

A Worldwide “Experiments of Concern” Resource Portal: Concept, Plan & Development Trajectory

Stephen M. Maurer, Robert M Cook-Deegan, Megan Davidson, Elisa D. Harris, Nikki M. Vangsnes, John Steinbruner & Laurie Zoloth

I. Summary

Advances in the life sciences offer important new ways of understanding and organizing DNA for human use, but also pose significant challenges to ensure that these uses do not include harmful ones, such as inadvertent or deliberate creation of dangerous new organisms that cause harm to people, animals, plants, or the environment. Scientists’ ability to obtain timely and competent advice before conducting “experiments of concern” has been identified as a priority, and we propose a new channel for providing such advice. Recent work commissioned by two of us (JS & EDH) suggests that a precise and narrowly defined “experiments of concern” category would have affected some 2500 researchers at 300 facilities in the US between 2000 and mid-2005.¹

We are currently seeking in joint funding from the Carnegie, MacArthur, and Sloan Foundations to build an on-line Portal where interested parties can obtain advice about actual or potential experiments of concern. If granted, this will permit us to construct and operate the proposed Portal for one (1) year. We expect this initial experience to validate the Portal’s value and (if appropriate) justify additional requests for support beyond the first year. Joint funding will send a powerful signal that foundations expect users to obtain impartial, outside advice before proceeding. Joint funding will also let multiple Foundations provide advice and input. We plan to use this input, along with conversations with other stakeholders (academic scientists, IBCs, and NSABB members) to refine the current Portal design in ways that best reflect the scientific community’s needs and enhance the ability of existing biosafety and biosecurity bodies to perform their missions.

As set forth below, the Portal will provide a convenient, confidential on-line service where individual scientists and institutions can obtain clearly and timely advice and information about the ethical, social, legal, and scientific issues raised by proposed experiments. It will also provide constructive advice so that scientists can modify proposed projects to make them safer and more prudent. Establishing a mechanism to conduct reviews of research proposals that raise “dual use” concerns will complement and build on other projects that have explored this issue by proposing and conducting peer review.² The Portal would also provide an open (unclassified) knowledge base for more permanent, government-mandated solutions.

¹ The research in question involved a survey of journal articles published in the US during that timeframe. See John Steinbruner, Elisa D. Harris, Nancy Gallagher, Stacy Okutani, *Controlling Dangerous Pathogens: A Prototype Protective Oversight System*,” December 2005 at pp. 64-5.

² J.Steinbruner *et al.*, *supra*.

This document presents the rationale for adopting a Portal approach; sets explicit goals that any successful Portal must satisfy; and provides a first-draft description of how the proposed Portal would function. Because the rapid pace of science requires a serious and timely response, it concludes by listing the steps needed to make the Portal a reality within six to eight months of being funded.

II. Rationale

The US National Research Council³ and UK Royal Society⁴ have repeatedly found that researchers contemplating experiments of concern do not receive sufficient expert advice and that the resulting biosecurity challenge is potentially catastrophic. The proposed Portal will provide a convenient new channel for delivering timely, clear, and authoritative advice to investigators and institutions. Preliminary surveys of biologists suggest support for such a capacity, at least within the synthetic biology community.⁵

A Portal design offers multiple advantages. These include:

- *Specialized Expertise.* Competent biosecurity advice is intrinsically interdisciplinary. Furthermore, many of the required disciplines cannot be found in every research institution. By contrast, an on-line Portal can draw on expertise wherever it exists
- *Economies of Scale.* The total number of experiments of concern at most universities and research centers is likely to be small. At present, many institutions do not have sufficient numbers of experiments of concern to merit a separate, in-house review and advice service. The Portal shares the costs of establishing a review mechanism and avoids wasteful duplication.
- *Policy Development.* There is no firm agreement on what constitute “experiments of concern,” let alone the principles and policy responses needed to address them. Refining this definition is a key goal of the National Science Advisory Board on Biosecurity. A Portal will generate regular, repeated, and practical interactions with scientists around the world. The resulting knowledge base will point the way to “lessons learned,” “good practices,” and policy insights. Since none of the Portal’s work will be classified, this information will be open to all.

³ US National Research Council, *Globalization, Biosecurity, and the Future of the Life Sciences* (2006) and *Biotechnology Research in an Age of Terrorism: Confronting the Dual Use Dilemma*,” (2003).

⁴Royal Society and Wellcome Trust: “Do No Harm: Reducing the Potential for the Misuse of Life Science Research (2004), available at <http://www.royalsoc.ac.uk/displaypagedoc.asp?id=10360>.

⁵ S. Maurer, K. Lucas & S. Terrell, *From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology* (2006), available at <http://gspp.berkeley.edu/iths/UC%20White%20Paper.pdf>.

- *Consistency and Fairness.* Developing biosecurity policy at the level of individual universities and research centers runs the risk of generating inconsistent outcomes and policies. Similarly, an institution-by-institution approach potentially creates conflict-of-interest problems by requiring faculty to evaluate each others' experiments. Both of these dangers will be much reduced under a Portal-based approach that spans multiple institutions.
- *Internationalism.* A worldwide Portal will automatically promote the development of consistent, consensus approaches across national boundaries and the recognition of patterns of common problems across international boundaries.
- *Timeliness and Flexibility.* Institutional Biosafety Committees are increasingly being called upon to provide biosecurity advice. The Portal will provide resources to these bodies and support their missions. In the longer term, NIH's National Science Advisory Board for Biosecurity (NSABB) is currently studying possible institutional frameworks for reviewing and managing experiments of concern. This process is expected to take several years. An academically based Portal will provide a valuable knowledge base for NSABB's deliberations and encourage responsible self-governance until more formal institutional oversight arrangements are established. In the longer term, we expect to modify (or possibly eliminate) the Portal to conform to whatever government policies ultimately emerge in this area.

III. Goals.

A successful Portal design must achieve multiple goals:

- *Connecting Problems With Expertise.* Experiments of concern cannot be adequately reviewed by individual scientists on their own, as they have an inherent self-interest in seeing their work proceed. Most scientists also lack the background and expertise required to evaluate dual-use concerns. Responsibility is ultimately in the hands of investigators, but the Portal can enable individual scientists to address this responsibility drawing on others' expertise.
- *Low Cost/User Friendly.* As an unofficial mechanism, the Portal is entirely dependent on voluntary participation by scientists. Scientists will not use the Portal if it is burdensome. The Portal must be carefully designed so that scientists can use it with a reasonable amount of time and effort.
- *Timeliness.* Scientists will not use the Portal unless it is timely. Our preliminary goal is for the Portal to provide a full response to ninety percent of all inquiries within thirty days. Scientists who do not receive a full response in this time will be advised (a) the reason(s) for delay, and (b) a firm commitment on when the requested advice will be forthcoming.

- *Confidentiality.* Scientists will not use the Portal if it allows competitors to monitor and “scoop” research ideas. Absent consent from the affected scientists, the Portal will keep all opinions confidential for a period of one year. Thereafter, scientists may request additional six month extensions unless and until the proposed experiment is (a) abandoned, (b) completed and published, or (c) becomes public knowledge. Posted opinions will *not* normally include the researcher’s name or institution.
- *Candor and Clarity.* In order to be useful, the Portal’s advice must be clear and unambiguous. All Portal opinions will reach one of three recommendations: the experiment can be performed; the experiment should only be performed if modified in certain clearly enumerated respects; or the experiment should not be performed. Each Portal opinion will also provide a short, complete analysis explaining the basis for the decision. Finally, opinions may contain short dissenting views where reviewers cannot achieve consensus. Portal staff will work closely with reviewers to avoid dissenting views wherever possible.
- *Transparency.* The Portal would not be classified. Portal opinions will normally be posted on the Internet within one year of issuance.
- *Viewpoint.* Portal advice will be limited to dual-use concerns. Subsequent expanded versions of the Portal may eventually offer broader bioethical, biosafety, and/or political viewpoints as well. Portal opinions will be based on input from a multi-disciplinary group that includes bench scientists, ethicists, social scientists, lawyers and policy analysts in this field.
- *Attribution and Credit.* The Portal site will give all Portal contributors (including project leaders, staff, and reviewing experts) full credit and attribution.

IV. Portal Design.

Availability & Scope. The Portal will respond to inquiries from any person, group, or institution (hereinafter called “users”) responsible for deciding whether to proceed with an experiment of concern. All inquiries must relate to imminent, specific, and practical choices. The Portal will not prepare advisory opinions concerning general principles or hypothetical experiments. Typical users may include (a) bench scientists, (b) institutional biosafety committees, (c) NIH’s Recombinant DNA Advisory Committee, and (d) any other person or group seeking biosecurity expertise related to a proposed experiment of concern.

The Portal will initially focus on providing whatever scientific, technological, and policy analysis may be needed to determine whether a given experiment will materially improve the ability of states and/or terrorists to develop biological agents or toxins that could be used against human, animal or agricultural targets. Any bioethics and/or biosafety advice will be directed to this focus. Users who require responses to other ethical or safety

questions will be asked to seek it elsewhere through IBCs, IUCACs, the RAC, and other existing channels.⁶

The Portal will maintain a complete record of all users who contact it and all opinions prepared for those users. The Portal will keep all opinions delivered to users confidential as provided below. Users who receive Portal opinions will be free to share and/or publish them as they see fit. The Portal will hold an annual conference at which it will report on the opinions and other advice it rendered during the previous year.

Architecture. The Portal will make maximal use of our University of Maryland collaborators' BRSS system and its extensive documentation base. The current BRSS system is a secure and scalable system written in PYTHON with multiple levels of encryption. The system is based on a thin-client model in which data reside on a remote server and can be accessed using an ordinary web browser. One of BRSS's most important features is a "semantic backplane" in which information workflows are rigorously defined according to strict, internal rules. We will exploit and extend this feature to create a powerful development tool ("Unified Modeling Language" or "UML") that displays BRSS workflows in graphical form. This will allow our IT team to extend BRSS into PLONE, a powerful open-source web applications server program that is both highly scaleable and secure. Once the Portal architecture has been designed at a graphical level, the UML will be automatically converted to code. This will provide a cost-effective solution to implementing the initial Portal design while ensuring built-in flexibility to revise the system as needs evolve over time.

Work Flow. The Portal will manage incoming requests for advice as follows:

- *Initial Contact.* Users requesting advice will initiate contact by logging onto the Portal's web site and filling out a series of standard intake forms. This process will normally take about thirty minutes. Users who prefer a live interview will be asked to leave contact information. Portal staff will normally respond within two business days. Staff will use the standard intake form in conducting live interviews.
- *Follow-Up Contact (A).* Portal staff will review each submitted intake form and assign it a case number within 24 hours. In some cases, information may be so ambiguous or incomplete that further review would not be practical. Portal staff will contact users as necessary to obtain this information.
- *Preliminary Analysis and Routing.* Portal staff will compare the intake form against its list of available expert reviewers.⁷ A minimum of three reviewers will

⁶ Second-generation versions of the Portal may be more ambitious, potentially offering new advice categories (bioethics, biosafety...) and/or inviting input from governments, advocacy groups, and other actors beyond the academic science and policy communities.

⁷Experts holding security clearances would be strongly encouraged to participate as reviewers. However, they would be cautioned against revealing classified information and the Portal would not knowingly accept such information under any circumstances.

then be selected based on the expertise required to review the proposal effectively. The Portal Oversight Committee members will have one business day to approve, delete and/or add suggested reviewers. Portal staff will telephone each suggested reviewer to confirm their availability. Thereafter, reviewers will immediately receive: (a) a complete copy of the intake forms and all known information about the case, (b) a short statement of the specialized disciplines and/or expertise that the staff believes are needed to provide a competent opinion, (c) a form for requesting additional information from the user, and (d) a computerized worksheet for reviewers to complete once they have formed an opinion..

- *Expert Review (Phase I)*. Within one week of receiving an electronic case file, each reviewer will notify Portal staff (a) whether any additional specialized discipline or expertise will be needed to address the case, and (b) whether any additional information needs to be obtained from the user.
- *Follow-Up Contact (B)*. In those cases where one or more reviewers request additional expertise, Oversight Committee members will consider the request and obtain additional reviewers as necessary. Portal staff will collect additional information requests from all assigned reviewers and promptly contact users to obtain these data. Every effort will be made to spare users unnecessary or repetitive contacts.
- *Expert Review (Phase II)*. Portal staff will promptly forward any additional information received from users to reviewers. Each reviewer will then form an opinion, fill out the computerized worksheets provided, and forward this information to the Portal staff. This phase of the review process should normally be completed within two weeks. Reviewers will hold all case materials in confidence.
- *Preliminary Opinion*. Once the reviewers' comments have been received, Portal staff will prepare a draft Preliminary Opinion reflecting and insofar as possible reconciling the opinions of all reviewers. The Preliminary Opinion shall consist of a short, clear statement of all material facts; a clear recommendation that the experiment can go forward; should only go forward if modified in some specific respect(s); or should not go forward. The opinion shall also contain a clear and complete explanation of the reasoning behind this recommendation. Opinions should not normally exceed two single-spaced pages and will normally keep the user's identity and home institution confidential.⁸ The Portal staff will promptly distribute copies of the draft Preliminary Opinion to all Oversight Committee members together with all reviewer comments. Oversight Committee members will then promptly consult in person, by conference call, through e-mail, or via some other reasonably secure method to review and discuss any needed modifications. The goal will be to achieve a full exchange of views among the entire Oversight Committee. The staff will then circulate the final Preliminary

⁸ Users may waive this requirement at any time.

Opinion to each reviewer to ensure that it accurately reflects their analysis. Reviewers who cannot reconcile their analysis with the final Preliminary Opinion will be asked to prepare a short dissenting opinion.

- *Follow-Up Contact (C).* The Portal staff will provide a copy of the final Preliminary Opinion to the user for review and comment. User comments will be promptly forwarded to the Oversight Committee and reviewers so that the Preliminary Opinion can be modified as necessary. Such modifications may include suggestions for a revised experiment designed to reduce or eliminate the biosecurity concerns. All modifications must be agreed by both the reviewers and the Oversight Committee. This process should normally be completed within two weeks. The resulting Interim Opinion will promptly be forwarded to the user and become final one week thereafter unless the user asks for an appeal.
- *Appeals.* Users who disagree with an Interim Opinion can appeal by submitting a succinct statement of their objections to the Oversight Committee within one week. The statement may, but need not, be accompanied by supporting communications from individuals and institutions in support of the objections. The Committee will promptly forward by email a copy of the objections and Interim Opinion to all reviewers assigned to the case. The reviewers will then have one week to respond. The Oversight Committee shall withdraw the Interim Opinion if, after one week, a majority of responding reviewers agrees with one or more objections and shall issue a new Interim Opinion based on its decision. Absent a successful Appeal, the original Interim Opinion will become final.
- *Records.* The Portal will promptly provide a copy of the Final Opinion to the user and to any person(s) or group(s) designated by the user. The Portal will normally keep all Final Opinions confidential for a period of one year. Thereafter, scientists may request additional six month extensions unless and until the experiment of concern is (a) abandoned, (b) completed and published, or (c) otherwise becomes public knowledge. Posted opinions will *not* include the researcher's name or institution.

Staff & Oversight Committee. Portal staff will normally consist of postdoctoral candidates with a strong interest in biology, security policy, or other related fields. All staff will be closely supervised by at least one member of the Oversight Committee. The Oversight Committee will also be broadly representative in terms of the expertise of its members and include at least one individual from each institution and/or group participating in the Portal project.

Outreach. Portal members will mount an outreach campaign to ensure that scientists know about the Portal and what it has to offer. Components will include:

- *Informal Contacts.* Project members will publicize the Portal's existence and potential usefulness to friends and colleagues who (a) serve or have previously served on IBCs, NSABB, RAC, American Society for Microbiology, Centers for

Disease Control and Prevention activities, biodefense research programs, NAS or NRC committees, or other bodies responsible for biosecurity, (b) have biosecurity-related research interests, and (c) are otherwise known to have an interest in biosecurity.

- *Press.* Project members will publicize the Portal's existence and potential usefulness through editorials and news coverage in both the general and scientific press.
- *Professional Societies.* Project members will make presentations introducing the Portal to US and overseas professional societies whose members have either contemplated experiments of concern in the past or are likely to do so in the future.
- *Pledge Drive.* Survey evidence⁹ suggests an emerging norm at least among synthetic biologists that scientists contemplating experiments of concern should always obtain a competent, independent advice before proceeding. Project members plan to promote this norm (and, indirectly, the Portal) by creating an Internet page that lists the names of scientists who have pledged to seek such advice before proceeding with any experiment of concern.
-
- *Annual Conference.* The Portal will host an annual conference to review developments over the preceding year, identify emerging principles, and discuss "lessons learned." Reporters notes will be prepared for each conference and posted on the Portal.

Additional Resources. The Portal will be the central component of a broader program to make biosecurity knowledge available to non-specialists who need it. Additional related web pages will eventually include a public information page summarizing the history of dual use experiments, a "Lessons Learned" page summarizing principles that have emerged from the Opinion-writing process, and a "Pledge Page" listing scientists who have promised not to perform experiments of concern without first seeking independent expert review. More elaborate, "second generation" projects are also possible. These include (a) a confidential on-line hotline where biologists can report biosecurity concerns or biosafety accidents, (b) a confidential on-line hotline where biologists who notice new biosecurity risks can report the information, (c) databases to record and collate the foregoing, and (d) "alert" services, review articles, and public talks designed to disseminate "lessons learned."

⁹ S. Maurer, K. Lucas & S. Terrell, From Understanding to Action: Community-Based Options for Improving Safety and Security in Synthetic Biology (2006), available at <http://gspp.berkeley.edu/iths/UC%20White%20Paper.pdf>

VI. Leveraging Existing Resources.

The Portal project will benefit from extensive related work that the collaborators either have done or are already planning to do at their respective universities. Last Spring, the Carnegie and MacArthur Foundations funded the UC and Northwestern collaborators to work with members of the synthetic biology community to identify and prioritize community-based options for improving biosecurity. The Portal concept is a direct outgrowth of this work. The Carnegie Foundation has also provided funds to provide biosecurity advice within the UC Berkeley/Lawrence Berkeley National Laboratory community. These resources will be used to support various travel, workshop, and preliminary IT design service for the Portal. The Portal will also build on extensive work already performed by our University of Maryland collaborators to define research activities that should be subject to prior review, to develop risk-benefit assessment criteria for use in the review process, and to create a data management system -- the Biological Research Security System, or BRSS -- for reporting information during the oversight process. BRSS is a sophisticated "expert program" that asks a series of carefully designed questions that quickly identify and then gather detailed information on areas of concern in proposed experiments. BRSS's performance and user-friendliness have been extensively demonstrated in tests with real biologists describing realistic examples of proposed experiments. The Portal will work closely with BRSS's IT team to get full value from the system's architecture and documentation. The Duke collaborators operate an existing biosecurity advice service for academic researchers within their region and will make this unique experience base available to the collaboration. Similarly, our Northwestern collaborator is currently building an advice service for Chicago-area nanobiotechnology researchers, funded by the National Science Foundation, and involving senior scholars in law, religion, philosophy and the humanities from Northwestern University, Berkeley, and the University of Arizona. The Portal plans to draw extensively on these resources and experience base.