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Approaches to Developing an Institutional Conflict of Interest Policy - Section Seven

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SECTION SEVEN: Case Studies

Case Study #1 – Dr. Blue and Dr. Green and Pain Management

The Office of Technology Transfer (OTT) at Pink Medical Center (PMC) has filed a patent application on an invention of Dr. Blue for a therapeutic that seems to offset the negative side effects of some opiates used in pain management. OTT is seeking a private licensee. Dr. Green would like to institute a clinical trial under a Food and Drug Administration Investigational New Drug (IND) application to test the therapeutic developed by Dr. Blue. [The case assumes all Food and Drug Administration regulatory requirements have been met.]

QUESTIONS:

- Does [mere] disclosure of a potential therapeutic to the tech transfer office and a patent application create an Institutional COI for Pink Medical Center (PMC)?
- Does PMC's Institutional COI Policy address patent applications and potential licensing process as potential Institutional COI?
- Should PMC take any special steps to anticipate managing an Institutional COI while the OTT is trying to locate a private licensee?
- What is the significance of IND (in the name of Dr. Green) responsibility for institution?

MANAGEMENT STRATEGIES:

Some institution's individual and/or institutional COI policies would not consider disclosure and patent application a conflict of interest until such time as a licensing partner has been identified and serious negotiations are underway. Other institutions consider the disclosure of discovery to OTT and patent application as potential COI and begin management strategies at the time of patent application. Institutions could anticipate license options that might reduce or eliminate institutional COIs as PI intends to pursue clinical trial. Such consideration might include: (1) avoiding institutional equity position as part of license terms; (2) If licensing to publicly traded company, institution could direct institutional royalties or other financial benefit to educational or research benefit unrelated to investigator or the academic/clinical unit's interests, e.g., the institutional share could be assigned to scholarship fund.

The IRB may also have special oversight strategies to suggest if the institution wants to go forward with clinical trial. Such oversight could include a special protocol design, recruitment, and data and safety monitoring committee, possibly including external advisors.

When the technology is licensed to a company, the institution could have the company assume responsibility for IND and clinical trial development with independent advisors and possible independent trial site(s).

Even if this case does not present a conflict of interest that needs management, the institution may decide to, as normal course of business, indicate a potential financial interest on human subject informed consent documents, or include that a patent is pending on press releases announcing the clinical trial.

Case Study # 2 – Dr. Gray & the PharmaCo Connection

Dr. Gray is the Chairman of Cardiology and consults for PharmaCo. Dr. White is in Dr. Gray's department and has developed a gene therapy approach to an often fatal congenital heart defect in newborns. Consider the following relationships or scenarios with PharmaCo concerning Dr. White's therapy.

1. PharmaCo would like to license the technology
2. PharmaCo already is the Licensee of the technology and wants to conduct Phase I Clinical Trials
3. PharmaCo is the Licensee and wants to sponsor additional research in Dr. White's lab and wants an option to any resulting intellectual property from that research.

Scenario 1. PharmaCo would like to license the technology:

QUESTIONS

- What are normal and customary terms of a proposed license agreement? In this case, should equity be included in license?
- Is Department Chair Dr. Gray's consulting relationship with PharmaCo and issue to be considered in the proposed license agreement?

MANAGEMENT STRATEGIES

Some institution may decide that if there is no equity included in the license and there are no related financial interests or relationships with other institutional decisions makers or trustees, there would not appear to be institutional conflicts of interest to manage beyond the usual issues of oversight of licensee's performance by the Technology Transfer staff.

If, however, there is any financial relationship between members of the Board, officers, directors, etc. the license should be referred to Institutional COI oversight process before final license is executed.

Some institutions may decide that since a licensee has been identified and there is a possibility of future royalties, that the financial interest does constitute a potential conflict that requires management.

If the consulting role is not *de minimums*, Dr. Gray should probably recuse himself/herself from deliberations of institutional conflict of interest.

Scenario 2. PharmaCo already is licensee of the technology and wants to conduct Phase I Clinical Trials

QUESTIONS: In addition to the issues identified in scenario #1:

- Who is proposed PI for clinical study?
- What does institution's individual COI policy or inventor's management plan say about whether Dr. White can be PI or involved in any way with clinical trial?

- Does institutional royalty/income distribution include a share to Dr. White's laboratory? To Dr. White's department (chaired by Dr. Gray who is a consultant to PharmaCo)? Or to Dr. White's college dean's office?
- Who is writing protocol for study – Dr. White or PharmaCo?
- Is the proposed clinical trial limited to institution's site or is this a multi site trial? [Phase I trial typically is quite limited in number of subjects, likely to be single site.]

MANAGEMENT STRATEGIES:

Since the discovery is already licensed, the license is an indication of commercial interest with needed preclinical data. Institution probably would be prudent to do a risk assessment of Phase I protocol, including outside reviewers or otherwise disinterested, knowledgeable reviewers.

Under individual COI policy, Dr. White may be precluded from serving as PI or have an otherwise restricted role in Phase I trial – for example, Dr. White may not be permitted to recruit or get consent from the subjects; a data safety and monitoring committee should be formed (possibly with external membership) to review study data.

In the absence of equity relationship with PharmaCo, institutional COI policy may permit the institution to participate in the clinical study, with special oversight. Some institutions may consider conducting a clinical trial even with an equity relationship if the circumstances are compelling enough. Consideration of a compelling circumstance might include the nature of the research, magnitude of the financial interest and the degree to which it is related to the research and the degree of risk to the subjects inherent in the protocol. The review might consider the extent to which the interest is amenable to effective oversight and management. In the case of some therapeutics and/or devices, the involvement of the inventor needs to be carefully weighed.

The institutions should disclose both Dr. White's and the institution's financial interest to any research project participants, staff and collaborators, and designate a contact person if there are any concerns. This disclosure of individual and institutional potential financial benefit should be included on consent forms and any publications or presentations of study results.

If institution determines that special circumstances support the institution conducting Phase I trial, it should have a predetermined plan for Phase II involving multi sites and perhaps even excluding the institution as Phase II site.

Finally, the dean's office may wish to review Dr. Gray's consulting agreement to assure the chair's consulting obligations do not interfere with or involve evaluation of study data from this trial.

Scenario 3. PharmaCo is the Licensee and wants to sponsor additional research in Dr. White's lab and wants an option to any resulting IP from that research.

QUESTIONS: Assume that the proposed research is preclinical research, and no clinical research such as described under #2 above is in play:

- Does institution's individual COI policy, or any policy, restrict the ability of the inventor, Dr. White, from serving as PI on research supported by the licensing company, PharmaCo, to continue research development?
- Does PharmaCo want publication restrictions?
- Are research results to be treated as proprietary information by PharmaCo?
- Is Dr. Gray's consulting agreement related in anyway to the scope of the research proposed in Dr. White's lab?
- If the institution holds equity in PharmaCo through the existing license, are there special considerations that should be weighed?

MANAGEMENT STRATEGIES:

Unless the institution's individual COI policy precludes this work, the arrangement is not all that unusual and in fact usually helps the company to advance the understanding and potential public benefit of the discovery. Nonetheless, the institution should consider whether the scope of work is appropriate for academic environment.

Terms and Conditions of sponsored research agreement should meet all the normal and ordinary research agreement conditions regarding indirect cost recovery, data rights, publication rights, etc. If the normal and customary terms are to be modified, Dr. Gray should recuse himself/herself from recommendations about acceptance of conditions that may be contrary to institutional policy.

Terms of agreement regarding option to newly-developed intellectual property should be carefully reviewed to avoid granting rights that would be problematic with respect to tax exempt status of institution. For example, such limits on publication or exclusive arrangements may make the funds provided through the agreement subject to unrelated business income tax. The exclusivity may affect the ability of the institution to house the research in facilities financed through tax-exempt bonds.

CAUTIONS and REMINDERS

In all of the above clinical research scenarios, the role of the Institutional Review Board (IRB) in determining whether the management of both individual as well as institutional COIs are satisfactory given the clinical risks to the subject is very important. The IRB's role in matters of institutional COI is not well understood; practices by many institutions for management of institutional COIs may be absent or minimal. Institutions should consider whether the IRB Chair should be a member of the Institutional COI committee, in all cases or those involving biomedical research. An alternative is to designate that IRB Chair as a resource consulted by the Institutional COI Committee during its consideration of the proposed relationship between company and institution for any clinical research in which the institution has a financial interest.

There is considerable debate concerning the effectiveness of the disclosure of institutional COI in informed consent forms. There is little literature or evidence to suggest that potential subjects have a good understanding of institutional COIs.

The importance of external involvement in assessing institutional COIs when high risk clinical research is involved is obvious. The institution should also build firewalls to insulate the institution from the financial interests of the technology transfer staff and any

individual who also stand to benefit financially from the commercialization of the invention or discovery.

Case Study # 3 – Dr. Black & Trustee Bigwig

Dr. Black has a research program funded by the National Science Foundation to study longevity of organic light-emitting diode (OLED) devices in consumer electronics. The Office of Technology Transfer (OTT) has filed a patent on a discovery by Dr. Black of a technique that will increase the longevity of OLED devices from 10,000 to 50,000 hours. Mr. Bigwig sits on the University Board of Trustees and is CEO of BigCo. BigCo wants to license the technology and sponsor research in Dr. Black's lab to further the development of this technology.

QUESTIONS:

- Did Mr. Bigwig have preferential insight of the potential success of the invention?
- Does the institution have a conflicts of interest policy that governs its Board of Trustees (BOT)?
- Does the institution's policy define personal financial interests of senior institutional officials as institutional COIs? If so, are BOT members included in this definition of senior institutional officials?
- Is BigCo an established and financially sound company?
- Does the institution allow for sponsored research funded by the licensee in an inventor's University lab?

MANAGEMENT STRATEGIES:

This case presents interesting challenges because a University trustee, Mr. Bigwig, who could equally benefit by the license, generates the institution's potential financial interest. Most institutions will have a separate policy governing the potential conflicts of interest of its Board of Trustees that will require disclosure of the financial interest, and then deliberation of the proposed transaction by a separate Board "conflict" committee.

If the BOT conflict committee approves of the transaction, there may be requirements that will be imposed on the transaction to mitigate the conflict and adhere to Internal Revenue Service and other federal requirements. In this case, we will assume that the BOT conflicts committee recommends that this license can be pursued under certain conditions (e.g., Mr. Bigwig can not be a direct party to the negotiations of a potential license or suggest any of its terms, etc.).

The institution should ensure that the OTT is apprised of Mr. Bigwig's conflict, that it can remain neutral in its negotiations with BigCo, and that the institution selects the licensee that can best commercialize the technology. It may be appropriate to enlist an outside third party to review potential terms with BigCo, if it is the best potential licensee, to ensure that these are fair and reasonable.

While it goes without saying, the institution should stress that University officers do not attempt to influence the OTT's decision. While this seems straightforward, there are often times that the OTT may directly report to a University officer, and all parties must acknowledge the sensitivity of this situation.

If the license is ultimately negotiated with BigCo, there are several management strategies that can be utilized to manage any potential conflict:

- The institution should maintain all usual and customary due diligence requirements in the license agreement and not grant exceptions except as stipulated by University policy.
- The agreement to sponsor research back into Dr. Black's lab should be made in accordance with standard University policies. As noted in Case Study 2.3, institutions may allow these arrangements if the research helps to advance the understanding and potential public benefit of the discovery. If institutional policy prohibits a licensee from sponsoring research in the inventor's lab, an exception should not be made in this case.
- The terms and conditions of the sponsored research agreement should meet all the normal and ordinary institutional research agreement conditions regarding indirect cost recovery, data rights, publication rights, etc. Any terms of the agreement regarding an option to newly developed IP should be careful not to grant rights that would be problematic with respect to facilities bonding and tax exempt status of institution. In this case, it may also be prudent for an outside and unbiased third party to review the terms of the research agreement.
- Because of the unique set of circumstances, it may be wise to develop an individual COI plan for Dr. Black.
- Disclose both Mr. Bigwig's and the University's financial interest to any research project participants, staff and collaborators, and designate a contact person if there are any concerns.
- Disclose the University's financial interests in any press releases, presentations or publications on either the licensing arrangement or resultant study publications.

CAUTIONS and REMINDERS

While potential institutional conflicts of interest may be especially problematic when human subjects are involved, and the university will wish to take particular care with respect to management of these potential conflict, it should not ignore potential conflict that surround the physical and social sciences. Some universities or divisions that do not house biomedical research may tend to dismiss both individual and institutional conflicts as these are justified as part of the institutional or divisional culture. Those cases that do present an institutional financial interest that could directly and significantly affect, or appear to affect, institutional processes for the conduct, review and oversight of research – regardless of discipline – should not be ignored.

Case Study # 4 – Dr. I.C. Itall & ShineThrough Inc.

Sunshine State University (SSU) has recently licensed a platform technology for innovative radiological scanning to an SSU start-up company, ShineThrough Inc. The inventor of the scanning technology, Dr. I.C. Itall, continues to receive National Institutes of Health (NIH) funding on further research and development of the imaging technology. She proposed to NIH that SSU conduct a small-scale pilot clinical trial to compare the new imaging platform to conventional diagnostic tools. Dr. Itall discloses a potential COI in her proposal and the fact that the institution will manage the perceived individual fCOI if awarded. Good news! The grant is awarded.

QUESTIONS:

- Does the institution's policy allow Dr. Itall to be an investigator for a Phase I clinical trial under its individual COI policy? What are the criteria in which this would be allowable? Are there any firewalls that need to be established in order for the NIH grant to go forward?
- What does the institution's COI policy state with respect to participation in a clinical trial if an institutional financial interest exists? Does it distinguish between the phase of the trial and/or the role of the institution if it is a multi-site trial?
- Does the institutional COI policy distinguish between an equity negotiated in a license vs. potential future royalties? What did SSU negotiate with ShineThrough and do the terms make a difference in terms of COI management in this case? (In a case with a start-up, we can assume that the SSU took equity in lieu of milestone payments.)
- Are there other clinical sites identified in the NIH grant (in this case, we can assume that there are not)?
- What is the potential risk to the subjects?
- Are there any other institutions that could conduct the clinical trial?

MANAGEMENT STRATEGIES

Some universities have policies that will prohibit the institution from participating in any clinical trial given an institutional COI, and in this case, the NIH grant will need to be modified if at all possible in order to identify and select another lead site. Other institutions will participate in the study only if compelling circumstances exist. For example, there is no other institution or investigator that can conduct an early phase trial given particular expertise. Under compelling circumstances, a COI management plans are put into place.

Since the discovery is already licensed, the license is an indication of commercial interest with needed preclinical data. It would probably be prudent for SSU to conduct a risk assessment of the protocol, including outside reviewers or otherwise disinterested, but knowledgeable reviewers.

Under the individual COI policy, Dr. Itall may be precluded from serving as PI or have an otherwise restricted role in the Phase I trial – for example, Dr. Itall may not be

permitted to recruit or get consent from the subjects; a data safety and monitoring board or committee (DSMB) should be formed (possibly with external membership) to review study data. Other co-investigators may have been identified to actually conduct the trial. The institution should ensure that the individual COI management plan is being monitored.

Even with an equity relationship with ShineThrough, the institutional COI policy may permit participation in the clinical study, with special oversight. Some institutions may explore other impartial entities to hold and manage the equity interest.

If the institution chooses to conduct the study, it may be required to form a monitoring committee (over and above a DSMB) to formulate, adopt and oversee compliance with an institutional COI plan, and the related individual COI plan. It may be prudent for this committee to be chaired by a respected scientist from outside the university community who has no real or apparent conflict of interest in the study. If institution determines that special circumstances support institution conducting Phase I trial, have a predetermined plan for Phase II involving multi sites and perhaps even excluding institution as Phase II site.

The institution should disclose both Dr. Itall's and SSU's financial interest to any research project participants, staff and collaborators, and designate a contact person if there are any concerns. This disclosure of individual and institutional potential financial benefit should be included on consent forms, any publications or presentations of study results and press releases.

Cautions and Reminders

Especially in clinical trial situations, if the institution makes the decision that they can manage the potential conflict and chooses to either conduct or participate in the study, strict adherence to the COI plans is critical. As noted in this section, the components of an individual COI plan are also some of the same components of an institutional plan, thus it is critical that an unbiased individual or body can monitor or oversee both.

Case Study # 5 – Snow Belt College & the Big Gift

Snow Belt College (SBC) has licensed a novel optical material for use in night vision goggles to Big Defense Contractor (BigDefCo). BigDefCo is selling the goggles for government use, but also has found a big market for bird enthusiasts following nocturnal migration patterns. BigDefCo also happens to be owned by a College alumnus who is in the process of donating a large gift to SBC's School of Engineering. BigDefCo (unknown to the alumnus!) approaches SBC and the inventor of the optical material with a research proposal to adapt the material for scuba equipment.

QUESTIONS:

- In what fields of use was the technology for the novel optical material licensed to BigDefCo?
- Did BigDefCo fund the initial research that rendered the novel material? If so, was any preference beyond the option to license given to Big DefCo?
- What, if any, control will the inventor have over how the gift funds are expended?
- What, if any, restrictions will be placed on the use of the gift funds i.e. support of research in the lab of the inventor?
- Does the inventor have any other relationship with BigDefCo such as outside consulting, significant financial interest, or advisory? If so, would compensation exceed thresholds set by institutional policy for COI?
- Is there an institutional conflict?

MANAGEMENT STRATEGIES:

Universities should have processes in place for sharing of information among research, technology licensing and development as well as the committee and officers responsible for managing objectivity in research. In this case, the anticipated gift from Alumnus, particularly if targeted to the inventor's lab, needs to be disclosed to all affected offices – technology transfer, sponsored research, and the department.

If the gift is targeted to the inventor's lab, care must be taken to maintain separation between the use of the gifted funds and the funding of the research with no special consideration for licensing of the intellectual property resulting from the sponsored project.

Case Study # 6 – The “Expert” Dean

Dean Senior at Superior University has been asked to sit on the Board of Directors of a University start-up company. The company, specializing in nano-materials for air purification systems, has become a publicly traded company. Dean Senior has been asked to become a Board member because of her internationally recognized expertise in this field. She is not an inventor of the licensed technology, nor would she represent the University’s interests on the Board. As a member of the Board, Dean Senior will receive \$20,000 in compensation per year, reimbursement for travel to Board meetings (one of the Board meetings is in Bora Bora), options to company stock and an air purification system for her home and office.

QUESTIONS:

- Does Superior University have any equity interest in the University start-up company? If so, how would the University’s institutional COI policy factor into the Dean’s consideration of accepting the Board appointment?
- Does the dean have any direct or indirect supervisory role of the research on air purification systems in the college?
- Does the significant financial interest represent a conflict of commitment for the dean?
- How does the COI concern broaden due to the publicly traded nature of the company?
- What concerns are raised by the dollar thresholds including the dollar value of the in-kind perks for the Board position (stock options, air filtration system, travel, etc.).
- How does the institution’s COI policy limit such outside compensated activities of senior officials? Would a dean be defined as a senior official?
- Does the dean have any supervisory responsibility over those with responsibility for any funded research from University start-up?
- Is there an institutional conflict?

MANAGEMENT STRATEGIES:

In mapping this conflict along the continuum, the financial interest is significant, the perception of conflict would be quite pertinent in the event of adverse events particularly if human research participants were utilized in any research related to the efficacy of the air filtration system and a reasonable person would question the independence of judgment of the dean given the stock holdings. Whether or not there is any financial COI related to sponsored research, the level of compensation/benefits for service would require certainly raise flags and elicit scrutiny for ethical and conflict of commitment reasons. Additional oversight is needed because of the publicly traded status of the company. Involvement of the dean in any relationship between the company and funded research at the institution would need to be carefully managed or eliminated to ensure independence in decision making. If there is any equity interest held by the University, outside participating in the management committee is imperative.

Case Study # 7: State University and the STTR

The State University's College of Engineering Dean Widget encourages the faculty to partner with local businesses in transferring commercially viable ideas to the market place and, thus, promoting local economic development. Dean Widget developed an innovative low-cost strategy for cleaning dioxins from paper mill waste water and The State University licensed the technology to Waste Watchers, a local company that has focused on waste management at coal-powered plants. As the inventor, Dean Widget receives a share of the royalties and serves on the Board of Scientific Advisors for Waste Watchers. A member of the Chemical Engineering faculty, Dr. Bolt believes the technology can be used at coal-powered plants and is invited by Waste Watchers to participate on an NSF STTR grant-funded project to test the technology. Dr. Bolt will conduct his work in his lab; the company collaborator will work in Dean Widget's lab.

QUESTIONS:

- Should Dean Widget participate in the research in his laboratory?
- If students participate in the research activity in Dean Widget's lab, who should supervise the students working with the Waste Watchers investigator in Dean Widget's lab?
- Does Dr. Bolt have anything to disclose as an individual?
- Does State University have a conflict of interest to report to NSF?
- Is there an institutional financial conflict of interest?

MANAGEMENT STRATEGIES:

The Federal Small Business Technology Transfer (STTR) Program requires researchers at universities to play a significant intellectual role in the conduct of each STTR project. These university-based researchers, by joining forces with a small company, can spin-off their commercially promising ideas while they remain primarily employed at the research institution. A team approach is required in which at least one research investigator is employed by the small business concern as the Principal Investigator and at least one investigator is employed by the research institution as the Research Institution Investigator.

In this case, the institutional conflicts may lie exclusively with the role of Dean Widget in supervising students in his lab working on technology from which he will receive an indirect value through his royalty share. Nonetheless, the institutional and individual interests should be disclosed to the students and staff working in the lab and the supervision of the students might fall to Dr. Bolt.

The relationship between Dean Widget, as the chief college academic officer, and Dr. Bolt needs to be monitored to ensure that Dean Widget's interests do not adversely affect Dr. Bolt conduct of the research and Dr. Bolt's academic career.