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A Pilot Survey on the Licensing of DNA Inventions

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Abstract
Despite ethical concerns about gene patents, virtually no empirical evidence exists to support claims about either positive or negative effects, and extremely little is known about the intellectual property protection strategies of firms and universities. This article discusses the results of a pilot study to examine patenting and licensing philosophies, policies, and practices of different types of institutions and to describe the contractual conditions for licensing DNA sequence inventions.

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Précis

Despite ethical concerns about gene patents, virtually no empirical evidence exists to support claims about either positive or negative effects, and extremely little is known about the intellectual property protection strategies of firms and universities. This article discusses the results of a pilot study to examine patenting and licensing philosophies, policies, and practices of different types of institutions and to describe the contractual conditions for licensing DNA sequence inventions.

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Intellectual property in biotechnology invention provides important incentives for research and development leading to advances in genetic tests and treatments.[1] However, there have been numerous concerns raised regarding the negative effect patents on gene sequences and their practical applications may have on clinical research and the availability of new medical tests and procedures.[2] One concern is that licensing policies attempting to capture for the benefit of the licensor valuable rights to downstream research results and products may increase the financial risks and diminish potential payoffs of – and therefore motivation for – performing downstream research and development.[3] In addition, very broad patent claims allowed by the U.S. Patent and Trademark Office, the sheer growth in patents claiming genetic sequences, and threats of overlapping patents create a veritable minefield for researchers in both academia and industry. The concern is that research may be stifled because of the high cost and hassle of negotiating access. Despite the ethical and policy concerns about gene patents, virtually no empirical evidence exists to support claims about either positive or negative effects.[4] Importantly, extremely little is known about the licensing behavior of firms and universities. To begin to examine emerging licensing issues for patents claiming genetic sequences, examine how gene-

based technology is propagating, and understand how patents are influencing the sharing and use of fundamental genetic inventions, we performed this pilot interview study.

METHODS

We developed an open-ended telephone interview guide and piloted it with two technology transfer executives. The interview guide first examines patenting and out-licensing strategies, including the process of determining what gets patented and to whom licenses are granted. Then, we asked several questions addressing license negotiations, including issues of exclusivity, research or diagnostic uses of patented sequences, and particular terms that are difficult to negotiate. Finally, we asked about protecting nonpatented genetic technologies, and the use of Material Transfer Agreements (MTAs) and Nondisclosure Agreements (NDAs).

We identified institutions that have patented human nucleic acid sequence inventions by searching the Delphion patent database for patents in U.S. class 435/6 (molecular biology, involving nucleic acid sequence) that have "Seq. I.D." in their claims.[5] We identified forty-eight for-profit companies and sixty-two non-profit institutions that were assigned three or more patents (mean number of patents held = 19.4, range = 3–192). We excluded all foreign institutions. We included in our sample thirty-three non-profit institutions (thirty-two universities or research centers, and one institute in the National Institutes of Health (NIH)) and thirty-two companies; for analysis purposes, we treated the NIH as a non-profit institution. We selected the ten companies and ten non-profit institutions assigned the highest number of patents, and then randomly selected twenty-two companies and twenty-two institutions from the remaining samples of those who held three or more patents. We oversampled firms to address a concern that company technology transfer executives would be less willing to participate.

During August and September of 2001, we called the technology transfer, licensing, or legal departments of these organizations, identified the individual or individuals responsible for genetic technology licensing, and attempted to conduct phone interviews regarding their patenting and licensing strategies and practices.

At the conclusion of the interviews, we requested copies of respondents' standard (template) licensing agreements relevant to sequence inventions. We also asked that a licensed patent or technology be chosen, and copies of license documents be mailed to us, with redaction of any specific information that our respondents believed would be commercially sensitive (e.g., licensor and licensee identity, covered technology, payment amounts). We secured the agreement of a University of Pennsylvania law professor to act as a third party for collecting and ensuring the anonymity of licensing agreements. We sent a fax or email reminder for the collection of agreements to respondents two weeks after the interviews.

After initial review of the interview data, we found that several respondents mentioned the term "research tool" in their discussions regarding the distinction between the research and clinical or diagnostic use of a patent. To better understand what was meant by this term, we sent an email follow-up question to twenty-seven respondents for whom we had email addresses asking them to clarify and define the term and give examples.

This study was approved by the University of Pennsylvania Committee on Studies Involving Human Beings, and by Stanford's Administrative Panel on Human Subjects in Non-medical Research. Oral informed consent was secured over the telephone from participants following a description of the study. All but two interviews were conducted by one of us (MRH), and responses were recorded in the form of written notes.

Qualitative analysis of the interviews and license agreements were conducted. Two of the authors (MRH and JFM) developed a coding strategy and performed the coding.

RESULTS

We contacted sixty-five organizations. Of these, nineteen did not participate. Five technology transfer executives contacted did not return phone calls; three said that although they were the correct contact at their organization, they did not have enough experience to help; five declined because of a staffing shortage or heavy workload; five declined as part of a policy not to participate in interviews or because they simply had received too many requests to participate in them; and one declined without explanation. We conducted interviews with representatives of nineteen of thirty-two companies (59%) and twenty-seven of thirty-three non-profit institutions (82%) ($\chi^2 = 3.96$, $p < 0.05$), for a total sample of forty-six organizations. Our final response rates from the initial sample were nineteen of forty-eight firms (40%) and twenty-seven of sixty-two non-profits (44%). There was no relationship between number of patents held and willingness to participate for either firms or non-profit institutions. We received a total of ten anonymized license agreements and standard licensing templates. In this paper, we present the results of the interviews only.

Patenting strategies

Our results show that respondents in universities have different patenting strategies than those representing commercial entities. We asked respondents to describe their strategies for patenting DNA sequences. There were two predominant models that emerged, largely associated with the profit-status of the organization. Five respondents from companies, and only one respondent from a non-profit, discussed maintaining patent portfolios as part of their overall business

strategy. These firms detailed a “blocking” approach to keep others out of an intellectual property area and a “defensive” approach to defend a stake in an area. These firms mentioned strategies such as filing patent applications for all inventions and then dropping technologies later if there was no commercial interest, patenting only those technologies related to current programs or interests, and patenting as a way to prevent others from commercializing. Non-profit institutions appeared to be more selective. Respondents from fifteen non-profit institutions and three companies stated that determining patentability (novelty, usefulness, and non-obviousness) is a necessary step in the patenting strategy. Demonstrating that an invention meets these requirements is mandatory for all patent applications, and the added emphasis placed on this step suggests that non-profits may undertake a more careful and discriminatory approach to deciding what merits filing a patent application.

This difference in selectivity is evident when the number of invention disclosures received is compared to the number of patent applications respondents had filed on nucleic acid sequence inventions in the prior two-year period. Excluding one extreme outlier from our sample, companies reported that they received an average of thirty-seven invention disclosures **(**range = 0–100) and filed an average of thirty-two patent applications (86%) in the last two years. Non-profits received an average of 163 disclosures (range = 0–600) and filed an average of twenty-four applications (15%). A recent study conducted by Mowery et al., examining the practices of three university technology transfer offices (Stanford, Columbia, and the University of California system) similarly found that between 1986 and 1990, disclosure to application filing rates of these academic institutions were between 15% and 17%.[6]

Licensing strategies

We asked about strategies for licensing out technology, including methods for finding licensees, preferred licensing positions, difficulties in negotiations, and ways in which nonpatented nucleic acid sequences are protected.

Marketing and purpose of out-licensing

Companies and non-profits granted licenses to their DNA sequence patents at a relatively similar rate (42% of firms' total owned portfolio of DNA sequence patents versus 51% of non-profits') but reported differing strategies for finding a licensee to commercialize their technologies. Non-profits were more likely than firms to report careful market analysis to ensure a patent would be licensed even prior to the filing for a patent application. Six non-profit institutions actively market to attract potential licensees, while no respondents from commercial firms noted this as part of their licensing strategy. Three respondents from commercial firms mentioned a preference for cross-licensing and five noted a strategy of licensing out technologies of no immediate interest, while respondents from non-profit institutions did not comment on either strategy. Licensing was essentially used only to transfer inventions into industry for commercialization, and licensing to universities by companies was the exception with only four firms saying that they have licensed to universities.

Character of licensees

Under the Bayh-Dole Act, patent holders of products resulting from federally sponsored research must demonstrate preference in licensing to small businesses.[7] Perhaps reflecting compliance with this federal requirement, six respondents from non-profit institutions expressed a preference for licensing out to small companies and start-ups. Two companies and thirteen non-profit institutions said that they were willing to accept equity and payment plans involving higher royalties, as well as milestone payments in lieu of large up-front sums, from these small

companies. Regardless of profit status or size, fourteen respondents remarked that smaller companies were easier to work with than either large or mid-size for-profit organizations or non-profit institutions. Likewise, fourteen respondents noted that having a previous successful relationship with the licensee or experience in negotiating licenses for other gene sequence patents made the deal go more smoothly.

Exclusivity

We were interested in examining the usage patterns and prevalence of exclusive versus nonexclusive licensing. There were wide disparities in reported strategies, ranging from those who grant only exclusive licenses to those who grant no exclusive licenses, with the majority using them selectively. In a previous study of a select sample of genetic diagnosis patents, Schissel et al. found that exclusive licenses were frequently used by non-profit universities and hospitals.[8] Here, we found that companies were substantially less likely than non-profits to license DNA sequence inventions exclusively. Of all licenses ever granted to these technologies, companies reported an average of 27% to be exclusive (standard deviation = 38.1, range = 0–100%) compared to 68% of those granted by non-profits (standard deviation = 26.0, range = 0–100%) (Kolmogorov-Smirnov test for equality of distribution $p = 0.001$).

We also asked respondents under what circumstances exclusive licensing is used. Six respondents stated that exclusive licenses were used as incentives to attract licensees. Additionally, two non-profits mentioned that they offered exclusive licenses to small companies. Respondents from five companies and seven non-profit organizations noted the use of nonexclusive licenses for access to research tools and non-patented materials, and two firms and two non-profit organizations noted a preference for nonexclusive licenses in general. Further reflecting wide variation of licensing strategies, one respondent noted the sole use of exclusive

licenses for diagnostic applications while another emphasized the use of nonexclusive licenses for these. Respondents also commented on the nature of both exclusive and nonexclusive licenses, saying that as part of their strategies, revenues generated from exclusive licenses must cover patent costs and have milestones, while nonexclusive licenses allow more leeway in negotiating financial terms (including the amounts and timing of payments, and the taking of equity).

Research versus clinical uses and research tools

In light of concerns that licensing arrangements may stifle downstream research as well as the ability of industry to develop diagnostic or predictive tests that are based on patented genes or disease-gene associations, we asked if respondents distinguish between research and clinical or diagnostic uses in licensing.

Fourteen companies and twenty-three non-profit institutions indicated that they distinguish between research and clinical uses in the licensing of nucleic acid sequence inventions. When asked to define the term "research," twelve respondents defined research as noncommercial use, seven defined the term as "internal" research and development, four said that research does not require regulatory approval (apparently distinguishing FDA-approved products), and four commented that commercial firms are unable by definition to perform noncommercial research. Six respondents said that they reserved the right to continue with their own institution's research when they licensed out technology. Six respondents said that they made the distinction between research and clinical uses by granting field of use licenses. Overall, thirty-six of the forty-six respondents noted generally that they resort to field of use or claim limitations to facilitate dividing a patent into multiple licenses as well as to retain rights to continue their own use of the invention.

Several respondents broached the topic of research tools during this discussion. Respondents from one commercial firm and six non-profit institutions said that research tools should be licensed nonexclusively and widely disseminated. Two interviewees commented that DNA is a research tool, one said that non-human genes are research tools, and one noted that their licensing arrangements for research tools do not include reach-through provisions or royalties.

To better understand what technologies fall under the term "research tool," we emailed twenty-seven respondents who had provided their email addresses during the initial interview, and asked them to define "research tool" and provide examples of inventions that they consider tools and those they do not. Eleven interviewees (41%) responded, all via email. In general, research tools were described as "a composition, sequence, method or process" that is useful in biomedical research for discovering, verifying, or studying another material or process.

Respondents discussed the development, patenting, and licensing of technologies they considered to be research tools. Respondents commented that tools do not require much development in order to be useful (n = 3), do not require patent protection because they "would not become a commercial product or part of a product" (n = 3), are typically licensed nonexclusively (n = 2), and should not be subjected to reach-through terms (n = 2).

Of the nucleic acid sequence technologies that could be considered research tools, respondents cited the Cohen Boyer Recombinant DNA technology (U.S. Pat. No. 4,237,224), DNA vectors and probes, polymerase chain reaction (PCR) primers, and genes themselves. Among the materials that respondents gave as examples of gene sequence technologies that are *not* research tools were materials being used to develop a diagnostic test, those that have

potential therapeutic use, such as the monoclonal antibody that is currently being used as a treatment for Crohn's Disease, and biological reagents with diagnostic or commercial potential.

Two respondents representing non-profit institutions specifically noted the distinction between a "tool" and a "target." One of these respondents commented that "a drug target or a disease diagnostic is not generally considered a research tool," and the other remarked "genes that are drug targets are viewed by large companies as research tools, but small companies feel that they are *not* research tools" (emphasis was the respondent's own). Several respondents noted that often a technology used as an investigative tool by one organization was itself originally researched and developed into an end product by another. It is evident from the responses that the definition is in part attributable to the perspective of the organization, and encompasses the intended use of the material.

Licensing experiences

Terms negotiated

In an attempt to determine whether research or other activities have been inhibited or facilitated by patents and licenses, we asked whether any licensing negotiations failed, and if so, how many in the last year, why, and what licensing terms were most problematic. In the negotiation of licenses, material transfer agreements (MTAs) and nondisclosure agreements (NDAs), each party has contractual terms and conditions that are sticking points, as well as some specific issues that could potentially break the deal. We were interested in looking at the most common terms negotiated, whether or not these were the same across all types of negotiations, and whether they were related to the profit status or size of the organization. (see Table 1).

(Insert Table 1 about here)

In licensing agreements, three main areas of difficulty arose: payment terms, terms that shift contract risks, and the retention of rights to downstream development (so-called reach-through clauses). Determining the value of a technology is a critical step in developing a solid licensing plan, and other financial terms, such as royalty schedules and amounts, are based on this initial assessment. Financial terms, including the amount of upfront payment, royalty rates, and milestone payments, were the most prevalent source of disagreement. Another area of difficulty for both companies and non-profit institutions was negotiating and defining rights to the use of the invention and subsequently derived products. Overall, respondents conveyed the idea that the licensor often wishes to retain rights to future intellectual property, as well as rights to continue work with the licensed technology, and the licensee often wishes to gain the right to sublicense the invention. Contract risks, including issues of indemnification, warranties, enforcement and due diligence, were the third most troublesome to negotiate.

Rights to future intellectual property

Most licensing programs involving DNA sequence inventions must account for downstream technologies derived from the invention. Respondents stated that agreeing on the distribution of reward from future discoveries and developments from the licensed invention is among the most difficult issues in licensing of patents (n = 18), MTAs (n = 25), and NDAs (n = 2). Reach-through clauses are a leading concern, regardless of profit status or size of the licensor organization, and were cited by four interviewees as a cause for negotiation breakdown.

Negotiation breakdown

Nearly three-quarters of all respondents (n = 33) said that they had at least one negotiation break down without agreement in the past year. Sixteen respondents representing commercial firms reported at least one negotiation in the past year that was not completed, and

seventeen representatives of non-profits responded similarly. Financial terms, as described above, were the primary cause of failed negotiations (n = 24), followed by problems with agreeing on the field and scope of use (n = 6). The next largest causes of negotiation failures were not term related, but rather personality conflict (n = 2) or a diminished interest in completing the deal (n = 3).

Material transfer agreements and nondisclosure agreements

All respondents reported using MTAs and NDAs for protection of nonpatented proprietary information and materials. Only one respondent reported that MTAs were not required, although they were still used in most transfers of materials into the institution and out to both for-profit and non-profit institutions. According to respondents, MTAs are used for unprotected (i.e., unpatented) or nonvaluable materials that are to be evaluated by potential licensees, or materials or data that are being used purely for research purposes. Ten companies and seventeen universities said that they used MTAs with both universities and companies. Four respondents commented that they used two templates, one for transfer to industry and the other to non-profit institutions, while seven universities specifically said that they used the Uniform Biological Material Transfer Agreement (UBMTA) drafted by the National Institutes of Health.[9]

Most respondents commented that of all negotiations, NDAs were the simplest, most standardized, and least troublesome. This is evidenced by the fact that there were only eight sticking points mentioned in NDA negotiations, compared to seventeen in licensing agreements, and twelve in MTA negotiations. (see Table 2)

(Insert Table 2 about here)

We asked the question how – aside from the use of patent licenses, MTAs, and NDAs – are nucleic acid sequence technologies protected. A few respondents mentioned tangible research

material licenses or tangible property licenses (n = 2) and bailments (n = 2). In discussing these alternatives, respondents commented that tangible research material licenses for research use require less negotiation, and therefore less time, and have fewer risks than do standard patent licenses. Bailments were described as a stronger form of transfer than MTAs, falling in between MTAs and licenses, and restricting use for research purposes only. Bailments were used with commercial entities, and were always nonexclusive.-

Licensing agreement collection

Despite the firewall safeguards we set in place (i.e., securing the agreement of a law professor to collect and anonymize agreements), respondents were, for the most part, unwilling to provide us with copies of negotiated agreements. The primary reasons for refusal were that respondents were simply too busy to devote the time involved in choosing an appropriate license agreement and removing identifying information from it, or were concerned that they would have to secure approvals from their licensees because of confidentiality clauses.

DISCUSSION

There are two primary findings of this pilot study. First, our results suggest that companies and non-profit institutions differ in patenting selectivity and patterns of exclusive license use. For-profit respondents reported the more expensive strategy of broadly filing patent applications, compared to the strategy of non-profit respondents (who received more invention disclosures than firms) of selective filing. Second, we find that non-profit academic, health-care, and research institutions are slightly more likely to license their DNA sequence inventions than for-profit firms, and are much more likely to grant exclusive licenses to these patents.

For comparison, a survey of academic technology transfer executives showed that roughly 50% of licenses granted by universities in 1999 are exclusive,[10] while only about 22% of licenses granted by the NIH in 2001, and fewer than 16% of active licenses managed by the NIH Office of Technology Transfer, are exclusive.[11] Thus, the use of exclusive licenses by non-profit institutions seems to exceed that of firms for the same technology, as well as the use by universities and the NIH for all technologies.

The asymmetries in patenting and licensing strategies may be related. These disparities may suggest a fundamental difference in the types of invention generated by companies and non-profit institutions (primarily universities). As previously indicated, numerous respondents noted a difference between research tools and research targets, commenting that the definition is partially attributable to the perspective of the organization, and encompasses the intended use of the material. Respondents also stated that tools useful for performing research should be licensed nonexclusively and be made broadly available, while exclusive licensing was viewed as necessary to promote investment in downstream research on promising targets and development of products.[12] Basic sequences are useful as targets for downstream development of therapies, and previous research by Thomas et al. showed the predominance of universities and other public institutions in basic genetic discovery.[13] Therefore, the high prevalence of exclusive licensing by universities may reflect a desire to make targets available for development while the less extensive use of exclusive licenses by companies suggests that firms are less likely to license targets to others for development, that their research does not generate targets, or that targets are simply a smaller fraction of their research product.[14]

The high proportion of exclusive licenses by non-profits raises the implication that invention coming out of non-profit institutions is more likely to be tied up with exclusive rights.

However, our results, and those of Mowery et al.[15] show that only 15% of university DNA sequence inventions are patented, suggesting that the bulk of such inventions will be made freely available upon scientific publication. Non-profit inventions (as defined by invention disclosures) are much less likely to be patented at all, are slightly more likely to be licensed and, if licensed, are much more likely to be on an exclusive basis. However, since universities are not in the business of making, using, or selling patented products or services, they use patents for licensing out their technologies so that they may be further developed. The authors do not know of any cases of universities patenting either offensively or defensively.[16] Thus, overall, the majority of DNA sequence based inventions generated in non-profit institutions appear not to be patented or licensed, and therefore not bound up by intellectual property claims.

Aside from somewhat uniform treatment of research tools, our study shows that there is no standard approach of institutions to exclusive licensing, and our respondents reported practices that vary widely. For example, the disagreement about the exclusivity of diagnostics suggests that there is no broad agreement in the biotechnology market about how best to move an invention into use, particularly when little or no further development is required. This poses some difficult questions regarding the best use of government-funded inventions, including those developed in academic institutions.[17] Importantly, exclusivity may be inappropriate if the sole licensee of a technology restricts public access in some way, thereby undermining the goal of federal funding benefiting the general public. Bayh-Dole mandates that preference be given to small businesses in licensing government-funded technology exclusively. All respondents from non-profit institutions reported that they license to small businesses. Small – and particularly start-up – businesses, in turn, may require exclusive rights to establish competitive advantage and give them access to high-risk capital. The prevalence of exclusive licenses granted by non-

profits may reflect the preference for licensing to small businesses mandated by Bayh-Dole, although we cannot determine this based on our results. If this is so, then an unintended consequence of the preference may be the frequent use of exclusive arrangements in transfer of technology discovered with federal monies. Exclusive licensing raises several concerns, including the risk that competition might be stifled as firms are prevented from pursuing particular areas of research. The problem posed may be compounded if the small business preference results in licensing of parties who are not in the best position to move an invention toward commercial viability, due to limited access to capital and other resources (including, for example, access to underlying intellectual property and technical know-how as well as personnel with necessary competencies).

Companies were more likely to adopt a broad patenting strategy to develop portfolios that could be used to block others from developing an area or to defend the firm's ability to work in a particular field. Broad patenting can be used by companies to ensure return on investments, to give them bargaining power with competitors and collaborators, and, defensively, to protect their ability to work and compete in a particular field or area. Non-profits were more likely to report that they undertook careful market analysis to ensure a patent would be used before filing. Several non-profit respondents reported filing provisional patent applications to retain rights to an invention while exploring whether there was a market for the invention.

There are continuing concerns that an increase in use of the patent system to divvy up proprietary rights to the human genome may delay dissemination of research tools among scientists, and therefore hinder or even stifle research. The 1998 Report of the National Institutes of Health Working Group on Research Tools addressed difficulties for biomedical researchers in negotiating access to research tools. The Working Group broadly defined research tools to

include all resources used in the laboratory, and to exclude all that would be sold to nonresearch consumers. Included in this definition are "cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools (such as PCR), methods, laboratory equipment and machines, databases and computer software."[18] The Working Group advised that guiding principles regarding the transfer of research tools acceptable across all segments of the biomedical research community be developed. Although those who responded to our question regarding the definition of nucleic acid sequence research tools did not differ greatly in their interpretations, there was no single approach to defining the difference between the research and clinical or diagnostic use of a nucleic acid sequence. Respondents' definitions of each of these terms varied extensively (e.g., the definition of "clinical" ranged in meaning from an entrance into clinical trials to being a term interchangeable with "commercialization").

Furthermore, overvaluation of new technologies may be common among the discoverers and was cited by several respondents as a barrier to successful negotiations. We believe that this problem will persist in the short term, but ultimately market forces will result in greater consensus regarding valuation, as licensing and technology transfer executives gain experience and successfully move inventions into the development pipeline.

STUDY LIMITATIONS

There are several limitations of this study. First, this was a pilot study of a limited number of licensing and technology transfer managers in universities, government agencies, and companies, and was not designed to estimate the frequency with which issues and problems arise. Second, we asked about a very narrow class of invention**,** nucleic acid sequences**,** and it is quite likely that respondents generalized from their broader licensing experiences to this narrowly defined

class of invention. However, this is not necessarily a problem because it may indicate that they treat these inventions the same as other technologies that they patent and license.

Finally, respondents stated that agreeing on the distribution of reward from future discoveries and developments from the licensed invention is among the most difficult issues they face in licensing. We did not collect detailed-information from respondents regarding what specific terms are being negotiated or how the issue is being resolved. Further study of this issue is warranted to understand how the market is distributing the long-term financial benefits and risks of gene-based discoveries and downstream developments.

CONCLUSION

The results presented in this paper demonstrate widely varying strategies used by companies and universities to protect gene sequence discoveries and to commercialize their gene sequence patents. Further, we find that there are several main areas of contention in negotiating access to these technologies, particularly those involving the distribution of the financial risks and potential benefits resulting from downstream developments. Further study is necessary to evaluate whether these practices, or the asymmetry between companies and non-profit organizations, have effects on the diffusion of technologies and the ability of university and commercial researchers to conduct research and bring gene-based products to market.

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18. See NIH, *supra* note 2.

Table 1: Difficult Issues in Licensing Negotiation

	Nonprofit n = 27 (%)	For-Profit n = 19 (%)	Total n = 46 (%)
Financial terms (amounts of and timing of payments, the taking of equity)	18 (67)	12 (63)	30 (65)
Future intellectual property/sub-licensing (distribution of reward from future discoveries and developments)	9 (33)	9 (47)	18 (39)
Indemnification/warranties	7 (26)	4 (21)	11 (24)
Scope of patent, license, or field of use	3 (11)	7 (37)	10 (22)
Due diligence (insurance that the technology will not languish)	4 (15)	1 (5)	5 (11)
Patent prosecution costs	4 (15)	0 (0)	4 (9)
Retention of rights to continue own use of the invention for research	4 (15)	0 (0)	4 (9)
Enforcement of patent rights	1 (4)	2 (11)	3 (7)
Choice of law/venue	3 (11)	0 (0)	3 (7)
Publication (concerns about delay and control)	2 (7)	1 (5)	3 (7)
Nonfinancial terms (respondents specifically commented that difficulties were not financial)	3 (11)	0 (0)	3 (7)
Duration of agreement	1 (4)	1 (5)	2 (4)
Assignment of patent costs	2 (7)	0 (0)	2 (4)
Exclusivity	0 (0)	2 (11)	2 (4)
Other (third-party-sponsored research, rights of first refusal)	2 (7)	2 (11)	4 (9)
None	1 (4)	(0)	1 (2)

Table 2: Difficult Issues by Type of Agreement

	Licenses n = 46 (%)	MTA n = 46 (%)	NDA n = 46 (%)
Financial terms (amounts of and timing of payments, the taking of equity)	30 (65)	1 (2)	1 (2)
Future intellectual property/sub-licensing (distribution of reward from future discoveries and developments)	18 (39)	25 (54)	2 (4)
Indemnification/warranties	11 (24)	3 (7)	1 (2)
Scope of patent, license, or field of use	10 (22)	3 (7)	0 (0)
Due diligence (insurance that the technology will not languish)	5 (11)	0 (0)	0 (0)
Patent Prosecution	4 (9)	1 (2)	0 (0)
Retention of rights to continue own use of the invention for research	4 (9)	0 (0)	0 (0)
Enforcement	3 (7)	0 (0)	0 (0)
Choice of law/venue	3 (7)	1 (2)	5 (11)
Publication (concerns about delay and control)	3 (7)	15 (33)	1 (2)
Non-financial terms (respondents specifically commented that difficulties were not financial)	3 (7)	0 (0)	0 (0)
Duration of agreement	2 (4)	2 (4)	21 (46)
Assignment of patent costs	2 (4)	1 (2)	0 (0)
Exclusivity	2 (4)	0 (0)	0 (0)
Definition of materials	0 (0)	2 (4)	0 (0)
Writing requirements (putting confidentiality agreement into writing)	0 (0)	1 (2)	5 (11)
Injunctive relief	0 (0)	0 (0)	2 (4)
Confidentiality (what is confidential, how many people are allowed access to confidential information)	1 (2)	1 (2)	6 (13)
Other (third-party-sponsored research, rights of first refusal)	3 (7)	1 (2)	0 (0)
None	1 (2)	1 (2)	0 (0)