



Genetically Engineered Self-Spreading Vaccines for Wildlife: Promise, Case Studies, and the Precautionary Imperative

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Chapter 1

Introduction

PATHOGENS circulating at the human-animal-environment interface have repeatedly converted ecological disturbance into public-health and conservation crises. Rabies, Ebola, Lassa fever, avian influenza, and coronaviruses demonstrate how infections maintained in wildlife reservoirs can spill over to humans with global consequences. At the same time, wildlife diseases such as chytridiomycosis in amphibians and white-nose syndrome in bats have driven severe population declines, eroding ecosystem functions already stressed by habitat loss, climate change, and pollution. These pressures have intensified the search for tools that can operate at the scale of populations rather than individuals.

Genetically engineered self-spreading vaccines were conceived to meet that challenge. The basic proposition is straightforward: genetically engineer a replicating vector – typically a virus with a narrow host range – to express protective antigens, inoculate a small number of individuals, and allow ordinary contact to disseminate immunity across the population. In theory, such an approach could immunize elusive, nocturnal, or highly mobile species at a fraction of the logistical cost of capture-and-release inoculation or oral baits, and could thereby reduce zoonotic risk while supporting conservation goals.

This is not a new idea. Since the 1980s, research programmes have explored replicating vaccinia and cytomegalovirus vectors, and, later, pox- and herpesvirus backbones tailored to specific hosts. In the 1990s, proposals targeting rabbit haemorrhagic disease and

myxomatosis in Australia were promoted as close to practical use. Similar claims resurfaced in the early 2000s with advances in molecular virology and again after COVID-19, when renewed interest in pandemic prevention rekindled optimism about rapid progress. Despite these cycles of enthusiasm, no transmissible vaccine has advanced to environmental deployment; most remain mathematical models, *in vitro* work, or contained *in vivo* studies. The recurrent portrayal of “near-readiness” reflects a pattern of rebranding the same concept rather than the resolution of its core uncertainties.

Those uncertainties are structural. Transmissibility, persistence, and autonomy – features central to the concept – also remove the very levers of control upon which biosafety and biosecurity depend. Once released, a replicating construct cannot be reliably recalled, and small genetic changes can shift host range, alter virulence, or modulate transmission. Interactions with circulating pathogens may yield recombinants or immune interference that models cannot anticipate at landscape scales. Because wildlife populations cross borders and interact in complex networks, even modest perturbations of survival or fecundity can cascade through food webs, changing predator-prey dynamics, seed dispersal, or vector ecology in ways that are difficult to monitor and impossible to reverse.

These biological realities collide with existing governance. The Cartagena Protocol on Biosafety and related national frameworks were built on the premise that living modified organisms can be localized, monitored, and, if necessary, withdrawn. Risk-assessment procedures, liability and redress expectations, and transboundary safeguards all implicitly assume containment and reversibility. Transmissible vaccines invert those assumptions by design. Moreover, meaningful participation by potentially affected States and Indigenous Peoples and local communities – an ethical expectation reflected across international environmental law – is hard to operationalize when neither the spatial nor temporal bounds of an intervention can be specified in advance.

Against this background, self-spreading vaccines have become a revealing test of precautionary governance. They force a shift from the familiar question – can we build them safely? – to the prior question of whether there exists any credible pathway to contain and constrain their risks once they leave containment. They also expose an asymmetry between the accelerating capacity to engineer replicating systems and the comparatively slow development of ecological data, long-term monitoring infrastructure, and international oversight mechanisms that would be prerequisites for any responsible field consideration.

This paper takes up that challenge in three steps. First, it traces the persistence of the idea across decades, emphasizing why claims of imminent application have repeatedly outpaced evidence. Second, it examines three emblematic targets – Lassa fever in *Mastomys* rodents, rabies in bats, and white-nose syndrome in North American bats – because they span zoonotic control and conservation imperatives and because they are the cases most often invoked to argue feasibility. Third, it situates the analysis within the objectives of the Convention on Biological Diversity (CBD) and its Cartagena Protocol on Biosafety, clarifying why current scientific understanding and regulatory architecture are misaligned with self-propagating agents.

The aim is not to dismiss innovation but to specify the conditions under which it could be responsibly evaluated. By separating conceptual appeal from operational reality, and by grounding the discussion in ecological dynamics and international law, the paper argues for a disciplined application of the precautionary principle: confinement of research to laboratory and strictly contained settings, coupled with deliberate investment in ecological monitoring, predictive modelling, and transboundary governance capacities. Only under such conditions could a future debate about environmental release be more than an expression of technological optimism.

Chapter 2

Case Studies

THE following cases are selected because they recur most frequently in scientific literature and policy conversations as plausible early applications of genetically engineered self-spreading vaccines, and because each illustrates a distinct motivation: reduction of a high-burden zoonosis at its reservoir (Lassa fever in *Mastomys* rodents), mitigation of a persistent zoonotic threat in a highly mobile keystone taxon (rabies in bats), and conservation of species under acute disease-driven decline (white-nose syndrome in North American bats). Across all three, similar promises and problems recur: modelling suggests theoretical feasibility at low seeding effort, but empirical evidence remains confined to laboratory or contained studies; ecological externalities and governance requirements expand with every plausible transmission pathway; and “near-product” rhetoric has repeatedly outpaced what risk assessment and monitoring can credibly support.

Lassa Fever in *Mastomys* Rodents

Lassa fever is endemic in West Africa, with the multimammate rat *Mastomys natalensis* serving as the primary reservoir and frequent peri-domestic contact sustaining human exposure. Conventional measures – improved housing, grain storage, environmental sanitation, and rodent control – have struggled to interrupt transmission at scale. A transmissible vaccine appears attractive because even modest reductions in reservoir competence could, in theory, translate into substantial decreases in human incidence.

From the early 1990s onwards, proposals have focused on narrow-host-range viral backbones, most commonly rodent cytomegaloviruses engineered to express Lassa antigens. Computational work has explored threshold conditions under which a small number of initially inoculated animals could drive vaccine establishment and spread. Laboratory studies have demonstrated stable expression of heterologous antigens in related systems and partial protection in inoculated individuals, but no construct has advanced to field trials. The gap between modelled spread and demonstrated field behaviour remains the central evidentiary limitation.

Mastomys natalensis is abundant, fecund, and ecologically influential, contributing to seed dispersal and serving as prey for multiple predators. Increasing survival or altering fecundity via vaccine-mediated changes in disease burden risks rodent population booms, crop damage, and shifts in predator-prey dynamics. Although species specificity is a design goal of a genetically engineered vaccine, imperfect host restriction is a recurring challenge in replicating vectors; closely related murids and commensal rodents share habitats and may be exposed. Over successive passages, mutations or recombination could adjust transmission, tissue tropism, or host range in ways that models cannot safely predict.

Rodent populations cross administrative and national borders with ease. A release of a genetically engineered vaccine in one jurisdiction would likely create transboundary exposure, activating obligations for prior informed consent and cooperative risk management that are difficult to operationalize when spread is the intended property. Communities most exposed to *Mastomys* – often rural households and market settings – would bear concentrated risks, yet meaningful, informed participation is hard to guarantee for an intervention without clear spatial or temporal limits.

The reservoir-focused logic is compelling, but the ecological leverage points are numerous and weakly understood. Without credible mechanisms to confine spread, detect early deviation from expected behaviour, or redress harms that may emerge slowly and unevenly across borders, the Lassa case remains a theoretical demonstration rather than a candidate for environmental deployment.

Rabies in Bats

Rabies imposes a persistent burden on human health and livestock. In Latin America and parts of Africa and Asia, bats – including *Desmodus rotundus* – are important reservoirs. Traditional oral-bait strategies that proved effective in terrestrial carnivores are impractical for volant, nocturnal, socially gregarious species. Because many bats engage in social grooming and have dense roosts, a transmissible vaccine that spreads via direct contact is frequently proposed as a “natural fit”.

Concepts span attenuated rabies backbones and recombinant pox-, herpes-, or cytomegalovirus vectors that express rabies glycoprotein while aiming for host specificity. Experimental work has shown that some bat herpesviruses can persist and disseminate within colonies, and modelling studies suggest that limited seeding could disrupt rabies circulation. Nonetheless, empirical evidence of safe, predictable spread in free-ranging bat populations is lacking, and the few demonstrations of within-colony dissemination rely on controlled contexts, not open environments with species turnover and migration.

Bats deliver outsized ecosystem services: pollination of key plants, long-distance seed dispersal, and suppression of agricultural pests. Colony histories, species mixing at cave systems, seasonal migrations, and reproductive pulses create complex contact networks that defy simple compartment models. A transmissible construct could persist for multiple seasons, reshaping immunity profiles and age structure. Cross-species transfer is plausible where roosts are shared, and even subtle effects on survival or

fecundity could cascade into altered plant regeneration or insect population dynamics. The evolutionary potential of replicating vectors in the context of co-infections and environmental stressors (e.g., food scarcity, heatwaves) is an additional unknown.

Because bats are highly mobile and transboundary by nature, any release of a genetically engineered vaccine in this case would effectively engage multiple national jurisdictions from the outset. The impossibility of defining a stable “receiving environment” undermines the risk-assessment premise of bounded exposure and manageable monitoring. In many regions, cave systems and bat roosts are culturally significant; ethical obligations to inform and seek agreement from affected communities collide with the practical impossibility of delimiting who is “affected”.

The bat case epitomizes the tension between conceptual fit and ecological irreversibility. The more realistic the contact structure becomes, the less credible it is to assert controllable spread or robust recall, leaving the proposal on the far side of what current governance and monitoring can bear.

White-Nose Syndrome in North American Bats

White-nose syndrome, caused by the fungus *Pseudogymnoascus destructans*, has precipitated severe declines in multiple bat species across North America, with some hibernacula experiencing catastrophic mortality. This acute conservation emergency has driven interest in interventions that operate at colony and metapopulation scales, including ideas for transmissible vaccination that might spread protection during the prolonged close contact of hibernation.

A recombinant raccoonpox-virus platform, among other poxvirus concepts, has been discussed as a vehicle to disseminate antifungal immunity. The biology seems initially favourable: cold, dense aggregations in hibernation sites, repeated close contact, and seasonal synchrony that could support spread. Yet risk reviews have highlighted the broad host range and genomic plasticity

of poxviruses, their recombination potential, and the uncertain interplay between immunomodulation and fungal pathogenesis in stressed bats. As a result, work has remained *in silico* or in containment, without environmental trials.

Populations affected by white-nose syndrome are already stressed, with skewed age structures, altered behaviour, and reduced genetic diversity. Introducing a genetically engineered replicating vector into such systems risks compounding fragility. Even if a construct were nominally host-restricted, sympatric mammals frequenting caves and mines could encounter the vector; non-target infection would carry both ecological and reputational costs for conservation programmes. Overwinter metabolism, torpor-arousal cycles, and immune suppression introduce further uncertainty into vector replication, transmission, and persistence across seasons.

The conservation imperative is strong, but urgency cannot substitute for the absence of control and recall. Many hibernacula lie on mixed-ownership landscapes – federal, state/provincial, tribal/Indigenous, and private – complicating any unified consent process. The temporal and spatial indeterminacy of spread makes it impossible to guarantee meaningful participation of all affected parties in advance. Liability and redress frameworks provide no workable path to compensate harms that could surface years later in remote roost networks.

Despite the conservation need, the combination of population fragility, vector plasticity, and mixed-jurisdiction landscapes renders transmissible vaccination unsuitable under current scientific and governance capacities.

Taken together, these cases show that the most frequently invoked targets for genetically engineered self-spreading vaccines are exactly those where governance and ecology are most unforgiving: peri-domestic rodents embedded in human livelihoods; bats that knit ecosystems together across vast ranges; and collapsing populations where any additional stressor could tip dynamics

towards irreversible loss. In each example, design goals – narrow host range, stable antigen expression, controllable transmission – collide with realities of mutation, recombination, species mixing, and landscape heterogeneity. The inability to specify a bounded or defined receiving environment or credible recall mechanism is not a detail to be engineered away but the central fact that keeps these proposals theoretical. Under present conditions, the scientific uncertainty and governance deficits do not merely slow deployment; they define its inadmissibility outside strictly contained research.

Chapter 3

Discussion

ACROSS more than four decades, self-spreading vaccines have followed a familiar arc: conceptual excitement, confident predictions of imminent application, and eventual return to caution once ecological and governance realities reassert themselves. The persistence of this cycle does not signal steady progress towards field readiness; it reveals how easily technical ingenuity can be mistaken for control over living systems. Each new platform – recombinant vaccinia, herpes- and cytomegalovirus vectors, and, most recently, synthetic biology tools – has refreshed the promise without resolving the structural issues that keep the technology confined to containment.

Those issues are rooted in biology rather than in engineering polish. A vaccine that propagates through a host population is, by definition, a replicating agent evolving in open systems. Small mutational changes, recombination with circulating viruses, shifts in tissue tropism, and modulation of host range are not outlying cases but ordinary features of viral evolution. In heterogeneous landscapes – where age structure, seasonality, co-infections, and species mixing shape contact networks – these evolutionary dynamics intersect with ecological feedback loops that models cannot safely predict. Even modest perturbations of survival or fecundity can alter food webs, seed dispersal, and disease ecology at scales that elude monitoring. Once established, a genetically engineered transmissible construct cannot be meaningfully recalled; uncertainty is not a temporary obstacle but a durable property of the intervention.

The ethical implications follow directly. Introducing self-replicating genetic material into wildlife populations is an irreversible alteration of shared environments. Communities most exposed – often Indigenous Peoples and local populations coexisting with reservoir species – would bear concentrated risks while having limited practical pathways to give or withhold informed agreement. Free, prior, and informed consent loses meaning when neither the spatial nor temporal bounds of an intervention can be specified in advance. Public narratives that describe these systems as “vaccines that vaccinate themselves” risk masking the scale of open-ended uncertainty and eroding trust when promised control proves illusory.

Existing governance frameworks were not built for this problem. Under the Cartagena Protocol on Biosafety, genetically engineered self-spreading vaccines fall within the definition of living modified organisms, yet the core assumptions of Annex III on risk assessment – bounded receiving environments, manageable exposure, and potential withdrawal – do not apply to agents designed to move autonomously across borders. Provisions on unintentional transboundary movement and on liability and redress likewise presuppose containable releases with traceable causality; they offer no workable path to assign responsibility or compensate harms that may surface years later or thousands of kilometres away. At the level of the Convention on Biological Diversity, premature deployment could undermine all three objectives of the CBD: conservation, by disrupting population genetics and interspecies interactions; sustainable use, by destabilizing ecosystem services; and fair and equitable benefit-sharing, by globalizing putative benefits while localizing risk.

A further asymmetry compounds these deficits: the capacity to engineer replicating systems is advancing faster than the capacity to evaluate and govern them. Modular cloning, rapid design-build-test cycles, and improved modelling have lowered the barrier to creating transmissible constructs, while the ecological baselines needed for credible assessment – long-term field data

on host-pathogen co-evolution, cross-species transmission networks, and landscape-scale feedbacks – remain sparse. Intellectual property constraints and limited data transparency further impede independent scrutiny. Innovation thus outpaces comprehension, not because scientists are careless, but because the relevant evidence accumulates on ecological timescales that laboratories and grant cycles cannot compress.

In this context, precaution is not a rhetorical posture but a practical standard. The principle articulated in the Rio Declaration and reflected in the Cartagena Protocol requires that the locus of activity remain where uncertainty can be bounded: laboratories and strictly contained trials. Confinement is a governance choice that acknowledges current limits while preserving the possibility of future evaluation. It should be paired with deliberate investment in three enabling capacities: ecological monitoring systems that can detect subtle, long-horizon change; modelling frameworks that integrate evolution, multispecies dynamics, and spatial heterogeneity; and international arrangements for notification, consent, oversight, liability, and redress scaled to self-propagating risks. Only with such foundations could any later debate about environmental release be more than an expression of technological optimism.

The larger lesson is about governance. To treat ecosystems primarily as substrates for technological intervention is to underestimate the depth and autonomy of living systems. Genetically engineered self-spreading vaccines are compelling precisely because they promise leverage at population scale; but they are untenable because they withdraw the levers of control on which responsible biotechnology depends. Recognizing that tension – and resisting the recurring allure of “near-product” narratives – allows policy to be guided not by the speed of invention but by the pace at which knowledge, monitoring, and accountability can credibly keep up.

Chapter 4

Conclusion

GENETICALLY engineered self-spreading vaccines endure in scientific and policy imagination because they promise leverage where conventional tools falter: reaching elusive wildlife at population scale, damping zoonotic reservoirs at their source, and rallying conservation in the face of rapid decline. The same features that make them attractive – transmissibility, persistence, autonomy – are, however, the reasons they remain confined to models and containment. In open, multispecies landscapes, a replicating construct is not a static product but a moving process. It evolves, encounters novel hosts, and feeds back into ecological networks in ways that cannot be bounded by current methods of prediction or control. After more than four decades, this is not a failure of ingenuity so much as a recognition that the intervention's defining properties place it beyond the reach of present biosafety practice.

The governance implications are decisive. Frameworks under the Convention on Biological Diversity and the Cartagena Protocol on Biosafety presuppose receiving environments that can be delimited, exposures that can be managed, and releases that can be reversed or at least arrested. Self-propagating agents invert these premises. Liability and redress become intractable when causality disperses over time and distance; meaningful participation by potentially affected States and communities becomes aspirational when the bounds of "affected" cannot be specified in advance. In this setting, authorization would shift risk from regulated actors

to ecosystems and communities with no credible pathway to consent or remedy.

Ethically, releasing a self-replicating construct into wildlife is an irreversible alteration of shared environments. The burdens would fall most immediately on those living alongside reservoir species, including Indigenous Peoples and rural communities, while any benefits would be diffuse and global. This asymmetry is difficult to reconcile with commitments to equity and with the precautionary duty that underwrites public trust in biotechnology and conservation alike. Assurances that “design fixes” can deliver controllable spread, narrow host range, or intrinsic containment remain conjectural in the settings where they would matter most – heterogeneous, changing landscapes.

The appropriate policy response is therefore not to foreclose inquiry but to relocate it. Research on genetically engineered self-spreading vaccine concepts should remain in laboratories and strictly contained trials, where uncertainty can be bounded and error does not propagate. In parallel, international effort should be directed to building the preconditions for any future evaluation: ecological monitoring systems capable of detecting subtle, long-horizon change; modelling frameworks that integrate evolution, multispecies dynamics, and space; and multilateral arrangements for notification, consent, oversight, liability, and redress tailored to self-propagating risks. Only once these capacities exist – and only if they demonstrate that risks can be credibly bounded – would a discussion of environmental release move from technological optimism to responsible assessment.

Discussions under the Convention on Biological Diversity and its Cartagena Protocol on Biosafety have already recognized the relevance of genetically engineered self-spreading vaccines within the broader synthetic biology agenda. Earlier deliberations, specific to self-propagating genetic elements, highlighted the need for further in-depth assessment, inclusive of ecological, socioeconomic, cultural and other impacts; mechanisms to ensure the free, prior, and informed consent of all potentially affected

communities; and examination of whether there is an appropriate evidence base on which to justify potential field tests or commercial use. Yet this work has not advanced beyond this preliminary scoping. As scientific exploration continues, it is essential that this issue be brought back to the attention of the international biosafety community. Re-engaging through the Convention's and Protocol's established mechanisms – such as ad hoc technical expert groups, voluntary guidance, and the Biosafety Clearing-House – would ensure that any future consideration remains grounded in the principles of precaution, transparency, and equity that anchor the global biosafety regime.

Seen in this light, precaution is not a brake on progress but is necessary for legitimacy. It aligns scientific ambition with the tempo of ecological knowledge and democratic accountability, preserving options rather than foreclosing them through irreversible action. The lesson of the past 40 years is that genetically engineered self-spreading vaccines are compelling as an idea and untenable as a field intervention under present conditions. Until the scientific, monitoring, and governance architecture catches up with the scale of the claims, environmental deployment should not be pursued. Protecting biodiversity and public health requires tools that work with, rather than against, the autonomy of living systems. By keeping genetically engineered self-spreading vaccine research within containment and investing in the capacities that make prudent judgment possible, the international community affirms that the measure of progress in biotechnology is not speed to release, but the strength of the knowledge, assessment, and accountability that accompany it.

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Self-spreading vaccines have been proposed for over four decades as a way to achieve population-level immunity in wildlife by allowing genetically engineered vectors to passively disseminate protective antigens from host to host. Since the 1980s – through successive waves of recombinant vaccinia, herpes- and cytomegalovirus constructs, and post-COVID synthetic biology platforms – the concept has repeatedly been promoted as close to field-ready. Yet no candidate has progressed beyond models and contained experiments. The distance between promise and practice persists because the very traits that make these vaccines attractive – transmissibility, persistence, and autonomy – create risks that current science and governance cannot effectively address.

This paper reassesses the paradigm through three frequently cited targets – Lassa fever in *Mastomys* rodents, rabies in bats, and white-nose syndrome in North American bats – chosen because they span zoonotic control and conservation imperatives and because they have repeatedly been presented as “near-product”. Across these cases, the scientific rationale is plausible, but ecological and evolutionary behaviour in open systems remains inherently unpredictable: small genetic changes can shift host range or virulence; interactions with circulating pathogens can produce unintended dynamics; and once established, a transmissible construct cannot be reliably recalled.

Situated within the objectives of the Convention on Biological Diversity (CBD) and Cartagena Protocol on Biosafety, the analysis shows that existing risk-assessment procedures, liability and redress provisions, and transboundary safeguards presume containment and reversibility – assumptions incompatible with self-propagating agents. Ethical commitments, including meaningful participation of potentially affected States and communities, are likewise difficult to realize when spatial and temporal boundaries are indeterminate. The conclusion is therefore precautionary and practical: research on genetically engineered self-spreading vaccines should remain confined to laboratory and strictly contained settings, while international efforts focus on developing credible ecological monitoring, long-term modelling, and governance mechanisms that would be prerequisites for any future consideration of environmental release.

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