



National Leadership Grants for Museums

Sample Application MG-249168-OMS-21

University of Wisconsin - Madison

Amount awarded by IMLS:	\$590,952
Amount of cost share:	\$0

The project description can be viewed in the IMLS Awarded Grants Search:
<https://www.imls.gov/grants/awarded/mg-249168-oms-21>

Attached are the following components excerpted from the original application.

- Narrative
- Schedule of Completion

When preparing an application for the next deadline be sure to follow the instructions in the most recent Notice of Funding Opportunity for the grant program and project category (if applicable) to which you are applying.

PROPOSAL NARRATIVE

The University of Wisconsin–Madison, in collaboration with a consortium of 24 partners in zoos, zoological associations, academia and industry, seeks a National Leadership Grant in the Collections Care and Public Access category. Together, we propose a global orang-utan genomic study, both to fully understand the emerging threats to them in zoos, and to build the much-needed capacity for a global management plan. That plan will facilitate exchange to the United States of those orang-utans with the greatest genetic value, with a view to securing a sustainable future for these species in American zoos.

1. Project Justification

1.1. What field-wide need or challenge will your project address, and how was it identified?



Three species of orang-utan (*Pongo* spp.) survive in the wild, in the South-East Asian countries of Indonesia and Malaysia (Supporting Document 2 – S2). All three are critically endangered; principally due to habitat loss and conversion to oil-palm, and illegal hunting and the pet trade [1-3]. Just ~57,000 Bornean orang-utans (*P. pygmaeus*) remain on the island of Borneo, in an area smaller than the state of Wisconsin [4]. Their populations declined by ~100,000 individuals from 1999-2015; more than 50% are affected by natural resource extraction [5-6]. On neighboring Sumatra, fewer than ~13,800 Sumatran orang-utans (*P. abelii*) still exist in the island's northern tip, in an area smaller than the state of New Jersey [7]. Further south, not more than 800 Tapanuli orang-utans (*P. tapanuliensis*) survive in a single and highly fragmented population, in an area half the size of Rhode Island [8]. The status of wild populations is thus extremely bleak. If every surviving wild orang-utan could sit in the seats of the SoFi Stadium in Inglewood, CA – host of the 2021 Super Bowl – the stadium would be at just 72% of its maximum capacity.

In the face of declining orang-utan numbers in the wild, their *ex-situ* populations in zoos are becoming increasingly important [9]. At least 1,100 orang-utans live in zoos globally, comprising 1.5% of all those remaining on Earth. Of these, 223 live in US zoos accredited by the Association of Zoos and Aquariums (AZA) [10]. While these animals play an essential role in educating and inspiring the American public [11], our prior research has cast doubt on their long-term viability. Specifically, with \$23,000 in seed funding from the AZA's Conservation Grants Fund, we identified six specific challenges facing orang-utans in US collections. Our underlying science has been extensively peer reviewed, including by the AZA Molecular Data for Population Management Scientific Advisory Group (SAG) (S3):

1) *Bornean and Sumatran orang-utan hybrids are living undetected in US zoos*

Bornean and Sumatran orang-utans cannot naturally inter-breed in the wild, having diverged ~700,000 years ago and dispersed on to separate islands (S2). When artificially introduced, however, they can successfully hybridize and produce viable offspring – as was the case in zoos until the 1980s [12-13]. Because orang-utans of all species look virtually identical, a chromosomal 'karyotyping' test was performed thereafter, to separate the species into two populations [14-15]. This was performed with a view to avoiding 'outbreeding depression', which might manifest as health and reproductive issues in the offspring of parents who are too genetically different [16-17].

It is now known that karyotyping cannot distinguish hybrids after the first generation of offspring. This means that any orang-utan that previously tested as Bornean or Sumatran – and now their descendants – may in fact be a hybrid. Indeed, using data accompanying our manuscript, in review at the Oxford journal, *Bioinformatics*, it can be shown that numerous third-generation hybrids have persisted undetected in breeding programs (S4). As such, the genetic integrity of orang-utans in living collections is compromised. There is now an urgent need to re-test all animals using modern methods.

2) Recently described Tapanuli orang-utans have lived undetected in zoos for the last five decades

The Tapanuli orang-utan was only described in the wild in November 2017; prior to this, individuals from its small population were assumed to have been Sumatran. In our papers now in review at *Biology Letters* (S5) and *Nature* (S6), we report that at least 3% of all Sumatran orang-utans in US zoos are in fact Tapanuli hybrids. This greatly compounds concerns regarding outbreeding depression [16-18]: though Bornean and Sumatran orang-utans diverged ~700,000 years ago, the Tapanuli and Sumatran species last shared a common ancestor ~3.4 million years ago [8]. Identifying these hybrids – and understanding the effects of such hybridization – is now critical to their management.

3) Three Bornean subspecies have now been described and are highly admixed in US zoos

Following genetic studies in 2001 [19], Bornean orang-utans were subdivided into three subspecies in eastern, central and western Borneo (S2) – two decades after the establishment of the Bornean zoo population. Through genetic testing in our pilot phase, we found that the ‘Bornean’ population in US zoos is in fact highly admixed between all three subspecies. In the wild, these diverged ~176,000 years ago and markedly differentiated over the last ~82,000 years [20]. Consequently, Bornean orang-utans in zoos comprise a ‘cocktail’ of asynchronous genes that could not normally exist in the wild. In our paper published in *Scientific Reports* (S7), we justified concerns that outbreeding depression could afflict subspecies hybrids, in spite of their more recent shared ancestry [17]. A full-scale study of outbreeding is therefore warranted, to determine how we might mitigate the effects of any depression.

4) Cardiovascular and chronic respiratory diseases are killing zoo-housed orang-utans

Cardiovascular disease (CVD) is the primary cause of mortality among orang-utans in zoos. It typically presents post-mortem as myocardial fibrosis – thus, by the time it can be diagnosed, it has already proven fatal. From 1980-2008, 28.9% of all sub-adult and adult orang-utan deaths in US zoos were attributed to CVD, which was otherwise a contributing factor in 12% of all other deaths [21-22]. Concurrently, chronic respiratory disease (CRD) accounts for 16% of adult mortality and is reported in up to 40% of orang-utans in US zoos [23-24]. It presents as chronic sinus drainage and infection of the laryngeal air sac; gram negative rod infection and bronchiectasis [24]. As neither disease has been observed *in-situ* in wild orang-utans, both are thought to be captive conditions that arise from intensive genetic and environmental management [25-27]. Through molecular studies in our pilot and scaling stages, we observed that CVD is probably Mendelian inherited – and thus passed down from parents to offspring. In contrast, we observed that CRD might instead present as an immune response to the introduction and/or hybridization of orang-utans too genetically distinct and ill-adapted to each other’s novel pathogens. A fuller understanding is paramount to reducing their incidence in zoos.

5) Captive managed breeding programs are not based on DNA data

Breeding and transfer recommendations are currently determined via pedigree-based Mean Kinship (MK) [28]. This approach utilizes the International Studbook (ISB) – *i.e.* the central, global record of zoo

orang-utan pedigrees, upon which all population management decisions are based [10] – to identify and prioritize the breeding of animals from genetic lines that are underrepresented. In the United States, this endeavor is undertaken by the AZA Orangutan Species Survival Plan (SSP); abroad, national and regional equivalents manage their populations by the same means. The ISB is not based on DNA data, however: rather, all wild-caught founders are assumed to have been unrelated and are assigned MK values of zero. This purports that they share zero percent of their genes with the rest of the population. Relatedness among descendants is subsequently calculated via the pedigree, and breeding recommendations are determined by pairing individuals with the values most amenable to increasing genetic diversity [28]. In practice, we have since empirically shown that some of the earliest wild-caught founders in the US population were parent-offspring or sibling dyads that were captured and imported together: inbreeding is thus higher than previously thought. Notably, in our manuscript in review at *Biology Letters* (S5), we describe a pair of wild-caught orang-utans, who – though presumed to be unrelated – were in fact full siblings. The pair produced 17 inbred descendants. Genetic diversity in US zoos is therefore much lower than is currently assumed via current MK measures.

6) *There are too few orang-utans in the United States to secure their long-term survival*

Of the 223 orang-utans in AZA zoos, 96 are presumed Bornean and 90 are presumed Sumatran [10], based on 1980s karyotypes. The remaining 37 are hybrids that are either contracepted or otherwise unable to breed. The AZA aspires to retain $\geq 90\%$ of genetic diversity in each population for at least 100 years, through the aforementioned pedigree-based Mean Kinship approach [13]. Yet even if we can address the previous five challenges – by determining true genetic composition, and preventing new cases of CVD or CRD – there are still too few animals in the US to secure our populations' long-term sustainability. Inevitably, we must source new orang-utans from zoo associations abroad.

The need for global species management – versus that on national or regional scales – is widely recognized as a field-wide need for securing the sustainability of living collections (S8). Such efforts, termed 'Global Species Management Plans (GSMPs) herein, whether or not they are administered under the World Association of Zoos and Aquariums' (WAZA) framework (S9), should supplement the largely 'closed' plans of zoos and zoo associations in disparate countries and continents (S8). In recent years, there have been several efforts to introduce novel genes to the US orang-utan population, in the absence of a GSMP: from 2009-2018, for example, eight orang-utans were imported from Germany, New Zealand and Australia. All were selected via pedigree-based Mean Kinship values, however, and thus were unlikely to have been the most genetically appropriate of all those available in zoos worldwide. In 2018, with co-authors from across the zoo industry, we articulated that an underlying GSMP is essential to captive orang-utans' long-term sustainability, in our peer-reviewed paper in the journal, *International Zoo Yearbook* [9, S10]. In the absence of a global genomic study, however, it is impossible to understand which orang-utans are most genetically suitable for international exchange.

1.2. How will the museum field benefit from your project?

Given our small orang-utan populations in US zoos, it is impossible to address these issues without international collaboration. Consequently, we propose a two-pronged approach to resolving these six key challenges: **1) by performing a global genomic study of all orang-utans in zoos, filling critical gaps in data that are needed to address the six key challenges; and 2) by applying this scientific foundation to develop an Orang-utan Global Species Management Plan. That Plan will facilitate exchange to the United States of those orang-utans with the greatest genetic value, securing a sustainable future for these species in American zoos.**

Genomic analyses of ~953 orang-utans will be performed in our laboratory at UW-Madison, either by Project Staff, or – in the case of DNA samples derived from eight countries with limited molecular capacity – by an early-career scientist from each (see Project Work Plan). During a 10-day Genomics Workshop at UW-Madison, they will analyze DNA samples from their country’s zoos, building capacity for a new generation of museum professionals to care for and manage their living collections. Under our tutelage, each will acquire transferable skills that could later be applied to develop similar projects.



Results from the genomic study will first be shared with studbook keepers and population managers from the national, regional and world zoo associations; many of whom are Project Consultants and/or Key Partners. Each will learn the true genetic diversity, kinships and pedigrees for their respective populations; confirm taxonomic compositions; understand when outbreeding may (or may not) result in depression; and determine how CVD and CRD might potentially be ‘outbred’ through selective breeding. Aside from our pilot data, no orang-utan genomic work has been performed in any zoo population since the 1980s. This study is therefore imperative in guiding any scale of population management.

We will then bring all these stakeholders together, for a 3.5-day Orang-utan Global Species Management Workshop at UW-Madison. Collectively, this coalition will plan and initiate a GSMP that can transcend national and regional borders. Through long-term implementation of that GSMP, the value of this project to the museum field would extend far beyond the conclusion of an award.

1.3. How have the beneficiaries been involved in the project’s planning?

This proposal includes 24 Key Partners, comprising all 14 of the major zoological associations that house or manage orang-utans globally; 4 academic partners; 2 industry sponsors; and 4 partner non-profits. Twenty-one orang-utan population managers and/or studbook keepers were involved in developing this proposal; most serve as Project Consultants. Importantly, the proposal was planned with input from the AZA Molecular Data for Population Management SAG, which advises the AZA Animal Population Management Committee and the AZA Orangutan SSP on how best to apply molecular data. The SAG will represent AZA’s interests throughout this project and has committed to peer-reviewing all research findings (S3). Notably, Dr Jamie Ivy, the SAG Chair, serves as a Project Consultant (Résumé 4 – R4).

1.4. What is the relevance of your proposed research for current practice?

Our proposal builds on the outputs of six prior IMLS grants; each of which validated the pressing need to address our six key challenges. We used the PMx software [29], supported by IMLS in 2005 and 2019 [30-31], to calculate pedigree-based mean kinship, and the PEDSAM software, funded in 2015 [32], to identify orang-utans for inclusion in our study. We have a longstanding research agreement to share data with the

Great Ape Heart Project, now funded with five IMLS grants from 2010-2022 [33-36], to facilitate joint analyses of CVD data (S. We will also advance an ongoing effort to better understand CRD incidence, in partnership with California State University, Fullerton, to exchange our genetic findings with their survey data on symptoms. Additionally, we leveraged successful examples of existing GSMPs (e.g. Amur tiger, *Panthera tigris altaica*, S11; Goodfellow's tree kangaroo, *Dendrolagus goodfellowi*, S12). Dr Tara Harris, Chair of the Amur Tiger GSMP (S13, R5), and Dr Kristin Leus, the population advisor to numerous global programs (S14, R6), will each serve as Project Consultants.

1.5. How will your project address NLG goals and align with your chosen project category?

Though we target the Collections and Care and Public Access category, we have aimed to address all seven essential ideas in the IMLS Strategic Plan [37]; in particular, the Build Capacity goal. Given the absence of genetic data, there is simply no capacity at the present time to address the emerging threats to orang-utans in zoos. This project is intended to build that capacity for American institutions.

2. Project Work Plan

2.1. What are the specific research questions and what is your theoretical framing?

We worked closely with our Project Consultants and Key Partners to develop the following six research questions. These are framed around the six field-wide challenges outlined in Section 1:

- 1) What are the true taxonomic compositions of orang-utans in living collections?
- 2) Are existing pedigree-based (versus DNA-based) measures of Mean Kinship correct?
- 3) Does inter-breeding distinct orang-utan taxa lead to outbreeding depression?
- 4) Are CRD and CVD genetic, and could we screen for these conditions?
- 5) Are outbred or unrelated animals more vulnerable to CRD affliction?
- 6) Which orang-utans should be exchanged internationally to sustain our living collections?

2.2. What specific activities, including evaluation, will you carry out, and using what research methods? What type of data will you gather and how will you analyze and use the data?

In collaboration with our industry partners at Promega (S15) and Roche (S16), we have developed novel molecular methods – just accepted for publication in *BMC Genomics* (S17) – to study orang-utan ancestry and health. On the advice of IMLS, we provide a layman's summary here, and technical details in S18.



Research methods flowchart: a) A DNA sample is collected from an orang-utan; in this case, a non-invasive, voluntary saliva swab; b) the DNA is extracted on the automated Promega Maxwell RSC robot; c) sections of DNA relevant to this study are 'enriched' using proprietary 'SeqCap' technology donated by Roche Sequencing Solutions (S16); d) the enriched portions are 'sequenced' on an Illumina HiSeq 4000 or MiSeq instrument; e) the resulting sequences come back in digital form for subsequent computational analysis.

Our method enables us to precisely and consistently analyze the following regions of orang-utan DNA:

- Up to ~177,500 highly variable positions, which can be used to infer ancestry and kinship at high resolutions. This approach is similar to 23andMe.com or Ancestry.com in humans.
- 109 genes known to be pathogenic for cardiovascular disease, including – but not limited to – those linked to cardiomyopathy and sudden cardiac death.
- 43 genes pathogenic for respiratory disease, including – but not limited to – alpha-1-antitrypsin deficiency, cystic fibrosis, ciliary dyskinesia and chronic obstructive pulmonary disease.
- 59 genes identified by the American College of Medical Genetics as being implicated in a majority of other human diseases, and which may thus be linked to cardiac and chronic respiratory disorders, or implicated in outbreeding depression [38].

We will gather data using this method in **Years 1 and 2**, from ~953 orang-utans in living collections worldwide. All were selected based on either, **a)** intention of the host country to participate in a Global Species Management Plan, and to facilitate international orang-utan transfers *sensu* [9]; or **b)** the individuals were identified (using the IMLS-supported PEDSAM software [32]) to be high priority for sampling, due to their value in filling data ‘gaps’ that are essential to answering our research questions:

- 226 in the US & Canada
- 330 in Europe
- 68 in Malaysia*
- 65 in Mainland China*
- 55 in the UK
- 46 in Japan*
- 35 in Taiwan*
- 25 in Singapore
- 22 in the Philippines*
- 21 in Thailand*
- 18 in Australia
- 15 in South Korea*
- 18 in Russia
- 6 in Vietnam*
- 3 in New Zealand

We began collecting DNA samples in 2011. We have already applied these methods to ~198 of the orang-utans in the US and Canada, as detailed in our manuscripts in review at *Biology Letters* (S5) and in press at *BMC Genomics* (S17). This serves as successful proof of concept from our pilot and scaling phases. Of the remaining 755 orang-utans, 362 have already been sampled (and the samples transferred to our lab); sampling is underway for a further 362, and approval has been sought for the remaining 31. Though most of our existing samples are blood- or tissue-derived, we have now validated a new method of DNA collection via non-invasive, voluntary saliva swab: this will facilitate rapid sampling in the event of an award. Moreover, we have an unrestricted five-year CITES permit to import orang-utan samples to the United States (S19). Samples from the eight countries marked with an asterisk (*) will be analyzed at the **Year 1** workshop by early-career scientists from each. The remainder will be analyzed by **Project Staff** throughout **Years 1 and 2**.

Capitalizing on UW-Madison’s capacity in high-throughput computing (S20), we will computationally analyze the resulting sequence data to address our research questions. We will do so first at the level of each population (*i.e.* for each separate breeding program in each country/region), and then again for all samples globally. As with the molecular methods, we defer detailed computational protocols to S21, on advice of the IMLS Program Officer. Put simply, we will test 11 principal hypotheses:

- 1) Distinct Bornean and Sumatran populations in zoos in fact include hybrids thereof.
- 2) Tapanuli orang-utans have hybridized and introgressed within those populations.
- 3) Bornean orang-utan populations are too admixed to manage at the subspecies level.
- 4) Orang-utans with CVD feature specific mutations with a Mendelian inheritance pattern.
- 5) Orang-utans with CVD are in predominantly inbred, not outbred, lineages.
- 6) Orang-utans with CRD are more genetically admixed than those without.

- 7) Orang-utans with CRD are in predominantly outbred, not inbred, lineages.
- 8) Orang-utans with CRD are more genetically distinct from their co-housed conspecifics than those without CRD symptoms.
- 9) Samples from orang-utans with CRD will include circulating viral DNA.
- 10) Not all wild-caught orang-utan population founders were unrelated.
- 11) Pedigree-based mean kinship has overestimated population-wide genetic diversity.

Findings will be shared with national and/or regional population managers, and with the WAZA International Studbook Keeper, as quickly as we produce them in **Years 1 and 2**. This will facilitate immediate implementation on a local scale, e.g. removing a known carrier of familial cardiomyopathy from a national breeding program. Our 3.5-day Orang-utan GSMP Workshop will be held in **Year 2**; a draft schedule is attached as S22. Implementation of that GSMP will begin (and continue beyond) **Year 3**. Data publication and dissemination will comprise much of our efforts in the final year of the project.

2.3. What are the risks to the project and how will you mitigate them?

As closely related and charismatic mammals, orang-utans tend to evoke strong human attachments. We recognize that some stakeholders feel strong responsibility for their local or regional programs, and are less receptive to the concept of a GSMP and the ‘interference’ that global management could bring. We have also observed many differences in opinion; for example, in how orang-utan populations should be managed, and what roles hybrid animals might play. Consequently, by far our biggest challenge is uniting those with disparate views. For this reason, we selected the Conservation Planning Specialist Group (CPSG) of the International Union for the Conservation of Nature (IUCN) to facilitate our GSMP Workshop: the CPSG has led population management programs since 1979, and is internationally respected as both experienced and impartial (S23). By deferring this role to the CPSG, we avoid any suggestion of interference in implementation. Population managers can be reassured that they will retain the responsibility for developing and implementing orang-utan management strategies.

The COVID-19 pandemic has also presented challenges. Consequently, we have minimized all but necessary travel. In the event that travel is still unrealistic at the time of an award, we can use our five-year CITES permit to import samples for analysis at UW-Madison by Project Staff, in lieu of the proposed early-career scientists from each country. Though an in-person Orang-utan GSMP Workshop is strongly preferred, CPSG has successfully led numerous virtual meetings during the pandemic, and would be able to adapt our Workshop for teleconferencing (e.g. with ‘Zoom’) [39].

2.4. Who will plan, implement and manage your project? For what purpose will partners be engaged?

This project will be planned and managed by Dr Graham L Banes (R1) of the Wisconsin National Primate Research Center, with Dr Emily D Fountain (R2), an Assistant Researcher. Five undergraduate students will be recruited in each project year (R3), at no cost to IMLS, via UW-Madison’s Undergraduate Research Scholars Program. In pursuit of the ‘Wisconsin Idea’, this program recruits those from underrepresented groups to advance scholarly diversity and inclusivity on campus. In **Year 1**, they will ‘pair-up’ with the foreign early-career scientists to perform the genomic study. In **Year 2**, they will lead practical demonstrations at the Orang-utan GSMP Workshop. In **Year 3**, they will write and contribute to peer-reviewed publications, and co-author manuscripts in peer-reviewed journals.

All 13 zoological associations that house or manage orang-utans will be represented throughout the project, and in-person at the **Year 2** Orang-utan GSMP Workshop, by their respective delegates. Most are Project Consultants, with résumés and/or supporting letters attached (S24-S38; R7-R17):

- Megan Elder, WAZA Intl' Studbook Keeper and Vice Chair, AZA Orangutan SSP (S24, R7)
- Dr Jamie Ivy, Chair, AZA Molecular Data for Population Management SAG (S3, R4)
- Clemens Becker, Chair, EAZA Orang-utan Endangered Species Program (EEP) (S25, R8), which also comprises the British and Irish Association of Zoos and Aquariums (BIAZA) (S26)
- Neil Bemment, Co-Chair, EAZA Orang-utan EEP (S27, R9)
- Simone Schehka, Co-Chair, EAZA Orang-utan EEP (S25)
- Jim Kao, Chair, SEAZA Orang-utan Species Management Plan (SMP) (S28, R10)
- Wendy Chua, Co-Chair, SEAZA Orang-utan SMP (S29, R11)
- Pei Enle, Chinese Association of Zoological Gardens (CAZG) (S30, R12)
- Dr Kazutoshi Takami, Japanese Association of Zoological Gardens (JAZA) (R13)
- Dr Nian-Hong Jang-Liaw, Taiwan Association of Zoos and Aquaria (TAZA) (S31, R20)
- Noel Rafael, Secretary, Philippine Association of Zoos and Aquariums (PHILZOOS) (S32, R19)
- Ampika Thongphakdee, Zoological Parks Organization of Thailand (ZPO) (S33)
- James Biggs, ASMP Manager, Australasian Association of Zoos and Aquariums (AAZ) (S34, R14)
- Amanda Embury, Chair, Orang-utan Australasian Species Management Plan (ASMP) (R15)
- Malaysian Association of Zoological Parks and Aquaria (MAZPA) (S35)
- Korean Association of Zoos and Aquariums (KAZA) (S35)
- Vietnam Zoos Association (VZA) (S35)

The Orang-utan Global Species Management Plan Workshop will be led by Dr Kathy Traylor-Holzer (S23, R16) of the IUCN CPSG, who also serves – with Chua – on WAZA's Committee for Population Management. Dr Morgane Tidiere, Research Scientist, will represent the interests of Species360 (R17). Additionally, this project is also an approved and branded conservation 'Partner of WAZA' (S36, S37).

2.5. When and in what sequence will your activities occur? What resources will you need?

We attach a three-year Schedule of Completion; Budget and Justification, and List of Key Personnel.

2.6. How will you track your progress toward achieving your intended results?

Continued evaluation will follow the five-stage framework of the Conservation Measures Partnership, *i.e.* the Open Standards for the Practice of Conservation (OSPC, S39), as implemented in the software program, *Miradi* [40]. This proposal manifests as the first two stages (*Conceptualize* and *Plan*) of the OSPC Management Cycle. In Years 1 and 2, we will undertake stages three and four – *Implement* and *Analyze and Adapt* – through weekly lab meetings for Project Staff; in quarterly 'Zoom' meetings with all Project Consultants; in biannual updates to all participating zoos (*i.e.* those providing DNA); and – in Year 2 – at our Orang-utan GSMP Workshop. Moreover, at the conclusion of each project year, we will distribute surveys based on IMLS Performance Measure Statements (S40) to Project Staff and Consultants. This will enable us to track progress and adapt our Project Work Plan to maximize its impact. Stage four will continue into Year 3, when we will concurrently address Stage 5: *Share*.

2.7. How and with whom will you share your project's results? How will you report the information?

The IMLS describes Stage 5 of the OSPC as "*communicating results and sharing discoveries.*" As all tangible project results will take the form of digital products, we detail specific actions in the Digital Product Form. In sum, and to the maximum extent possible, all data and results will be placed into the public domain. Peer-reviewed manuscripts will be submitted to open-access journals or archives; digital data will be published in open-access repositories. That data will be shared prior to publication with the Great Ape

Heart Project (S41) and with California State University, Fullerton (S42), to advance their research goals in CVD and CRD, respectively. Finally, though not a focus of this proposal, a dedicated website and public outreach effort would also accompany this project, produced with Jordana Lenon, the Public Information and Outreach Specialist at the WNPRC (S43, R18).

3. Project Results

3.1. What are your intended results, and how will they address the need, problem or challenge? What models, tools, research findings, and/or services will result from your project? How will you ensure that they are broadly adaptable by others and are widely disseminated to the field?

Our project will generate the following research findings:

- Genomic data from 953 orang-utans. We will use these data to computationally test the hypotheses associated with our six field-wide challenges. Moreover, we will deposit these in a public repository, enabling other scientists to build on our research. As detailed in the **Digital Product Form**, this approach will enable perpetual public access and use.
- A new software module for use by population managers, comprising a new algorithm for inferring kinship directly from DNA sequence data. This will export a kinship matrix for analysis in the software program, *PMx*, which is used by all population managers to generate breeding and transfer recommendations [29]. By importing our custom kinship matrix to *PMx*, it will be possible to calculate Mean Kinship values through combination of pre-existing pedigree data and empirical DNA-derived relatedness measures. This will complement a similar approach in development by our colleagues at UW-Milwaukee, with IMLS support from 2015 [32]. In contrast with their algorithm, ours will be compatible with outbred populations, *i.e.* those comprising multiple species, subspecies or taxonomic units. This result will enable other admixed species to be managed using DNA directly in *PMx*, facilitating broad adoption by a wide range of population managers.
- An understanding of the effects of outbreeding on orang-utans, including potential depression. We anticipate that population managers will be able to mitigate many ill effects through strategic and targeted captive breeding, *e.g.* by not pairing individuals whose offspring will inherit deleterious genes. Our results will also have broader impacts for understanding outbreeding depression. In mammals, this phenomenon is poorly understood; principally due to a lack of experimental possibilities. In non-mammals, outbreeding is typically studied by deliberately infecting hybrid animals with disease, and evaluating their immune response compared to non-admixed individuals [*e.g.* 41]. The main alternative for such a study in mammals is to analyze DNA from a large and admixed population that was sampled over many generations. As our samples include orang-utans that lived as far back as the 1950s, this proposal presents a rare opportunity for our discipline.
- A scientific basis to guide *in-situ* reintroductions. More than 1,500 orphaned and displaced orang-utans await reintroduction: yet, as the effects of outbreeding are unknown, all must be repatriated prior to their return to the wild [17]. Our findings will inform the extent to which such repatriations are necessary, *e.g.* at the species, subspecies or subpopulation levels.
- Publications in peer-reviewed journals, disseminating our findings to the scientific community. Our research will serve as a model study for potential expansion to other taxa.

Additionally, we expect the following outcomes for each national and/or regional zoo association:

- Corrected DNA-derived pedigrees, facilitating captive breeding that pairs the most genetically appropriate individuals. As shown in our six key challenges, the present pedigree-based Mean Kinship approach can be demonstrably harmful in the absence of empirical kinship data.
- Corrected species affiliations, enabling population management at precise taxonomic resolutions. This is imperative for securing sustainable populations in living collections; particularly as Tapanuli orang-utans are known to persist undetected in zoos (S8).
- An understanding of which individuals might carry harmful or otherwise deleterious alleles (genetic variants) and which should, on that basis, be contracepted. This form of preventive conservation will improve the health of living collections.
- Using our new algorithm, as implemented for use with PMx [29], population managers will be able to generate breeding and transfer recommendations that directly incorporate DNA data. This will empower them to continue direct management without further input from Project Staff, ensuring the long-term sustainability of this work far beyond the conclusion of the award.

Globally, living collections in zoos will benefit from the following outputs:

- An updated and corrected WAZA Orang-utan International Studbook [10]. As the core foundation upon which all breeding programs are based, our results will build capacity for accurate and science-based population management across every country and region.
- A Global Species Management Plan for orang-utans, which integrates national and regional collection plans. This result directly addresses WAZA’s field-wide vision for securing the sustainability of endangered populations in zoos (S8, S9). Our GSMP may or may not be branded under the WAZA umbrella – the pros and cons of WAZA endorsement will be evaluated by stakeholders at the Year 2 workshop (e.g. this might exclude participation by China, which cannot be a WAZA member under Chinese law). Moreover, based on the genomic results, each zoo association will need to decide the extent to which participation is possible. Nonetheless, as aforementioned, successful examples of current GSMPs are attached (S11, S12). Plus, we include letters of support from the managers of various GSMPs – both WAZA- (S13) and non-WAZA branded (S14) – that demonstrate the feasibility of globally managed programs.
- By training early-career scientists from countries with limited molecular capacity, we build new capacity for those professionals to care for and manage their living collections.

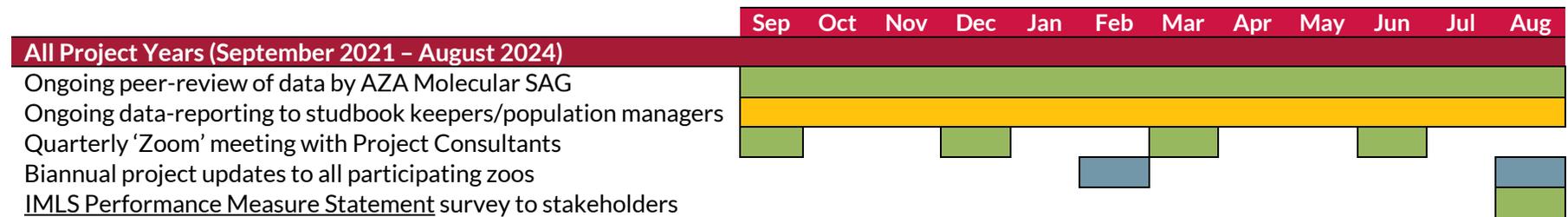
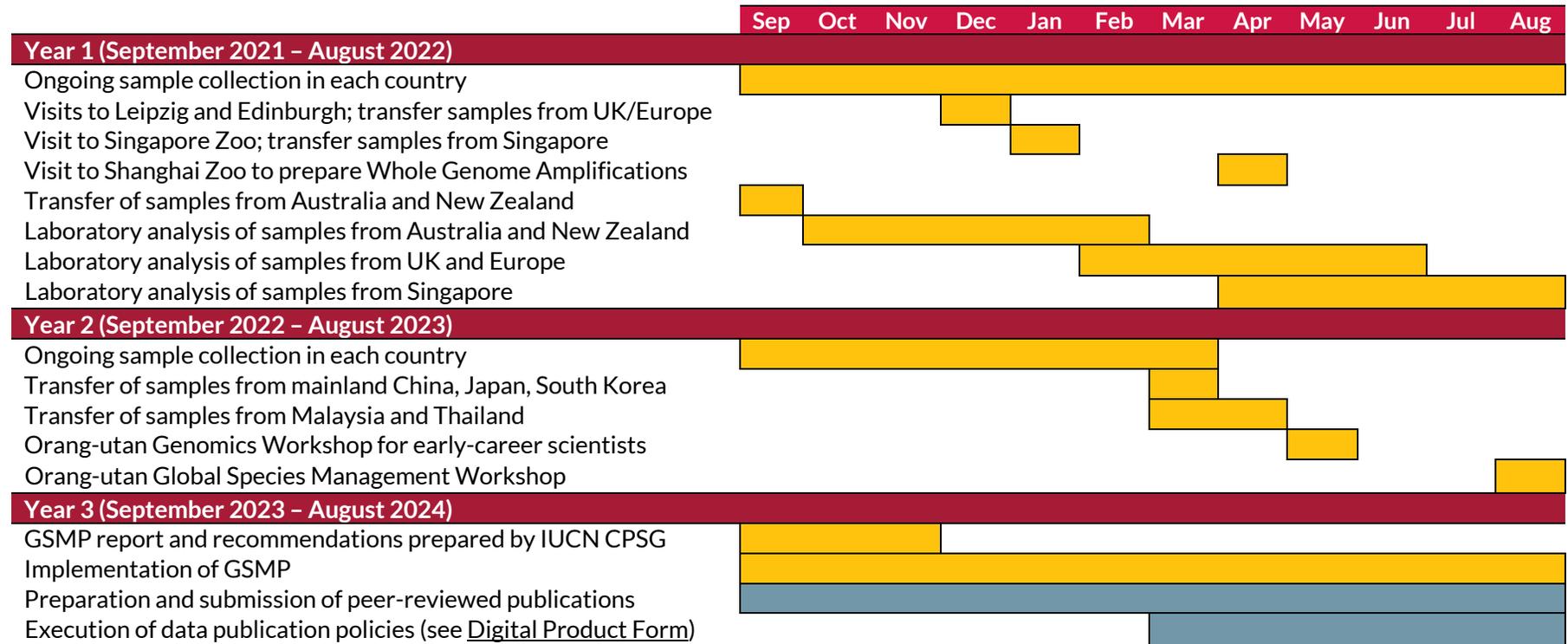
3.2. How will you manage the research data and make it available for future use (RQ)?

We have attached a Digital Product Form that details data management and publication plans.

3.3. How will the knowledge, skills, behaviors and/or attitudes of the intended audience change? How will you sustain the benefits of your project?

At UW-Madison, our role serves to empower our Project Consultants and Collaborators with the tools and data they urgently need to resolve the six field-wide challenges. This research will allow us to provide those resources, and to bring all those stakeholders together. Our approach will therefore build the capacity for long-term global management, and without further input by Project Staff – securing not only the sustainability of orang-utans in zoos, but the long-term viability of this project.

SCHEDULE OF COMPLETION



Implement and Analyze Colors indicate Management Cycle Stages from the Open Standards for the Practice of Conservation (S38).
Adapt As explained in the **Project Narrative**, we use the OSPC (as implemented in the software program, *Miradi* [40, S39] to track progress toward achieving our intended results and to evaluate our Project Work Plan in the context of IMLS Performance Measure Statements (S40).
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