Need a Reagent? Just Sign Here ...

Free exchange of materials is supposed to be a hallmark of academic research, but nowadays, if you ask a colleague for help you will probably have to sign away some cherished rights

Last June, Jane Gitschier and Yien Ming Kuo of the University of California, San Francisco (UCSF), asked a colleague at Oxford University in Britain to help them with a research project. They wanted some mammalian DNA sequences engineered by the Oxford scientist for an experiment with transgenic mice. It was a routine request, but it prompted a response that researchers say is becoming is all too common in hot fields of biology: Before sending the DNA out, Oxford asked the UCSF scientists and their sponsor, the Howard Hughes Medical Institute of Chevy Chase, Maryland, to sign a letter surrendering all property rights on discoveries "contingent upon" the use of Oxford's materials. Oxford also asked for the right to preview and comment on articles before submission to a publisher. These are strong terms, yet all parties accepted them.

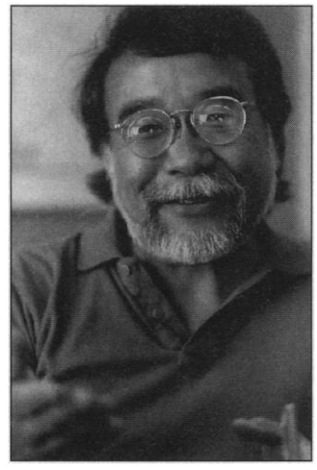
The UCSF scientists are not discussing the contract, called a materials transfer agreement (MTA), a copy of which has been obtained by *Science*. Gitschier merely says: "I signed some papers and got some materials." Like many in academia, she doesn't quibble about legal issues, so long as the research goes forward. For its part, Oxford says it puts few limits on scientific exchanges, but sometimes its hand is forced by a sponsor of the research. The Oxford scientist in this case works at the Wellcome Trust Centre for Human Genetics. Richard Liwicki of the university's research and commercial services office says "the university does have to be particularly careful" in handling materials from Wellcome Trust projects, which are governed by regulations on charities.

Even researchers who routinely accept such conditions—or ask collaborators to do so—bemoan the tangled web that MTAs have become. Researchers who want materials from colleagues find themselves signing away some of their freedom to publish, while colleagues eager to send out samples and reagents are forced—sometimes by outside sponsors of research, and sometimes by their own universities—to hold off until the lawyers have sewn up all the proprietary rights. These legal barriers are only adding to the toll that the intense competition in biomedicine is already taking on the tradition of sharing among academics (*Science*, 23 June 1995, p. 1715). If every university insisted on legal protections like those Gitschier and her colleagues were forced to sign, says UCSF molecular biologist Henry Bourne, "it would make it impossible to get anything done." He adds: "I think these [MTA] agreements will just sour everything."

Indeed, the situation has gotten so bad that some research leaders, including a group of UCSF faculty members, are urging the National Institutes of Health (NIH) to use its clout to try to set some reasonable ground rules for MTAs. NIH has tried before. But even when guidelines for acceptable MTAs have been agreed upon in the past, they have been overlooked by universities and rejected by industry. This time, NIH director Harold Varmus has set up a special task force to look into the concerns, and NIH staffers have invited biomedical researchers to send detailed comments to NIH's Office of Technology Transfer, headed by Maria Freire. She and an outside panel chaired by law professor Rebecca Eisenberg of the University of Michigan, Ann Arbor, plan to discuss the issue at an NIH meeting later this year.

Prepublication review of manuscripts "endangers the academic tradition of free and open publication."

—Keith Yamamoto



DAVID POWERS

A "spreading virus"

There will be no shortage of comments, both from researchers and university technology transfer officials. The increasing complexity of MTA contracts, and the time and effort devoted to negotiating them, is "a horrendous problem," says Kate Phillips, a staffer at the Council on Governmental Relations, a nonprofit outfit in Washington, D.C., that represents 142 research schools and is coordinating universities' responses to NIH.

Much of the pressure to draw up restrictive MTAs comes from corporate sponsors of research, says Niels Reimers, former chief of technology licensing at UCSF, who worries about a "spreading virus" of restrictions. "Virtually every university is gearing up to compete for industry dollars," he adds, and he worries that universities "may be sacrificing some of their principles" to please their corporate supporters.

But Phillips says that nonprofits, who are honor bound to protect their faculty members' freedom to publish, are not free of blame. "I'm dismayed that we've talked about it for 10 years, but it has only gotten worse," Phillips says. Even when there's no pressure from outside, some university offices adopt restrictive clauses in MTA agreements.

Among the most outspoken critics of the system are a group of UCSF faculty members led by biologist Keith Yamamoto. In a 16 September letter to Varmus, Yamamoto complains of "burdensome" MTA letters. And the demand for prepublication review of manuscripts, he writes, "endangers the academic tradition of free and open publication." Yamamoto warns that "universities will be overwhelmed by the immense bureaucracy required simply to keep adequate records of compliance with [MTA] restrictions."

Academic licensing officials contacted by *Science* agree that MTAs are a growing headache. Louis Berneman, director of the technology transfer center at the University of Pennsylvania, says the number of MTAs reviewed by his office doubled over the past year, from 197 to 425. He says that exchanges between research scientists, once regarded as routine, are increasingly treated like "minilicenses that have to be negotiated before you have data one."

Asked to describe a problem case, an East Coast U.S. university official cited an MTA used by Novartis Pharma of Basel, Switzerland, one of the world's largest drug companies. (Like many researchers discussing specific incidents, this official declined to be identified for fear of embarrassing colleagues or annoying research sponsors.) Novartis,

she said, made great demands in return for sharing a compound that has been in the clinic for 2 decades. The proposed MTA agreement says that "all data obtained" from the academic experiment would have to be submitted to Novartis before publication and that the company could use the data "without restriction." The company's initial attitude, according to the university official, was: "It's our candy jar, and we can do what we want." It eventually agreed to milder terms, but only after months of negotiation.

Joyce Brinton, Harvard's technology chief, says that nonprofit outfits can usually be talked out of imposing sweeping conditions. "When you get back in touch, it gets fixed," she says. Companies are tougher. "What we don't want" in a company agreement, she says, is to be told "we can't do something just because a provider of a tool says we can't." Julie Norris, director of the Massachusetts Institute of Technology sponsored research office, shares this sentiment. She comments in a 29 August letter to NIH that relations with industry are "deteriorating rather than improving." She writes that "no amount of education has lessened the companies' attempts" to gain control or outright ownership of discoveries arising from the use of shared materials.

Failed negotiations

The Eisenberg panel will have a tough time cutting through the morass of MTAs to find a consensus. And it has several cautionary examples before it. Two years ago, NIH published the "uniform biological materials transfer agreement," a model document hammered out by university administrators under the leadership of Harvard's Joyce Brinton. It was a kind of peace treaty endorsed by more than 100 universities, says Brinton, designed to let researchers share reagents without relying heavily on lawyers. Originally, the group hoped to create a second model MTA that could be used for interactions with private companies, but nothing came of it.

NIH began a new effort in 1995 to help companies shape a model contract for transfers from company labs to nonprofit institutions, after the nonprofit agreement was in place. These talks began, according to Freire, at a time when AIDS activists were pushing industry and NIH to speed up AIDS drug development. NIH consulted with 18 executives in the Inter-Company Collaboration for AIDS Drug Development, hoping to come up with a model MTA that was acceptable to industrial and academic labs. After many meetings and document revisions, NIH devised a three-level scheme of increasingly complex legal formats based on the degree of clinical testing completed for material that was to be shared. It was acceptable to the universities. But in the end, according to George Johnston, the Hoffmann-La Roche patent counsel who represented the industry group, his colleagues declined to sign off. After polling the companies, he says, "we found that the members were not comfortable working with language that was prepared by an external organization."

Freire declines to comment on industry's reaction. But she confirms that she received a letter in August from Johnston, ending the talks. She was disappointed but not surprised: "When the rubber meets the road, it is a very difficult thing to have an intellectual-property agreement that everybody is going to be satisfied with." It may be worth trying for a consensus once again, Freire thinks, but this time, she may aim for agreement on a set of principles rather than specific legal language.

And while industry balks, universities appear to be ignoring the standard MTA they put together for their own use in 1995, according to many technology transfer officials. They're opting instead for local "improvements" of the standard language. But the situation has not improved, academic leaders say: The terms for sharing reagents are getting more complex and more intrusive.

This sorry history has led several participants in the debate to conclude that the notion of standardizing the MTA form used in nonprofit transactions won't work. For example, David Owen of the U.K. Medical Research Council (MRC) acknowledges that MTA negotiations are becoming "a huge problem," yet he adds that, "I don't like universal forms." He says they, too, introduce rigidity. He proposes instead that everyone abide by a set of ethical principles, chiefly the MRC's golden rule: Don't ask anyone to sign an agreement you wouldn't sign yourself. The Eisenberg panel may have a difficult time coming up with anything better.

–Eliot Marshall

Devilish Details

Oxford University isn't the only nonprofit research institution that's been known to write tough materials transfer agreements (MTAs) limiting the use of reagents. A few other examples:

GEORGETOWN

Georgetown University in Washington, D.C., last July sent an MTA to a prominent biologist asking for a preview of any research that might result. The agreement says the recipient must "provide Georgetown an advance copy of any proposed publication that makes reference to the material." And if Georgetown sees anything patentable, it insists upon the "opportunity to request that recipient delay publication until after a U.S. patent application(s) has been filed."

Georgetown's technology transfer chief, Carol Tracy Carr, says that while this might lead to a 2-month delay, it wouldn't impose a burden. She says, "It's rare that [scientists] just knock off [reports] and send them out the door." Furthermore, "I always view [the publication clause] as negotiable." In this case, Georgetown only asked the researcher to send in a manuscript when submitting it for publication.

Duke University of Durham, North Carolina, uses a similar clause in a standard MTA form it sends out to scientists at nonprofit institutions. According to Linda Abruzzini, who handles MTAs, Duke commonly requires the recipient to "furnish Duke with a copy of the manuscript or abstract disclosing [research] results prior to submission thereof to publisher. ..." This must be done "not less than 30 days prior to publication to allow Duke an opportunity to protect proprietary or intellectual-property rights. ..." Duke agrees that the total delay should not exceed 90 days.

PENN

The University of Pennsylvania also has its own MTA for nonprofits. If the recipient wants to file a patent, the MTA requires that he or she first contact Penn's technology office and negotiate a deal. These restrictions, according to another clause, apply not only to the shared materials, but to "any substance that is replicated or derived therefrom." There is no attempt to delay publication, but Penn asks for a copy of any published work based on the materials.

Penn's tech transfer director, Louis Berneman, says that MTAs create "a no-win situation" for his office. Researchers get mad if you hold up an exchange to check the fine print, and they get mad if you don't protect them from bad contracts. There's always "hell to pay," Berneman says. Everyone hates MTAs, he adds, but "I don't know of a better alternative."

–E.M.