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Research Alliance for Veterinary Science and Biodefense BSL-3 Network (RAV3N): Report on network origin and phase I activities

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Abstract

Recent disease events have heightened awareness for the need for collaboration between the nation's public health and veterinary infectious disease communities to improve preparedness for current and future biological threats. To address this need, the U.S. Department of Agriculture's National Bio- and Agro-Defense Facility (USDA NBAF) has partnered with Texas A&M University through its Global Health Research Complex (TAMGHRC) to establish the Research Alliance for Veterinary Science and Biodefense BSL-3 Network (RAV3N). As a collaborative network of U.S. university and federal BSL-3Ag/BSL-3/BSL-4 laboratory research facilities, the objective of RAV3N is to establish strategic and coordinated approaches for harnessing collective large-animal biocontainment infrastructure and research capacity to improve bio-surveillance, diagnostics, and countermeasure development against high-consequence pathogens of veterinary and zoonotic importance. Here, we describe the origin and development of RAV3N, detail phase I activities, and summarize the proceedings of its first membership meeting held in August 2022.

1. Introduction

Recent emergence and re-emergence of high-consequence diseases pose a threat to national and global economies and food security. Most recently, severe acute respiratory syndrome

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

coronavirus 2 (SARS-CoV-2) caused over 6.5 million human deaths worldwide and is responsible for devastating global disruptions to public health and the economy. However, prior to this zoonotic pathogen, Ebola and Nipah viruses caused disease outbreaks in Africa and Asia. Meanwhile, notable animal health pathogens such as African swine fever virus (ASF) and highly pathogenic avian influenza (HPAI) have resulted in millions of losses in the swine and poultry industries. In response to these outbreaks and increasing concerns over global health biosecurity for humans and animals, the U.S. government has released National Security Memorandums 15 and 16 (National Security Memorandum (NSM-15), 2022; National Security Memorandum (NSM-16), 2022), which call for enhancing the nation's protection against biological threats and strengthening food and agriculture security, respectively. Similarly, the unique biodefense concerns related to the food and agricultural sector have been highlighted in a May 2022 report by the Bipartisan Commission on Biodefense (Boots on the Ground, 2022). These reports call for increased focus on One Health initiatives that utilize a multidisciplinary approach to collectively secure the nation's public health, veterinary, and agricultural interests.

In response to this recognized need for a coordinated approach to preventing and responding to biological disease threats, the Research Alliance for Veterinary Science and Biodefense BSL-3 Network (RAV3N) was established in 2021 as a national association of academic and federal BSL-3Ag/BSL-3/BSL-4 laboratories engaged in biodefense research for infectious animal diseases. The specific objectives of the network relate to providing a framework utilizing existing large-animal biocontainment infrastructure and expertise for a rapid and efficient response to emergent pathogens and continued research of known high-consequence pathogens of veterinary importance.

Addressing dangerous threats safely and securely requires a national network of federal and academic biocontainment laboratories (Le Duc, 2020). Due to the specialized considerations for diagnostics and research of high-consequence pathogens, coordination and open communication between laboratories with biocontainment capacities are essential and have led to the formation of collaborative networks including the Biosafety Level 4 Zoonotic Laboratory Network (BSL4ZNet; Pickering et al., 2019), National Institute of Allergy and Infectious Diseases (NIAID) Biodefense Laboratory Network, and Centers for Research in Emerging Infectious Diseases (CREID) Network (https://creid-network.org/). However, these groups are limited in number and have yet to focus specifically on the unique needs of research conducted in large-animal biocontainment. These needs include understanding the specific challenges of working with large agricultural and wildlife species in biocontainment, from both a scientific and operational perspective. For example, utilizing animal models in which the above-mentioned diseases naturally occur (e.g., studying Ebola or Nipah virus in pigs) requires a highly skilled and knowledgeable team of veterinarians, scientists, technicians, and animal caretakers, as well as expert biosafety professionals and facility management. Despite a growing number of active high-containment research facilities across the nation, these unique enterprises typically operate in a siloed manner – failing to capitalize on the broad collective expertise of the biocontainment laboratory professional community, resulting in an inefficient and redundant response to emerging pathogens.

This report details the origin and development of RAV3N and summarizes the proceedings of its first membership meeting, which was held August 23–25, 2022.

2. Origin and development of RAV3N

2.1. Origin

RAV3N was established during the U.S. government fiscal year 2020 using federal appropriations from U.S. Department of Agriculture (USDA) National Bio- and Agro-Defense Facility (NBAF) funding. Both USDA Animal and Plant Health Inspection Service (APHIS) and USDA Agricultural Research Service (ARS) contributed to form the secretariat for RAV3N with the goal of improving coordination between U.S. federal and academic laboratories focused on animal health, biodefense, and high-containment (BSL-3/BSL-4) research. To minimize duplication with other established, international high-containment laboratory networks that are also supported by USDA, the focus of the RAV3N is laboratories located in the U.S. Specific emphasis is placed on coordination of research, biosurveillance and diagnostics, laboratory biosafety, operations, workforce development, and sharing of laboratory best practices. Texas A&M University's Global Health Research Complex (TAMGHRC) serves as the network's headquarters in College Station, Texas.

2.2. Network structure and development

An Executive Committee was established to oversee and guide subsequent network activities. This committee consists of 8 representatives from USDA-ARS, USDA-APHIS, and TAMGHRC. The secretariat for the network consists of a project manager, a project coordinator, and the director.

To avoid duplicating other laboratory networks, the initial list of prospective network members was determined by the Executive Committee using agreed-upon criteria. These criteria were as follows: (i) U. S.-based laboratory and animal research holding facilities capable of handling large animals (livestock and wildlife species) at BSL-3 or BSL-4 and BSL-3Ag/ABSL-3 or ABSL-4 biosafety levels, combined with pro-grammatic capability to address transboundary animal and zoonotic diseases and One Health research questions; and (ii) program interest and mission emphasis on solving agricultural research problems in the U.S. and globally.

In addition to representatives from NBAF and TAMGHRC, representatives from 16 potential member institutions were invited to a virtual informational meeting on March 16, 2021. A primary point of discussion was the uniqueness of RAV3N that would not duplicate the efforts of other biocontainment networks like BSL4ZNet, a well-established international network of BSL-4 laboratories. The following points were offered as unique aspects of RAV3N. (i) It includes both federal and university membership in a directed partnership. (ii) It focuses on pathogens of agricultural importance, particularly in large-animal and avian species. (iii) It recognizes the livestock-wildlife interface and includes wildlife agencies. (iv) It promotes biocontainment training and workforce development. Finally, (v) it advances and supports the pursuit of collaborative funding opportunities by member organizations. In response to requests from potential members, a one-page informational document was

circulated to the potential network members to outline network objectives as well as membership requirements and benefits to encourage institutional participation.

2.3. Inaugural virtual workshop (May 5–6, 2021)

Attendees of the informational meeting were tasked with considering membership and consulting relevant institutional parties as appropriate. Any organization planning to join the network was asked to attend a 1.5-day inaugural workshop on May 5–6, 2021, which was held virtually due to the ongoing SARS-CoV-2 pandemic. The objectives for the first day were to introduce members, identify commonalities (e.g., facility biocontainment level, research focus, animal species, and agents of interest), and prioritize network activities. Member institutions were provided prompts that addressed the following areas: (i) name of organization and affiliation, (ii) core capabilities, (iii) mission focus and specialty areas of expertise, and (iv) key opportunities and challenges for the next 3–5 years. Sixteen representatives presented slides about their organizations, with sessions moderated by Executive Committee members. The day concluded with a group discussion to identify common goals, challenges, and priorities.

The second day opened with a recap of the network's objectives and a review of a draft of the network's charter, provided by the program management team. Terms of the charter were collaboratively discussed and modified, including the objectives and membership criteria and responsibilities. The remainder of the workshop was spent confirming network objectives and discussing the establishment of technical working groups, including topics, structure, and initial priorities and goals. A set of tangible deliverables was developed for each working group to pursue as part of the initial activities. As the working groups develop and identify gaps, subsequent objectives will be defined with input from the larger network. The revised charter was distributed following the meeting with the charge for each representative to sign the charter on behalf of their institution, thus committing to abide by the responsibilities and guidelines established therein, as well as by the confidentiality and etiquette agreement.

3. Network structure and governance

The proposed list of membership criteria and strategic program focus areas of the network to consider when inviting future members was confirmed by the inaugural network members. Provisions to expand membership are to be determined and agreed on by the inaugural network members depending on evolving issues or needs as they arise. Membership is by invitation only, and new members will be invited based on their ongoing operation and management of major biocontainment facilities (e.g., BSL-3Ag/BSL-3/BSL-4 public health and/or large animal and laboratory agricultural research facilities) in the U.S. combined with success of their infectious disease scientific program missions. Institutional membership will require an ongoing commitment to participate in technical working groups by freely sharing technical knowledge (e.g., training guidelines, standard operating procedures [SOPs], etc.) and ideas while also maintaining strict confidentiality of any information shared among the network members.

As of August 2022, RAV3N includes a total of 18 member organizations. Federal-level membership includes 6 USDA laboratories as well as laboratories from the U.S. Department of Homeland Security (DHS), the Center for Disease Control and Prevention (CDC), the U.S. Geological Survey (USGS), and the NIAID. In addition to Texas A&M University, academic membership includes laboratories at the University of Texas Medical Branch, the Ohio State University, the University of Missouri, Kansas State University, Colorado State University, and Boston University (see Table 1).

3.1. Phase I objectives and accomplishments

The principal representative of each member facility was charged with designating appropriate representatives to serve as members of the working groups. All working groups convened for the first time in June of 2021 and continued to meet monthly using a virtual platform. A Microsoft Teams site was also developed to facilitate communication and information sharing, with secure private channels provided for each individual working group as well as general channels accessible to all members of the network. The primary objective for Phase I was to establish the technical working groups and build relationships, so that a mutual trust would allow for subsequent sharing of ideas, practices, and procedures (Table 2).

3.2. Technical working groups

3.2.1. Workforce development and capacity Building—The overall purpose of this working group is to address the shortage of qualified candidates that bring veterinary and infectious disease experience to positions in the biocontainment laboratory community and to achieve the network goal of fostering the education and training of world-class personnel, providing job opportunities for graduates of member universities, and producing well-trained and experienced employees for U.S. federal and university high-containment laboratory facilities.

In Phase I, the Training and Workforce Development Working Group had 15 members representing 12 institutions. Several common challenges were identified by the group, most notably the difficulties in retaining staff; the high turnover rates were attributed to candidates leaving academic and government positions for private industry positions, which tend to offer significantly higher compensation. The working group members collectively shared an interest in modernizing biocontainment training, citing that current methods, such as reading SOPs as training material, are outdated and ineffective. The group explored novel teaching techniques and their potential applications to biocontainment training, such as virtual and mixed-reality methods.

3.2.2. Animal Husbandry and Health Management in Containment—This working group is comprised of veterinary and animal husbandry experts that represent a community of practitioners facing the unique challenges of managing agricultural and livestock species in containment facilities. The collective experience of the members, coupled with their broad veterinary expertise, enables the exchange of ideas and information to maximize the health and welfare of a wide range of research animals in containment, including rodents, small animals, livestock and poultry, non-human primates, and wildlife

species. In Phase I, the Animal Husbandry and Health Management in Containment Working Group had 13 members representing 10 institutions. Through presentations, discussions, and the development of best practice documents, the members shared their practical experiences and lessons learned in working with a wide range of animal species in containment.

3.2.3. Science Excellence and capacity—The aim of this working group is to identify both core areas of collective expertise and knowledge gaps across member institutions, and to subsequently provide a platform for exchanging ideas as well as support for programs to address gaps.

RAV3N facilitates open communication and resource maximization across specialized facilities to promote scientific excellence individually and collectively for network members. In Phase I, the Scientific Excellence Working Group had 18 members representing 16 institutions. This group hosted a monthly scientific lecture series at which member institutions presented seminars to showcase their research and capabilities.

3.2.4. Operations, Biosafety, and Biorisk—This group was developed to exchange operational knowledge and collective best practices obtained through years of successful, safe biocontainment operations across the network member institutions.

The network encourages staff visits, work exchanges, and training opportunities between member institutions to create a national technical capacity that can be drawn upon during an emergency response. In Phase I, the Operations, Biosafety, and Biorisk Working Group was the largest working group, with 23 members representing 15 institutions. It worked closely with NBAF staff to identify and prioritize monthly topics for discussion, including incident response plans, occupational health programs, and periodic lab shutdowns. Group members reported finding it very useful to include participants from biosafety and facilities and operations in the same group so that perspectives from both fields could be considered when discussing shared issues and challenges.

4. First in-person membership meeting

The first in-person membership meeting was held in College Station, Texas, on August 23–25, 2022. Thirty-six members representing 16 agencies attended in person, with 5 additional members attending virtually (Fig. 1). In addition to RAV3N member presentations, the workshop included invited guest speakers Dr. Claudio Mafra, Professor at the Federal University of Vicosa (Brazil); Dr. Gerald Parker, Associate Dean for Global One Health and Director of the Pandemic Preparedness and Biosecurity Policy Program at Texas A&M University; and keynote speaker Dr. Glennon Mays, Director of Recruitment and Student Service and Clinical Professor, College of Veterinary Sciences and Biomedical Medicine at Texas A&M University.

The workshop featured presentations from all represented RAV3N member laboratories. In addition to presenting an overview of their capabilities, members were asked to address the following prompts in their presentations:

- How have your facility's capabilities changed since we performed this exercise one year ago?
- What are your facility's current highest priorities and greatest needs?
- How has SARS-CoV-2 affected your research activities? Are you currently working with this virus, and/or other diagnostic efforts?
- Do you have any suggested or requested areas for collaboration with other RAV3N laboratories?

These presentations enabled RAV3N member organizations to quickly and efficiently brief one another on recent changes, priority topics, and areas of greatest need. This information was used to guide and enhance discussions throughout the remainder of the workshop, including a roundtable session to discuss the common challenges that had been identified and the role the RAV3N network might play in addressing them. Common themes and shared challenges that emerged include the following:

Scientific

- Surveillance, diagnostics, and countermeasure development for high-consequence emerging diseases (African swine fever virus, monkeypox, Japanese encephalitis virus, tick-borne diseases).
- Increased demand for genetic sequencing and bioinformatics as the field expands beyond pathogen identification to include characterization and epidemiology. This requires expertise and capability, bringing new challenges like mechanisms for securely storing massive amounts of data.

Operational

- Concerns over lack of funding to operate and maintain high-containment facilities, including upgrading and modernizing facilities and equipment.
- Lack of well-trained and qualified personnel (issues with both recruitment and retention of staff for biocontainment positions).
- Pandemic challenges included reduced staff, maintaining social distancing in shared spaces, and supply chain issues (personal protective equipment [PPE], critical lab supplies and reagents), which put a strain on keeping mission-critical activities going.

A noteworthy topic of discussion was the contribution of RAV3N member biocontainment facilities to the SARS-CoV-2 pandemic response. Activities at nearly all of the RAV3N facilities were impacted, largely through a temporary shift in mission to SARS-CoV-2 surveillance and/or diagnostic testing (for humans and/or animals) as well as participating in the development of animal models and countermeasures. This shift in activity was largely driven by agency requests (federal laboratories) and the acquisition of grant funding for SARS-CoV-2 research by principal investigators (academic laboratories). As a consequence, other work was de-prioritized for a year or more. This delay was commonly observed across all research enterprises, but biocontainment research was particularly impacted due

to the unique constraints on space, animals, and labor/staff when working in containment. International shortages of PPE supplies were particularly challenging, as biocontainment work cannot be performed without appropriate PPE to ensure the safety of staff and containment of pathogens. Building on these shared experiences and the lessons learned, the project co-principal investigators, Drs. Kurt Zuelke and Alfonso Clavijo, then facilitated a roundtable discussion on coordinating biocontainment laboratory responses to emerging pathogens. These preliminary discussions support a broad objective of the RAV3N network, which is to enhance national response preparedness and surge capacity to support U.S. agriculture and biodefense needs.

The diversity of workshop attendees was displayed during the poster session, in which 13 participants with broad subject matter expertise presented on a variety of topics ranging from the development of a cost-effective strategy for molecular surveillance of SARS-CoV-2 variants to process validation for custom steam sterilization cycles. This session further enhanced the exchange of ideas and information between RAV3N members and resulted in development of new collaborations.

One objective of the workshop was to launch Phase II of RAV3N, which will cover years 3 and 4 of the project. Common needs identified during the previous sessions were prioritized and tied to overall strategic focus areas, and input was sought from the members to define working group activities and deliverables. The meeting concluded with a close-out discussion and reiteration of the plan for Phase II based on member input during the workshop. This was followed by a tour of the Texas A&M Global Health Research Complex, a biocontainment research facility featuring large animal BSL-3Ag capabilities, which opened in 2020 and currently serves as the RAV3N network headquarters.

For many attendees, this conference was their first travel since the onset of the Covid-19 pandemic, and participants expressed great appreciation for the ability to congregate in person. While technology allowed for many meetings and other events to be held virtually, the ability to discuss critical topics in-person with a large group significantly enhanced the connections that had been forged and promoted member buy-in for active participation in Phase II of the network.

5. Phase II and future directions

Building on previous successes, collaborations, and relationships from Phase I, the RAV3N membership collectively identified four additional strategic focus areas for Phase II: (i) biorisk preparedness; (ii) science communications; (iii) leveraging member capabilities; and (iv) workforce development and capacity building. Broadly, these strategic areas would focus on topics and gaps identified by members as being valuable to the network and the high-containment community as a whole. Specifically, the aims for these areas are to *enhance preparedness* of the national biocontainment research community to *rapidly respond to emerging infectious disease biorisks* that threaten animal health, agricultural enterprises, and public health interests through harnessing the collective expertise and experience of the membership; to address member-identified gaps in *science communications* and improve skills related to communicating their research to their peers as well as the general public; to

leverage network member expertise and experience in order to foster cooperation between network members and support operational readiness activities at NBAF; and to develop, support, and promote training initiatives and *workforce development opportunities* for career paths pertaining to biocontainment research facilities.

To address these four strategic focus areas, specific activities planned for Phase II include the launch of an additional technical working group focused on technology transfer and commercialization, hosting a biosafety gap assessment workshop, and developing outreach programs to increase awareness and exposure to biocontainment career opportunities.

6. Conclusions

RAV3N was successfully established during the U.S. government fiscal year 2020 and includes a total of 18 member organizations. Phase I of the initial network agreement was completed in summer of 2022, transitioning the network to Phase II activities that will continue until the fall of 2024. Moving forward, the network will continue to engage and inform member organizations with the original aim of fostering collaboration among the nation's public health and veterinary infectious disease research communities to improve preparedness for future biological threats.

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Data availability

No data was used for the research described in the article.

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Fig. 1. First in-person membership meeting participants (2022).

From left to right, back row: Les Shupert (NIAID-NIH RML), Doug Eckery (USDA-APHIS NWRC), Paul Anderson (U Missouri LIDR), Connie Holubar (UTMB GNL), Miguel Grimaldo (UTMB GNL), Mark Ackermann (USDA-ARS NADC), William Wilson (USDA-ARS NBAF), Brandon Dominguez (TAMU GHRC), Muzafar Makhdoomi (USDA-APHIS FADDL), Kurt Zuelke (TAMU GHRC), Michael Puckette (DHS S&T); Middle row: Tonia McNunn (USDA-ARS NADC), Michael Bowen (CDC), Juliette Hanson (OSU PAAR), Lindsay Gabbert (DHS S&T), James Chung (U Missouri LIDR), Rachel Olson (U Missouri LIDR), Dana Vanlandingham (KS State BRI), Bonto Faburay (USDA-APHIS FADDL), Susan Brockmeier (USDA-ARS NADC), Elizabeth Rieder (USDA-ARS FADRU), Mike Jones (NIAID-NIH RML), Chad Mire (USDA NBAF), Steven Witte (USDA NBAF), Gerald Parker (TAMU), Alfonso Clavijo (USDA-ARS NBAF), John Neilan (DHS S&T); Front row: Sankar Chaki (TAMU GHRC), Renata Landers (RAV3N Program Coordinator, TAMU GHRC), Lisa Hensley (USDA-ARS NBAF), Colleen Thurman (Boston U NEIDL), Carrie Hunt (RAV3N Program Manager, TAMU GHRC), Jessica Spengler (CDC), Missy Pearce (CDC), Andre Mendonca (TAMU GHRC); Virtual participants (not pictured): Angela Bosco-Lauth (CSU IDRC), David Swayne (USDA-ARS SEPRL), Karthik Shanmuganatham (USDA-APHIS NCAH), Katie Richgels (USGS NWHC), Roxann Motroni (RAV3N Executive Committee, USDA-ARS).

Table 1

RAV3N member organizations and locations.

Organization	Acronym	High-Containment Laboratory Capabilities*	Location	Affiliation
Biosecurity Research Institute at Kansas State University	BRI	BSL-3; ABSL-3; BSL-3Ag; ACL-2; ACL-3	Manhattan, Kansas	Academic
Centers for Disease Control and Prevention	CDC	BSL-3; BSL-4; ABSL-3; ABSL-4	Atlanta, Georgia	Federal
DHS Science & Technology Directorate, Plum Island Animal Disease Center	PIADC	ABSL-3; BSL-3Ag	Orient Point, New York	Federal
Galveston National Laboratory at University of Texas Medical Branch	GNL	ABSL-3; ABSL-4; ACL-2; ACL-4	Galveston, Texas	Academic
Infectious Disease Research Center at Colorado State University	IDRC	ABSL-3; ACL-1; ACL-2; ACL-3	Fort Collins, Colorado	Academic
Laboratory for Infectious Disease Research at University of Missouri	LIDR	BSL-3; ABSL-3; ACL-2; ACL-3	Columbia, Missouri	Academic
National Emerging Infectious Diseases Laboratory at Boston University	NEIDL	ABSL-3; ABSL-4; ACL-2; ACL-3	Boston, Massachusetts	Academic
NIAID, NIH Rocky Mountain Laboratories	RML	ABSL-3; ABSL-4	Hamilton, Montana	Federal
Plant and Animal Agrosecurity Research Facility at Ohio State University	PAAR	ABSL-3; BSL-3Ag; ACL-2	Wooster, Ohio	Academic
Texas A&M Global Health Research Complex	GHRC	ABSL-3; BSL-3Ag; ACL-2; ACL-3	College Station, Texas	Academic
USDA - National Bio- and Agro-Defense Facility	NBAF	ABSL-3; BSL-3Ag; ABSL-4; BSL-4Ag; ACL-2; ACL-3	Manhattan, Kansas	Federal
USDA-APHIS National Veterinary Services Laboratories	NVSL	BSL-3; BSL-3Ag	Ames, Iowa	Federal
USDA-APHIS Foreign Animal Disease Diagnostic Laboratory (satellite laboratory of NVSL)	FADDL	BSL-3; BSL-3Ag	Orient Point, New York	Federal
USDA-APHIS National Wildlife Research Center	NWRC	N/A	Fort Collins, Colorado	Federal
USDA-ARS Foreign Animal Disease Research Unit	FADRU	BSL-3; BSL-3Ag	Orient Point, New York	Federal
USDA-ARS National Animal Disease Center	NADC	ABSL-3; BSL-3Ag	Ames, Iowa	Federal
USDA-ARS Southeast Poultry Research Laboratory	SEPRL	ABSL-3; BSL-3Ag	Athens, Georgia	Federal
US Geological Survey – National Wildlife Health Center	NWHC	ABSL-3	Madison, Wisconsin	Federal

ABSL, animal biosafety level; BSL, biosafety level; Ag, agriculture; ACL, arthropod containment level; N/A, not applicable - indicates ≤ BSL-2 laboratory capabilities.

*Capabilities listed are specific to high-containment (BSL-3 and/or BSL-4, equivalent ABSL level laboratories) and/or arthropod containment laboratories (any BSL). RAV3N secretariat can facilitate contact with individual RAV3N member biocontainment facilities (https://rav3n.tamu.edu/).

Table 2

Overview of the RAV3N working groups (Phase I).

Working group	Aim
Training and Workforce Development Working Group	To address the shortage of qualified candidates that bring experience in biosafety, facility operations, animal handling, and veterinary medical experience to positions in the containment laboratory community.
Animal Husbandry and Health Management in Containment Working Group	To facilitate the development of a best practices and lessons learned repository from a community of veterinary experts that face the unique challenges of managing animals in containment.
Scientific Excellence Working Group	To identify core areas of collective expertise and any gaps in knowledge represented across member institutions and subsequently provide a platform for the exchange of ideas and support for programs to address gaps.
Operations, Biosafety, and Biorisk Working Group	To exchange operational knowledge and collective best practices obtained through years of successful and safe biocontainment operations across the network member institutions.