6. A Compensatory Liability Regime to Promote the Exchange of Microbial Genetic Resources for Research and Benefit Sharing – Jerome H. Reichman

Bunyan S. Womble Professor of Law
Duke University School of Law

Scientists know only about 1 percent of the world's microbial resources. A good selection of known and scientifically validated microbial resources are held in hundreds of public culture collections around the world, which have accumulated these precious resources over a long period of time. Many other semi-public collections are held by government departments, especially in the U.S., and by universities around the world, who assemble materials for specialized research purposes. About 600 of the public collections are loosely organized under the World Federation of Culture Collections (WFCC) which operate under agreed quality and security standards. The original principle underlying the establishment of the WFCC was that their cultures belonged to the common heritage of mankind, in the same way that plant genetic resources were initially treated by the United Nations Food and Agriculture Organization (FAO). The members of the WFCC make these resources publicly available for research purposes, with the holdings listed in open catalogs and, of particular importance, the member collections are obliged to authenticate all their resources and to track all uses.

By the late 20th century, there was a tug of war to propertize these resources, some of which had acquired commercial (and strategic) value. One response was that some public culture collections began to devise material transfer agreements (MTAs) that progressively restricted access to, use of, and redistribution of their microbial materials for research purposes. A leader in this trend has been the American Type Culture Collection (ATCC), but many others within the WFCC have followed its example by imposing restrictions on access and use that one would expect to find in the private sector. For example, the ATCC's standard MTA for materials available to non-profit affiliates contains the following prescriptions, according to the ATCC model contract:

1) use in a single laboratory only;
2) no redistribution without permission;
3) limitations on derivatives;
4) a built-in reach-through claim on any and all derivatives (which replicates the copyright law's derivative work model); and
5) a need to negotiate and obtain permission for each pending transaction in connection with any given material.

Moreover, this highly proprietary model, which applies to not-for-profit and for-profit researchers alike, has been imitated by the other collections to varying degrees, with a view to addressing their potential relations with commercial clients. While some culture collections have tried to preserve space for public research, even here the tensions between making microbial resources available and limiting both access and use remain visible. One result has been the progressive privatization of upstream resources that are needed for research.

A second response was that, after 1992, the Convention on Biological Diversity (CBD) established the principle that genetic resources of every kind found within the territorial boundaries of nation-states are subject to the sovereign rights and control of those states. Under Article 15, access must be obtained on mutually agreed terms, subject to prior informed consent and to further obligations concerning benefit sharing and the transfer of end-use technology. Over time, the trend has been for developing countries to restrict access to their microbial resources for virtually all uses, including public research uses, and to assert ownership claims to resources held in the public collections of developed countries that were not obtained in conformity with the principles set out in the CBD.

Let us now ask what is fundamentally wrong with this picture? The growing trend on both sides of the development divide is to view each microbial resource as if it were potentially as valuable as gold. Sometimes, of course, when the proprietor has a known or likely commercial application for a specific microbe, strong restrictions on access, use, and reuse make sense. Some of the special collections deposited at ATCC provide examples of such a situation.

Generally speaking, however, the bulk of all microbial materials residing in public culture collections all over the world have no known or likely commercial applications whatsoever. In reality, the only value that the bulk of these materials possess is to serve as research materials, as inputs for basic scientific research. The hoarding and proprietary tendencies that increasingly predominate thus undermine and risk defeating the research potential of university research scientists everywhere. Academics depend on their ability to screen large collections of raw materials against leads developed in their laboratories either by phenotypical observations or by genetic analysis, or by some combination of the two. Needless to say, as we observed in an article regarding the hoarding of small molecule libraries (Rai et al. 2008), narrowed access to these upstream research resources actually leads to fewer commercial payoffs in the end, a situation in which everybody loses.

Not surprisingly, serious researchers have reportedly devised informal means of their own to ignore or avoid these restrictive practices. Such measures are especially prevalent at universities, which may hold a large amount of microbial resources at varying states of validation. To this end, single laboratories or research units informally exchange biological resources among themselves for public research purposes on the basis of mutual trust and reciprocally recognized quality controls, without entering into any formal legal undertakings. In effect, this informal network, which antedates the use of MTAs and reportedly still accounts for approximately 60 percent of all microbial materials exchanged, converts the private goods of the single participants into a type of "club goods" available to trusted members. This informal system thus tries to maintain the original sharing norms of the WFCC within a carefully selected group of likeminded researchers.

The result is an informal, closed semicommons based on “group loyalty” and reciprocity gains that drive a large but shrinking part of the research domain.
Some characteristics of these informal exchanges are summarized as follows:

- Ad hoc verbal agreements are usually preferred to MTAs; and the standard norm is “use in lab only." This practice likely violates the rules of university technology transfer offices and transnational regulations. There is little or no tracking or independent authentication (with concomitant risks).

- These cooperative networks have generated some push-back against formal restrictions on research as well as some interest in more science-friendly MTAs, such as the one on which the Science Commons has been working.
- On the whole, without any unified MTA, these informal exchanges have diminished over time as more laboratories tend to restrict at least so-called commercial uses for fear of lost opportunities, especially a lost blockbuster.
- The end result is unacceptably high transaction costs and growing restrictions on freedom of research with the concomitant risk of fewer commercial payoffs for both researchers and the public at large.

To break out of these two existing options—overly restrictive formal legal MTAs or loosely organized informal exchanges based on mutual trust—we offer a third option. Adopting a formula Paul Uhlir and I first put forward in relation to data exchanges in 2003, we propose to "formalize the informal sector" on a more research-friendly basis, by adopting standard contractual templates, i.e., to devise a contractually constructed research semicommons for publicly held microbial resources all over the world. (Cf. Reichman & Uhlir, 2003).

Designing a Third Option

In order to build a third option on a solid legal foundation, there must be a standardized material transfer agreement that contractually regulates the relations between all the participating microbial research communities and their members. Enforcement of such a standard-form agreement would be the province of a governing body or trusted intermediary that is generally responsible for oversight and management of the projected microbial research infrastructure.

A key premise underlying this initiative is that any deposit in the proposed materials semicommons does not forfeit all rights to benefit from downstream commercial applications, if they should emerge later on. This premise is necessary to heighten the potential reciprocity gains from participating in the research pool by directly addressing fears of losing commercial opportunities later on.

Participants will not normally contribute materials that have known or likely commercial potential. Why not? Because if a participant's microbial material already has a known or likely commercial application, he or she stands to gain more from holding out than from the basic research opportunities flowing from participation in the semicommons. (See Minna Allarkhia's presentation summary in this volume at Chapter 20.) Those high-value materials will logically flow to ATCC and other entities equipped for this purpose.

Hence, the third option that we envision would receive only deposits of microbial materials that lack any known or likely commercial uses at the time of deposit. This premise would capture the bulk of all materials in the public culture collections, not to mention the unvalidated resources outside those collections in universities, government agencies, or *in situ*.

There would be various other criteria for materials to be included in the pooled collection we envision. For instance, high-quality standards should be set and maintained for admission, including measures for authentication, validation, and tracking. To qualify,

participants would have to meet these standards (through which the semicommons continues to expand). However, many university laboratories would not qualify without upgrades.

Within the semicommons, there would be no restrictions on upstream public research functions with respect to deposited materials except that specimens could only be redistributed to member collections meeting the agreed quality standards. That is, we start with a built-in, absolute research exemption to achieve the broadest possible upstream research domain with no unworkable distinctions between commercial and noncommercial research. Instead, we would address future commercial outputs directly, as will be seen.

There would be strict and careful tracking of all uses of materials from the pooled collection in order to maximize the scientific verifiability of results, as already occurs in some form at most WFCC public culture collections. The attribution and reputational benefits of all depositors would be preserved to the fullest extent possible, and, of course, biosafety and security regulations must be fully observed.

The economic logic underlying this model is that the providers of microbial materials would presumably obtain more potential reciprocity benefits from the vast upstream research opportunities generated by the semicommons than would accrue from operating in isolation. But fears of losing unknown future commercial opportunities could undermine the prospect of these potential research gains, so we address this concern directly with a built-in provision for benefit sharing from unknown future downstream commercial applications. That is, we would build a so-called “compensatory liability rule” for downstream commercial applications into the system, yielding equitable compensation for the providers or their designate representatives under international law, while fulfilling international obligations under the CBD. This component thus gives providers a means of securing equitable compensation from future commercial applications, unknown or unlikely at the time of deposit, that ultimately resulted from research uses of the deposited materials. A liability rule means that one may freely take the materials for any research purpose, without need of any permission to use, on condition that a duty to pay equitable compensation arises if and when the application itself accrues commercial gains. It is neither an “absolute permission” rule (i.e., comparable to an exclusive property right) nor a pay-per-use rule; it is a “take and pay” rule, as I will explain in a moment.

Recall that only about one percent of the world’s existing microbial population has actually been identified. Most of those identified microbes possess largely unknown properties and characteristics of no commercial interest. Some of these are held by private industry in collections whose contents have not been publicly certified. One may accordingly describe the bulk of the holdings in existing public microbial collections as "pre-competitive" in the sense that they have elicited little active scientific interest at the present time and—perhaps for that very reason—have no known or likely high payoff commercial applications.

In other words, the bulk of the microbial materials currently and prospectively to be held in public collections may properly be characterized as building blocks of future knowledge. Yet, the existing MTAs applicable to these materials tend to impose restrictive conditions on use and reuse that make scientific research costly and difficult to conduct. Such constraints particularly impede collaborative research involving large and diverse microbial populations that may be subject to high-throughput screening or other

advanced research methods (especially when computational biology and the use of automated knowledge discovery tools is envisioned).

The payoff from our proposal is that any scientist authorized by dint of his or her connection to a participating institution could roam and explore a vast expanse of known microbial research space, with a view to maximizing future abilities to add to, identify, and develop value-adding contributions about specific contents. This would include the linking of federated, distributed collections in a virtual semicommons by digital means.

Nevertheless, it remains possible that access to the pooled resources, which are made available to scientists under a regime of minimum research restrictions, could lead to the discovery of a later commercial application of a given material that was neither likely nor foreseeable in advance. Such discoveries are welcome contributions to social welfare. They are a product of skilled efforts and the investment of time and labor, which should not be confused with parasitic or free-riding uses that undermine incentives to innovate.

To internalize and capitalize on these gains, we seek not only to develop a broad research commons, but also to encourage investment in downstream commercial applications by careful use of *ex ante* liability rules that do not impede downstream patents on end products. Liability rules are "take and pay" rules (like the non-exclusive licenses covering the Cohen–Boyer patents), not absolute permission rules, like exclusive rights. The latter only work well when the values of potential uses are known relatively well *ex ante*. They do not work when each party over-values his or her property because nobody knows its true worth (which is what we have here). (See T. Lewis and J. H. Reichman, 2005).

With a liability rule, the message is not, "You cannot use my microbial materials for commercial purposes." It is instead the opposite: "Please find commercial uses for my research materials, and, when you patent the end results, please pay me a reasonable royalty from your gross sales." Notice that this is not a compulsory license *ex post*. It is a built-in automatic *ex ante* license to use and pay—a pre-existing obligation to share a small percentage of any eventual economic returns with depositors and with the culture collections that maintain and regulate them, both of which contributed to the downstream commercial payoff. (Cf. J. H. Reichman, 2001). Notice, too, that there is a built in possibility of lottery effects if many downstream commercial applications spin off from any given microbial resource as actually occurred with the Cohen –Boyer patents.

The end result we propose is thus a kind of built-in public-private partnership. The culture collections from which the microbes were taken would manage any resulting income streams from downstream applications. We envision relatively low royalty rates—2 to 4 percent (comparable to those used in Canada when medicines were subject to a license of right). A part of this revenue stream should go to the collection to help defray its costs. The rest would go to the upstream scientists and laboratories that provided the materials (thus enabling downstream commercial applications) or to designated authorities in developing-countries for materials deposited under the CBD. No depositor would be able to write or limit research restrictions, however. Full use of deposits for all scientific research is the *sine qua non* of participation and cannot be bargained away. Such an approach would thus improve on the Food and Agriculture Organization's International Treaty on Plant Genetic Resources for Food and Agriculture (2001), which was the first international convention to codify a "compensatory liability regime" along the lines I first advocated in 2001. Finally, governance rules, including mediation and dispute resolution, would be needed.

To recapitulate our basic thesis, start with the notion that liability rules—"take and pay" rules—go beyond current applications of club economics to the formation of knowledge semicommons by avoiding the limitations of exclusivity. At the same time, such rules still provide enough economic incentives to contribute to the pooled resources from which scientific researchers would derive more benefits than they could obtain working alone. This approach provides an intermediate zone, where Creative Commons licenses are insufficient but exclusive rights and concomitant restrictions on research would impose unnecessary overkill in relation to the still uncertain value of the upstream inputs. Nevertheless, the liability rule is triggered via standard-form licenses that keep transaction costs low, in the manner of a Creative Commons license. And the use of liability rules fully preserves and promotes the benefits of the collaborative research model. In fact, it enables that research model by alleviating fears of lost downstream gains.

The approach we propose must further be reconciled with three other unresolved problems:

1. What Fiona Murray calls the "Big Refrigerator Problem." How much capacity can the public culture collection muster, and how does one reach more of the unvalidated materials held by academics outside of the public culture collections? We envision a federated network of distributed collections building on the World Federation of Culture Collections prototype that would be managed within a single, overarching governance scheme.

2. What will be the future impacts of genetic research techniques on the collections and on the scheme as a whole? We think it likely that upstream genetic resources can be pooled and managed under a similar framework. In any event, the evidence suggests that genetic research results must be squared with living and evolving cultures over time.

3. Will we need an international treaty, like that of the International Treaty on Plant Genetic Resources for Food and Agriculture, which is governed by an international organization under the auspices of the Food and Agriculture Organization? We hope it would not become necessary to go outside scientific circles, but some, such as Michael Halewood at this symposium, think an intergovernmental organization will be necessary.

In the future, the long-term goal should be that culture collections become a means of combining materials, plus relevant literature and data, into a digitally integrated whole. This would be the true long-term payoff from creating the materials semicommons, and it is discussed in the later chapters of our forthcoming book.

REFERENCES

Helfer, Laurence R. 2005. Using intellectual property rights to preserve the global genetic commons: The International Treaty on Plant Genetic Resources for Food and Agriculture, in *International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime* (K.E. Maskus & J. H. Reichman eds., Cambridge U. Press, 2005).

Lewis T. and J. H. Reichman 2005. Using Liability Rules to Stimulate Local Innovation in Developing Countries: Application to Traditional Knowledge, *in International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime*, Ch. 13 (K.E. Maskus & J. H. Reichman eds., Cambridge U. Press, 2005).

Rai, A.K., J. H. Reichman, P. F. Uhlir, and C. Crossman. 2008. Pathways across the valley of death: Novel intellectual property strategies for accelerated drug discover. *Yale Journal of Health Policy, Law & Ethics* 8:53–89.

Reichman, J. H. 2001. Of green tulips and legal kudzu: Repackaging rights in subpatentable innovation. *Vanderbilt Law Review* 53(6):1743–1798.

Reichman, J. H., and P. F. Uhlir. 2003. A contractually reconstructed research commons for scientific data in a highly protectionist intellectual property environment. *Law and Contemporary Problems* 66:315–462.

Reichman, J. H., T. Dedeurwaerdere, and P. F. Uhlir. Designing the microbial research commons: Global intellectual property strategies for accessing and using essential public knowledge assets (Cambridge Univ. Press, forthcoming 2013).

Question and Answer Session

PARTICIPANT: With regard to the royalty amounts and the decision between having something on the order of 2 to 4 percent, how is that decided, and then what happens when other technologies intervene or other licenses come into the finalized product? How do you accommodate the royalty stacking provision?

PROF. REICHMAN: Well, there would have to be a royalty stacking provision. There is something at the end of our draft chapter that talks about the model, but we have not yet actually worked through the model to do it. You need a royalties stacking provision, and you need a mediation and dispute resolution arrangement. It may well be that different communities would have different royalty values.

The International Treaty for Plant and Genetic Resources put a very low royalty on their pooled genetic resources, but they broke new ground. This was the first time it had ever been done at the international level, and I think they decided on a 0.5 percent royalty. I think that was a mistake, but if you are serious that the primary object is

research, not gain, the point is to not be left out of the game so that you can support the research. You do not want to encumber these downstream licenses with a heavy reach-through amount, otherwise you get the pharmaceutical sector on your back and you may have lots of problems.

I published an article in the Vanderbilt Law Review in 2001 called "Of Green Tulips and Legal Kudzu" (Reichman, 2001). It is about repackaging rights in sub-patentable innovation generally, and I introduced the "compensatory liability regime" there. So, in different contexts you might have different percentages of royalties, but I do not think they should ever be very large because, by definition, the materials in question are so far upstream that you have not added enough value at this point to justify a commercial payoff. If you are fairly certain that there will be a commercial application, then you will need a tailor-made license, and the microbe will not enter the research pool. You will know what it is worth. You will have enabled it later on. So, we think 3 to 5 percent is not too much, but not too little either. Increments above a baseline royalty of 3 percent could depend upon the amount and quality of valuable information, if any, that is disclosed with the microbe. You will notice that in government use licenses of patented inventions, the U.S. government usually offers 4 percent as a starter. It generally never goes above 6 percent, although one or two licenses went to 10 percent. I am an expert on government use licenses. So, in that range, we think ours is a pretty fair estimate *ex ante*.

MR. HALEWOOD: I am with Bioversity International, which is one of the international agricultural research centers supported by the Consultative Group on International Agricultural Research (CGIAR). I have two questions, or one point and a question. One has to do with, under the treaty, the swapping of the right to keep things open for research downstream and the requirement to pay. In the plant-breeding community there have traditionally been two forms of intellectual property rights. One is plant variety protection rights, which allow downstream research, and the other is patent rights, which do not. People who were very much involved in the negotiations of the treaty wanted to, in a sense, punish the patenters and give support to those who were still resisting that. So that is why they wanted to have a mandatory benefit-sharing clause that complemented the pre-existing division, if you will, on one side.

The other thing I wanted to ask was something you wrote about in your paper and hinted at in your presentation. You talked about membership or conditions of entry into the pool, and you linked that to quality management criteria and said that that would limit, initially at least, the number of organizations that could be members. I wonder if you could not split that in two, looking at this from a development perspective. You could have a limited pool of entrants as suppliers, given their need to respect and meet high standards, but recipients could be global and anybody. I do not know why you could not make it that way.

PROF. REICHMAN: That is a very interesting proposal. I am not against it, especially if you were thinking of developing countries. I can see some problems about free riding though, and you have to make sure that the people who go in think they are getting enough out of it. There is some recent research that came up at the COMMUNIA workshop in June of this year. There were some economists from Germany who had done very good empirical research verifying the real importance of this reciprocity hypothesis, and I am a little nervous about undermining the reciprocity gains expected from membership in the pool at the beginning, until it is established. Once it is established,

then everybody can see the payoffs, as is the case with so many of these other genomic commons, and then you can relax the admission standards. I certainly think your goal is desirable, and I would endorse it. I just think it has to be handled carefully because, at the moment, you are trying to get the people who are already in it to stay in it.

Another limiting factor is that the pooled microbes can be widely distributed for in-lab research, but they cannot be widely redistributed without quality and security controls, including authentication, validation, and the tracking of all uses. This limitation is built into the present-day microbial research model, to preserve the purity of research results.

PARTICIPANT: Could you quickly clarify how you would handle third-party transfers? Are they allowed?

PROF. REICHMAN: Third party transfers would be handled entirely by the downstream people in the normal way that it is being done already. If you are in the stream and you come up with something that now is known or likely to be profitable, then you are going to negotiate that deal with third parties out there. Of course, the tracking of the microbes in question must be used. But when you are transposing into the downstream world, you will still owe the commons under a "reach through" liability rule. You do not owe them anything else, however, and you are free to do what you want with your work.
Then what do you do? You go to the pharmaceutical company, you go to the fertilizer company, or you go to the beer company, and you negotiate your own deal, and they are going to go through the patent process, the clinical trial process, the whole nine yards. Everybody is aware, however, that there is a built-in reach-through agreement that must be respected in the end. That agreement does not say that you have to negotiate with me. It says you have to pay me a reasonable royalty from your ultimate gross returns, and that passes on all the way down the line.

PARTICIPANT: I come back again to the question about royalties. It is a royalty-stacking question. There are two kinds of royalty-stacking issues. One is that there will be other technologies that do not involve the use of microbial material, which will be under patent or copyright, and there will be charges. But let us put that aside. It is a question of the science: In how many cases is the model of innovation that you go from a single microbe to a commercial use? That is sort of the model in conventional chemistry.

PROF. DAVID: If you need to use an ecology of microbes, then the question of royalty-stacking arises.

PROF. REICHMAN: Yes, that is right. You have to address it.

PARTICIPANT: Who would have jurisdiction? When I first read about this provision that you put in, I said, No, this is not an *ex-ante* liability rule. I am not a lawyer, but from what I have learned from working with lawyers, the liability rules work on the basis that you show essentially that you have been injured by the use.

PROF. REICHMAN: Well, that is the tort law origin of them, but we are adapting it to intellectual property. It becomes an *ex ante* entitlement, i.e., a built in, automatic license rather like a non-exclusive license, and it has to do with notions of equity, not injury.

PARTICIPANT: Well, no, it is an adaptive view, but what it is, is a pass-through license without claiming intellectual property.

PROF. REICHMAN: Yes and no. It is a form of intellectual property rooted in liability rules rather than exclusive rights. You underestimate the fact that it remains an *ex ante* entitlement, like all other intellectual property rights, some of which are non-exclusive from the get-go (e.g., trade secret protection).

PARTICIPANT: So, you have a pass-through license. Now, the question is: Since you want to encourage downstream use, why are you not using a flat fee? Because, first of all, incentives like flat fees are less distorting. It is a lump sum payment. It is predictable. It gives greater incentive, on the one hand, to people to go for a use which will be very commercially attractive because it is a fixed fee. The fixed fee can be justified on the basis of the costs of meeting the quality standards, of devoting time to the curation and to the running costs of collections. It also has another positive feature that it is administratively easier. You do not have to have these *ex-post* negotiations to deal with stacking problems because you are not seeking a percentage of the revenues. And that is economically more efficient because it reduces the pricing of the end products, and therefore tends to increase the ultimate social benefit because you do not have the dead weight.

PROF. REICHMAN: Yes, it has some advantages. These are friendly comments.

PARTICIPANT: Yes, and we want to make it better.

PROF. REICHMAN: These questions are coming from one of the world's leading economists in this area, so I am very grateful for them. On the second question, the problem is that you do not know enough to assess a flat fee. It will likely be either too little or too much, like literary authors who should not accept a flat fee for their books. You really do not know in advance, and you have this "lost blockbuster" complex. The flat fee might work in the example that you gave this morning about the specialized collections. Flat fees sometimes work when you are just making a research tool available, like the Cohen-Boyer patents. You would probably get a lot more action and a lot more science done with them. This is practical, however, because you know the value of the research tool in advance.

But, here, how do you know at the beginning what value to put on microbial resources? It is like the .5 percent in the treaty on plant genetic resources. Well, 0.5 percent in certain cases could be all right, but in most other cases it looks too low. So, you are worried about the blockbuster. Well, if your microbe turns out to be part of the cure for cancer, then you will want a piece of that action.

PARTICIPANT: Well, that is a different case because you are trying to get a piece of the action and not promote downstream use.

PROF. REICHMAN: You are trying to promote it, but I do not think you are hindering it. You do have a possible royalty stacking problem, however. We found that in our "Pathways Across the Valley of Death" article, as well, and I think we have some

innovative solutions. In that context, you could have a group of small molecules of which only one is going to be the winner, but all four were necessary to arrive at the winning result. We go out of our way to state in that article that all four of those molecules participate in the liability rule, but you cannot stack the royalties, while the winner gets a tailor-made license with the patentee.

There is not a separate valuation for each relevant microbe. They divide the proceeds from the liability rule, but the winner gets a negotiated contract with the patentee, and the losers get a share of the return based on the *ex ante* liability rule. In our "Pathways" article, we suggest that that is a workable way to defer a lot of the risks, to spread the costs of the risk premium that people are getting because if you had one of the relevant small molecules but not the big one, at least you would get a small piece of the action, and that helps you cover the losses when your clinical trials go bad.

In some of these and other cases, we will need the mediation and dispute resolution mechanisms discussed in our book. I do agree with you that the stacking problem will require an express provision. So, I thank you very much for that and thank you for your questions.