INDIANA UNIVERSITY

CENTER FOR BIOETHICS

Final Summary Report: Review of Merck-Regenstrief Partnership

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EXECUTIVE SUMMARY

Arrangements between university researchers and industry have been commonplace for decades.[1-3] The typical arrangement involves a private sponsor, such as a pharmaceutical company providing a grant, contract or some other form of financial support to an academic investigator to conduct an individual study (e.g., a clinical trial) or pursue a line of research (e.g., a set of studies examining different forms of treatment for heart disease) that is of interest to the company and also falls within the scientific expertise and interest of the investigator. While such relationships are, at least *prima facie,* intended to be mutually beneficial, they can present conflicts of interest and commitment for the university-based researchers. It was because of these risks of conflict that rules, regulations, and guidelines for managing such conflicts were developed by federal regulators, professional associations and the academic community generally.[4-9] Indeed, the level of scrutiny for such arrangements has never been greater.[10]

A separate type of industry-academic arrangement is also appearing in the form of broader partnerships, platforms and collaborations where joint agreements are developed to pursue common areas of research, data analysis or drug development.[11,12] These arrangements vary but they differ in substantive ways from the more traditional grant-supported investigator model, often in the length of the time horizon, the arrangement's financial structure, its expectations of reciprocal benefit, and potential for impact at both organizations. The Massachusetts Institute of Technology was among the first to develop and implement these kinds of arrangements.[13] Indeed, even the country's premier public biomedical research sponsor, the National Institutes of Health, ventured into this territory when it announced in 2012 that its National Center for Advancing Translational Sciences (NCATS) "has unveiled a collaborative program that will match researchers with a selection of pharmaceutical industry compounds to help scientists explore new treatments for patients".[14]

In 2012, the Regenstrief Institute entered into a new partnership with the pharmaceutical company Merck with the goal of improving "the health of patients through data analytics, health care innovation, education and research that supports evidence-based health care."[15] In March of 2013, the Indiana University Center for Bioethics (IUCB) was asked to evaluate the Regenstrief component of the partnership from an ethics perspective. This was a unique opportunity since few such assessments have been reported in the literature.

The Study

The principal goal of the IUCB study was **to provide substantive actionable recommendations to minimize the risk that potential or actual conflicts of interest** might affect the scientific processes and outcomes of Regenstrief and its investigators. The study was also designed to provide an assessment of how well the partnership was meeting a standard for what an "ethically credible" partnership should look like. Although frameworks have been developed for assessing ethical acceptability in other areas of health care,[16,17] the idea to apply such an approach to

academic-industry partnerships was new. Therefore, the study provided an opportunity to design new tools that would help Regenstrief assess its current partnership and, if they proved useful, to aid in assessing future partnerships. The study was undertaken from October 2013 to September 2014 and conducted by faculty and staff from the IU Center for Bioethics (www.bioethics.iu.edu) using an approach consisting of five components:

(1) **Regular meetings** with Regenstrief leadership involved in the partnership that provided regular feedback to the project team, including one focus group to understand needs;
(2) Comprehensive **review of the scholarly literature** to identify current empirical findings about successful and unsuccessful partnerships, ethical assessments, and policy analyses;
(3) **Analysis of key partnership documents** including the master contract, handbooks for investigators and related materials;
(4) Development of a new evaluation tool consisting of a set of 9 substantive ethical **principles** and 23 **benchmarks** for ethically credible academic-industry partnerships (See Table 1) and;
(5) Conduct of **an online, anonymous survey** of Regenstrief investigator knowledge of and attitudes about the partnership to further inform the analysis.

The group provided two deliverables:

Deliverable #1: An annotated bibliography arising from the review of 25 publications from the peer reviewed literature; the ethical principles; and the benchmarks.

Deliverable #2: A final report including analysis of survey results and proposed recommendations.

Main Conclusions

1. While it was not task of this study to declare the Merck-Regenstrief partnership as "ethical" or "unethical," we concluded that **Regenstrief is engaged in an "ethically credible" partnership.** We came to this conclusion by determining that a majority of the ethical principles and benchmarks developed for ethically-credible partnerships were met. Regenstrief is engaged in an innovative and exciting partnership which substantially met the evaluative criteria that were jointly developed for this purpose.
2. Regenstrief's governance practices include procedures and policies that anticipate and address many of the key ethical issues that would be expected to arise in such partnerships.
3. While some principles and benchmarks were not fully met or a clear assessment was not possible, specific recommendations were made that, if followed, could assist Regenstrief in meeting or exceeding the benchmarks in the future. Indeed, we are convinced that with minor modifications, the approach taken by Regenstrief may serve as a model for other academic-industry partnerships.

Recommendations

In general, the recommendations addressed three main areas: (1) transparency and knowledge about the partnership; (2) conflict of interest policy; and (3) ongoing review of the partnership and its perception among Regenstrief investigators. Attending to these items could commend this type of partnership to others who are contemplating similar arrangements.

Recommendation #1: Increase transparency by providing more opportunities for investigators to become educated about the partnership, especially in areas where lack of understanding could potentially lead to an erosion of trust among Regenstrief investigators.

We believe that this can be achieved in a number of ways:

- In addition to the handbook that emailed to all eligible investigators, Regenstrief could hold an annual meeting where projects recently completed or being conducted in the partnership are reported to all investigators. This could spur interest in the partnership and also correct misinformed opinions about the partnership.
- At the conclusion of this review, hold a "town hall" meeting where these results could be presented to Regenstrief investigators and leadership would be able to provide information where seemingly problematic issues arise and investigators could further elaborate on the identified areas.
- At the conclusion of this review, write a memorandum of the findings joined with educational information on the partnership to be sent to all Regenstrief investigators.

Recommendation #2: Increase transparency in the project selection process by establishing and making explicit to all investigators how projects are selected and what criteria are used.

We believe that this could be achieved in a number of ways:

- Providing details about the process, and include it in the investigator handbook for the partnership.
- Allow an unaffiliated and unbiased observer to sit in on the project selection meetings in order to form an objective description of the process. This person would ideally be qualified to offer recommendations on improving process after seeing how the committee selects projects.

Recommendation #3: Regenstrief should seek additional ways to engage more investigators in the partnership.

We believe that this could be achieved in a number of ways:

- Distinguishing announcements for this call for proposals from all others (e.g., NIH, PCORI, etc.) so as to draw attention to them in Regenstrief email.

- Holding an annual Regenstrief WIP on the research outcomes of the partnership and use the opportunity to discuss the partnership and the next call for proposals.

***Recommendation #4*: In addition to the extant conflict of interest disclosure policies required by the IU School of Medicine, Regenstrief should establish and publicize widely partnership-specific conflict of interest (COI) policies.**

We believe this could be accomplished in a number of ways:

- Requesting COI self-disclosure from investigators akin to the IU policy when selected projects are funded.
- Requesting COI self-disclosure from investigators akin to the IU policy as a part of the initial proposal process. That is, an essential part of the proposal submitting process includes disclosing potential conflicts of interest.
- Issue a join position paper by Regenstrief and Merck on conflicts of interests and circulate it to relevant bodies and personnel.

***Recommendation #5*: Regenstrief should continue to reach out to investigators who may have concerns about the partnership and provide opportunities for learning, consultation and input.**

This could be accomplished in a number of ways:

- Conduct a more comprehensive assessment of Regenstrief investigator knowledge and attitudes about this partnership and other partnerships, which includes one-on-one interviews or focus groups.
- Providing an open and non-threatening opportunity for investigators to express concerns about the partnership.
- Ensure that Regenstrief investigators are aware of and encouraged to make use of the CTSI Bioethics and Subject Advocacy Program consultation service.

Methodological Considerations

Given that this study was one of the first of its kind undertaken, we are aware that there are areas where improvement could be achieved. Since the use of principles and benchmarks has, to our knowledge, never been used to assess the ethical credibility of an industry-academic partnership before, further research may be needed to confirm the value of this approach and refinements made as necessary. We chose to use the results of an investigator survey as empirical indicators of achievement, but other methods may be equally or more appropriate.

Table 1.

PRINCIPLES	BENCHMARKS
Academic Freedom	1. Promote investigator-initiated science and protect the ability to attract and maintain federal research support. 2. Permit investigators to initiate or continue collaboration with any other qualified group, person, or entity. 3. Ensure that all investigators involved in the partnership are given equal opportunity to submit proposals for funding. 4. Avoid obligating faculty to work outside their own self-defined scientific area.
Conflict of Interest Policy and Management	5. Protect students, fellows, and post-doctoral fellows involved in collaborative projects from exploitation. 6. Ensure that effective mechanisms exist to eliminate, control or manage conflicts of interest in the partnership.
Intellectual Property	7. Ensure all investigators and both partners retain their proprietary and intellectual property rights throughout and after the partnership.
Data Sharing, Access	8. Ensure that data sharing arrangements are explicit and that all rights to access data are fairly negotiated at the outset of the partnership.
Effective Governance	9. Establish parameters for what type of projects will and will not be funded (e.g. add-on projects, training, pilot studies). 10. Create ways to protect each party from an unexpected end to the partnership. 11. Assess formally the efficiency, effectiveness, and achievements of the partnership on an annual basis. 12. Ensure that clear, comprehensive, and efficient procedures exist for all governance entities of the partnership and are known to all investigators.
Protection of Human Subjects	13. Ensure that all investigators, staff and other participants in the partnership have adequate training in the responsible conduct of research and related ethical issues. 14. Ensure that all projects in the partnership aim to satisfy the highest ethical standards.
Publication	15. Ensure the right of all researchers associated with the partnership to publish. 16. Disseminate all research results at the conclusion of collaborative studies in a timely fashion. 17. Ensure authorship follows ICMJE guidelines.
Social, Scientific, and Industrial Value	18. Maintain competitive advantage in the specified research domains. 19. Structure the research to maximize potential benefit for communities and society. 20. Structure the partnership to have the best chance of benefiting both partners and harming neither.
Transparency	21. Widely publicize the partnership agreement and collaborative opportunities to the public and employees. 22. Establish procedures for frequent and effective communication between partners. 23. Ensure both partners are aware of other partnerships each may be involved in.

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I. Background and Introduction

In 2012, the Regenstrief Institute and Merck entered into a 5-year partnership with the goal of improving "the health of patients through data analytics, health care innovation, education and research that supports evidence-based health care."[1]

In March of 2013, the IU Center for Bioethics (IUCB) received a Request for a Proposal from Dr. William Tierney, President/CEO of the Regenstrief Institute to formally evaluate the current Merck-Regenstrief partnership with the expectation that it be done on an annual basis, and the results be published in the peer reviewed literature. The goal of this evaluation was to provide substantive actionable recommendations to minimize the risk that potential or actual conflicts of interest in the Merck-Regenstrief partnership would adversely affect the scientific processes and outcomes of the partnership. In so doing it would be further expected that the Merck-Regenstrief partnership would become a model for other public-private collaborations.

An initial proposal for the review was submitted on October 6, 2013. A revised version of the proposal focusing only on Regenstrief's activity in the partnership was resubmitted on December 9, 2013, and subsequently accepted.

The IUCB review consisted of the following elements:

1. The development of **principles** and **benchmarks** for ethically credible academic-industry partnerships. This involved :
    a. An assessment of key documents including: the Merck-Regenstrief Master Collaboration Agreement, an investigator guide to the partnership ("Handbook for the Merck-Regenstrief Collaboration") and an internal report of investigator and staff experiences in the first year of the partnership ("Summary of Year-End Interviews of Regenstrief Participants in the Merck Collaboration, Year 1").
    b. A comprehensive literature review of academic-industry collaborations.[2]
    c. Convening a focus group with the members of Regenstrief's steering and operations committees for the partnership.
2. A survey of Regenstrief investigator attitudes, experiences, and perspectives about the partnership.
3. A final report to include recommendations.

This report constitutes Deliverable #2 as outlined in the accepted proposal.

[1] Merck Press Release, "Merck and Regenstrief Institute establish evidence-based care collaboration." November 8, 2012
[2] This document was previously submitted as Deliverable #1

II. Development of Benchmarks for Ethically Credible Academic-Industry Partnerships

The IUCB constructed a set of principles and benchmarks for ethically credible academic-industry partnerships meant to be the primary tool for the review (Appendix 1, pg. 45). These benchmarks enabled a holistic review of the partnership and provided a common framework for conducting the focus group, crafting the investigator survey instrument, conducting the retrospective analysis of relevant findings, and making final recommendations.

In addition to the purposes of this review, these benchmarks have been designed so that Regenstrief can apply them to their ongoing partnership with Merck as a set of standards against which actions and policies can be assessed, and used on a regular basis as part of any internal program evaluation. Furthermore, Regenstrief can apply the benchmarks to future partnerships that it enters into with other organizations.

Along with a memorandum, these benchmarks were presented as Deliverable #1 to Dr. William Tierney, President/CEO of Regenstrief Institute, and Dr. Jon Duke, Regenstrief Director of the Merck-Regenstrief Partnership, on December 30, 2013, for comment.

In what follows is a detailed description of the initial stages of the review and how the principles and benchmarks were created.

A. Initial Assessment of Merck-Regenstrief Collaboration Agreement and other Key Documents

In order to build the knowledge necessary for this review, the IUCB requested copies of the Merck-Regenstrief Master Collaboration Agreement and other key documents so as to understand, in detail, the nature of the relationship, the commitments made by the partners, what expectations were created, what benefits are expected to flow to each partner, and how the partnership is managed. These documents were distributed to the authors of this report in early October and everyone was asked to read them.

B. Literature Review of Academic-Industry Collaborations

An initial search of the literature on ethical issues in academic-industry collaborations was conducted by IUCB research assistant, Avril Rua in mid-2013, and then updated by a second RA, Joshua Rager in late 2013. These papers were identified through OVID Medline using the Medical Subject Headings (MeSH terms):

> **Industry AND Academies and Institutes/or Universities AND Cooperative Behavior AND Ethics**

Other searches were conducted by adding and combining “Conflict of Interest,” “Academic Medical Centers,” “Private-Public Sector Partnerships,” “Drug industry,” and “model[text word]” in various combinations. Google Scholar and PubMed searches were conducted using similar keyword searches.

Papers were selected based on publication year, relevant content, and journal of publication. In total, 29 papers were selected. Each IUCB investigator read a set of the papers gathered and reported in weekly meetings on their usefulness for creating the benchmarks.

These papers were also read by IUCB research assistants Avril Rua Pitt and Joshua Rager, annotated, and then compiled into an annotated bibliography. The citations in the annotated bibliography are organized by their content relevance to each principle. The annotation that follows each citation includes the paper's key argument and the relevant findings and conclusions for industry-academia partnerships (Appendix 2, pg. 48).

It is noteworthy that while a somewhat robust literature exists on academic-industry relationships generally, it focuses mostly on those arrangements where industry supports academic researchers and where the principal ethical issue is conflict of interest. A much smaller literature can be found that focuses on arrangements of the kind Regenstrief is now beginning to engage in with industry, i.e., as collaborative partners. This annotated bibliography reflects these developments.

C. Creation of Principles and Benchmarks

Principles can be ubiquitous concepts in bioethics and are meant to be general action guides for ethical behavior and policy. Nonetheless, stand-alone principles do not provide specific guidance for every situation without some degree of interpretation and specification. In contrast, benchmarks are more granular and less abstract than principles and serve as achievable metrics for satisfying goals. The use of principles and their corresponding benchmarks is a relatively recent addition to the bioethics toolbox and is adapted from Emanuel et al.[3] In this format benchmarks confirm the extent to which a principle is satisfied. With these concepts in mind, the principles and benchmarks of ethically credible partnerships have been designed and written with the intention to:

- establish a practical and achievable floor for partnerships of this kind;
- provide more direct guidance than principles alone in applying this document;
- allow considerable freedom to accommodate the variety ways an individual benchmark may be achieved.

In addition to the benchmarks, descriptions of the principles are given (Appendix 1, pg. 45) and the methodology used to create them.

1. Method

At the conclusion of our initial literature search, items such as exemplars, best practices, challenges, and suggestions for academic-industry partnerships were gathered from three sources: (1) the literature cited in the annotated bibliography, (2) admirable items within the

[3] Emanuel EJ, Wendler D, Grady C, What makes clinical research ethical. JAMA. 2000;283:2701-2711; Emanuel EJ, Wendler D, Killen J, Grady C What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research The Journal of Infectious Diseases 2004; 189:930–7

Merck-Regenstrief contract, and (3) the expertise of IUCB faculty. These items were compiled into one document and transformed into an initial set of 60 original benchmarks. The IUCB faculty investigators met 10 times from October 2013 to December 2013 to draft, discuss, refine, and add to this original document. This process led to 23 final benchmarks for ethically credible academic-industry partnerships. As these benchmarks were being drafted, they were grouped according to common themes which were then identified as the 9 principles in the present document.

On December 30, 2013, these benchmarks, along with the annotated bibliography, were presented to Drs. Bill Tierney and Jon Duke of Regenstrief. Comments, feedback, and suggestions were solicited. Comments were received from Dr. Tierney on February 21, 2014. These comments were reviewed and revisions made accordingly in early March 2014.

D. Focus Group with Regenstrief Leadership of Merck-Regenstrief Partnership

On March 25, 2014, the IUCB convened a focus group with Regenstrief members of the Steering and Operations Committees for the Merck-Regenstrief partnership to understand and assess the perspectives of key leaders involved in managing the partnership based on the ethical principles and benchmarks of a model collaboration.

1. Method

An interview guide (Appendix 3, pg. 56) was drafted by IUCB faculty investigators from February 2014 to March 2014 based on the principles and benchmarks document. A current list of the Regenstrief leadership in the partnership was obtained from Jennifer Gatz, Managing Researcher at Regenstrief, in early March 2014. Prior to convening the focus group, a copy of the principles and benchmarks along with a study information sheet were emailed to participants on March 11, 2014. A second email with the same attachments was sent to participants on March 24, 2014 to remind them of the focus group.

This study was determined to be exempt by the IU IRB (Study #1401404759). Taping and note taking occurred throughout the session. Recordings were uploaded and sent for transcription to The Processed Word (www.mdtheprocessedword.com). Transcriptions were received on Monday, March 31, 2014 and cleaned for errors (See Appendix 4 for key quotes from transcript, pg. 61). The transcripts were then read and analyzed for content and pertinence to the benchmarks.

2. Outcomes

Five representatives of the Regenstrief steering and operations committees participated in the focus group. Representation included: 3 members of the operations committee, 1 member of the steering committee, and 1 participant who served on both the steering and operations committees. There was one invitee who was not in attendance. The session lasted 2 hours. Further analysis of the focus group will occur in Section IV.

III. Survey of Regenstrief Research Scientists and Affiliated Scientists

To better understand the experiences, knowledge, and perspectives of Regenstrief Research Scientists and Affiliated Scientists, we designed and implemented an online survey using RedCap consisting of 30 questions that used a 6-point Likert scale. Several questions permitted free-text responses.

1. Method

At the conclusion of the focus group in late March, the IUCB began drafting a survey instrument based on the benchmark document and results of the focus group. From April 2014 to June 2014, involved members of the IUCB met 9 times to create, draft, and edit the survey instrument. The instrument was reviewed by internal expert, Dr. Aaron Carrol, Director of the IU Center for Health Policy and Professionalism Research, and he offered comments and suggestions. Email addresses (e.g., Listservs) of eligible Regenstrief participants were obtained from Jennifer Gatz.

Prior to our request to participate, potential participants were sent an email from William Tierney, CEO/President of Regenstrief, encouraging their participation. On July 10, 2014, all potential participants were sent an email containing a study information sheet, a request for their participation, and a link to the online survey. Reminders were sent to potential participants on July 16, 2014, and July 22, 2014. The survey closed on July 28, 2014. This study was deemed exempt by the IU IRB (Study #1406322622).

2. Results

93 Regenstrief research scientists and affiliated scientists were invited to participate in the survey and we received 35 partial or complete records for a response rate of 38%. To count as a record, the respondent must have answered at least one question beyond the first four demographic questions (Appendix 5, pg. 73). Of the total 93 invited to participate, 51 were identified as research scientists and 42 as affiliate scientist. We received 26 research scientist records and 9 affiliate records for response rates among these two groups of 51% and 21%, respectively. Additionally, of those records received, 8 reported having been supported by the partnership and 27 having never been supported.

3. Method for Interpreting Results

We used a color-coding system (as seen above in the results section) to identify responses suggesting:

- good or acceptable achievement (GREEN);
- caution or attention (YELLOW);
- notable concern and needed attention (RED).

To identify and classify these areas we used the rubric below:

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
GREEN	**61%-100%**	**0-30%**	**0-10%**
YELLOW	**31%-60%**	**31%-60%**	**11%-20%**
RED	**0%-30%**	**61%-100%**	**21%-100%**

Some questions were intentionally written as negative statements, i.e., statements which, according to the benchmarks, one would not want to see high rates of agreement (**Questions 10, 13, 14, 22, 23**). In these cases, the percentage criteria for the strongly agree/agree and strongly disagree/ disagree columns would switch to determine which color and category it should receive. For example, in Question 23 we stated "I feel there is a conflict between my professional goals and the goals of the partnership." Guided by notions of conflict of commitment and the principle "Conflict of Interest Policy and Management," we would not want to see a high percentage of respondents agreeing with this statement. In this instance, 67% of respondents either disagreed or strongly disagreed with statement and only 3% either agreed or strongly agreed with this statement. As such, the 67% satisfies the Green criterion for strongly agree/agree and the 3% for the Green criterion in strongly disagree/disagree which suggests good or acceptable achievement.

Other questions do not lend themselves to strict use of this rubric (**Questions 1 and 24**). In these instances, the possible responses (e.g., knowledgeable, somewhat knowledgeable) are grouped according to what has been deemed appropriate by the authors of this report and then the rubric is applied.

4. *Results for Each Question.*

Q1: In your opinion, how knowledgeable are you of the Merck-Regenstrief partnership? (due to a computer glitch, the first 12 records did not contain this question)

	VERY KNOWLEDGEABLE	KNOWLEDGEABLE	SOMEWHAT	NOT
TOTAL N=27	4 (15%)	5 (19%)	12 (44%)	6 (22%)
	AT LEAST SOMEWHAT KNOWLEDGEABLE			NOT
	21 (78%)			6 (22%)

Q2: The Merck Regenstrief partnership has an acceptable data sharing policy.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	12 (34%)	23 (66%)	0%

Q3: The Merck-Regenstrief partnership is likely to benefit society.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=33)	24 (71%)	10 (29%)	0%

Q4: The Merck Regenstrief partnership ensures that all Regenstrief investigators are given equal opportunity to submit proposals for funding in the partnership.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	15 (43%)	16 (46%)	4(11%)

Q5: The Merck-Regenstrief partnership chooses research areas of focus that prioritize Merck's interests.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	15 (43%)	20 (57%)	0%

Q6: The Merck-Regenstrief partnership adequately protects investigators' intellectual property rights.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	7 (20%)	28 (80%)	0%

Q7: The Merck-Regenstrief partnership promotes investigator-initiated science.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	14 (40%)	17 (49%)	4 (11%)

Q8: The Merck-Regenstrief partnership is beneficial to Regenstrief.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	27 (77%)	8 (23%)	0%

Q9: The Merck-Regenstrief partnership effectively disseminates the funding opportunities to all investigators who are eligible to apply

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	12 (34%)	16 (46%)	7 (20%)

Q10: The Merck-Regenstrief partnership chooses research areas of focus in ways that are problematic.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=35)	2 (6%)	24 (69%)	9 (25%)

Free response:

"funds projects not likely to be funded by traditional government or foundation sources"

"focus on evidence from practice such as NLP applications in clinical text "

Q11: The Merck-Regenstrief partnership permits investigators to continue on-going collaborations with other research collaborators or teams.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	18 (53%)	16 (47%)	0%

Q12: The Merck-Regenstrief partnership is likely to benefit patients.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	18 (53%)	16 (47%)	0%

Q13: The Merck-Regenstrief partnership pressures faculty to work outside of their own research interests.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	1 (3%)	17 (50%)	16 (47%)

Q14: The Merck-Regenstrief partnership results in the exploitation of students and fellows.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=32)	1 (3%)	15 (47%)	16 (50%)

Q15: The Merck-Regenstrief partnership explains the procedures for applying for funding to all eligible investigators.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	14 (41%)	14 (41%)	6 (18%)

Q16: The Merck-Regenstrief partnership chooses research areas of focus that prioritize Regenstrief's interests.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	9 (26%)	21 (62%)	4 (12%)

Q17: The Merck-Regenstrief partnership has established clear criteria for which projects will be funded.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	5 (15%)	22 (64%)	7 (21%)

Q18: The Merck-Regenstrief partnership has been beneficial to me

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	8 (24%)	14 (41%)	12 (35%)

Free response for those who selected strongly agree/agree:

"I acquired salary support, new collaborators, and a mechanism to pursue science related to my goals."

"Projects chosen are priorities for Merck and RI so will benefit me directly or indirectly"

"Both support &opportunity to pursue meaningful collaborations"

"I am receiving support for my research."

"Has helped, in part, advance Gopher and OpenMRS"

"funding, publications, collaborations"

"Funding, furthering my interests, well run and organized"

"Funding received has benefited my specific area of research, which is of general interest to Merck but allows me to specifically pursue an area not yet recognized/funded by other agencies. With this support we have been able to collect valuable pilot data and collaborate with pharma scientists to further understand/promote the research area."

Free response for those who selected strongly disagree/disagree:

"It hasn't negative affected me it just hasn't affected me in anyway that I am aware of"

"no negative impact, just no beneficial impact"

"Has not been of direct benefit to me and has contributed to the strain between the IUSM and RI. It may have created conflicts of interest or conflicts of commitment that bring into question how the relationship with Merck is helping RI's role as a support organization to the School of Medicine (as opposed to serving primarily RI's needs more directly)."

"I am new to Regenstrief Institute and do not have sufficient knowledge about the Merck-Regenstrief partnership."

QUESTIONS 19-21 ONLY AVAILABLE TO THOSE WHO STRONGLY AGREED/AGREED IN QUESTION 8

Q19: Partnering with Merck has benefitted Regenstrief by providing more research funding

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=25)	25 (100%)	0%	0%

Q20: Partnering with Merck has benefitted Regenstrief by creating an environment more supportive to partnering with outside entities.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=25)	23 (92%)	2 (8%)	0%

Q21: Partnering with Merck has benefitted Regenstrief by creating a more effective system for managing projects.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=25)	8 (32%)	12 (48%)	5 (20%)

Q22: I have concerns that some projects conducted in the partnership are unethical.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=34)	0%	12 (35%)	22 (65%)

Q23: I feel there is a conflict between my professional goals and the goals of the partnership.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=33)	1 (3%)	10 (30%)	22 (67%)

Q24: The Merck-Regenstrief partnership has had the following effect on my ability to compete for research funding.

	STRENGTHENED	NEITHER	WEAKENED	DON'T KNOW
TOTAL (N=33)	8 (24%)	25 (76%)	0%	0%
	STRENGTHENED/ NEITHER		WEAKEND/ DON'T KNOW	
	33 (100%)		0%	

REST OF QUESTIONS ONLY AVAILABLE TO THOSE WHO REPORTED HAVING BEEN SUPPORTED

Q25: The Merck-Regenstrief partnership has effective mechanisms to manage conflicts of interest.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	3 (43%)	3 (43%)	1 (14%)

Q26: The Merck-Regenstrief partnership ensures the right of all investigators to publish.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	6 (86%)	1 (14%)	0%

Q27: The Merck-Regenstrief partnership encourages timely dissemination of research results.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	5 (71%)	2 (29%)	0%

Q28: There is effective communication between Regenstrief and Merck co-investigators.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	5 (72%)	1 (14%)	1 (14%)

Q29: My right to publish research findings from my work in the partnership does not differ from my right to publish from my work on other projects.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	6 (86%)	0%	1 (14%)

Q30: The projects I've been involved in the partnership are undertaken according to the highest ethical standards.

	STRONGLY AGREE/AGREE	NEITHER/ I DON'T KNOW/ NA	STRONGLY DISAGREE/DISAGREE
TOTAL (N=7)	7 (100%)	0%	0%

IV. Findings

A. Specific Findings

1. Method

Survey results were used to assess whether Regenstrief met a benchmark or not.

We used a rough three-part distinction in making what is a somewhat subjective assessment:

- To conclude that a benchmark has been MET, we required that **greater than or equal to 50%** of respondents to the questions relating to that benchmark Agreed or Strongly Agreed.
- To conclude that a benchmark has NOT BEEN MET, we required that **less than 30%** of respondents to the questions relating to that benchmark Agreed or Strongly Agreed.
- To conclude that the JURY'S OUT on whether a benchmark has been met we required that **between greater than 30% and up to 49%** Agreed or Strongly Agreed.

	STRONGLY AGREE/AGREE
MET	≥ 50%
NOT MET	< 30%
JURY'S OUT	30% - 49%

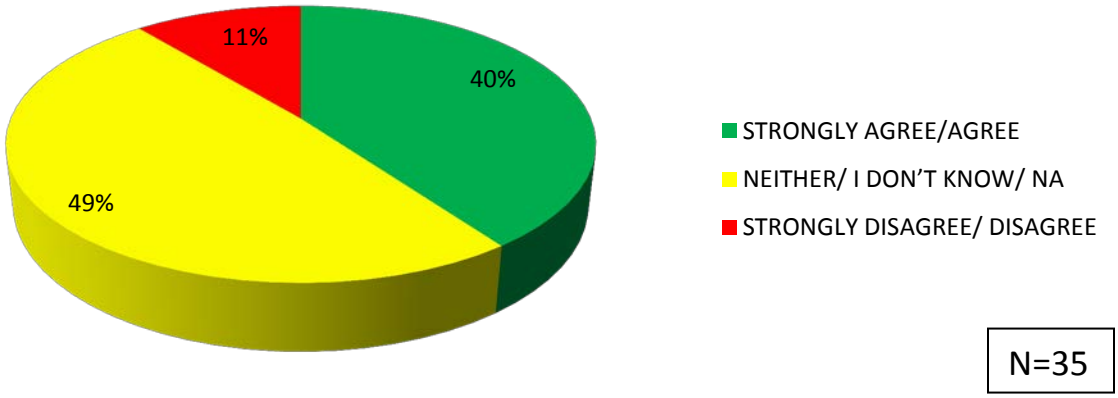
Instances where the questions are posed as negative statements (i.e., the opposite of a benchmark, **Questions 10, 13, 14, 22, 23**), we would want to see ≥ 50% of strongly disagree/disagree. To keep the graphs visually consistent, the color green is used for strongly disagree/disagree for these questions.

There were also cases where the benchmark was not appropriate to include in the investigator survey. This occurred when the benchmark pertained to an organizational- or systems-level policy or partnership arrangement that investigators would not be expected to know. In these situations, a consensus opinion of the research team was employed to determine whether the benchmark had been met or not.

There are also instances where one benchmark has multiple questions that inform whether or not the benchmark has been met. In some case, both questions suggest the benchmark has been MET but in others, the responses suggest varying levels of achievement. In the case of the latter situation, a paragraph follows both graphs describing what weight is given to each question.

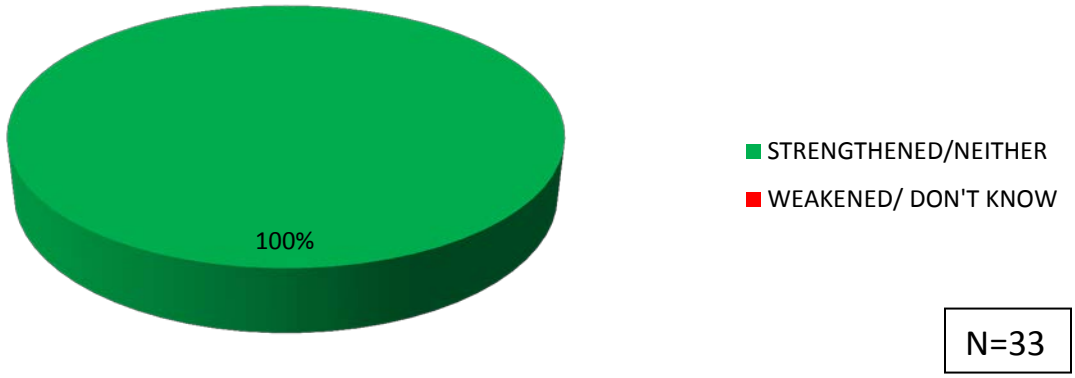
BENCHMARK 1: Promote investigator-initiated science and protect the ability of investigators to attract and maintain federal research support.

Question 7: The Merck-Regenstrief partnership promotes investigator-initiated science.



- Jury's Out: Benchmark has not been clearly MET or NOT MET
- 49% Neither Agree Nor Disagree or Don't Know/NA
- 11% Disagree or Strongly Disagree

Question 24: The Merck-Regenstrief partnership has had the following effect on my ability to compete for research funding.

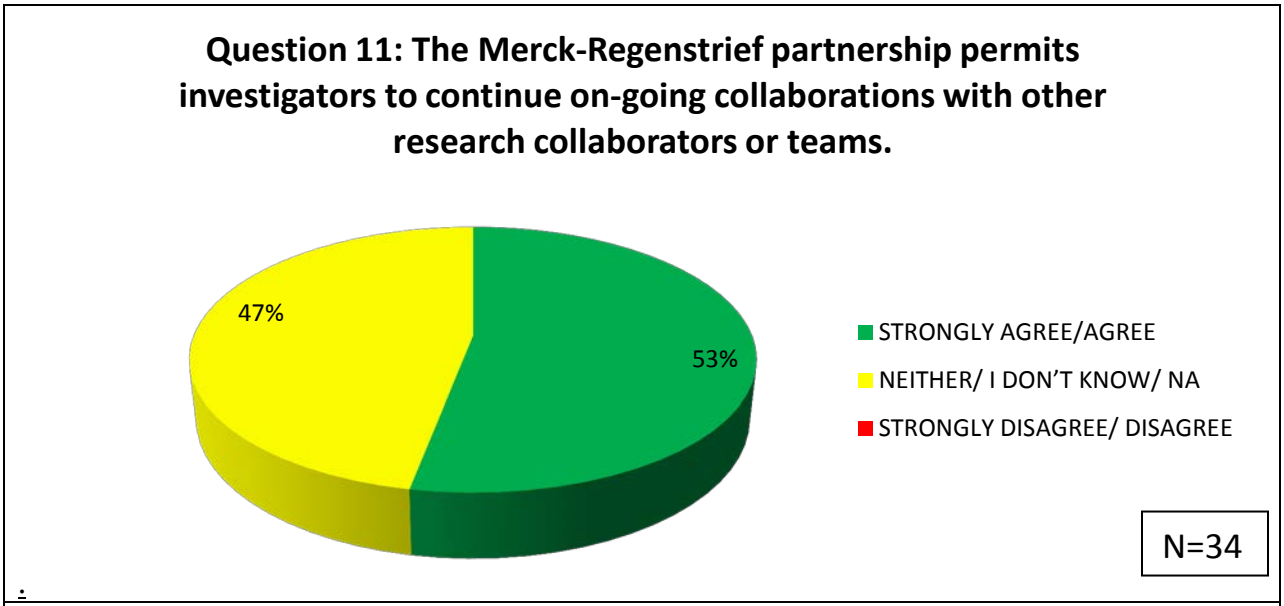


- Benchmark MET

Given these two pieces of information, we believe that the JURY'S OUT for Benchmark #1. We make this conclusion because while we found the responses to Question 24 in accordance with the benchmark, only 40% of respondents agreed or strongly agreed with Question 7 and a small but significant number of respondents (4) disagreed or strongly disagreed with the statement in Question 7. The greater weight we gave to Question 7 over Question 24 in this case is based on our sense that the component of benchmark #1 covered in question 24 simply asks for noninterference from partnership—a negative right of sorts—whereas the component addressed

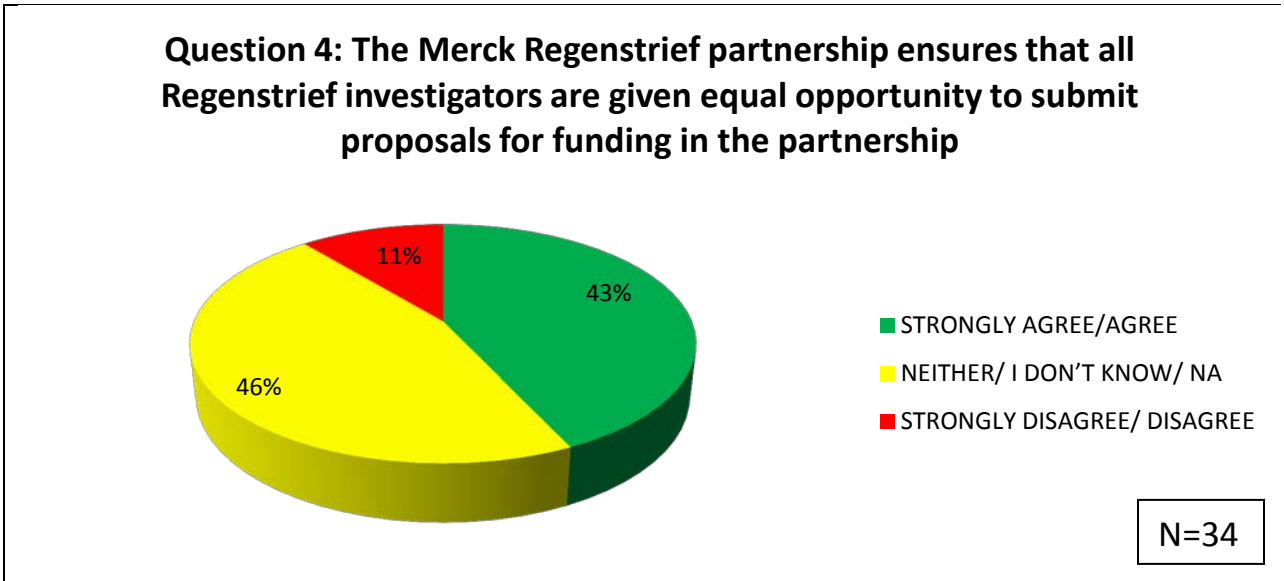
by Question 7 requires more of the partnership to ensure and promote investigator-initiated science.

BENCHMARK 2: Permit investigators to initiate or continue collaboration with any other qualified group, person, or entity.



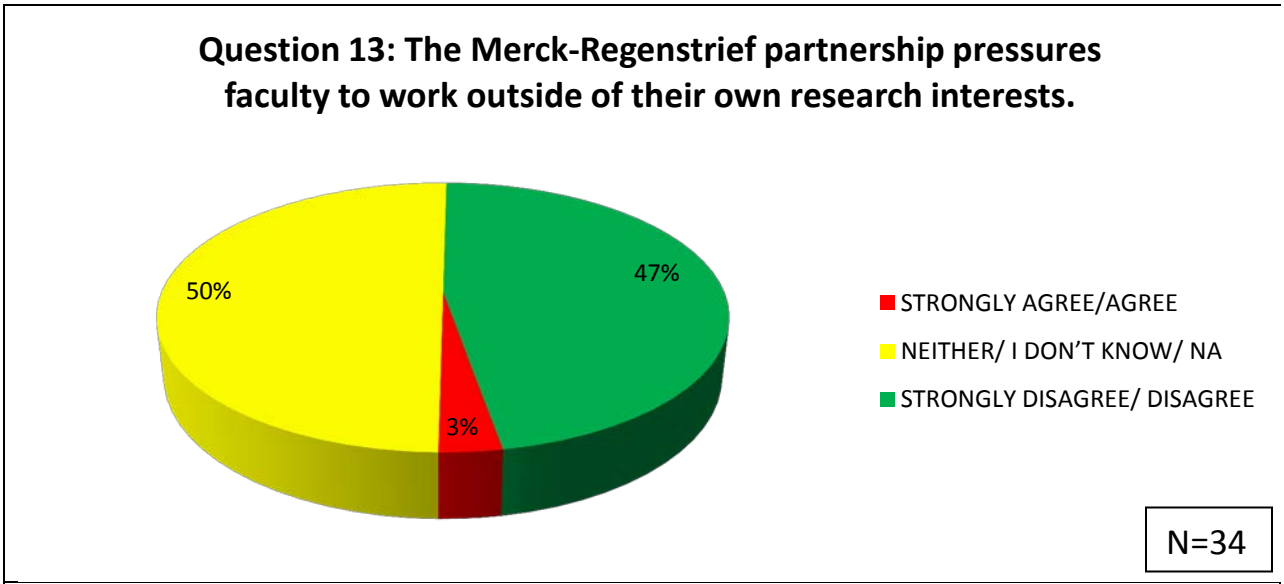
- Benchmark MET

BENCHMARK 3: Ensure that all investigators involved in the partnership are given equal opportunity to submit proposals for funding.



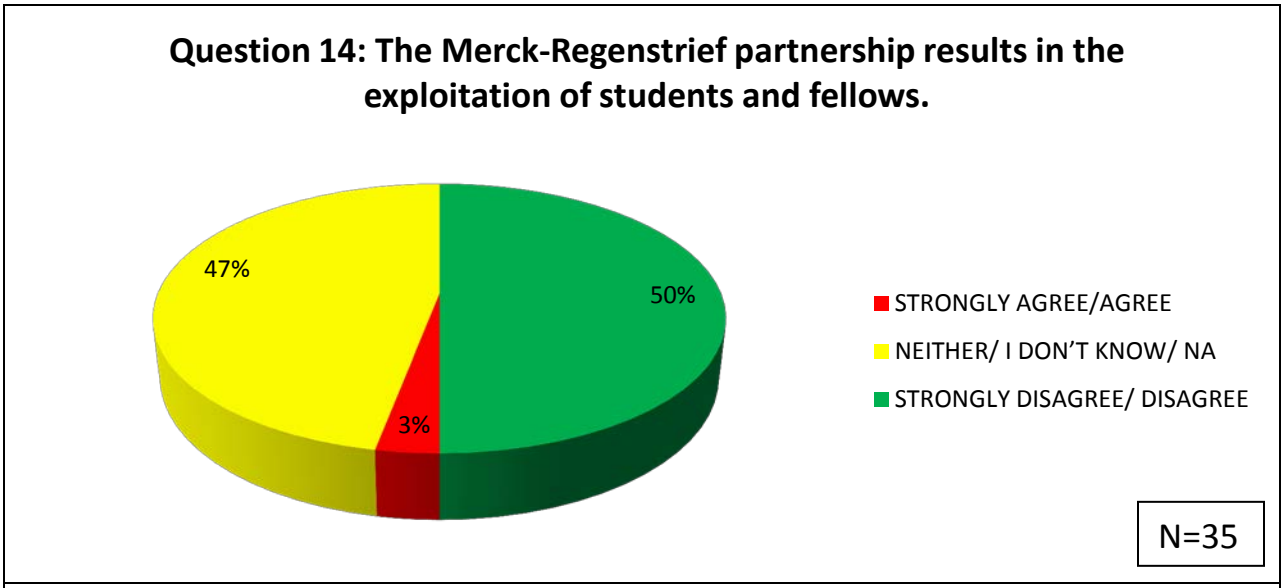
- Jury's Out: Benchmark has not been clearly MET or NOT MET
- 46% of respondents Neither Agree Nor Disagree or Don't Know/NA
- 11% disagree or strongly disagree

BENCHMARK 4: Avoid obligating faculty to work outside their own self-defined scientific area



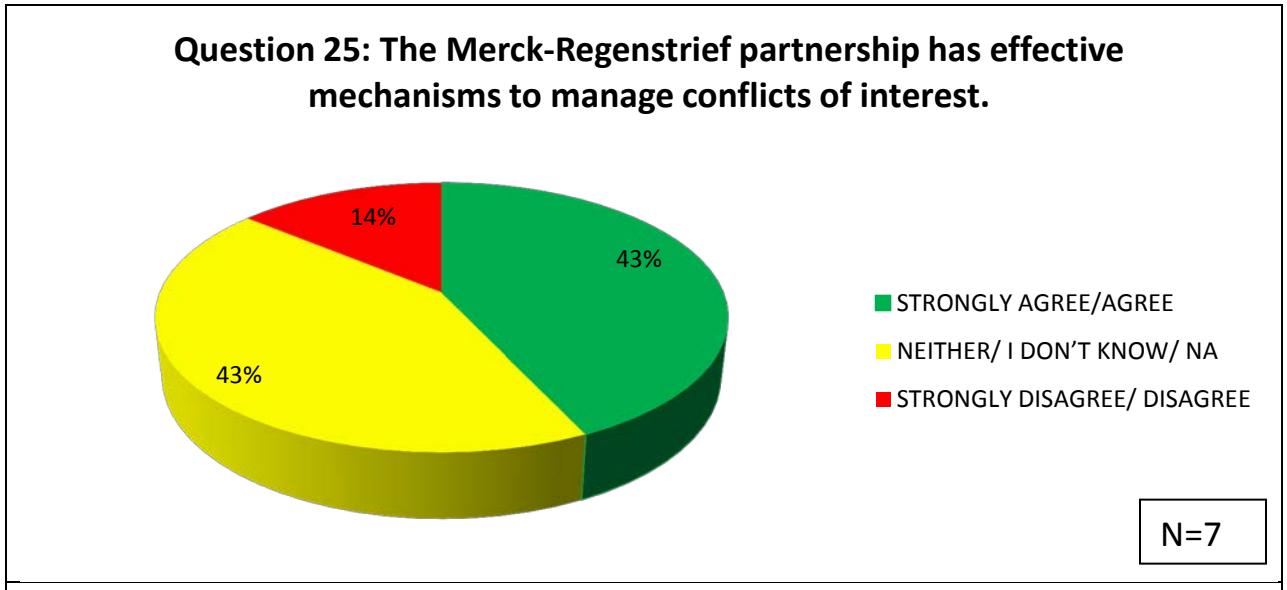
- Jury's Out: Benchmark has not been clearly MET or NOT MET
- 50% of respondents Neither Agree Nor Disagree or Don't Know/NA

BENCHMARK 5: Protect students, fellows, and post-doctoral fellows involved in collaborative projects from exploitation.



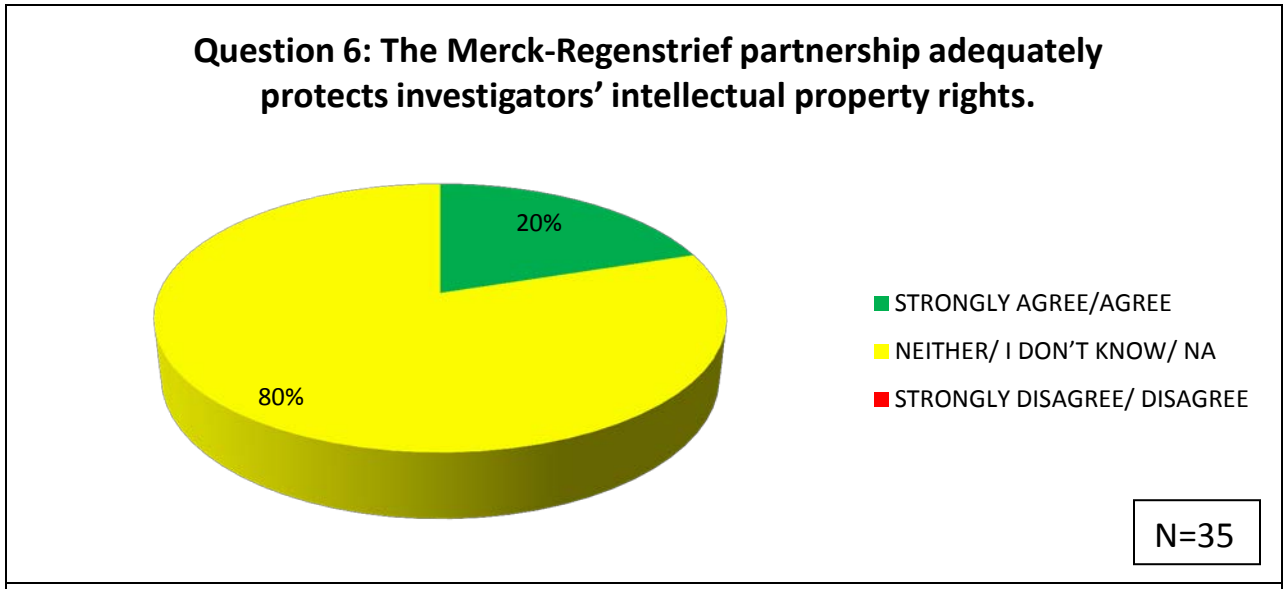
- Benchmark MET
- However, 47% of respondents Neither Agree Nor Disagree or Don't Know/NA

BENCHMARK 6: Ensure that effective mechanisms exist to eliminate, control, or manage conflicts of interest in the partnership.



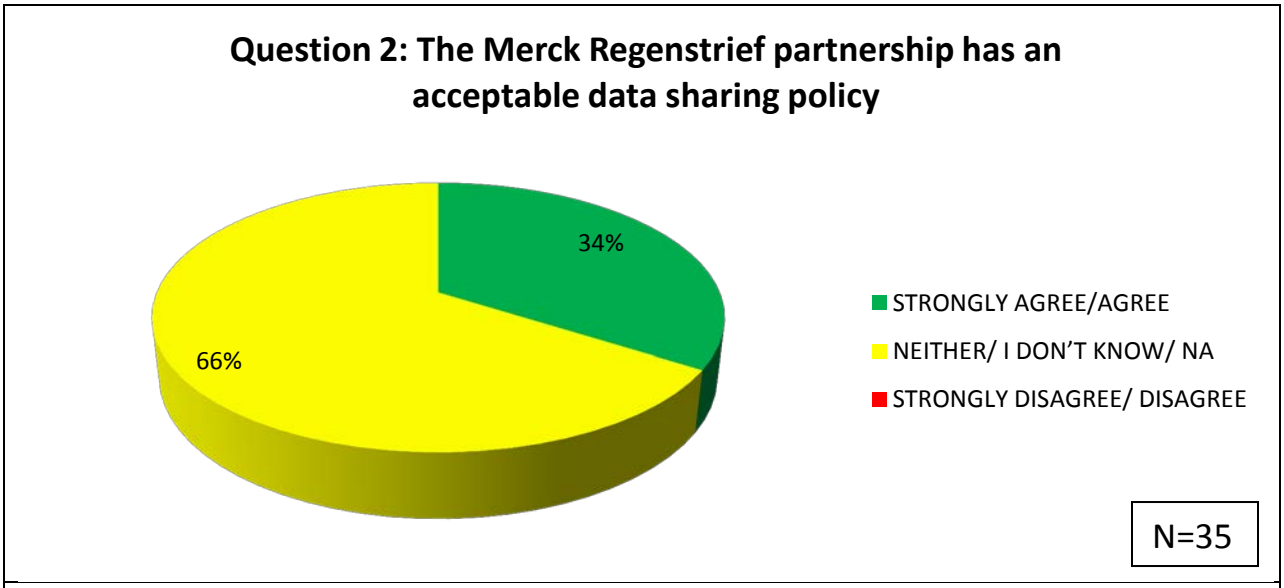
- Jury's Out: Benchmark has not been clearly MET or NOT MET
- 43% of respondents Neither Agree Nor Disagree or Don't Know/NA
- 14% of respondents disagree or strongly disagree.
- Notable that this question was only asked of those who have been supported by the partnership.

BENCHMARK 7: Ensure all investigators and both partners retain their proprietary and intellectual property rights throughout and after the partnership.



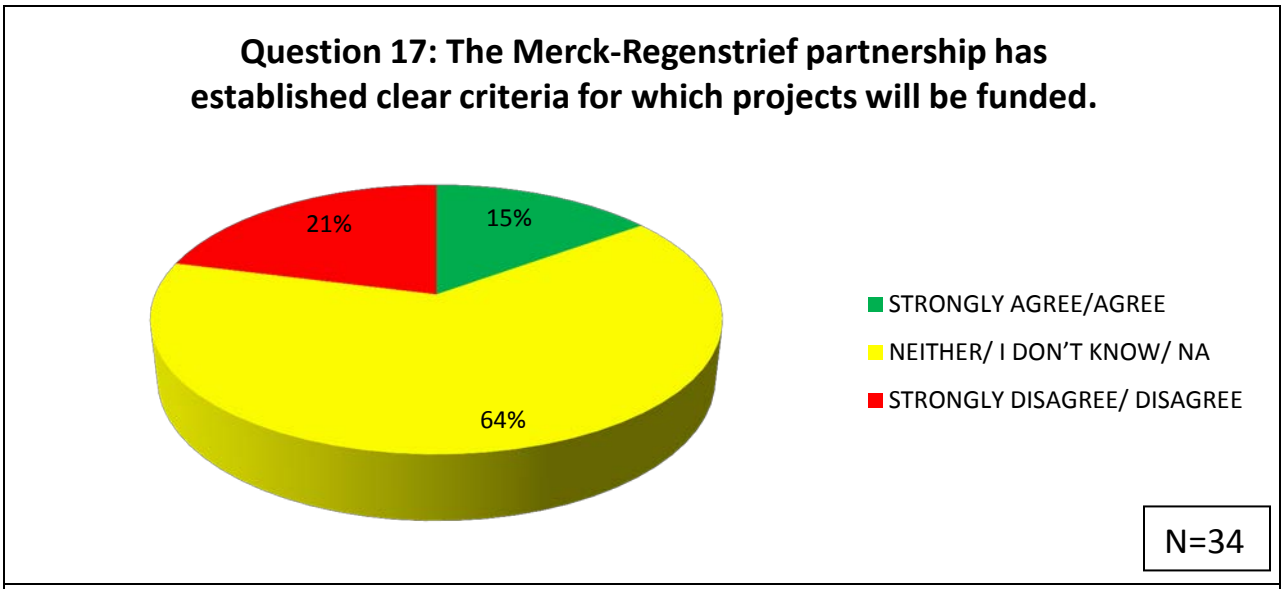
- Benchmark NOT MET
- 80% of respondents Neither Agree Nor Disagree or Don't Know/NA

BENCHMARK 8: Ensure that data arrangements are explicit and that all rights to access data are fairly negotiated at the outset of the partnership.



- Jury's Out: Benchmark has not been clearly MET or NOT MET
- 66% of respondents Neither Agree Nor Disagree or Don't Know/NA

BENCHMARK 9: Establish parameters for what type of projects will and will not be funded (e.g., add-on projects, training, pilot studies).



- Benchmark NOT MET
- 64% of respondents Neither Agree Nor Disagree or Don't Know/NA
- 21% of respondents disagree or strongly disagree

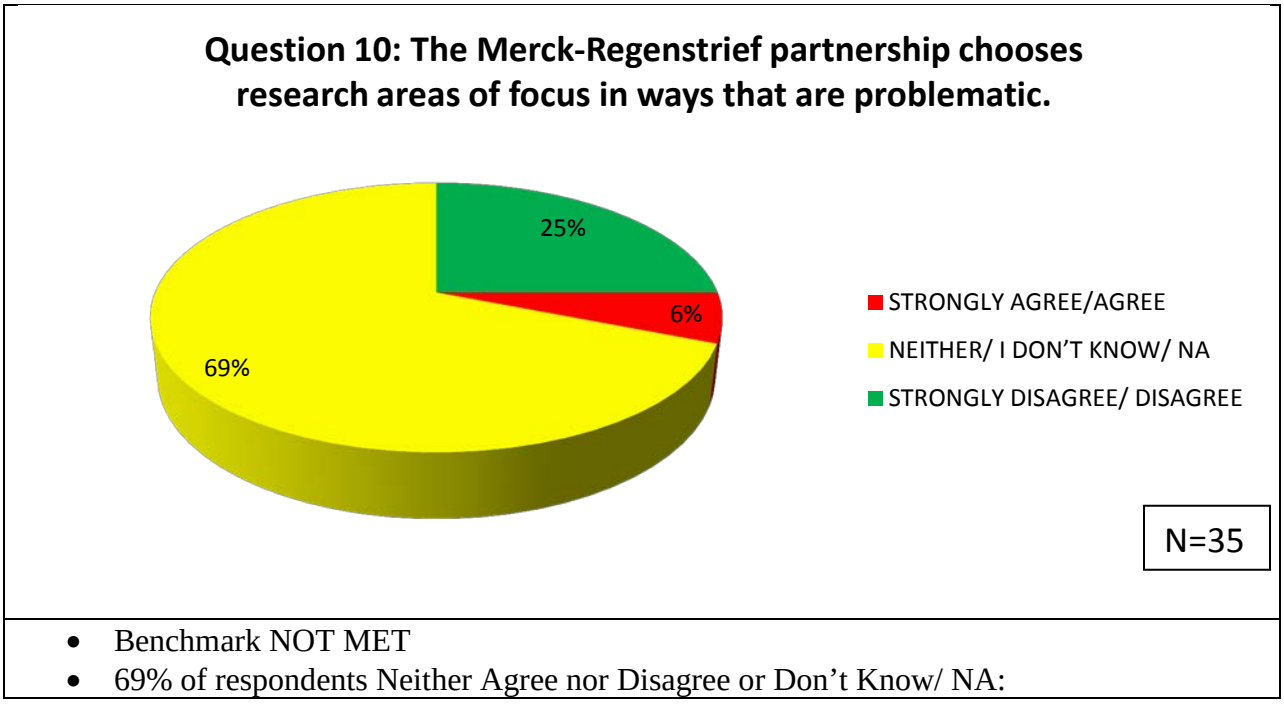
BENCHMARK 10: Create ways to protect each party from an unexpected end to the partnership.

No survey data were sought. We did not ask investigators about procedures in the event of a premature dissolution of the partnership given such decisions would made by leadership and not investigators. However, given that each section of the collaboration agreement contains formal procedures for early termination of the contract, we can reasonably conclude that this benchmark has been satisfactorily met.

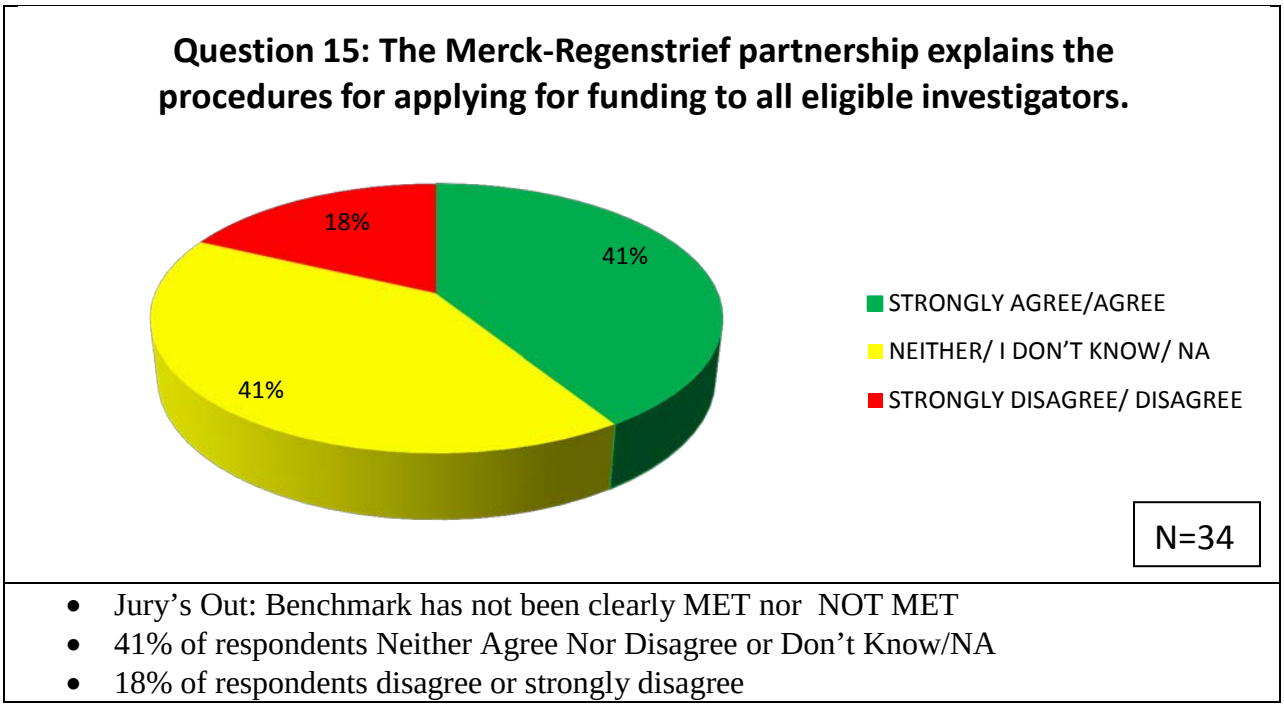
BENCHMARK 11: Assess formally the efficiency, effectiveness, and achievements of the partnership on an annual basis.

No survey data were sought. We did not ask investigators about formal review of the partnership given that such a benchmark is established primarily for partnership leadership. However, by virtue of this report, we can reasonably conclude that this benchmark has been satisfied.

BENCHMARK 12: Ensure that clear, comprehensive, and efficient procedures exist for all governance entities of the partnership and are known to all investigators.



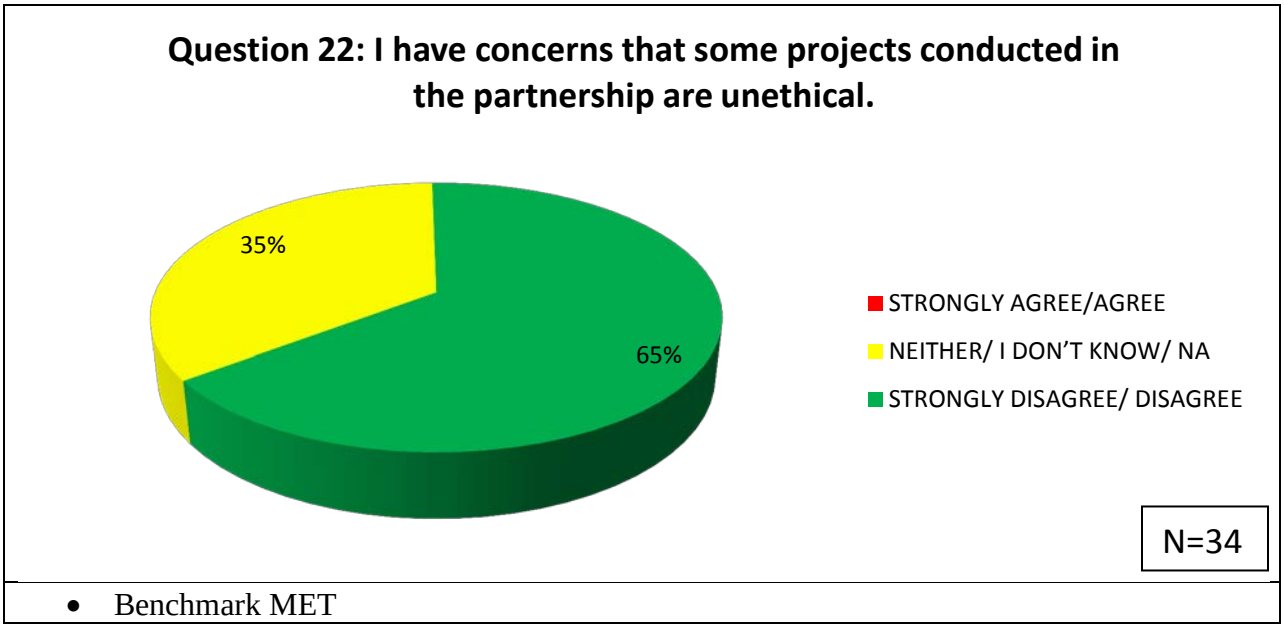
- Benchmark NOT MET
- 69% of respondents Neither Agree nor Disagree or Don't Know/ NA:



- Jury's Out: Benchmark has not been clearly MET nor NOT MET
- 41% of respondents Neither Agree Nor Disagree or Don't Know/NA
- 18% of respondents disagree or strongly disagree

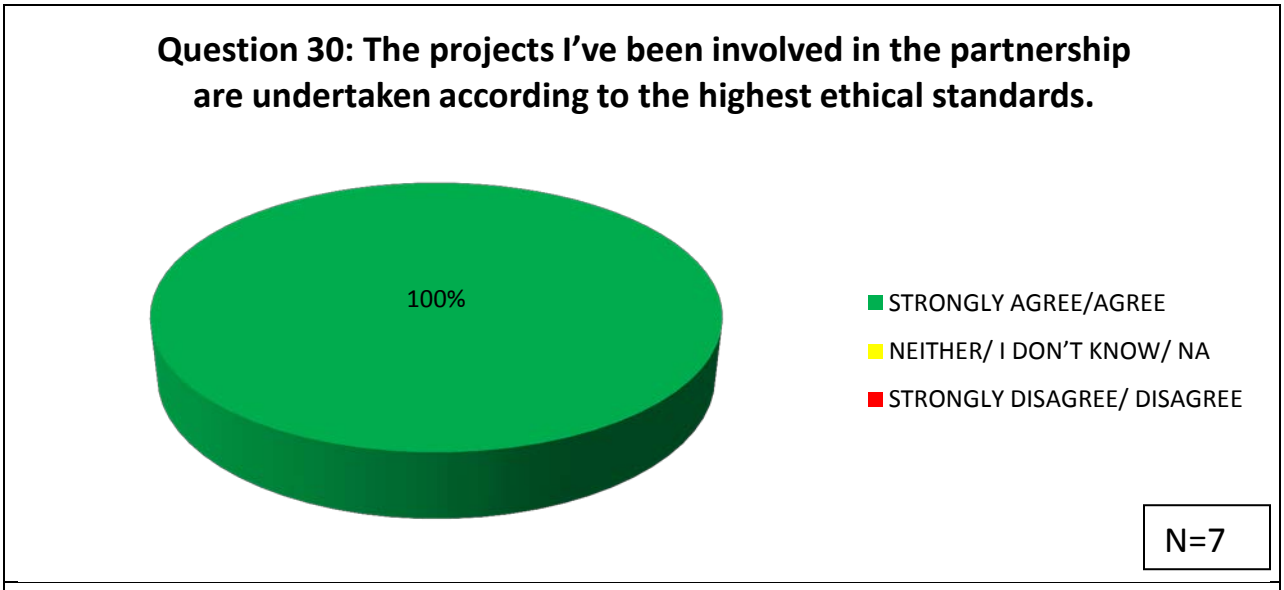
Given these two pieces of information, we conclude that the benchmark has NOT been met given the responses to Question 10 but also because 59% of respondents to Question could not confirm that the partnership explains the procedures for applying for funding to all eligible investigators.

BENCHMARK 13: Ensure that all investigators, staff, and other participants in the partnership have adequate training in the responsible conduct of research and related ethical issues.



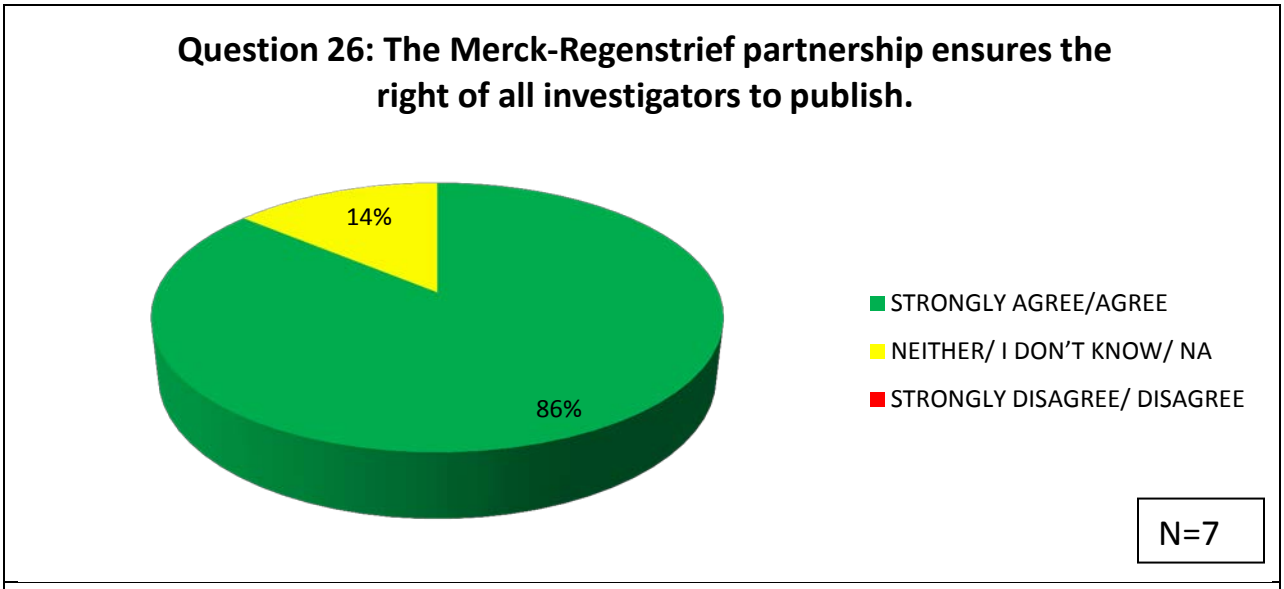
- Benchmark MET

BENCHMARK 14: Ensure that all projects in the partnership aim to satisfy the highest ethical standards.

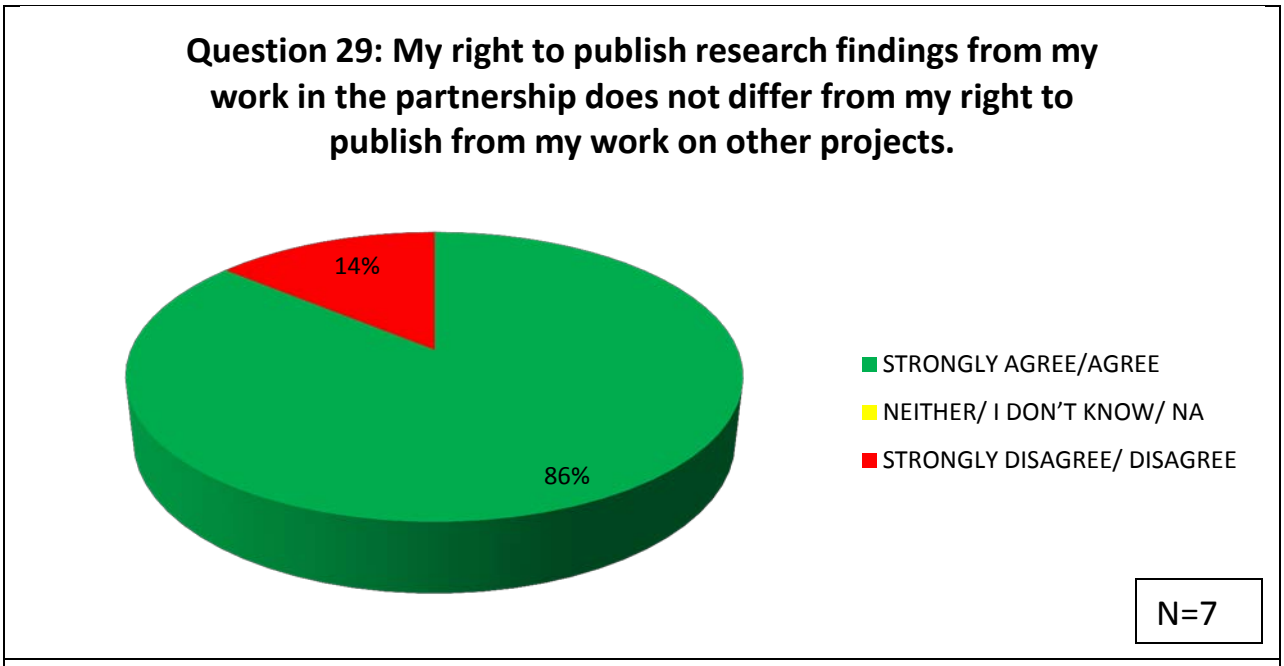


- Benchmark MET
- Notable that this question was only asked to those that have been supported by the partnership.

BENCHMARK 15: Ensure the right of all researchers associated with the partnership to publish.

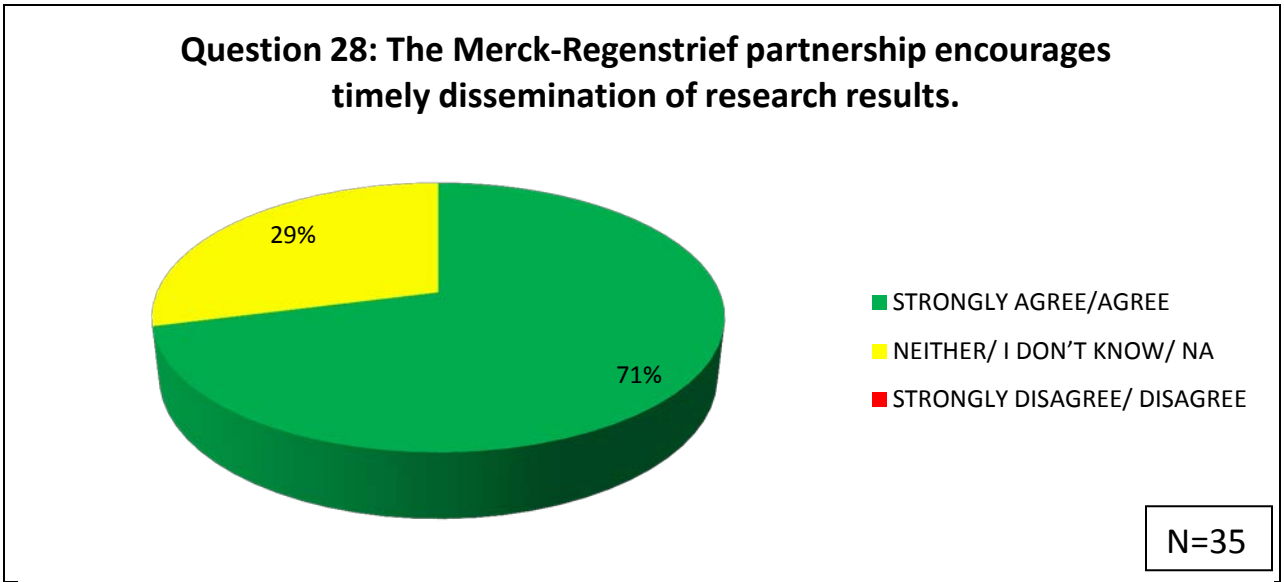


- Benchmark MET
- Notable that this question was only asked to those who have been supported by the partnership



- Benchmark MET
- Notable that this question was asked only to those who have been supported by the partnership

BENCHMARK 16: Disseminate all research results at the conclusion of collaborative studies in a timely fashion.

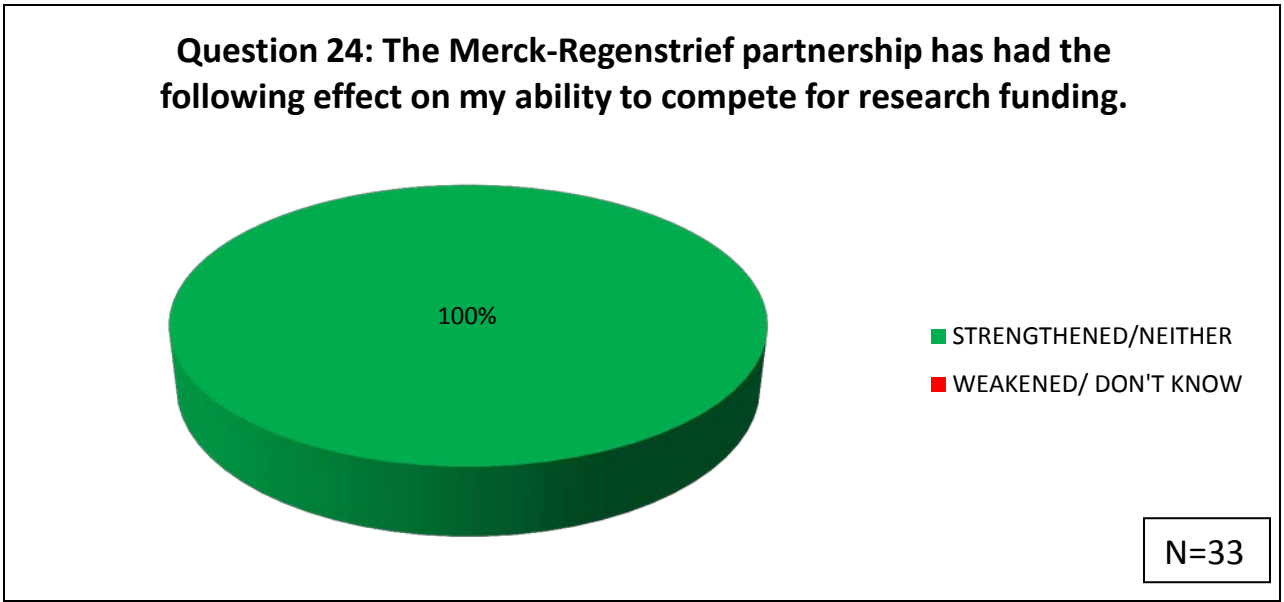


- Benchmark MET

BENCHMARK 17: Ensure authorship follows ICMJE guidelines.

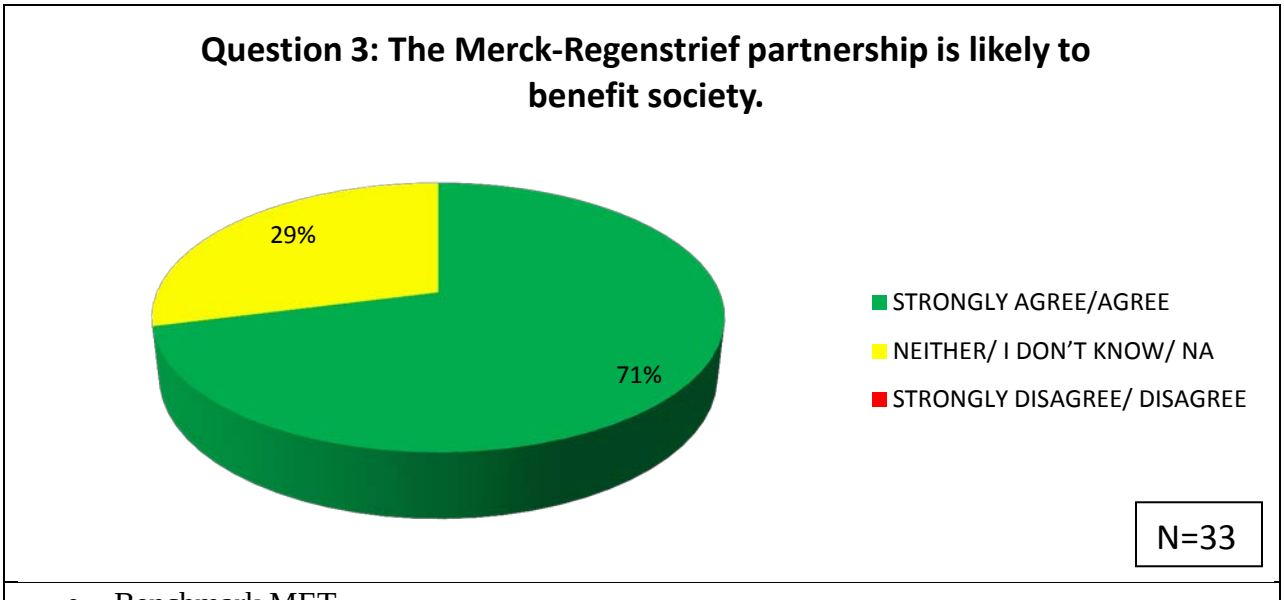
No survey data were sought.. Additionally, there isn't any evidence in the documents we've been provided with that suggest publications resulting from the partnership follow these guidelines. Given that journals require these authorship guidelines be followed, we assume but cannot confirm or disconfirm that the benchmark has been met. Inconclusive findings.

BENCHMARK18: Maintain competitive advantage in the specified research domains.

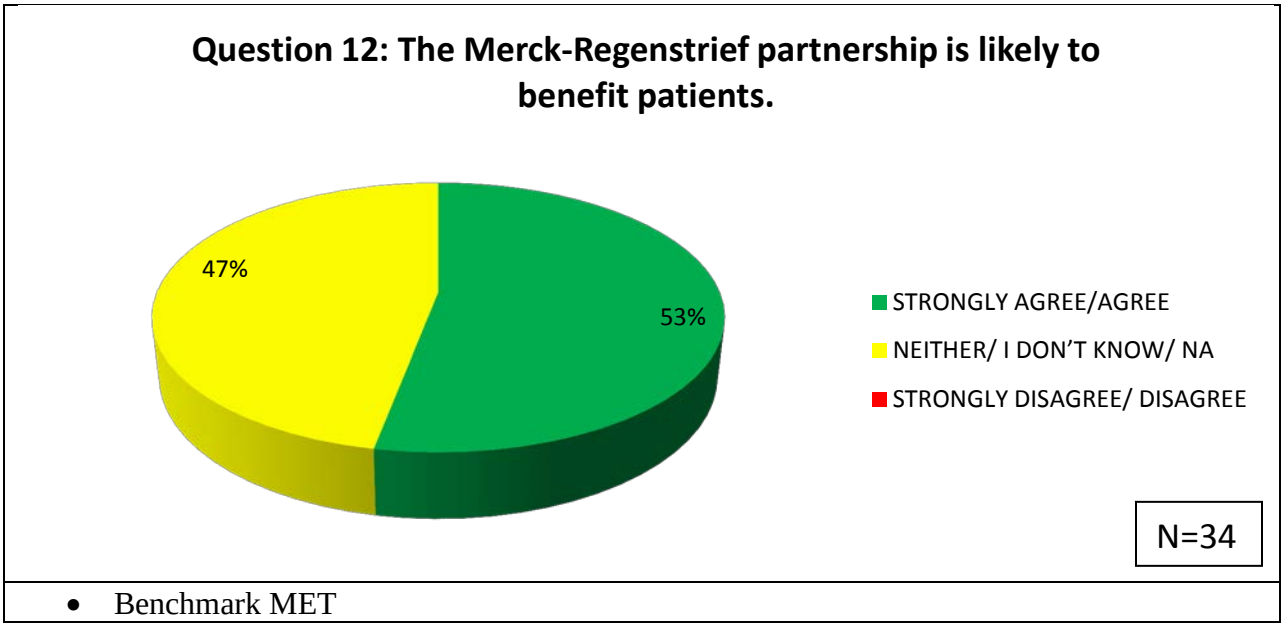


- Benchmark MET

BENCHMARK 19: Structure the research to maximize potential benefit for communities and society.



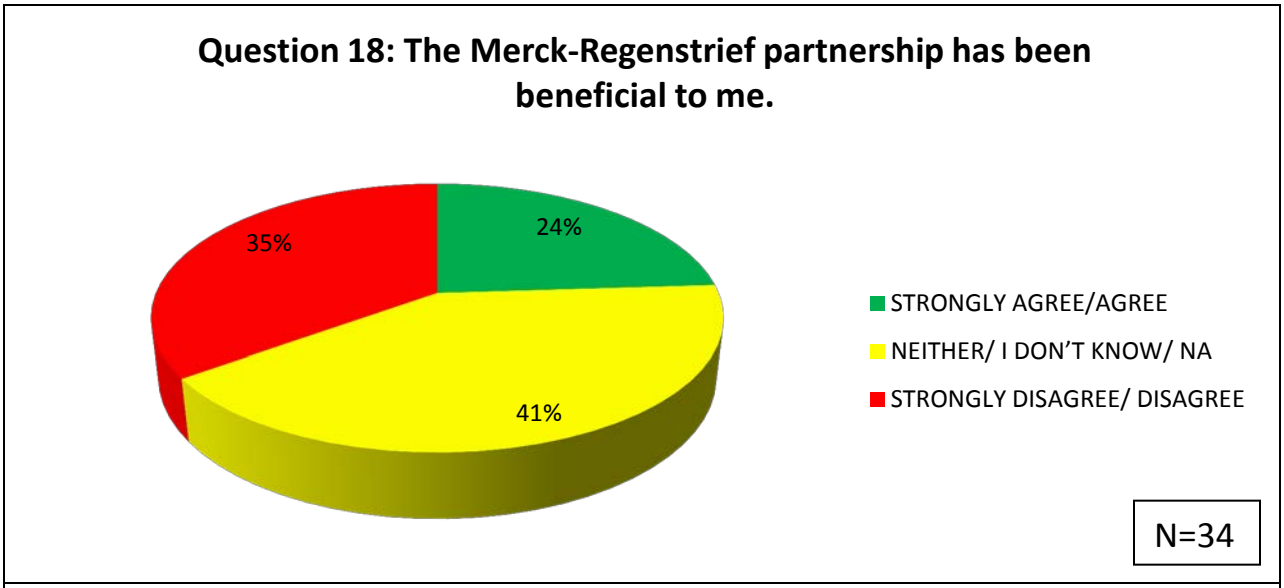
- Benchmark MET



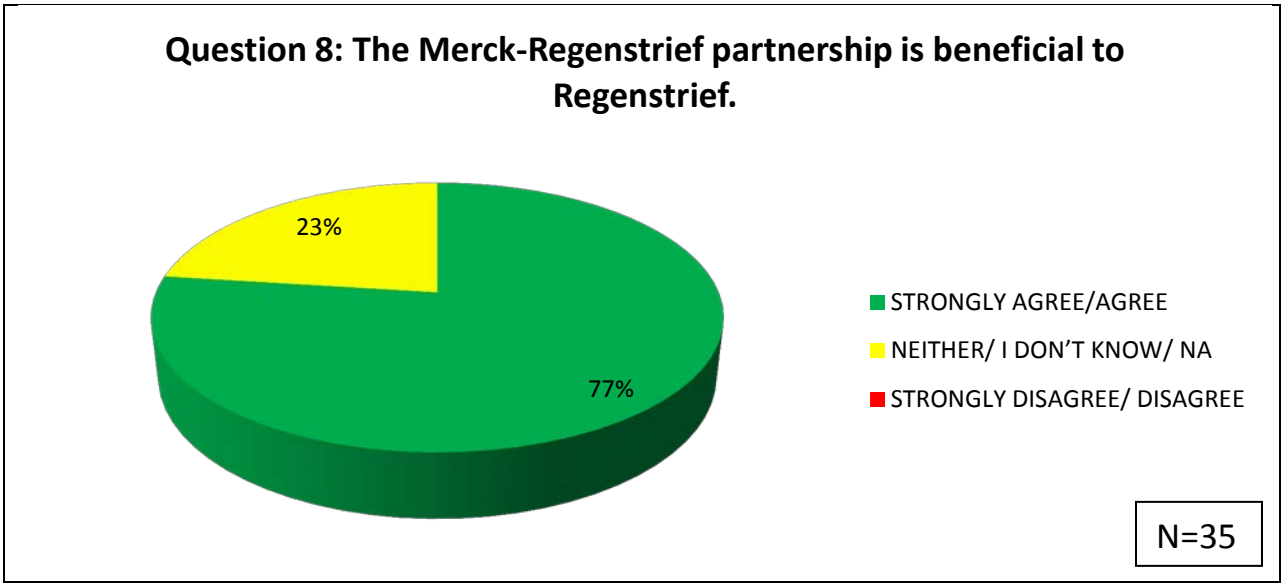
- Benchmark MET

Both questions suggest the benchmark has been MET and so we conclude that the benchmark has been MET.

BENCHMARK 20: Structure the partnership to have the best chance of benefiting both partners and harming neither.



- Benchmark NOT MET
- 41% of respondents Neither Agree nor Disagree or Don't Know/NA
- 35% of respondents disagree or strongly disagree with the statement



- Benchmark MET

Despite the fact that the responses to Question 18 suggest that the benchmark has not been met, free responses to this question indicate that while some investigators may not directly benefit from the partnership, investigators indicated that it neither harmed them as well:

"It hasn't negative affected me it just hasn't affected me in anyway that I am aware of"

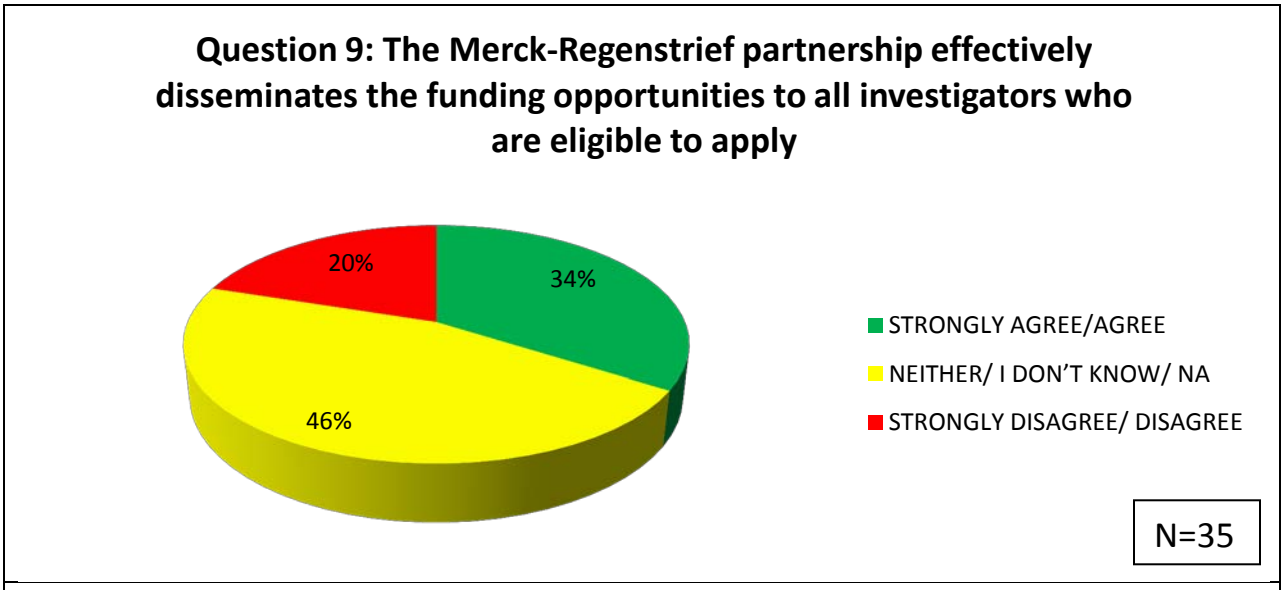
"no negative impact, just no beneficial impact"

As can be seen in the survey instrument (Appendix 5, pg. 73), we asked respondents that if they disagree or strongly disagree with the statement in Question 18 but felt the partnership didn't harm with either, to leave the free response blank. Only one respondent indicated being harmed but even in this response, the harm appears to be less individual and more institutionally-minded:

"Has not been of direct benefit to me and has contributed to the strain between the IUSM and RI. It may have created conflicts of interest or conflicts of commitment that bring into question how the relationship with Merck is helping RI's role as a support organization to the School of Medicine (as opposed to serving primarily RI's needs more directly)."

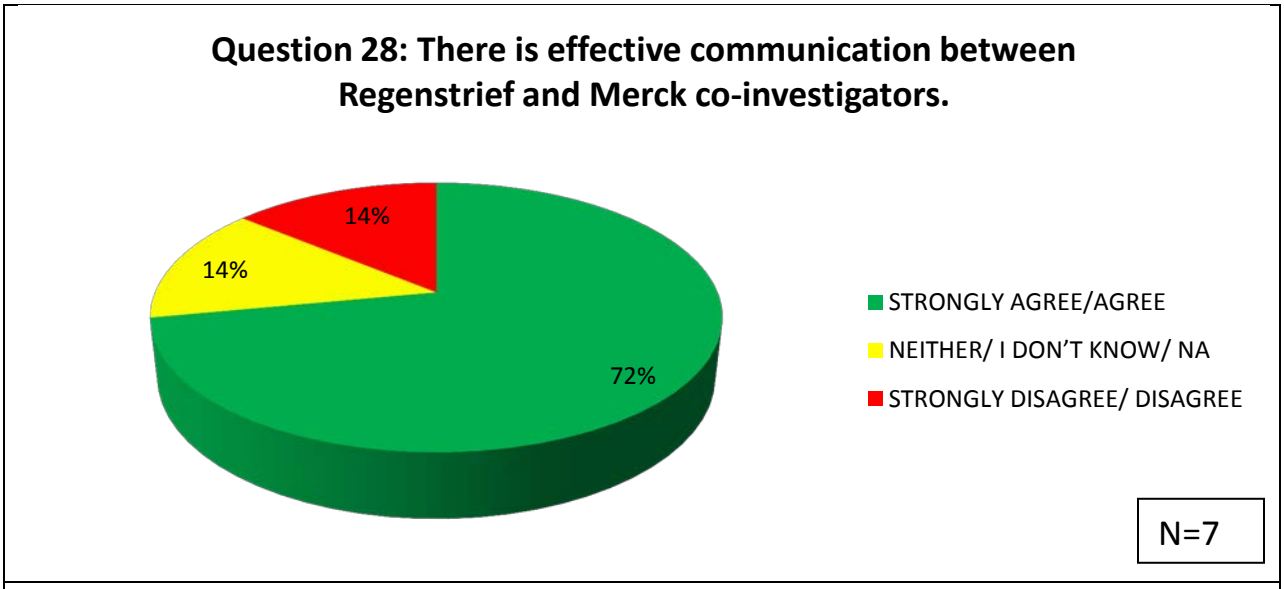
However, given the available responses, we reasonably conclude that this benchmark has been MET.

BENCHMARK 21: Widely publicize the partnership agreement and collaborative opportunities to the public and employees.



- Jury's Out: Benchmark has not been clearly MET nor NOT MET
- 46% of respondents Neither Agree nor Disagree or Don't Know/NA
- 20% of respondents disagree or strongly disagree with the statement

BENCHMARK 22: Establish procedures for frequent and effective communication between partners.



- Benchmark MET

BENCHMARK 23: Ensure both partners are aware of other partnerships each may be involved in.

No survey data were sought. Additionally, there isn't any evidence in the documents we've been provided with that suggest each partner knows of other formal partnerships the partner may be engaged in. However, this lack of evidence does not confirm the benchmarks has not been met but simply there isn't any evidence suggesting one way or the other. Inconclusive findings.

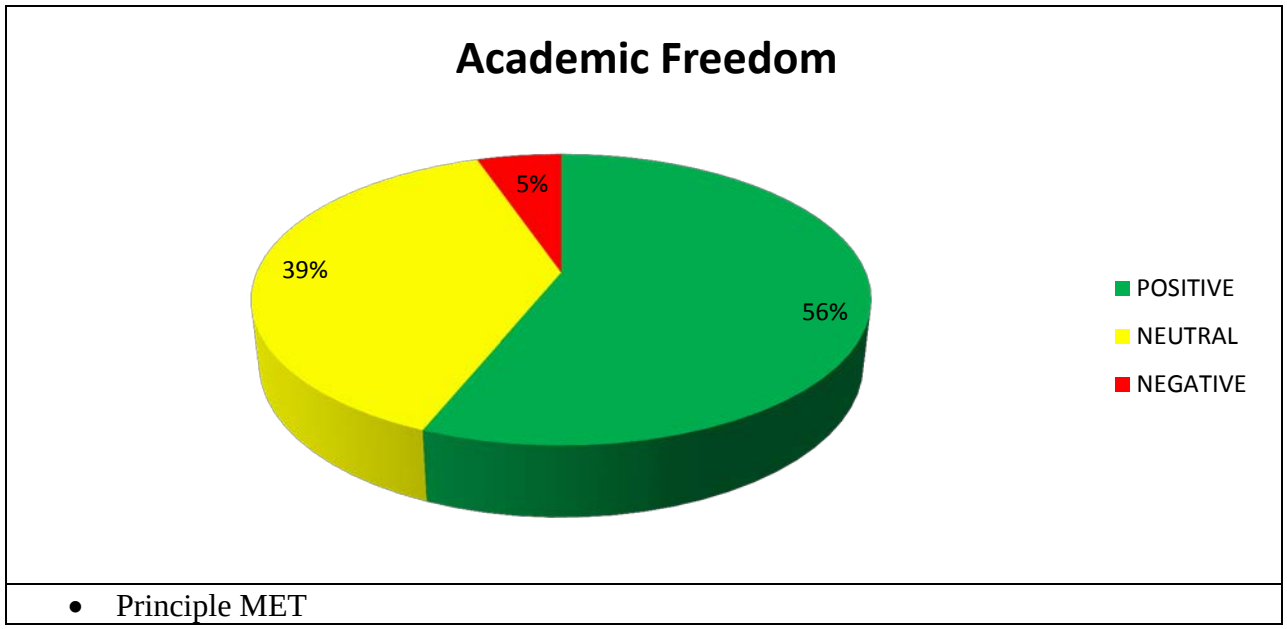
B. General Findings

We compiled the raw data from each question according to the principle that is associated with its analogous benchmark to ascertain general findings. To determine whether or not the principle has been MET, NOT MET, or JURY's OUT we used the following thresholds:

	POSITIVE
MET	≥ 50%
NOT MET	< 30%
JURY'S OUT	30% - 49%

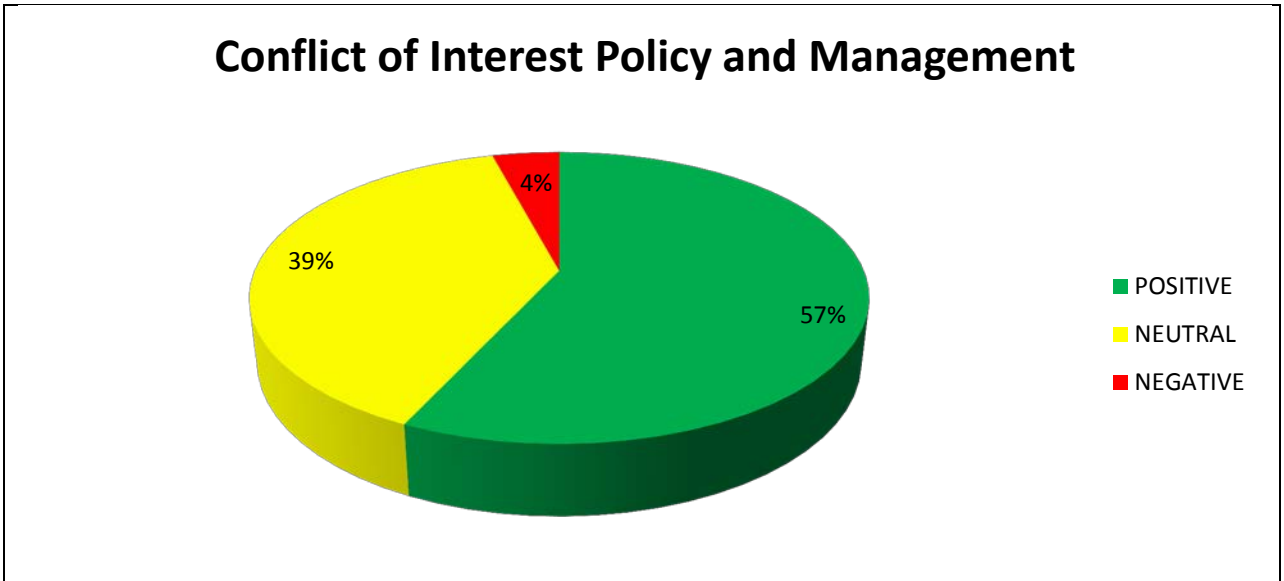
The term positive means the response is in agreement with the given benchmark.

ACADEMIC FREEDOM



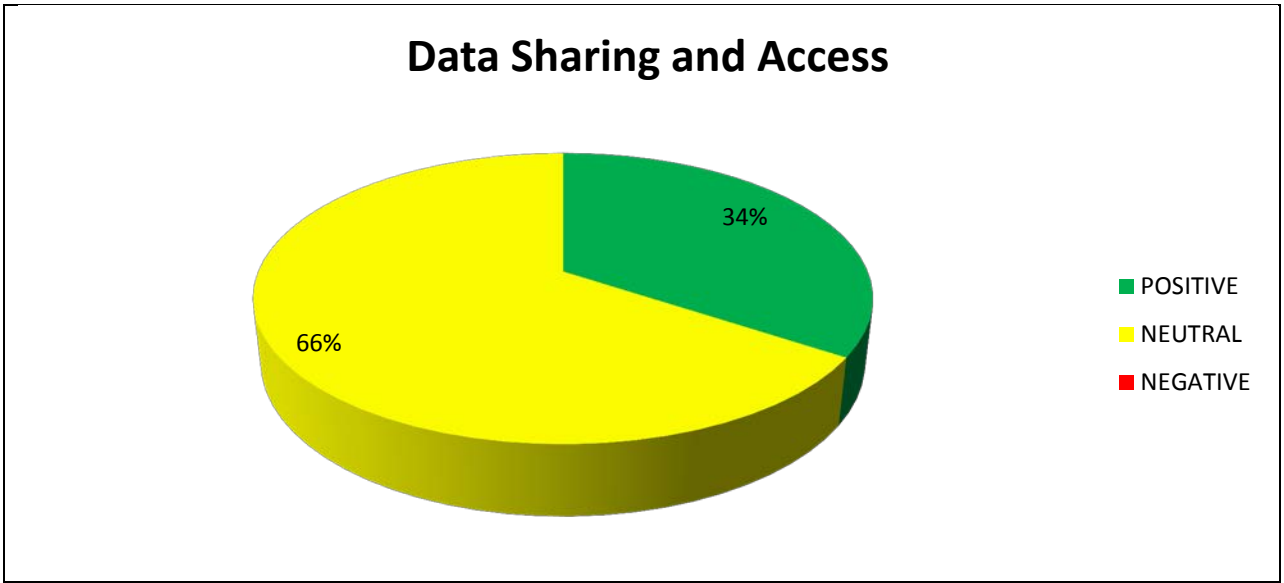
- Principle MET

CONFLICT OF INTEREST POLICY AND MANAGEMENT



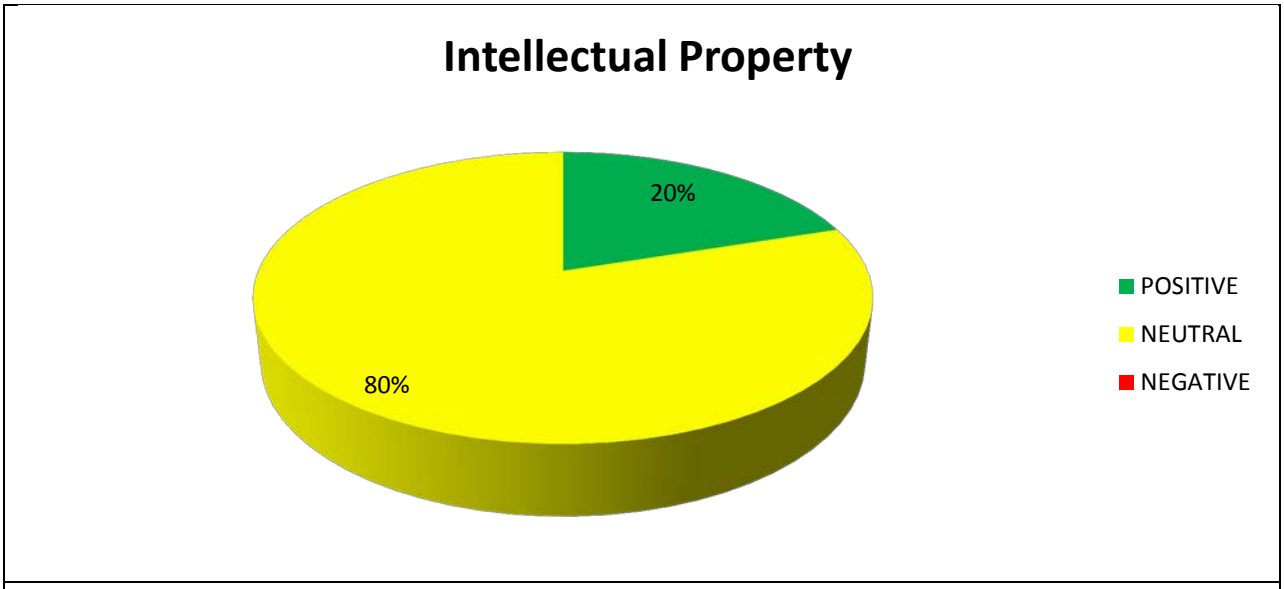
- Principle MET

DATA SHARING AND ACCESS



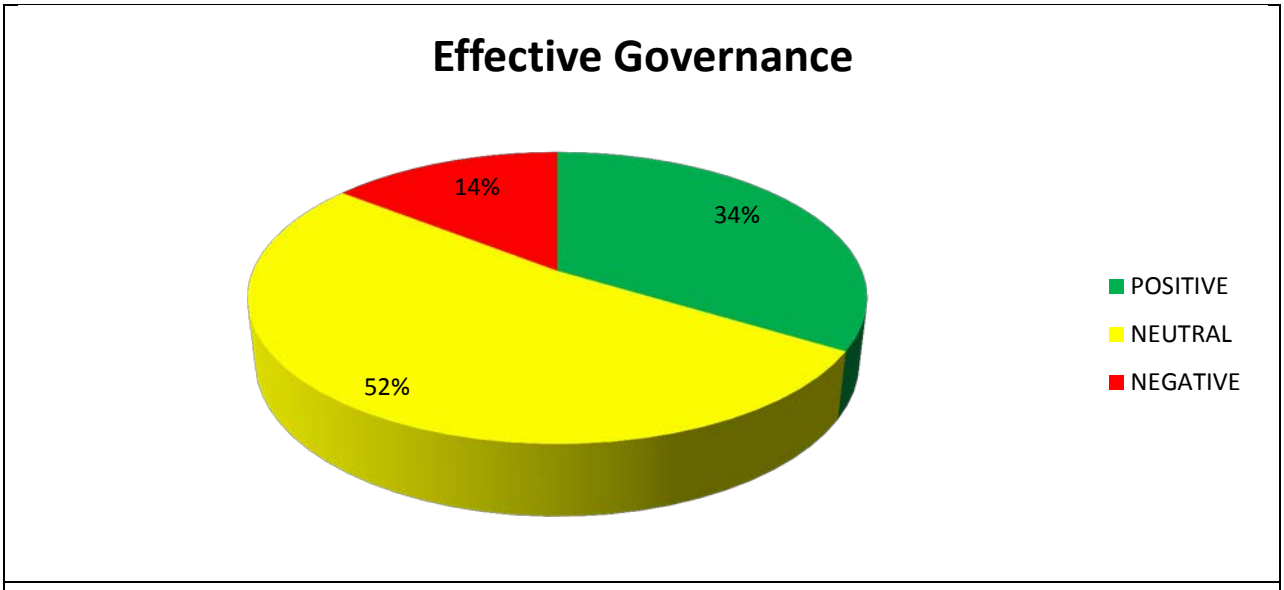
- Jury's Out: Principle has not been clearly MET or NOT MET

INTELLECTUAL PROPERTY



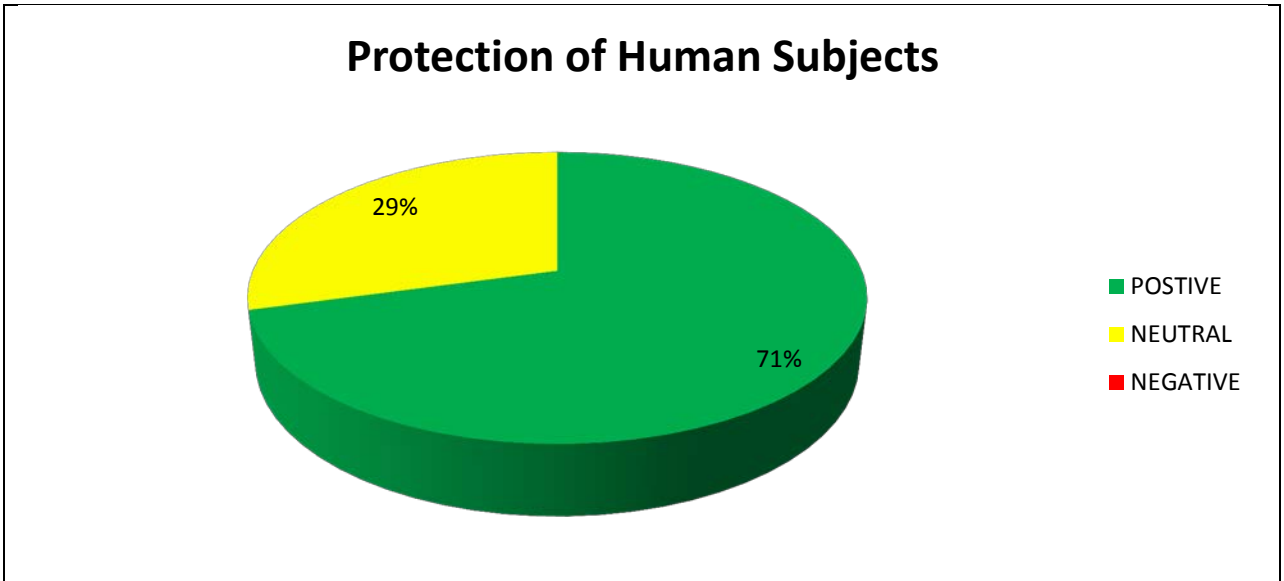
- Principle NOT MET

EFFECTIVE GOVERNANCE



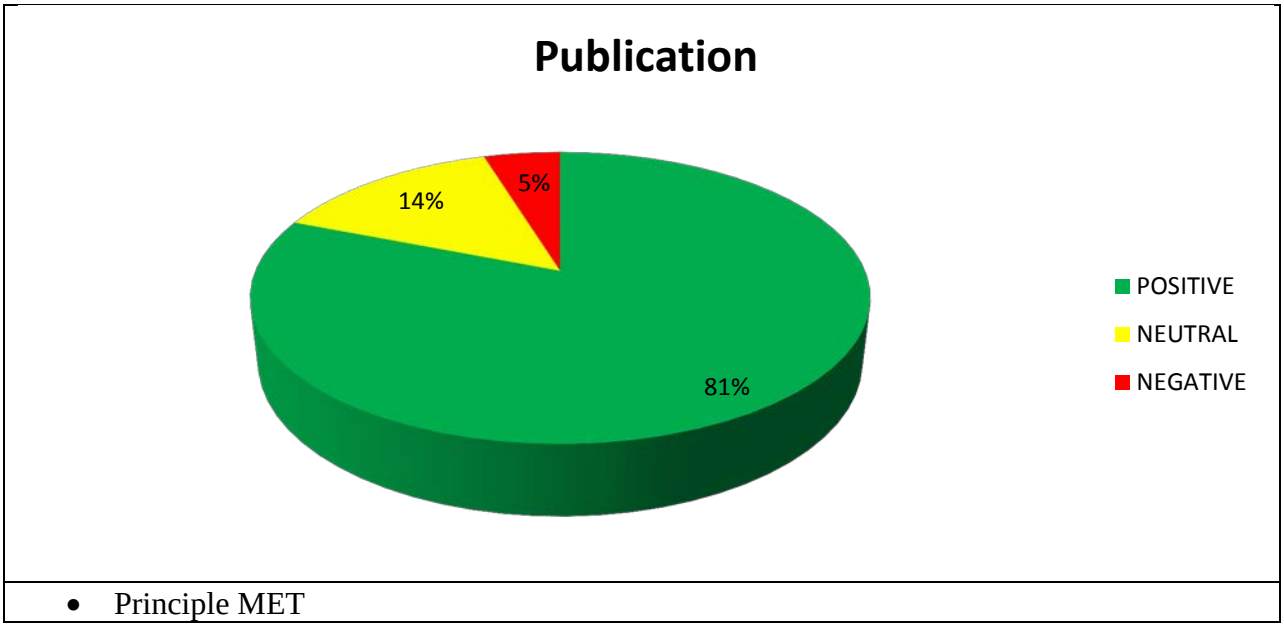
- Jury's Out: Principle has not been clearly MET nor NOT MET
- 52% of respondents gave responses that were neutral towards effective governance concerns

PROTECTION OF HUMAN SUBJECTS



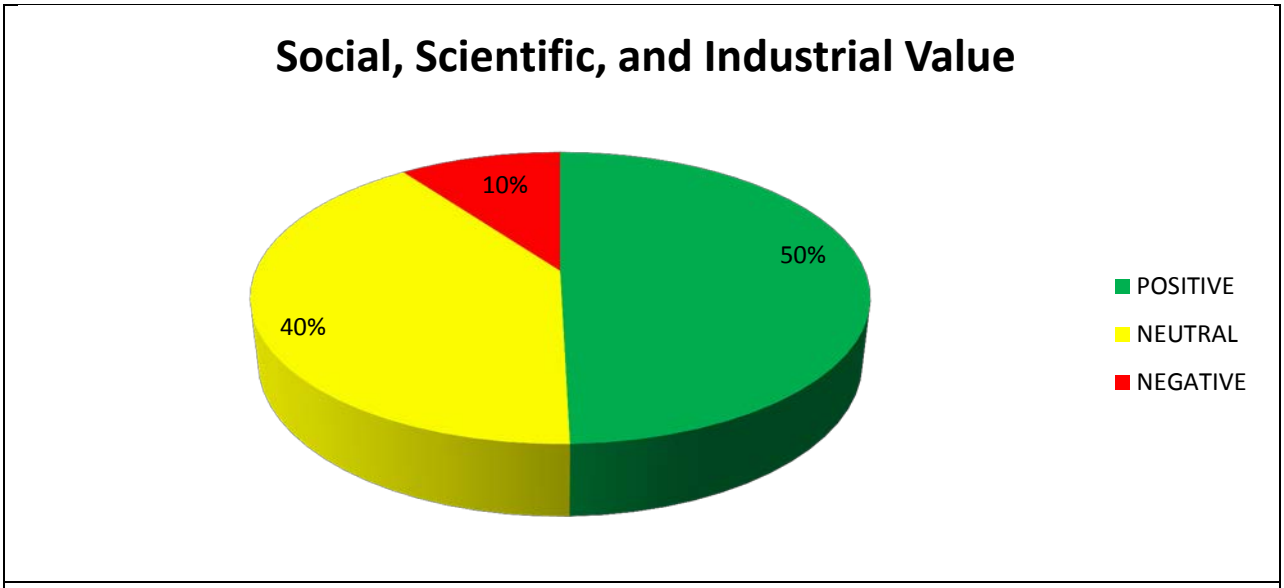
- Principle MET

PUBLICATION



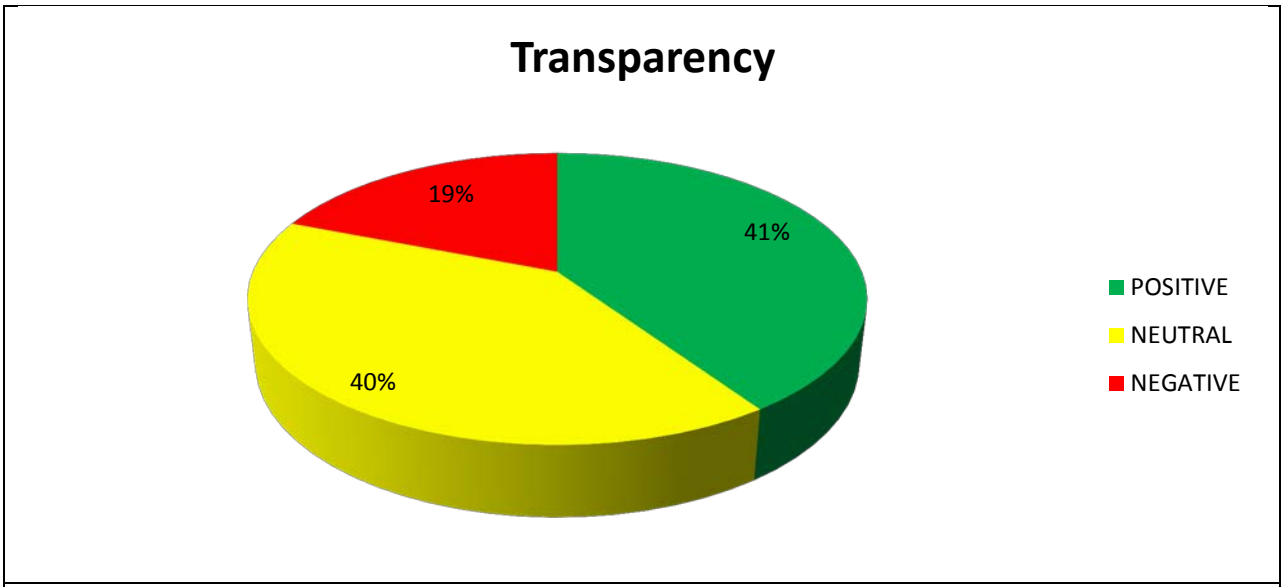
- Principle MET

SOCIAL, SCIENTIFIC AND INDUSRIAL VALUE



- Principle MET

TRANSPARENCY



- Jury's Out: Benchmark has not been clearly MET nor NOT MET

A. Summary of Findings

Of the 23 benchmarks, we concluded that

- **12 have BEEN MET** (Benchmarks #2, 5, 10, 11, 13, 14, 15, 16, 18, 19, 20, 22),
- **4 have NOT BEEN MET** (Benchmarks #7, 8, 9, 12), and
- **6 benchmarks, the JURY'S OUT** (Benchmarks #1, 3, 4, 6, 21).
- **4 were not applicable** to the survey format, but based on the research team's consensus opinion,
    - **2** benchmarks **have BEEN MET** (Benchmarks #10, 11)
    - **2** benchmarks, the **JURY'S OUT** (Benchmarks #17, 23).

Of the 9 principles, we found that

- **5 have BEEN MET** (Academic Freedom; Conflict of Interest Policy and Management; Protection of Human Subjects; Publication; Social, Scientific, and Industrial Value),
- **2 have NOT BEEN MET** (Intellectual Property; Data Sharing and Access),
- **2** principles **the JURY'S OUT** (Effective Governance; Transparency).

Included in Appendix 6 (pg. 76) is a visual summary/"report card" of these results.

B. Limitations.

1. The response rate of 38% was low, as were the number of survey participants making it difficult to report these results as representative of all Regenstrief Scientists and Affiliates.
2. The standards for determining whether a benchmark or principle was met, not met, or jury's out was subjective to a great extent. That said, raising the percentage of agree/strongly agree to 60%, 75%, 95% (for example) as the standard by which a benchmark was met; or lowering the percentage of agree/strongly agree to 25%, 20% or 10% (for example) as the standard by which a benchmark was assessed to have not been met would have changed the results dramatically.
3. The method for determining whether a principle was met, not met, or jury's out may have been skewed due to the varying number of respondents among the questions. Thus, whether or not a principle was met was largely determined by the responses given in questions with the greatest number of respondents.
4. Despite the conceptual relevance, the heterogeneity of the questions and benchmarks that fall under a given principle means that the results of aggregating the data by principles should be interpreted loosely and used only as a baseline for a future review. At times, this also produced what seems to be a qualitative disparity in the specific findings and general findings.
5. These results are based almost exclusively on how Regenstrief investigators think the partnership matches up with the principles and benchmarks for ethically credible partnerships. As such, what may otherwise be achievement in a benchmark given only

data from the contract and key leadership informants, this review relied on the attitudes and perspectives—however informed—of Regenstrief investigators to judge the partnership based on our standards.

6. The relative uniqueness of this partnership (e.g. bioinformatics-based, Regenstrief as a support organization to the IU School of Medicine) means that this review and the standards used to judge it may be idiosyncratic, thus questioning generalizability to other academic-industry partnerships.
7. In times where no survey data was not sought, the writers of this report used consensus to determine whether the benchmark had been met or not. This is a subjective measure based only on internal discussion and what evidence was available to us.

V. Recommendations

Based on these findings, we make the following recommendations:

Recommendation #1: **Increase transparency by providing more opportunities for investigators to become educated about the partnership, especially in areas where lack of understanding could potentially lead to an erosion of trust among Regenstrief investigators**.

The areas of notable concern for this recommendation include Benchmarks #7 and 8. While there is evidence in the contract that these principles and benchmarks have been addressed, it is imperative that investigators know how intellectual property is protected and awarded in partnership projects and also, the agreed upon terms for data use by Merck in partnership projects. Additionally, other benchmarks that we found to have been NOT MET or for which the JURY'S OUT (Benchmarks #1, 2, 4, 6, 9, 12, 21) included high rates of no opinion or little knowledge on the matter. As such, education in these areas may ameliorate these issues.

We imagine that this can be achieved in a number of ways:

- In addition to the handbook that emailed to all eligible investigators, Regenstrief could hold an annual meeting where projects recently completed or being conducted in the partnership are reported to all investigators. This could spur interest in the partnership and also correct misinformed opinions about the partnership.
- At the conclusion of this review, hold a "town hall" meeting where these results could be presented to Regenstrief investigators and leadership would be able to provide information where seemingly problematic issues arise and investigators could further elaborate on the identified areas.
- At the conclusion of this review, write a memorandum of the findings joined with educational information on the partnership to be sent to all Regenstrief investigators.

Recommendation #2: **Increase transparency in the project selection process by establishing and making explicit to all investigators how projects are selected and what criteria are used**.

While Benchmarks #9 and #12 were addressed in Recommendation #1, we feel that these benchmarks need specific attention given that they comprise 2 of the 4 benchmarks that were NOT MET and that education measures alone may not remedy the issues here.

We believe that this could be achieved in a number of ways:

- Providing details about the process, and include it in the investigator handbook for the partnership.
- Allow an unaffiliated and unbiased observer to sit in on the project selection meetings in order to form an objective description of the process. This person would ideally be qualified to offer recommendations on improving process after seeing how the committee selects projects.

<u>Recommendation #3</u>: **Regenstrief should seek additional ways to engage more investigators in the partnership.**

We also found that despite what we feel is a process that lends itself to investigator-initiated science, the survey results indicate otherwise. Only 40% of those surveyed agreed or strongly agreed with the statement that the partnership promotes investigator-initiated science (Question 7). Additionally, less than half of respondents disagreed or strongly disagreed with the statement that the partnership pressures faculty to work outside their own self-defined research area (Question 13). Notably however, of those surveyed who had been supported by the partnership, 7 out of 8 either agreed or strongly agreed with the statement in Question 7 and 6 out of 8 disagreed or strongly disagreed with the statement in Question 13.

This could be accomplished by:

- Distinguishing announcements for this call for proposals from all others (e.g., NIH, PCORI, etc) so as to draw attention to them in Regenstrief email.
- Holding an annual Regenstrief WIP on the research outcomes of the partnership and use the opportunity to discuss the partnership and the next call for proposals.

<u>Recommendation #4</u>: In addition to the extant conflict of interest disclosure policies required by the IU School of Medicine, Regenstrief should establish and publicize widely partnership-specific conflict of interest policies.

Only 3 of 7 respondents who have been supported by the partnership could confirm that the partnership has effective mechanisms to manage conflicts of interest. While this question was not posed to the entire population surveyed, we feel that this demographic—by virtue of their participation in the partnership—would likely have the best chance of knowing whether or not conflicts of interest are effectively managed. Given this data, we make the recommendation above. While we feel the existing IU COI policies are sufficient, additional steps taken in this area may help to curb or quell a perception that COIs are inherent problems in academia-industry partnerships.

We believe this could be accomplished in a number of ways:

- Requesting COI self-disclosure from investigators akin to the IU policy when selected projects are funded.
- Requesting COI self-disclosure from investigators akin to the IU policy as a part of the initial proposal process. That is, an essential part of the proposal submitting process includes disclosing potential conflicts of interest.
- Issue a join position paper by Regenstrief and Merck on conflicts of interests and circulate it to relevant bodies and personnel.

<u>Recommendation #5</u>: Regenstrief should continue to reach out to investigators who may have concerns about the partnership and provide opportunities for learning, consultation and input.

This could be accomplished in a number of ways:

- Conduct a more comprehensive assessment of Regenstrief investigator knowledge and attitudes about this partnership and other partnerships, which includes one-on-one interviews or focus groups.
- Providing an open and non-threatening opportunity for investigators to express concerns about the partnership.
- Ensure that Regenstrief investigators are aware of and encouraged to make use of the CTSI Bioethics and Subject Advocacy Program consultation service.

APPENDIX 1

INDIANA UNIVERSITY
CENTER FOR BIOETHICS

Principles and Benchmarks for Ethically Credible Partnerships

Principles

Academic Freedom—refers to researchers, their interests, and their ability to pursue these independent interests as they see fit.

Conflict of Interest Policy and Management—refers to the competing or potentially competing interests and commitments of involved parties and persons, including financial conflicts of interests and conflicts of commitment. Managing such conflicts can be achieved through establishing tested methods for assessing potential conflicts of interests.

Data Sharing, Access— includes the importance of developing mutually agreed upon procedures for accessing each partner's data and other relevant clinical information in order to facilitate research.

Intellectual Property—this principle emphasizes the need to protect the property rights of each partner and investigators that predate the partnership and arise from work conducted within it.

Effective Governance—emphasizes the importance of effectively managing and leading the partnership. Governance addresses legal issues, administrative duties/obligations, priority setting, and fosters fairness, cooperation, and communication within the partnership. Effective governance should be bureaucratically structured in a way that sufficiently leads and enables research and is minimally burdensome. The rules and conditions set by and for the partnership's governance entities would preferably be set at the outset of the collaboration.

Protection of Human Subjects—establishes that collaborative research should adhere to the highest ethical standards, including compliance with applicable standards relating to the privacy and confidentiality of personal health information.

Publication—focuses on issues of authorship and how research findings are to be published, disseminated, or made known to others. Usually this principle can be satisfied through publishing in the peer-reviewed literature.

Social, Scientific, and Industrial Value—refer collectively to the benefits for and goals of each partner in the collaboration. These include industry values, scientific values, medical values, and social values. The partnership should seek to create new knowledge that will improve the well-being of citizens and be of significant importance to the academic and industrial partner.

Transparency—concerns the degree to which the collaboration is known by and visible to relevant parties and the public including its function and initial agreement. Transparency is primarily achieved through open communication.

Definition of Benchmarks

Benchmarks are specific standards or practices that are used to confirm the extent to which a principle is satisfied. The benchmark framework is adapted from Emanuel et al (2004) and the present draft of benchmarks seeks to establish practical and achievable baselines for Industry-Academia collaboration while still allowing for considerable freedom as to how they may be achieved. The substance of the benchmarks is pulled from the literature on this topic, admirable items within the Regenstrief-Merck contract, and the IU Center for Bioethics' own experience and expertise in policy and ethics.

PRINCIPLES	BENCHMARKS
Academic Freedom	1. Promote investigator-initiated science and protect the ability to attract and maintain federal research support. 2. Permit investigators to initiate or continue collaboration with any other qualified group, person, or entity. 3. Ensure that all investigators involved in the partnership are given equal opportunity to submit proposals for funding. 4. Avoid obligating faculty to work outside their own self-defined scientific area.
Conflict of Interest Policy and Management	5. Protect students, fellows, and post-doctoral fellows involved in collaborative projects from exploitation. 6. Ensure that effective mechanisms exist to eliminate, control or manage conflicts of interest in the partnership.
Intellectual Property	7. Ensure all investigators and both partners retain their proprietary and intellectual property rights throughout and after the partnership.
Data Sharing, Access	8. Ensure that data sharing arrangements are explicit and that all rights to access data are fairly negotiated at the outset of the partnership.
Effective Governance	9. Establish parameters for what type of projects will and will not be funded (e.g. add-on projects, training, pilot studies). 10. Create ways to protect each party from an unexpected end to the partnership. 11. Assess formally the efficiency, effectiveness, and achievements of the partnership on an annual basis. 12. Ensure that clear, comprehensive, and efficient procedures exist for all governance entities of the partnership and are known to all investigators.
Protection of Human Subjects	13. Ensure that all investigators, staff and other participants in the partnership have adequate training in the responsible conduct of research and related ethical issues. 14. Ensure that all projects in the partnership aim to satisfy the highest ethical standards.
Publication	15. Ensure the right of all researchers associated with the partnership to publish. 16. Disseminate all research results at the conclusion of collaborative studies in a timely fashion. 17. Ensure authorship follows ICMJE guidelines.
Social, Scientific, and Industrial Value	18. Maintain competitive advantage in the specified research domains. 19. Structure the research to maximize potential benefit for communities and society. 20. Structure the partnership to have the best chance of benefiting both partners and harming neither.
Transparency	21. Widely publicize the partnership agreement and collaborative opportunities to the public and employees. 22. Establish procedures for frequent and effective communication between partners. 23. Ensure both partners are aware of other partnerships each may be involved in.

APPENDIX 2

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Annotated Bibliography

Academic-Industry Partnerships

(Prepared by: Josh Rager, Avril Rua Pitt, December 2013)

Executive Summary

Academic-Industry partnerships have been on the rise in the last couple of decades. These relationships have been said to have two major benefits: increases patient access to medical advances, and accelerates medical innovation. (Johns et al., 2003). Despite these benefits, these relationships have raised several ethical, legal and policy issues spanning from intellectual property, to restrictions and disclosures of conflicts of interest and publication of results. The overarching view held by authors is that there is a need to protect investigators and academic institutions from undue influence from industry sponsors that may arise from the unique position created by divergent interests. The literature suggests that a lot still remains to be done in order to protect the integrity of research, and promote the conduct of research between academia and industry.

Academic Freedom

Carpenter Jr, W. T., Koenig, J. I., Bilbe, G., & Bischoff, S. (2004). At Issue: A Model for Academic/Industry Collaboration. *Schizophrenia bulletin*, *30*(4), 997.

Carpenter et al describe a collaboration between the Maryland Psychiatric Research Center at the University of Maryland, Baltimore and Novartis Pharma AG. The authors outline the main concerns of each party preceding the agreement and discuss the nature and content of the collaboration's contract as well the anticipated benefits for each party. Additionally, the authors describe the function and structure the collaboration in practice as well as issues that arose and how these were resolved. In the postscript, the authors reflect on the early termination of the collaboration.

Vitiello, B., Heiligenstein, J. H., Riddle, M. A., Greenhill, L. L., & Fegert, J. M. (2004). The interface between publicly funded and industry-funded research in pediatric psychopharmacology: opportunities for integration and collaboration. *Biological Psychiatry*, *56*(1), 3-9. doi: http://dx.doi.org/10.1016/j.biopsych.2004.03.011

The authors of this paper stress the importance of investigator-initiated grants in industry-funded research and discuss some of the limitations involved in industry sponsorships including the need for unfettered access to databases and issues and biases arising in the publication of collaborative findings.

Conflict of Interest

Bekelman, J. E., Li, Y., & Gross, C. P. (2003). Scope and impact of financial conflicts of interest in biomedical research: a systematic review. *JAMA: the journal of the American Medical Association*, *289*(4), 454-465. doi: 10.1001/jama.289.4.454

Bekelman et al reviewed quantitative studies on the extent, impact and management of financial conflicts of interest, concluding that such financial relationships are pervasive and problematic. Areas addressed include the effect of industry sponsorship on the study conclusion, design, and quality and investigator behavior. Studies on the management of financial COIs, noting that this is an area that is largely discretionary.

Boyd, E. A., & Bero, L. A. (2000). Assessing faculty financial relationships with industry. *JAMA: the journal of the American Medical Association*, *284*(17), 2209-2214. doi: 10.1001/jama.284.17.2209

This case study of the University of California, San Francisco (UCSF) disclosure forms and official documents from the Office of Research Administration sought to analyze the extent of personal financial relationships with sponsors, their nature and efforts made to address disclosures and perceived conflicts of interest. Discussed in the article are the characteristics of positive financial disclosures, institutional responses and management strategies.

Kuszler, P. C. (2001). Curing conflicts of interest in clinical research: impossible dreams and harsh realities. In *Widener L. Symp. J.* (Vol. 8, p. 115).

This in-depth article discusses different sources of funding of clinical research (federal, private sponsor, third party payer, patient out-of pocket).; financial and non-financial conflicts of interest; and current methods of addressing financial conflict of interest (laws and regulations, institutional policies – disclosure v. prohibition). Ways of redressing conflicts of interest are then discussed.

Lo, B., Wolf, L. E., & Berkeley, A. (2000). Conflict-of-Interest Policies for Investigators in Clinical Trials. *New England Journal of Medicine*, *343*(22), 1616-1620. doi:10.1056/NEJM200011303432206

After analyzing conflict of interest policies in 10 US medical schools that receive the largest amount of NIH funding, this article concludes that these policies vary greatly from institution to institution. These policies were also weaker than other industry-sponsored clinical trials. The

authors conclude that there should be higher standards for university based clinical trials than commercial organizations.

Martin, J. B., & Kasper, D. L. (2000). In Whose Best Interest? Breaching the Academic–Industrial Wall. *New England Journal of Medicine, 343*(22), 1646-1649. doi:10.1056/NEJM200011303432213

In this article, the authors note an increase in industry funded research conducted by academic institutions over the last couple of decades, which has led to a breach in the wall between the academic and industrial worlds. After analyzing the change in nature between academic-industry partnerships and the disadvantages of breaching this academic wall, the paper concludes that the criteria for conflict of interest applied in the public sector are appropriate for the academic sector as well. Investigators should be free from any influence by the industry sponsor. In cases of patient-oriented research, the authors suggest a minimal financial relationship for an investigator to research on a product that may be commercialized.

Taylor, P. L. (2013). Innovation Incentives or Corrupt Conflicts of Interest? Moving Beyond Jekyll and Hyde in Regulating Biomedical Academic-Industry Relationships. *Yale J. Health Pol'y L. & Ethics, 13,* 135-198.

Taylor assesses the present COI regulatory framework for academic-industry collaborations and critiques its lack of scrutiny from a number of legal perspectives. Suggesting reform, Taylor offers a way to rectify the defects, proposes collecting data on COI regulation to better inform choices on forms of collaboration, offers a set of interim rules until such collection can be performed, and recommends the creation of “how-to” models for collaborations and anticipating COIs.

Data Sharing, Access, and Intellectual Property

Blumenthal, D., Causino, N., Campbell, E., & Louis, K. S. (1996). Relationships between Academic Institutions and Industry in the Life Sciences — An Industry Survey. *New England Journal of Medicine, 334*(6), 368-374. doi:10.1056/NEJM199602083340606

Blumenthal et al considered the characteristics of these relationships between academic institutions and industry, the benefits realized by companies, the difficulties of collaboration arising from various sectors including internal policies and intellectual property, and withholding of data. The paper discusses both the benefits and challenges of such relationships. (Note: This is a 1996 article.)

Melese, T., Lin, S. M., Chang, J. L., & Cohen, N. H. (2009). Open innovation networks between academia and industry: an imperative for breakthrough therapies. *Nature Medicine, 15*(5), 502-507.

Melese et al describe the various models of industry-academia collaborations and suggest four steps for future collaborations to actualize the potential outcomes of such partnerships. The authors suggest that each party should weigh the value of their assets with those of their potential partner and concurrently assess these values with the value in the potential, collaborative outcome. The authors also suggest that industry-academia collaborations should be managed like an investment portfolio, adopt a new attitude about sharing information, and seek to create new models for collaborative innovation.

Moses, H., Perumpanani, A., & Nicholson, J. (2002). Collaborating with industry: choices for Australian medicine and universities. *Medical Journal of Australia*, *176*(11), 543-546.

This article focuses on ways of enhancing Australia's collaboration between industry, Australian medicine and universities. The growth of collaboration in the US is discussed. The authors categorize conflicts into 6: conflict of commitment, conflict of interest, breach of trust, distraction from basic discovery, compromised academic independence and different mandates. The Australian perspective is then offered addressing legislative obstacles, sources of funding and scale, noting that some Australian inventions migrate to the US which has more funding opportunities, larger markets and stronger legislative frameworks.

Jones, R., Wilkinson, D., Lopez, O., Cummings, J., Waldemar, G., Zhang, R., . . . Gauthier, S. (2011). Collaborative research between academia and industry using a large clinical trial database: a case study in Alzheimer's disease. *Trials, 12*(1), 233.

Jones et al describe a collaborative effort between Pfizer and a group of academic researchers to investigate novel aspects and treatments of Alzheimer's disease using Pfizer's pre-existing clinical databases. The authors detail how the academic team was assembled, how the specific investigations were agreed upon, and how the projects and collaboration were managed. Additionally, the authors report the successes of the collaboration as evidenced in published articles and advocate the scientific value of data mining.

See also:

Mello, M. M., Clarridge, B. R., & Studdert, D. M. (2005). Academic Medical Centers' Standards for Clinical-Trial Agreements with Industry. *New England Journal of Medicine, 352*(21), 2202-2210. doi:10.1056/NEJMsa044115

Effective Governance

Mello, M. M., Clarridge, B. R., & Studdert, D. M. (2005). Academic Medical Centers' Standards for Clinical-Trial Agreements with Industry. *New England Journal of Medicine, 352*(21), 2202-2210. doi:10.1056/NEJMsa044115

This article studied institutional standards for restricting investigator control over clinical-trials agreements in 107 institutions, revealing a great degree of variance in institutional procedures.

The paper analyzes acceptability of restrictive contractual provisions, tensions in negations and disputes with industry sponsors, and tools and practices used to facilitate negotiations with industry sponsors. Several strategies are proposed, among them the need for information sharing among institutions with the aim of building appropriate standards.

Schulman, K. A., Seils, D. M., Timbie, J. W., Sugarman, J., Dame, L. A., Weinfurt, K. P., . . . Califf, R. M. (2002). A National Survey of Provisions in Clinical-Trial Agreements between Medical Schools and Industry Sponsors. *New England Journal of Medicine, 347*(17), 1335-1341. doi:10.1056/NEJMsa020349

This survey on the content of academic-industry clinical trial agreements contains provides scores for site agreements and coordinating center agreements between medical centers and industry sponsors. The survey revealed that some academic institutions do not adhere to the International Committee of Medical Journal Editors' (ICMJE) Uniform Requirements for Manuscripts submitted to Biomedical journals.

The Ad Hoc Committee on Industrial Partnership Review. (2003). MIT's Industrial Partnerships. Internal Report. Massachusetts Institute of Technology. http://web.mit.edu/chancellor/IndlPartnershipsRpt.pdf

This is an internal report of an ad hoc committee at MIT created to review the university's numerous partnerships with industry. Included in this report is a summary and history of MIT's partnerships as well as lists and discussions of the benefits and risks of MIT's industry collaborations. The committee's report also includes a description of best practices in industry-academia collaborations and recommendations for future partnerships.

Joint Project of the National Council of University Research Administrators and the Industrial Research Institute. (2006). Guiding Principles for University-Industry Endeavors: National Council of University Research Administrators.

Joint Project of the National Council of University Research Administrators and the Industrial Research Institute. (2006). Living Studies in University-Industry Negotiations: Applications of the Guiding Principles for University-Industry Endeavors. B. M. K. James J. Casey Jr., National Council of University Research Administrators.

University-Industry Demonstration Partnership Researcher Guidebook Worling Group. (2012). Researcher Guidebook: A Guide for Successful Institutional-Industrial Collaborations. Atlanta, Georgia Tech Research Corporation.

University-Industry Demonstration Partnership Working Group. (2012). Partnership Continuum: Understanding & Developing the Pathways for Beneficial University-Industry Engagement. Atlanta, Georgia Tech Research Corporation.

University-Industry Demonstration Partnership. (2012). Contract Accords 1-10: For University Industry Sponsored Agreements. Atlanta, Georgia Tech Research Corporation.

University-Industry Demonstration Partnership. (2013). Contract Accords 11-15: For University Industry Agreements. Atlanta, Georgia Tech Research Corporation.

These publications are guidebooks created and compiled by the University-Industry Demonstration Partnership. Included in these documents are guiding principles for university-industry collaborations, case studies, materials for both academic and industrial researchers new to these collaborations, and methods for constructing fair and comprehensive contracts. All of these publications can be found at http://sites.nationalacademies.org/PGA/uidp/PGA_055253

See also:

Carpenter Jr, W. T., Koenig, J. I., Bilbe, G., & Bischoff, S. (2004). At Issue: A Model for Academic/Industry Collaboration. *Schizophrenia bulletin*, *30*(4), 997.

Melese, T., Lin, S. M., Chang, J. L., & Cohen, N. H. (2009). Open innovation networks between academia and industry: an imperative for breakthrough therapies. *Nature Medicine*, *15*(5), 502-507.

Protection of Human Subjects

Klitzman, R. (2013). How IRB Leaders View and Approach Challenges Raised by Industry-Funded Research. *IRB: Ethics & Human Research*, *35*(3), 9-17.

Klitzman reviews responses by IRB chairs, administrators and members on challenges they face in industry-funded research. It also reviews IRB decisions and responses to assessing and weighing problematic studies with perceived low social benefit. Issues mentioned include uncertainty as to the suitability of an institution in conducting a study, studies that diminish the scientific utility of research, and whether some industry funded studies are even research.

Publication

Bodenheimer, T. (2000). Uneasy Alliance — Clinical Investigators and the Pharmaceutical Industry. *New England Journal of Medicine*, *342*(20), 1539-1544. doi:10.1056/NEJM200005183422024

After a brief background on the clinical drug trial system and the tensions and shift from academic medical centers to contract-research organizations and site-management organizations, the article discusses the industry-investigator relationship with regard to trial design, data analysis, publication of results and control of publication, and authorship. The authors conclude

that academic-industry drug trials have the potential of balancing the commercial interest of industry and scientific goals of investigators.

Wager, E., Field, E. A., & Grossman, L. (2003). Good publication practice for pharmaceutical companies. *Current Medical Research and Opinion*, *19*(3), 149-154. doi:10.1185/030079903125001767

The authors propose Guidelines on Good Publication Practice (GPP) aimed at ensuring that industry sponsored clinical trials by pharmaceutical companies are published ethically and responsibly. The article describes how these guidelines came about, the need for more guidelines, issues addressed by the GPP, and how they should be applied. The guidelines apply to phase II, III and IV trials, and exclude independently published studies.

See also:

Carpenter Jr, W. T., Koenig, J. I., Bilbe, G., & Bischoff, S. (2004). At Issue: A Model for Academic/Industry Collaboration. *Schizophrenia bulletin*, *30*(4), 997.

Blumenthal, D., Causino, N., Campbell, E., & Louis, K. S. (1996). Relationships between Academic Institutions and Industry in the Life Sciences — An Industry Survey. *New England Journal of Medicine, 334*(6), 368-374. doi:10.1056/NEJM199602083340606

Schulman, K. A., Seils, D. M., Timbie, J. W., Sugarman, J., Dame, L. A., Weinfurt, K. P., . . . Califf, R. M. (2002). A National Survey of Provisions in Clinical-Trial Agreements between Medical Schools and Industry Sponsors. *New England Journal of Medicine, 347*(17), 1335-1341. doi:10.1056/NEJMsa020349

Vitiello, B., Heiligenstein, J. H., Riddle, M. A., Greenhill, L. L., & Fegert, J. M. (2004). The interface between publicly funded and industry-funded research in pediatric psychopharmacology: opportunities for integration and collaboration. *Biological Psychiatry, 56*(1), 3-9. doi: http://dx.doi.org/10.1016/j.biopsych.2004.03.011

Social, Scientific, and Industrial Value

Clackson, T. (2006). Translational Research in Academia and Industry. *Experimental Biology and Medicine, 231*(11), 1685-1689.

This article considers two case studies: Epidermal Growth Receptor Biomarkers, and Chemical Dimerization. Factors necessary for successful academic-industry relationships are considered.

Johns, M. M., Barnes, M., & Florencio, P. S. (2003). Restoring balance to industry-academia relationships in an era of institutional financial conflicts of interest. *JAMA: the journal of the American Medical Association, 289*(6), 741-746.doi: 10.1001/jama.289.6.741

Johns et al concludes that industry-academic partnerships should not be allowed if they only serve the pecuniary interest of the holder without directly or materially furthering scientific advancements referred to as the justification test. The article discusses the nature and operation of financial conflicts of interest and strategies for dealing with them. It also proposes a justification test in order to reduce the appearance and potential of bias.

See also:

Blumenthal, D., Causino, N., Campbell, E., & Louis, K. S. (1996). Relationships between Academic Institutions and Industry in the Life Sciences — An Industry Survey. *New England Journal of Medicine, 334*(6), 368-374. doi:10.1056/NEJM199602083340606

Carpenter Jr, W. T., Koenig, J. I., Bilbe, G., & Bischoff, S. (2004). At Issue: A Model for Academic/Industry Collaboration. *Schizophrenia bulletin*, *30*(4), 997.

Transparency

See:

Carpenter Jr, W. T., Koenig, J. I., Bilbe, G., & Bischoff, S. (2004). At Issue: A Model for Academic/Industry Collaboration. *Schizophrenia bulletin*, *30*(4), 997.

APPENDIX 3

Introduction: [To be read out loud].

Thank you all for agreeing to meet with us today. Before we begin, we'd like preface our discussion with a reminder of the background to this review and outline what we'll be doing today.

In 2013, the IU Center for Bioethics was invited by Dr. William Tierney, President/CEO of the Regenstrief Institute to formally evaluate the Regenstrief Institute's role within the current Regenstrief-Merck partnership with the expectation that it be done on an annual basis, and the results be published in the peer reviewed literature. The evaluation is being done under contract to the IU Center for Bioethics.

The particular focus of the evaluation is Regenstrief's role in the partnership with the main goal being to provide substantive actionable recommendations to Regenstrief. In so doing, it is intended that this evaluation will aid in the ongoing Regenstrief-Merck partnership and that it will also become an exemplary model for other public-private collaborations undertaken by Regenstrief.

Part of the evaluation involves understanding and assessing the perspectives of key leaders involved in managing the Regenstrief-Merck Partnership. That is the focus of today's session.

You were selected as a participant because you are a member of the Regenstrief-Merck Steering and/or the Operations Committees. Today you will be asked to answer questions about the Regenstrief-Merck partnership.

To facilitate this discussion we will refer to a set of **ethical principles** and an accompanying list of **benchmarks** for model partnerships. They have been developed by the IU Center for Bioethics specifically for this project. We'll be asking you about how these benchmarks and principles are reflected in the Merck-Regenstrief partnership. We expect that they will stimulate discussion.

The session should last approximately 90 minutes to 2 hours. In addition to note-taking, we will be recording and transcribing the discussion for analysis. We will not identify individuals by name, and all audio recordings and transcriptions will be destroyed once we have completed the analysis. However, we do intend to publish a scholarly article based on the results of the overall evaluation and may include quoted material from this focus group in the publication. The IU IRB determined this project to be exempt from review.

Your participation in this study is completely voluntary, and if for any reason you wish to discontinue your participation today, you are welcome to leave. If any issues or concerns should arise after your participation in this study, you're welcome to raise them now or to follow up with me afterwards.

Are we ready to begin?

***

Lead-in question: The first principle is **academic freedom** which concerns researchers' ability to pursue their own, individual academic interests as they see fit. Do you feel this is important? Have you confronted any issues related to this? Was this something that you anticipated or thought about at the outset of partnership? What have you all done to promote and ensure academic freedom?

Probe on:

- Promoting investigator-initiated science and continued ability to attract federal research support
- Permitting investigators to initiate or continue partnerships with other qualified persons, groups or entities
- Ensuring all investigators have equal opportunity to submit for funding
- Not obligating faculty to work outside their own self-defined scientific area
- Others?

Follow-up: How well do you think the partnership has done promoting this? Have any issues arisen regarding this principle either within this group or among the investigators?

Lead-in question: The next principle is **Conflict of Interest** that is, managing the competing or potentially competing commitments and/or financial conflicts of involved parties and persons. Has this been a challenging issue for you? What measures have you all taken to eliminate, manage or control such potential (or actual) conflicts?

Probe on:

- Protecting students, fellows, and post-docs involved from exploitation
- Ensuring effective mechanisms exist to eliminate, control, or manage COIs.
- Others?

Follow-up: What mechanisms are in place? And, if any issues have arisen, how have you all dealt with them?

Lead-in question: The third principle concerns **protecting the intellectual property and proprietary** rights of each partner throughout and after the partnership, including fair data sharing and data access agreements. These issues were addressed in your contract with Merck. What have you all done to promote and ensure this principle? [4]

[4] At the time of the focus group, we combined the principles "Data Sharing, Access" and "Intellectual Property," but subsequently split these into two principles giving us the present total of 9 principles. The investigator survey and final analysis were all conducted under the 9 principle format represented throughout this report.

Probe on:

- Ensuring all investigators and both partners retain their proprietary and intellectual property rights throughout and after the partnership.
- Ensuring that data sharing arrangements are explicit and that all rights to access data are fairly negotiated at the outset of the partnership.
- Others?

Follow-up: How well do you think you've done in promoting and ensuring this principle? Have any issues arisen concerning this topic (if so, how were they resolved)?

Lead-in question: The fourth principle concerns how the partnership is managed and led including but not limited to legal issues, administrative duties and obligations, priority setting and managing conflicts. All of which may be captured under the term **governance**. What do you think are some essential features for effectively managing a partnership like this in a way that is fair and enabling toward the investigators? If asked to list important parts of effective governance, most people would list fairness, cooperation, and communication. Do those sound right to you? Are there other goals you would suggest? How well do you think you've done in accomplishing these?

Probe on:

- Establishing parameters for what type of projects will and will not be funded (e.g. add-on projects, training, pilot studies).
- Creating ways to protect each party from an unexpected end to the partnership.
- Assessing efficiency, effectiveness, and achievements of the partnership on an annual basis.
- Ensuring that clear and comprehensive procedures exist for all governance committees and are known to all investigators.
- How are the Areas of Interest decided? How are decisions made as to what projects will be funded?
- Others?

Follow-up: Can you give examples?

Lead-in question: The fifth principle focuses on the requirement that the research conducted within the partnership should adhere to the highest ethical standards **for protecting human subjects**. Have there been issues that have arisen for you in this area? Were they affected at all by the fact that it was a partnership? What have you all done to promote and ensure this principle?

Probe on:

- Ensuring that all investigators, staff and other participants in the partnership have adequate training in the responsible conduct of research and related ethical issues.

- Ensuring that all projects in the partnership aim to satisfy the highest ethical standards.
- Others?

Follow-up: How well do you think you've done? If any issues have arisen, how were those issues resolved?

Lead-in question: The sixth principle concerns issues of a**uthorship and how research findings are to be published**, disseminated, or known. Have there been issues that have arisen for you in this area? Can you give some examples? What have you all done in regards to ensuring good publication practices and adherence to authorship rules?

Probe on:

- Ensuring the right of all researchers associated with the partnership to publish.
- Disseminating all research results at the conclusion of collaborative studies in a timely fashion.
- Ensuring authorship follows ICMJE guidelines.
- Others?

Follow-up: How well do you think you've done?

Lead-in question: The seventh principle concerns the **benefits to each partner** and the goals of each partner in the collaboration. The general idea is that the partnership should create new knowledge that will improve the well-being of citizens and be of significant importance to the academic and industrial partner. Does that sound like an important goal to you? Is it one that you have had to think about or apply so far? Examples? What have you all done to promote and ensure this principle? What are some the potential or actual benefits of collaborating with Merck for both you, the company, and society? Are there any potential or real harms to collaborating with Merck?

Probe on:

- Maintaining competitive advantage in the specified research domains.
- Structuring the research to maximize potential benefit for communities and society.
- Structuring the partnership to have the best chance of benefiting both partners and harming neither.
- Others?

Follow-up: How well do you think you've done in promoting this principle? Have any issues concerning this topic arisen?

Lead-in question: The eighth principle concerns how well the collaboration (its function and agreement) is **known by and visible to** relevant parties and the public. Do you feel the collaboration is well enough known in this way? Has this been a concern of yours? What have you all done to increase and ensure transparency?

Probe on:

- Widely publicize the partnership agreement and collaborative opportunities to the public and employees.
- Establish procedures for frequent and effective communication between partners.
- Ensure both partners are aware of other partnerships each may be involved in.
- Others?

Follow-up: How well do you think you've done? Have there been any surprising issues that have arisen on this topic?

Closing Remarks: Thank you for your time. Please remember that if there are any additional concerns or comments after this group is adjourned, feel free to contact me or any members of our team. Once we have gathered and analyzed our data for this review, we look forward to reporting back to you all.

APPENDIX 4

Academic Freedom

“It's safe to say that we were very keen on protecting it, which means we must have worried that it would be at risk, you know?...what I thought at the time was, yeah, we want to be sure that we're not either a shill for or just a guardian of stuff that's for purely industry purposes so it was on the radar.” (6)

“but I think the greatest risk here is that we were going to be taking an investigator who might better spend his time focusing on something else more on the line of his or her previous research. Because that person needed research funding support and are unable to get it themself, we're gonna buy that person to work on our stuff and unfocus his research career.” (6)

“ this is one of the early discussions we had is that we need to find ways that their research interest and our research interest overlap so that the investigators on both sides are doing what, as a mutual interest, otherwise the partnership is not gonna make it. And that, I think, is a way of kind of coll - academic freedom in a collaborative way. So, we each have the freedom to brainstorm and pick things that turn us on and then propose them and then we can decide to fund them or not fund them depending on relevance and interest and rigor and all those other kind of things, but at the end of the day, we did give people the - we didn't just say, OK, Merck wants this project done.” 6

“we talked about that in early meetings as a very general term, and John came up with this notion and we'll look for things that co-PIs on both sides and throw things - and each group will throw things on the table.” 7

“I would say that I have come to - since we're worrying more about academic boredom than academic freedom, you know, that you're just gonna be doing something… That's the statement because that's the reality, is that you're just doing something which is like, yeah, we can do it. We can run that analysis. We can look at this. We can look at that and, in part, which is why Jennifer put together this exploratory studies project, which was sort of a mini - kind of people want to take a quick look at something. It doesn't require a lot of research or support. We found mechanisms to do sort of run of the mill things, but that real issue about like is it just gonna be a also ran tenth time somebody's looked at this issue. So, I think around academic freedom, that's sort of exactly what Bill is saying. Is it gonna careen somebody's career by just doing mediocre science?” 7

“So, the exploratory studies project, we started it last summer, so about a year and a half into the project, into the whole collaboration, and the point was to be able to do these little research questions that aren't full projects that don't need a lead on both sides and the full rigor of what we do for regular projects, but can just be sort of either they don't have a Regenstrief lead or they don't really need all of that planning so they can just be kind of quick one-offs, and one example

of how this has been useful recently is that we had a group at Merck who was looking at ,I think it was for chronic kidney disease, one of those drugs. So, we had a phone call and we had someone from IU who's like an expert in this call in and so the call didn't go very well, and they didn't really come together. Afterwards, he emailed us and said, you know, these aren't interesting questions. This has been done. Basically for business reasons, I'm not interesting in spending my time on this. So, he felt very free to do that. There was no coercion. There was no - he didn't suggest somebody else because he knew no faculty member would want to spend time on this, but we still have a mechanism just with our data core and our project management structure to do those sorts of things without impeding on anyone else's time." 7

"The proposal process really highlighted this…if an idea came from Merck and there was no interest here, then there was no interest here and same with ours….Jennifer would do is solicit ideas from IU people and then her counterpart would solicit ideas from Merck and then we'd put it all together and socialize them." 8

"I realized that I didn't really understand what Merck did. What are the diseases that they focus on? I know these companies have hot diseases within them where all the drug development is focusing on, and they put hundreds of millions of dollars into stuff, and I had no idea. I go, shouldn't I know that? So, I asked the question, and it was amazing. They kinda didn't know that cause these were all working in epidemiology and in global health. Whatever it was, they had snippets, like somebody knew something. So they threw out the things they knew about, but nobody had kind of global knowledge about it." 8

"But the point is that to serve the academic freedom, we took big A academic. In other words, we a broker and one of Regenstrief's notions that we're supposed to broker research and look beyond our walls. So, it may not have served our investigators, but it serves our customers, which is the university. We're here to support the university." 9

"They have spent what is probably hundreds of hours to get thing finalized because of the incredibly ridiculous, odorous, but that's the right way to do regulation. So, just in general, there's a huge amount of sensitivity to ensuring that there's not the perception of a - so just to kind of lay that out." 10

", if there is not a compatriot found, then it just dies. So, there shouldn't be any circumstance where someone is coerced into studying something that is outside of their own self-defined scientific area. Everybody should - there's no pressure to do that." 10

". A lot of the Merck scientists, and I think I'm the only person who has led, who has PI'd these projects, are better than us. They're better. They're scientifically better at certain things than we are. I'll just be honest with you. They provide suggestions and insights that are more rigorous, of higher quality, higher scrutiny, better defined than what we came up with…. It was nothing in their interest, it was just methodology, random crap, but they've got scientists who are very good, in some cases better than we are, and I think that we have to have that recognition, like academic

freedom to be like, you know, you are actually getting advise from somebody who knows maybe more than you do about some things. To me, that's an interesting part of the story." 10

"The investigators here don't always recognize that in their Merck counterparts because they will come back with something, and they'll be - they'll say, oh, just - they're trying too hard to tightly control it, but she was right. You can't control that. You can't compare that as a control group because she's right. They don't match or whatever. It usually comes up with methodology in a study design and not even like you were saying, but it's interesting to listen to both sides of that." 11

"there is a bias towards if you're a really smart investigator, you stay in academia. If you want to essentially be told what to do and run some other studies, you go to industry and those who have actually worked with people have realized there's some really smart people out there. We do not have the corner on the market of intelligence, and so I don't think any of us, it was a revelation when people are saying, well, of course, but I think there is a bias amongst some of our colleagues, both in the institute and outside the institute that we're kind of smarter than they are and part of our kind of grooming people to be part of this is to level the playing ground on both sides. And I must say that on the financial side of stuff, on the resources side of stuff, it's the opposite. That Merck thinks they're rich and we're poor... He says we're putting money on the table, we make the rules, and I said money is the cheapest thing on the table right now. The toughest thing on the table is our intellectual capacity. That's - you know, so it was not a matter that we're subjugated to you. You bring something and we're bringing something to the table. I argue that money's a lot cheaper than a kind, and so we leveled the playing field by that. So, there were biases on both sides based on assumptions about the other guy, neither one of which was valid." 11

EMM suggestion of academic curiosity

"I see a lot more curiosity. Maybe it's just my interest biases, but curiosity in the developments side. The folks who are coming from the IT side who say let's build out a new thing for an [INAUDIBLE]. Those guys are much more like let's experiment and explore new ground. With the methodology folks, we get some of that same kind of thing where I think there's sort of an academic curiosity. I think with a straight analytics projects, which is probably for lack of a better word, sort of the bread and butter, look at adherence in patients, less of a curiosity driven thing to me, but that's just my –" 12

" So, there are - I think some of the curiosity is on the methods and not on the focus, and that's where you sometimes get. I want to do this in melanoma. I don't want to do this. Well, fine I don't care about melanoma, but I want to do that. So, that's the marriage, and if it weren't that way, how are you going to find people, enough people who want to do melanoma to put a project together. Its such a narrow corner."12

"Go get a grant" 13

“We - it's a little bit - it's not quite bilaterally symmetrical because, you know, I'm sure if nobody at Regenstrief was interested, John would knee jerk reaction might be, well, then we're not interested, but one of my roles is to be a matchmaker and to work the interfaces and stuff like that. So, I will push it. We'll see if there's somebody else around here that might be interested in that because it both make Merck happy and it makes Regenstrief important - I can tell you that, for example, endocrinology thinks much more highly of us now than they did before we have the osteoporosis center, and it's spontaneous to see how wonderful Regenstrief is. Cause we've created some nice opportunities for them that weren't anticipated and really don't benefit us very much. So, there's some collateral benefit for us which is tremendous and what's it cost us? We're bringing more money in. We get to claim it all as part of our grant so our board says, god, that's a lot of money. That's great. You created this other center. That's terrific and for us, it's just OK, we'll do that and it's been modest amount of work on our part and a huge amount of benefit for the university.” 13

Conflict of Interest and Commitment

“I can't think of any conflicts or anything that's come up in this area.”13

“But we haven't asked, right? We've never asked our people if they own stock, own competing stock.”14

“I only just make sure they fill it out in the IRB.”14

“The one conflict that came to my mind potentially in this area is that the bone center often serves and is serving as a test facility for the clinical trial for Odanacatib, which is the new Merck osteoporosis drug. And I don't know how that - I don't think there's been an impact, but it's there. It's the same guys.” 14

Back and forth among participants about who fills out a COI form and who doesn’t. 14-16

“There have been questions from our folks about how to do the conflict of interest, you know, on a publication and what sort of phrasing should they use to describe this.” 16

“But let me clear - there's an exploration of this that actually never came up until last week and that is that, for example, our investigators just a fraction of their salary paid. They don't personally get honoraria or anything for this. It's just buying their time to work for the institute, and I'm assigning the work on this. We're actually doing it for things not Merck, too. So, this isn't the only thing we're using this method for. But, you know, I'm the president of the institute and the institute, if the institute succeeds, do I benefit from that? So, if the institute is benefitting, is that a conflict of interest for me? “ 16

“the fact that I represent an organization that itself can benefit becomes an important conflict of interest at times, and I don't know how to factor that into this yet.” 17

“Well, I think the problem is because none of us personally benefits from this. We just get our salary paid. OK?... You're losing because it's pulling your focus away from helping what direction of your career to go, and we're benefitting from that lack of focus. And the other thing, if I'm gonna be supporting 20 percent of a whole bunch of people to be working on this from other things, they're now working for the institute for the institute's benefit, and I think it's gotta be clear that it's not necessarily for their benefit, and it has to be up front acknowledgment because there's, at times, gonna be a conflict of commitment.” 18

“It's not real money, and we're attracting people away from what would be considered more academic lucrative things to be doing, chasing the easy money and dangling it in front of them. I don't know. I can see that argument happening.” 18

“maybe you're taking advantage of faculty and that's sort of a conflict of interest with us in doing it. I think another side that I find totally know how to reckon is relationships with other companies or parties who are interested in us and how our relationship with Merck affects that…I mean, I know you can say well, that's just a tangled web you weaved, but it could just as well be like maybe I shouldn't apply for this $100,000 NIH grant to study the risks associated with Cycliftin because that's Merck. You know, so I think there's also stuff that actually affects the way I look at other relationships which is sort of a conflict of interest maybe in a way that I'm benefitting from or it's actually disadvantageous for me, but there's some effect.” 19

IP, Data Sharing, Access

“I think, from a faculty perspective, people probably feel like Regenstrief underleverages IP as generated here.” 19

“Well, we've just built a hell of a lot of stuff over the last 40 years and a lot of foundational work and don't really have the IP to show for it.” 20

“The relationship we have with Merck is an interesting one insofar as the contract says that they have the right of first refusal for anything developed under this agreement. The NLP stuff might be a good example of that. That they have the right of first refusal to take it and market it and actually had trouble signing that aspect of the contract until we had our agreement signed with IU. Because for 25 years, our investigators have been signing a form with IU saying f\IU owns all the intellectual property. They've been signing a form for Regenstrief, saying Regestrief owns all the intellectual property, and we finally resolved it so that depending on who funded the project, if a property belongs to either IU or Regenstrief… we have the ability to market stuff, and we're going to be doing more of it, but the issue is one that has not been discussed a lot until the past year among the faculty, and now it's being discussed a whole lot among the faculty and we're moving to support it.” 20-21

“In the contract, I think it was definitely much more - certainly, the Merck side said a, we want things to be - we want - want we develop it together that we can assign the IP and exactly as Bill

referenced, the biggest issue was that we would not be able to cleanly assign IP because IU had official ownership stake. The whole thing almost cratered until I remembered Thursday afternoon, one week I was in clinic and I had to call Mr. Betley and say, as chairman of the foundation and the board, etc., the only thing that's left that can save this is you simply saying you will personally make assurances that - like if Regen - if IU tries to come in and swoop it, and that's what it took. Then, eventually, we got a real contract signed. So, in practice, it was Regenstrief. I mean, it was Merck. In reality, they've been very big on the open source sort of agenda that we have here because most of our development from an IP standpoint has been IT and they are very interested in building things that get other people to use it to be able to produce data that can be leveraged for other purposes. So, supporting open MRS is a very big interest of theirs. They haven't seen like, "oh there's huge money in them thar hills" because we built this. Rather, they see it in getting it out more broadly and making Merck look great and all of that as having more value." 21

"We haven't had any IP generated in the sense that we've built stuff, but we haven't had any patents submitted for our IP. We haven't had any things that have executed on that yet. I think that will be coming this year. " 22

"We haven't fought over any IP." 22

". They explicitly said it obviously reflects well to be working with an independent organization like Regenstrief Institute and of course, that's a tip of the hat to the public relations benefit of working with an organization that's respected and that is known for its openness. So, that's one benefit. Two is, we've taught them and they have taught us a lot about partnering. We are - I mean, the process that we've built. Jennifer, primarily, and these guys over the past couple years has proven to be extremely potent and reusable, and they now extend it to nine other partnerships, and so we were sort of this prototype partnership which they learned from, and I think that they have sort of held us up also as an example of just an effective, from almost a social level, that –" 22

"Who wants to argue that's a certain amount of intellectual property. Although it can't be patented, it certainly can be modeled. It can be –"22

"Well, we're writing a paper on it so I guess we're shooting it out about the structure of the partnership in terms of that." 23

"I think our proposal process is really good…His name is Arnaud and working very closely with him has been very important just to communicate. I never really speak with the investigators on the Merck side, but he does and so if I have a question, I go through him. So, just having sort of the two - I'm the contact for our group, and he's the contact for their group, it's been really useful in keeping things smooth and making sure that we don't have a lot of cross communication." 23

Benefits/Value

“model by the way we internally structure the finances for this was unique. It took me nine months to get IU to agree to it, starting at the level of the person that we would be setting up accounts at IU all the way up through the university president and getting a commitment that the institute could actually buy time of faculty… When you're doing a $13 million project, all the sudden, it gets people's attention and all of the paranoia about you're just getting around trying to pay indirect costs and stuff like that. And so, so this got us a chance - if the institute was gonna actually change its business model to a certain degree. We're still gonna support our investigators, but actually become something the institute itself does, then you're not gonna be able to set that up unless you just do it. You can't set it up as a thought process… actually do work as an institute rather than just this notion of supporting a bunch of independent agents, then I've gotta work through the processes. We've got to get approvals, we've got to send money through. It's gotta actually work, and people gotta get rid of their paranoia and it actually served that purpose reasonably well, but not without its heartaches. It took IU despite the fact that they dictated the terms and we followed them to the letter, it took them 18 months to sign the agreement and even then, they only signed it because the departments are screaming that we had more than $1 million in the transfer account and they couldn't download it without a signed agreement. And they still don't feel comfortable with it. So, it's - and I'm not exactly sure why. It's just different, and IU is allergic to different.” 24

“The benefit to me was we've got a chance to actually do it. A huge benefit to the institute cause we're now getting ready to roll it out maybe institute-wide. “ 24

“So, I would say - you talk about the financial structure, but the logistical structure, the operational structure of executing projects has also evolved which has been extremely effective in terms of the cores, the biostat score, data core, NLP core, operations, just the structure. I feel like it's so much easier. Now, if we had a project coming from anybody. Like forget Merck, just like somebody came along and wanted to do a project, we just stuck it into the pipeline, we would know exactly how to channel it, manage it, get it done, wrap it up, turn it back. I mean, we have a system. We didn't have a system so –“ 24

“the process to propose and review projects works extremely well and if you could sit in the session with us when the steering committee meets, it's a mini study session. It's kind of a low key study session. We go over methods, we go over values.” 24

“If Merck comes by and says how much money do they put into it, we just go down until it adds up and we fund everything above the line. I mean, it works extremely well and everybody… So, everybody is very comfortable with that. It's fair, it's effective, it's not time consuming. They deal - the projects are these little concept proposals. They're called -… Charters. Doesn't make any sense, but these little concept papers, three or four page paper that's got an estimated budget, and we end up - it ends up being really a highly effective way that if we didn't have something like this to force us to do this, we wouldn't have discovered it, and it's now, I think, an executable model in a lot of different potential partnerships.“ 25

“and I think the funding relationship is such that we can, if we have a great idea or we have something that we're cooking, we could reach out to an organization that's interested in all kinds of stuff and say this wasn't part of our plan, but what do you guys think about, you know - are you interested in this space that we're getting into. So, from a funding perspective, it's great… We're able - right now it would be very difficult for me to come up with a small idea outside of our innovation challenge, go to the NIH and say I need this, but with Merck, we can say we want to build out our hidoop cluster. Are you interested in helping support that or something, and they may be or they may not.” 25

“Well, benefits to the participants. A couple of times, we've had projects that have been successful and that people have been really interested in, and the collaboration gets the investigators an option to submit for a second year if they want to expand the research or if the team's working very well together, but I can't –“ 26

“I've had some good science come out of mine. I know we spent a lot of time looking at - well, it doesn't matter about the details, but essentially, there's a bunch of people who have chronic kidney disease who might be getting a drug they shouldn't be getting so that was something we were able to ascertain.” 26

“The efficiency says something. I mean, if you said, well, as a member of society, we have a researcher here at this university that just received a five year award to investigate potential risks of bisphosphates in patients with renal dysfunction and in 2018 -… OK. OK. That's good, but if you said there's a group to be working and in 12 months' time they're going to come forward and have a planned strategy recommendation for this group to understand the incidence and their whole - you know, you might say, as a member of society, yeah, I'd take that latter one.” 27

“So anybody with a DEXAscan in this area and your patient, you can look them up and find a result. Until we started doing that, zero were available electronically. So, for a population of a million people, we're gonna have all of their scans. Well, that's huge. People use those data all the time, and they're not available if you didn't do the scan, if you don’t have the paper result. So, by building infrastructure for us to do the research and making that infrastructure part of the system and not just part of a research project, we've benefitted the system, and that was one of our goals, was can we make the system better and then do research, and the system itself has to benefit from it. That was a very explicit goal on the part of both Regenstrief and Merck to make this available. Obviously, we're going to take advantage of it, but long after we're gone, they're still gonna be being captured cause we've automated that process.” 27

“We'd be hurting if it hadn't been for the industry partnership, and its not just this fund. There are other ones, but this is a huge one for us. This is the biggest one, and it's a model for how, in this day and age of funding, we need to have an effective governance system so that we can take advantage of the fact that there is certain sectors of the life sciences industry that are looking for partners like us, and we'd be more than happy to serve that interest if it serves our interest at the

same time, and that's the key. We just chase the dollars and survive, we can survive and be soulless. So we have to make sure that we stick to our mission and keep that emblazoned on our walls so that we use this as a way to continue it at a time when other funding is tenuous." 28

"we hire investigators who have an interest in - their mission and our mission are at least co-linear if not overlapping, and if our investigator is interested in doing something - if there's something our investigators aren't interested in doing something, we're not gonna do it because, by default, we have to have a local partner, and so as long as our investigators stay focused on their personal mission and it's tied to our mission, I think we're OK… but as long as it's answering the research question you're interested in and you were hired because you had interesting research questions you were interested in, I think we're OK, and we" 29

"there's no question that they derive benefits from some of the stuff we're doing, and some of the stuff we're doing, we might not have done had they not proposed it, but we cert –" 29

"Maybe one of the suggestions from this is that in our charters, there ought to be a line as what's the benefit to science, what's the benefit to society? Maybe that will be something we explicitly consider with each charter, and it ought to be in things that are otherwise balanced, equal. Maybe that ought to be the deciding factor. This thing is actually gonna have more downstream benefit than another one. And maybe just be explicit about it so that when somebody says what the hell good is this, we have an answer up front cause that was actually a plan from the beginning. That might actually be useful and it takes almost no time." 30

"The first year it was us because it a long time for the Merck investigators – for it to perculate throughout Merck for Merck to figure out that there's something here, but once they came this year, it was very heartening to see that of all the things that plopped on the table, there was Merck that had a half and Regenstrief had the other half, and it was –" 31

Transparency

"We tried to go pretty wide. So we sent it - I got help from the CTSI using their listserv" 32

"And then anyone who is part of Regenstrief, our affiliates, our investigators. We sent out just a very general email about what the collaboration is and what we are looking for, and our steering committee prior, the one immediately prior to this initial call, we had - I think we had five minutes at the end of that one to talk about well, what are you guys interested in for this year and ask Merck what general areas and they listed some, but they were very general and kind of all over the place so that wasn't all the helpful. So, I put that in the email that said we'll accept proposals from anything. So, I got a lot of responses here. I don't remember exactly how many, but 30-40, maybe, people. And at that point, all we asked for was a couple of sentences. It wasn't a lot of work on the investigators' part to do that and then I put all of those in a spreadsheet. We sent them to my counterpart at Merck and the steering committee members from Merck and said do you all have anyone on your end who would be interested in any of

these and then, likewise, my counterpart did the same thing on his side and sent me a spreadsheet that we circulated." 32

"I mean, it was sort of obvious that like here's stuff that's kind of about drugs and clinical stuff. Here's stuff that's kind of about informatics and things. So, I think to look at it, you would probably so, oh, I'm guessing this is stuff that Merck cares about and stuff that Regenstrief cares about." 33

"But we certainly didn't have like a document of how we arrived at that." 33

"There's a difference between who can look at and from who or for whom it's intended to benefit." 33

"we didn't design it to make everybody have a home." 33

"But we shared it as broadly as possible. " 33

"That aren't disease-specific in our focus that, and if you look at the projects, they're kind of all over the place except for in this Center for Excellence for Osteoporosis. They're obviously going to focus on osteoporosis. The other projects are really all over the place, and as much method - half of them are really methodologic as opposed to disease-focused. I don't think you look at it and say they obviously have a bias against something." 33

"And we've made it pretty clear that in the announcements that it's blue sky. If you've got an idea - essentially, that idea for which you - that some of our resources would prove useful if you had some money to access them, and I want to get that before we finish here." 34

", I think, even just the process was beneficial to the investigator. I think of one. We had a researcher in human sexuality proposed something related that was not of interest at all to Merck, but he wasn't really aware of Regenstrief or the INPC so just going through the process, I introduced him to the data corp, and he met up with a researcher at Merck, and they didn't get funded ultimately, but he had said, you know, this is great. I didn't even know this was here and now this is something that I can do. So, even the people who ended up having these areas that were way outside of what Merck was talking about and were interested in, they got something useful there." 34

"but it essentially divides things into something that's high interest, moderate interest and really no interest, low interest, and eventually things that go to low interest, they don't get asked to flush out their charters and the hot and moderate ones end up with the proposals. We go and kind of just say same three categories and then among the hot interest say which ones we definitely want to do and then Merck has to say how much money they have and then if we get all the hot ones, then we have to go down and rank the moderate ones and go down and get those. So - and it's nice that we can end up funding - 30-40 percent of the proposals that are initially submitted are ultimately funded. So it's not a matter of you just taking a real small tip of

the iceberg, and so there is an opportunity to go down and there's opportunities where they say, this is one you ought to move up a little. We really want - there's somebody who really wants to do this and a couple places, somebody else at Merck said I want to do that one. I'll put extra money into this. Merck actually shopped these things in their own shop to find extra money for them." 35

"One is that there are people who are non-voting members who sit at that decision meeting. So there's three people on each side who vote, but there are some non-voting folks who are present and are able to give feedback and share. For whatever that's worth." 35

"The second is that the priorities, we probably read these and evaluate them as more than just - you know, we think about the teams, right? So we'll look and say this person was on - last year, this team worked together. They were an extremely good team, which might be the way the investigator is evaluated in NIH section, but we know like these guys work well together or don't, and also priorities shift… and it's sort of the same thing where like there are things that we took and then between the RFP cycle and the voting cycle, they have major changes in their priorities at Merck, and it affected what was selected and so some people get the short end of the stick. So, I think it can happen in both scenarios." 36

"There were a couple of projects where they said, you know, they're not ready for this yet. They're still developing this whatever the approach was and so let's let this percolate another year and it will almost certainly get funded next year. So, it's kind of like revise and resubmit….well so we know what's coming. We've got a sense for it, and yet, I don't - I haven't gotten the sense from the process - and I'm pretty sensitive to this - that there's bias involved. I think that there's - that certain people who come up with ideas, those ideas resonate and they percolate to the top, and that happens in a little bit different way. I don't get a sense that Merck is either openly or surreptitiously driving the agenda, and I don't think we are either. …The ones that are in the middle, but these people kind of churn and through the thing, it kind of percolates more towards the top, and it gets rewarded for doing that, and they do it with help and advice from us at each step of the way." 36

"In other words, if we've selected things that fit with the declared mission of our partnership, is that fair? If we selected things that fit with our RFP that we sent out four months ago, is that fair? In other words, to whom do we owe this fairness and, you know, how is that defined?" 36 and erics response

Protection of Human Subjects

"Only the IRB refusing - counting so many things as exempt. We're like we want you to please review this, and they won't. They say it's exempt." 37

"We circulate the ICMJE guidelines and say you have to abide by them, but they're pretty broad and so…They're not signing. They're encouraged." 38

“The reason Merck came to us is we're sitting on a mountain of data that's somebody else's data. And yeah, we follow all the IRB rules. We following the INPC rules, etc. … But in the end, we don't own the data. We're getting value from the data that other people are paying to put there, and they know that we're using them for research, and I know that the health organizations think that we get rich off of our grants, and they don't get anything off of them… years that we could be called on, especially when we are making money off of this that's supporting our research mission. Now, we're not individually making money off of it, but it's supporting our research mission. It's part of our organization and we're moving the company forward based on somebody else's asset, and Deloit is a good example. Their first approach to us was send us all your data. Sell us all of your data, and I don't know that there is anything that would have prevented us from doing that because there is nothing in the INPC charter that says we can't do it. We'd have to get permission to do research on the data, but it's not to say that we can't upload it somewhere because we're already uploading it to us.” 39

“And I - I'm guessing this issue is gonna show up in other places as other information exchanges happen, as other organizations put in health records, and they don't really know how to deal with them. This is gonna bubble up, and I'd like to have a better answer for it than we currently have.” 40

APPENDIX 5

SURVEY INSTRUMENT FOR:

Survey of Regenstrief Investigators and Staff on Experiences, Knowledge, and Perspectives of the Regenstrief-Merck Partnership

PI: Eric M. Meslin, PhD

Introductory Statement to Participants: Thank you for agreeing to participate in this study. When responding to the statements and questions contained in this survey, please remember that we are inquiring about your opinions of the Merck-Regenstrief partnership.

We'd also like to remind you that your participation in this study is completely voluntary, and if for any reason you wish to end your participation in this survey, you can stop participating at any time. We ask that you take this survey in a private space and on a secure network. If any issues or concerns should arise after your participation in this study, you may contact the PI at emeslin@iu.edu. This survey should last approximately 10 minutes and we ask that you only take the survey once.

Preliminary Questions

1. What is your affiliation with Regenstrief Institute?
    a. Research Scientist
    b. Affiliated Scientist
2. Have you ever been directly supported by the Merck-Regenstrief partnership?
    a. YES
    b. NO
3. In what capacity or role were you supported by the partnership?
    a. Principal Investigator
    b. Co-Investigator
    c. Other
        i. If "Other," please specify
4. In your opinion, how knowledgeable are you of the Merck-Regenstrief partnership? (**Likert Scale)**
    a. Very knowledgeable
    b. Knowledgeable
    c. Somewhat knowledgeable
    d. Not knowledgeable

Questions for Those Who Selected either (b) or (a) in Question #1:

(Unless otherwise noted, participants will be asked to respond to the statements from the options given in the Likert Scale below.)

Likert Scale: Strongly Agree, Agree, neither agree nor disagree, disagree, strongly disagree, I don't know/not applicable

Stem: The Merck-Regenstrief partnership:

5. Promotes investigator-initiated science
6. Permits investigators to continue on-going collaborations with other research collaborators or teams.
7. Ensures that all Regenstrief investigators are given equal opportunity to submit proposals for funding in the partnership.
8. Effectively disseminates the funding opportunities to all investigators who are eligible to apply.
9. Pressures faculty to work outside of their own research interests.
10. Results in the exploitation of students and fellows.
11. Adequately protects investigators' intellectual property rights.
12. Has an acceptable data sharing policy.
13. Has established clear criteria for which projects will be funded.
14. Chooses research areas of focus in ways that are problematic.
    a. **Branch**: if participant chooses strongly agree or agree:
        i. Please describe why or in what ways you feel the research areas of focus are chosen in problematic ways. Please cite specific examples if able. **(Text Box)**
15. Chooses research areas of focus that prioritize Merck's interests.
16. Chooses research areas of that prioritize Regenstrief's interests.
17. Explains the procedures for applying for funding to all eligible investigators.
18. Is likely to benefit patients
19. Is likely to benefit society
20. Is beneficial to Regenstrief
    a. **Branch**: if agree or strongly agree:
        i. Partnering with Merck has benefited Regenstrief by:
            1. Providing more research funding (**Likert Scale)**
            2. Creating an environment more supportive to partnering with outside entities (**Likert scale)**
            3. Creating a more effective system for managing projects (**Likert Scale)**
21. Has been beneficial to me
    a. **Branch**: if agree or strongly agree
        i. Please describe the ways in which the Merck-Regenstrief partnership has benefitted you. (**Text Box)**
        ii. **If disagree or strongly disagree**

iii. If you believe the Merck-Regenstrief partnership has negatively affected you in some way, please describe why you believe this and in what ways it has done so. If the partnership has simply not been to your benefit but has neither been to your detriment, please leave the text box blank.

NO STEM

22. I feel there is a conflict between my professional goals and the goals of the partnership.
23. I have concerns that some projects conducted in the partnership are unethical.
24. The partnership has had the following effect on my ability to compete for research funding (**different likert scale)**:
    a. **Strengthened** it.
    b. Neither strengthened nor weakened it.
    c. **Weakened** it.

Additional Questions for those who answered "(a) YES" in Question #1 (i.e. only those who HAVE been supported by the partnership):

STEM: The Merck-Regenstrief partnership:

25. Has effective mechanisms to manage conflicts of interest.
26. Ensures the right of all investigators to publish
27. Encourages timely dissemination of research results.

NO STEM:

28. There is effective communication between Regenstrief and Merck co-Investigators.
29. My right to publish research findings from my work in the partnership does not differ from my right to publish from my work on other projects.
30. The projects I've been involved in the partnership are undertaken according to the highest ethical standard

APPENDIX 6

PRINCIPLES	BENCHMARKS
Academic Freedom ☑	1. Promote investigator-initiated science and protect the ability of investigators to attract and maintain federal research support.
	2. Permit investigators to initiate or continue collaboration with any other qualified group, person, or entity.
	3. Ensure that all investigators involved in the partnership are given equal opportunity to submit proposals for funding.
	4. Avoid obligating faculty to work outside their own self-defined scientific area.
Conflict of Interest Policy and Management ☑	5. Protect students, fellows, and post-doctoral fellows involved in collaborative projects from exploitation.
	6. Ensure that effective mechanisms exist to eliminate, control or manage conflicts of interest in the partnership.
Intellectual Property ⊗	7. Ensure all investigators and both partners retain their proprietary and intellectual property rights throughout and after the partnership.
Data Sharing and Access ⊗	8. Ensure that data sharing arrangements are explicit and that all rights to access data are fairly negotiated at the outset of the partnership.
Effective Governance ⚠	9. Establish parameters for what type of projects will and will not be funded (e.g. add-on projects, training, pilot studies).
	10. Create ways to protect each party from an unexpected end to the partnership.
	11. Assess formally the efficiency, effectiveness, and achievements of the partnership on an annual basis.
	12. Ensure that clear, comprehensive, and efficient procedures exist for all governance entities of the partnership and are known to all investigators.
Protection of Human Subjects ☑	13. Ensure that all investigators, staff and other participants in the partnership have adequate training in the responsible conduct of research and related ethical issues.
	14. Ensure that all projects in the partnership aim to satisfy the highest ethical standards.
Publication ☑	15. Ensure the right of all researchers associated with the partnership to publish.
	16. Disseminate all research results at the conclusion of collaborative studies in a timely fashion.
	17. Ensure authorship follows ICMJE guidelines.
Social, Scientific, and Industrial Value ☑	18. Maintain competitive advantage in the specified research domains.
	19. Structure the research to maximize potential benefit for communities and society.
	20. Structure the partnership to have the best chance of benefiting both partners and harming neither.
Transparency ⚠	21. Widely publicize the partnership agreement and collaborative opportunities to the public and employees.
	22. Establish procedures for frequent and effective communication between partners.
	23. Ensure both partners are aware of other partnerships each may be involved in.

KEY TO REPORT CARD

GREEN	Benchmark MET
YELLOW	JURY'S OUT on Benchmark
RED	Benchmark NOT MET
WHITE	Insufficient evidence
☑	Principle MET
⚠	JURY'S OUT on Principle
⊗	Principles NOT MET