

## Offering Results to Research Subjects: U.S. Institutional Review Board Policy

By Christa Kozanczyn, Katie Collins, and Conrad V. Fernandez

*This article is reprinted from Accountability in Research, 14:4, 255-267 (<http://dx.doi.org/10.1080/08989620701670179>). It may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden. The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material. Full terms and conditions of use are at <http://www.informaworld.com/terms-and-conditions-of-access.pdf>.*

### Abstract

Background: This study aims to determine the nature of United States Institutional Review Board (IRB) policy in a broad spectrum of research settings regarding the return of results to study participants. Method: IRB policies or standard operating procedures of 207 Medical School, Industry and Nonmedical School IRBs were examined on-line to determine if they incorporated specific reference to the return of results to participants at the conclusion of the research. Results: The majority of IRBs had no available policy regarding the return of research results to participants [56% (n=116)]. A further third [36.3% (n=75)] had policies that were defined as vague or that only indirectly mentioned the return of results. Medical School IRBs were more likely to have a policy than Industry or Non-medical University IRBs, respectively (odds ratio, 4.63; 95% confidence interval, 1.84 to 11.66 and odds ratio, 3.03; 95% confidence interval, 1.75 to 5.25). Few provided any guidance as to the process of return of results. Of the IRBs that had a research results policy, 54.9% (n=50) specifically addressed genetic research. Conclusions: Our findings demonstrate a marked lack of uniformity in IRB policy regarding the return of study results with over half providing no guidance.

### Introduction

Respect for persons requires researchers to ensure participants are treated ethically, prior to, during, and after the completion of the research. While a number of authors advocate offering to share results in the majority of clinical research settings (Fernandez et al., 2003a; Partridge and Winer, 2002; Zlotnik Shaul et al., 2005), there are those who object to a routine practice of offering results to all research participants (Markman, 2006; Ravitsky and Wilfond, 2006). These objections are based on possible harms related to unreliable results, costs, adverse psychological impact, and potential insurance consequences (Dixon-Woods et al., 2006; Schulz et al., 2003). Participants, on the other hand, indicate that they wish to receive results, even if potentially negative (Fernandez et al., 2006; Partridge et al., 2005). Despite participant interest and potential benefits, researchers infrequently offer research results – on average less than 40% do so regularly (Partridge et al., 2004; Rigby and Fernandez, 2005). Given the ubiquitous implications in all aspects of human research and the marked complexity of how and when to provide research

results in a respectful manner, there is a strong need for consistent and detailed guidance from IRBs on this important issue.

There are no overarching regulatory policies in place governing the release of research results to the research participants in U.S. federal guidelines. Specific limited circumstances are addressed. The U.S. Common Rule requires that researchers provide research subjects with information on "significant new findings developed during the course of research which may relate to the subject's willingness to continue participation" (45 CFR 46.116, 2001). In addition, the Common Rule states that in the case where "research involves no more than minimal risk to the subject. . . whenever appropriate, the subjects will be provided with additional pertinent information after participation" in lieu of the required formal informed consent (45 CFR 46.116). These measures leave researchers with no guidance as to how to consistently offer research results in the vast majority of human research.

Outside of the U.S., international regulations are also inconsistent in addressing the issue of offering research results to participants. The Canadian TriCouncil Policy (2002) governing human research does not address this issue and perhaps explains the finding that few Canadian university-based research ethics boards (REBs) have policies on returning results (Macneil and Fernandez, 2006), despite the fact that REB chairs highly support the concept (Macneil and Fernandez, 2006). The document of The World Health Organization Operational Guidelines for Ethics Committees that Review Biomedical Research focuses on "community considerations" in making available results of the research (WHO, 2000). However, these guidelines do not explicitly indicate the need to consider this issue for individual participants.

There is an important gap in this emerging issue whereby participants are beginning to expect an offer of research results (Fernandez et al., 2007; Partridge et al., 2005) but researchers are lacking guidance as to how to do so. The offer of research results is particularly relevant to clinical trials where tangible benefits with respect to improved health outcomes may be available. It is also crucial to have a model of how to approach returning results to individuals and communities in genetic research (Ravitsky and Wilfond, 2006; Shalowitz and Miller, 2005). The IRB review provides a key opportunity to support researchers offering research results to participants, when appropriate.

We hypothesized that IRBs would be unlikely to have policies that addressed the return of research results or that contained concrete details. We examined a large sample of U.S. IRBs representing all medical school, industry, and a geographically representative sample of university-based IRB policies to ascertain a better understanding of the specific guidance that is provided to researchers for the return of research results. This is a fundamental step in determining the scope of regulatory intervention that is needed to improve guidelines promulgated by IRBs for researchers.

## **Methods**

We reviewed all available on-line Institutional Review Board policies from all U.S. medical schools, all industry IRBs as specified through an industry listing site (commercial independent IRBs not associated with any specific health care institution), and a geographically representative selection of Non-Medical School University IRBs from the American Association of State Colleges and Universities (AASCU) and the Office for Human Research Protections listing. These were abstracted from the public domain, Web sites from American Universities engaging in research using human subjects and industry Institutional Review Boards. Universities and IRBs were identified through the Internet. A total of 207 IRBs were identified from four Web sites:

<http://www.aamc.org/medicalschoools.htm>

<http://www.advamed.org/solutions/reviewboards.shtml>

<http://ohrp.cit.nih.gov/search/asearch.asp#ASUR>

<http://www.aascu.org/members/default.htm>

Out of a possible 125 Medical School Web sites listed on the AAMC Website, 123 were accessed. Two sites were not available at the time of searching; 30 of the 33 Industry IRBs' Web sites listed on the AdvaMed Web site were available; 3 listed Industry IRB Web sites were unavailable or did not exist at the time of searching; 54 non-medical school university IRBs were identified by using the listing of schools available on the AASCU Web site and cross-matching with the first possible match on the OHRP listing of IRB assurances by state. This represents a selection of nonmedical university IRBs characterizing all states in the U.S. and thus approximately 12% of the non-medical universities on the AASCU Web site.

One reviewer (CK) reviewed all Web sites using a standard scoring template. A second reviewer (CF) examined 20 Web sites at two separate times, ten sites being reviewed at each time. The first ten Web sites were examined at the beginning of the study by both reviewers to determine that the questions being asked were complete and that the definitions being used were clear. There was concurrence on the search strategy being used. The second set of Web sites was reviewed to determine the accuracy of the application of the previously defined questions and search. A discrepancy was found in the application of the search for mention of the Belmont Report, and the first reviewer rechecked all 207 Web sites to determine the presence or absence of the term and the presence or absence of a specific reference or link to the document. There was full agreement on other aspects of the data collection.

The standardized template was developed through a combination of literature review and review of a previous similar study (Macneil and Fernandez, 2006) to determine selected characteristics of the institutions, as well as characteristics of the IRB guideline documents. Data collection included the number of members of each IRB, as well as the categories of research reviewed at the institution (medicine, social science, humanities, law, non-medical health science, and other). Size of the institution (student enrollment) and the amount of federal research expenditures were acquired from the document Student Characteristics: Headcount, Part-Time Enrollment, Degrees from [http://thecenter.ufl.edu/AnyFed1990-2000-II/Student\\_Characteristics.xls](http://thecenter.ufl.edu/AnyFed1990-2000-II/Student_Characteristics.xls). The most recent available published data on student enrollment is from 2003-2004. The data on federal research expenditures is from the 2002 fiscal year from the same document.

Searches were made of each Medical School, Non-medical University and Industry IRB Web site to find guidelines or standard operating procedures. The IRB policy did not have to be specific to the Medical School. An acceptable IRB for review included those designated by the medical school Web site but affiliated with the university. The guidelines were searched using, when possible, the search/find function for the following search terms: adverse, unanticipated, results, return, outcome, termination, closure, finding, summary, Belmont, offer, inform, genetic, and deception. Relevant sections were read in their entirety. The sites were also visually scanned to ensure no relevant sections were missed. When the search/find function was unavailable, the policies were read in their entirety for the same information.

Presence or absence of IRB guidelines or standard operating procedures (SOP) and the details contained within the guideline were recorded as Yes, No, or Vague. Vague was utilized for Web sites with guidelines or SOPs referring to return of research as an abstract concept with no details provided. Data recorded included the following IRB requirements: to report adverse events to the IRB, to return data regarding adverse events to the study

participants, and to return the study findings or results to the study participants at the conclusion of the study.

## Statistics

Statistical analysis was performed in SPSS version # 13.0, published Chicago, Illinois. Descriptive statistics were used to report the frequencies of the availability of guidelines, the frequency of policies with details on reporting adverse events to study participants, and/or on the return of research results to participants.

We examined a number of associations determined a priori. These included the presence of a policy regarding the return of results to participants and the type of institution (Medical School, Industry, Non-medical School University), the size of the institution determined by student enrolment, the amount of federal research expenditures allotted to the institution (in a specific year) and the U.S. census geographic region of the institution (east, south, midwest, west). Industry IRBs were excluded from this part of the analysis as they do not have available funding data nor is the size of the institutions they represent meaningful. In order to analyze these associations, the data was recoded as dichotomous data. The institutions that had a Yes or Vague recorded for the presence of policy were recoded as Yes. This was done as it allowed for the possibility that even a Vague policy stipulation meant that the IRB was considering this issue. Significant P values were set at .05. Odds Ratios are reported with 95% confidence intervals.

## Results

Of the 207 University and Industry Institutional Review Boards reviewed, 164 (79%) had their IRB Guidelines online and an additional 15 (7.2%) had a portion of their guidelines available online. Requirements for reporting adverse events to study participants were found in 140 (67.6%) of all the institutions and vague guidelines regarding this issue were found in an additional 6 (4.9%). The number of institutions which had, within their guidelines, policies regarding the return of research results to study subjects is found in Table 1 and is subdivided by type of institution.

**Table 1. Presence of an IRB Policy or Guideline Details Regarding the Return of Research Results to Study Participants Described by Institutional Setting**

	<b>All N=207</b>	<b>Medical School N=123</b>	<b>Non-Medical N=54</b>	<b>Industry N=30</b>
No	116 56.0%	47 38.2%	43 79.6%	26 86.7%
Yes	16 7.7%	12 9.8%	4 7.4%	4 13.3%
Vague	75 36.3%	64 52.0%	7 13.0%	0 .0%

Medical School IRBs (N=123) had guidelines that contained policies, or the mention of policies, on the return of research results at the conclusion of the research to study participants 61.8% of the time (N=76), although over half of these were categorized as vague. These results were significantly different from Industry IRBs and Non-Medical Universities (chi square 22.69,  $p < .005$  and chi square 25.76,  $p < .005$ , respectively). Universities with Medical Schools were 4.63 and 3.03 times more likely (Odds Ratio 4.63, 95% confidence interval 1.84 to 11.66 and Odds Ratio 3.03, 95% confidence interval 1.75

to 5.25) to have policies than Industry IRBs or Non-Medical University IRBs, respectively. There was no significant difference between Industry IRBs and Non-Medical IRBs. IRB policies regarding the return of results were examined for specific details. These are shown in Table 2. Of the 91 institutions that had policies regarding the return of research results to study participants, 50 (54.9%) of them included genetic research as part of the policy.

**Table 2. Presence of Additional Policy Details within IRB Guidelines Regarding the Return of Research Results to Study Participants**

Policy detail	Yes	Vague	No
Who disseminates data to study participants	3 3.3%	9 9.9%	79 86.8%
What information is released to study participants	0 .0%	28 30.8%	63 69.2%
Requirement of peer review prior to dissemination	0 .0%	0 .0%	91 100.0%
Offer of study conclusions with informed consent document	17 18.7%	29 31.9%	45 49.5%
Budget requirements for the return of research results	0 .0%	1 1.1%	90 98.9%
Maintaining contact with study participants	1 1.1%	13 14.3%	77 84.6%
Readability of information released	1 1.1%	0 .0%	90 98.9%

There was no correlation between the student body size of the university or geographic location and the likelihood of a policy regarding the return of results to participants within their IRB guidelines. Chi square statistics show that there is a significant difference (chi square 14.44,  $p < .005$ ) in the presence of a policy regarding the return of research results with increasing research dollars (Table 3).

**Table 3. Presence of Policy Regarding the Return of Research Results to Study Participants Compared to Annual Research Grant funding (U.S. Dollars) of University Institutions**

		Presence of policy on the return of research results to participants		
		No	Yes	Total
2002 Grant funding as described by the Center "Student Characteristics" document	<1 Million	6 100.0%	0 .0%	6
	1-5 Million	7 53.8%	6 46.2%	13
	5-20 Million	21 67.7%	10 32.3%	31
	>20 Million	46 40.0%	69 60.0%	115

Industry IRBs had the lowest scores over all in virtually all categories. Of the 30 industry IRBs that had Web sites, only 11 (36.8 percent) had their policies on their Web sites. The

11 Industry IRBs that had policies online contained only details consistent with the Common Rule in mandating return of information that may affect the subject's willingness to continue. Only 4 (13.3%) had vague policies on returning research results to study subjects. There were no details regarding who was to give the information or what information was to be offered and no details on the offer of the return of results with the consent form. There was no mention of returning research in the context of genetics research.

## **Comment**

Our research shows that there is no systematic approach to the return of research results to study participants within guidelines provided by U.S. IRBs. Although almost half of the IRBs studied had some form of policy dealing with the issue, the operational details on how to respectfully return research results were vague or absent in the majority. Only one institution had details about the need for budget planning for the dissemination of results, even though adequacy of funding is a potential major impediment identified by researchers (Fernandez et al., 2003a; Fernandez et al., 2004). Medical Schools and Universities with large research budgets fared better in terms of having policies regarding the return of study results to participants. However, of the Universities that had research budgets of greater than U.S. \$20 million annually, only 60% had IRB policies that referred to the return of study data to participants. This reflects a missed opportunity for leadership in the academic community.

Industry IRBs frequently did not have their policies available online for potential clients to view nor did they have comprehensive policies when they were available online. These findings underscore the important point that regulatory guidance is required to ensure that ethical principles are being upheld by all researchers engaged in human research, regardless of setting (ASCOP, 2003). No significant association was observed between the presence of a policy on returning research results to study participants and the geographic location of the institution.

We noted that a high proportion of the institutions that had policies did so in the context of genetic research. Although in our study, the details of the policies regarding genetic research were not differentiated from those of generalized research, this is an important topic that requires a more thorough investigation. This is an emerging and highly debated topic with many difficult issues potentially impacting the individual participants, their families, and their communities (Bookman et al., 2006; Knoppers et al., 2006; Shalowitz and Miller, 2005; Weijer and Emanuel, 2000). It is recognized that there are special risks that are perceived to be present in genetic results (whether obtained clinically or by research). It is striking that despite these special risks, only 50 IRBs had specific guidelines regarding genetic results. This very complex area highlights a potential issue of justice that requires that we respect individuals in whichever jurisdiction their research is conducted. Guidelines developed for the results of genetic research obviously have the potential to provide lessons that can be utilized in less contentious areas of human research.

The 1979 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 'The Belmont Report' (1979), states that in order to conduct ethical research, a number of principles must be respected and maintained. These include respect for persons, beneficence and justice. The debate over the offering of research results to study subjects is in part a debate over the interpretation of what is meant by respect for persons. The Belmont Report states that volunteers engaging as research subjects should be treated as autonomous agents and as such have their personal goals and opinions respected. We argue elsewhere that the principle of respect for persons should extend to valuing choices made by all participants whether or not they accept an offer of research

results (Fernandez et al., 2003b). We have previously examined the presence of policies addressing this issue in Canada and found a similar lack of consistency (Macneil and Fernandez, 2006). Almost certainly this inconsistency relates to the absence of central regulatory guidance and points to a potential solution. The modification of regulatory guidelines to encompass this issue would certainly assist in bringing a strategic and uniform approach to this complex topic.

There are a number of strengths in this study. We have reviewed a highly representative number of IRBs including all U.S. Medical School IRBs. All of the available Industry IRBs were examined. Over 12% of U.S. Non-Medical Universities were reviewed with a broad geographic representation. Potential limitations of our findings come from the possibility of human error while visually scanning the IRB guidelines. We believe we minimized this by utilizing the search/find function for key words in the online IRB documents. The associations we have identified as significant show a large effect suggesting that the differences in presence of policies would have been retained even if some policies were missed. The utilization of online IRB Web sites for our data source has the potential to identify outdated information or an inaccurate reflection of an existing written policy. However, many researchers use these sites in preparing IRB submissions, thus making the lack of a policy or an inaccurate one potentially detrimental. Industry IRBs must have policies regarding the research they review. Since so few Industry IRB policies were available online there is the potential for an underestimation of the frequency of Industry IRB policy with regards to the return of results to study participants. However, the Internet is a frontline tool that is used by researchers and the absence of accurate Web site information is of little use to researchers seeking guidance on the ethical conduct of research.

## **Conclusion**

There is a marked lack of guidance and consistency from IRBs on the question of the return of research results to study participants. This is despite clear arguments for a moral accountability to consider doing so on the part of researchers (Fernandez et al., 2003b; Zlotnik Shaul et al., 2005). It is unlikely that IRBs will respond in a uniform manner without an overarching regulatory framework. Although rigorous self-driven attention to ethical issues in the conduct of research is required from all researchers, policy from IRBs to guide researchers in the offer and return of research results is clearly needed to provide a just and uniform approach in situations where the offering of results is generally agreed upon to be appropriate.

## **Acknowledgments**

We thank Charles Weijer, M.D., Ph.D., Department of Bioethics, University of Western Ontario, London, Ontario, Canada and Anthony Otley, M.D., Department of Pediatrics, IWK Health Centre and Dalhousie University, Halifax, Nova Scotia, Canada for critical review of an earlier draft of the manuscript.

This study was funded by the Dalhousie Medical School Research Fund and the IWK Health Centre Foundation, Halifax, Nova Scotia, Canada.

The funding sources had no role in design or conduct of the study; the collection, management, analysis, or interpretation of the data; or the preparation, review, or approval of the manuscript.

## References

- Department of Health and Human Services. (1979). Protection of human subjects: Belmont Report—Ethical principles and guidelines for the protection of human subjects of research, *Federal Register*, 44(76): 23192–23197.
- TriCouncil Policy Statement. (2000). Ethical Conduct for Research Involving Humans. Ottawa: Medical Research Council of Canada.
- Department of Health and Human Services. (2001). Title 45, Code of Federal Regulations, Part 46. Protection of Human Subjects. National Institutes of Health, Office for Protection from Research Risks.
- American Society of Clinical Oncology Policy. (2003). Oversight of clinical research, *J Clin Oncol*, 21(12): 2377–2386.
- Bookman, E. B., Langehorne, A. A., Eckfeldt, J. H., Glass, K. C., Jarvik, G. P., Clag, M., Koski, G., Motulsky, A., Wilfond, B., Fabsitz, R. R., and Luepker, R. V. (2006). NHLBI working group. Reporting genetic results in research studies: Summary and recommendations of an NHLBI working group, *American Journal of Medical Genetics*, A, 140(10): 1033–1040.
- Dixon-Woods, M., Jackson, C., Windridge, K. C., and Kenyon, S. (2006). Receiving a summary of the results of a trial: qualitative study of participants' views, *Bmj*, 332(7535): 206–210.
- Fernandez, C. V., Kodish, E., Shurin, S., and Weijer, C. (2003a). Offering to return results to research participants: Attitudes and needs of principal investigators in the Children's Oncology Group, *J Pediatr Hematol Oncol*, 25(9): 704–708.
- Fernandez, C. V., Kodish, E., and Weijer, C. (2003b). Informing study participants of research results: An ethical imperative, *Irb*, 25(3): 12–19.
- Fernandez, C. V., Santor, D., Weijer, C., Strahlendorf, C., Moghrabi, A., Pentz, R., Gao, J., and Kodish, E. (2007). The return of research results to participants: Pilot questionnaire of adolescents and parents of children with cancer, *Pediatr Blood Cancer*, 48(4): 441–446.
- Fernandez, C. V., Skedgel, C., and Weijer, C. (2004). Considerations and costs of disclosing study findings to research participants, *Cmaj*, 170(9): 1417–1419.
- Knoppers, B. M., Joly, Y., Simard, J., and Durocher, F. (2006). The emergence of an ethical duty to disclose genetic research results: international perspectives. *Eur J Hum Genet*, 14(11): 1170–1178.
- Macneil, S. D., and Fernandez, C. V. Attitudes of Research Ethics Board Chairs toward disclosure of Research results to research participants. Results of national survey. *Journal of Medical Ethics*, 33(9): 549–553.
- Macneil, S. D., and Fernandez, C. V. (2006). Informing research participants of research results: analysis of Canadian university based research ethics board policies. *J Med Ethics* 32(1), 49–54.
- Markman, M. (2006). Providing research participants with findings from completed cancer-related clinical trials: not quite as simple as it sounds. *Cancer* 106(7), 1421–4.
- Partridge, A. H., Hackett, N., Blood, E., Gelman, R., Joffe, S., Bauer-Wu, S., Knudsen, K., Emmons, K., Collyar, D., Schilsky, R. L., and Winer, E. P. (2004). Oncology physician and nurse practices and attitudes regarding offering clinical trial results to study participants. *J Natl Cancer Inst* 96(8), 629–32.

- Partridge, A. H., and Winer, E. P. (2002). Informing clinical trial participants about study results. *JAMA* 288(3), 363–5.
- Partridge, A. H., Wong, J. S., Knudsen, K., Gelman, R., Sampson, E., Gadd, M., Bishop, K. L., Harris, J. R., and Winer, E. P. (2005). Offering participants results of a clinical trial: sharing results of a negative study. *Lancet* 365(9463), 963–4.
- Ravitsky, V., and Wilfond, B. (2006). Disclosing Individual Genetic Results to Research Participants. *AJOB* 6(6):8–17.
- Rigby, H., and Fernandez, C. V. (2005). Providing research results to study participants: support versus practice of researchers presenting at the American Society of Hematology annual meeting. *Blood* 106(4), 1199–202.
- Schulz, C. J., Riddle, M. P., Valdimirsdottir, H. B., Abramson, D. H., and Sklar, C. A. (2003). Impact on survivors of retinoblastoma when informed of study results on risk of second cancers. *Med Pediatr Oncol* 41(1), 36–43.
- Shalowitz, D. I., and Miller, F. G. (2005). Disclosing individual results of clinical research: implications of respect for participants. *Jama* 294(6), 737–40.
- Weijer, C., and Emanuel, E. J. (2000). Ethics. Protecting communities in biomedical research. *Science* 289(5482), 1142–4.
- WHO (2000). Operational guidelines for ethics committees that review biomedical research., Vol. 2006. WHO.
- Zlotnik Shaul, R., Reid, L., Essue, B., Gibson, J., Marzinotto, V., and Daneman, D. (2005). Dissemination to research subjects: operationalizing investigator accountability. *Account Res* 12(1), 1–16.

## **Authors**

Christa Kozanczyn, School of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada  
Katie Collins, School of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada  
Conrad V. Fernandez, Division of Pediatric Hematology/Oncology, Department of Pediatrics, Halifax, Nova Scotia, Canada; IWK Health Centre and Department of Bioethics, Dalhousie University, Halifax, Nova Scotia, Canada; Email: conrad.fernandez@iwk.nshealth.ca