Framework for Conducting Productive and Responsible International Research Collaborations

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Contents

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Abstract

Openness and collaboration provide a foundation for scientific progress, facilitating advancement as scientists build upon each other's work. Scientists are increasingly participating in international research collaborations, bringing many benefits to researchers and to the scientific community. However, collaborations also come with risks and challenges, from disagreements to how the research is performed or how credit is given, to conflicts surrounding research standards and ethics. Additional risks arise when collaborations involve research with a high potential for misuse, such as weaponization or other misuses. Raising awareness about these risks and promoting best practices can help researchers benefit from collaborations while minimizing potential issues. We have surveyed peer-reviewed literature, grey literature, and policies and developed a unifying framework, which can be used by researchers and institutions to make informed decisions regarding participating in international collaborations. This framework consists of four pillars: Knowing Your Partner, including their values, personality, and background before embarking on a partnership; Planning the Partnership, by discussing expectations and any needed agreements; Technology Risk and Benefit Assessment, which can be used to assess risks and benefits of the proposed research; and Institutional Guidelines, where institutions create policies and guidelines for approving and participating in partnerships to help their staff follow best practices. Using the guidelines and activities suggested through these pillars, scientists, with the support of their institutions, can make informed decisions about how to engage in responsible and productive research collaborations.
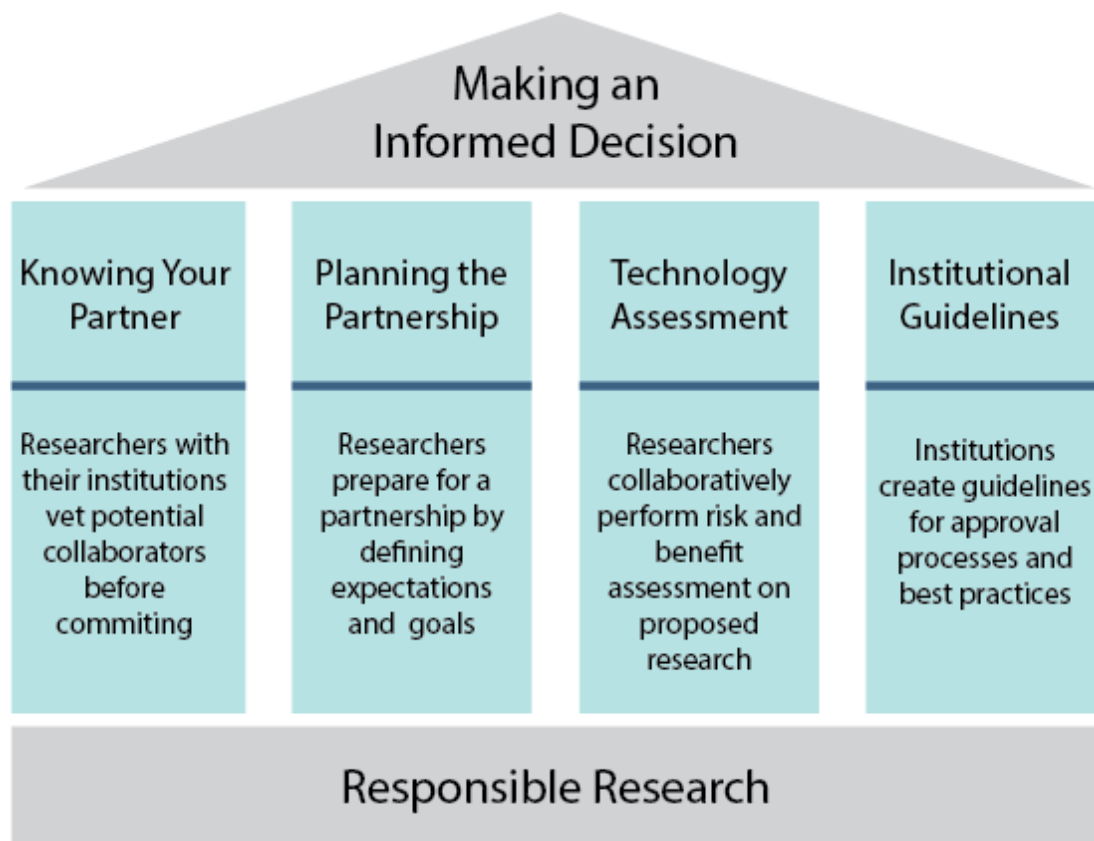
Introduction

Openness and collaboration are foundational for the scientific community. Generally, sharing of technology and information among parties is encouraged as part of the open dissemination of scientific ideas. Especially in today's interconnected world, scientific knowledge is disseminated freely through a plethora of means, including publications, research conferences, collaborations, faculty visits, open-source archives and scientific alliances. This sharing is a core component of science, creating a platform for scientific advancement as scientists build upon each other's work. On a global level, international collaboration accelerates technological advancement, promotes health equity,[1] and brings to bear a necessary diversity of skills, stakeholders, resources, and perspectives on critical scientific questions. Trends suggest that global collaboration in science is growing at a greater than exponential rate due to an increased need for specialization and a broadening distribution of scientists worldwide.[2]

Scientists may find numerous benefits of international collaborations, including gaining access to unique expertise and resources, increased access to funding opportunities, improving the impact by exchanging ideas and sharing data, or achieving greater international prominence. At the institution level, universities' involvement in programs to host foreign students can help institutions attract top talent and open the doors to new international collaborations, as well as diversify the student population. Researchers may participate in these international programs because they have a passion for training students and want to increase global scientific capability.

The benefits of openness and collaboration within the scientific community are clear. However, international collaborations come with a variety of risks and challenges. Examples of these challenges include misunderstandings between partners, differences in opinion about research goals, or disagreements about intellectual property (IP) rights or authorship credit. Researchers rely on authorship credit for career advancement, and IP benefits allow institutions to recoup research costs and provide resources for further innovation; therefore, addressing these challenges is critical for successful international collaborations.

Other risks come from a difference in values between collaborators leading to disagreements about research standards and ethics. Research partnerships may exacerbate risks inherent to the research itself—such as safety and security risks, ethical risks, or risks of misuse of research outputs—because collaborators may have different awareness or understanding of these concepts. Research that is intended to provide benefit but also has the reasonable potential to be misused for harmful purposes is called dual-use research. Dual-use research has historically spanned many fields, including nuclear energy, biotechnology, materials science, and artificial intelligence (AI).[3] Working with and sharing information about research with dual-use potential creates an ethical dilemma because it can potentiate both societal advantage and societal harm.[4] With this in mind, many have expressed the importance of industry and academic research institutions protecting their data from access by those who would misuse it.[5]

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[1] Andrade PA, Carvalho DBBd. (2015) International cooperation for science and technology development: a way forward for equity in health. *História, Ciências, Saúde-Manguinhos.* 22**:** 49-67.

[2] Ribeiro LC et al. (2018) Growth patterns of the network of international collaboration in science. *Scientometrics.* 114 (1)**:** 159-179.

[3] Williams-Jones B, Olivier C, Smith E. (2013) Governing 'dual-use' research in Canada: A policy review. *Science and Public Policy.* 41 (1)**:** 76-93.

[4] Selgelid MJ. (2009) Governance of dual-use research: an ethical dilemma. *Bull World Health Organ.* 87 (9)**:** 720-723.

[5] Paile S et al. (2018) Do academic activities contribute to WMD proliferation? European Studies Unit.

Even if much of the research findings will be published, collaborations between laboratories exacerbate risks of misuse by providing opportunities to gain more tacit knowledge than simply accessing a publication and by enabling access to unpublished data.[6] Foreign collaborations in particular may increase the risks of theft, as has occurred in cases where visiting scientists or collaborators illicitly access and distribute unpublished data or intellectual property.[7] Additionally, local institutions or funding agencies finance projects and visiting students but may not reap the benefits if the acquired skills and know-how are being exported.[8] Even through legal means, technology acquisition becomes a concern when transfers are one-sided or when technologies can be misused for harmful purposes.

Clearly defining the goals and terms of a partnership is essential—not just to improve the probability of success through shared understanding about roles and responsibilities, but also to reduce the risk of unintended access to and misuse of earnest research findings and skills. Institutions and researchers should be equipped with the tools to evaluate potential collaborations and minimize risk within their partnerships. We performed an extensive literature search and found that no comprehensive framework existed for developing productive and responsible research collaborations. However, many resources pointed to relevant themes, and frameworks exist for some components of the process for creating research collaborations. We have taken the themes found in the literature and developed a unifying framework with four pillars, which can be used by researchers and institutions to make informed decisions regarding participating in international collaborations:

> *Knowing Your Partner* - Institutions and scientists create a review process to evaluate potential collaborators.

> *Planning the Partnership* - Scientists prepare for a potential partnership by thoroughly defining the expectations of each collaborator and the goals of the collaboration.

> *Technology Risk and Benefit Assessment* - Scientists, with the input of other experts, assess both the positive value and the potential for causing harm of the research they are proposing.

> *Institutional Guidelines* - Institutions create policies for approval processes and best practices that their faculty and staff are encouraged or required to follow.

Institutions and scientists can utilize the information gathered on potential partnerships in connection with institutional policies to make an informed decision whether and how to proceed with an international collaboration. Understanding and following these principles can help institutions make the most of their foreign collaborations. Importantly, however, despite the focus of this framework on international partnerships, many of the practices discussed here apply valuably to domestic partnerships as well. This paper will discuss each of these four pillars in detail, including examples of how institutions implement these practices.

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[6] Joshi T. (2018) The Dynamics of Knowledge Sharing in the Biotechnology Industry: An Indian Perspective. *Technology Innovation Management Review*. 8 (1).
[7] Barry E. (2019) Stolen Research: Chinese Scientist Is Accused of Smuggling Lab Samples. *The New York Times.* 31.
[8] Hamilton C, Joske A. (2017) Australian universities are helping China's military surpass the United States. *The Sydney Morning Herald*.

Knowing Your Partner

Realizing the benefits of a collaboration requires thoughtful planning regarding with whom to collaborate and how. Bringing in a partner with unique expertise, resources, and experiences can greatly benefit a project. In addition to providing access to critical resources—including funding and expanded technical know-how—collaborators can offer unique perspectives to evaluating and planning research. However, differences in culture, communication style, priorities, project leadership style, scientific expertise, and research standards can all create challenges. Researchers may find potential partners through regional networks of scientists, incidental meetings at conferences, or through mutual acquaintances, but ensuring successful outcomes for the partnership should not be left to chance. Spending some time to ensure a potential collaborator is the right fit can help researchers proceed with confidence in planning their partnership.

When working with a new partner, there are many things to consider in order to determine if both parties will work well together. We have suggested a few ideas for researchers to consider when getting to know a potential partner.

> *Experience and Expertise* – What is their previous research experience? What is their status at their institution? Do they have any accreditations? What is the experience of the other researchers who may be staffing the project? How is the technical expertise of both parties complementary?

> *Personality* – How does their personality influence the way they handle various situations that might come up during a partnership? It may be useful to consider a personality test to get to know each other's personalities.

> *Leadership styles* – Do they have experience leading similar projects? Do leadership styles differ, and if so, how will those differences be navigated?

> *Cultural considerations* – Are there cultural differences in work style? How do they communicate? Will you be able to work through differences in time zones or language barriers?

> *Research values* – Do you understand each other's opinions on ethical questions in science, and are there differences that could cause issues? Do you have similar values and priorities?

Asking some of these questions will help determine if a potential partner is the right candidate for a partnership, before beginning the planning process (detailed in the "Planning the Partnership" section below).

In addition to the need to ensure partners will be able to contribute positively to a partnership, when participating in an international collaboration, researchers and institutions must have confidence regarding with whom data and resources are being shared and used. Foreign collaborations can be extremely beneficial, but they create new access points to research information that could be misused and thereby can increase the risk of unwanted and ill-intentioned access to research outputs. Through a definitive breach of contract or due to incongruence between verbal communication and signed contracts, collaborators may misuse the data for their own gain. They may also allow it to fall into the wrong hands (intentionally or unintentionally), or otherwise increase the risks of the research through negligence or

unawareness. This misuse may occur through means such as commercial endeavors which exclude rightful owners of the intellectual property or usurp the intended beneficial application of the innovation, or by sharing the information with other groups without consent of all parties involved in the research. Below, we discuss a number of factors and potential vulnerabilities that one should consider about their potential collaborator.

Partnering Institutions – In determining if a potential partner is the best fit for a collaboration, it is important to understand where differences in values and ethical frames of reference between the two participating institutions may exist. For example, military institutions contribute substantially to global scientific research, but in certain cases (particularly those involving dual-use research) a potential partner institution's military connections may warrant closer scrutiny. Similarly, private sector entities can serve as valuable partners, but evaluating shared values and visions for research (e.g., commercialization goals for the technology under development) can be particularly important when considering collaborations with businesses—especially when those businesses operate under unfamiliar foreign regulations and market cultures. While institutions may choose to collaborate with partners with non-academic (e.g., military or business) affiliations, such affiliations are important to consider in making partnership decisions surrounding research output protections. The boundaries between categories like public versus private, civilian versus defense, and industry versus academia can vary dramatically nation to nation, so familiarizing oneself with regional differences could aid in making well-informed assessments about potential international collaborators.

Professional History – "Knowing your partner" extends beyond the affiliations of an individual person or organization. Any potential partner will likely have an assortment of other past and present relationships that could be relevant, and this is especially important in the context of an international partnership. To start, exploring a potential collaborator's research and publication history is a simple but effective technique to get a sense of their past and present work as well as their partner and funding relationships. This can provide insight into whether they have the research experience needed for the topic on which they will be collaborating. When appropriate, talking to mutual acquaintances can give those acquaintances an opportunity to vouch for the potential partner. Such strategies can facilitate more effective collaborations not only by broadening an understanding of what skills a potential collaborator might bring to the table, but also by providing context on how they might conduct themselves in a partnership.

Gaining insight about the potential collaborator's research and relationships can also be a risk mitigation strategy. Such evaluations can provide insights into other competing interests that a potential partner may be balancing, sources of funding, and the types of entities that are interested in their work. For example, it would be especially important to know if a potential international collaborator worked closely with particular foreign government agencies or business interests. The flow of funds and information in such relationships, as well as the data permeability, would be important to assess before continuing with a partnership. In rare cases, a search may also reveal other issues involving the potential collaborator, such as redacted publications due to ethical concerns or similar issues regarding standing within professional societies.

Verification of work and educational history can be used to ensure that potential partners have presented their experience honestly. For scientists further in their career, publication history will likely provide significant information; however, for those beginning their careers, such as graduate students or post-doctoral fellows, institutions can call employers, universities, or graduate advisors to verify employment or attendance. In addition to verifying employment, it may be beneficial to verify the legitimacy of the institution to avoid issues such as scientists

utilizing alternate names to hide connection to, for example, a military institution. This can include checking for an institutional website, verifying with third party websites which corroborate, and confirming the physical address of the institution. In the case of hiring international scientists or if concerns arise, background checks may also be used to verify identity.

Problematic Indicators – Certain indicators may suggest an increased risk that an individual or institution may intend to misuse data or information gained during a collaboration. Red flags associated with increased risk include hiding or downplaying commercial or military connections, having a publication record that doesn't match the research that is being proposed, or, in some cases, providing false information regarding work or education history. As an example, many scientists have been caught using the names of fake institutions on their resumes, sometimes to hide military affiliations.[9] Additionally, almost 2% of scientists have published fraudulent data, which can become the responsibility of collaborators if it is in a shared publication.[10] Especially for new collaborations with unfamiliar partners, research scientists and institutions should consider pausing to get to know their potential partner before committing to a collaboration to avoid some of these potential issues. This validation process can be used prior to potential collaborations, as well as before sharing samples or data.

In doing these kinds of preliminary research on potential collaborators, researchers and institutions gain the opportunity to reevaluate before committing to a partnership if red flags arise. In some instances, further investigation may alleviate concerns and the collaboration can proceed. However, in some cases, individuals or institutions may need to reconsider whether the collaboration is in their best interest. By taking the time to verify information concerning potential partners, parties can move forward with foreign collaborations with more confidence that their research will be used for its intended purposes.

Planning the Partnership

Even when working with a trusted partner, collaborations can bring challenges. Thoughtful planning and open communication with partners are key to realizing the benefits of the collaboration while avoiding some common issues. Before embarking on a new partnership, scientists and institutions should assess what they hope to gain from the partnership and the most effective way to go about it. There are numerous reasons to embark upon a research collaboration and any potential partner will also have their unique motivations as well as their own way of operating. In order to maximize positive outcomes, it is important to have open discussions with potential collaborators to make sure all parties agree on the aims of the partnership. Defining the collaboration ahead of time will not only be useful for deciding whether to go through with the collaboration but can also help reduce the chance of future disagreements or potential roadblocks. The following suggestions for questions to discuss with a potential partner are geared towards research collaborations, but can also be used for other situations such as exchange programs or visiting scientists, as applicable:

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[9] Joske A. (2018) Picking Flowers, Making Honey: The Chinese Military's Collaboration with Foreign Universities. *Australian Strategic Policy Institute*. https://www.aspi.org.au/report/picking-flowers-making-honey. Accessed March 29, 2022.

[10] Fanelli D. (2009) How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data. *PLOS ONE.* 4 (5)**:** e5738.

Aims of the partnership – What are the main goals? What are the priority outcomes? What are the motivations for the project? Do you intend to patent or publish your findings? What do you need to accomplish to consider this project successful?

Accomplishing the goals – How will workload be divided? How will you adjust if unexpected problems arise? How long do you expect it to take? Do either of you have time or resources to accommodate unexpected research needs? How will progress be reported between parties?

Communication – What are your communication plans to ensure parties have the opportunity to discuss project needs and updates? Will travel be required or can all discussions take place virtually? Who will be a part of project communications?

Funding and resources – What resources will each partner provide? How will funding be divided and how are ongoing cost sharing decisions going to be made? Who will handle monitoring the budget? Does either partner have existing funding relationships that could affect the partnership? For new funding, what agencies will partners target, and do those agencies have any rules relevant to the collaboration, such as disclosure requirements?

Ending the collaboration – Is this collaboration for a single project or an ongoing collaboration? Does it end when a paper is published, or some other time?

Rights and authorship – What is the expectation for authorship credit on publications? Who will have the intellectual property rights and data ownership (or are they shared) and why? Who will have the rights to specimens collected? When and with whom can any data be shared? Is the project likely to result in a patentable technology? If so, what are the regulations surrounding patents in each country, and how will decisions be made regarding the patent?

Research standards – What are the requirements of each partner's Institutional Review Board or other research evaluations? What standards will be used for an ethical review, such as a human subjects study review? Which biosafety levels can each facility handle, and by what measures does each partner make that determination? Where differences may exist between institutional policies or codes of conduct, how will they be reconciled? What risk-benefit analyses will be conducted for the project?

Disputes – How will disputes be handled? Do both parties have a legal team, or internal processes for handling disputes? Is there a mechanism for making changes during the collaboration? Are there terms and conditions, such as a force majeure clause?[11]

Legal issues – Are there any conflicts of interest? Do data sharing laws, export control, technology transfer laws, or any other laws impact your collaboration?

Signing an agreement – Are all parties willing to sign a Memorandum of Understanding (MOU), an IP non-disclosure agreement, or other type of agreement? Are you on the same page about what should be included in the agreement, regarding IP rights, resources, and expectations regarding the share of work responsibilities and share of royalties or credit?

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[11] Legal Information Institute, Cornell Law School (2021). Wex.

Overall, it is important in pursuing new collaborations, both international and domestic, to normalize these types of partnership-defining conversations. Bringing up these topics proactively, even with a potential partner that feels familiar, can unearth problems before they take root. The value of this practice extends beyond harmonizing multiple systems of responsible research conduct; partners must understand one another's governance, standards of practice, institutional responsibilities, and even basic work styles to generate a successful relationship. Communicating frankly, early, and often is the best way to establish such concordance—and, importantly, it may be the only way to identify differences in practices and project goals or gaps in understanding that would be prohibitive to continuing with a partnership. This list of questions provides a starting point to open up conversations between potential collaborators. For further reading on what to discuss before beginning a collaboration, we suggest reading '10 Simple Rules for Establishing International Collaborations'[12] and the guide for international partnerships by Universities United Kingdom (UK).[13] Additionally, online resources, such as the World Intellectual Property Organization, have example guidelines for things to consider when drafting an agreement, and it is advised to seek help from a legal professional in drafting any agreement.[14]

Scientists will likely require outside expertise in intellectual property agreements before beginning any collaboration that is likely to produce results intended for commercialization, or any time there is concern over legal ramifications from misuse of research findings. Legal professionals can help scientists draft agreements that are unique and appropriate to their collaboration. While many resources can help researchers get an idea of what types of signed agreements they may want to make, these resources should not be used in lieu of a legal consult; contract agreements for international partnerships will be specific to the two countries involved, the type of collaboration, the funding being used, the research involved, and the mutual agreement regarding intellectual property rights.

Having open and honest conversations allows researchers to become more aware of the benefits and drawbacks of entering into a collaboration. Understanding these pros and cons will help researchers make an informed decision as to whether they want to move forward in seeking institutional approval for a collaboration.

Technology Risk and Benefit Assessment

Research collaborations may involve research with a high potential for risk, such as dual-use risk. The effects of ill-intentioned access to research outputs with dual-use potential can be greater than other research, so collaborations involving such research should include ethical consideration of the risk of societal harm. The first step in mitigating dual-use research risk is to recognize what risks and benefits are posed by various experiments. In this way, analyzing the research itself for dual-use potential can help inform the overall risk of the collaboration. If scientists recognize the ethical concerns of what they are doing and what would happen if that research fell into the wrong hands, they can weigh that against the benefits of their research and apply precautions appropriate to the level of risk involved. Some institutions require faculty and staff to assess the risks and benefits of all research performed at their institution to mitigate dual-use risk. These assessments can then be included in the overall approval process for

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[12] de Grijs R. (2015) Ten Simple Rules for Establishing International Research Collaborations. *PLoS Comput Biol.* 11 (10)**:** e1004311.
[13] UK High Education International Unit. (2013) International Partnerships - a Legal Guide for UK Universities. 3rd edn.
[14]World Intellectual Property Organization. Intellectual Property Policies for Universities. https://www.wipo.int/about-ip/en/universities_research/ip_policies/#database. Accessed August 12, 2021.

foreign collaborations. Research with dual-use potential does not necessarily need to be avoided, but risks should be understood and reduced where possible.

In a recent review paper, Tensmeyer et al. describe a variety of risks to consider in performing a risk assessment.[15] Negative outcomes from research output can generally occur in one of three ways: accidents, intentional misuse, and inadvertent outcomes (negative outcomes that were not the result of misuse or accidents, such as intentional application of pesticides causing unintentional health and environmental hazards). Each of these risks can be amplified through international collaborations. For example, other countries may not have the same regulations for safety standards resulting in increased risk of an accident. Additionally, sharing research outputs with unfamiliar partners may increase the risk of misuse or unauthorized access to data.

The types of risks that can contribute to negative outcomes are many. The following non-comprehensive list presents some of the many potential risks that may be particularly relevant to researchers considering international collaborations along with examples of how such risks may manifest.

> *Epidemiological and public health risks* – e.g., poor biosafety practices in handling uncharacterized clinical samples in-transit lead to an outbreak of a novel pathogen
>
> *Risks to human rights* – e.g., newly discovered DNA motif allows for identification and targeting of a racial minority
>
> *Weaponization* – e.g., new production methodologies for ammonia also simplifies the DIY manufacture of chemical weapons
>
> *Risks to civil liberties* – e.g., new developments in photosensitive materials allow for illegal High Definition (HD) video surveillance of political dissidents
>
> *Mental and behavioral health risks* – e.g., research into behavioral conditioning is misappropriated by an intelligence agency for unethical interrogation techniques
>
> *Impacts on public opinion and trust* – e.g., poor communication surrounding the ethics of human fetal experimentation results in public outcry and subsequent reactionary legislation that unnecessarily inhibits earnest scientific inquiry
>
> *Environmental risks* – e.g., a new industrial process for the efficient manufacture of sustainable biofuels generates a novel pollutant
>
> *Resource risks* – e.g., a new high-efficiency battery technology places pressure on a highly limited natural resource
>
> *Economic risks* – e.g., breakthroughs in quantum computing render standard-of-practice encryption for financial transactions obsolete
>
> *One Health and animal health risks* – e.g., use of antimicrobials leads to generation of a resistant pathogen that rapidly spreads through animal populations

Performing research may lead to any of these types of risk, but in many cases, involving collaborators can increase the likelihood of such risks because the researchers have even less control over how their research is used. In line with some of the examples above, a collaborator may poorly communicate the results of the research to media outlets resulting in impacts on public opinion. Similarly, they may share results with business enterprises or military institutions, resulting in any number of outcomes such as weaponization.

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[15] Tensmeyer, et al. (2023) The Role of Technology Risk Assessment Frameworks in Research. *SSRN.*

While national and international agencies may attempt to regulate and define dual-use research broadly, due to the pace of scientific innovation much of the responsibility for assessing the dual-use risks of specific research will necessarily fall to researchers. The landscape of cutting-edge research is rapidly changing, making it difficult for policy makers to assess the risks associated with emerging technologies and identify specific technologies of concern in time for those risks to be mitigated completely. For example, a list of experiments with dual-use potential generated in the early 2000s would have no notion of the concerns involving genomics or nanotechnology, or the way AI would be impacting biotechnology today. And again, if experts today were to generate a list of research activities with dual-use potential, this list would quickly become outdated as new technologies emerge and our understanding of current technology expands. Additionally, just because a research topic has dual-use potential does not mean that every type of experiment within that topic has the same level of concern, or that risks of an experiment outweigh benefits. This variation in risk is well demonstrated by pathogen research, where experiments with massive potential benefit can range from being totally benign to being fraught with hefty biosafety considerations.

Recognizing the limitations of a list-based approach to dual-use policy, the research community is in the best position to evaluate work happening in their own field, given their technical knowledge and familiarity. As members of the scientific community, researchers have a responsibility to discern what constitutes risky research in their own fields. And, in addition to mere responsibility, the scientific community has an incentive to self-regulate about research— namely, that avoiding reactionary regulation can protect the benefits of earnest openness in science for posterity, and a culture of awareness creates an environment where explicit regulation is less necessary.

Understanding that risk and benefit analysis is an on-going process throughout the research cycle is a key tenet of many frameworks and initiatives for ethical research. For example, Malaysia's Responsible Conduct of Research (RCR) program is designed not only to inform project planning, but also serve as a resource throughout projects as risks and ethical considerations evolve.[16] The frameworks are most useful when they provide tools to enable consistent reevaluation of risk mitigation techniques to be built into study design. Frameworks can also be more powerful when, like Malaysia's RCR program, they are developed in accordance with the cultural, institutional, and governance contexts in which they are intended to operate.

Many other frameworks have been published to assist researchers with such risk analysis, including generalist frameworks and more detailed guides that apply to specific technologies, research settings, or audiences. Broadly, frameworks fall into three different categories: conceptual, compliance-based, and evaluative. Evaluative frameworks are the most likely to apply to decision-making about research partnerships. These can be further subdivided into whether they strive for an objective analysis of a particular technology or project, or whether they seek a subjective analysis of risk to a particular asset. **Table 1** outlines these categories and provides examples of each.

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[16] Yusoff K et al. (2017) The Malaysian Code of Responsible Conduct in Research. *Science 2 Action*, Malaysian Industry-Government Group for High Technology. Selangor, Malaysia.

Table 1. Categorization scheme to inform choosing a risk and benefit assessment framework(s).

Category	Description	Example
Conceptual	Intended for broad policymaking, higher-level thinking, and informing ethical mindsets and governance	Responsible Research and Innovation (RRI)[17]
Compliance-based	Intended to guide project development and execution in accordance with existing governance (e.g., a set of laws or a code of ethics)	National Institutes of Health (NIH) Companion Guide[18]
Evaluative	Intended to provide a targeted evaluation for a particular project or technology of the risks posed to external stakeholders or society	Societal Risk Evaluation Scheme (SRES)[19]

Evaluative frameworks can also be further characterized by whether they include analyses of risks and benefits or risks only, and whether they provide a qualitative or quantitative output. Qualitative frameworks have the benefit of being more flexible and allowing for a more holistic view of the risks. The disadvantage is that qualitative frameworks often do not provide guidance in how much to weigh each factor contributing to an overall risk calculation. Quantitative frameworks assign weights to different factors, and risks are given ordinal or numerical values. Quantitative risk assessments can be valuable when sufficient data are available regarding risks. However, if the assessment includes a high degree of uncertainty, these risk assessments can appear more rigorous with no added confidence in the results.[20]

For more details on technological risk assessment frameworks, we recommend the recent review paper, written by Tensmeyer *et al*.[21] No single framework is categorically superior to another. Researchers and institutions can use their understanding of the concepts evaluated in each of the frameworks to select the one—or several—most applicable to their research. Furthermore, unless a framework reveals that the research is against local regulation, none of these frameworks prescribes a specific response based on the ethical considerations of the research evaluation. The critical thinking and discussions performed during a technological risk assessment provide context for researchers and institutions to understand what risks are

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[17] Harmon SHE. (2016) Modernizing biomedical regulation: foresight and values in the promotion of responsible research and innovation. *J Law Biosci.* 3 (3)**:** 680-686.

[18] National Institutes of Health. (2014) Tools for the Identification, Assessment, Management, and Responsible Communication of Dual-use Research of Concern.

[19] Cummings CL, Kuzma J. (2017) Societal Risk Evaluation Scheme (SRES): Scenario-Based Multi-Criteria Evaluation of Synthetic Biology Applications. *PLOS ONE.* 12 (1)**:** e0168564.

[20] Bowman K et al. (2020) Assessing the Risks and Benefits of Advances in Science and Technology: Exploring the Potential of Qualitative Frameworks. *Health Secur.* 18 (3)**:** 186-194.

[21] Tensmeyer, et al. (2023) The Role of Technology Risk Assessment Frameworks in Research. *SSRN.*

associated with specific research projects—and begin to think about how those risks might be affected by participating in a collaboration.

Once one or multiple technological risk assessment frameworks are chosen or adapted, each will have its own prescribed methods or instructions for application. Research scientists can include these assessments when evaluating whether or not they think that a potential collaboration is ethical and will ultimately result in positive scholarly and societal impacts. In the context of partnerships, implementing a risk benefit assessment may involve some added complexity. It can be valuable to conduct assessments in cooperation with potential partners, but in many cases (especially when making decisions about whether or how to commit to an international partnership) the partnership itself may need to be factored into the risk calculus. For example, an evaluative framework might return a favorable result for going forward with a project if conducted by a single entity but factoring in an international collaborator introduces additional risks that sensitive data might be accessed by unintended third parties abroad. Such added considerations might tip the risk/benefit calculus in the other direction or might indicate the need for higher-level mitigation efforts. Similarly, applying compliance-based frameworks can become daunting if multiple partners from multiple countries are subject to divergent legal restrictions.

It is important to note that risk identification is only the first step and can't itself prescribe a course of action. Therefore, analyses of risks and benefits should be used to build broader risk mitigation strategies replete with anticipation mechanisms and contingency plans to apply as research projects progress and future findings come to light. Decision-making surrounding dual-use research is ever ongoing, and is rarely black-and-white, so establishing a flexible risk mitigation strategy at the outset can help ensure even the most complex dual-use research projects maximize benefits and minimize potential negative outcomes. See the "Making a Decision" section below for more on how to incorporate risk mitigation strategies into a research plan for collaborations.

As researchers are planning partnerships, it will be important for them to understand what research guidelines exist for both parties and identify ways to harmonize and meet the expectations of different review panels. For these reasons, collecting robust information about any potential partners is critical before embarking on a risk assessment—see "Knowing Your Partner" above.

Institutional Guidelines

As the regulatory intermediaries between scientists and broader governance, institutions have a critical role to play in mitigating risks and ensuring successes for their researchers' partnerships. While the complexity and singularity of research partnerships mean that decision-making responsibilities must often ultimately boil down to individual researchers, institutions can instill the peace of mind that proven frameworks and backstops exist. Strong institutional guidelines help researchers by setting explicit expectations, outlining standardized procedures, and imparting confidence in best practices. They can also empower researchers to proactively seek out collaborations that fit their needs, rather than having to assess a path forward retroactively in response to an externally proposed partnership. Beyond simply establishing policies, institutions can engage in active oversight and outreach to ensure their researchers have the resources they need to plan partnerships and follow the requirements of funding agencies. By developing guidelines for planning and participating in international collaborations, institutions can help ensure researchers automatically comply with all applicable laws and take part in productive, positive collaborations that can benefit the researcher, the institution, and the world.

Governments and national-level funding agencies have enacted regulations and policies regarding both research with dual-use potential and foreign involvement in scientific research that represent a minimum standard for scientists to follow. These policies require disclosure and sometimes approval for certain activities, such as exporting novel proprietary technology during collaborations. However, while compliance with these policies helps mitigate the risks of foreign collaborations, these policies cannot cover every risk without over-regulating. Furthermore, legislation cycles can't match the pace of change in science. Rapid rates of innovation often mean national policies will lag behind the cutting edge, failing to address emergent dual use threats or other risks from the latest discoveries. Therefore, research institutions themselves must fill the gaps in what constitutes risk in a particular field, and how to apply the most up-to-date understandings of risk to any decisions and mitigation strategies regarding international collaborations. The U.S. National Science Advisory Board for Biosecurity has stated as much, asserting that policies governing dual use potential and information security considerations for research should be enacted both nationally and at the institutional level, with the direct engagement of individual scientists conducting the research.[22]

Because government and national-level institutions are not equipped to evaluate every research project in detail, individual research institutions are uniquely positioned to provide guidelines that take into consideration the nuances of the risks and benefits of specific research activities during partnerships. These guidelines can support and complement national policies, which helps ensure that researchers are following legal requirements. Many research universities have been proactive in developing guidelines that fit the needs of their institution. Here we identify some policies that institutions commonly utilize to reduce risk when participating in foreign partnerships. The processes utilized across institutions can be summarized in four key components:

1) Research institutions designate an oversight body for international partnerships, identifying individuals or offices responsible for developing institutional guidelines and ensuring all research and teaching activities that take place at the institution are in line with those guidelines.

2) Institutions create guidelines for policies and best practices concerning collaborations (especially international ones), including how dual-use research and information protection will be handled during partnerships.

3) As part of their policies, institutions develop approval processes, so that collaborations and research activities can be evaluated on a case-by-case basis to ensure they comply with institutional guidelines.

4) Institutions raise awareness among faculty and staff and foster a culture of collective responsibility in ensuring research and teaching activities work toward the benefit rather than harm of the institution and society.

Oversight Mechanism

Institutions can designate an office or person(s) whose responsibility it is to develop and enact guidelines and policies and ensure they are being followed by faculty, staff, and students. An oversight entity, in addition to its enforcement role, can also serve as a resource for consultation

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[22] National Science Advisory Board for Biosecurity. (2007) Proposed Framework for the Oversight of Dual-use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information.

by any member of the institution, and can impart a level of confidence that an institutional authority is available if any unique or difficult-to-evaluate cases arise. Many institutions have successfully created similar offices of oversight, such as Institutional Biosafety Committees (IBCs) and Institutional Animal Care and Use Committees (IACUC). The policy components outlined above may already be a part of existing (perhaps separate) offices. For example, institutions may choose to make dual-use risk evaluation of life science research the responsibility of the principal investigator and the biosafety committee; approval for collaborators may exist within an office of research administration; and internal compliance programs may already be responsible for export controls. A one-size-fits-all recommendation for institutional oversight cannot and should not be made because existing strengths, weaknesses and needs differ by institution. In addition, laws differ regionally, and different types of research require different policies. However, there are a few key features that are often part of the oversight mechanisms at research institutions.

Knowledge of requirements – Institutions can consider training or hiring someone to be fully informed regarding government regulations and funding level requirements that are relevant to the scientific research that is being performed at that institution. While fundamental research, and academic research more generally, are often exempt from export control laws in many countries, this may depend on the exact nature of the research and local laws. Furthermore, funding agencies such as the National Institutes of Health (NIH) and National Science Foundation (NSF) in the U.S. require full disclosure of international collaboration and foreign funding on all grant proposals. Institutions can train or hire someone who knows the ins and outs of external requirements to ensure that institutional policies are in line with regulations. Because every country and funding agency is different, institutions need someone familiar with the applicable local laws and funders' requirements who can update institutional guidelines for compliance. It may also be beneficial to designate an institutional point of contact who is an expert on mitigating risks of research misuse. Some institutions define a point of contact that is available to walk faculty and staff through the process of obtaining approval, answer questions, and provide needed guidance.

Information regarding requirements can be disseminated by the responsible office or officer to faculty and staff to promote compliance. This can include scheduled trainings or providing written or mixed media resources. Having a basic understanding of requirements can help faculty and staff follow guidelines and know how and when to reach out for help.

Oversight over relevant activities – Institutions create oversight mechanisms for aspects of research with increased risk. These oversight activities may be handled by a central office or distributed across several offices. Some of the activities that institutions may want to monitor include:

- Research of dual-use potential
- International partnerships
- International visiting students or faculty
- Compliance with external regulations and funders' requirements
- Animal and human subjects research

Motivating an entire organization to adopt new compliance regulations can be complex, particularly in large universities where busy researchers have numerous responsibilities. Administrators for large institutions might especially benefit from a "push-pull" approach, where the necessary resources are abundantly available through multiple access points, where researchers are regularly and actively engaged by administrators, and where researchers are

both incentivized and mandated to apprise themselves of new compliance regulations. It is important to recognize that many aspects of oversight are tied closely to government regulations, and thus failure to comply may result in penalties; therefore it is an institution's responsibility to ensure compliance.

Best Practices

As noted above, by gaining awareness of the risks associated with certain activities, institutions can make informed decisions about which policies fit their institutional needs to mitigate risk while realizing the benefits of research. Understanding commonly used best practices can help institutions develop guidelines for which activities the institution will choose to approve, as well as measures the institution will take to mitigate risks for approved activities. Institutions should consider policies regarding regulatory compliance, international collaborations in all forms, visiting scientists, international travel abroad, and intellectual property.

Institutions and scientists can implement commonly used measures to mitigate risk while conducting research in the context of approved collaborations. Many such measures are part of any good research conduct, but extra precautions can be taken for research involving sensitive materials or data—including data that may be relevant to competitive research, patentable technology, or research of dual-use potential. Some examples of best practices are in Table 2.

Table 2. Research Best Practices for Mitigating Risk and Protecting Data

Data Security	- Password-protecting computers. Dual-factor authentication and physical security measures can be strong additions - Cybersecurity measures for archived data, such as encryption - Placing lab notebooks away securely, treating them as components of the lab's proprietary knowledge - Granting access to sensitive data only on a need-to-know basis - Employing vigilance, frequent updates, and professional input on appropriate measures for network cybersecurity
Intellectual Property	Creating an intellectual property policy—see for guidance the Lambert toolkit[23] or the World Intellectual Property Organization[24]
Visitors	- Requiring visiting scientists to sign a non-disclosure or other confidentiality agreement[25] - Ensuring visitors do not remove material without appropriate approval (e.g., samples or data)

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[23] University and business collaboration agreements: Lambert Toolkit. https://www.gov.uk/guidance/university-and-business-collaboration-agreements-lambert-toolkit. Last Updated 2019. Accessed July 26, 2021.
[24] World Intellectual Property Organization. Intellectual Property Policies for Universities. https://www.wipo.int/about-ip/en/universities_research/ip_policies/#database. Accessed August 12, 2021.
[25] UK High Education International Unit. (2013) International Partnerships - a Legal Guide for UK Universities. 3rd edn.

	• Screening visitors before sharing sensitive information—see "Know your Collaborator" section
Collaborations	• Requiring faculty to disclose and, if applicable, obtain approval for foreign involvement in research • Obtaining legal advice before beginning a collaboration • Signing appropriate non-disclosure, confidentiality, intellectual property, or other agreements • Mandating institutional screening procedures for faculty and principal investigators (PIs) to follow before establishing foreign collaborations—see "Know your Collaborator" section • Guidelines and approval processes for beginning new collaborations
Dual-Use Research	• Engage faculty, staff, and students on issues of dual-use and laboratory risk management, including biosecurity and biosafety principles • Provide yearly trainings • Establishing a disclosure and, if applicable, approval process for research with dual-use potential • Establishing a dual-use research office or convening an oversight committee as needed to adjudicate unique cases—see "Oversight Mechanism" section

Many institutions implement such practices to mitigate risks. For example, the University of Rochester provides their faculty with a comprehensive document that details guidelines for a variety of collaboration activities.[26] Universities UK, a nonprofit organization representing 140 research universities in the UK, published a guide that includes best practice policies and guidance for scientists and institutions to assess the risks and benefits of a potential collaboration.[27] Institutions may consider creating similar resources for their own faculty and staff to turn to when they have questions regarding the institution's foreign collaboration policies.

Culture of Awareness

As institutions develop and implement policies governing collaboration, they will need to avoid the tendency to create bureaucratic exercises that are followed out of necessity (i.e., "box-ticking") but aren't driving true risk evaluation. Policies will instead be most effective when designed and enacted within a culture of awareness, in which all stakeholders (researchers, administrators, safety personnel, etc.) understand and share the same goals of effective and safe collaboration. To foster a culture of awareness, institutions can inform faculty on the rationale behind institutional policies. As institutions raise awareness, they can place an

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[26] Waugh R et al. (2019) International Research & Global Collaboration: Guidance for the University of Rochester Community. Committee on Science and Security UoR (ed.).

[27] UK High Education International Unit. (2013) International Partnerships - a Legal Guide for UK Universities. 3rd edn.

emphasis on the ethical considerations of the misuse of research, and help faculty gain a sense of collective responsibility in research and engagement.

One possible method of working towards a culture of awareness is creating a statement that describes international collaborations as an institutional priority, while maintaining a commitment to academic freedom.[28] During seminars or faculty conversations, institutions can encourage scientists and students to consider the societal impact of their research activities, including the use of technology for other societal harm.[29] In recognizing the importance of teaching ethics to young scientists, institutions can encourage a code of conduct that is regularly discussed both with faculty and with students. There are numerous examples of codes of conduct, both at a national level, such as the Malaysian Code of RCR[30] and at an institutional level, such as the Code of Ethics in Research put forth by Ateneo de Manila University in the Philippines.[31] Teaching staff how these research conduct principles apply in collaborative research projects will help them conduct responsible collaborations.

The increased level of access associated with international collaborations increases the chance of misuse, but proactively creating a culture of responsibility can help reduce risks. Because such incidents of misuse can result in reactionary policies swayed by public opinion, in addition to societal harm, self-regulation by the research community can help protect scientific freedom in the long run.[32] When scientists take ownership of ethical research responsibilities, they become good global stewards of science and the worldwide research enterprise benefits.

As institutions place a greater emphasis on security in relationships, it is also important to foster a community where diverse students and scientists feel welcome as visitors and collaborators. When discussing collaborations (both domestic and international), institutions should place an emphasis on non-discrimination, ensuring they are maintaining equity as well as security. This may take the form of a specific non-discrimination policy if institutions do not already have one. A strong non-discrimination policy can work as an effective counterweight against a strong security policy, and both institutional arms can work together to establish a productive balance. A commitment to diversity and a commitment to security can foster one other; the perception that these two priorities are at odds is inaccurate and can lead to misguided decision making. Equity and diversity are important priorities driving collaboration and need not be sacrificed in protecting research. In fact, international partnerships are a key medium for the global advancement and distribution of equity values in the scientific community.

Approval for International Collaborations

Consistent disclosure of foreign collaborations can also be utilized by institutions to make decisions in an approval process for foreign collaborations. Creating an appropriate approval process allows institutions to keep track of foreign collaborations and help investigators mitigate the risks of those collaborations. This process can also be used to determine both the risks and benefits of a proposed research collaboration, considering the nuances of each request to make an informed decision. Approval processes can be utilized for many research activities, including:

- Research partnerships

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[28] Paile S et al. (2018) Do academic activities contribute to WMD proliferation? European Studies Unit.

[29] Joske A. (2019) The China defence universities tracker. *Australian Strategic Policy Institute. November.* 25.

[30] National Science Council. (2017) The Malaysian Code of Responsible Conduct in Research.

[31] Loyola Schools Ateneo de Manila University. Code of Ethics in Research. https://www.ateneo.edu/code-ethics-research. Accessed September 15, 2021.

[32] Marchant GE, Pope LL. (2009) The problems with forbidding science. *Sci Eng Ethics.* 15 (3)**:** 375-394.

- Involvement in foreign recruitment programs
- Receipt of foreign grants and gifts
- Sharing samples or data with foreign institutions
- Foreign components of federally funded research
- Hosting short-term visitors
- Hosting foreign students and researchers
- Travelling abroad
- Establishment of an MOU
- All other foreign agreements

Institutions can determine their own approval process for each of these activities, creating streamlined processes for activities of lower risk (such as hosting a one-time lecturer) versus more comprehensive reviews for activities with more considerations concerning risk (such as extensive research collaborations). It may be useful for institutions to create a guide for researchers considering international collaborations, including forms needed for administrative purposes, templates or requirements for research agreements, and necessary documentation. Required documents will be unique in every country and also depend on funding agencies' and institutions' requirements. The guide can also suggest many of the themes discussed previously, such as ideas for evaluating partners and planning the partnership. By asking researchers to report on each of these areas, it allows review committees to make informed decisions about approvals.

As an underlying theme for this process, a requirement for institutional approval is not meant to limit scientists' ability to openly collaborate and have meaningful global partnerships. Instead, this process is meant to help researchers identify the most mutually beneficial collaborations and minimize associated risks. While institutional policies regarding foreign partnerships generate some up-front costs, these policies can help scientists engage in positive collaborations and protect the institution from ill-intentioned access to research information. Good institutional practices can improve the likelihood that the advances derived from earnest scientific openness contribute to broader societal welfare.

Making a Decision

Many factors should be weighed to make an informed decision to proceed with a potential collaboration. Steps that can be taken to inform this decision include those described throughout this paper: taking the time to know the potential collaborator and their institutional values, planning the potential partnership in order to understand the benefits and requirements of the collaboration, and performing a technological risk assessment to thoroughly analyze the impacts of the research that is being performed. This information can be utilized in line with the institutional policies regarding foreign collaborations to evaluate both the risks and benefits of a potential partnership.

Unfortunately, there is no clear formula for determining whether to proceed with a foreign collaboration. Analyzing the risks and benefits of a collaboration can't alone yield a conclusion, but such tools can be used to see the bigger picture and build broader risk-mitigation strategies when a simple "yes or no" cannot answer the question of whether to pursue a particular collaboration. Risk mitigation strategies are best designed on a case-by-case basis to ensure they're sufficiently flexible, durable, and reactive to future inputs, but institutions can combine multiple frameworks and draw from past examples to determine the decision-making process that works best for them. It may be useful to include discussions within a committee or between faculty for any potential partnership that is high risk.

We also note that it is important to sufficiently weigh benefits when evaluating a potential collaboration. If a proposed project is associated with risk but has the potential to positively impact society and the institution, then it may be a collaboration worth pursuing. On the other hand, if there are ways to achieve the same positive results while lowering the risk of accidents or the inadvertent or deliberate misuse of technology or innovations, it may be worth considering other avenues. In line with the Responsible Research and Innovation (RRI) framework, when weighing risks and benefits scientists can consider not only whether a research collaboration is an acceptable course of action but if it is the *best* course of action for creating the most positive impact for their institution and society.[33]

Relying largely on the four pillars discussed throughout this paper, we have suggested a few questions to consider when making decisions about international collaborations.

> *Knowing your partner:* Are their personalities, leadership and communication styles, and values a good fit? Do they have the right experience and expertise? Do they apply appropriate research standards? Has their background information been vetted and verified? Taken together, is all the information you know about this partner sufficient to trust them to be a productive and responsible partner?

> *Planning the partnership:* Were you able to come to an agreement on plans and expectations for the partnership, including cost-share, work responsibilities, intellectual property or data rights, authorship credit, among others? Do you feel confident that you have a plan to work through setbacks? Are all parties in agreement on goals?

> *Technology risk assessment:* Do you understand the risks associated with any data or products generated by this project? Have you considered how working with this partner may affect those risks? Do you have appropriate risk mitigation strategies in place?

> *Institutional guidelines:* Is this partnership plan in line with institutional guidelines, as well as regulations and funding agency's requirements? Have you worked with your institution to ensure appropriate information has been provided in order to facilitate the approval process?

If, after a thorough evaluation of the risks and benefits of a potential partnership, scientists and their institutions determine that proceeding with the collaboration is in their best interest, institutional resources and support systems should be used to ensure the collaboration is successful. While risks of issues with a partner and research misuse will always exist, following best practices within a collaboration can help mitigate these risks. Researchers should work with their institutions to develop plans for their collaboration to ensure best practice policies are being followed.

Conclusion

A successful partnership generates new knowledge that, without the multi-sourced perspectives, data and resources afforded by the collaboration, researchers may not be able to achieve on their own. Some discoveries can only occur as a result of broadened horizons and an effectively applied diversity of ideas. Successful partnerships not only offer gains for participants, but can also establish lasting institutional connections, define models for others to

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[33] Harmon SHE. (2016) Modernizing biomedical regulation: foresight and values in the promotion of responsible research and innovation. *J Law Biosci.* 3 (3)**:** 680-686.

follow, and open new channels of social discourse—both within and without the scientific community. Individual researchers benefit from new tools and can reach ground that would have been inaccessible alone, while at a geopolitical level entire nations can benefit from the resulting innovations and international scientific allegiances. At their best, scientific collaborations are important standard-setters for cross-disciplinary, cross-cultural, and cross-border problem-solving.

Following best practices for partnerships will increase the likelihood of success of these collaborations, not only in protecting scientists and earnest innovation while mitigating the risks of participating in international collaborations, but also by ensuring that all researchers and institutions involved in the work agree on the parameters of the collaboration and are ready to take on a new endeavor together. While this process may increase up-front effort for international collaborations, institutions and researchers can proceed feeling more confident that their partnerships will be successful. When international partnerships are safe, secure, and successful, they allow the global community, through good stewardship of science, to benefit from innovation without fear of those same innovations being misused.