CONVENTION ON INTERNATIONAL TRADE IN ENDANGERED SPECIES
OF WILD FAUNA AND FLORA

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IUCN SSC'S GUIDING PRINCIPLES ON CREATING PROXIES OF EXTINCT SPECIES FOR CONSERVATION BENEFIT

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IUCN SSC Guiding Principles on Creating Proxies of Extinct Species for Conservation Benefit

Version 1.0

International Union for Conservation of Nature

Species Survival Commission

IUCN SSC Guiding Principles on Creating Proxies of Extinct Species for Conservation Benefit

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Drafting process and acknowledgements

A "De-extinction Task Force" was established in April 2014 under the auspices of the Species Survival Commission (SSC) and charged with drafting a set of *Guiding Principles on Creating Proxies of Extinct Species for Conservation Benefit* to position the IUCN SSC on the rapidly emerging technological feasibility of creating a proxy of an extinct species. The core group of the Task Force was chosen to represent a wide range of expertise relating primarily to species conservation, but with no *a priori* position, either for or against the concept of species "de-extinction". The drafting process started with the production of a scoping document to define the terms of reference for the group, and to clarify the scope of the proposed document. Several preliminary drafts were circulated, reviewed and amended by Task Force members.

The Task Force was chaired by Philip Seddon, co-chaired by Axel Moehrenschlager, and comprised H. Resit Akçakaya, Liz Bennett, Mike Bruford, Neil Cox, Piero Genovesi, Henry T. Greely, Claire Marris, David Oehler, and Will Turner. Additional input and advice during the preliminary drafting phase was provided by Paul Smith, Craig Hilton-Taylor, Claudio Campagna, Tammy Steeves, Patrick Whittle, and Richard Maloney. Mike Hoffmann served as the SSC Steering Committee liaison, while Simon Stuart retained oversight for this project.

A first draft was presented to SSC Chair Simon Stuart, and submitted to the SSC Steering Committee, its Subcommittees, all Specialist Groups and Task Force Chairs, and affiliates for review between May and September 2015. A further consultation was held during the SSC Leaders' Meeting in September 2015, in Abu Dhabi ,UAE. A revised draft was submitted to the SSC Steering Committee in April 2016. The final draft was submitted to the SSC Steering Committee on 25 May 2016.

The Task Force would like to express heartfelt thanks to each and every person that contributed to the development of the guidelines. We also acknowledge the support of home institutions and organisations of all contributors for allowing them the time to carry out this work. We hope that these guidelines contribute to the appropriate development of new conservation tools and approaches.

The following people provided insights, suggestions, comments, and critiques, at various stages in the drafting process:

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Section I. Introduction

The prospect of species “de-extinction”, defined as the process of creating an organism that resembles an extinct species (but see Note on Terminology below) has moved from science fiction to plausibility within the last decade, but has been debated widely only within the last few years. The increasing public profile of species “de-extinction” has been driven in part by rapid advances in the technical capacity to read and manipulate genetic code. The discussion around revival of extinct species has shifted from “could we?” to “should we?” As with almost any new technology, enthusiastic endorsement needs to be balanced against significant concern over any possible harmful consequences.

To date, “de-extinction” candidate lists have featured species that are beloved, missed, charismatic, i.e. primarily larger mammals and birds. This taxonomic bias that pervades “de-extinction” wish lists tends to mirror the bias in current ecological research and conservation management, and to some degree even our knowledge of what has gone extinct. However, the stated primary rationale for pursuing the creation of proxies for extinct species has been framed around ecological enrichment, and the case has been made that “de-extinction” with environmental release is fundamentally a conservation translocation issue that seeks to re-establish populations of proxy species in suitable areas of habitat to achieve ecosystem conservation benefits.

The requirement for sufficient area of habitat might be most easily met for species that have gone extinct in very recent times when ecological conditions were similar. The creation of proxies for species that went extinct in the more distant past is more likely to face significantly different ecological conditions in potential recipient sites, increasing uncertainty and the risks of unwanted outcomes, and reducing the likelihood that any conservation benefits would be achieved.

This document sets forth SSC guiding principles on the creation of proxies for extinct species, as defined in Section II, as a potential conservation tool to restore biological diversity, to enhance ecosystem stability and resilience, and to engage in meaningful dialogue with the public about the role of proxy creation for conservation.

This is a controversial topic, supported or opposed on the basis of a wide range of biological, economic, political, and ethical viewpoints. This document does not aim to cover all aspects of “de-extinction”, but is focussed on the potential for the creation of ecological replacements for extinct species to yield conservation benefits while minimising the likelihood of negative impacts on current conservation efforts, extant species, the environment, and local livelihoods.

The principal objectives of these guidelines are: to outline the current SSC consensus view of the key issues, considerations, and implications of species “de-extinction”; to highlight critical areas of concern; to acknowledge opportunities, and uncertainties; to link this issue with other areas of SSC policy; and to set out guiding principles that seek to maximise conservation benefits and minimise harm.

Note on Terminology

The term “de-extinction” is misleading in its implication that extinct species, species for which no viable members remain, can be resurrected in their genetic, behavioural and physiological entirety. These guidelines proceed on the basis that none of the current pathways will result in a faithful replica of any extinct species, due to genetic, epigenetic, behavioural, physiological, and other differences[1]. For the purposes of these guidelines the legitimate objective for the creation of a proxy of an extinct species is the production of a functional equivalent able to restore ecological functions or processes that might have been lost as a result of the extinction of the original species. Proxy is used here to mean a substitute that would represent in some sense (e.g. phenotypically, behaviourally, ecologically) another entity – the extinct form. Proxy is preferred to facsimile, which implies creation of an exact copy. The guidelines do not consider the application of techniques to address the conservation of extant species, such as cloning of extant rare species or the introduction of genetic variation into extant species that are at risk of inbreeding.

“De-extinction” is therefore here used in a limited sense to apply to any attempt to create some proxy of an extinct species or subspecies (hereafter “species”) through any technique, including methods such as selective back breeding, somatic cell nuclear transfer (cloning)[2], and genome engineering (see Section V). Where possible the term “proxy” will be used to avoid the connotations of “de-extinction”.

1 Shapiro (in press)

2 The precautionary terminology adopted in these Guidelines is not intended to create an obstacle to equally precautionary cryo-banking of endangered species, and it is acknowledged that advances in interspecies cloning might open up the best pathway to the production of faithful genomic copies of an extinct species in some taxonomic groups.

Section II. Scope of this guidance

To achieve conservation benefits, proxies of extinct species need to be more than attractions or laboratory test cases. They would have to be translocated into suitable areas of habitat where they would be free to interact with other species. For this reason these guidelines proceed on the basis that proxy creation for conservation benefit is in large part a conservation translocation issue, where conservation translocation is defined as "*the intentional movement and release of a living organism where the primary objective is a conservation benefit: this will usually comprise improving the conservation status of the focal species locally or globally, and/or restoring natural ecosystem functions or processes*" [3]. Therefore the focus of these guidelines is based on achieving species-and-ecosystem-level conservation goals through conservation translocations, including ecological replacements (*sensu* [3]). The guidelines were not written to apply directly to other uses of the relevant technologies, such as for exploitation, biological research or for public display, although they might have some relevance in those settings.

"De-extinction" could be said to have been achieved with the live birth, hatching, or germination of any reasonable proxy of a once extinct species. Such a "revival", either of a few individuals or by creating a captive breeding population, might by itself have some research, educational, or entertainment value, but the wider success as a conservation tool must consider post-release performance and the status and persistence of a re-established population, and the wider ecological impacts.

The current focus is on vertebrates, especially birds and mammals, reflecting the focus of current and proposed "de-extinction projects". However, these guidelines are intended to be applicable, as appropriate, to "de-extinction" of any taxon. For example, risk of impacts on biodiversity and ecosystem services will be relevant to all taxa.

These guidelines should not be construed as endorsing, encouraging, or facilitating the creation of proxies of extinct species for conservation benefit, nor do they assume that proxy creation will inevitably become part of the conservation toolkit. The guidelines do intend to highlight the considerable risks and uncertainties any such projects would entail, and to set out principles which, if adhered to, might head off ill-conceived projects and enhance the net conservation benefits of responsible projects.

Framing statement

It is now widely believed that technological advances will soon make it possible to produce sufficient numbers of sufficiently genetically diverse individuals to form functional proxies of some extinct species. It is therefore timely to ensure that this endeavour, if it is pursued at all, is pursued responsibly, with minimal harmful impacts, so that demonstrable, explicit, additive, conservation benefits in terms of enhanced ecosystem stability and resilience can be realised.

"De-extinction", or proxy species creation, as with some current conservation interventions, poses a moral hazard (see also Section III) – a situation whereby one party takes more risks because another party will bear the costs of those risks. Changing public perceptions could undermine current and future conservation efforts if proxy creation is seen as providing a techno-fix to the crisis of species extinctions and biodiversity loss. Efforts in this arena should be positioned to the public as supporting, not replacing, the conservation of extant species and ecosystems.

Conservation prioritisation is a valid means to apportion scarce resources for species conservation, but should not consider technological advances as providing a viable means of even temporarily suspending efforts to avert the extinction of some species in the expectation of later revival, since even if appropriate cryo-preserved samples are kept, the complexity of the original species and its full ecological role and interactions are unlikely to be fully restored.

The priority must remain the preservation and enhancement of extant biodiversity, with proxy species creation in an attempt to restore biodiversity being undertaken only when consistent with preserving existing biodiversity

3 IUCN 2013

Section III. Background information

“De-extinction” has captured the attention of sections of the scientific community and the general public alike. Not only is the breadth of public engagement substantial, the sophistication of informed debating points, both pro and con, is growing.

Synthetic Biology

The technical capabilities to read and manipulate genetic code are increasing eightfold every year, and costs have been reduced over the last 15 years by a factor of 6x to 11x per year. As a result in the last 40 years there have been rapid advances in the technological feasibility of proxy species creation via cloning, the reading of ancient DNA, and the reconstruction of extinct genomes scaffolded on extant species. Further advances can be expected to provide additional tools in genetic engineering.

Proxy species creation, specifically via the genome engineering pathway (see Section IV3), is here considered a subset of the wider field of Synthetic Biology, broadly defined as “the construction of new biological parts, devices and systems, and the redesign of existing natural biological systems for useful purposes”[4]. The inevitable advancement and refinement of techniques, such as CRISPR (Cluster Regularly Interspaced Short Palindromic Repeats)-based editing (see Section V.3.), will improve the accuracy and reduce the costs of genome engineering for proxy species creation. Unprecedented progress in this arena seems likely in the coming decade.

Ethical and economic issues

As an ethical point “de-extinction” represents a form of “moral hazard”. Moral hazard, initially used in economics, refers to a situation where one party takes more risks because another party, willingly or unwillingly, will incur the costs if things go badly. In the “de-extinction debate”, the moral hazard is that the prospect of “de-extinction” will cause the current generation to believe that any extinct species can be resurrected by future generations, resulting in reduced societal and political support for conservation measures to prevent species extinctions, or situations whereby future generations will inherit any problems caused by “de-extinction” efforts. Such moral hazard issues are unresolved and need to be debated at all levels.

Other concerns might arise from a view of the natural world having a well-ordered and unchanging nature, to a charge of the hubris of believing that scientists can improve on nature, through to concern that biotechnologists have insufficient understanding of the things we are manipulating to be able to avoid unacceptable impacts.

It is believed that humans have a moral obligation not to render species extinct, but it is unclear if this extends to a moral obligation to resurrect them. It has been argued that humans alive today owe a debt of restorative justice where humans were responsible for past extinctions, although the exact cause of past extinction is often unclear. The counter argument to this line of reasoning goes that species, especially those that no longer exist, cannot be owed a debt of restorative justice. The individual organisms that were wronged by extinction are not alive today and nor are those who caused the extinction, so a debt cannot be paid by those who owe it to those who are due it[5].

Economic aspects of “de-extinction” include the issue of effective use of financial resources. The technical stages of proxy species creation – in creating the first few specimens and then managing a captive population – will have costs. Unless new funding is attracted to proxy species creation by funding sources, which would not otherwise invest in conservation, diversion of funds might be at the expense of efforts to conserve extant species.

Concern has been expressed that proxy species creation is being pursued for commercial gain, rather than for conservation benefits. Realistically, legitimate commercial elements will likely be involved in “de-extinction” technology development and implementation, but the underlying motives around such support will need to be addressed and should be made explicit from the outset.

In balance proxy species creation might have a negative utility via unwise expenditure if projects use funds that could contribute to preventing extinctions happening in the first place or if there is reduced investment in conservation due to the expectation of future technical fixes to current problems; through health concerns if proxy species are vectors for pathogens or provide novel selection pressures for pathogens; due to the deleterious environmental impacts if released proxies become invasive or pests. Although there will be concerns and issues around animal welfare during laboratory, rearing and post-release stages, these are not immediately the focus of these guiding principles.

“De-extinction” efforts could be associated with a positive utility primarily via environmental benefits, but also through proxies as a source of inspiration; for the advancement of scientific knowledge in general; for specific technological advancement, and through educational and cultural values.

Assuming humans do not have an overriding ethical obligation to resurrect long-extinct species, ecological, welfare, legal, moral, and socio-economic concerns need to be addressed for the creation of proxies of extinct species to be ethically acceptable.

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4 Redford et al. 2014

5 Sandler 2013

Section IV. Technical overview: the three pathways of proxy creation, potential, and limitations

Currently three pathways for proxy creation are recognised: selective breeding, cloning, and genome engineering.

1. Selective back-breeding

An extant close relative, descendant, or hybrid form of the extinct species is selectively bred for ancestral traits, relating to genotype, phenotype, or behaviour (animals), or signalling (plants). No direct manipulation of genetic material is involved as only traditional selective mating is used, and there is little control over which suites of traits might be retained within each generation. Efforts might be guided primarily by the physical appearance of the resulting offspring, but also by genetic comparisons, in relation to what is known of the extinct form.

Examples

Some domestic breeds of cattle (*Bos taurus*) have been selectively bred for size and colouration to resemble the extinct Auroch (*Bos primigenius*) from which they descended[6].

Plains zebra (*Equus quagga*) have been selectively bred for pelage colouration and patterning to closely resemble the quagga (*E. quagga quagga*), a now-extinct subspecies[7].

It has been proposed that giant Galapagos tortoise hybrids could be selectively bred, guided by genetic screening, to concentrate original alleles in an attempt to restore the genetic integrity of an extinct form[8].

Potential

When the functional role of an extinct form is adequately understood, selective back breeding could have the potential to create a functional equivalent.

Limitations

Forms derived via selective back breeding might most commonly be phenotypic proxies and perhaps functional equivalents of the extinct form; the degree of genetic similarity might be unknown but is likely to be limited due to hybridisation or the many generations and multiple selection pressures since the descendant form was separated from the original. The greater the genetic difference relative to the original form, the greater the uncertainty over the post-release performance of the proxy.

This approach is dependent on there being one or more suitable descendant or related form assumed to retain the genetic potential for expression of ancestral traits or some of the relevant ancestral alleles.

There is potential for ongoing hybridisation with related species, with unknown implications.

2. Somatic Cell Nuclear Transfer (Cloning)

For mammals, the nucleus of a somatic cell taken from an individual of an extinct species is removed and inserted into the enucleated egg cell (cell from which the nucleus has been removed) of a suitable surrogate species. The cell is induced to start to divide and the embryo is implanted into the surrogate host to gestate to term. Cloning is currently most advanced for mammals and amphibians; the first ever clones were of northern leopard frogs in the 1950s.This has been done successfully with many mammal species, with more or less safe results for offspring.

The first mammal to be cloned from non-embryonic/non-fetal cells was Dolly the Sheep (*Ovis aries*) in 1996. Dolly was cared for at the Roslin Institute in Edinburgh until her death five months before her seventh birthday. The first threatened species to be cloned was the gaur (*Bos gaurus*); a baby bull named Noah was delivered in 2001, but died within 48 hours due to common dysentery. The banteng (*Bos javanicus*) is the second threatened species to be successfully cloned; the first cloned bantang calf was born in 2003 and lived at San Diego Zoo for seven years, dying there in 2010. In 2008 clones of a grey wolf (*Canis lupus*) were born from somatic cells harvested post mortem. As of early 2015, nearly 20 mammalian species have been cloned using somatic cell nuclear transfer.

For birds, somatic cell nuclear transfer currently seems impossible. The problem with cloning birds is that egg cell contains a large quantity of yolk that makes identification of the nucleus extremely difficult, and the female must be killed to obtain a newly ovulated egg because by the time an egg is laid the embryo has already begun to develop on the yolk. Genomic engineering techniques, discussed below, will be needed for birds. Cloning techniques have been developed for plants and amphibians, but is not yet clear whether reptiles can be cloned.

If the cryo-preserved cells are gametes then in vitro fertilisation might be possible, thus avoiding the considerable challenges of somatic cell nuclear transfer, though the use of gestation surrogates would still be necessary for mammals, with the attendant issues

6 Stokstad 2015.

7 The Quagga Project http://www.quaggaproject.org

8 Poulakkis et al. 2008.

around interspecies cloning[9][10].

Example

The only example of cloning of an extinct taxon, and the only example of taxon "de-extinction" to date, is the partially successful cloning of a bucardo (Pyrenean ibex; *Capra pyrenaica pyrenaica*) in 2003. One bucardo kid was born alive but died in a few minutes from a birth defect[11].

Recent and current projects are seeking to clone the extinct gastric brooding frog (*Rheobatrachus spp.*)[12], the Thylacine (Thylacinus cynocephalus)[13], and the woolly mammoth (*Mammuthus primigenius*)[14], though the existence of any mammoth cells suitable to be nuclear donors seems highly unlikely.

Potential

The production of clones has the potential to come close genetically to the resurrection of an extinct species. Rapid technological advances in the cloning of extant species, including species of conservation concern, and the increasing commercialisation of cloning applications, are leading to improvements in success rates and the health of clones. Cloning is suitable currently only when cryo-preserved tissue samples are available, most likely limiting the application of this approach to the resurrection of recently extinct species.

Limitations

Cloning is currently a relatively inefficient process for many species. In mammal cloning, for example, many eggs are required to derive viable embryos, and many embryo implantations are required to achieve even partial gestation and few live births.

Clones in many species have had a tendency to developmental abnormalities and premature aging, leading to suffering and to short lives, which has led to significant ethical concerns and would negate any potential for conservation benefits.

Cloning is fully dependent on the availability of intact somatic cells that have been stored appropriately, restricting the application of this approach to efforts on recently extinct species.

Finding a suitable surrogate host for mammals, and bird cloning, pose some significant additional technical challenges.

Production of multiple clones from one source will not provide any basis for population restoration. Multiple separate successful clones are necessary to ensure sufficient genetic diversity for a founding population.

Epigenetic effects, the influence of the rearing environment, the absence of appropriate conspecific learning opportunities, and other factors (e.g. microbiome and inheritance of the mtDNA of the gestational surrogate in interspecies mammal cloning[15]) could result in the creation of proxies that differ in unknown and unpredictable ways from the extinct form, even as clones of the original.

3. Genome engineering[16]

With genome engineering, the genome of the extinct species is first read with reference to many specimens – likely of skin, bone, feather, seed, spore, pollen, and other tissue suitably preserved in museum collections. If there are gaps in the genome sequence of the extinct form, they can be filled in with the genome of a nearest living relative. The genomes of living relatives will also be sequenced and cell lines will be created from the cells of a genomically similar extant species. Cells in that cell line will then be edited, using CRISPR/Cas9 or other technologies, to replace important DNA sequences characteristic of the extant species with synthesized DNA with the extinct species' sequence. The nuclei from these cells would then be inserted into a cell capable of forming an embryo, effectively performing somatic cell nuclear transfer. The embryo is implanted into a surrogate for gestation and birth (for mammals). For birds, the cells would be introduced into the reproductive organs of similar extant bird species to produce chimeras that were birds of the extant species that had germ cells from the extinct species. Male and female birds with the extinct species' germ cells would then be mated to produce individuals with the genome of only the extinct species. This method could also be done with mammals, algae, fungi, and plants, where it might prove easier than cloning.

Examples

There are no higher-order examples of proxy species creation using this genetic reconstruction and hybridization technique, but in 2005 researchers reconstructed the virus responsible for the 1918 Spanish influenza pandemic, recovering material from autopsy samples and from a victim buried in Alaskan permafrost, and using non-coding regions from a closely related influenza virus[17].

High profile efforts working with ancient DNA and using an allele transfer technique include projects on woolly mammoth and pas-

9 Gomez et al. 2009

10 Lanza et al. 2000

11 Folch et al. 2009

12 White, 2013

13 Fletcher 2014

14 Shapiro 2015

15 Hwang et al. 2013

16 Church and Regis 2012

17 Tumpey et al. 2005.

senger pigeon (*Ectopistes migratorius*)[18].

Potential

This is a feasible approach for the creation of proxies of species that went extinct before suitable cell samples could be collected and frozen, but recently enough so that good DNA sequencing is possible. It is made possible by advances in the ability to read and reassemble ancient DNA, and to make rapid, multiple changes in base pairs. It extends back in time the potential of species "de-extinction" to pre-historic extinctions hundreds of thousands of years ago, but not to millions of years.

One approach is to use an understanding of the extinct genome to re-engineer extant forms to express specific desirable traits once present in the extinct species, such as cold-tolerant elephants as proxies for woolly mammoths. In creating novel life forms that share an incomplete set of traits with the extinct species, this approach starts to move away from the essence of species re-creation. It does however, acknowledge (i) the current inability to fully resurrect a genetically faithful version of an extinct species, and (ii) an underlying objective of restoring ecological processes to benefit whole ecosystems[19], rather than just iconic focal species identical to their extinct counterparts.

The recent development of the CRISPR DNA-editing technique has made genetic modification easier, more accurate and less expensive[20]. The potential of this technique for human gene therapy could rapidly advance the technology and a spin-off benefit might be improvements in the ability to manipulate the genomes of a wide range of animal species, including for the reconstruction of proxies of extinct species.

Limitations

DNA is a fragile molecule and there are limits to how far back in time it will be possible to go since degradation of ancient DNA creates gaps and uncertainties. The more gaps the greater the proportion of the reconstructed genome that must derive from a near relative.

Genome engineering requires a suitable near relative to provide the appropriate gene sequences to fill gaps around the scaffold of the reconstructed genome and, in mammals, to act as gestational surrogates.

The resulting hybrids will not be genetically identical to the extinct form, and the expression of hybrid traits might be unpredictable, not least due to epigenetic effects. Significant technical challenges remain, but these are not considered to be insurmountable.

18 The Long Now Foundation http://longnow.org/revive/species/passenger-pigeon/

19 Shapiro 2015

20 de Souza 2015

Section V. Overview of potential benefits and disadvantages of creating proxies of extinct species

This section discusses the potential benefits and risks specifically of proxy species creation that involves the environmental release of resulting individuals. This is necessarily a simple list as many of the possible benefits and disadvantages in relation to the creation of proxies of extinct species have little or no published evidence or analysis.

Potential Benefits

Restore biodiversity

Loss or depletion of species from ecological communities can reduce the stability of ecosystems[21]. In contrast, restoring biodiversity, including through the establishment of populations of proxies of species that were there formerly or which are ecological equivalents of such species, or the creation of unique or distinctive evolutionary lineages, might increase ecosystem stability in the face of environmental change, promoting network diversity and reducing loss of other species.

Enhance ecosystem function and resilience

A defensible objective of proxy species creation for intended conservation benefit is enhancement of ecosystem resilience in the face of changes, the restoration of critical functions lost through extinction, and the re-establishment of ecosystem engineering functions that can serve to reverse changes.

Creation of proxy keystone species could support the restoration or maintenance of ecosystem services, including enhancing ecosystem resilience in the face of environmental change[22].

Engage public support

The hope of revival of once extinct species unfailingly captures public interest, and for many people the prospect of being able to see proxies of once extinct species could be a source of inspiration and wonder[23]. Proxies of extinct species successfully restored to a natural environment have potential to become flagship species for conservation, could provide a strong rationale for the preservation or restoration of habitat, and might be a means to reconnect people with the natural world in ways that could translate to conservation awareness beyond just the proxy.

Socio-economic impacts

Positive socio-economic impacts from released proxies could include direct effects through increased employment in projects or through associated tourism[24], and indirect impacts through beneficial effects on ecosystem services and cultural values.

Technological advances that could benefit extant species

Techniques relevant for proxy species creation, such as reading and reconstructing ancient DNA, allele transfer, and cloning, could be applied to the conservation of extant species[25], for example via genetic rescue as a means to increase the genetic diversity of relict populations through the reinsertion of genetic sequences retained only in museum specimens, or through enhanced techniques for the captive breeding of threatened species with mating systems that are not compatible with confinement.

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21 Dirzo et al. 2014

22 Zimov 2005

23 Sherkow and Greely 2013

24 Whittle et al. 2015

25 Jones 2014

Disadvantages

Financial and opportunity costs

To achieve the desired ecosystem-level goals, a population must be re-established in suitable areas of habitat, entailing translocation and post-release care and monitoring. The not-inconsiderable costs required for preparation, transport and release, and post-release management, will fall to conservation management bodies and will require resources, not just money but scarce human resources, that would otherwise be applied to the ex situ and in situ conservation of extant species.

Therefore work on proxy species will, to some extent, carry both financial and opportunity costs that must be balanced against expected conservation benefits. In addition, as with any conservation translocation, there needs to be assurance of funding for the anticipated life of the program, and contingency funding to address possible undesirable outcomes arising from releases of proxy species.

Decreased support for preventing extinctions

Public support for species conservation has been built around a sense of urgency and loss. There are valid concerns that even the prospect of species "de-extinction" could negate the powerful message that extinction is forever and lead to reduced support for the conservation of extant species[26], especially highly threatened species, because of views that these could subsequently "just be resurrected".

The precautionary creation of frozen zoos could reinforce a false sense of complacency in the face of impending extinctions. This represents a moral hazard (see Section III) that has been discussed in the context of "de-extinction" without any resolution, but which requires more discussion within the conservation community.

Unacceptable suffering by individuals

There are severe, well documented welfare concerns in relation to processes around the production of animal clones, including the suffering of new individuals and of gestational surrogates, around the provision of appropriate animal husbandry for proxies of once extinct species, and around post-release survival of animals following translocation into novel ecosystems[27]. Positive welfare states must be ensured for individuals to meet their physical and psychological needs.

Risks to surrogate species

Beyond animal welfare concerns for surrogate individuals, the requirement of near relatives for some proxy creation pathways might necessitate use of extant species that are of conservation concern themselves. This is equivalent to the risk to source populations harvested to provide founders for the captive breeding and/or translocation of extant species.

Uncertainty about species, behaviour, and post-release performance

These guidelines consider that none of the current pathways can fully replicate the offspring that would have resulted from natural mating of the focal species before extinction. Species "de-extinction" is therefore here described as proxy species creation. Proxies of extinct species might constitute novel species[28] by having unfamiliar ecological traits and being non-resident (having no recent evolutionary history) in a release area. In addition, there might be a lack of knowledge about the natural population dynamics of proxies, or lack of knowledge over behavioural deficiencies or their mitigation.

Invasiveness

A proxy species might become invasive if its establishment and growth causes damage to the environment, or to human economy or health. The negative effects of the proxy species might appear only long after its release into the wild. These negative impacts can be due to genetic factors associated with the proxy species creation process, or behavioural factors arising from the rearing environment, or because of ecological and environmental changes since extinction that mean any release will likely take place into an ecosystem where resident species have never encountered the original form of the proxy.

Novel disease vectors

No organism can be or remain entirely free of infection with micro-organisms or parasites. The release of a species that has been absent from an area, or of a proxy species never previously present, carries risk of spread of disease, particularly from captive facilities. Similarly, specialized parasites or pathogens might have been lost, and released individuals might be vulnerable to diseases they have never before encountered. The samples used to obtain DNA might harbour currently unknown pathogens. New associations with disease-causing agents not previously encountered might make proxy species novel vectors for disease.

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26 Pim 2013

27 Wells 2005.

28 Saul & Jeschke 2015

Inadvertent resurrection of ancient pathogens

Endogenous retroviruses reside in genomes and could be resurrected along with the proxy of the focal species. There is a small but non-negligible risk that any such retroviruses could become exogenous again.

Hybridisation with extant forms

There is a risk of hybridisation with closely related forms in the release area, jeopardising the genetic, population, or ecological properties of extant species. Hybridisation risk might be increased due to the process by which a proxy species has been created and by the use of surrogates for gestation and early rearing.

Ecosystem impacts

A proxy species, once placed in the wild, might have major undesirable and unforseen impacts at its destination on other species or on ecosystem functions. The post-release performance and impacts of proxy species will be subject to risk and uncertainty arising from genetic and epigenetic factors, the influence of the rearing environment, and unpredictable interactions with biotic and abiotic elements following release into what will possibly be novel ecosystems. The consequences of ecological replacements using proxies of extinct species might be more difficult to predict than if using extant species for which more is known.

Socio-economic impacts

Socio-economic impacts could include human-wildlife conflict and the risk of direct, harmful impacts on people (e.g. injury or death, spread of disease) and their livelihoods (e.g. livestock predation, crop raiding, reduced populations of wild-harvested species) from released proxy species, and indirect impacts through negative effects on ecosystem services and cultural values.

Re-extinction

There is a risk of project failure resulting in the (re)-extinction of the proxy species. Failure to establish a population of a proxy species might be due to a range of factors, including habitat mismatch, novel pathogens, unexpected inter-specific interactions, conflict with humans, the absence or aberrant expression of critical behaviours in the relation (e.g. behaviours related to foraging, predator avoidance, migration, breeding), and due to structural or physiological impairments (e.g. failure of the parallel restoration of an appropriate microbiome).

Section VI. Guiding principles

The IUCN SSC considers that the creation of a proxy of an extinct species, as described in Section II as including environmental release, will pose risks but has the potential to derive a conservation benefit when programmes incorporate the following components. It is also important to emphasise that none of the guidelines given below addresses the fundamental ethical issues discussed above (see Background). The IUCN SSC strongly encourages dialogue amongst opponents and proponents of "de-extinction", affected stakeholders, and the public, and the implementation of extremely precautionary policies and enforcement mechanisms prior to the undertaking of any "de-extinction" effort.

Expectation of conservation benefit

1. There should be *a priori* positive justification for engaging in proxy species creation based on the expectation of a positive conservation benefit, i.e. increasing ecosystem stability and resilience, and/or reducing losses in other species (see Section V). It is inappropriate for the creation and release of a proxy of an extinct species to be considered conservation neutral, as there will be at least some risks/costs in even ideal scenarios. If the objective for the creation of a proxy of an extinct species is the derivation of a functional equivalent able to restore ecological functions or processes that might have been lost as a result of the extinction of the original species, then the positive justification should be ecological, and in its absence "de-extinction" would seem unjustified.

Selection of "de-extinction" candidates

2. Alternative ecological replacements must be considered because in many cases a suitable ecological proxy might be found amongst extant species. Moreover, it would most likely be easier, less costly, and quicker to use extant proxies than to engage in the creation of proxies, and there would be more information available to predict ecological impacts. So, not only would the proxy form need to provide the anticipated ecological function, but it would need to do so better (and with less cost/risk) than the translocation of members of an extant species.

3. Selection of candidates should apply criteria in addition to the technical ability to recreate a species, considering among other factors: ultimate conservation benefits, invasive potential, generation time, human/wildlife conflict potential, the potential to control populations or reverse releases should unacceptable negative impacts occur, and overall ecological roles. The conservation goal of the programme should be clearly defined before the start, and a full species plan addressing all of these issues should be prepared before any programme is initiated.

4. Early candidate selection should evaluate the possibility to re-establish natural species assemblages through translocation into suitable areas of habitat where the primary threats that led to extinction in the first instance are absent or controllable, with the intention of establishing viable populations.

5. The 2013 *IUCN Guidelines for Reintroductions and Other Conservation Translocations* provide a suitable, comprehensive, and well-accepted framework to consider feasibility and risks associated with the translocation-related aspects of proxy species creation, with particular focus on recognition of the potential for environmental risks due to unwanted post-release effects. These guidelines should form part of the basis for candidate selection[29].

Release of proxy species

6. Once legal and other requirements have been addressed then the primary focus of translocation planning, implementation and post-release assessment is the desired performance of the focal species. Planning for "de-extinction" should include evaluation of the predicted population performance, behaviour, and ecological role of the proxy species. Some of this evaluation can take place, with more confidence, on *ex situ* captive populations of the proxy species before any decision is made whether to translocate them.

7. Local communities in areas considered for releases must give prior informed consent, and special effort should be made to obtain prior approvals from indigenous peoples.

8. Matching habitat suitability and availability to the needs of the focal species is critical to project success and needs to be central to translocation feasibility and design for any project.

9. The release of proxy species is not entirely different in nature from the translocation of extant species that have been absent from an area due to local extinctions, but might differ in the degree of uncertainty involved, both in its harms and in its benefits. Any release of proxy species should be preceded by an in-depth risk assessment. Risk assessment should make use of the most appropriate tools and should take into account uncertainty, as well as the potential long-term effects of factors of change, including climate change. There are parallels with the deliberate release of genetically modified organisms and the associated methods that have been developed to assess risks and monitor impacts.

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29 Seddon et al. 2014.

10. Risks involved in the release of proxy species will usually increase as the following increase:

    - The extent of environmental change since extinction
    - The time since extinction of the original form
    - The genetic differences between the original form and the proxy species
    - The likelihood of unacceptable ecological impacts
    - The potential for negative impacts on human interests
    - The anticipated role and degree of critical interactions between the proxy species and others
    - The extent to which critical behaviours must be learned from experienced conspecifics.

11. The main categories of risk to be considered in relation to the release of a proxy species should be ecological, disease, gene transfer, socio-economic, and risk of project failure. The main categories of potential benefit are ecological, but also socio-economic.

12. A proxy species might have major impacts within a release area on other species and on ecosystem functions; its own performance might not be equivalent to that of the original species. In evaluating risks a careful approach should treat the proxy species as non-native to the release site, even where this lies inside the indigenous range of the original form.

13. A trial translocation, involving confinement facilities and staged releases, should be used to evaluate post-release performance, and to enable refinement for future translocations, while retaining the ability to terminate the trial should prior thresholds of unwanted impacts be reached.

14. Disease risk assessment should be part of the early planning phase and subject to periodic evaluation.

15. The risks of hybridisation with closely related species should be evaluated.

16. The probability of either negative or positive socio-economic impacts and public attitudes should be assessed during project planning and periodically during implementation.

17. Any translocation of proxy species must have an exit strategy should unacceptable impacts occur, entailing removal of all individuals from a release area.

18. The chosen release area should meet the total biotic and abiotic needs of the focal species, at the time of release and for the foreseeable future. Locations and species should be chosen with this requirement in mind. The longer the time since the extinction of the original form the greater the likelihood of environmental change that affects habitat suitability and project success.

19. Released individuals should be tagged appropriately and monitored.

20. Close genetic monitoring of founder stock, released individuals, and wild relatives is required to assess both success over time and potential introgression.

21. The *2013 IUCN Guidelines for Reintroductions and Other Conservation Translocations* should be consulted in the planning and implementation of any translocation of proxy species.

<u>Criteria for defining success</u>

22. Programmes should include a set of criteria against which “success” is assessed.

23. Every “de-extinction” attempt should have clearly defined goals – a statement of the specific intended result that articulates expected conservation benefit (See also VI.1. Above).

24. For each goal there should be associated tangible objectives that detail how each goal will be realised.

25. Objectives should be developed that relate to the different components of a project. These could include:
    - Considering alternatives to achieve the desired conservation benefit
    - Feasibility studies
    - Project planning and consultation
    - Project implementation and evaluation

26. It should be understood that there is a strong possibility of significant differences from the original species, arising due to genetic variation, limited genetic variability, epigenetic effects, genetic stability, associated social and learning deficits, and the potential for altered ecosystem function in changed environmental conditions.

27. Genome-wide assessment and genetic architecture across taxonomic groups and their likely influence on success (above) need to be explored.

Avoidance of opportunity costs

28. No "de-extinction" attempt should risk extinction of any extant species, whether directly through negative interactions, or indirectly through opportunity costs – these are the benefit, profit or value that must be given up to achieve something else.

29. Although some of the costs, particularly in the early technical stages, might be met by funding sources that are not ordinarily available to conservation, proxy creation will likely require access to some level of resourcing that would otherwise be applied to the conservation of extant species; these resource costs must be made explicit, transparent, and understood by all stakeholders so that rational decisions can be made at all stages of project planning and implementation.

30. Evaluation of the costs and benefits of proxy species creation as compared to alternative management strategies to achieve similar conservation goals should be made as part of the early assessment of candidate and project feasibility. This should include consideration of selecting alternative ecological replacements from amongst extant species (see also VI.2).

Ethical management of proxy species

31. All efforts should be made to minimise the suffering of individuals, of focal species, of gestational surrogates, and of other affected species, at every stage of the "de-extinction" process

There are three options for the management of individuals of proxy species:

Maintain in captivity

32. From the perspective of seeking conservation benefits, the perpetual captive management of all individuals of a focal animal species should not be an expected outcome of any "de-extinction" program, but it is understood that some individuals might spend their lives in captivity.

33. Internationally acceptable standards for humane captive management must apply

Release

34. Translocation into a suitable area of habitat is a necessary action to realise the conservation goals of proxy species creation, and any translocation must apply conservation translocation best practice as detailed in *the 2013 IUCN Guidelines for Reintroductions and Other Conservation Translocations*.

35. Any translocation has risks and uncertainties and some post-release mortality is highly likely. These risks should be well understood, communicated to stakeholders and the public, and deemed acceptable in relation to anticipated benefits..

36. Care should be taken to minimise stress and suffering during all stages of the translocation process.

37. A program of post-release monitoring of individual health and welfare is necessary, and contingency plans should be in place to provide post-release veterinary care as necessary.

Euthanize

38. Euthanasia might be an appropriate action for individuals that are not suitable for release or for captive management that contributes to the establishment of wild populations. The conditions under which euthanasia would potentially be applied need to be identified in any project.

Section VII. Legal and Other considerations

Legal and legislative implications

- Legislation tends to categorise the protected status of native species on the basis of risks of extinction throughout the natural or the national range. Proxies of extinct species would initially have no calculable metrics of population decline or range contraction, lacking even a current range. A case could be made that any proxy assumes the historic range of the species for which it is intended to be the functional equivalent, though environmental change might make that unrealistic in some cases.
- Proxy species will be categorized differently by different authorities, and thus would not necessarily automatically replace extinct species within national or international legislation.
- Many laws prohibit the release of non-native species. Proxy species might be considered to fit this definition, so that any release would be possible only as an exemption.
- In addition to endangered species and invasive species laws, many jurisdictions have a range of wildlife and public land management laws that will significantly influence the creation and release of proxies of extinct species.[30]

International Conventions

- It is unclear how proxy species be dealt with in e.g. CITES, CBD, or other agreements around biodiversity management or targets, and it is beyond the scope of these guidelines to make convention-specific recommendations. Each proxy species will have to be separately evaluated with reference to each piece of specific legislation. For example, the cloned banteng is considered a hybrid by the US Fish and Wildlife Service and is therefore not considered part of the banteng population; the American Zoo and Aquarium Association however, considers the same animal to be a banteng and includes it in studbook records.

Proxy species as Genetically Modified Organisms

- Proxy species creation using cloning or genome engineering (see Section IV3) will produce genetically modified organisms that will be subject to specific national or international legislation and/or regulation that might limit the ability to move organisms across boundaries and to release them into the environment.

National regulations

- National regulations determine the status and degree of protection of organisms within national borders. It is beyond the scope of these guidelines to consider how national species/biodiversity management legislation might be applied in the case of proxy species creation, e.g. Endangered Species Act (USA), Species at Risk (Canada), Wildlife Act (NZ). Proxy species will need to be categorised on a case-by-case basis with reference to the terms of specific legislation.

Taxonomy and extinction risk

- Any proxy species could differ in some, and sometimes unpredictable, ways from the original form. Hence, its taxonomic name should reflect that.
- Internationally accepted guiding principles and standards of taxonomy, when such are available for created proxy species, should be followed.

Red Listing and species status implications

- The Red List criteria can be applied to any taxonomic entity, but apply only to wild populations inside their natural range, or populations resulting from conservation introductions; all individuals in a highly managed state or in captivity are excluded except in as much as a species can be listed as *Extinct in the Wild* as long as such individuals survive under such conditions
- Proxy species, therefore, might qualify for listing as *Extinct in the Wild* on the IUCN Red List[31], while all individuals remained in captivity or in a highly managed state, but this could be with the proviso that the proxy has survived beyond some as-yet-to-be determined period of time. It remains unclear how close a proxy would have to be to the original species to fully subsume its representation on the Red List.
- Before any proxy species are assessed for the IUCN Red List, IUCN SSC should develop standards for identifying such forms on the IUCN Red List. This could be a standard method of naming such forms (e.g. the name of the surrogate host species, followed by the name of the original form or the intended proxy species), in combination with an indication of the genetic method used.

30 Camacho 2015

31 IUCN 2012

Section VIII. The policy context

In large part there is a policy vacuum in relation to the specific issue of creating proxies of extinct species for conservation benefit. This is because few examples of such proxies exist, and even fewer where conservation benefits are sought. By necessity therefore, these guidelines are anticipatory. Nevertheless, there are some relevant policies that apply to particular aspects.

Two of the recognised pathways to proxy creation, cloning and genome engineering (see Section V), would result in the production of a genetically modified organism (GMO) as defined in the *Cartagena Protocol on Biosafety (CPB) to the Convention on Biological Diversity* (CBD 2000). The importation of GMOs is regulated by the CBD 2000, which regulates the international trade of GMOs with those countries that have ratified the CPB. It is a supplementary agreement to the 1992 Convention on Biological Diversity that "seeks to protect biological diversity from the potential risks posed by living modified organisms resulting from modern biotechnology." It establishes an Advance Informed Agreement (AIA) process to ensure that countries are provided with the sufficient information with which to make informed decisions before agreeing to the import of GMOs into their territory.

Individuals of proxy species could be classified as Living Modified Organisms (LMOs), defined in the *Cartagena Protocol* as "… any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology". The CPB uses the term LMO to distinguish living GMOs from GM products, because the scope of the CPB is the protection of biodiversity.

IUCN Resolution 3.007 (IUCN 2004) called for a moratorium on further environmental releases of GMOs until these can be demonstrated to be safe for biodiversity, beyond reasonable doubt; and directed the IUCN to support initiatives to ratify and implement the Cartagena Protocol on Biosafety.

The *IUCN Guidelines for the Prevention of Biodiversity Loss Caused by Alien Invasive Species* (IUCN 2000a) draw on and incorporate relevant parts of the 1987 *IUCN Position Statement on Translocation of Living Organisms* and the 1998 *IUCN Guidelines for Re-introductions* (now replaced by the 2013 *IUCN Guidelines for Reintroduction and other Conservation Translocations*). The guidelines are concerned with preventing loss of biological diversity caused by biological invasions of alien invasive species, but do not address specifically the issue of genetically modified organisms. Proxy species might fit the definition of "alien species" due to genetic differences from the original form and/or where releases take place outside the former indigenous range of the extinct species. Even a genetically identical proxy put into the former indigenous range might be considered invasive where, because of changes in the ecology of that range since extinction, it poses a threat to existing biological diversity. In particular the guidance on Intentional Introductions (5.3) is relevant to the release of proxy species, specifically:

> 5.3.2 Empowering the biosecurity agency, or other institutional mechanism, to decide whether proposed introductions should be authorized;
>
> 5.3.3. Urging the use of an environment impact assessment and risk assessment as part of the evaluation process before coming to a decision on introducing an alien species;
>
> 5.3.4. Requiring the intending importer to provide the burden of proof that a proposed introduction will not adversely affect biological diversity;
>
> 5.3.5. Recommending consultation with relevant organisations within government, with NGOs and, in appropriate circumstances, with neighbouring countries, in the evaluation process.
>
> 5.3.6. Where relevant, requiring experimental trials to be conducted as part of the assessment process.
>
> 5.3.7. Ensuring that the evaluation process allows for the likely environmental impacts, risks, costs (direct and indirect, monetary and non-monetary) benefits, and alternatives, to have been identified and assessed by the biosecurity authority in the importing country.

Proxies of extinct species would be classifiable according to *IUCN Red List Categories and Criteria* (IUCN 2012, 2014 a).

The IUCN *Guidelines on the Use of Ex Situ Management for Species Conservation* (IUCN 2014 b) present a 5-step decision making process for determining when ex situ management is appropriate. This emphasises a need for clarity over the role of ex situ management in species conservation, which could include the provision of individuals for all forms of conservation translocation. The guidelines also highlight a need for ensuring that the resources and expertise needed for ex situ management are suited to meet the specific conservation role, and are thus relevant to the captive management of proxy species.

The *IUCN Guidelines for Reintroductions and Other Conservation Translocations* (IUCN 2013) provide detailed guidance on the intentional release of any organisms for conservation benefit, and would apply to any proposed release of individuals of a proxy species. These Guidelines have many relevant provisions, including providing a basis for candidate selection, for assessment of the feasibility of releases taking into account species biology, habitat requirements, social feasibility, and regulatory compliance. Guidance is also given on release, monitoring, and ongoing management of newly establishing populations. Particular attention is given to risk assessment, and of specific relevance to the release of proxy species is Section 6.6, where the following is noted:

- Ecological risk: a translocated species may have major impacts (whether desirable/undesirable, intended/ not intended) at its destination on other species, and on ecosystem functions;
- Disease risk: as no translocated organisms can be entirely free of infection with micro-organisms or parasites, with consequent risk of their spread, disease risk assessment should start at the planning stage, with its depth in proportion to the estimated likelihood of occurrence and severity of impact of any prospective pathogen

- Associated invasion risk: separate from the risk of pathogen introduction, translocation design should be mindful of the wider biosecurity of the release area: care should be taken that potentially invasive species are not accidentally released;
- Gene escape: where organisms are moved outside their indigenous range, and there is a risk of hybridisation with closely-related species or subspecies, this may possibly result in lower fitness of offspring and/or loss of species integrity.

Also, the *IUCN Guidelines for Reintroductions and Other Conservation Translocations* (IUCN 2013) recommend that any translocation includes an “exit strategy” in the case of evidence of undesired and unacceptable consequences, to allow for orderly and justifiable reversal of any releases.

The *Guidelines for Wildlife Disease Risk Analysis* (OIE-IUCN 2014) propose a standardised and consistent Disease Risk Analysis (DRA) framework, that should be applied in any assessment of the disease risks potentially posed by proxies as the best way to analyse risks and generate the insights needed to make informed decisions about where to focus risk management actions.

The *US Coordinated Framework for Regulation of Biotechnology* (finalized in1986) sets out federal policy for regulating the development and introduction of products derived from biotechnology, which would apply to species created by cloning or genomic engineering (though not by back-breeding) in the US. The policy has three tenets: (1) a focus on the product of genetic modification (GM) techniques, not the process, (2) the evaluation of verifiable scientific risks is required, and (3) a conclusion that existing statutes are sufficient to review the products of GM.(President’s Domestic Policy Council Working Group on Biotechnology 1986).

Where individuals of a proxy species are confiscated by authorities for any reason, there is a responsibility on those authorities to dispose of them appropriately. The *IUCN Guidelines for the Placement of Confiscated Animals* (IUCN 2000 b) would apply. These state that the ultimate decision on the placement of a confiscated animal must (1) maximise the conservation value of the animals without harmful impact to wild or captive populations, (2) discourage irregular trade in the species, and (3) provide a humane solution.

The IUCN SSC Conservation Breeding Specialist Group (CBSG) has developed a One Plan Approach to integrated conservation planning to formulate and coordinate both *ex situ* and *in situ* conservation activities across a broad range of stakeholders. Such an approach could be followed for “de-extinction” projects to bridge the gap between captive and wild population management, policy, planning and implementation. Examples of the CBSG One Plan Approach are available at: www.cbsg.org/our-approach/one-plan-approach-conservation

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