APPENDIX A. EVIDENCE TABLES

Author/ Year	Study Design	Participants	Findings
Lo, 2000[100]	Analysis of COI policies	10 US Medical Schools receiving the largest amount of research funding from the NIH: Baylor, Columbia, Harvard, Johns Hopkins, UCLA, UCSF, U. of Penn, U. of Washington, Washington U., Yale	- all policies required disclosure of financial interests, including stock and stock options and income from salary, honorariums and consulting fees. -5 required disclosure of all financial interest, regardless of the value -5 required disclosure if > $10,000 -Further info on person required to disclose, to whom to disclose, prohibited interests
McCrary, 2000[99]	Deductive content analysis on COI policies to evaluate the documents according to certain domains	All US Medical Schools (n=127), and other research institutions (n=170) that received more than $5 million in total grants annually from the NIH or NHS, 48 journals in basic science and clinical medicine, and 17 federal agencies N= 250 institutions, 47 journals, 16 federal agencies	-250 institutions: 6% had no COI policies 91% adhered to the federal threshold for disclosure, 9% exceeded federal guidelines -Journals: 43% had policies requiring disclosure of COI -Federal agencies: 25% had policies that explicitly addressed COI 15/16- relied primarily on institutional discretion -Further info on 235 institutions with disclosure requirements including: type of conflict, person (or entity) with interest requiring initial disclosure, party to which initial disclosure must be made, when disclosure is required, how disclosure should be managed, penalty for nondisclosure.
Weinfurt, 2010[13]	Survey of financial conflict policies	199 sites in US with at least partial commercial sponsorship that contributed participants to phase 3 clinical trials, the results of which were published in either JAMA or NEJM. Response rate/(n) = 66% (61) for academic medical centers, 37% (77) for non-academic medical centers, and 27% (61) for nonacademic outpatient settings	Compared academic medical centers/ nonacademic medical centers/ outpatient nonacademic sites in various domains, including: Follow formal written policy on investigator financial relationships- 97%/ 87%/ 44% Also, whether required to report financial relationships, type of IRB review, the persons or groups with role in review of investigators' financial relationships, whether consideration of reasonableness of per capita payment amounts, whether institution has nonemployee investigators and reviews financial relationships of nonemployee investigators, whether institution uses monetary threshold below which there is no review of investigators/ financial relationships, whether institution uses NIH threshold, and whether there are prohibited financial relationships.
Weinfurt, 2007[96]	Focus groups, cognitive interviews and expert panel development and revision	16 focus groups with healthy adults, adults with mild chronic/ serious illness, parents of healthy/ seriously ill children; cognitive interviews (n=10) with a convenience sample from primary care clinic; an expert panel discussion	-developed model disclosure statement. included generic disclosure statement (person leading study might benefit financially), specific disclosure statement (how might benefit financially- including descriptions of salary support, money received outside of the study, per capita payments, finders' fees restricted to research uses, unrestricted finders' fees, researcher or university holding a patent or equity

Author/ Year	Study Design	Participants	Findings
Weinfurt, 2006[92]	Descriptive assessment of COI policies, most collected via publicly available information on internet	123 academic medical centers, with IRBs. Response rate/ (n) = 98% (120)	-goals of disclosure of COI should include: promoting autonomy, avoid legal liability, and deterrence. -majority of policies most consistent with goal of avoiding legal liability. -48% mentioned disclosure to potential research subjects. Of these, 58% required or suggested verbatim language for the informed consent document. -all required disclosure of the study sponsor, 38% required nature of financial relationship disclosed. -18% specified disclosing how funds allocated. -4% required notification that protocol reviewed by COIC or other administrative body. -5% made reference to nonfinancial interests.
Weinfurt, 2006[97]	Scripted interviews	10 US academic medical centers, 10 independent hospitals, 10 independent IRBs and 10 unaffiliated research entities N= 23 IRB chairs, 14 COIC chairs and 8 investigators	Coding of interview transcripts led to comparisons between investigators, IRB chairs and COIC chairs regarding circumstances in which conflicts of interest should be disclosed, rationale for or benefits of disclosure, information to be disclosed, negative effects or barriers to disclosure, timing of disclosure.
Campbell, 2006[93]	Survey on financial relationships between IRB members and industry	Random sample of 893 IRB members at 100 academic institutions in US. Response Rate/ (n), 67.2% (574)	78 reported at least one protocol came before their IRB with which they had COI 58% always disclosed the relationship to an IRB official 8% sometimes did 12% rarely did 23% never did Of the 62 who were voting members 65% never voted on a protocol 5% rarely did 11% sometimes did 19% always did
Vogeli, 2009[95]	Anonymous survey of IRB chairs	IRB chairs at the most research-intensive medical institutions in US Response Rate/(n) = 71.7% (211)	68% have written policy defining COI 22% did not 9% did not know Further info on to whom to report, how disclosure managed, confidence in policies/ procedures, how conflicts managed

Author/ Year	Study Design	Participants	Findings
Wolf, 2007[91]	Assessment of IRB policies regarding COI, most collected from IRB websites and IRB representatives	121 medical schools receiving NIH funding in fiscal year 2003	74% had written policies 79% of those defined what constituted a COI 10 required any financial interest disclosed 23 only > $10,000 4 significant (undefined) financial interests 14 no definition of a financial interest 99% referred to all IRB members, 1% only IRB chairs, 14% IRB staff, 20% ad hoc reviewers and consultants, 4% guests 4/92 address failure to comply
Brody, 2003[98]	Self-report questionnaire with 12 questions relating to policy for disclosure, institutional management of disclosed possible COIs, action by institution when COI is not disclosed	158 senior investigators, 297 senior research administrators, 195 bioethicists, 17 journal editors and 7 agency administrators	Overall, all supported disclosure to IRBs, research subjects, journals and funding agencies Only the bioethicists were strongly supportive of including research subjects
Weinfurt, 2009[94]	Examined 5 years of empirical data from the Conflict of Interest Notification study, to formulate 6 suggested goals of disclosure	n/a, data from study	6 goals of disclosure: promoting informed decision making, respecting participants' perceived right to know, establishing or maintaining trust, minimizing risk of legal liability, deterring troubling financial relationships, protecting research participants' welfare

APPENDIX B. PEER REVIEW COMMENTS TABLE

	Reviewer	Comment	Response
Are the objectives, scope, and methods for this review clearly described?	1	None	No response needed
	2	None	No response needed
	3	Yes – though the method of pursuing the item with multiple publications and no VA policy might be an odd way to set priorities.	No response needed
	4	Clearly described, but I believe fatally flawed in their limited scope.	See below for specific comments to specific critques
	5	None	No response needed
	6	Overall, the purpose of the review are clearly defined with good documentation on the methods, search terms, inclusion/exclusion criteria, etc.	No response needed
	7	None	No response needed
Is there any indication of bias in our synthesis of the evidence?	1	None	No response needed
	2	None	No response needed
	3	None	No response needed
	4	As indicated in my response to question 4. below, I believe that the authors have been even-handed in how they have synthesized what evidence they have collected.	No response needed
		I believe there are a number of important biases that resulted from how they have cast their review net that should really be addressed.	See below
		I suspect that Key question #1 is incomplete, and had they incorporated additional literatures as I have suggested below, that where they might have gone with Key question #2 might be entirely different than it is currently.	See below
	5	None	No response needed
	6	No indication of bias.	No response needed
	7	No bias was introduced from the methods but given the change in implementation of COI policies in the last decade, a more refined analysis should be considered. For example, dividing the time period into first five years versus second five years might be illuminating.	Unfortunately, we were not able to operationalize this good suggestion, since only one of the studies published during the second five year time frame collected data during the prior five years. All the other more recently published studies had data from before 2005.

	Reviewer	Comment	Response
Are there any published or unpublished studies that we may have overlooked?	1	I don't know of any "studies" that were missed, however, I think there are probably relevant white papers and other commentaries on these subjects that would have been relevant (e.g., from AAMC, PRIM&R, and AAHRPP, NIH and other Federal entities).	We searched the websites of each of these organizations and identified only COI policies or position papers, no empiric studies of COI. We added text to the methods regarding this.
	2	Pape T, Jaffe NO, Savage T, Collins E, Warden D Unresolved legal and ethical issues in research of adults with severe traumatic brain injury: Analysis of an ongoing protocol. J Rehabil Res & Devel. 2004;41(2):155-74.	We reviewed this paper and it describes legal and ethical issues with respect to adults with traumatic brain injury. It does not deal with COI and therefore we did not include it in our review.
	3	At least, I don't know of any and the methods seem comprehensive.	No response needed
	4	I've indicated a number of studies that I think may have been overlooked – but I have not tried to be exhaustive about this.	No response needed
	5	None	No response needed
	6	None	No response needed
	7	I believe there is literature expressing the opinion that disclosing financial COIs in the consent document or process might have undue influence if participants think the study is better designed or safer because the investigator has an interest.	We didn't find such studies and without a specific citation we can't check on this.

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	1	Policy development on VHA research conflict of interest has been underway for quite some time. I am surprised the authors do not seem to be aware of that fact. Dr. Brenda Cuccherini is the contact person in ORD. Also, the authors should look at the conflict of interest issues covered in VHA Handbook 1200.05.	The relevant sections of VHA Handbook 1200.05 are as follows: Disclosing Conflicts of Interests. This means disclosing to the IRB any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and complying with all applicable VA and other Federal requirements regarding conflict of interest. (p20) Conflict of Interest. No IRB may have a member participate in the IRB's initial or continuing review of any study in which the member has a conflicting interest, except to provide information requested by IRB (38 CFR 16.107(e)). (p38) Conflict of Interest. The IRB must ensure that steps to manage, reduce, or eliminate potential, actual, or perceived conflicts of interest related to all aspects of the research (financial, role (investigator-patient relationships), and other professional, institutional, or personal roles) have been taken. (p46) While these directions articulate general goals, it is the specifics of how they are operationalized that is the question of interest.
	2	COI as it relates to investigators seems to be monitored carefully now. Investigators are asked to disclose potential and actual COIs. The question of COI amongst IRB members and reviewers is not discussed as much. I think the authors have hit on a relative weakness in the system and further exploration is needed in this area.	No response needed
	3	If I were asked to consider the sources of conflict of interest in research review, the first thing that would come to mind did not even arise in this review. I would have first thought of the conflict of interest in the IRB with having to consider and defend the institutional interests of the sponsoring institution, as well as the well-being and autonomy of research subjects. This is a pervasive conflict of interest and may well be undercutting the IRB endeavor – since many IRBs seem to act more to defend their home institution from harm than to defend research subjects. I am sure I have read others commenting on this, though I don't know exactly where to point to without some additional research in the literature. Is it really the case that this did not arise in the literature search? Or is it that this did come up but was ruled out of scope for this project?	We did not find empiric studies of this. It may exist in policy statements but reviewing policy statements was not our scope.

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	4	The author's decision to focus on conflict of interest issues in research seems to have been driven largely by the number of articles they uncovered specifically in the PubMed database on the various potential issues of interest identified under the heading of **Key Question #1**. This is a potentially problematic decision for the entire review since the only literature database searched here was PubMed. This makes the review far from systematic. In particular, the PubMed database would miss a great deal of the social science literature on these topics. Inclusion of the main social science, legal, educational and perhaps humanities databases (e.g. Psychology Abstracts, Sociological Abstracts, Lexis, Westlaw, ERIC, etc.) would likely have uncovered additional literature on these specific topics as well as identifying additional topics that may have provided alternative foci of interest for this review. As one example, my sense is that there has been a great deal of discussion within humanities literature about what defines and distinguishes research activities from quality improvement activities. As another example, there's been voluminous discussion within a variety of social science literature's about whether IRB's that are predominantly biomedical in their composition and dispositions provide adequate and appropriate review of social science studies. This would seem to be a particularly relevant issue for the VA HSR&D program, since much of the research in that program employs social science methods and perspectives. The reviewers rejected a focus on the distinctions between research and quality improvement initiatives as a topic of interest for their in-depth review addressing Key question #2. They justify this decision by pointing out that VA has recently offered definitions of these concepts, which they include on pages 9 and 10 of the report. To this reviewer, the VA definitions seem to offer an equivocal position on the distinction between research and quality improvement initiatives, and do not seem to offer clear guidance to researchers or IRBs about the conditions under which various systematic activities should be exempted from IRB review. I say this as both a researcher, and as someone with a decade's worth of IRB service under my belt. It strikes me that this VA "policy" could in fact use some improvements, which might begin with a review of two very recent publications on this topic: 1) Emanuel and Menikoff in NEJM[1]; 2) Selker et al. – Discussion Paper of a working group drawn from the "Clinical Effectiveness Research Innovation Collaborative of the IOM Roundtable on Value & Science-Driven Healthcare."[2] On page v, the authors describe one of the topics uncovered in their literature search as "payment to patients." Here again is an issue that likely would have been more voluminously represented in the literature had social science databases been included in the author's search. I suspect that a search of those databases would have uncovered a great deal of discussion regarding not just payments to patients but more broadly speaking numerous issues around use of "incentives for research/study subjects." In survey-based research, the study of subject incentives if practically a cottage industry, and at least some of that work has taken up concerns with the ethics questions involved. The list of articles classified by the authors under the "miscellaneous" heading is surprisingly brief. Again I think this is likely indicative of the unfortunate decision to restrict their literature review to the PubMed database.	While we respect this reviewer's input, the decisions about where to focus the detailed review was made in consultation with VA Central Office stakeholders and is not something we can change. We reviewed the New Republic article by Lessig and were not as convinced as this reviewer that this is on target for this topic. The example used of JAMA's COI policy and the effect it had on a JAMA critic doesn't seem particularly relevant to investigators or IRBs dealing with possible financial interest in the research studies they conduct or review. If the point is that transparency of COI policies can have unintended consequences, that we agree with, but it is for empiric research to determine whether and to what magnitude such unintended consequences occur. We did devote a section of the review to potential harms of disclosure.We searched the internet for information on the VCU case and there has been no peer-reviewed publication about it, only one letter or commentary in BMJ.

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	4 (Cont'd)	Though it may have to do with search terms they have selected as well. As but one example of something I had expected to see here but did not is some very nice empirical work by Keith-Spiegel and colleagues on the issues of relationships between researchers and IRB's that is directly relevant to issues of research integrity.3,4 **Issues within the portion of the review dealing specifically with conflicts of interest.** The reviewed literature on COI seems to have focused almost exclusively on the issue of disclosure thereof. A very fundamental problem with this is that it jumps directly over the more obvious, but obviously more fraught approaches to COI emphasized by the two prominent reports (of the IOM and NIH) referenced on p. 2 of the current report. Specifically, both of those statements place emphasis primarily on the elimination and avoidance of conflicts of interest, and the active management of such conflicts where they cannot be eliminated or avoided, perhaps through formal means such as the creation of COI committees. Only lastly do they mention disclosure as an ameliorative, suggesting that they do not see this as a sufficient approach in and of itself. It would be striking had this just been an oversight of the report authors, but it is an astonishing blind-spot in the literature if there has been no empirical research into this. That the avoidance of COI has not been, and is not the focus of thought and discussion on this topic suggests that the community has yet to come truly to grips with the need to engage the problem at its roots. This reviewer is increasingly convinced that disclosure itself may be a really bad idea and likely has unanticipated consequences in undermining public trust, not preserving it. My own thinking on this topic has been influence by a 2009 article on the topic, written by Lawrence Lessig and published in The New Republic.5 Lessig makes what I find a very compelling case against relying on "transparency" as an antiseptic with respect to misbehaviors of those in government, arguing that such transparency would very likely undermine public trust and not accomplish its primary objective. I think his points translate largely into the realm of research and public trust as well. I was also very struck to see that the discussion of conflict of interest seemed to focus nearly exclusively on the issue of financial conflicts of interest that are introduced by individual researcher or IRB member involvement with industry in particular. Has there truly been no examination of institutional relationships (such as between University leadership decisions and funders, whether private OR public) as they may adversely impact the integrity of research? As one example, did the Martinson et al. 2009 article in Academic Medicine6 not get captured in the initial net that was cast? Has there been nothing published in the academic literature about the startling institutional conflicts of interest that were unearthed in 2008 between Philip-Morris and Virginia Commonwealth University? That controversy initially embroiled Frank Macrina (who was VP at VCU at the time), himself the author of the most widely cited textbook on responsible conduct of research! Was there no empirical work on the potentially conflicted nature of IRB service itself? Aside from the requisite community members and perhaps professional ethicists, most members of "local" IRB's are drawn from their own employing institution. This can readily put them in a conflicted position between loyalty to their employer and loyalty to the study subjects involved in the studies they are reviewing. I have witnessed this conflict first hand on a number of occasions in my own IRB service. One might view this as a concern about institutional conflicts of interest, which is again, another topic that I had expected to see arise in this review which is entirely absent.	

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	4 (Cont'd)	http://vabio.blogspot.com/2008/05/nyt-tobacco-research-is-secret-at-vcu.html	
		http://www2.richmond.com/business/2008/oct/01/vcu-report-on-tobacco-research-due-today-ar-627812/?referer=http://www.google.com/search&shorturl=http://bit.ly/dGHzhh	
		Minor points:	
		What is the correct number of articles identified under the topic of when quality improvement initiatives are considered research? At the top of page v the report indicates 31 whereas in the middle of page 10 indicates 32.	
		References:	
		1. Emanuel EJ, Menikoff J. Reforming the Regulations Governing Research with Human Subjects. *N Engl J Med*. 2011. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21787202. 2. Selker HP, Grossman C, Adams A, et al. The Common Rule and Continuous Improvement in Health Care: A Learning Health System Perspective - Institute of Medicine. Available at: http://iom.edu/Global/Perspectives/2012/CommonRule.aspx. Accessed February 8, 2012. 3. Keith-Spiegel P, Koocher GP. The IRB Paradox: Could the Protectors Also Encourage Deceit? Ethics & Behavior. 2005;15:339–349. 4. Keith-Spiegel P, Koocher GP, Tabachnick B. What Scientists Want from Their Research Ethics Committee. Journal of Empirical Research on Human Research Ethics. 2006;1:67–82. 5. Lessig L. Against Transparency: The perils of openness in government. The New Republic. 2009;(October 9). Available at: http://www.tnr.com/article/books-and-arts/against-transparency. Accessed March 4, 2012. 6. Martinson BC, Crain AL, Anderson MS, De Vries R. Institutions' Expectations for Researchers' Self-Funding, Federal Grant Holding and Private Industry Involvement: Manifold Drivers of Self-Interest and Researcher Behavior. Academic Medicine. 2009;84:1491–1499.	We obtained and reviewed the references cited by the reviewer. References 1,2,3 and 5 are opinions or commentaries and do not contain data and are therefore not included in our review. Reference 4 describes the result of a survey to identify the attributes of an "ideal" IRB from the perspective of researchers. While the results are interesting (the most highly valued item was "an IRB that reviews protocols in a timely fashion") they do not deal directly with the issue of COI or how it is applied. Reference 6 is a survey of 5000 randomly selected faculty from which 1703 yielded usable data, and while the results are revealing in terms of the relationship between funding source and potentially inappropriate behaviors, it does not deal with conflict of interest policies per se or their application.
	5	This draft report by Shekelle et al., detailed the results of their reviews of the literature from January 1, 2000, to February 11, 201, on issues related to the Institutional Review Board (IRB) including quality improvement initiatives, conflict of interest (COI) in research, multisite studies requiring multiple IRB approvals, and genetic research. A total of 116 articles were identified and reviewed. Although more articles were related to issues related to multisite studies requiring multiple IRB reviews (41 articles) and quality improvement projects (31 articles), the authors focused on issues related to research COI and IRB (11 articles), as currently VHA does not have a research COI policy. The review and analysis of the literature appeared to be adequate, and the draft report appeared to be well written. There are, however, a number of concerns: 1. As pointed out by the authors, the number of articles reviewed for the main topic, i.e., research COI and IRB, was small (i.e., 11 articles). In addition, there were substantial limitations in some of these articles including small sample sizes and low survey response rates. As a result, the draft report does not provide sufficient information/evidence to guide VHA policy makers in developing a research COI policy.	1. This is correct. The purpose of the review was not to assist VA in developing COI policies per se, but rather to examine the potential challenges in their application.

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	5 (Contd)	2. The authors repeatedly used the term "multisite institutional research board challenge." (see pages iv and 7) First of all, I believe they meant "multisite institutional review board (IRB) challenge." In addition, I believe they were talking about the challenge presented by multisite studies that required multiple IRB review and approval. The term multisite IRB is used for an IRB that covers a number of research facilities such as VA Central IRB. For example, VISN 4 has a VISN4 Multisite IRB located at the Coatesville VAMC that is being used as the IRB of record for not only Coatesville VAMC, but also for Wilkes-Barre VAMC (and Lebanon VAMC, and Erie VAMC in the past).	2. This sentence has been rephrased.
		3. On Page 9, the authors attempted to summarize VHA Handbook 1058.05 in Table 2. However, it really missed the essence of the Handbook. The following provides a better summary of the VHA Handbook 1058.05 entitled, "VHA Operations Activities that May Constitute Research." Health care operations activities such as quality assurance and quality improvement projects differ from research in that health care operations activities are specifically designed to support the operations of a health care institution, while research is specifically designed to contribute to generalizable knowledge (i.e., to expand the knowledge base of a scientific discipline or other scholarly field of study). Both health care operations activity and research utilize systematic investigation to achieve their objectives. Similar to research, the results of health care operations activity may be published in scientific journals and ultimately expand scientific knowledge base. Thus, neither systematic investigation nor publication effectively distinguishes health care operations activity from research. However, when a health care operations activity goes beyond its purpose of supporting the operations of a health care institution by adding elements specifically designed to expand the knowledge base of a scientific discipline or other scholarly field of study, the activity constitutes research.	3. This text was added
		4. On Page v, 3rd paragraph, it was stated that "Across studies, the amount of payment appeared related to the magnitude of the procedures to be performed or the time to participate in the study." However, on page 12, 1st paragraph, it was stated that "Across studies, there was, in general, no indication that the payment was related to the procedures to be performed or the time commitment required to participate in the study." (see also Pages vii and 23) Which one is correct?	4. This was a typographical error, it is "unrelated"
		5. On Page 2, 1st paragraph, it was stated that "IRBs also distinguish what constitutes a research study with human participation (i.e., an intervention that potentially subjects a patient to risk without guarantee of likely benefit and therefore requires IRB review) from quality improvement initiatives that do not directly involve participants." This statement is misleading. Human research does not have to directly involve participants. Likewise, quality improvement initiatives may directly involve human participants.	5. These revisions have been made.
		6. The numbers on page 6 do not add up! The number of references excluded should be 47, instead of 44 as stated in Pages iv and 6. In addition, it should be pointed out that the same two articles were included in Conflicts of Interest (N=11) as well as Genetics (N=8).	6. This sentence has been rephrased

	Reviewer	Comment	Response
Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	5 (Cont'd)	7. The second paragraph on Page 19 should have a new subtitle, as it does not belong to either "Who has Policies on Disclosure?" or "Conflict of Interest within an IRB." I suggest a subtitle such as "Which COI should be disclosed to Research participants?"	7. We have added to this section a modified version of this additional subtitle.
		8. Tables 1, 3, 4, 5 and 6 should be deleted, as they did not add any useful information. These references were already listed in Pages 28-35 under References.	8. We prefer to keep these in the text.
		9. On Page 15, there is a difference between "regulations" and "policies" or "guidelines." The NIH guidelines on financial conflict of interest are not "regulations."	9. According to NIH's website, the 2011 statements are "regulations" and so we continue to refer to them as such in the report. Please see: http://grants.nih.gov/grants/policy/coi/
		10. There were multiple typographic errors throughout the draft report (please see attached draft report in Track Change).	10. We identified and corrected the 3 typographical errors that were identified.
	6	Overall, this was a thorough summary of the literature. The use of frequencies in reporting articles and approaches helped convey the emphasis of the literature.	No response needed
	7	I put comments directly into the draft. The analysis and report are good. They should be published.	No response needed
Are there any clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.	1	None since policy already is well on its way to being promulgated, and some of the areas identified in the document already are addressed in VHA Handbook 1200.05.	No response needed
	3	PRIMR, the current review of the Common Rule by OHRP	No response needed
	6	It is likely that the report will help clarify and remove obstacles in conducting research in clinical settings.	No response needed
	7	AAMC has a group called FOCI that meets several times annually. That would be a good conference. It could be presented at the annual AAHRPP conference and PRIM&R conferences.	No response needed
Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.	1	This document is not relevant since some of the studies cited are from several years ago, and VHA research conflict of interest policy based on current thinking in government, academia, and the private sector has already drafted.	We believe it remains a suitable topic for research to determine the degree of variability that may exist within VA in the application of COI policies by both researchers and IRBs.
	2	Additional information for IRB administrators might be in order. The authors may want to make a recommendation as to what types of COI should be monitored.	This is a good recommendation but is for Central Office policy makers and not within the scope of the evidence report.
	3	The literature searches might well be stand-alone reports in a journal like Hastings or Hastings IRB journal.	No response needed

	Reviewer	Comment	Response
Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.	6	While the report did a good job of reviewing the literature, it would be helpful to have some mention or discussion about the implementation of the policies and the extent that how something is implemented (e.g., a conflicts of interest policy) may ultimately impact the overall effectiveness of a policy. The general emphasis—which was appropriate given the question—was on what the policies were, but the report leaves the reader with the impression that IRB and COI issues, for example, are primarily about defining the policy.	This important point was added to the future research.
Please provide us with contact details of any additional individuals/ stakeholders who should be made aware of this report.	1	Dr. Brenda Cuccherini, ORD	No response needed
	5	Dr, Brenda Cuccherini, Office of Research and Development	No response needed
	7	Ann Bonham, AAMC abonham@aamc.org I assume you have contacts at NIH.	No response needed

Additional Comments

Reviewer	Comment	Response
8	I agree with reviewer 9's main point as well. Since this is synthesizing evidence it would be appropriate to include some reference to the aggregated findings in the section below adding a very brief review (if possible at this late hour). Just an acknowledgement of the problem in a brief few lines should do it. Multisite Institutional Research Board Challenges We identified 41 articles that dealt with the challenges of having to submit a research protocol to IRBs at multiple institutions. Most were descriptive studies of how the same application was reviewed by different IRBs. VA has recently implemented a process whereby multi-site VA studies can be reviewed by a single, centralized IRB. Consequently, a detailed review of this issue would not be helpful to VA. Thanks for all those working on this.	We have added a brief statement (page 8) on the general findings within this topic.
9	The report is quite useful. As a consequence of the ESP and another document that addresses COI that HSR&D recently received, I will pursue an evaluation of COI both at an IRB and research project peer review committee levels. A few comments are attached: The presentation is clear, relevant, and useful. My only comment relates to the framing of Q2: "… for which no current policy exits." This framing results in statements that, "a detailed review of this issue would not be helpful to VA." To me, this sentence doesn't make sense, since my response is quite the opposite, i.e., because VA has determined that the issues are important (i.e., specific policy was developed), a detailed evaluation of the literature is also very important. HOWEVER, I am NOT proposing that the ESP be revised. It is truly useful as is. Rather, I suggest that the Key Question, and the rationale for focusing on COI, be revised. A few text revisions here and there in the Exec Summary (and perhaps in the body of the report) should be sufficient. Bottom Line – Nicely done. I greatly appreciate the consistent, high quality of the ES reports.	The phrasing of this key question has been revised to better frame its intent.