants: List any adjuvants used and the plan for their use. Provide a scientific justification for the use of Complete Freund's Adjuvant (CFA) and discuss why other less reactive adjuvants cannot be used. Provide dosages, volumes, route, number of injection sites, and injection locations. Specify frequency and method of injection site monitoring and include a response plan (for example, alternative endpoint and veterinary medical treatment) in the event of an adverse reaction.

V.4.4.4. Monoclonal Antibody (MAbs) Production: Provide a scientific justification for in vivo MAbs production. What in vitro methods of MAbs production were considered but not used? For in vivo MAbs production, specify the priming agent, animal monitoring frequency, number and frequency of abdominal taps, and fluid replacement therapy. Include a response plan (for example, alternative endpoint and veterinary medical treatment) in the event of an adverse reaction.

V.4.4.5. Animal Identification: Describe the method of animal identification used in this study. Examples include microchips, tattoos, ear tags, and cage cards.

Figure C–3. DOD animal use protocol format with completion aids—Continued

V.4.4.6. Behavioral Studies: Fully describe the use of aversive stimuli, food or water restriction, and so forth, that would affect the study animals. Include methods of monitoring physiologic or behavioral indexes, including criteria (for example, weight loss or state of hydration) for temporary or permanent removal of the animal from the study. Provide an appropriate scientific justification for this type of behavior modification. An IACUC policy may be included where applicable.

V.4.4.7. Other Procedures: Describe all procedures which have not been explained in other sections of this proposal that will be performed while conducting this research. Examples include electrocardiograms, radiology, and aerosol exposure.

V.4.4.8. Tissue Sharing: List what tissues will be shared, with whom, and for what purpose.

V.4.5. Study Endpoint: State the projected study endpoint for the animals (for example, recovery and return to issue pool, euthanasia, or death without early euthanasia). Indicate whether recovery, euthanasia, or death is expected; and the specific plan for determining when the animal experimentation phase will be stopped. The P.I. must ensure that unnecessary pain or distress is prevented by carefully considering "When is the experimental question answered?" so that the animals can be expeditiously removed from the study. Define specific criteria that will be used to determine study endpoint (for example, weight loss, loss of locomotion and significant lowering of body temperature, decreased food or water consumption, and decreased activity). Specifically address and scientifically justify any proposal in which critically ill or moribund animals are allowed to die as a result of the experimental procedures without the benefits of veterinary medical treatment or early euthanasia. Explain the plan for the disposition of surviving animals or animals removed from the study prior to its completion.

V.4.6. Euthanasia: If applicable, discuss the euthanasia method. The Animal Welfare Act defines euthanasia as "humane destruction of an animal by a method that produces rapid unconsciousness and subsequent death without evidence of pain or distress, or a method that utilizes anesthesia produced by an agent that causes painless loss of consciousness and subsequent death." The current American Veterinary Medical Association (AVMA) guidelines for euthanasia must be followed. Exceptions to the AVMA guidelines will be considered by the IACUC on a case-by-case basis. If requested, the attending veterinarian will assist in selecting the best method for euthanasia.

V.5. Veterinary Care: If requested, the attending veterinarian of the facility will assist PIs with preparing this section.

V.5.1. Husbandry Considerations: Federal regulations require that animal housing and living conditions must be appropriate to their species and contribute to their health and comfort. Briefly describe animal husbandry to include routine animal observations, caging methods, feed and water provisions, environmental parameters, sanitation schedules, and light cycles.

V.5.1.1. Study Room: Where will the experimental procedure be conducted? Will the animal be housed in this room for more than 12 hours?

V.5.1.2. Special Husbandry Provisions: Examples include micro-isolators, metabolic cages, food and water restriction.

V.5.1.3. Exceptions: Describe any deviations/exceptions to *The Guide for the Care and Use of Laboratory Animals*, the Animal Welfare Act regulations, or IACUC policy that have an impact on animal housing space, feeding, and sanitation. Deviations/exceptions must be justified by the P.I. and approved by the IACUC.

V.5.2. Veterinary Medical Care

V.5.2.1. Routine Veterinary Medical Care: Describe the routine veterinary medical care. State if the animals will be observed daily or more frequently. Indicate what will happen if the animal becomes ill or

Figure C–3. DOD animal use protocol format with completion aids—Continued

debilitated during the study and requires evaluation. List the criteria used for health evaluation while the animals are on study (for example, weight loss, ruffled fur, dehydration, decreased activity, and hunched body position). Include a response plan (for example, alternative early endpoint and veterinary medical treatment) in the event of debilitating illness or an adverse reaction.

V.5.2.2. Emergency Veterinary Medical Care: Describe emergency veterinary medical care.

V.5.3. Environmental Enrichment

V.5.3.1. Enrichment Strategy: Discuss enrichment provided to animal species listed in this protocol.

V.5.3.2. Enrichment Restriction: Provide written justification for restricting enrichment programs or activity programs of dogs, cats, or nonhuman primates. Single housing of nonhuman primates and dogs without sensory contact with conspecifics must also be justified and approved by the IACUC.

VI. STUDY PERSONNEL QUALIFICATIONS AND TRAINING: List the names, qualifications and training by procedure of all personnel working with animals assigned to this protocol. Personnel performing observations, procedures, and/or manipulations described in the protocol must be identified and appropriately trained and qualified to perform these procedures. Contact the attending veterinarian for assistance with this requirement.

VII. BIOHAZARD/SAFETY: Provide a list of any potential biohazards associated with the chosen animal model and this research proposal (for example, viral agents, toxins, radioisotopes, oncogenic viruses, and chemical carcinogens). Describe safety precautions and programs designed to protect personnel from biohazards associated with this research and any surveillance procedures in place to monitor potential exposures.

VIII. ENCLOSURES: Enclosures such as IACUC policies on adjuvants, monoclonal antibody production, tissue sharing, food and/or water restriction, prolonged restraint, pathology addenda, and pain assessment criteria may be included at the discretion of the PI unless directed by the IACUC.

Figure C–3. DOD animal use protocol format with completion aids—Continued

C–5. Personnel qualifications.

a. A Study Personnel Qualifications/Training table must be included in section VI of the protocol description. The table format is preferred by the IACUC for ease of reviewing the protocol. The table will contain the following four column headings:

(1) Name of the activity (for example, the procedure, observation, or manipulation to be performed, such as the venous catheterization of a dog).

(2) Name of the person performing the activity.

(3) Qualifications of the person performing the activity (for example, assistant laboratory animal technician (ALAT), 2 years experience).

(4) Training of the person performing the activity (for example, Canine Procedures Workshop, 1999).

b. Itemize each activity being performed in the protocol. List per species if there are multiple species in the protocol. If more than one individual is performing the activity, list each individual separately.

Appendix III: Comments from the Department of Defense

OFFICE OF THE UNDER SECRETARY OF DEFENSE
3030 DEFENSE PENTAGON
WASHINGTON, DC 20301-3030

RESEARCH
AND ENGINEERING

Mr. Cary Russell
Director, Defense Capabilities and Management
U.S. Government Accountability Office
441 G Street, NW
Washington, DC 20548

Dear Mr. Russell:

This is the Department of Defense (DoD) response to the Government Accountability Office (GAO) Draft Report, GAO-22-103992SU, Objectives and Performance Measures Needed to Monitor Use of Alternatives for Trauma Training, dated February 3, 2022 (GAO Code 103992). DoD appreciated the opportunity to support the GAO team's multi-year review of the Department's policies and practices involving use of animals.

DoD concurs with GAO's recommendations in the draft report. Enclosed are the Department's responses to GAO's recommendations. If you have any questions, please contact Dr. Ben Petro, Director, Human Systems, at (571) 372-6435 or james.b.petro.civ@mail.mil.

Sincerely,

MCQUISTON.BARBARA.K.1179839713 Digitally signed by MCQUISTON.BARBARA.K.1179839713 Date: 2022.03.15 15:53:18 -04'00'

Barbara K. McQuiston
Director of Defense
Research and Engineering
for Research and Technology

Enclosure:
As stated

GAO DRAFT REPORT DATED FEBRUARY 3, 2022
GAO-22-103992SU (GAO CODE 103992)

"DOD ANIMAL USE: OBJECTIVES AND PERFORMANCE MEASURES NEEDED TO MONITOR USE OF ALTERNATIVES FOR TRAUMA TRAINING"

DEPARTMENT OF DEFENSE RESPONSES
TO THE GAO RECOMMENDATIONS

RECOMMENDATION 1: The Secretary of Defense should ensure the Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight, in coordination with the Under Secretary of Defense for Research and Engineering and the military services, develops objectives, in specific and measurable terms, for monitoring the department's progress in refining, reducing, and replacing animal use in trauma training.

DoD RESPONSE: The Department concurs with this recommendation.

RECOMMENDATION 2: Once DOD has developed measurable objectives, the Secretary of Defense should ensure the Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight, in coordination with the Under Secretary of Defense for Research and Engineering and the military services, develops and uses performance measures – including determining what data need to be collected, to monitor the department's progress in refining, reducing, and replacing, animal use in medical training.

DoD RESPONSE: The Department concurs with this recommendation.

RECOMMENDATION 3: The Secretary of Defense should ensure that the Under Secretary of Defense for Research and Engineering ensures that the components use fully-approved guidance for animal use protocols for trauma training and clarifies which protocol elements, such as for literature searches and verification signatures, apply to animal use protocols for trauma training.

DoD RESPONSE: The Department concurs with this recommendation.

Appendix IV: GAO Contact and Staff Acknowledgments

GAO Contact

Cary B. Russell, (202) 512-5431 or russellc@gao.gov

Staff Acknowledgments

In addition to the contact named above, the following staff members made key contributions to this report: Sally Newman (Assistant Director), Alfonso Garcia (Analyst-in-Charge), Scott Hiromoto, David Jones, Mae Jones, Cindy Korir-Morrison, Terry Richardson, Amber Sinclair, Carter Stevens, and Samuel Woo.

Related GAO Products

Animal Use in Research: Federal Agencies Should Assess and Report on Their Efforts to Develop and Promote Alternatives. GAO-19-629. Washington, D.C.: September 24, 2019.

Animal Use in Federal Research: Agencies Share Information, but Reporting and Data Could Be Strengthened. GAO-18-459. Washington, D.C.: May 31, 2018.

DOD Animal Research: Controls on Animal Use Are Generally Effective, but Improvements Are Needed. GAO/NSIAD/HEHS-99-156. Washington, D.C.: July 8, 1999.

DOD Animal Research: Improvements Needed in Quality of Biomedical Research Database. GAO/NSIAD/HEHS-99-24. Washington, D.C.: December 14, 1998.

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