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Expert Insights
PERSPECTIVE ON A TIMELY POLICY ISSUE

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Policy Options to Prevent the Creation of Mirror Organisms

Most of the molecular building blocks necessary for life are *chiral*: They have three-dimensional structures that are different from their mirror images. All organisms on earth are partly made of chiral molecules that, similar to human hands, could come in left-handed and right-handed forms. DNA, RNA, and amino acids are all chiral molecules, and all are found only in one chiral orientation in life on earth (Blackmond, 2019; Church and Regis, 2014). Opposite-handed versions of these essential molecules can exist, but they are not used or produced by living organisms on earth (Blackmond, 2019; Church and Regis, 2014). One publication from December 2024, titled "Confronting the Unprecedented Risks of Mirror Life," by Adamala, Agashe, Belkaid, and colleagues (2024) identifies a radical and alarming development: Scientists are approaching the ability to create living organisms made of opposite-handed molecules, called *mirror life* (Bohannon, 2010; Bohannon, 2018).

This group of concerned scientists (Adamala, Agashe, Belkaid, et al., 2024) describes how research leading to creation of mirror life could put humanity (as well as nearly all plants and animals) at risk. If mirror organisms, specifically mirror bacteria, are created, it is likely that almost nothing in nature would be able to

restrain them. The spread of mirror bacteria throughout the biosphere could kill most or perhaps all animal and plant life on earth. In particular, mirror organisms might be unrecognized by immune systems of natural life forms (Brewster and Laskowski, 1992), and infection would likely lead to uncontrolled proliferation within host tissues, resulting in death (Adamala, Agashe, Binder, et al., 2024). Human immune systems recognize many molecular markers belonging to harmful organisms in a way that depends on the chiral orientation of these molecules, just as a right-handed glove fits on a right hand. A mirror organism would have molecular markers that likely would not be effectively recognized by the immune system, in the way a right-handed glove does not fit on a left hand. Natural predators of bacteria—protists, phages, and other bacteria—would likely be unable to recognize mirror bacteria. Although

Key Recommendations

In the near future, policymakers should

- state that they are deeply concerned about the warnings issued by scientific experts regarding mirror organisms
- pause any federally funded research programs aimed at creating mirror life and urge that other funders do the same, pending further assessment of that warning
- commission studies to evaluate the concerns that have been raised
- encourage other interested parties to conduct studies and analyses on that topic.

If concerns are not disproven by such studies, policymakers could

- make the recommended pause on federally funded research permanent
- add mirror organism research to the federal policy for oversight of dual-use research of concern and pathogens with enhanced pandemic potential
- designate mirror organisms as select agents and their creation as restricted experiments under the federal select agent program, which would capture all such work, independent of funding source
- broaden existing nonproliferation catch-all export controls so that they capture any exports supporting the development of mirror organisms
- draft, pass, and implement new legislation to prohibit the development of mirror organisms and to ban or regulate precursors
- ensure that the development of mirror organisms is banned everywhere in the world by engaging bilaterally with countries that have science and technology bases that could otherwise support mirror organism development
- work within a variety of existing multilateral institutions to establish binding international commitments prohibiting mirror organism development
- work toward the establishment of a new international treaty specifically designed to prohibit mirror organism construction and to regulate materials and technologies useful for mirror organism development.

some existing antibiotic therapies might be effective against mirror bacteria, most antimicrobial therapeutics would be unlikely to cure infection with mirror bacteria.

Mirror life does not exist at the time of this writing in late 2024. However, scientific research programs have made progress toward its creation through synthesizing increasingly complex mirror biomolecules (Harrison et al., 2023; Milton, Milton, and Kent, 1992; Wang et al., 2019; Zhao and Lu, 2014) and reproducing molecular functions, such as mirror DNA replication and the transcription of mirror RNA (Xu and Zhu, 2022; Pech et al., 2017). By assembling such molecular components using synthetic biology techniques (Gaut and Adamala, 2021), these research programs could create a functional mirror version of an existing organism, such as the abundant and robust bacteria *Escherichia coli*. The U.S. National Science Foundation has funded grants toward creation of mirror life at the Scripps Research Institute (Dawson, 2018) and a collaboration between the University of California at San Diego and Yale University (Devaraj, 2024; Isaacs, 2024). George Church's group at Harvard University (Church and Regis, 2014; "George Church—Life: What a Concept!" 2007; Service, 2022) led research efforts related to mirror life, and the laboratory of Ting Zhu at Westlake University in China (Peplow, 2018; Xu and Zhu, 2022) has been engaged in an active research program to establish mirrored versions of the core biochemical processes that would enable mirror life.

In Adamala, Agashe, Belkaid, and colleagues' article (2024), they state that "in the absence of compelling evidence for reassurance, our view is that mirror bacteria and other mirror organisms should not be created." They argue that even if mirror organisms are created that cannot grow outside the laboratory, such a safeguard is vulnerable to human error or natural evolution. Moreover, a malicious actor intending to cause global-scale harm or use the threat of such harm as leverage could deliberately remove such safeguards and gain the potential to cause catastrophic harm to human, animal, and plant life. These potential consequences create a critical public policy imperative to consider all available tools to prevent such organisms from being created, identify research and development that would be particularly enabling for these organisms' creation, and ensure that the additional technical breakthroughs required to permit their construction remain difficult to achieve. Were these tools to be implemented, any research program to develop mirror organisms would be forced underground, where it would have to surmount those technical hurdles on its own without the ability to take advantage of work to that end done by others.

Research on mirror biology might someday have commercial or other legitimate uses. However, Adamala, Agashe, Belkaid, et al. (2024) argue that the creation of mirror life for any purpose would make it far too easy to create a variant that could threaten most complex life. Even creating these organisms in the pursuit of countermeasures against their potential release by others would expose the world to the very danger that those countermeasures would be intended to counter.[1] As a result, these scientists recommend avoidance of these risks entirely over potential future benefits. Although Adamala, Agashe, Belkaid, et al. (2024) acknowledge that some mirror biomolecules may have beneficial applications, commercially useful mirror molecules could be produced without the use of mirror organisms.

In warning of the dangers of mirror biology, these authors have invited critical examination of their findings and have called for broad societal discussion of the

appropriate next steps. This paper is intended to contribute to that discussion by identifying and analyzing a suite of relevant policy tools. We draw on our own expertise and an examination of literature on governance of dual-use life science research (Epstein, 2001; Epstein, 2012) and government guidance. In particular, we consider possible U.S. policy, regulatory, and statutory mechanisms, along with international agreements that could establish legally binding obligations to prevent and prohibit mirror organisms from ever being constructed. An all-of-society response would also include actions on the part of scientific or professional organizations and other civil society institutions, which we do not address in this paper. Nor do we assess in depth the scientific case for the dangers of mirror organisms, the possible ecological or health consequences of mirror organism release, or the development of defenses or countermeasures against such organisms. Because any mirror organism constructed anywhere is a threat to all countries everywhere, actions to prevent the construction of mirror organisms would need to be coordinated internationally. Therefore, in addition to outlining domestic efforts, we address actions that the United States could take to motivate and catalyze similar efforts internationally.

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The Policy Challenge and Recommendations for Immediate Action

The potentially catastrophic risk posed by mirror life makes the stakes for effective public policy intervention very high. At the same time, some aspects of this risk make it easier to address than some other extreme risks. Building a mirror organism is beyond the existing state of the art, and years of dedicated effort would still be required to create one (Adamala, Agashe, Binder, et al., 2024). At least initially, potential malicious creators of a mirror organism would need to be exceptionally technically skilled. At present, it is unlikely that any covert program specifically dedicated to that objective exists. There is time to put preventive measures in place to prevent not only the creation of mirror organisms, but the widespread proliferation of the tools needed to be able to do so.

Any scientific progress by ongoing research programs irreversibly removes barriers to mirror organism creation. Progress in creation of synthetic nonmirror (natural chirality) cells could speed a subsequent program to create mirror

cells. Advances in artificial intelligence (AI) biology models and other biological advances that are not narrowly targeted could also shorten the time required for researchers to make significant progress toward creation of mirror life.

Recognizing that the recommendations of Adamala, Agashe, Belkaid, et al. (2024) are offered as a starting point for further discussion, we nevertheless identify actions that can be taken immediately. To avoid undercutting any future prohibition on research with the goal of creating mirror bacteria—a prohibition that Adamala, Agashe, Belkaid, et al. (2024) have called for—we recommend that the U.S. government take steps to pause any such ongoing research programs immediately. Such a pause can be lifted if a ban is not ultimately agreed to, but any research results discovered in the absence of a pause can never be unlearned if a ban is subsequently put into place. We also believe that the U.S. government should initiate work immediately to reduce any uncertainty in the conclusions of Adamala, Agashe, Belkaid, et al. (2024) and the technical report by Adamala, Agashe, Binder, et al. (2024) in ways that do not require creating mirror life. Immediate action could help convey the potential seriousness of the problem and establish U.S. leadership in galvanizing international measures to address the issues around the creation of mirror life. However, further scrutiny of these authors' concerns will likely be necessary to initiate some of the other policy options described here.

One challenge of any U.S. government policy response to the threat posed by mirror organisms is the need to engage effectively—not only with the life science community, but with the public at large. Many of the policy options discussed in this paper will require detailed technical understanding to formulate, and they will likely affect not only research directly intended to produce mirror organisms but other biological applications as well. Formulating and implementing these policies will need to be done in close consultation with the affected technical communities. However, the potential consequences of these policies go far beyond the technical community. These policies could affect every person—indeed, much of life—on the planet, which calls for broad stakeholder engagement beyond the technical community. That degree of outreach is daunting for any issue, but it will be especially challenging for this one because of the technical complexity of the underlying biology and the magnitude of the stakes.

U.S. Government Domestic Policy Options to Halt, Prohibit, and Prevent Mirror Organism Production

We catalog four categories of U.S. government domestic policy response roughly in the order of the complexity of their implementation. These categories are

- executive branch statements and norm-building actions, with both domestic and international goals
- executive branch actions regarding its own activities, including a federal funding ban
- executive branch regulatory changes under existing statutory authority; these would establish binding constraints on all activities under U.S. jurisdiction
- legislative changes; any such legislation would enable—and would need to be followed by—regulatory implementation by the executive branch.

Some of these actions could be taken immediately, but most would likely be contingent on more-widespread examination of the concerns of Adamala, Agashe, Belkaid, et al. (2024).

Executive Branch Statements

We recommend that the federal government take two immediate actions in response to the concerns of Adamala, Agashe, Belkaid, et al. (2024). First, as discussed previously, senior officials at research funding agencies should explain that because of the irreversible nature of scientific research, the U.S. government is taking the prudent course of pausing any federally funded research intended to develop mirror organisms until more is learned about the nature of this risk and about the costs and benefits of various policy measures to deal with it. The government should also recommend that other funders do the same.

The government should also seek to resolve, to the extent possible, questions that Adamala, Agashe, Belkaid, et al. (2024) have raised. One useful mechanism to do so would be by commissioning studies by government and national laboratory experts and by entities such as the National Academies of Sciences, Engineering, and Medicine (NASEM) to assess the validity of the concerns that have been raised regarding mirror organisms. Studies by additional organizations could also be encouraged. Findings from these studies that the concerns are sufficiently plausible and thus that they should be acted on could serve as triggers to initiate action on other policy tools developed in this paper.

Should the concerns not be refuted, government statements can also contribute to one of the most effective long-term means to ensure that mirror organisms are not developed, which is the establishment of a robust norm—indeed, a taboo—among the international scientific community that the inherent risk from mirror organisms must make their creation unthinkable. U.S. government officials cannot establish such a norm by themselves, but high-level scientific, security, health, and environmental officials can support such a norm by making the U.S. government's analyses and conclusions about the dangers of mirror organisms clear and—should those analyses warrant further action—by previewing actions that the federal government will be taking to prevent their construction.

Executive Branch Actions Regarding Its Own Activities

Assessment by NASEM: In a situation somewhat analogous to the warnings about mirror life (Adamala, Agashe, Belkaid, et al., 2024; Adamala, Agashe, Binder, et al., 2024), scientists Mario Molina and F. Sherwood Rowland published a paper in 1974 that concluded that the atmospheric release of *chlorofluoromethanes*—gasses used at the time in aerosol propellants and refrigerants—was destroying the earth's ozone layer (Molina and Rowland, 1974). Because ozone attenuates solar ultraviolet radiation that could cause skin cancer, cataracts, and immune system suppression, its loss would be a planetary health concern (U.S. Environmental Protection Agency, 2024). Molina and Rowland's paper led the National Research Council (an arm of the National Academy of Sciences) to convene an ad hoc panel to assess the urgency of the problem and recommend what further action NASEM should take. The panel recommended that NASEM conduct a more in-depth study

to follow up. NASEM approved such a study in November 1974, appointed a panel to conduct it in March 1975, and released the study in September 1976 (National Research Council, 1976). The study validated Molina and Rowland's conclusions (Kaufman, 1977).

Departments and agencies within the U.S. government often fund NASEM studies on topics relevant to their missions; they have sometimes been directed to commission NASEM studies by an executive order. A NASEM study on the threat from mirror organisms should be conducted in two phases: First, it should assess the scientific validity of the conclusions of Adamala, Agashe, Belkaid, et al. (2024), because a finding that those concerns warranted policy attention would likely be necessary before the government sought to pursue many of the remaining policy tools addressed in this paper. Given that subsequent government action would likely be contingent on the outcome of the studies it commissioned, taken in the context of other analyses that may have been conducted by other interested parties, the first phase of the NASEM study should be tightly limited in scope and completed on an expedited basis. If conclusions from the initial sets of studies warrant subsequent work, a second phase of the NASEM study would involve addressing technical questions that arise in implementing these policies.

This proposed second phase could cover the following topics that the U.S. government will need to better understand to implement policy to prohibit, prevent, and counter mirror organisms:

1. **Pathways and precursors:** Determine the set of technical pathways and precursors that are necessary to produce mirror organisms. Should the federal government establish the goal of preventing mirror organism construction, it would want not only to ban these organisms' final production but also make that construction essentially impossible by blocking the relevant pathways.
2. **Identification:** Identify ongoing or proposed research efforts that might contribute to the construction of mirror life.
3. **Commercial or scientific utility:** Assess the need for or utility of any commercial, scientific, or other legitimate applications of the precursors and pathways identified in step 1.
4. **Prospects for regulation:** Recommend which of these precursors and pathways should be categorically banned to prevent the construction of mirror organisms; which ones should be regulated to ensure that these precursors and pathways are not used to construct mirror life but could be available for legitimate use; and which ones (whether because they are impossible to control or because their relevance to mirror biology is so inconsequential compared with their legitimate applications) should not be regulated at all.
5. **Regulatory thresholds:** For those precursors and pathways that are deemed important to regulate, determine thresholds—if any—below which the regulations need not apply.
6. **Countermeasures:** Assess the feasibility of countermeasures that could ameliorate the health threats and environmental hazards of mirror organisms but that would not involve the advance creation of mirror organisms. For example, off-target effects or toxicity profiles of antibiotic therapies thought to be effective against mirror bacteria could be studied

without the creation of a mirror bacterium. In addition, assess the feasibility of any countermeasures that would require mirror organism development to determine whether contingency plans could or should be made to produce such countermeasures following the release of a mirror organism by others. Under such circumstances, there would no longer be any preventive value in refraining from constructing mirror organisms. However, any such planning would have to be deliberated very carefully, since those plans alone could reduce barriers to mirror organism construction. If a potential countermeasure drew on any of the precursors or pathways identified in step 1, that fact should be considered in developing regulations.

7. **Observables and signatures:** Identify observable signs and signatures that could be used to identify a research program to construct mirror organisms in order to support enforcement of regulations (and potentially treaties).

The NASEM studies provide several opportunities to foster the international engagement that will be necessary to address this problem on a global scale. NASEM can involve international experts in its studies. It can also act jointly with other countries' national academies, as it did when it worked with the UK Royal Society and the Chinese Academy of Sciences on studies of human germline editing (Royal Society, 2023). NASEM could also involve the Interacademy Partnership, a mechanism by which regional, national, and global academies of sciences work together on global problems (Interacademy Partnership, undated). However, international engagement could slow the overall response, buying international engagement at the price of responsivity.

Federal funding ban. In addition to making public statements, the executive branch could make the recommended federal funding pause permanent or initiate one if that had not been done already. The scope of such a ban might depend on the outcome of NASEM's analysis; one possible characterization could be that the government will refrain from funding experiments or the development of technologies that are intended to further the creation of mirror organisms or that substantially lower the remaining barriers to doing so. Because such a statement has normative value and a direct impact on research funding policy, its wording will be important. Assuming a decision has been made to make the initial funding pause permanent, the terms *moratorium* or *pause*, which have been applied in the past to certain categories of problematic research (Bonham, 2021), would not be appropriate because they denote temporarily halting ongoing activity. Calling the nontemporary federal funding halt a *ban* would be more accurate.

Unless a federal research program has been specifically mandated by Congress or court order, federal research funds are awarded at the discretion of funding agency program managers, so long as the research topic is consistent with agency policy and the broad constraints of congressional authorization and appropriations language. The discretion to award funding implies the discretion to withhold it, an outcome that can be mandated for certain subject areas as a matter of agency policy. Because all program managers in federal funding agencies work within a chain of command that eventually runs through the department or agency director to the President, a White House statement banning funding for the construction

of mirror life would provide sufficient policy guidance to ensure that program managers do not fund mirror organism development. However, funding guidance is ultimately conveyed to program managers and to the funded community through agency-specific policy documents, such as the National Institutes of Health (NIH) Grants Policy Statement (National Institutes of Health, 2024) or the National Science Foundation's *Proposal and Award Policies and Procedures Guide* (National Science Foundation, undated). Agencies have their own procedures for amending these documents, which will take time even when the substantive content of the changes is specified. In this case, as discussed in the following paragraphs, the precise parameters of the ban may need to be worked out as well.

For maximum effectiveness, we recommend that any federal funding ban be declared by the White House. First, it should be clear that all federal agencies are covered. Even if only one or two federal agencies would be logical places to fund mirror biology research, any U.S. government declaration will be weakened if it appears that the research might be funded by some other agency that would not explicitly be covered by the ban. Moreover, to the extent that proposals relevant to mirror biology research might be submitted to more than one funding agency, it would be important to ensure that all agency interpretations of that ban are consistent. Second, banning research funding is an unnatural act for a federal funding agency; the missions of such agencies are to fund research, not to ban it, so the impetus to initiate such a ban is unlikely to arise from the bottom up, no matter how socially responsible agency funding managers may be. Third, implementing the funding ban may require changes in the overall process of soliciting, reviewing, and funding research proposals; agencies may not welcome such changes, particularly given that the safety and security concerns motivating a ban on mirror biology research may not be the only external pressures seeking to shape the agency research portfolios and processes. Therefore, direction from the highest levels of government to implement a federal funding ban, notwithstanding the practical difficulties, may be important.

Withholding funding from projects specifically intended to create mirror organisms is conceptually simple, but the objective of such a ban may be not only to prevent the construction of mirror organisms but to ensure that precursors and intermediate technologies that would be needed to enable their construction remain out of reach as well. However, some precursors may have more general applicability beyond construction of a mirror organism that the funding agency may still wish to pursue. Analysis will be needed to determine what the exact boundaries of a funding ban should be, weighing the contribution that the research

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might make toward the development of mirror organisms against the opportunity costs of forgoing the benefits of that research in nonmirror-organism applications.[2] Agencies may need to establish internal processes to ensure that a funding ban, once in place, is being effectively implemented.

Adding mirror research to the federal Policy for Oversight of Dual-Use Research of Concern and Pathogens with Enhanced Pandemic Potential (DURC/PEPP policy). A ban on federally funded research that is intended to produce mirror organisms could be extended to certain nonfederally funded research by modifying the existing federal DURC/PEPP policy (Executive Office of the President, 2024). It is also possible that such modification could capture experiments leading up to but not attaining the final construction of a mirror organism.

The federal DURC/PEPP policy applies to nonfederally funded research conducted in institutions that receive government funding if the agency providing that funding is already authorized to oversee nonfederally funded research; the DURC policy alone confers no such authorization. (In contrast, the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules [NIH, Office Of Science Policy, 2024], which are incorporated by reference in the terms and conditions applied to all NIH grants [NIH, 2024], apply to all research involving recombinant or synthetic DNA, whether NIH-funded or not, that is conducted at institutions that receive NIH funding for research involving recombinant or synthetic DNA.) The DURC/PEPP policy states that when funding agencies are authorized to exert oversight over nonfederally funded research as a condition of awarding federal funding, they should establish that the research institutions they are funding are applying the DURC/PEPP oversight framework to their nonfederally funded research as well.

The federal DURC/PEPP policy establishes oversight mechanisms within federal funding agencies and research institutions over certain types of research that "can be reasonably anticipated to produce knowledge, information, products or technologies that could be misapplied to do harm with no, or only minor, modification" (Executive Office of the President, 2024, p. 8). At present, this policy covers two such categories of research: research with listed agents that results in or is reasonably anticipated to result in any of a list of covered experimental outcomes, called *Category 1 research* in the policy, and the creation of what it defines as *pathogens with enhanced pandemic potential (PEPPs)*, called *Category 2 research*. Neither category as defined would include any form of mirror biology research. Both categories involve the manipulation of pathogens, and even if creation of a mirror form of an organism would be considered a type of manipulation that is covered, the normal form of the organism chosen to be mirrored is very unlikely to be a pathogen. Moreover, a synthetic mirror organism might not closely resemble any existing organism at all, much less a pathogen.

However, the policy could be amended to explicitly include mirror organisms. For Category 1 research, mirror organisms (or organisms with a certain specified content of mirror molecules) could be added to the list of agents, and the creation of mirror organisms (or other experimental manipulations directly related to construction of mirror organisms) could be added to its list of covered experimental outcomes. Category 2 research is described in terms of experimental outcomes or actions with a "pathogen" that could create a PEPP. Modifying that definition to include

research with mirror organisms could be as simple as changing "pathogen" to *organism*, a change that would have negligible effect otherwise, although it is possible that such a modification would not capture mirror organisms that were not strictly mirror forms of existing organisms. Alternately or in addition, the existing text stating that Category 2 research can include the creation of *eradicated or extinct* potential pandemic pathogens could be broadened to include the creation of *novel* potential pandemic pathogens as well. Yet another approach would be to explicitly designate research with mirror organisms as falling within Category 2.

The policy would also have to be modified in terms of what was required of research that met the agent and experimental condition criteria. For Category 1 research, the policy requires that the research institution conduct a risk and benefit assessment and draft a risk mitigation plan; the federal funding agency then reviews and approves the plan and the assessment before the project receives funding. If the policy were to be used to ban the construction of mirror organisms, the mitigation option of not funding the research would have to be specified explicitly and not left up to institutional or funding agency discretion. Category 2 research also requires such a risk and benefit assessment, but that assessment faces stricter scrutiny in that the research must also satisfy each of seven criteria, one of which is that "the potential benefits to society justify the potential risks" (Executive Office of the President, 2024, p. 23). If mirror organisms were indeed judged to pose such catastrophic risks, research creating them would not be able to satisfy that criterion, making this policy (if amended to cover the creation of mirror organisms) an implicit ban on the use of federal funds.

Use of the DURC/PEPP policy to ban the construction of mirror organisms would not add significantly to what could be accomplished by a federal funding ban (discussed previously) other than possibly broadening it to some modest amount of nonfederally funded research. Moreover, the federal select agent program could be used, as discussed later, to ban the construction of mirror organisms in any research activity, regardless of funding source. What the DURC/PEPP policy could add, however, would be options to ban or prescribe other conditions on federally funded and certain nonfederally funded research that could help pave the way for production of mirror organisms but that did not actually attain that goal. However, such modifications are unprecedented and would be quite time-consuming to draft and approve. No provisions with that level of technical specificity are included in the existing policy for any of the categories of research that it now covers. Therefore, crafting revisions that delineate which mirror-related organisms would be covered, what experimental outcomes would be included, and what restrictions should be placed on research with those agents that achieved those outcomes could be time-consuming: Simpler revisions of government biosecurity policies take many months. To the extent that such restrictions would affect research that did not have the goal of constructing mirror organisms, review and comment by members of the affected communities would likely be necessary, adding time, and previous iterations of this policy did not take effect until one year after the final text was released. This approach would be useful to the extent that passage of mirror-biology–specific legislation, discussed in the following section, is either not pursued or would take even longer.

Executive Branch Regulatory Changes Under Existing Statutory Authority

In addition to executive action controlling its own activity, the U.S. government could use existing statutory authority to regulate action under U.S. jurisdiction. We describe several avenues for doing so.

Addressing mirror organisms under select agent regulations. The most direct way to establish regulatory control in the United States over mirror organisms in general (i.e., not just those that might be created in the course of federally funded research) would be to put them under the purview of the select agent regulations (7 CFR § 331; 9 CFR § 121; 42 CFR § 73), which govern the possession, transfer, and use of biological agents deemed by the Secretary of the U.S. Department of Health and Human Services (HHS) to have the "potential to pose a severe threat to public health and safety" (42 U.S.C. § 262a(a)(1)(A)) or by the Secretary of Agriculture to have the "potential to pose a severe threat to animal or plant health, or to animal or plant products" (7 U.S.C. § 8401(a)(1)(A)). In determining whether to designate an agent as a Select Agent, the HHS Secretary (in the case of a human pathogen) is to consider

1. the effect on human health of exposure to the agent or toxin
2. the degree of contagiousness of the agent or toxin and the methods by which the agent or toxins is transferred to humans
3. the availability and effectiveness of pharmacotherapies and immunization to treat and prevent any illness resulting from infection by the agent or toxin
4. any other criteria, including the needs of children and other vulnerable populations, that the Secretary considers appropriate (42 U.S.C. § 262a(a)(1)(B)(1)).

All institutions possessing, transferring, or using these designated agents, called *biological select agents and toxins*, and all individuals with access to them must register with the federal government. Congress has banned certain categories of people—called *restricted persons*—from accessing select agents, and all seeking access must undergo Federal Bureau of Investigation background checks to ensure that they are not in those prohibited categories or otherwise barred from having access (18 U.S.C. § 175b). The program also mandates certain safety, security, and emergency response requirements, including the reporting of any instances of loss, theft, or release of a select agent or toxin (Centers for Disease Control and Prevention and U.S. Department of Agriculture, 2023). Furthermore, the select agent regulations designate certain experiments as *restricted experiments*, which no one can conduct or possess products from without permission from the Secretaries of Agriculture or HHS (42 CFR § 73.13). Designating mirror organisms as biological select agents would criminalize their possession or use by anyone not registered to have them, which would serve as a total ban if nobody were to be so registered. Designating them as select agents would also allow defining their creation or use as restricted experiments, which would criminalize their creation by anyone without permission to do so—which could be everybody. Note, however, that categorically designating all mirror organisms as select agents is only possible if all mirror organisms would pose a severe threat to public health and safety, animal or plant health, or animal or plant products. If only some mirror organisms would pose such a threat,

only those would be eligible to be designated as select agents, and this route would not be able to categorically prevent the creation of any mirror organism.

Designating new select agents and restricted experiments could be done via a regulatory process conducted by the relevant executive branch agency (HHS or the Department of Agriculture); such a designation would not require congressional action. However, given that one of the statutory objectives of the select agent program is to ensure the "appropriate availability of biological agents and toxins for research, education, and other legitimate purposes" (42 U.S.C. § 262a(b)(4)), it is not clear to what extent the designation of mirror organisms as select agents could serve the purpose of totally banning their possession and use. It is possible that the relevant Secretaries might be able to determine that mirror organisms are so dangerous that their "appropriate availability" should be none at all and that the regulations should specify that no one should be allowed to construct, possess, or use these organisms. If writing such a ban into the regulations was seen to be inconsistent with statute, a de facto ban could still be implemented simply by refusing to grant permission to construct or use mirror organisms when requested. In any event, it will be important to communicate that notwithstanding that one objective of the select agent program with respect to all other select agents is to provide for their safe and secure use in research programs, the objective of designating mirror organisms as select agents would be to ban their creation completely.

Such regulatory changes could be enacted relatively quickly. Under normal circumstances, the process of reviewing the list of select agents, proposing changes, submitting them for public comment, reviewing the comments, and making the final changes can take more than a year. However, when a regulatory agency concludes that the typical process of initial publication, solicitation of public review and comment, evaluation, and final publication is "impracticable, unnecessary, or contrary to the public interest" (5 U.S.C. § 553(b)(B)), it can bypass the normal process and proceed directly to issuing an *interim final rule* that takes effect immediately. The agency will still

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solicit comments, but those will be used as the basis for possibly changing a rule that has already come into force as opposed to revising draft text that has not yet been formally issued. The select agent program has used this expedited process for changing the select agent list twice—once to add a newly discovered bacterial variant closely related to the causative agent of anthrax (HHS, 2016) and again to control certain chimeric viruses combining severe acute respiratory syndrome coronavirus (SARS-COV)-1 (a select agent) and SARS-COV-2 (the agent responsible for coronavirus disease 2019 [COVID-19], which is not a select agent) (HHS, 2021).

Issuance of an interim final rule would be the quickest way that the U.S. government could enact legally binding measures controlling the creation of mirror organisms, allowing the United States to send an urgent message about the unacceptability of this line of research. However, using the select agent regulations in this way would provide only a partial solution. It would restrict only the final step in mirror organism construction, leaving the development of the technical pathways to accomplish that end relatively unimpeded. Moreover, the use of regulation rather than statute to enforce these policies could leave the perception—and indeed the reality—that such a policy could relatively easily be reversed at any time. For that matter, designating the creation of mirror organisms as restricted experiments in a way that did not go on to ban such experiments completely could imply that although they would be restricted, such experiments were considered legitimate.

For these reasons, new legislation could be a more effective means of addressing this issue in the long term. As we discuss in the following section, such legislation could be designed to provide the necessary authorities to govern not only the final construction of mirror organisms but precursor materials and technical pathways leading up to that construction and could do so in ways that do not create the perception that these controls could be easily lifted. However, enacting new legislation is a time-consuming and uncertain process, and the regulatory revisions described previously could be enacted while legislation is prepared and debated.

A middle ground between quick but less inclusive regulatory change on the one hand and more-substantial but more time-consuming and uncertain statutory change on the other could be to make changes to the select agent regulations that capture precursor materials, intermediate biological constructs, and other aspects of the research and development pathways that enable the eventual creation of mirror organisms. Such changes would be unprecedented for the select agent program, and they may not even be consistent with statutory language that calls for the imposition of "appropriate safeguard and security

requirements for persons possessing, using, or transferring a listed agent or toxin" that are "commensurate with the risk such agent or toxin poses to public health and safety" (42 U.S.C. § 262a(e)(1)). Although extensive controls on entire pathways for their development might be justified as being "appropriate safeguard and security requirements" in the event that mirror organisms are designated as select agents, the reference to placing requirements on "persons possessing, using, or transferring a listed agent or toxin" could imply that regulatory authority exists only when tied directly to the actual select agents themselves and could not be extended to precursors or intermediate biological constructs (42 U.S.C. § 262a(e)(1)). Moreover, it is unclear whether those precursors or intermediate constructs can be regulated as select agents in their own right because by themselves, they might not be considered to pose a "severe threat to public health and safety" (42 U.S.C. § 262a(1)(A)).

Even if legal issues do not preclude broad regulatory control of the research and development pathways toward the creation of mirror organisms under the select agent program, such an approach would constitute a dramatic change from the existing regulations and would be quite unfamiliar to the agency officials who would be drafting them. More significantly, such a broad set of regulations might affect those using mirror precursors for purposes unrelated to constructing mirror organisms, and the perspectives of these users would need to be considered through the review and comment processes. Such enhanced regulations would take much more effort—and especially time—to draft, review, and implement than the minimalist approach of adding mirror organisms and mirror organism creation, respectively, to the existing lists of select agents and restricted experiments. Enhanced regulations would also come with the same perception issues as the shorter-term regulatory changes discussed previously in that they might be perceived as being readily reversible. Therefore, we would recommend against pursuing this approach unless a timely legislative solution is seen to be unfeasible.

Export controls. U.S. export controls—the Department of Commerce's Export Administration Regulations (15 CFR § 730–780) and the Department of State's International Traffic in Arms Regulations (22 CFR § 120–130)—regulate the ability of U.S. persons to export certain goods, services, and nonpublic information to foreign destinations, including (in the case of information) to foreign nationals within the United States.[3] Export controls can even govern the disposition of products made by foreign producers using equipment that is subject to U.S. export controls. In areas in which the United States and its partners and allies have technological advantages over adversaries, export controls can provide an important means of helping maintain those advantages.

For this reason, any decision to add mirror organisms, precursors, or production technologies to export control lists would have to be weighed very carefully because doing so might convey the impression that the United States would be seeking to develop mirror life or its components while suppressing the development of such organisms or components by adversaries. The fact that export controls do not apply to transactions between U.S. persons could reinforce such an impression. Any indication that the creation or use of mirror organisms served the national security interests of the United States and needed to be kept from adversaries would severely threaten attempts to build

a global norm against them and could even incentivize adversaries to pursue the creation of these organisms.

However, U.S. export controls could play an important role in strengthening an international norm against mirror biology without necessarily adding mirror organisms or associated technologies to control lists, just as export controls reinforce the norm against biological weapons. Biological weapons are banned by an international treaty to which the United States is a party. While this treaty and U.S. domestic law allow defensive research, U.S. domestic law bans any efforts by U.S. persons (including those working for the U.S. government) to develop biological weapons, making clear that the U.S. government is not reserving for itself the right to produce such weapons (18 U.S.C. § 175(a)).

Under these circumstances, an aspect of export controls called the *catch-all provision* provides a powerful tool for preventing U.S. persons from lending any assistance to such weapon programs without necessarily giving the perception that the United States seeks to conduct such activities itself.[4] These provisions require U.S. persons to obtain export licenses to export anything that they know, have reason to know, or are informed will be used in a biological weapon program. If the export is to make a "material contribution" to such banned weapons, the law requires that the license be denied (15 CFR § 744.4(a) and (d)(1); 15 CFR § 744.6(b)(3); 50 U.S.C. § 4813(d)). Because of the internationally proscribed nature of such programs, it is not likely that any such licenses will ever be requested, much less approved. But having the licensing requirement in place criminalizes any unlicensed export to such a program. Note especially that the export of *anything* in support of such a program—even pencils or toilet paper—would be covered, not just the export of items that were otherwise controlled (i.e., controlled under provisions other than the catch-all controls).

These catch-all controls could have an equivalent effect on mirror biology research programs if export control regulations were amended to establish that for the purpose of these catch-all provisions, the development of mirror organisms should be treated as the development of biological weapons. Such a designation does not imply that mirror biology research programs have ever had a weapons motivation. Rather, catch-all controls could reflect a government decision that further work to develop mirror life should face the same barriers as development as biological weapons. Extending the catch-all controls in this way would probably not serve to extend the statutory ban against providing a material contribution, but it would require licenses to be sought for any export that supports mirror organism development, and such licenses could be denied as a matter of policy. Such development efforts could be effective against foreign mirror organism development efforts even without specifically placing mirror organisms and related technologies on export control lists.

Any materials, constructs, or technologies relevant to mirror organisms that are not banned but rather regulated—either under the select agent regulations or under standalone legislation—should also be specifically included on export control lists, which would permit legitimate exports to be reviewed on a case-by-case basis. Any such controls, however, would need to be carefully synchronized with the equivalent domestic controls to prevent the perception issues that could result if mirror biology–related items that were not regulated domestically were placed under export controls.

Any materials that are banned under domestic law or regulation need not and should not be specifically placed under export controls because there would be no legitimate reason to export them. Any export of a banned material could be presumed to be in support of a foreign program to develop mirror organisms, thereby violating the catch-all provision; there would be no need to explicitly include such items on export control lists. In this respect, export controls on mirror biology–related materials and technologies would be simpler than for those related to biological weapons because in the latter case, defensive applications are permitted. Such items as genetically modified pathogens that might constitute a biological weapon in one context might be part of a legitimate defense program in some other context, and export controls specific to those materials are needed to control their legitimate use. No such distinction would be necessary for banned items related to mirror organisms.

Responding to the creation, release, or creation and release of mirror organisms. It will be important that any regulatory or statutory controls on possession and use of mirror organisms do not limit the actions of the U.S. government in the event that mirror organisms are created despite or in violation of the policies described in this paper. Under such circumstances, the U.S. government will likely need to collect and characterize such organisms and conduct other types of research with them. However, the government's ability to do so would have to be codified in a way that did not allow—and did not appear to allow—the U.S. government to work with them in any other circumstance.[5]

If mirror organisms are designated as select agents without any laboratories or individuals being authorized to work with them, one way to provide for such an ability in the event of their release by others would be to utilize the emergency authority that the Secretary of HHS has to "temporarily exempt an individual or entity from the requirements" of the select agent regulations "based on a determination that the exemption is necessary to provide for the timely participation of the individual or entity in response to a domestic or foreign public health emergency" (9 CFR § 121.6(f), 42 CFR § 73.5(e), 42 CFR § 73.6(e),(f)). Waiting until a mirror organism had actually been created before issuing any exemptions permitting its use in research would mitigate the perception that the United States was reserving the possibility of working with such organisms in advance of their creation by others. Such exemptions are limited to no more than 30 days; there is a possibility of a single additional exemption. If additional time were needed to develop countermeasures or other responses to the release of mirror organisms, 60 days should provide sufficient time to push through an interim final rule that extended this 60-day deadline, especially considering the extreme urgency that such research could warrant.

New Legislation

The executive branch actions discussed in the previous sections draw on the existing statutory armamentarium available to the U.S. government to halt, prohibit, and prevent the construction of mirror organisms. For this reason, they can be taken relatively quickly. But the most robust set of domestic safeguards against the development of mirror biology would be put into place by legislation specifically for that purpose. Such legislation would provide the only mechanism for comprehensively addressing all research, regardless of funding source. In addition, such legislation

could ban or regulate not only the final construction of a mirror organism, but various precursor materials and intermediate technical steps that build the pathway for ultimate mirror organism construction. Unlike the select agent legislation, legislation specifically addressing mirror biology would not need to have provisions to maintain "appropriate availability" of mirror organisms for "research, education, and other legitimate purposes"; unlike export control legislation, mirror biology legislation could govern activities of U.S. persons within the United States and would not be limited to goods, services, or information provided to foreigners.

Legislation could ban the development or possession of mirror organisms by anyone without exception. Such a scope would make clear that the U.S. government was not reserving for itself the right to develop mirror organisms.

A model for legislation that establishes criminal prohibitions relating to a specific microbiological entity is 18 U.S.C. § 175c on variola virus, the virus that causes smallpox. This legislation makes it unlawful to produce, possess, transfer, or work with variola without government authorization, establishes the circumstances in which the prohibited conduct is within the criminal jurisdiction of the United States, sets criminal penalties, and provides a technical definition for *variola virus (*18 U.S.C. § 175c(d)).[6] Variola virus is also a select agent, showing that regulating mirror organisms as select agents does not interfere with the ability to enact legislation regarding them.

Ban activities related to the construction of mirror organisms. Legislation could ban the development or possession of mirror organisms by anyone without exception (other than in the course of responding to the creation or release of mirror organisms, should they be developed in violation of such a ban). Such a scope would make clear that the U.S. government was not reserving for itself the right to develop mirror organisms, which would be critical in proposing a global ban. This provision would therefore differ from the corresponding language in the variola ban, which exempted actions conducted or authorized by the Secretary of HHS. Alternatively or in addition, this legislation could declare that any development, possession, or use of mirror organisms that was not in connection with emergency response had no "prophylactic, protective, bona fide research, or otherwise peaceful purpose." The U.S. criminal code defines any work with a biological agent that is not justified under any of those categories as being "for use as a weapon," and such a statutory declaration would have the effect of banning work with mirror organisms under existing biological weapons statutes.[7]

Include mirror organism development under the catch-all provisions of U.S. export controls. Legislation dedicated to mirror organisms could specify that for the purposes of U.S. export controls, mirror organisms would be considered to be biological weapons. Such a designation would automatically include such organisms within existing catch-all controls that restrict support to biological weapon programs anywhere in the world; this would extend to mirror organism development the existing statutory ban against providing a material contribution to biological weapon programs. Such a legislative requirement would remain in effect until removed by future legislation; it could not be removed by future executive branch action alone.

Regulate key precursor materials and intermediate constructs. Legislation could provide authority to a federal regulatory agency to regulate or ban precursors and constructs that are important for the production of mirror organisms. The intent of these regulations would be to create a "firebreak" around the ultimate creation of mirror organisms by working to ensure that key technical hurdles en route to their creation remained unsolved. Crafting these regulations would require applying a risk-benefit test to these materials and constructs, banning those for which their use in creating mirror organisms outweighed their potential benefits in other applications, and regulating others with compelling nonmirror biology applications to ensure that they were not used in mirror organism development. Regulators would also need to consider that precursor materials or constructs that were widely available and in high demand for "ordinary" (nonmirror) biotechnology might be infeasible to regulate at all.

Address software tools and AI models. Software tools and AI models could prove useful in the development of mirror organisms. However, regulating these tools for mirror biology purposes could be challenging because of the wide applications of such models in life science research, the difficulty in distinguishing mirror biology from nonmirror-biology applications, and the challenges in regulating software tools in general. Should effective approaches to mitigating the adverse biosecurity consequences of AI models be developed, such approaches may provide avenues for limiting such contributions to the development of mirror organisms.

Identify and investigate mirror organism development. Law enforcement agencies could be tasked with identifying and investigating programs to develop mirror organisms, which the proposed legislation would make illegal. If submission of information (e.g., sales data) from vendors of materials and services that could be relevant to mirror organism production would be useful to this end, regulatory authorities could be empowered to collect that information. Law enforcement agencies could also be tasked with accepting information voluntarily provided by bioeconomy material and service providers about orders that might have been intended to support mirror biology development, just as firms manufacturing synthetic DNA are encouraged, under existing U.S. government guidance, to contact law enforcement authorities if they believe that an order of DNA is or could be intended for illegitimate activities (National Science and Technology Council, 2024).

Exempt activities done in response to the creation or release of mirror organisms. Legislation on mirror organism development could provide for exemptions that would permit the U.S. government to authorize or conduct work with mirror organisms in the circumstance that they are ever created, released into the environment, or come to

infect humans, animals, or plants. Such a provision would have to be written in a way that did not appear to condone possession or use of mirror organisms by the U.S. government under any other conditions, yet did not tie the hands of the government in responding to such creation or release. No advance planning for any such release should be permitted to develop mirror organisms because making sure that such development remains impossible is the strongest defense that can be mounted.

The downside of seeking legislation is that it is a complicated and uncertain process that can be derailed by nominally unrelated political disputes. It is also not likely to be quick, meaning that it would not be a substitute for the more readily implemented executive actions outlined previously.

Moreover, any new regulatory regime that was enacted pursuant to new legislation could increase the compliance burden faced by research institutions under existing regulations. Any increased costs that were not accompanied by a corresponding funding stream would constitute an unfunded mandate, reducing the resources available to that institution for research and other mission-related activities.

No matter how robust a legal structure the United States puts into place, the world would remain at risk without equivalent structures established everywhere on the planet where the capability to create mirror organisms exists or could develop.

U.S. Government Options to Pursue International Action

The U.S. government could also pursue bilateral and multilateral activities to halt, prohibit, and prevent mirror organism production. No matter how robust a legal structure the United States puts into place, the world would remain at risk without equivalent structures established everywhere on the planet where the capability to create mirror organisms exists or could develop. Moreover, because research associated with mirror biology countermeasures could provide information relevant to the possible construction of mirror organisms—even if it did not involve the creation of mirror organisms themselves—it could be useful to establish international transparency and oversight measures over such work. The oversight system applied by the World Health Organization (WHO) to research with variola virus offers one model.

Options to pursue international action to prohibit, prevent, and counter mirror organisms include bilateral and multilateral diplomatic engagements or convenings; work within existing multilateral treaties, international organi-

zations, or informal multilateral associations; and the creation of new treaties or international organizations.

Bilateral and Multilateral Engagement and Convenings

If the U.S. government judges that the risks posed by mirror organisms warrant action, it could make prevention of the development of mirror organisms an important part of all its diplomatic engagements, including those with adversaries. Under such circumstances, it should seek for all countries to come to a shared understanding of the risk posed by mirror organisms and establish legal regimes against creation of mirror organisms. The United States can facilitate a common view of the problem by supporting the convening of an international forum to discuss the risk and approaches to mitigating it. For allies and partners, their willingness to take action to prohibit and prevent the development of mirror organisms could color other aspects of their relationships with the United States. For adversaries, ensuring that mirror organisms are not developed should be an area of common interest, even if other aspects of the relationship remain antagonistic. All countries would have an interest in being reassured that others are not working to develop mirror organisms, and all would have an interest in assuring others that they are not doing so either. Transparency by each state into its programs dealing with mirror biology will therefore be important.

Bilateral engagement with China will be particularly important, given China's status as an influential geopolitical actor, a technological superpower, and a world leader in mirror biology research. Engaging China early in U.S. diplomatic efforts and suggesting joint action spearheaded by both countries is likely to be more productive than inviting China to participate in what it might perceive to be a subordinate role.

Existing Multilateral Institutions and Organizations

Just as the most expedient way for the United States to establish some safeguards against mirror biology would be to take advantage of existing laws and regulations, the most straightforward way to mobilize international action against such organisms would be through existing organizations. Just as in the domestic case, existing organizations may not be truly fit for purpose, but they can provide some relevant capabilities.

The Australia Group. The Australia Group is an informal association of countries that seek to harmonize their export controls on goods and technologies that could assist in the proliferation of chemical and biological weapons (Arms Control Association, 2021b). It could provide a useful forum for U.S. representatives to discuss with representatives from other countries the applicability of export controls on any items that might be useful for the development of mirror organisms. Through the Australia Group, the United States could encourage other countries to adopt export control policies that are similar to the ones suggested for the United States because lack of harmonization could serve to undercut existing U.S. controls.

Even though the Australia Group's objective is to prevent the proliferation of chemical and biological weapons—an internationally agreed goal, given widespread adherence to the chemical and biological weapons conventions—its membership is not universal. For example, neither Russia

nor China is a member. Furthermore, states cannot join simply by opting in. New members are accepted only by a consensus of existing members, and new states must prove that they are in compliance with the Chemical and Biological Weapons Conventions and have effective national export control and export enforcement systems. Some states have argued that multilateral export control agreements, such as the Australia Group, are discriminatory and that they are a means by which the United States and its allies act to suppress technological development in developing countries (Beck, 2000; Meier and Hunger, 2014). As recently as December 2024, a United Nations (UN) General Assembly committee adopted a resolution noting "with concern" that nonproliferation export controls unduly interfere with international scientific cooperation for peaceful purposes and that nonproliferation obligations are best met through "multilaterally negotiated, universal, comprehensive and non-discriminatory agreements" (UN General Assembly, 2024). Given the political overtones associated with Australia Group membership and the need to have all countries—including adversaries of the United States—work to prohibit and prevent mirror organisms if such policies are to succeed, the Australia Group may not be the best venue to seek international engagement on this topic.

The Biological Weapons Convention (BWC). The United States could seek agreement among states parties to the BWC that there can be no legitimate use for mirror organisms because of the extreme danger that such organisms pose.[8] Under the treaty, such a finding would be tantamount to declaring mirror organisms to be biological weapons. The BWC prohibits biological weapons by banning the development, production, stockpiling, acquisition, or retention of biological agents or toxins that are "of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes." This wording, called the *general purpose criterion*, avoids the need to define exactly what a biological weapon is, and it makes the treaty robust to any unspecified or unanticipated biological agents that are not used for a legitimate purpose (Biological Weapons Convention, 1975).

The argument that BWC states parties can deem mirror organisms to be biological weapons by declaring that they have no legitimate peaceful purpose may be controversial, given that mirror biology research has never had a weapon-related motivation. We believe that the very nature of the BWC's general purpose criterion allows such an argument to be made, but we acknowledge that it may not be a consensus view.

The BWC is one of the world's most-signed treaties; 187 states parties have done so. Four states have signed but not ratified the BWC, and only six countries have done neither (UN, Office for Disarmament Affairs, undated).[9] The treaty is an incorporation of the international norm against biological weapons, which is strong. No country openly maintains a biological weapon program, and states asserted to be violating the treaty do so secretly.[10] The BWC has no verification or enforcement mechanisms other than calling for dialogue among states or referring potential violations to the UN Security Council. Nevertheless, the BWC can establish a consensus among states parties—which is virtually a world consensus—that mirror organisms can serve no legitimate purpose and should therefore be considered biological weapons. Because Article IV of the BWC obligates all states parties to "take any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition or retention" of biological

weapons anywhere within their jurisdictions or under their control (Convention on the Prohibition of the Development Production and Stockpiling of Bacteriological [Biological] and Toxin Weapons and on their Destruction, 1996), that consensus would establish a legally binding obligation for all BWC states parties to include mirror organisms in their biological weapon controls.

BWC states parties arrive at and document their collective views on treaty-related matters at five-year review conferences. These conferences have no power to formally amend the terms of the treaty, but they can and have issued declarations memorializing shared understandings. For example, although the treaty does not explicitly ban the "use" of biological weapons—instead, it refers to the Geneva Protocol, which does (Geneva Protocol, 1928)—the Final Declaration of the 1996 BWC Review Conference states that the use of any biological agents in ways that are "not consistent with prophylactic, protective, or other peaceful purposes . . . is effectively a violation" of the BWC (Convention on the Prohibition of the Development Production and Stockpiling of Bacteriological [Biological] and Toxin Weapons and on their Destruction, 1996). Similarly, the Tenth Review Conference—most likely to be held in 2027—could codify the assertion that mirror organisms have no prophylactic, protective, or other peaceful purpose, and their development or possession would constitute a treaty violation.

Since 2002, BWC states parties have held intersessional meetings annually, so it might not be necessary to wait until 2027 for such a declaration to be issued. However, states parties have not empowered these annual sessions to issue the kind of collective findings or interpretations, such as those that have been made at review conferences (Arms Control Association, 2021a; Bansak, 2011). BWC states parties could use the upcoming annual meeting to make such a statement, but because taking such action would require consensus among the participating states, it is not clear whether this would be feasible. Perhaps the urgency of preventing the development of mirror organisms could create a consensus that has eluded BWC states parties in other circumstances.

The Environmental Modification Convention (ENMOD). The Environmental Modification Convention bans the "military or any other hostile use of environmental modification techniques having widespread, long-lasting or severe effects as the means of destruction, damage or injury to any other State Party," and it explicitly includes deliberate manipulation of the Earth's "biota" as constituting an "environmental manipulation technique" (ENMOD, 1978, Articles I and II). The effects to which mirror organisms have been alleged to lead would certainly be "widespread, long-lasting, and severe," placing them

Perhaps the urgency of preventing the development of mirror organisms could create a consensus that has eluded BWC states parties in other circumstances.

within the ambit of the treaty. In addition to constraining the behavior of states parties, the treaty obligates each state party "to take any measures it considers necessary in accordance with its constitutional processes to prohibit and prevent any activity in violation of the provisions of the Convention anywhere under its jurisdiction or control" (ENMOD, 1978, Article IV).

However, this treaty only has jurisdiction over "military or other hostile" actions, and, in fact, explicitly protects not only "the use of environmental modification techniques for peaceful purposes" but also "the fullest possible exchange of scientific and technological information" for such purposes (ENMOD, 1978, Article III). To forestall such a justification for promotion of mirror organism development, the states parties to ENMOD would need to collectively agree that there are no legitimate or peaceful uses of mirror organisms that warrant the global environmental risk that they pose, and therefore, any effort toward their development should be considered military or hostile. It may be that such a view could not gain consensus among ENMOD members, given that mirror biology research has never had a military motivation.

ENMOD would probably not bring qualitatively different tools to constrain the development of mirror organisms beyond what the BWC offers, and with 78 states parties, it has far fewer members (UN, undated). Moreover, review conferences for ENMOD have been held only in 1984 and 1992. Neither treaty has verification provisions other than general calls for states to consult and cooperate to discuss compliance concerns, and neither provides for enforcement mechanisms other than referral to the UN Security Council. However, ENMOD would engage different government ministries (i.e., environmental ministries rather than defense or public health ministries), and it would bring this issue before the world community from a different perspective. Therefore, working within ENMOD would complement working within the BWC, and the United States could pursue both avenues.

The WHO. The WHO does not have any existing programs or activities that would deal with the risk from mirror organisms, which do not exist in nature. However, the WHO oversees research with the variola virus, which has been eradicated in nature but still exists in two WHO-authorized repositories in the United States and Russia. A similar approach could provide international transparency and oversight for research related to mirror organisms, including the development of countermeasures.

Following the eradication of smallpox, the WHO required all remaining laboratory samples of variola virus to be consolidated in the two repositories, and it placed restrictions on the research that could be done with those samples. Any research with live variola virus at either of the repositories requires WHO authorization. Any other laboratories seeking to do research with individual variola genes must comply with restrictions intended to prevent the possible reconstruction of variola or a virus that will manifest similar symptoms (World Health Organization, 2016). Variola research oversight is performed by the WHO Advisory Committee on Variola Virus Research (ACVVR), established by the WHO's governing World Health Assembly in 1999. ACVVR consists of up to 25 international experts in a broad variety of disciplines that are relevant to variola virus research, and it makes recommendations to the WHO Secretariat, which retains authority over the use of variola samples. Because research into mirror organism countermeasures would not involve any organisms

or materials that were under WHO control, neither an advisory body for mirror biology research nor the WHO itself would have any binding authority to approve or disapprove research proposed by member-states. However, such a committee at the WHO could provide international visibility and expert review of proposed research activities. In particular, such a body would provide a forum in which the state of research relevant to mirror biology could be assessed, and it could make recommendations to nation-states regarding which activities should be banned to prevent the development of mirror organisms; which should be regulated because, while having some relevance to mirror organism creation, they also have beneficial applications; and which should remain unregulated. Such a committee could provide international visibility and oversight for mirror biology–related activities, helping to assure countries that the benefits of permitted yet regulated research would be made equitably available to all, while potentially concerning activities are carefully and transparently scrutinized.

The UN Security Council. The United States could seek a UN Security Council resolution prohibiting the creation of mirror organisms. The Security Council is responsible for the "maintenance of international peace and security" (UN Charter, 1973, Article 24). Not only can it issue resolutions that are legally binding on all UN member-states, but under Chapter VII of its charter, it can authorize nonmilitary or even military measures be taken to "maintain or restore international peace and security" (UN Charter, 1973, Articles 39, 41, 42). Given the catastrophic threat that mirror organisms could pose to all countries, the Security Council could find that mirror organisms do not have any legitimate function that justifies the risks that they pose. Accordingly, it could therefore determine, under Chapter VII of its charter, that the development of mirror organisms—or any work contributing to that end—would constitute a "threat to the peace, breach of the peace, or act of aggression," and it could direct that all UN member-states take actions to halt, prohibit, and prevent their development.

There is no precedent for the type of threat posed by mirror organisms and certainly not a precedent for UN actions to deal with such a threat. However, the UN Security Council has taken actions throughout its history to deal with weapons of mass destruction. In January 1992, the Security Council—meeting at the heads-of-state level—issued a statement that "the proliferation of all weapons of mass destruction constitutes a threat to international peace and security" (UN Security Council, 1992). This statement alone did not authorize any action by the UN or its member-states, but it did place proliferation on the Security Council's agenda. On April 24, 2004, the Security Council adopted Resolution 1540 under Chapter VII, which reaffirmed that the proliferation of nuclear, chemical, and biological weapons constituted a threat to international peace and security and called on member-states to take "appropriate actions" to prevent their acquisition by nonstate groups (Arms Control Association, 2021a). This resolution, which did not authorize the use of force or indeed any enforcement measures at all—directed that UN member-states

- "refrain from providing any form of support to non-State actors" attempting to pursue such weapons
- "in accordance with their national procedures . . . adopt and enforce effective laws" to prohibit any nonstate actors from pursuing such weapons

- "take and enforce effective measures to establish domestic controls," including border controls, export controls, physical protection, and material accountancy, to prevent the proliferation of such weapons (UN Security Council, 2004).

Although this resolution was adopted unanimously, it attracted some criticism. For example, Pakistan's ambassador to the Security Council, while voting for the resolution, emphasized that it did not seek to prescribe "specific legislation" on the part of UN member-states. In fact, he stated that the Security Council could not "legislate for the world" because, with 15 members, it was not a "representative body"(UN, 2004). Other critics objected to Resolution 1540's sole focus on nonproliferation without parallel attention to disarmament, and still others were concerned that the Security Council might later use Resolution 1540 to impose sanctions or other punitive measures on states that were not seen as sufficiently compliant (Arms Control Association, 2021a). The resolution would have been even more controversial—perhaps to the point of precluding its passage—had it specifically addressed enforcement actions. Instead, it expressed the Security Council's intention, "at the appropriate level, to take further decisions which may be required" to address any shortcomings in implementation (UN Security Council, 2004).

In the years since Resolution 1540 was adopted, the Security Council has remained comfortable with the approach taken in in that resolution, having extended it in a series of unanimously adopted resolutions (Arms Control Association, 2021a). Looking beyond this resolution, the Security Council has acted under Chapter VII of the UN Charter in a variety of cases and in a variety of ways over the past decades. An analysis of these cases has concluded that when the Security Council intends to mandate compliance with a resolution, it should

- explicitly "determine the existence of a threat to international peace, a breach of the peace or act of aggression" under Article 39 of the UN charter
- make reference to acting "under Chapter VII"
- use the verb "decides" in the resolution's operative paragraphs (Security Council Report, 2008).

To enact a legally binding worldwide ban against mirror organisms, the United States could seek Security Council passage of a resolution to that effect that is modeled on Resolution 1540. If effectively implemented, such an action would, in effect, create a global regime to prevent creation of mirror organisms. Such a resolution could determine that the development of mirror organisms by any state or nonstate party would constitute a threat to international peace and security under Article 39 of the UN Charter, could state that the Security Council was acting under Chapter VII, and could state that the Security Council decides

- that all states shall refrain from manufacturing, acquiring, possessing, developing, transporting, transferring, or using mirror organisms
- that all states, in accordance with their national procedures, shall adopt and enforce appropriate effective laws to prohibit any nonstate actor to manufacture, acquire, possess, develop, transport, transfer or use mirror organisms
- that it would convene to review any evidence of mirror organism development that was presented to it

- that it would then determine whether action under Article 40 (nonmilitary measures) or Article 41 (military measures) would be warranted to address that threat.

Such a statement goes further than Resolution 1540 in explicitly contemplating enforcement measures; in that way, it would be unprecedented—but so could be the risk from mirror organisms.

As it did in Resolution 1540, the Security Council could include a provision in a mirror organism resolution to create a committee to report back to the Security Council on the "implementation of this resolution" (UN Security Council, 2004, operative paragraph 4). If the WHO did not establish a mechanism to oversee mirror biology research, or if the Security Council wished to assume that responsibility from the WHO, it could use this proposed resolution to establish such a mechanism.

The North Atlantic Treaty Organization (NATO) and other multilateral security organizations. In their mutual defense treaties, the United States and its allies agree that an armed attack on any party would be dangerous to all, and the parties commit to come to one another's defense under such circumstances. Although the development and therefore the possible release of mirror organisms by any entity could represent a catastrophic threat to all treaty partners, it is not clear that such a scenario would be considered an *armed attack* as envisioned by these treaties. Neither is it clear that a military response would be able to address that threat. However, each of these treaties also establishes communication mechanisms by which allies can discuss threats to their security, and all of them could use these mechanisms to consider appropriate responses if other states or nonstate groups appear to be developing mirror organisms. The United States could raise the threat of mirror organisms with its NATO and other mutual defense treaty allies, seeking cooperation in banning their development domestically and otherwise responding to the threat of such organisms' development by others.

On the other hand, discussing the risk from mirror organisms within security alliances that are perceived as hostile by U.S. adversaries, or at least giving any such discussions a high profile within such an alliance, could be counterproductive to mobilizing international cooperation against the development of mirror organisms among all countries, including U.S. adversaries.

A New Treaty Dedicated to Mirror Biology

Just as new legislation specifically designed to control mirror biology may be more fit for purpose than attempting to issue new regulations under existing statutory authority, a treaty crafted for the specific purpose of imposing a global ban on mirror organisms may be able to do so more effectively than relying on existing international instruments. The UN Security Council, which has the authority to establish binding international law that bans mirror organisms, is not the forum to negotiate technical details that would differentiate those activities, precursor materials, and intermediate biological constructs that would need to be banned from those that should be permitted but regulated. If the Security Council left that level of detail to member-state implementation, the differing national results likely would be uncoordinated and perhaps even incompatible. Those details could be addressed through treaty negotiations, but negotiating and securing the ratification of treaties is often a complex and

time-consuming process that can fall hostage to preexisting diplomatic disputes.

On the other hand, a dedicated mirror biology treaty could have tremendous urgency, given the threat; it could be focused, given the narrowness of the topic to be controlled; and although there may be future applications of mirror organisms that would have to be forgone under a mirror organism ban, few institutions have a strong vested interest in their creation. Therefore, factors that could complicate the negotiation of a new treaty could be minimized in the case of mirror biology.

One example of the world's ability to respond in this manner to a global environmental risk is the Montreal Protocol on Substances That Deplete the Ozone Layer. Following Molina and Rowland's 1974 *Nature* publication explaining how chlorofluorocarbons (CFCs) destroyed stratospheric ozone, and the National Academy of Sciences' 1976 validation of that work, Congress passed amendments to the Clean Air Act in 1977 that called for regulation of substances "reasonably anticipated to affect the stratosphere" (Nemecek, 1997). By 1980, the United States, Canada, Sweden, and Norway had banned CFC-based aerosol propellants (Parson, 2003, p. 50). Growing concerns about ozone depletion led to international negotiations to protect the ozone layer—concerns that were exacerbated when the "ozone hole" over Antarctica was discovered (Farman, Gardiner, and Shanklin, 1985). Although it was not yet known whether the ozone hole was caused by CFCs, the Montreal Protocol, calling for an immediate reduction in CFCs, was signed on September 16, 1987, and entered into force on January 1, 1989. The Montreal Protocol was later amended to totally ban CFCs in the developed world by 1995 and in the developing world by 2010 (Nemecek, 1997).

Many years elapsed between the discovery of the global environmental risk posed by CFCs and the conclusion of an international treaty to ban them, which is not a good precedent for the world's ability to rapidly respond to a global environmental crisis. However, the more optimistic interpretation is that this treaty was concluded despite significant initial opposition by industry. CFC producers challenged the science linking CFCs and ozone depletion and argued that it did not justify banning them, especially given that obvious alternatives did not exist for CFC use as refrigerants—a substantially bigger market than aerosol propellants (American Chemical Society, undated).

A treaty banning mirror organisms, shutting down the pathways by which they could be synthesized, and requiring states to regulate certain precursor materials and intermediate constructs should face fewer political obstacles. As serious as global ozone depletion would be, the threat posed by mirror organisms may be perceived as far graver, and it does not appear that there are significant economic interests that would be harmed by a mirror organism ban. Such a treaty, if concluded, could also establish an international oversight mechanism for mirror biology–related issues, including mirror biology countermeasure research.

Even if the UN Security Council is willing and able to use its Chapter VII authority to mandate a mirror organism ban, it is not well suited to work out the technical details associated with a regulatory regime. To complement a UN Security Council resolution, the United States could seek to initiate international negotiations on a treaty addressing the threat of mirror organisms. The process of negotiating a treaty, just like the process of stakeholder engagement and review-and-comment rulemaking that is used in domestic regulation, would provide an opportunity

for the various interests involved to design and come to agreement on appropriate solutions. Whether that opportunity could be realized depends on whether states see coming to agreement on an international regime to ban mirror organisms as more important than using the negotiations as leverage in unrelated areas of contention.

International Response to the Release of Mirror Organisms

Just as U.S. law preventing the construction, possession, or use of mirror organisms would have to be written carefully to permit their authorized study in response to the actual creation or release of mirror organisms into the environment, any multilateral arrangement or declaration would have the same requirement. And like U.S. law, any such treaty provisions would have to be written in a way that did not allow or appear to allow the construction of mirror organisms in advance of such an event. One way that the states parties to a treaty banning mirror organisms could respond to the changed world circumstances of a mirror organism release would be for the treaty to specifically anticipate those provisions of the treaty that would have to be voided or changed. However, because several detailed provisions might be implicated, and because the actual circumstances of the release might matter, it could be difficult to anticipate exactly what changes would have to be made.

An alternative way to allow for states' obligations under a treaty to be revised in the event of a mirror organism release—a mechanism that would address constraints under existing treaties, as well as any assumed under a newly negotiated one—would be through the UN Security Council. According to Article 103 of the UN Charter, "In the

It does not appear that there are significant economic interests that would be harmed by a mirror organism ban.

event of a conflict between the obligations of the Members of the United Nations under the present Charter and their obligations under any other international agreement, their obligations under the present Charter shall prevail" (UN Charter, 1973, Article 103). Recognizing that Article 25 of the charter states that UN member-states "agree to accept and carry out the decisions of the Security Council," Article 103 has been interpreted as meaning that Security Council resolutions can override treaty obligations that states might otherwise have (Liivoja, 2008).[11] This mechanism was implicitly utilized in UN Security Council Resolution 2118, which authorized member-states to "acquire, control, transport, transfer, and destroy [Syrian] chemical weapons . . . consistent with the objective of the Chemical Weapons Convention," notwithstanding the actual language in Article I of that treaty, which categorically commits states parties to never acquire chemical weapons "under any circumstances" (UN Security Council, 2013). A similar Security Council resolution, passed after the creation or environmental release of mirror organisms, could authorize member-states to take protective measures that might oth-

erwise violate a mirror organism ban treaty or other international arrangement.

Conclusion

The creation and release of mirror organisms could have catastrophic consequences for life on earth. A variety of U.S. government domestic and international policy actions could assist in halting research into the creation of mirror life and precluding its development everywhere. The policy actions described in this paper offer several avenues for achieving these goals. These policy actions, in most cases, are mutually supportive and could be pursued in parallel. Some of the actions described here, such as long-term regulation under the federal select agent program and the implementation of standalone legislation—might be redundant; if legislation is passed, regulation under the select agent program would not be necessary or desirable.

Those actions that can be taken immediately—executive branch statements, commissioning of a NASEM study, and implementation of a pause on federal funding with the goal of developing mirror organisms—should be taken immediately. These actions would not necessarily have long-term effects, but they would convey the importance that the U.S. government attaches to the possible consequences of mirror organisms, and these actions should signal to researchers that unless countervailing evidence is discovered, mirror organism development should no longer be considered a legitimate area of scientific endeavor.

Regulatory changes could take more time, but such changes could also serve to impose force-of-law constraints on some actions relevant to mirror organism construction. Ultimately, standalone legislation devoted to banning or regulating mirror organisms and the means of creating them could be necessary.

International engagement will be necessary to extend these unilateral bans worldwide. A new treaty dedicated to banning mirror organisms would be the most effective international instrument, but useful actions that will be easier to implement can be taken through existing bilateral, multilateral, and international engagements and institutions. The United States should explore these international actions as well.

Notes

[1] One precedent for a countermeasure creating the problem it was intended to ameliorate is the 1977 H1N1 influenza epidemic, which was caused by an H1N1 virus that was much more similar to a virus isolated in 1950 than it was to H1N1 viruses that circulated between 1947 and 1956. The most plausible explanation is that the 1977 outbreak was caused by the accidental or intentional release (for example, through its administration as a vaccine) of virus obtained directly from a sample of the 1950 strain that was preserved for research or clinical use in a laboratory. Had that virus been circulating in animal hosts during the 27 years between the two sample collections, a much greater difference would have been observed (Racaniello, 2009).

[2] Given the discretionary nature of awarding federal funding, agencies are free to make rather arbitrary decisions about exactly what the boundaries of a funding ban should be. Delineating the boundaries of a ban on mirror biology that would be incorporated into regulation or law, as is discussed later, would be more impactful because violation of those boundaries could incur civil or criminal penalties.

[3] According to the Export Administration Regulations (15 CFR § 772.1), the term *U.S. persons* includes U.S. citizens, U.S. permanent residents, certain categories of people with protected status under U.S. immigration law, and entities (*juridical persons*), such as corporations and associations that are organized under U.S. jurisdiction.

[4] Catch-all controls also apply to exports intended for nuclear weapon programs or programs to develop certain delivery systems, but the United States is not party to any treaty or arrangement categorically banning such programs, and it reserves the right to develop, build,

possess, and use such weapons. In these cases, the existence of catch-all controls for exports supporting these remaining weapon programs does not necessarily serve to reinforce an international ban against them, although they do serve nonproliferation efforts to prevent such programs from succeeding.

[5] U.S. criminal law contains a provision that could complicate the ability of the U.S. government to provide assurance that the select agent regulations could prevent the government itself from making mirror organisms. The U.S. Code (18 U.S.C. § 175b(a)(3)) states that criminal penalties for violating one specific provision of the select agent regulations "shall not apply with respect to any duly authorized United States governmental activity." It is not clear how broadly this provision was meant to apply or whether it is being applied at all; to our knowledge, U.S. government researchers and laboratories that possess, use, or transfer select agents do so in compliance with the select agent regulations and do not take advantage of this literal "get out of jail free" card. Nevertheless, this language could give rise to the perception that the U.S. government did not consider itself bound by whatever select agent regulations it enacted to restrict or ban mirror organisms. (Note that this apparent exemption for official U.S. government–authorized activities does not apply to the Biological Weapons Statute, 18 U.S.C. § 175. Anyone developing biological weapons in the United States, including government employees, would be violating this criminal provision; there is no "duly authorized United States governmental activity" exemption to this criminal prohibition.)

[6] Arguably, the definition of *variola virus* in 18 U.S.C. § 175c(d) is ambiguous in that it could be interpreted as also capturing smallpox vaccine—a nonpathogenic virus that is so closely related to variola that it can induce immunity to variola but does not itself cause the disease. The Justice Department subsequently issued an interpretation stating that it did not consider the vaccine to be banned (see Bradbury, 2008).

[7] 18 U.S.C. § 175. Importantly, note that language in a subsequent section of the criminal code (18 U.S.C. § 175b) that excludes authorized U.S. government activities from certain aspects of the select agent regulations does not apply to the prohibitions with respect to biological weapons in 18 U.S.C. § 175.

[8] *States parties* is the BWC's term for its signatories.

[9] The states parties include the State of Palestine, which is not recognized as a state by the United States. The signatories that have not ratified are Egypt, Haiti, Somalia, and the Syrian Arab Republic; nonsignatories are Chad, Comoros, Djibouti, Eritrea, Israel, and Kiribati.

[10] The United States asserts that China and Iran conduct biological activities that "raise questions" regarding their compliance with the BWC and that Russia and North Korea both maintain offensive biological weapon programs and are "in violation" of their obligations under the treaty (U.S. Department of State, 2024).

[11] The full extent to which Security Council resolutions have priority over treaty obligations is a complicated one having to do with, among other things, whether the Security Council's actions are consistent with the UN Charter and other compelling international norms. (See, for example, Heieck, 2018.)

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Abbreviations

AI	artificial intelligence
BWC	Biological Weapons Convention
CFC	chlorofluorocarbons
DURC	Dual-Use Research of Concern
ENMOD	Environmental Modification Convention
HHS	U.S. Department of Health and Human Services
NASEM	National Academies of Science, Engineering, and Medicine
NATO	North Atlantic Treaty Organization
NIH	National Institutes of Health
PEPP	Pathogens with Enhanced Pandemic Potential
UN	United Nations
WHO	World Health Organization

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About This Paper

If ongoing research programs continue, scientists are likely to be able to create *mirror organisms* whose molecular components, including genetic material, are mirror images of those found in nature. Mirror bacteria could proliferate throughout the biosphere and evade major components of natural hosts' immune systems. A publication released in December 2024 (Adamala, Agashe, Belkaid, et al., 2024) and its accompanying technical report (Adamala, Agashe, Binder, et al., 2024) describe the potential risks—to human, animal, and plant life, as well as to the ecology of earth—posed by development and release of mirror life. Furthermore, Adamala, Agashe, Belkaid, et al. (2024) argue that mirror life cannot be developed safely, that any "guardrails" could be removed via established techniques in synthetic biology, and that any benefits from the development of mirror life are outweighed by the risks. Fortunately, mirror organisms do not exist, and early action to prevent their construction could help avert global-scale catastrophe. In this paper, we describe U.S. and international policy mechanisms that could contribute to halting research and development programs to create mirror organisms. Domestic policy options could include executive branch statements and norm-building actions (e.g., the issuance of high-level statements and a National Academies of Sciences, Engineering, and Medicine study), a ban on federal funding of research toward the creation of mirror organisms, regulatory changes under the existing statutory authority in the federal select agent program and export controls, and legislation tailored to prohibiting and preventing the construction of mirror organisms. Policy options in the international arena include bilateral and multilateral engagement; invoking and using the authorities of the Biological Weapons Convention, the Environmental Modification Convention, and the United Nations Security Council; and the creation of a new treaty banning the development of mirror organisms.

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