Center for Zoonomics

The Center for Zoonomics integrates conservation and medical genomics to improve human, animal, and ecosystem health.

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1. Abstract

A central goal in medical genomics is to elucidate genetic and environmental predictors of disease susceptibility, onset, and progression in humans and animals. As in humans, diseases pose critical threats to the health of wildlife (Deem et al, 2001). For example, the spread of a single fungal pathogen (chytridiomycosis) is thought to have contributed to the population decline of over 500 amphibian species (Scheele et al, 2019). Moreover, like humans, non-human species suffer from diseases due to deleterious genetic variation (Lande, 1995). While conservation biologists have focused on the consequences of such deleterious genetic variation at the population level (e.g., inbreeding depression), medical genomics has focused on the proximate biological mechanisms that cause disease at the level of the individual, in order to develop methods for prevention and treatment. Applying genomic research methods to wildlife species can inform our understanding of disease and health in humans, while also improving the health and welfare of individual animals, and advancing the successful management of wildlife populations.

The aim of the Center for Zoonomics is to build the capacity to apply medical genomics to wildlife species in order to promote the health and wellbeing of wildlife, ecosystems, and people. To identify the needs and contributions of a Center, a three day planning workshop, spearheaded by Dr. Eric Baitchman of Zoo New England, was held in November 2021 at the Broad Institute of MIT and Harvard. The workshop's twenty-eight participants included specialists from zoo, medical, veterinary and academic research communities. The workshop was professionally facilitated by Dr. Kathy Traylor-Holzer of IUCN Species Survival Commission's Conservation Planning Specialist Group.

Workshop participants identified several benefits that could result from medical genomics research in wildlife species, with particular focus on research of *ex situ* populations. Participants also discussed major needs that a Center should address to facilitate research. Three broad topics were discussed by break-out working groups:

- Engagement with population managers and other stakeholders.
- Considerations of values and feasibility when choosing species that would benefit most from research.
- Development of a standardized system and database for collecting, storing, and sharing biospecimens and associated health and phenotypic data for research.

2. Background

A. Unique advantages of studying *ex situ* populations

The Center aims to enable research of wildlife populations, including both *in situ* (i.e., located in the natural habitat) and *ex situ* (i.e., captive environment) populations. *Ex situ* wildlife populations are particularly amenable to, and ripe to benefit from, genomics research coordinated through the Center for two broad reasons. First, the Center has strong partnerships with Association of Zoos and Aquarium (AZA) institutions (which primarily maintain *ex situ* populations), thereby making it feasible to both perform research and implement actionable outcomes for *ex situ* populations. Second, these *ex situ*

populations provide several unique advantages that can be leveraged to study biological processes related to disease and health. These advantages include:

1. Species-specific disease predilections are common. These diseases are documented by experts such as zoo and wildlife veterinary clinicians and pathologists.
2. Due to small founder population sizes, deleterious mutations that cause disease—which are rare within large populations— may be more common within *ex situ* populations. Critically, the relatively high frequency of deleterious recessive mutations in *ex situ* populations increases statistical power to associate such genetic variants to phenotype.
3. Diverse data related to health and lifetime reproduction are collected from pedigreed animals, longitudinally, throughout the lifecourse (e.g., clinical and pathological data, and breeding opportunities and reproductive success, have been collected from managed species in AZA institutions for decades).
4. Necropsies are performed for virtually all animals in AZA institutions, such that cause of death is often known (unlike *in situ* populations, in which cause of death is rarely known). This affords the opportunity to model effects of disease on lifetime reproductive success and population viability.
5. Long-term management of zoological institutions allows for biospecimen collections to be built up over time. This is valuable because, as a consequence of most research funding being limited to, at most, five years, a major research bottleneck is that samples need to be ready up front for grant applications to be competitive for research funding.
6. Many species maintained *ex situ* have evolved unique solutions to living healthily under diverse circumstances, which can inform biology in ways that humans and model species cannot (e.g., hibernation; divergent "solutions" of species to have long lifespans; low prevalence of cancer).

B. Current barriers to studying *ex situ* populations

While *ex situ* populations offer an array of unique advantages for informing biology and health, and the genomics era has dramatically advanced opportunities to perform exciting research on diverse species, major bottlenecks exist that hamper research of *ex situ* populations. The workshop identified the following primary barriers:

- Lack of a uniform system across AZA institutions for collecting biospecimens, and lack of a uniform (but flexible) consent system for research use. At present, a handful of AZA institutions have biobanks for research use, each of which is locally established.
- Lack of a central database for connecting AZA biospecimens to phenotypic and health data.
- Lack of researcher engagement with AZA institutions during design and implementation of research using AZA-provided biospecimens. Researchers may direct outcomes towards the research community, rather than collaborating with the institutions that provided biospecimens and metadata to identify and provide return of results that could inform actionable outcomes. This lack of engagement of AZA institutions in research design may contribute to a general culture within AZA institutions of closely guarding ownership of biospecimens and data.

3. Vision and strategy

The central aim of the Center is to integrate conservation and medical genomics to improve human, animal, and ecosystem health. The Center will enable research of wildlife species by developing and maintaining infrastructure for a network of **contributing institutions** to carry out standardized collection and storage of wildlife biospecimens and associated metadata, to provide for research use following a uniform consent process.

Critically, the Center will emphasize the engagement of contributing institutions (institutions that contribute biospecimens to the biobank), appropriate AZA committees, and related agencies in research design, so that projects have maximum potential to promote healthy wildlife populations and ecosystems by providing return of results that may have actionable outcomes.

To achieve these goals, workshop participants identified key needs that a Center should address. These needs include:

- Engagement of potential contributing institutions to learn their needs, and discuss research benefits, risks, and feasibility of maintaining a biobank for research use.
- Discussions with population managers (e.g., within the AZA community) to identify species for which both research and actionable outcomes would be most valuable and feasible, to be included in a biobank.
- Establishment of a biobank network, in which biospecimens are collected and stored by contributing institutions in a uniform manner.
- Establishment of a uniform, but flexible, consent process for research use of biospecimens.
- Establishment of a central database to store all data related to biospecimens, including health data across the lifecourse of each sampled animal.
- A public-facing website with biobanking protocols and guidelines, and other relevant information (e.g., guidelines for biospecimen collection, storage, and shipping; consent forms).

4. Engagement of contributing institutions and the research community

Contributing institutions, which may manage *ex situ* or *in situ* populations, and which contribute biospecimens to the biobank, are foundational for enabling research of wildlife. Below is a list of potential stakeholders from contributing institutions.

- Within AZA:
    - Species Survival Plan (SSP) coordinators (or consortium member or institution managing species)
    - Taxon Advisory Group (TAG) chairs
    - TAG Veterinary advisors
    - Population biologists (who advise the program coordinators)

    - Molecular Data for Population Management Scientific Advisory Group (MSAG) chair
    - Animal Health Committee
- Other animal management agencies:
    - United States Fish and Wildlife Service (USFWS), state agencies, United States Geological Survey (USGS)
- Field researchers working with the same species (may already be connected with SSP or Saving Animals From Extinction (SAFE) programs).
- SAFE coordinators- these programs are focused on conservation of *in situ* populations. They may have a link to *ex situ* management stakeholders or researchers in the field.
- International Union for Conservation of Nature (IUCN) taxon specialist groups. They may link in with TAGs, field researchers, and other species experts and managers.

Through management of *ex situ* populations, contributing institutions not only have the potential to collect biospecimens, but also collect detailed phenotypic and health records of animals, have expertise on different species' unique biology, care, and welfare, and have the potential to act upon research results to improve animal and population health, wellbeing, and management. However, contributing institutions may not be aware of, or may not have access to, the rapidly evolving research technologies that could potentially be used to modernize and improve their endeavors. On the other hand, biological and biomedical researchers have expertise in scientific questions and methods within their research fields, but may not be aware of, or have access to, the wealth of biological information that could be gleaned from wildlife species.

Thus, a critical need for the Center is to engage stakeholders from both contributing institutions and the research community. The following guidelines are inspired by the All of Us program (Precision Medicine Initiative Working Group, 2015; see References), which we find applicable to the Center.

- Contributing institutions and researchers should be equal partners in the design and implementation of a biobank and resulting research.
- A foundation of trust must be built at the beginning. The convening of stakeholders for the planning workshop was an important first step, but their continual involvement in development of the Center will be critical.
- Needs and concerns by contributing institutions should be heard and addressed.
- Realistic expectations of scientific outcomes and timeframes, in addition to the goals, benefits, and risks of research, should be communicated to contributing institutions from the beginning.
- Data protection and privacy, and secure computing, should be prioritized.
- Contributing institutions should be regularly informed as research progresses.
- A framework of **return of results** (i.e., researchers return results to contributing institutions that may lead to actionable outcomes that benefit the study species) should be established with participation from contributing institutions, which researchers will be expected to provide when data are generated.

While certain research endeavors can take several years (e.g., identifying genetic variants associated with a trait) or may not have direct conservation application, data generated for that research can still be valuable for informing conservation and management efforts. For example, genomic data could provide fundamental population genetics information describing the genetic diversity in a species, which could be used to inform population management. Therefore, population managers, or others involved in biospecimen collection, alongside researchers, should be involved in identifying a return of results that would best suit their needs.

Increasingly, wildlife and *ex situ* population managers are using the IUCN SSC *Guidelines for the Use of Ex Situ Management for Species Conservation* (IUCN/SSC, 2014) to identify ways in which *ex situ* living populations and biobanks can support research that provides conservation benefit for species. This tool is used by the European Association of Zoos and Aquaria (EAZA) for its regional collection planning, which may help identify research needs common to species held in AZA institutions.

Pathways for research project implementation and return of results to population managers

Requests to the Center to use biospecimens for research are welcome from anyone. We envision two main pathways for initiating projects (Figure 1): 1) The project is conceived by program managers [e.g., SSP coordinator, SSP veterinary advisors]; or 2) the project is conceived by researchers (e.g., researchers at contributing institutions, academic institutions, or the Center).

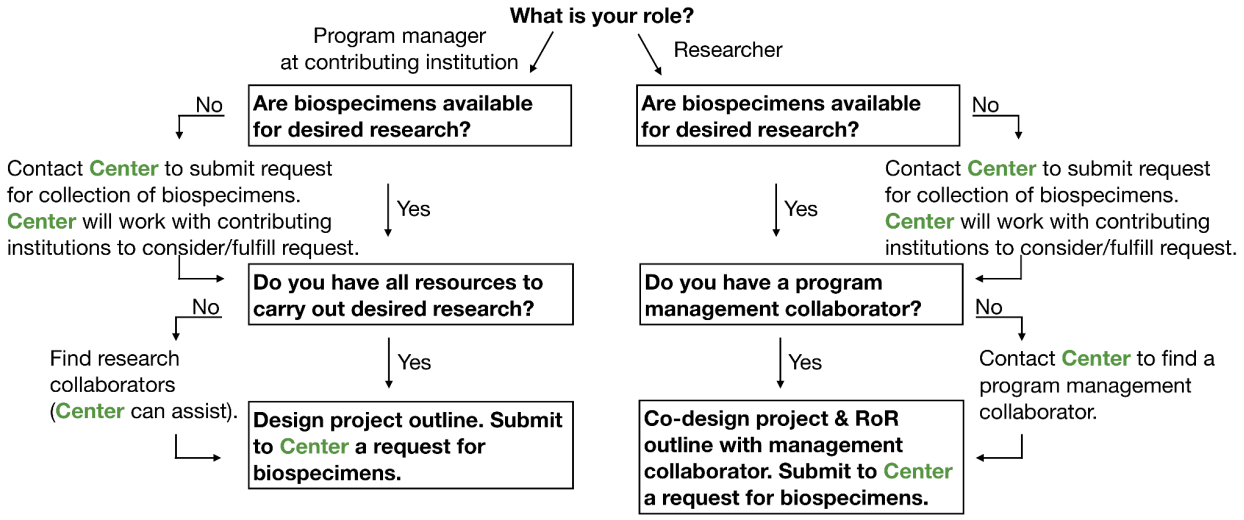
If a project is conceived by a program manager, we anticipate that the program manager would reach out directly to the Center, or, if not aware of the Center, to AZA's Molecular Data for Population Management Scientific Advisory Group (MSAG). The MSAG would connect the program manager with the Center. The Center would then work with the program manager on next steps.

If a project is conceived by a researcher, the researcher can reach out directly to the Center. Given that a central aim of the Center is to improve the health and well-being of wildlife and their ecosystems, every request to use biospecimens for research must designate a collaborating program manager (or other appropriate expert) from a contributing institution to participate in the design and regular assessment of return of results that could lead to actionable outcomes that benefit the health, wellbeing, or viability of the study species. The Center can help the researcher identify a collaborating program manager.

Once the species program, researchers, and the Center are connected, the next step is gathering stakeholders to assess the value and feasibility of return of results. As part of that process, the Center may help to identify additional collaborators. Importantly, the aim of this process is to discuss potential actionable outcomes of the project, limitations, and realistic timeframes at the outset, and have stakeholders continue to review and reassess those outcomes during the whole process. In particular, it would be helpful for the Center to attend Breeding and Transfer planning meetings that occur regularly (yearly or every

other year), both to familiarize the Center with the management decision-making process, but also to familiarize program managers on how return of results may (or may not) impact breeding recommendations.

Figure 1. Workflow for initiating a project.



Outreach

We recommend the Center establish an advisory board to help connect the Center with the following organizations. The advisory board may change over time based on the needs of the Center. This section focuses on outreach, but members of the advisory board should be diverse and able to help in other areas (e.g., advice on project selection; strategizing funding). The Center should develop specific goals and a timeline for establishing these relationships.

- Molecular SAG of AZA
- Institution and SSP/Program Vets (AAZV conference; ACVP meeting to reach pathologists; AZA Animal Health Committee; Veterinary Advisory Group)
- Program managers/SSP coordinators (Animal Program meetings at AZA Mid-year and Annual Conferences)
- Other AZA professionals (Zoo directors, educators, public relations)
- Wildlife agencies
- Wildlife sanctuaries and rehabilitation centers
- Clinical and Translational Science Awards (CTSA) programs - these programs are funded by NCATS, and some of the "hubs" are at veterinary schools, such as Tufts.
- Academic research community
- In addition, the Center should develop a public-facing website that outlines what the Center is doing, with info on different projects. Include the website URL (first ensure that the URL won't change) in Animal Care Manuals or Breeding and Transfer plans.

5. Species prioritization for biobanking

To help prioritize species to be included in a biobank, we list considerations for determining species that would be valuable and amenable to both research and actionable outcomes (e.g., outcomes that would benefit animal health, welfare, or population management). The considerations can also be used as a rubric to identify any potential gaps that would need to be addressed to carry out a project. The criteria are intentionally not ranked. All of them are important, and the presence of any combination, or lack of any combination, could be a project "dealmaker" or "dealbreaker," respectively. Moreover, any combination could fit a particular funding source or mission, and the Center should seek to act on impactful projects.

Considerations for value:

- Species of conservation concern. The value may come from both private and public sector interests in understanding and improving the long-term health of a population or species. Available criteria that could be used include: SAFE species, IUCN Red List categories, and the Endangered Species Act.
- Species that may provide biological or biomedical insight, for example serve as a model for:
    - Infectious diseases
    - Heritable diseases
    - Aging or developmental biology
    - Social, behavioral, or environmental determinants of health
    - Novel biological adaptations (e.g. species that are remarkably resilient to a disease common in humans; hibernators; unusually long-lived animals).
- Species of cultural value, such as iconic species that have high visibility to the public. For these species, research or management outcomes will likely result in public excitement and engagement.
- Capstone species with significant ecosystem services, such as apex predators, scavengers, and ecosystem engineers.
- Species in which disease phenotypes affect population viability and/or welfare that can be diagnosed with genomics or biotechnologies.
- Well-organized infrastructure around a species for management or treatment (e.g. SSP/TAG/SAFE/Recovery), such that programs can act upon research results.
- Phenotypes that have relevance to reintroduction programs (e.g., diagnosing and managing diseases that impact fitness).
- Generation and sharing of genomic data with the scientific community that enables additional research, both in conservation and in the biological and biomedical sciences (e.g. Brandies et al. *Genes* 2019; Stephan et al, in review, *PNAS*).
- Research projects whose protocols and results can be applied to other species, including humans.
- Research projects that can provide opportunities for training and capacity development, including education and public outreach.

Considerations for feasibility:

- Well-functioning organizational infrastructure (SSP, TAG, SAFE, Recovery, etc) enables coordinated collections of biomaterial and phenotypic data, from animals with known pedigrees. These programs have buy-in from a high proportion of stakeholders (e.g. holding facilities or administrators) to participate in prospective studies.
- Clearly defined phenotypes are critical for research. Phenotypes should be:
    - Objective - Phenotypes should be as objective and quantitative as possible.
    - Defined with a case definition that is applicable irrespective of the observer.
    - Complete - Phenotypes should be noted for all known measurements such that “wildtype” or “control” is easily distinguishable from “not examined” or “not applicable”.
    - Repeatable - Additional individuals should be able to be phenotyped using the same methods in the future.
- Biospecimens can be made available, accessible, and are appropriate for the study.
    - The number of banked or bankable biospecimens provides adequate statistical power to address research questions.
    - Samples are of sufficient quality for generating the data.
    - Structure in the data can be appropriately controlled for (e.g. confounding factors are recorded in the metadata).
    - Samples should appropriately represent genetic and phenotypic diversity. Biases introduced from sampling (subsetting of a population used for biospecimens) should be minimized. For building a biospecimen collection without a specific research question, the biospecimens should be from a set of animals representative of the phenotypic and genetic variation in the entire population/species.
    - Samples have been approved for the relevant use by the contributing institution
- Regulatory challenges/laws regarding sampling have been, or can be, addressed in a timely manner.
- Consent for research use is available.
    - Many precious biospecimens are banked, but current practice, especially for increasingly threatened populations, tends towards setting highly restrictive permissions.
- A sufficiently successful breeding program exists to act on research findings.
    - Potential exists for manipulation of breeding or environment.
    - A program has the ability to continuously collect and analyze biospecimens for ongoing management.

6. Biobanking

The Center should adapt and apply best practices from human medical genomics to guide collection, barcoding, storage, permitting, and sharing of biospecimens paired with phenotypes and metadata. The Center's approach should be guided by the principle that, while biospecimen collection should be optimized where possible, any biospecimen is

always better than no biospecimen, and some metadata are always better than no metadata, as technological advances can improve the usability of samples.

A. Sample collection and storage

Collection and reliable storage of biospecimens maximizes opportunities to collect high-quality genomic or other data useful for a wide range of research applications. The Center should adopt and adapt best practices from human biomedicine to standardize collection of high-quality biospecimens to potentiate future discoveries. The Center should pilot these conventions at directly affiliated zoological institutions, and make what we learn about best practices publicly available.

Establishing and disseminating best practices for sample collection

- The Center should create zoo-adapted guidelines for sampling best practices from existing protocols in the biomedical field (e.g. the All Of Us research program; https://allofus.nih.gov/) and guidelines established by existing zoological collections (e.g. the San Diego Frozen Zoo).
- The Center should also consult managers of existing biorepositories such as the Cornell Veterinary Biobank to identify features especially useful for multi-species biobanking.
- The Center should work with AZA's Biobanking Scientific Advisory Group to disseminate information to AZA institutions.
- The guidelines should specify the highest-priority types of biospecimens to be collected, volume/quantity, and conditions for biospecimen preservation.
- Guidelines for biospecimen collection should be made publicly available on the Center's website, and Center staff should update them regularly to reflect innovations in the field.
- Beta testing of the biospecimen collection guidelines will be implemented at Zoo New England.

Supporting both opportunistic and project-oriented sampling

The Center should advocate collection of both project-specific biospecimens and opportunistically collected biospecimens useful for a wide range of potential future applications.

Euthanized animals may be a high-impact source of material for biospecimens. Online guidelines for biospecimen collection should focus on ensuring collection of high-quality biospecimens useful for a variety of potential future research applications, while minimizing time burden on zoo staff when animals are euthanized.

B. Biospecimen barcoding

In human clinical care and biomedical research, sample barcoding is ubiquitous. It reduces workload for technicians, eliminates errors in transcribing labels, and ensures that samples do not get disconnected from patients. In contrast, barcoding is not yet routine in zoo medicine. Often, samples are labeled by hand and without a systematic encoding system. This presents major impediments to high-quality zoo-based biomedical research: (1) connecting biospecimens to associated phenotypes ad hoc is time-consuming; (2) many

biospecimens are unusable because those connections are lost; (3) errors are common, adding imprecision to projects and impeding successful research.

The Center should adapt best practices from human biomedicine to implement barcoding of zoo medicine samples. We identified two junctures where barcoding is crucial.

1. Biospecimens must be **barcoded at the point of collection**. Implementing this will require identifying systems and products that will not increase, and ideally reduce, workload for zoo staff. This may include: (1) providing preprinted stickers and barcodes; (2) providing easy access to a database for biospecimen information that would be useful both during biospecimen collection and for reviewing collections (e.g. an app); (3) provide prelabeled "universal kits'' for use at necropsy, or designed for specific projects. For example, for the meerkat project, the Center could produce a meerkat heart disease project-branded kit to collaborators, with all the information and materials needed to provide biospecimens and phenotype data.
2. Biospecimens must be confirmed to have barcodes when they are received by the Center. Biospecimen providers should be provided with prelabeled tubes and shipping materials, and complete a preformatted form with required information. No biospecimen should enter the Center without a barcode. The Broad Genomics Platform already implements this system, and should be consulted by the Center.

The Center should consult biomedical institutions that have existing, robust barcoding systems, including the Broad Institute, to develop a system for biospecimen barcoding. The system will be piloted at Franklin Park Zoo. Importantly, barcoding need not replace text or handwritten labels. Text labels are useful for identifying samples in freezers, and can continue to be applied in conjunction with barcodes. For more sophisticated set ups, barcode printers can provide barcode stickers that also include human readable labels.

7. Data

A. Pairing biospecimens with metadata, phenotype data, and genomic data

Metadata are essential for nearly every question in genomics. Studies assaying population features such as overall genomic diversity, or genomic regions depleted of diversity, require information on the time and location of biospecimen collection, and studies focused on identifying the genomic basis of disease require clinical phenotypes and, especially for investigation of later-onset diseases, information on the age of the animal at the time of sampling.

At present, many barriers impede robust pairing of metadata with biospecimens. Staff members working directly with animals often have extensive, longitudinal information on individual animals, but unless a specific genomic study is already underway, this information may never be recorded or stored. Phenotypes are sometimes collected in the context of a specific study, but stored (by necessity, in part) separately from the biospecimens to which they pertain. As time passes, institutional memory is lost and the probability of ever reconnecting the metadata with the biospecimens is diminished. Additionally, free-standing Excel sheets get stored locally and changed, so eventually there

are several copies, often slightly variable, and it is impossible for any researcher with a local copy to know whether it is the most up-to-date version.

The Center should work towards the pairing of biospecimens and associated metadata, according to the following principles.

- Even the most carefully collected biospecimens have essentially no value if there is no information about the animals they derive from, or if this information cannot be linked.
- A core goal of the Center should be to develop an electronic "staple" that will permanently link all available phenotype data - including data that continue to emerge over the lifetime of the animal - to the biospecimen, and hyperlinks to any data that derive from it (e.g. genomic data in repositories such as the NCBI Sequence Read Archive).
- Attaching *some* phenotypes to data, even basic phenotypes (e.g. sex or age), is always better than attaching no phenotype.
- Minimum metadata types may include: sex, age at sampling, biospecimen tissue types collected, geographic location of sampling, any available photographs, video, or audio recordings.
- At any given time, there must be only ONE copy of the data repository that is known to all users as the official version.

B. Electronic data platform

Linking samples, metadata, and phenotypes via barcodes will require a central, electronic repository that is universally recognized as containing the most up-to-date information on a given biospecimen. Components of the requisite platform already exist in various systems, and a core goal of the Center should be to review each of these (e.g. Species360's ZIMS used by most AZA institutions; Terra used by the Broad) before deciding whether to add new functions to an existing system, or to instead develop a new, free-standing platform tailored to the specific needs of genomics research.

Considerations for the Center to address

- De-identification, either prior to researcher access or at the time of publication, may be important for the willingness of contributing institutions to collect biospecimens. De-identification should be discussed early on with both participating institutions (who will collect biospecimens) and research collaborators to discuss needs of all stakeholders and risks associated with a lack of de-identification.
- Specific caveats for considering ZIMS as a database:
    - The Center would need to discuss with Species360 staff the potential for expanding ZIMS capabilities.
    - The ZIMS software already addresses some of the needs of a database (e.g., health data and some pedigree info are available). The proposed database for the Center may serve well as an extension on the existing ZIMS platform.
    - While the ZIMS platform already exists, and people at AZA institutions already know how to use it, access to different modules is varied across staff.
    - Not all institutions use ZIMS.

C. Use permission

The Center should create its own material transfer agreement (MTA), specific to the Center, designed to provide flexibility regarding biospecimen use and ownership. The Center should consider a model that allows zoo-based biospecimen owners to opt in to different levels of permission (e.g., exclusive to a specific research project, open to similar areas of research, or open access for not-for-profit research purposes [within the bounds of pre-established parameters to define "research"]) for each biospecimen or collection of biospecimens.

- The Uniform Biological MTA, which aims to protect the rights of the contributing institution if materials are patented, should be investigated to determine whether it is appropriate to the Center's needs.
- Pre-established institutional relationships may specify levels of use permission prior to biospecimen collection via a standardized data collection method (connected with the barcode system).
- The Center should identify a core network of zoological institutions from which samples are most likely to be requested for project-oriented sampling (projects are expected to be taxa based). It is of utmost importance that the Center keeps MTAs up to date with those institutions in order to facilitate the timely transfer of biospecimens.
- For certain key collaborators, the Center should consider establishing a category for "Research Partners", for which memorandums of understanding (MOUs) and a standing MTA may be established that facilitate sharing of biospecimens. MTAs with other institutions may include a level of permission that allows sharing with only the Center, or all Center Research Partners.
- The Center should consider piloting this MOU system with the San Diego Zoo and Smithsonian.

8. Policy

Policies appropriate to the goals and needs of the Center, contributing institutions, and participating researchers will need to be established, including policies surrounding: use agreements from contributing institutions; review process for biospecimen requests; design and implementation of return of results; data protection, access, and sharing. The Center should establish an advisory board, which should include substantial representation from the contributing institutions, to:

- Help the Center connect with diverse stakeholders.
- Help identify priority species of interest from the perspective of both population management and research.
- Provide coordination of the activities of the Center.
- Oversee the development and implementation of policies related to the return of aggregate and/or individual results to contributing institutions.

- Help develop an evaluation and approval process for researchers to access data and biospecimens.
- Provide guidance for the design and implementation of the biobank network.
- Help identify partners that can provide a full service biobank that manages all aspects of collection, processing, storage, retrieval, and biospecimen tracking. Partners must have the bandwidth to fulfill biospecimen requests in a timely manner.
- Ensure protection of data is held to the highest standards and kept up to date.

9. References

Brandies, P., Peel, E., Hogg, C. J., & Belov, K. (2019). The value of reference genomes in the conservation of threatened species. *Genes*, *10*(11), 846.

Deem, S. L., Karesh, W. B., & Weisman, W. (2001). Putting theory into practice: wildlife health in conservation. *Conservation biology*, *15*(5), 1224-1233.

IUCN/SSC. (2014). Guidelines on the Use of *Ex Situ* Management for Species Conservation. Version 2.0. Gland, Switzerland: IUCN Species Survival Commission.

Lande, R. (1995). Mutation and conservation. *Conservation biology*, *9*(4), 782-791.

Precision Medicine Initiative Working Group, Precision Medicine Initiative Cohort Program. National Institutes of Health, 2015. Available at: https://www.nih.gov/sites/default/files/research-training/initiatives/pmi/pmi-working-group-report-20150917-2.pdf

Scheele, B. C., Pasmans, F., Skerratt, L. F., Berger, L., Martel, A. N., Beukema, W., ... & Canessa, S. (2019). Amphibian fungal panzootic causes catastrophic and ongoing loss of biodiversity. *Science*, *363*(6434), 1459-1463.