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OFFICE FOR PROTECTION OF HUMAN SUBJECTS
2150 SHATTUCK AVENUE, SUITE 300
BERKELEY, CA 94704-5940

(510) 642-7461
Web Site: http://cphs.berkeley.edu
FWA: #00006252

November 16, 2017

Research Compliance Advisory Committee
Office of Environment, Health and Safety
317 University Hall, #1150

Professor G. Steve Martin
Interim Vice Chancellor for Research
119 California Hall, #1500

Lisa Garcia Bedolla
Chair, Committee on Committees
Chancellor's Professor
5639 Tolman Hall

Attached is the 2016-2017 Annual Report for the Committee for Protection of Human Subjects (CPHS). CPHS and the Office for Protection of Human Subjects (OPHS) strive to offer excellent customer service while ensuring the health, welfare and safety of subjects and supporting institutional regulatory compliance. CPHS and OPHS continue to lead the UC System in reviewing and revising our policies and practices and implementing increased flexibility for non-federally regulated, minimal-risk biomedical, social-behavioral, and educational research projects. This minimizes regulatory burden on many investigators and has been greatly appreciated by the faculty. In light of the forthcoming changes to 45 CFR 46, the Code of Federal Regulations governing human subjects research, CPHS and OPHS will continue to revise policies and update guidelines in order to maintain regulatory compliance while streamlining processes and reducing administrative workload for faculty conducting human subjects research.

Please contact us with any questions or comments regarding this report:

- Rebecca Armstrong, Director, Research Subject Protection
  Email: rda@berkeley.edu Tel: (510) 642-1180

- William Jagust, CPHS-1 Chair
  Email: jagust@berkeley.edu Tel: (510) 643-6537

- Jane Mauldon, CPHS-2 Chair
  Email: jmauldon@berkeley.edu Tel: (510) 642-3475

Respectfully Submitted,

William J. Jagust, M.D.
Chair, Committee for Protection of Human Subjects (CPHS-I)
Professor, School of Public Health and Helen Wills Neuroscience Institute

Jane Mauldon, Ph.D.
Chair, Committee for Protection of Human Subjects (CPHS-2)
Associate Professor, Goldman School of Public Policy

Enc. CPHS Membership Roster 2016-2017

Cc: Patrick Schlesinger, Interim Associate Vice Chancellor for Research
Rebecca Armstrong, Director, Research Subject Protection

Report to the Research Compliance Advisory Committee

I. Committee Title and Report Period

Committee for Protection of Human Subjects - Report for July 1, 2016 - June 30, 2017.

II. Executive Summary

In 2016-2017, the Office for Protection of Human Subjects (OPHS) and the Committee for Protection of Human Subjects (CPHS) reviewed and approved 1895 applications, an increase of 222 protocols over last fiscal year. New, continuing review, and amendment approvals were up over last year, especially continuing reviews as a result of protocols with three-year approvals coming up for renewal. Noncompliance submissions went up as well, along with official determinations of "not human subjects research" (NHSR). The number of withdrawn applications was down. Despite a substantial increase in workload and reduced staff (see below for further details), OPHS review turnaround times remained steady (see tables 5 and 6). UC Berkeley research remains primarily social-behaviorally focused, at 73% of total approved submissions. Of the 1895 applications approved, 33% of them were federally-funded. As described in further detail below, an FDA audit in February resulted in good news for UC Berkeley.

In late 2015, UC Berkeley was the first UC System institution to roll out an Exempt Category #7. This new category permitted minimal risk, non-federally funded or regulated research studies, which formerly had to be reviewed under expedited level review processes, to now be reviewed under exempt level processes. Category #7 continues to benefit researchers in many ways, from filling out a shorter application form and reducing review time, to eliminating the need for continuing review. As displayed by a marked increase in exempt application submissions during the last fiscal year, UC Berkeley's research community is making use of this option.

Furthermore, UC Berkeley continues to grant 10-year approval periods to qualifying, expedited level, minimal risk studies; and, OPHS staff continue to serve as alternate CPHS members in order to review minor amendments and continuing review applications to help reduce review timelines. Throughout the fiscal year, CPHS and OPHS revised and created several guidelines and revised three policies. The full listing can be found at the end of this report.

In response to continuing conversations with UC Berkeley's research community, CPHS/OPHS implemented additional changes to increase flexibility within the regulations in order to facilitate the IRB review process for investigators. These changes included relaxing amendment requirements for non-federally regulated, minimal risk research, as detailed in the following guidance document: Attachment Requirements for Surveys, Questionnaires, and Interview Guides. In addition, OPHS staff implemented changes to internal policies for protocol review in an attempt to facilitate the review process for investigators and reduce the number of comment cycles needed before approval.

OPHS experienced a number of staff changes over the 2016-2017 fiscal year. Assistant Director Tanya Prestage left OPHS in September 2016 after three years of service and assumed a Director position at UC Santa Cruz. In October 2016 Emily Harden was promoted to the RCA-3 level and in February 2017 Adrienne Tanner was promoted to Assistant Director. IRB Coordinator Sarah Donnelly joined OPHS in February 2017 as well. Colleen Kohashi started taking over CPHS-2 committee work in spring 2017 and was promoted to IRB Administrator at the beginning of July. IRB Administrators Louise Tipton and Diana Holt retired at the end of June 2017 after 12 and 8 years of service to UC Berkeley, respectively.

III. Committee Membership and Number of Meetings During the Report Period

The Committee is comprised of two panels, CPHS-1 and CPHS-2, and both review biomedical and social-behavioral research. CPHS-1 convened 11 times and CPHS-2 convened 9 times during the ’16-’17 fiscal year. CPHS-1 had 14 members and CPHS-2 had 12 members (the 2016-2017 CPHS Membership List is attached).

Professor Bill Jagust, MD served as CPHS-1 Chair and Professor Jane Mauldon served as CPHS-2 Chair. Professor Jack Lesch served as CPHS-1 Vice Chair and Professor Oliver John served as CPHS-2 Vice Chair. OPHS Director Rebecca Armstrong served as a designated CPHS reviewer assisting with the expedited review of minor protocol amendments (e.g., reviewing the addition of funding), continuing review/renewal applications, and deviation reports. OPHS staff were authorized as alternate members for Dr. Armstrong in order to complete IRB review and approval duties, as determined appropriate based on their experience and role in OPHS.

IV. Summary of Research Protocols Reviewed

Approvals

The total human subjects research review activities for CPHS and OPHS increased by 222 submissions for 2016-2017. New protocol submissions were up slightly overall in comparison to last year, with a substantial increase in new exempt reviews due to the increasing popularity of exempt category #7. New full board applications decreased by 26 applications, while new expedited applications remained steady at 287. Amendments were up for expedited protocols, while full board amendments dropped and exempt amendments remained steady. The sharpest increase was for expedited continuing review applications, up by 193 over last year. This increase is due to applications with three-year approvals coming up for renewal for the first time. Three-year approvals were first granted in April 2013. In April 2016, CPHS further extended the standard approval period to 10 years. As we continue to grant 10-year approvals for minimal risk, non-federally regulated research, we expect continuing reviews numbers to substantially decrease in the future. Further, new 45 CFR 46 regulations, scheduled to take effect in January 2018, no longer require continuing review for minimal risk research regardless of funding.

Figure 1 shows the total number of applications approved over the last five years. Table 1 breaks down the applications approved over the same period of time based on the type of submission and level of review. These data exclude cases of potential noncompliance, adverse events, unanticipated problems, administrative actions, and withdrawn submissions.

Figure 1. Total applications approved over 5 years

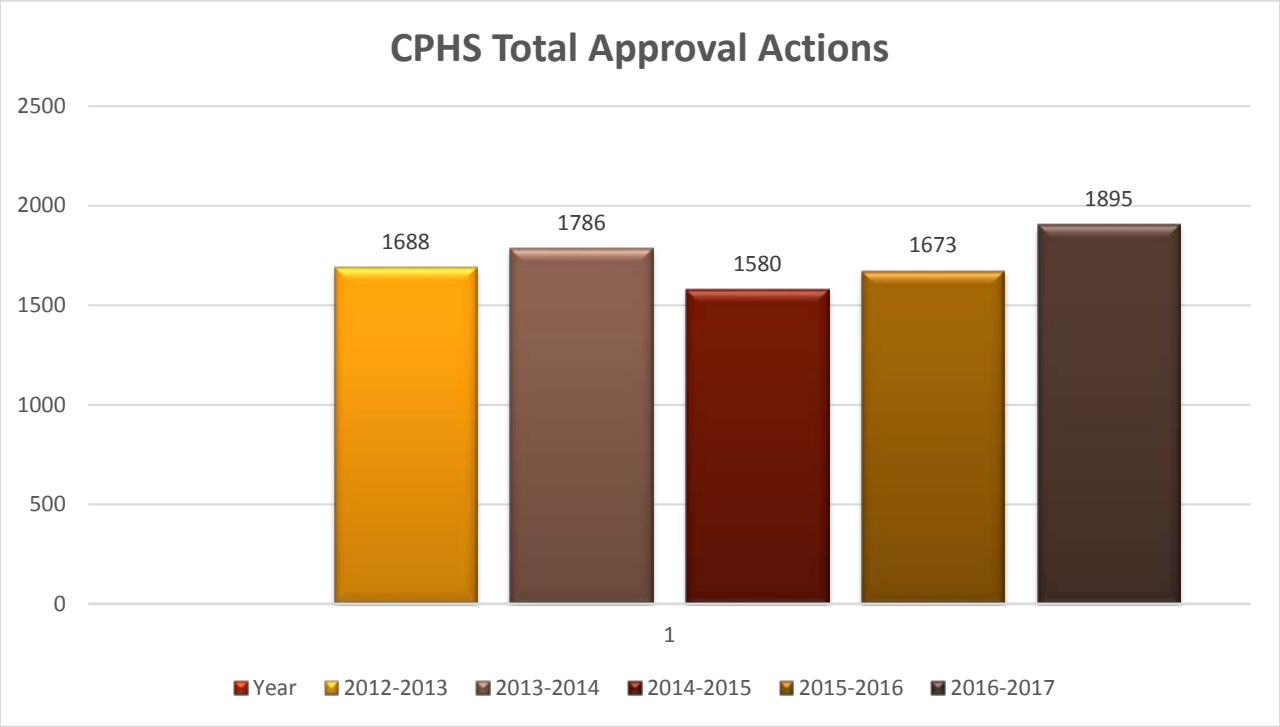


TABLE 1. Types of applications approved over 5 years

Application Type		2012-13	2013-14	2014-15	2015-16	2016-17
New	Exempt:	210	205	178	200	244
	Expedited:	238	309	355	290	287
	Full Board:	27	29	44	81	55
	TOTAL	475	539	577	571	586
Amendment	Exempt:	74	100	116	132	131
	Expedited:	500	494	592	661	679
	Full Board:	14	27	34	19	13
	TOTAL	588	621	742	812	823
Continuing Review	Expedited:	582	603	235	260	453
	Full Board:	43	23	26	30	33
	TOTAL	625	626	261	290	486
Total Activity		1688	1786	1580	1673	1895

Withdrawn applications

There are times when applications received by CPHS/OPHS are reviewed, then later withdrawn from consideration by the researchers before final approval. The majority of these are new applications, but also include amendments, continuing reviews, and deviation submissions. Table 2 shows applications withdrawn over the last five years by level of review. Out of the 153 applications that were withdrawn this year, 62 were exempt applications, 82 were expedited applications, and 9 were full board applications.

TABLE 2. Applications withdrawn by level of review

Reporting Period	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
Exempt	61	60	54	75	62
Expedited	65	64	88	96	82
Full Board	6	5	16	19	9
Total:	*132*	*125*	*158*	*190*	*153*

Adverse Events and Unanticipated Problems
There were 10 potential unanticipated problems reported in the last year; however, none were determined to be unanticipated problems involving risk to subjects or others.

Noncompliances
Whenever a study deviates from the approved protocol, or when activities occur outside of an approval, this is deemed noncompliance and must be reported to CPHS. Most often these are found to be cases of simple noncompliance, such as exceeding the approved total number of subjects. Sixty-two cases of potential noncompliance were reviewed in the last year, none of which were found to be serious or continuing noncompliance.

TABLE 3. Noncompliance

Reporting Period	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
Noncompliance cases	36	66	46	54	62

Subject complaints
OPHS received three subject complaints this past year which were unsubstantiated or the issue was quickly resolved with the Principal Investigator.

Administrative actions
OPHS provides consultation on whether an activity is or is "not human subjects research" (NHSR). At times a journal or sponsor may require an official determination of NHSR. If the request is made by email, OPHS issues a determination letter. Eleven official NHSR determination letters were issued last year. Many more determinations were issued informally by email through ophs@berkeley.edu. If a protocol is submitted through eProtocol that is *not* found to meet the threshold definition of human subjects research, OPHS makes a NHSR determination. Last year, 39 determinations were made in eProtocol. The eProtocol system provides a NHSR determination action notification for researchers as proof of determination.

OPHS also processes requests for one institution to rely on the IRB review of another. The process helps prevent duplicative IRB reviews of collaborative projects that involve more than one institution. Investigators can make use of the UC System Memorandum of Understanding (MOU) that permits one campus to rely on the IRB review of another. Outside of the UC system, investigators may request that

UC Berkeley either review for or rely on another institution they are collaborating with. These requests must be reviewed and approved by the OPHS Director. For non-UC collaborations, institutions may enter into Inter-Institutional IRB Authorization Agreements (IIAs), either formally documented with an IIA form or listed on a spreadsheet, depending on protocol specifics. Table 4 lists the number of active projects with MOUs and/or IIAs for the past five years. Table 4 shows an increase in MOUs and IIAs, indicating increased collaboration among institutions and decreased duplicative work for investigators and IRBs alike.

In addition, this past year UC Berkeley signed on to the IRB Choice single IRB (sIRB) agreement that may be used for NIH funded clinical trials and collaborative research.

TABLE 4. Memoranda of Understanding and Inter-Institutional IRB Authorization Agreements

Reporting Period	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
Reliances under UC MOU					
UCB Reviewed	88	97	87	124	134
UCB Relied	30	30	30	29	137
Total:	*118*	*127*	*117*	*153*	*271*
Reliances under IIAs					
UCB Reviewed	86	101	85	113	102
UCB Relied	20	15	18	27	41
Total	*106*	*116*	*103*	*140*	*143*

2016-2017 Turnaround times

The tables below show the amount of time (in number of calendar days) that a new application or amendment spent with CPHS/ OPHS and the amount of time spent with the investigator(s) between submission and approval. Time spent with CPHS/OPHS includes the time taken to assign the submission to an OPHS analyst, time the analyst spent on the preliminary review, and time spent by the convened IRB or designated reviewer. Time is measured in calendar days and a value of "0" indicates that action was taken by that party in less than 24 hours. Continuing review turnaround times are not included as they are processed by expiration date.

On the CPHS/OPHS side, turnaround times for this period compared to last period were similar, despite reduced staff and an increase in protocol submissions. (We focus here on the median values – see table below.) Days spent with CPHS/OPHS for new submissions went up 6 days for exemptions, down 4 days for expedited protocols, and down 2 days for full board applications. Days with investigators (which is not under CPHS control) went down in every category.

Table 5. Turnaround times for new protocols

Application Type		Calendar Days with CPHS/OPHS				Calendar Days with Investigator(s)		
		2013-14	2014-15	2015-16	2016-17	2014-15	2015-16	2016-17
Exempt	Range	-	-	0 to 62	0 to 47	-	0 to 217	0 to 159
	Median	4	8	11	17	6	9	6
	Average	6	9	13	17	17	18	13
	# protocols	205	178	200	244			
Expedited	Range	-	-	0 to 229	3 to 130	-	0 to 242	0 to 206
	Median	29	38	46	42	12	14	10
	Average	33	39	47	44	25	26	18
	# protocols	309	355	290	287			
Full Board	Range	-	-	11 to 83	19 to 141	-	0 to 217	0 to 178
	Median	28	38	40	38	38	22	16
	Average	42	42	42	45	15	32	29
	# protocols	29	44	81	55			

On the CPHS/OPHS side, turnaround times for amendments went up by 1 day for exempt and expedited protocols, and remained steady at 7 days for full board protocols. Turnaround times on the investigator side remained steady for expedited and full board protocols, and went down by 1 day for exempts.

Table 6. Turnaround times for amendments

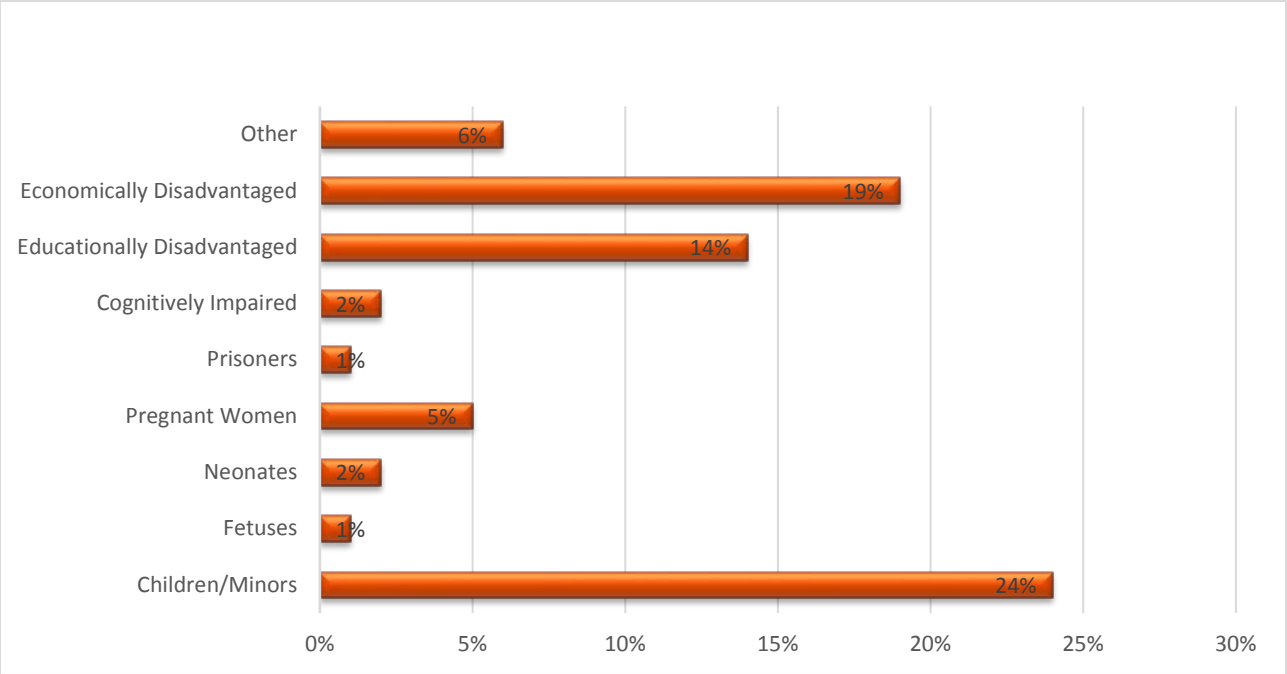
Application Type		Calendar Days with CPHS/OPHS				Calendar Days with Investigator(s)		
		2013-14	2014-15	2015-16	2016-17	2014-15	2015-16	2016-17
Exempt	Range	-	-	0 to 56	0 to 29	-	0 to 176	0 to 223
	Median	2	2	4	5	-	1	0
	Average	3	4	5	7	15	9	5
	# protocols	100	116	132	131			
Expedited	Range	-	-	0 to 78	0 to 73	-	0 to 308	0 to 228
	Median	6	8	7	8	-	0	0
	Average	9	11	11	11	19	7	5
	# protocols	494	592	661	679			
Full Board	Range	-	-	0 to 41	0 to 72	-	0 to 41	0 to 63
	Median	6	7	7	7	-	0	0
	Average	10	13	10	14	15	4	5
	# protocols	27	34	19	13			

Significant details for 2016-2017 research

- *Social-behavioral vs. biomedical research:* 73% of protocols (new and continuing review applications) approved were for social-behavioral research.
- *International research:* 20% of the protocols reviewed and approved included international sites.

- *Federally funded research:* 33% of the protocols reviewed and approved indicated that they were supported by federal funds.
- *Research with vulnerable subject populations:* 40% of the protocols reviewed and approved included at least one vulnerable population. Economically and educationally disadvantaged subject populations are often present in the same study.

FIGURE 2. Vulnerable subjects 2016-2017



V. New Laws, Regulations, and Standards

Updated Common Rule

Changes to regulations governing human subjects research, as outlined in the Common Rule, 45 CFR 46, were published in the Federal Register in January 2017. The rule changes are scheduled to take effect on January 19, 2018. The amended rules are the first significant changes to human subjects regulations since 1991. While some changes will reduce the burden on researchers and institutional compliance areas, other requirements come with additional responsibilities. Assuming there is no delay in the implementation dates for these new regulations, OPHS/CPHS is working to update its policies, guidelines, and research applications to adhere to the new regulations.

NIH's Revised Clinical Trial Policies

Good Clinical Practice Training: Effective January 1, 2017, NIH expects all NIH-funded clinical investigators and clinical trial staff who are involved in the design, conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP).

Implementation of New NIH Clinical Trial Definition and Procedures:

In 2014, NIH began a multi-faceted effort to enhance the quality, relevance, feasibility, and transparency of NIH-funded clinical trials. A key element of these stewardship reforms was the development of a clearer, more comprehensive definition of clinical trial. The NIH clinical trial definition is:

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes (https://grants.nih.gov/policy/clinical-trials/definition.htm).

The revision is designed to make the distinction between clinical trials and clinical research studies clearer and to enhance the precision of the information NIH collects, tracks, and reports on clinical trials. When determining whether or not a study qualifies as a clinical trial, investigators must ask the following questions:

a) Does the study involve human participants?
b) Are the participants prospectively assigned to an intervention?
c) Is the study designed to evaluate the effect of the intervention on the participants?
d) Is the effect being evaluated a health-related biomedical or behavioral outcome ?

If the answer to all four questions is "yes," then the clinical study would be considered a clinical trial according to the NIH definition. All NIH applications proposing clinical trials that are submitted on or after 1/25/2018 must be submitted under a funding opportunity announcement (FOA) designated specifically for clinical trials. There has been some concern within the research community about this change, especially as it applies to behavioral studies that might previously have been considered basic research. As a social-behaviorally focused institution, this change might affect studies here at UCB that were not previously considered to be clinical trials.

NIH Single IRB Policy
The Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research issued June 2016 states that all domestic sites of NIH-funded non-exempt multi-site studies where the same research protocol is being conducted at more than one site must use a single IRB (sIRB) for review, while all other sites rely upon that single review. The policy does not apply to multi-site studies when the sites have different roles in carrying out the research. With certain exceptions in their proposals, investigators must submit a plan to NIH stating which IRB is the sIRB. The policy was originally scheduled to be enforced starting May 25, 2017. However, in response to feedback from the national research community, the implementation date has since been delayed to January 25, 2018. Guidance and Frequently Asked Questions to assist in the implementation of the policy are available at: https://osp.od.nih.gov/clinical-research/irb-review/.

VI. New or Modified Campus Procedures and Programs

OPHS staff updated and/or created a large amount of content on http://cphs.berkeley.edu over the last fiscal year to aid investigators and research participants alike:

CPHS Guidelines
OPHS and CPHS updated the following guidelines for investigators:

- Attachments Check List for Exempt Applications
- Attachments Check List for Non-Exempt Applications
- Children in Research
- Child Assent and Parent Permission
- Compensation of Research Subjects

- Exempt Research
- HIPAA and Human Subjects Research
- Informed Consent
- Magnetic Resonance Imaging (MRI) in Research
- Secondary Analysis of Existing Data

OPHS and CPHS developed the following guidance:
- Attachment Requirements for Surveys, Questionnaires, and Interview Guides (new)

CPHS Policies and Procedures
OPHS and CPHS updated the following policies:
- IRB Meeting Administration
- Categories of Action
- Unanticipated Problems and Adverse Event Reporting

CPHS Website
- An FAQ on electronic consent signatures was developed and added: http://cphs.berkeley.edu/faqs.html#e7
- An FAQ on volunteer research assistants was developed and added: http://cphs.berkeley.edu/faqs.html#e13
- The CPHS/OPHS glossary of terms was updated: http://cphs.berkeley.edu/glossary.html
- Consent builder was updated: http://cphs.berkeley.edu/consentbuilder.html
- Consent/permission/assent templates were updated: http://cphs.berkeley.edu/informedconsent.html
- Worksheet to Determine Whether Human Subjects Are Involved in Research When Obtaining Existing Data/Biological Specimens was developed and added.
- Working With Research Study Participants: An Overview was developed and added as an educational resource.
- About Research Participation was created for research participants.

VII. Agency Inspections and Enforcement Actions

The FDA audited CPHS/OPHS in February from 2/16/17-2/23/17. OPHS staff worked tirelessly to prepare for the unannounced audit while maintaining their normal workload. The Auditor began his audit by reviewing a select number of FDA-regulated protocols as well as meeting materials, minutes, rosters, and policies. The Auditor found no regulatory noncompliances (i.e. no 487's were issued) and noted just two minor observations that were promptly corrected. The Auditor predicted the final outcome from the FDA's compliance office would be a *No Action Needed (NAI)* letter and that it would be approximately five years before CPHS/OPHS might expect another FDA auditing visit. As of November 15, 2017, CPHS/OPHS has yet to receive an official outcome letter from the FDA.

VIII. Education and Outreach

Education of UCB's research community
OPHS conducted 18 training sessions for the research community in the past year, similar to last year's 17 presentations. See a breakdown of presentations by unit in the below table.

Table 7. Education Outreach

College/School/Department	# of Presentations

Anthropology	2
CSS Team 2 ERSO Managers	1
Graduate Student Workshop	2
Joint Medical Program	1
McNair Scholars	1
Psychology	1
RAC Forum for Research Administrators	1
Research Administrator Professional Development Program (RAPDP)	1
School of Public Health	3
School of Social Welfare	1
Sociology	3
SURF/Haas Scholars	1

Education/professional development of OPHS staff
Alexis Clasca, Colleen Kohashi, Carmen Lam, and Adrienne Tanner presented at the 2016 Advancing Ethical Research Conference organized by Public Responsibility in Medicine and Research (PRIM&R) held in Anaheim, CA (see below for details). Director Rebecca Armstrong continued serving on the education sub-committee for PRIM&R Board.

Clasca, A., & Lam, C. (2016, November). *Implementing Flexibility and Being Flexible*. Poster session presented at the annual meeting of Public Responsibility in Medicine and Research, Anaheim, CA.

Kohashi, C., & Tanner, A. (2016, November). *Conducting Research in an International Setting: Resources and Guidelines.* Poster session presented at the annual meeting of Public Responsibility in Medicine and Research, Anaheim, CA.

OPHS staff participated in the following webinars:

- UCOP, "Responding to Noncompliance in Human Subjects Research," November 2016.
- Public Responsibility in Medicine and Research, "Primer on the Revised Common Rule" in January 2017.
- Public Responsibility in Medicine and Research, "Introduction to Research Misconduct for IACUC, IRB, and IBC Professionals" in May 2017.
- SBER Virtual Roundtable: "Understanding FERPA and its application to SBER", June 2017

General issues under discussion in the IRB world (in addition to items described above regarding new regulations, policies and definitions):
- Implementation of updated Common Rule.
- sIRB use and implementation issues.
- Data repositories and Big Data.