ADVANCING THE COMMON GOOD THROUGH PUBLIC PRIVATE RELATIONSHIPS FOR BIOMEDICAL INNOVATION

CENTER FOR PRACTICAL BIOETHICS
GUIDANCE AT THE CROSSROADS OF DECISION

Summary of
March 2016 Meeting

Convened at the Ewing Marion Kauffman Foundation by the Center for Practical Bioethics and the Duke Initiative for Science and Society

Kansas City, Missouri

> "Research involving human participants has become a vast academic and commercial activity, but this country's system for the protection of human participants has not kept pace with that growth.
>
> On the one hand, the system is too narrow in scope to protect all participants, while on the other hand, it is often so unnecessarily bureaucratic that it stifles responsible research."
>
> *— National Bioethics Advisory Commission, 2001*

Robust relationships and collaboration among commercial, non-profit, and government sectors are critical for innovation in biomedicine. While these relationships afford opportunities for great public benefit, they also present special challenges to carefully balance divergent primary and secondary interests between public and private actors. There is no broad consensus on the effective mechanisms to manage these conflicting interests (COI). Public-private partnerships (PPP) are often the subject of vociferous criticism due to these competing interests. Yet, others argue, with equal fervor, that these collaborations are necessary to find new therapeutics and diagnostics to quickly meet patient needs. We are at an impasse that impedes biomedical innovation.

New models which uphold the integrity and independence of the scientific process while allowing, under specified conditions with appropriate mechanisms, public-private partnerships to make scientific progress, are required. There are too few effective tools to manage the COIs associated with such collaborations and too little public understanding of the need to achieve a new balance point: a more robust scientific "common good." To this end, co-sponsors -- the Center for Practical

Bioethics and the Duke Initiative for Science and Society -- invited key stakeholders to an inaugural meeting March 10-11, 2016, at the Ewing Marion Kauffman Foundation in Kansas City, Missouri.

The meeting began with a dinner that was followed by an inspiring and thought-provoking presentation, *Conflicts of Interest and Public-Private Partnerships: Can we Move Beyond the Ugly House?*, presented by Lisa Rosenbaum, National Correspondent for the *New England Journal of Medicine*. Rosenbaum argued that we are trapped in an "ugly house" paradigm where public private partnerships are perceived negatively in virtually all situations. Currently, the public and many policy makers give little or no weight to more charitable interpretations of differing views or suggestions to change existing ways of thinking.

She reasoned that we have devolved into a dualistic view, i.e., options are "black or white" and there is little tolerance for ambiguity or novel or innovative approaches. This is the case even though there are fundamental scientific questions that are unanswered about the efficacy and wisdom of our current approaches to identifying, managing, and regulating conflicts of interest.

Rosenbaum noted that a 2009 Institute of Medicine (IOM) report, *Conflict of Interest in Medical Research, Education and Practice*, concluded that "on many topics related to conflicts of interest, no systematic studies are available. For other topics, data are suggestive rather than definitive." For example, although the consensus opinion is that the effect of pharma gift-giving has a negative impact on clinical care, there are actually no studies that demonstrate a negative impact on patient outcomes. In fact, some studies showed a potential benefit to physicians in terms of their ability to identify new and potentially better treatments in the course of pharmaceutical representative visits. Furthermore, the premise of many opinions about pharma's impact on clinicians is fundamentally biased in a negative direction. To state this is almost to akin to stating a heresy.

An excellent example of this is the negative view of research, policy or advocacy efforts to improve

chronic pain care funded by charitable grants from pharmaceutical manufacturers. The abuse of prescription pain medications by those struggling with substance use disorders (SUD) has led to allegations by public officials and the media that the drug companies are not contributing funds to support good research or program and policy development, but rather, to buy influence and to use those to whom they contribute to advance their corporate interests and enhance their profits. Historically, disclosure of financial relationships was deemed to be an adequate safeguard against such conflicts of interest.

However, Rosenbaum pointed out that we do not fully understand the limitations of disclosure and "transparency" in managing COIs. For example, psychological and social science research indicates that financial disclosure may have the opposite of its intended effect. Rather than making people more skeptical, someone who discloses COI is perceived as more trustworthy, not less, simply because he or she is being "honest" enough to disclose. Furthermore, the emphasis on financial disclosure of COI minimizes what may be more important non-financial biases, such as the pursuit of fame or commitment to advocating a particular ideology that might have significant impact on patient outcomes. We have many bias blind spots. Many so-called "conflict free" individuals may actually have a strong bias to disbelieve any data, no matter how sound, coming from the pharmaceutical industry, and will, therefore, overstate the risk and underestimate the benefits of potentially breakthrough treatments. This kind of bias contributes to the disproportionate focus on the industry's failures relative to the contributions it makes to the health and well-being of our society.

In general, with respect to COIs we operate on an emotional rather than scientific plane. In January 2016, Harvard medical students demonstrated this emotional response to COI when they told a *New York Times* reporter that they felt "violated" when they learned that one of their professors did not sufficiently reveal his or her COI before a lecture. The ferocity of the comments and letters to the editor in response to Dr. Rosenbaum's commentaries in the *New England Journal of Medicine* calling for more careful thinking about COI provide another example. Much of the discourse about and response to COI takes the form of moral outrage, rather than pragmatic, reasoned argument.

Rosenbaum's presentation informed the discussions about COI and PPPs that were to follow the next day, particularly her conclusions that:

- Empirical rather than reactive approaches to understanding and managing COIs are required.
- Bias must be understood in all directions—especially biases which lead one to ignore the negative effects of over-regulation.
- Rational and scientifically-based approaches mush be promoted above those based on "moral grandstanding."

The following morning, meeting facilitator Richard Payne reflected on Dr. Rosenbaum's presentation from the previous evening and the ensuing discussion.

He explained that the day was organized around three sessions:

1. *Everything You Wanted to Know About Public/ Private Collaborations but were Afraid to Ask*
2. *A Brief History of FDA Sponsored PPPs*
3. *COI Challenges for Non-Profits Working in Medical/Life Sciences*

Dr. Payne then pointed to the irony that the group had gathered to discuss conflicts of interest but had required no disclosure of potential conflicts among those present. He then asked the group to consider how disclosure about potential sources of bias should be handled throughout the meeting. Ross McKinney, the person responsible for managing conflicts of interest at Duke University, suggested that each person disclose what they would want to know about another in order to be alert to potential biases or conflicts of interest. The group accepted his suggestion and agreed to volunteer brief self-disclosure

statements before speaking so that the audience could make their own judgments on possible biases inherent in presentations and the discussions that followed.

— Session One —

Participants: Jim Ferris, *Director, Center for Philanthropy and Public Policy, University of Southern California*

Richard Payne, *John B. Francis Chair at the Center for Practical Bioethics and Esther Colliflower Chair, Duke School of Divinity*

John Tyler, *General Counsel, Secretary and Chief Ethics Officer, Ewing Marion Kauffman Foundation*

Jim Ferris opened this session by noting that although there is a continuum of partnership arrangements, ranging from simply sharing information to actually co-creating a project, he is "not a big fan" of many formal PPPs because they have "very high transaction costs." For partnerships to work, they must have a well-defined value proposition and committed leadership or champions. Ferris suggested that perhaps the greatest value that the government brings to partnerships is not money, but rather knowledge, expertise and networking opportunities. He also pointed out that due to the erosion of trust in government institutions, PPPs can provide benefit by bridging the credibility gap and reducing skepticism about the value of governmental involvement.

Working across silos and different sectors can be "extremely difficult." Ferris offered the example of private foundations that promote collaboration and PPPs as a way of leveraging their resources but in practice have difficulty working together across silos. In fact, the concept of an Office of Strategic Partnerships was borne out of difficulty for foundation presidents in the Los Angeles area to work together. Partnerships are difficult, in part because there is little accumulated knowledge about how to create them, make them work efficiently and maximize return on investment (both human and capital resources)—thus startup and transaction costs are very high.

Richard Payne shared his observations about the Analgesics Clinical Trial Translations, Innovations, Opportunities and Networks (ACTTION) program and the related Initiative on Methods, Measurement and Pain Assessment in Clinical Trials (IMMPACT)—a PPP between academics, the pharmaceutical industry and the FDA. ACTTION and IMMPACT were created to address an important scientific problem: the increasing failure of clinical trials to bring new and better analgesics to market. The problem seemed to lie in the methodology of the clinical trials rather than in inherent inefficacy of the pharmaceutical agents. (Technically this seems to be the case because agents that had FDA-defined efficacy in other therapeutic areas could not be separated from placebo in many pain clinical trials.) Despite a carefully designed Memorandum of Understanding (MOU) created by senior officials at the FDA and the University of Rochester (the lead academic institution) and the productivity of IMMPACT—by one count 65 papers published in high impact academic journals advancing the conduct of analgesic clinical trials—the ACTTION/IMMPACT PPP was publically criticized and (many say mistakenly) characterized as an "elaborate pay-for-play scheme."

Payne pointed out that a strategic communication strategy may have prevented the use of "loose and inappropriate language" in several email communications between the academic participants that fueled the accusations. In the course of discussion, there was strong agreement that well-defined and strategic communication goals should be part of any PPP. Mechanisms should be in place to defend PPPs from unfounded accusations. Although ACTTION continues and is still productive, the momentum of the program was set back, and the reputations of several highly respected individuals were besmirched.

John Tyler discussed the hypocrisy of taking what he labeled a "purist" approach to identifying and managing COIs in the context of PPPs. Tyler defined

this approach as one in which an individual claims a complete absence of self-interest. He argued that a purist philosophy requires "magical thinking" because it seeks the unattainable. There can never be complete absence of "interests" among collaborating partners with enough expertise in a content area to do productive work. He pointed out that those advocating for strict purity and who complain that it is compromised by COI among the parties in a PPP often have unacknowledged political agendas which present a COI in and of themselves. The purists discount or are blind to the lost opportunity costs that can be incurred by cutting off prospects for partnerships (see McKinney example below), and thus harm can be done by taking an absolutistic perspective.

Absolutistic or deontological decision-making can only work when the parties are completely homogeneous, share the same values and hold them in the same hierarchy. This is not likely to be the case in a PPP emerging within a competitive, pluralistic, capitalistic society. In a society like our own, compromise is always essential. Therefore, "purist" positions against creating PPPs are simply not realistic. On the other hand, it is wrong-headed to believe that the values "purists" hold primary are not important and act effectively as a "deal-breaker" for anyone outside the purist camp. It was suggested that, with agreement of all parties, a "rule" utilitarian approach could be employed, i.e., certain values or rules could be recognized as inviolable and others could be assigned lesser value. For example, members of a PPP could agree that treating all parties fairly is a primary value. However, they could also agree that determining what is fair should be contingent upon merit rather than complete equity. In the end, agreement on a hierarchy of values is critical to an ongoing and productive PPP. If, for whatever reason, one party cannot compromise on a particular value, it is better to know that at the beginning of the relationship prior to significant investment of time or money.

Questions posed by the presenters for discussion:

- Since Lisa Rosenbaum gave many examples of big partnerships already existing that were created for good reasons, what do you lose if the partnership is not working and you have to pull back? What do you give up, and is it possible that there is something gained by cutting your losses in that sense?

- Should the creation of PPPs prioritize communication strategies to engage the public in their rationale for creation and in sharing the important findings and success of the collaboration?

- How do we define the moral interests that compete among the parties in a PPP? Is it the notion that money and the profit motive which underlies capitalism and competition is an essential part of our social fabric, and if strict requirements on the so-called absence of conflicts of interest "derail the profit motive," are we not undermining capitalism? Is academic freedom another critical moral interest?

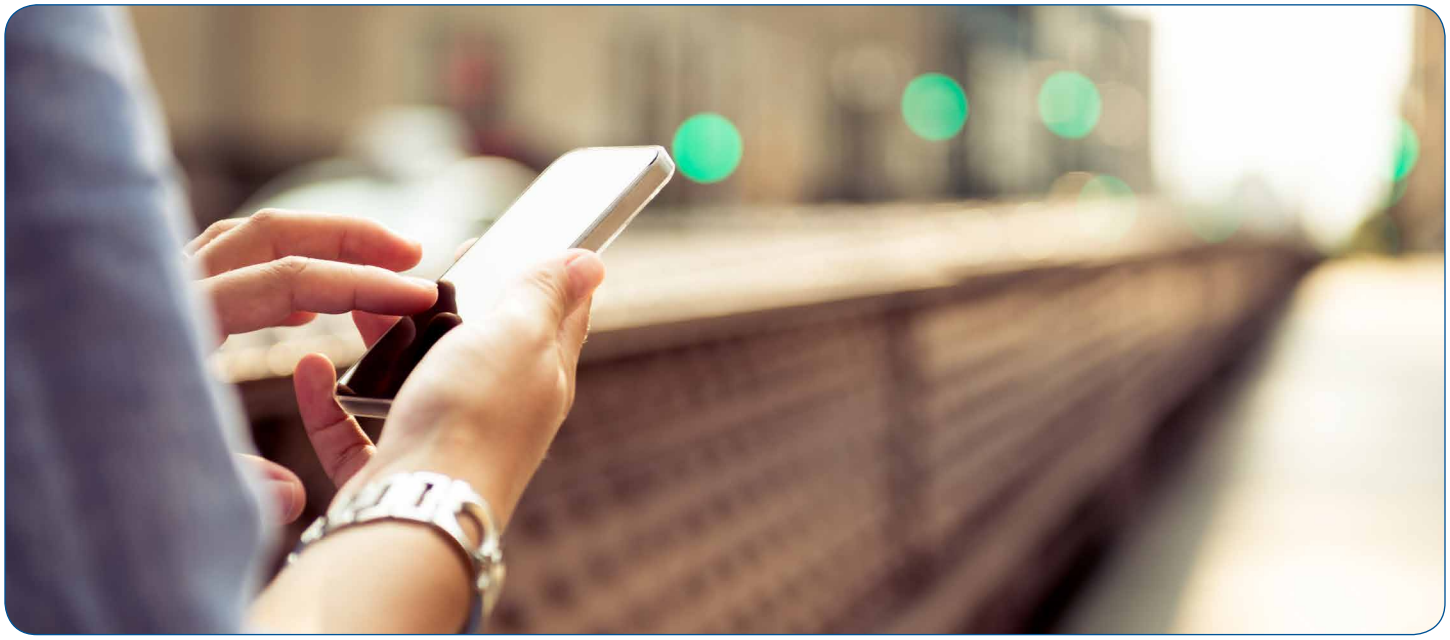
Participant comments and questions following panelist presentation:

- Are there negative and unintended consequences to our society as a whole related to the proliferation of PPPs? Could the proliferation of PPPs lead to the "commercialization or corporatization" of our society, resulting in the loss of a sense of shared common values? Do the ends justify the means, and should PPPs have transparent grounding in ethical principles as well as an emphasis on producing specific outcomes? Although the Supreme Court has ruled that corporations are moral agents, how is that expressed in this context and who among the various agents has authority to act on behalf of the corporate entity?

- It was agreed that a new ethical framework is required for underpinning successful public private partnerships and preserving the public's trust in them.

    › Ethical principles and values should be used as tools for addressing or ameliorating tensions and disagreements in the context of PPPs.

    › They should not be used as weapons against well-intended agents or a means of one party to dismiss or devalue the views of another.



  - › Veracity is essential to the preservation of public private partnerships, and the trust of the public is essential to their success.
  - › All values are not equal, and in the context of any partnership, the ranking of values can and should be negotiated at the beginning.
  - › Those decisions/rank orderings can also be reconsidered and values re-assigned as the situation changes and/or the fact base is amended.

- Many parties, even those in the so-called purist camp, are more willing to compromise in a time of crisis. (See Ross McKinney's comments in Section 2.) We are always somewhere in between purity and the practical, balancing between pure notions of principle and the consequences of our acts. Purity is often "a code word for truth or justice."

- The reality of the digital world, particularly the popularity of the 140 character "tweet," works against communicating subtle and complex topics. Yet, Twitter is more ubiquitous and increasingly popular as a communication vehicle in the public space, so it cannot be ignored. Should agents be designated who can and cannot speak on behalf of the PPP or individual participants? Should parameters be established for internal and external communication?

- The purist position can be an "exclusionist position," as exemplified by the state of FDA advisory committees where the most experienced people are excluded from advisory committees because of the current interpretation of COI rules.

- PPP participants need to be careful that "communication strategies" are not a euphemism for spin control. It is important to recognize that truth is based on "facts," which in medicine and the life-sciences evolve over time, and people should only be held accountable for sticking to the "facts" in the context of a given situation. A pragmatic but principled approach is needed to ameliorate the harms of "us vs. them" approaches to public policy.
  - › In the current political environment, people seldom give the most charitable interpretations to what other parties say—particularly when they disagree.
  - › Better communication strategies and expertise in general are needed about pain issues.

- We shouldn't be naïve about the power of emotional stories and anecdotes and how they often trump intellectual, rational thought—particularly in the digital social media environment and world of images.

- Medicine should take examples from other industries, for example the energy sector, in how they frame public messages. It is ironic that medicine, which is closer to the individual than other industry sectors, has not been as effective in framing public messages about a common good.

- In structuring better communication strategies, we need to identity *values* that motivate us such as improved health care, treatment, etc.

— Session Two —

Participants: Wendy Sanhai, *Senior Managing Scientist, Exponent*

Laurie Burke, *Founder, Lora Group*

Ross McKinney, *Director, Trent Center for Bioethics, Humanities, and History of Medicine, Duke University*

Wendy Sanhai discussed the critical elements of PPPs from the perspective of the Federal Food and Drug Administration and related Health and Human Services agencies. Reinforcing an earlier point, she noted that there must be a business case to address the current high cost and long development time to bring drugs to market. The status quo is unsustainable. Therefore, it is in the public interest to leverage resources and expertise, and PPPs are a way to do this. Input from stakeholders must be transparent to secure and maintain public trust. PPPs are most useful when there is an important scientific and public health need that is unmet by government or private industry. For example, there are critical scientific and medical gaps both in the development of better biomarkers for disease monitoring and of improved methodology of assays or clinical trials to advance new drug and medical device delivery. PPPs could be developed to more effectively address these issues.

The number of PPPs has been increasing steadily over the years. Sanhai argued this would not be the case if they were not productive. (There was some disagreement with this analysis. Others argued that the increase in PPPs is due more to budget deficits and decreased government funding than their successes.) Most of the FDA-related PPPs are disease specific, and the FDA typically is involved in the pre-competitive phase of drug or product development, thereby minimizing the perception that the agency is giving a specific company a competitive advantage. Sanhai stated clearly that FDA participants absolutely cannot say or do anything that would give a competitive advantage to competitors. The focus of the FDA PPPs has been "lifting all boats in the field" to develop broad-based tools and platforms, to address safety issues, etc.

Sanhai identified several key elements in PPPs:

d. Identify unmet public health and/or medical need; look at gaps and do landscape analysis

e. Comprehensive assessment and identification of stakeholders

f. Have specific mission and governance statements and structures

g. Have feasibility and sustainability plans

h. Include the patient voice as an important component

i. Policy concerning how intellectual property is to be handled

j. Data sharing policies

k. Research and evaluation is important—want to learn how to better design and implement PPPs

Laurie Burke highlighted the challenges posed by the complexity of many PPPs. Using the example of the Patient Reported Outcome (PRO) Consortium, she explained that efforts are often duplicated. What is more, meeting FDA requirements requires extensive coordination within multiple organizations and overcoming many bureaucratic hurdles. There are many challenges related to working with diverse work cultures and values. In the end, out of 35 potential projects identified by the PRO Consortium, only one has come to fruition so far.

Ross McKinney recounted his generally positive experiences with an "accidental PPP" that emerged to develop AIDS drugs. The PPP was effective, in the main, because there was a sense of crisis, and people were willing to compromise on purist and idealistic positions about partnerships and COIs in order to achieve a common goal. They were also willing to set aside profit motives (at least temporarily) because of the perceived severity of the immediate situation. It helped that the initial major pharmaceutical company partner, Burroughs Wellcome (a for-profit entity), was owned by a non-profit foundation which did not prioritize stock price. In addition, McKinney (and presumably other) primary investigators in the PPP were paid through the NIH, not by a private company, thereby reducing some concerns about COI. The situation changed when Burroughs Wellcome was acquired by GlaxoSmithKline, and ultimately, the competitive space around AIDS drugs changed as a result of the early successes.

McKinney also emphasized the role of patient advocacy groups. Early on, Act Up and other advocacy groups were disruptive as they attempted to assert the voice of HIV/AIDS patients. Over time, the PPP gained the advocates' trust, which led to constructive engagement and ameliorated political tensions that were encumbering progress. This particular PPP led to critical early successes and positive change in a timeframe that was much shorter than had been originally anticipated, particularly in the development of biomarkers which enhanced drug discovery. The sense of urgency surrounding the early AIDS crisis produced a more progressive approach to owning intellectual property among potentially competitive partners in the PPP. There is much to be learned from the success of this model; it serves to demonstrate the potential power of well-constructed PPPs.

Questions posed by the presenters for discussion:

- Given the complexities of developing and managing PPPs, do the benefits outweigh the costs?
- How are leaders and champions of these efforts chosen? Are there leadership characteristics that should be considered when constructing PPPs? Has a profile emerged of the ideal PPP leader?
- Do the coordinating, interoperability and silo problems associated with PPPs present an opportunity for an Office of Strategic Partnership to provide benefit in a complex agency and environment such as the FDA, other federal agencies or in a broader national context?

Participant comments and questions following panelist presentations:

- There seem to be a few identified "non-negotiable" factors when considering PPPs:
  - Public trust must not be compromised.
  - There should be no product specific discussions outside of the formal FDA Advisory Committee process.
  - Data sharing in public domain is required.
- With the proliferation of PPPs across multiple agencies, could we inadvertently be creating more silos that actually impede innovation? How can we emphasize greater connectivity, coordination, and interoperability so that the advantages of PPPs can be amplified?
- How do you define patient participation? Does the FDA really want the patient voice or that of the advocate? What would it mean to add a fourth P for "patient," i.e., to create public private patient partnerships?

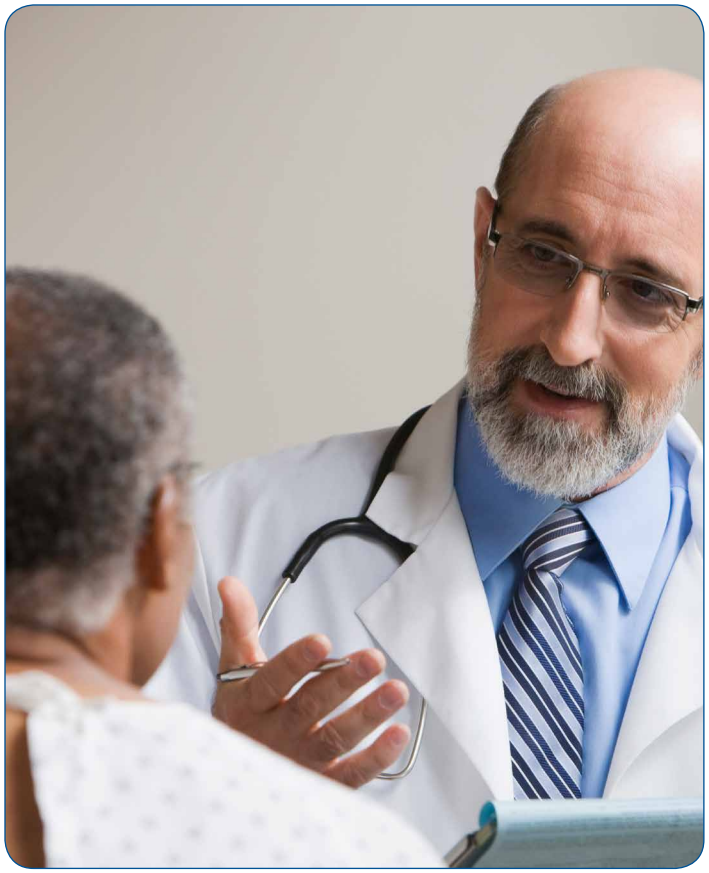
Buz Waitzkin offered a summary of the three different PPP experiences recounted and asked the group to discuss potential lessons that could be drawn from them.

- ACTTION/IMMPACT was operating successfully until language and communication issues significantly compromised their operation and impugned the integrity of the principals.
- The FDA's PRO consortium eventually became quite complex, and diverging interests made it inefficient.
- The HIV Consortium was informal and operated in a sense of crisis, which promoted a common purpose and focused the mission. It worked very well until they successfully got over the crisis and developed effective high active anti-retroviral drugs (HARTs). Then the companies started competing, and the PPP became less effective.

Lessons learned:

- PPPs will work when people are willing to compromise purist principles because they share an urgent mission. However, these circumstances may be unusual; the anti-retroviral PPP is still viewed as unique within the FDA.
- The concept of "harm reduction" incorporates these notions of compromise, common mission and purpose and sacrifice across different interests. Potential partnerships between the pain advocacy and addiction communities present an opportunity to utilize this concept.
- Medicine is fundamentally different from other industries because everyone involved must shoulder the social responsibility to promote human health. However, economics are aligning to drive a confluence of interests.
- Is it a good thing that the anti-retroviral division within FDA is seen as an outlier or "cowboy," if they are productive?

- For-profit companies are not value neutral. That can be a positive factor when it motivates improved care. When there is non-alignment (e.g., Merck in the Vioxx case), there is anger and distrust. There has been an evolution in some corporate structures in the way of "benefit corporations," L3Cs and "social purpose corporations," which have the effect of acknowledging that the business structure is not actually neutral. These structures hope to induce flexibility to balance profits and social purpose.
- In focusing on the problems of PPPs and interpreting conflict rather than confluence of interests, we are debating against a strawman idealistic and purist



perspective. Everyone has biases. However, the fury of the response to Lisa Rosenbaum's commentaries suggests that these are not felt as abstract ideals.

— Session Three —

Participants: Myra Christopher, *Kathleen M. Foley Chair and former CEO, Center for Practical Bioethics*

Julie Wood, *Senior Vice President for Health of the Public and Inter-professional Activities, American Academy of Family Physicians*

Jess Rabourn, *Director, WideTrial*

Greg Koski, *Co-Founder, President and CEO, Alliance for Clinical Research Excellence and Safety (ACRES)*

Myra Christopher recounted her experience with an initiative led by the Center for Practical Bioethics (CPB) that involved Kansas City research institutions. The Center initiated *The Research Integrity Project* in response to a 1998 report from the Office of the Inspector General titled, *INSTITUTIONAL REVIEW BOARDS: A TIME FOR REFORM*. One of the report's major findings was:

> Clinical research provides revenue and prestige to the institutions to which many IRBs belong. The institutions expect IRBs to support these interests at the same time that they protect human subjects. The resulting tension can lessen the IRBs' focus on their basic mission. The minimal "outside" representation that typically exists on IRBs deprives them of an important counterbalance to the institutional interests. For independent IRBs, the dependence on revenues from industry sponsors exerts similar possibilities for conflict.

In collaboration with Kansas City's three medical schools, other health delivery systems, and private enterprise engaged in human research, CPB attempted to promote the conduct of responsible research and improve human research protections by relocating the function of Institutional Review Boards from academic and healthcare providing institutions into a community-based not-for-profit that would develop, support and maintain four community-based review boards – one focused on pediatrics, two focused on adult health and another focused on behavioral health. The project was funded by Aventis Pharmaceuticals.

Christopher described an extensive effort on behalf of the Center to be transparent about funding; however, this project led to allegations that CPB's funding relationship with Aventis created a conflict of interest, and the Center was criticized by bioethicists and journalists. Although there was virtually no "fact checking" by the media, this situation had the effect of impugning the character of those leading the project (as in the ACTTION/IMMPACT case) and, ironically, with the complicity of other bioethicists. The Center's effort to manage and mitigate potential COI by publicly disclosing their source of funding was turned against the project. Critics ignored the purported value of

transparency and disclosure and instead focused only on appearance of COI.

This situation occurred in a very problematic research regulatory environment, particularly at the local IRB level. In fact, one of the participants said, "If we were to grade the current process of human subject protection and IRB processes, it would get a double F-. "He gave the example of a study in Nova Scotia, Canada that found over a two year period that despite all of the regulatory review and bureaucracy, the IRB review process did not change anything substantive in the protocol; instead, the IRB reviews often made the consent forms more complex and inaccurate. Furthermore, there may be a conflict of interest in maintaining the bureaucracy and local power of the IRB in many cases. Given the need to promote innovation of regulatory science, it may be necessary to "blow up" the current research regulation paradigm.

Jess Rabourn discussed his WideTrial initiative, an effort to make cohort-level Expanded Access trials more feasible for drug development stakeholders by way of a central non-profit sponsor. Their approach is to partner with disease foundations and trial sites and then offer low cost or zero cost Expanded Access solutions to drug companies under individual bilateral agreements. WideTrial has bilateral agreements with drug companies to get access to their drugs and to share data. Financial conflicts of interest have not been a significant concern because the drug companies are not giving them money—only access to their drug. However, they do worry about the appearance of COI if the project is perceived as a designed marketing agent for drug companies. Rabourn pointed out that among recent ideas exploring new paradigms in clinical research and human protection oversight has emerged the idea of certifying investigators using a "TSA Pre-Check model" to enhance efficiency and minimize the burden imposed on experienced investigators with a track record of conducting safe, ethically appropriate research. In this model, investigators would be credentialed through a rigorous process and then they would be presumed "safe" to conduct human research. However, they would be audited periodically.

Julie Wood discussed the potential COI related to industry funding of continuing medical education (CME) and the efforts of the American Academy of Family Physicians to keep the educational content as free from bias as possible. In response to this, it was noted that the AMA has adopted the following position: "Unless extraordinary circumstance dictate, we shouldn't seek outside support for CME." However, there is significant pushback from practicing physicians on this position.

Greg Koski discussed how the Alliance for Clinical Research Excellence and Safety (ACRES) functions as a neutral (non-profit) third party in managing complex PPPs. This role is exemplified by the recently announced cancer "moonshot" initiative. ACRES will promote a cloud-based system bringing together investigators, systems and technologies and large Fortune 500 companies to work on a large complex common goal. ACRES will function as a "neutral broker."

The question that emerged from these presentations and the discussion that followed was *"Has the bioethics community been sufficiently engaged in productive and constructive work on conflict of interest issues?"* Some felt that it has not up to this point, but it was agreed that the bioethics community has an important role to play in creating new models that advance biomedical research, protect human subjects, and instill confidence in the American public about the integrity of public private partnerships.

— Conclusion —

Meeting participants identified many areas where much more work needs to be done. Several themes and research questions eventually emerged from the group's discussion.

Emerging themes concerning COIs and PPPs

1. Future discourse should be based on scientific thinking and rational discussion as opposed to moral grandstanding.

2. Communication strategies for explaining the rationale and potential benefits of PPPs and the management of COIs should 1) be deliberate,

Some Examples of Public Private Partnerships

ACTTION: Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks. http://www.acttion.org/

The mission of the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) public-private partnership with the United States Food and Drug Administration (FDA) is to identify, prioritize, sponsor, coordinate, and promote innovative activities — with a special interest in optimizing clinical trials — that will expedite the discovery and development of improved analgesic, anesthetic, addiction, and peripheral neuropathy treatments for the benefit of the public health.

ACRES: Alliance for Clinical Research Excellence and Safety. http://www.acresglobal.net/

ACRES allies are committed to finding the most effective, innovative, ethical means of building, implementing and maintaining an integrated, comprehensive global system for clinical research, in a timely and cost efficient manner–and then do it!

Clinical Trials Transformation Initiative: http://www.ctti-clinicaltrials.org

CTTI engages all stakeholders as equal partners to analyze existing research impediments and recommend consensus-driven, actionable solutions that will lead to a more sustainable and effective clinical trial system.

Critical Path Institute: https://c-path.org/

Critical Path Institute, founded in 2005 in Tucson, Arizona, is an independent, non-profit organization dedicated to bringing scientists from the FDA, industry and academia all together to collaborate and improve the drug development and regulatory process for medical products.

based on the best available evidence concerning effectiveness, 2) emphasize potential lost opportunity costs from over-regulation, and 3) recognize the need to attend to and manage emotional responses to the perception of COI.

3. PPPs that are grounded in a common mission and purpose and designed to address a critical medical need (e.g., AIDS informal consortium) or significant scientific question (ACTTION/IMMPACT) can be productive, even in the face of challenges to their integrity.

4. The proliferation of PPPs at the federal level has had the unintended consequence of creating more complexity, inefficiency and siloing, and risks impeding progress in innovation. An Office of Strategic Partnership may make sense in this environment to coordinate activities, provide common resources, and bridge the silos.

Possible research questions and topics to address concerning COIs and PPPs

1. Research is needed to produce a systematic description of the collective experience of PPPs and analysis to extract lessons learned going forward.

2. In considering COIs, current regulations and rules governing research and education, we need to more thoroughly consider benefits that are lost because of over-regulation and over-interpretation of the current rules. This will require exploration of the landscape of entrepreneurs and investigators and surveys to explicate examples of lost opportunities.

3. New paradigms for regulating clinical research need to be explored and evaluated. Is a "TSA Pre-Check" approach to credentialing investigators and presuming they are "safe unless alarms go off" viable? There are several research questions embedded here:

    d. Does credentialing and certifying investigators matter? Can you show differences in research quality, efficiency and safety?

e. Does a TSA-like approach work? Is it feasible?

4. A systematic analysis of for-profit vs. non-profit PPPs would be illuminating.

5. Research is needed to determine how much of the success or failure of a PPP is determined by the personality of its leaders. What are the leadership skills that are required to promote PPPs? How does structure, mission or concept impact PPPs and their potential for success?

6. What is the social science of public perceptions of PPPs?

7. Is a neutral third party required to manage complex PPPs, such as will be engaged by the cancer moonshot? Is ACRES an example of this kind of neutral third party, and if so, what are the characteristics that promote success?

Possible Outcomes and Next Steps:

Several ideas were generated at the meeting and thereafter, via emails and telephone conversations, about possible next steps. Those included:

1. Host an additional meeting to continue the discussion.

2. Establish an ongoing forum focused on developing new paradigms for public private partnerships and managing conflicts of interest. (This would necessitate expanding the group of invitees.)

3. Tease out from this meeting a research agenda to underpin new models and develop a strategy to advocate for that agenda.

4. Meet with the FDA and/or the administration to explore their interest in establishing an Office for Strategic Partnerships.

5. Submit an article based on this meeting to the *New England Journal of Medicine*.

6. Approach the *American Journal of Bioethics (AJOB)* about publishing a special issue focused on this topic.

Since the meeting, ACRES approached the Center for Practical Bioethics to discuss their interest in a collaborative initiative to assure that ACRES fully integrates ethics and regulatory science into all its activities. CPB and ACRES are engaged in discussions about hosting a meeting in 2017 to explore these issues in more detail and planning to co-convene a national symposium in 2017.

Participants

Gaylene Anderson – *Senior Innovations Manager, Cleveland Clinic*

Laurie Burke – *Founder, LORA Group*

Myra Christopher – *Kathleen M. Foley Chair and former CEO, Center for Practical Bioethics*

James Ferris – *Director, Center for Philanthropy and Public Policy, University of Southern California*

Kathleen M. Foley – *Memorial Sloan Kettering Cancer Center Chair*

Audiey Kao – *Vice President of Ethics, American Medical Association*

Kevin A. Klock – *Director of Operations and Advisor to the President for the Foundation for the National Institutes of Health (FNIH)*

Greg Koski – *Co-Founder, President and CEO, Alliance for Clinical Research and Safety (ACRES)*

Ross McKinney, Jr. – *Director, Trent Center for Bioethics, Humanities, and History of Medicine, Duke University*

Heather Pierce – *Senior Director for Science Policy and Regulatory Counsel, Association of American Medical Colleges*

Jess Rabourn – *Director, WideTrial*

Lisa Rosenbaum – *National Correspondent, New England Journal of Medicine*

Steven Ross – *Partner, Akin, Gump, Strauss, Hauer, and Feld LLP*

Wendy Sanhai – *Senior Managing Scientist, Exponent*

John Tyler – *General Counsel, Secretary and Chief Ethics Officer, Ewing Marion Kauffman Foundation*

Julie Wood, *Senior Vice President for Health of the Public and Inter-professional Activities, American Academy of Family Physicians*

Facilitators

Richard Payne – *John B. Francis Chair in Bioethics, Center for Practical Bioethics*

Michael 'Buz' Waitzkin – *Deputy Director, Duke Initiative for Science and Society, Duke University*

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