



July 14, 2015

VIA ELECTRONIC MAIL

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SACHRP Chair
Jerry A. Menikoff, MD, JD
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SACHRP Executive Secretary
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Dear Drs. Botkin and Menikoff:

The undersigned members of the Physician Clinical Registry Coalition (“the Coalition”) appreciate the opportunity to submit these comments prior to the July 21-22, 2015 meeting of the Secretary’s Advisory Committee on Human Research Protections (“SACHRP”). Several members of the Coalition plan to attend and provide public comment at the SACHRP meeting on Tuesday, July 21, when the Committee is scheduled to discuss the application of Department of Health and Human Services regulations to registries, including the topic of benchmarking in human subjects research. The Coalition is a group of more than 20 medical society-sponsored or physician-led clinical data registries that are working together to advocate for public policy changes that will help promote and/or remove barriers to the development of such registries. The Coalition is very encouraged by SACHRP’s recommendations in its report, titled “Human Subjects Research Implications of ‘Big Data’ Studies” (“Big Data Advisory Document”),¹ as well as Dr. Menikoff’s June 25, 2015 letter responding to previous questions and requests from the Coalition. A copy of Dr. Menikoff’s letter is attached for your convenience, along with the Coalition’s September 23, 2013 letter to the Office for Human Research Protections (“OHRP”).

This letter sets forth some background on the ongoing concerns of clinical data registries with respect to the application of the Common Rule to their activities and lists the key issues we would like to cover in our comments at next week’s SACHRP meeting.

¹ http://www.hhs.gov/ohrp/sachrp/commsec/hsimplicationsofbig_datastudies.html.
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Background

Generally speaking, the Coalition members collect identifiable patient information or protected health information (“PHI” as defined by the HIPAA Privacy Rule) primarily for purposes of quality improvement for the participating sites relating to the procedures or diseases covered by the registry. This quality improvement effort is typically achieved by developing benchmarks on performance/treatment outcomes from data submitted by all registry participants and sharing those benchmarks with each registry participant. In doing so, these registries typically will enter into HIPAA-compliant business associate agreements with their participating hospitals or medical practice groups. Many registries also will obtain waivers from an institutional review board (“IRB”) of the HIPAA authorization and Common Rule informed consent requirements to allow for the collection and use of PHI for research purposes. The registries obtain these waivers even though, according to OHRP guidance, the Common Rule generally should not apply to the majority of registries because they do not receive federal funding or conduct federally-regulated research. In addition, existing OHRP guidance and Dr. Menikoff’s June 25 letter confirm that health care providers that submit data collected in the course of regular clinical care to external third-party researchers are not engaged in human subjects research and therefore such submissions are not covered by the Common Rule.

Nonetheless, many hospitals and other data sources will not submit data to a registry that engages in some research analysis of their data without such IRB waivers. Despite the precautionary steps described above, many hospitals take the position that they must obtain separate waivers from their local IRBs notwithstanding OHRP’s clear statements that the hospitals could rely on a central IRB waiver obtained by the clinical registry covering such data submission. Even worse, many hospitals believe they must obtain HIPAA authorizations and Common Rule informed consent from patients before submitting their data to a clinical data registry that conducts research on the data, even if such research uses de-identified data or a limited dataset as defined by HIPAA. These positions are creating significant barriers to the development of clinical data registries.

Requested Clarifications

The Coalition greatly appreciates the clarifications that OHRP has already provided on the application of the Common Rule to the activities of clinical data registries. However, we believe further, more prominent guidance from OHRP is necessary to alleviate barriers to registry development due to the confusion about whether the Common Rule applies to clinical data registries or health care providers submitting data to registries. Most of these requests are supported by the SACHRP’s Big Data Analysis Document. All of our requests would fall within the scope of Section 511 of the Medicare Access and CHIP Reauthorization Act of 2015 (HR 2) that the Secretary issue a clarification or modification with respect to the application of the Common Rule to clinical data registries.

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The principal issues and requested clarifications we would like OHRP and SACHRP to consider are as follows:

1. We appreciate Dr. Menikoff's confirmation that health providers that submit clinical outcomes data to a data registry that conducts some research with that data does not cause such data sources to be engaged in human subjects research themselves. This position is based on Section III.A.6. of the OHRP "Guidance on Engagement of Institutions on Human Subjects Research" at <http://www.hhs.gov/ohrp/policy/engage08.html>, which states that "Institutions whose employees or agents release to investigators at another institution identifiable private information or identifiable biological specimens pertaining to the subject of the research" are not engaged in human subjects research. The SACHRP recommends that OHRP reiterate its position on this issue. We would go one step farther and ask that the agency amend its current guidance on this issue specifically to add a reference or example for outcomes data submitted to clinical data registries by hospitals, physicians, and other data sources. We would also expect this issue would be covered by the Secretary's guidance document in response to Section 511 of HR 2.
2. We remain concerned about OHRP's position on benchmarking for quality improvement purposes. We appreciate the statement in Dr. Menikoff's letter "that some benchmarking activities—for example, ones that are designed solely to measure performance levels by participating practitioners or institutions and not to produce new knowledge regarding the relationship between specific procedures and health outcomes—will not satisfy the definition of research and thus will not activate the regulatory requirements." He further states that the agency continues "to look for better ways to clarify this distinction." Dr. Menikoff indicated that his statements are based on the SACHRP's analysis of this question. We applaud the SACHRP for its thoughtful discussion of this issue and agree that the focus should be on risk analysis and protection of the data, regardless of the purpose. We disagree, however, with the premise that benchmarking itself can meet the definition of research. Rather, benchmarking by definition is conducted solely to measure the performance levels of registry participants. Benchmarking results may also be used for research purposes, but such use of de-identified, aggregate data does not trigger HIPAA requirements and should not implicate the Common Rule either. Alternatively, we would support an effort to distinguish between "low risk" research conducted using big data, including data collected from clinical encounters unrelated to specific clinical studies, versus "higher risk" research based on clinical studies or investigations that involve direct interactions with patients.
3. We appreciate Dr. Menikoff's confirmation that to the extent a clinical data registry's collection of identifiable patient information requires IRB review and approval or an IRB waiver of the Common Rule consent requirements, a central IRB review and approval or

waiver would satisfy the regulatory requirements—meaning that the sites submitting data to the registry may rely on that central IRB waiver and should not need to obtain a separate waiver from their local IRBs. We continue to believe that more prominent guidance on this point would be helpful. At a minimum, this principal should be included in the Secretary’s guidance on the application of the Common Rule to clinical data registries under Section 511 of HR 2.

4. The Coalition generally applauds the SACHRP’s recommendation that OHRP consider creating a new Common Rule exemption for registry studies based on clinical outcomes data where the registries’ data collection efforts are subject to HIPAA’s rigorous privacy and security requirements and there is no direct interaction with patients. The Coalition recommended such an exemption in its 2013 letter to Dr. Menikoff and in other communications with OHRP and Congress. As the SACHRP Big Data Advisory Document states:

There have been recent proposals that registry studies tracking delivery of standard of care and that involve entities covered by HIPAA (including the institution in which the research is conducted) are so low risk, and their potential benefit so great, that a new exemption should be adopted, allowing these studies to proceed without any IRB review. Establishing such an exemption would eliminate transaction costs and delays for these studies, and would pose risk to subjects that would be vanishingly small, as long as the protections of HIPAA are applied to the data.

While we appreciate the SACHRP’s support of this proposed exemption, we do not believe it should be tied to new transparency requirements or solicitation of input from patient focus groups or community advisory boards, as suggested in the Big Data Advisory Document. The point of the exemption is that the relevant HIPAA privacy and security rules provide more than adequate protection for patient data. Unless there is some direct interaction with patients, the Common Rule only adds confusion and cost, but not tangible additional protection of patient rights or welfare. Layering additional new requirements would defeat the purpose of the exemption—*i.e.*, to simplify and reduce the cost of developing clinical data registries.

That said, the Coalition is open to discussions about transparency of clinical data registry methods and public reporting of registry data. But such discussions should not be tied to the adoption of a HIPAA exception to the Common Rule for pure data collection activities by clinical data registries.

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Thank you again for the guidance you have provided on these important issues. We look forward to discussing them at the SACHRP July 21 meeting and working together after that to ensure the achievement of the dual goals of protection of PHI/identifiable patient data and development of clinical data registries to improve patient care. If you have any questions, please feel free to contact Rob Portman at 202-872-6756 or rob.portman@ppsv.com.

Sincerely,

AMERICAN ACADEMY OF NEUROLOGY
AMERICAN ACADEMY OF OPHTHALMOLOGY
AMERICAN ACADEMY OF PHYSICAL MEDICINE AND REHABILITATION
AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS
AMERICAN JOINT REPLACEMENT REGISTRY
AMERICAN COLLEGE OF SURGEONS
AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
AMERICAN SOCIETY OF CLINICAL ONCOLOGY
AMERICAN SOCIETY OF NUCLEAR CARDIOLOGY
AMERICAN SOCIETY OF PLASTIC SURGEONS
AMERICAN SOCIETY FOR RADIATION ONCOLOGY
AMERICAN UROLOGICAL ASSOCIATION
NORTH AMERICAN SPINE SOCIETY
SOCIETY OF INTERVENTIONAL RADIOLOGY
SOCIETY OF NEUROINTERVENTIONAL SURGERY
SOCIETY FOR VASCULAR SURGERY
THE SOCIETY OF THORACIC SURGEONS

Enclosures



JUN 25 2015

Robert M. Portman, JD, MPP
Principal
Powers Pyles Sutter & Verville PC
1501 M Street, N.W., Seventh Floor
Washington, D.C. 20005-1700

Dear Mr. Portman:

This is in response to your communications with the Office for Human Research Protections (OHRP) on behalf of the Physician Clinical Registry Coalition regarding the application of the Department of Health and Human Services (HHS) protection of human subjects regulations at 45 CFR part 46, subpart A (the “Common Rule”) and the activities of clinical data registries. In a letter sent to us on September 23, 2013, you requested a number of clarifications by OHRP related to the application of the Common Rule to clinical data registries. Since that time we posted on the OHRP website the OHRP correspondence with Dr. Anthony Asher on behalf of the National Neurosurgery Quality and Outcomes Database, in which we responded to some of the same issues.

http://www.hhs.gov/ohrp/policy/Correspondence/correspondence_regarding_the_application_of_45_cfr_part_46_to_the_activities_related_to_a_national_health_registry.html. And as noted below, we asked the Secretary’s Advisory Committee on Human Research Protections (SACHRP) to consider some of these issues, which it has now done. While that correspondence and the SACHRP deliberations address some of your concerns, this letter replies directly to your specific requests.

The first request is that OHRP “confirm that providers and groups that submit clinical outcomes data to a data registry primarily for ‘health care operations purposes’ (as defined by the HIPAA privacy rules) are not engaging in human subjects research (as defined by the Common Rule).” With regard to this issue, we note that any institution - including practice groups, hospitals or other clinical care providers - that solely releases private identifiable information that was obtained in the course of patient clinical care to a clinical data registry is not “engaged” in human subjects research, and no regulatory requirements of the human subjects regulations apply. This is true even if the clinical data registry will be conducting nonexempt human subjects research with that information. You suggest that OHRP amend its [Guidance on Engagement of Institutions on Human Subjects Research](#) to specifically refer to this circumstance. We note that this circumstance corresponds to scenario B(6) of non-engagement in the current guidance document, (available at <http://www.hhs.gov/ohrp/policy/engage08.html>) although releasing information to clinical data registries is not specifically mentioned. While we do not have current plans to revise that guidance document, we agree that it would be appropriate to add that specific example, and thus will keep this suggestion in mind with regard to possible future revisions.

The second request is “...that OHRP recognize that using a registry to aggregate and analyze data pertaining to care quality is not considered human subjects research under the Common Rule”. OHRP’s view is that such a statement is overly broad, given the regulatory definition of “research.” As indicated in the correspondence with Dr. Asher, some benchmarking activities may involve human subjects research, while other activities may not. With this request in mind, OHRP asked SACHRP to consider this topic, which they did at their meetings on October 29-30, 2014 and March 24-25, 2015. Their conclusions can be found in this document:

http://www.hhs.gov/ohrp/sachrp/commsec/hsrimplicationsofbig_datastudies.html. We acknowledge that some benchmarking activities – for example, ones that are designed solely to measure performance levels by participating practitioners or institutions and not to produce new knowledge

regarding the relationship between specific procedures and health outcomes -- will not satisfy the regulatory definition of research and thus will not activate the regulatory requirements. We continue to look for better ways to clarify this distinction.

The third request is that OHRP “confirm that a clinical data registry conducting human subjects research would not be covered by [the] Common Rule as long as it were not receiving federal funding, conducting research pursuant to a federally-regulated activity, or conducting research under a Federal Wide Assurance where the entity has voluntarily chosen to have all research conducted under the Common Rule.” We confirm that this is indeed the case.

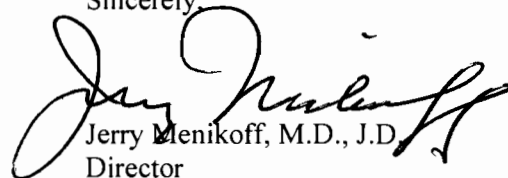
The fourth request is that OHRP comment on the use of a single IRB to review and approve a clinical data registry’s nonexempt human subjects research. As noted above, institutions that are providing data to the clinical data registry, but are not engaged in the research activity, do not need any IRB review. Thus, only review by a single IRB would be required if there is only one institution that is actually engaged in conducting the research. But even if there are multiple institutions that are engaged in the conduct of the research, it is still possible to have a single IRB reviewing the study. The participating institutions that are engaged in the research could put in place an Institutional Review Board (IRB) Authorization Agreement (IAA) in which they designate that single IRB as being responsible for satisfying all of the relevant regulatory requirements, including those that pertain to waiver of informed consent. In that circumstance, no other IRB review would be required.

The fifth request is that OHRP “confirm that the release of de-identified data by a clinical data registry for research analysis does not implicate the Common Rule because the use of de-identified data does not constitute human subjects research.” It is true that the activity of releasing de-identified data for research does not meet the regulatory definition for research involving a “human subject,” and that consequently the requirements of the Common Rule do not apply to that release of data. In addition, with regard to the entities that receive the data and analyze it, since that activity would not involve the use of a “human subject,” obtaining and analyzing the de-identified data for research also does not invoke any regulatory requirements of the Common Rule.

The sixth request is to discuss creating an exemption from the regulatory requirements for clinical data registries. In response to this request, we asked SACHRP to consider this question. Its conclusion can be found in the report mentioned above at http://www.hhs.gov/ohrp/sachrp/commsec/hsimplicationsofbig_datastudies.html. OHRP would welcome continuing discussion of the advisability of creating such an exemption.

We hope this information is helpful.

Sincerely,

A handwritten signature in black ink, appearing to read "Jerry Menikoff". The signature is fluid and cursive, with a large initial "J" and "M".

Jerry Menikoff, M.D., J.D.

Director

Office for Human Research Protections

September 23, 2013

VIA ELECTRONIC MAIL

Jerry A. Menikoff, MD, JD
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U.S. Department of Health & Human Services
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Jerry.Menikoff@hhs.gov

Dear Dr. Menikoff:

Thank you again for recently meeting with representatives of the Physician Clinical Registry Coalition regarding the application of the Common Rule to clinical data registries. As you know from our previous discussions, the Coalition is a group of 20 medical society-sponsored or physician-led clinical data registries that are working together to advocate for public policy changes that will help promote and/or remove barriers to the development of such registries. A list of Coalition member groups is attached.

Background

Generally speaking, the Coalition members collect identifiable patient information or protected health information ("PHI" as defined by the HIPAA Privacy Rule) primarily for purposes of quality improvement for the participating sites relating to the procedures or diseases covered by the registry. In doing so, these registries typically will enter into HIPAA-compliant business associate agreements with their participating hospitals or medical practice groups. They also will typically obtain waivers from an institutional review board (IRB) of the HIPAA authorization and Common Rule informed consent requirements to allow for the collection and use of PHI for research purposes. The registries obtain these waivers even though, according to OHRP guidance, the Common Rule generally should not apply to the majority of registries because they do not receive federal funding or conduct federally-regulated research. However, many hospitals and other data sources will not submit data to a registry that engages in some research analysis without such IRB waivers. Despite these precautionary steps, many hospitals take the position that they must obtain separate waivers from their local IRBs or, even worse, that they must obtain HIPAA authorizations and Common Rule informed consent from patients before submitting their data to a clinical data registry that conducts research analysis of the data, even if such analysis uses de-identified data or a limited dataset as defined by HIPAA. These positions are creating significant barriers to the development of clinical data registries.

Requested Clarifications

The Coalition believes these barriers to registry development could be alleviated by the clarification of several issues that would help reduce confusion about whether the Common Rule applies to clinical data registries or the individuals or entities submitting data to registries. The principal issues and requested clarifications are as follows:

1. It would be very helpful to registry development if OHRP would confirm that providers and groups that submit clinical outcomes data to a data registry primarily for “health care operations purposes” (as defined by the HIPAA privacy rules) are not engaging in human subjects research (as defined by the Common Rule). This is important to assure reporting providers and groups that they do not need to obtain separate approval or waivers from a local institutional review board (IRB) before submitting the data. In our previous discussions with the agency, OHRP stated that when a hospital, physician, or other health care provider simply supplies data collected in the course of clinical care to a clinical data outcomes registry, the data source is not engaged in human subjects research. You indicated that this position was based on Section III.A.6. of the OHRP “Guidance on Engagement of Institutions on Human Subjects Research” at <http://www.hhs.gov/ohrp/policy/engage08.html>, which states that “Institutions whose employees or agents release to investigators at another institution identifiable private information or identifiable biological specimens pertaining to the subject of the research” are not engaged in human subjects research. Please confirm that hospitals or other individuals or entities that submit data obtained in the course of clinical care to data registries are not engaged in human subjects research. Please also confirm that this conclusion applies regardless whether the clinical data registry is engaged in human subjects research covered by the Common Rule. We also ask that OHRP amend Section III.A.6. of the Guidance on Engagement of Institutions on Human Subjects Research to make specific reference to clinical data registries—*e.g.*, “Institutions whose employees or agents release to investigators at another institution or to other external entities, such as clinical data registries, identifiable private information or identifiable biological specimens pertaining to the subject of the research” are not engaged in human subjects research.
2. We ask that OHRP recognize that using a registry to aggregate and analyze data pertaining to care quality is not considered human subjects research under the Common Rule. Data aggregation consists of gathering PHI and other data from multiple data sources, aggregating and analyzing the data to develop average or standard performance levels/metrics (benchmarks) across all sources, and then reporting back to each source how its performance compares to the group average. The benchmarks themselves do not contribute to generalizable knowledge. Registries may make secondary use of the data to perform research (usually using data in the form of a limited dataset as defined by HIPAA or de-identified data), but the purpose of the benchmarking itself is to improve quality care at the participating sites. These are classic health care operations that clearly do not implicate

the definition of research and do not require IRB approval or waiver of authorization. Common examples include derivation of regional, national, or other benchmarks and creation of limited or de-identified data sets alone. Likewise, these activities should not be regarded as human subjects research or otherwise implicate the Common Rule and should not require IRB approval or waiver of informed consent. Treating benchmarking as human subjects research could lead hospitals and other data sources to unnecessarily seek IRB review and approval for activities that are not research. Therefore, the Coalition requests that OHRP clarify that data aggregation for a variety of purposes, including benchmarking, by clinical data registries is not research unless the registry is engaged in other activities that meet the definition of research under the Common Rule.

3. Please confirm that a clinical data registry conducting human subjects research would not be covered by Common Rule as long as it were not receiving federal funding , conducting research pursuant to a federally-regulated activity, or conducting research under a Federal Wide Assurance where the entity has voluntarily chosen to have all research conducted under the Common Rule.
4. OHRP has previously stated that sites participating in a multi-center research study may rely on central IRB review and approval of such study and are not required to also obtain separate local IRB review and approval. See “ANPRM for Revision of Common Rule,” 76 Fed. Reg. 44412, 44521 (July 26, 2011). In our recent meeting, OHRP staff agreed that this principal applies to data registries—*i.e.*, if a clinical data registry obtains an IRB waiver of the Common Rule informed consent requirement for the collection and use of identifiable patient data in research, the sites submitting data to the registry may rely on that central IRB waiver and should not need to obtain a separate waiver from their local IRBs. Please confirm your agreement with this statement. We also request that OHRP issue formal guidance on this point, whether in the proposed and final revisions to the Common Rule or in another guidance document.
5. Please confirm that the release of de-identified data by a clinical data registry for research analysis does not implicate the Common Rule because the use of de-identified data does not constitute human subjects research.
6. At our recent meeting, we discussed the Coalition’s position that a clinical data registry should be deemed to fit within an exempt category of the Common Rule where the registry can demonstrate that it complies with the HIPAA privacy and security rules in connection with its use and disclosure of PHI and where registry participation will not require any human subjects intervention, including but not limited to subjects interviews. While human subjects research conducted by clinical registries includes the collection and analysis of identifiable patient information, the HIPAA rules are much more protective of identifiable patient information than the more general requirements of the Common Rule that apply to human subjects research. The Coalition would like to continue discussions with OHRP on this proposal.

Jerry A. Menikoff, MD, JD
September 23, 2013
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Thank you again for meeting with the Coalition and for considering the foregoing requests for clarification in the application of the Common rule to clinical data registries and their data sources. I look forward to your response. If you have any questions, please feel free to contact me at 202-872-6756.

Sincerely,

A handwritten signature in black ink, appearing to read "Robert M. Portman". The signature is fluid and cursive, with a prominent loop at the end.

Robert M. Portman, JD, MPP
Principal

Enclosures

PHYSICIAN CLINICAL REGISTRY COALITION MEMBERS

AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS

AMERICAN ACADEMY OF OPHTHALMOLOGY

AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS/AMERICAN JOINT REPLACEMENT REGISTRY

AMERICAN COLLEGE OF CARDIOLOGY

AMERICAN COLLEGE OF EMERGENCY PHYSICIANS

AMERICAN COLLEGE OF GASTROENTEROLOGY

AMERICAN COLLEGE OF SURGEONS

AMERICAN GASTROENTEROLOGICAL ASSOCIATION

AMERICAN SOCIETY OF ANESTHESIOLOGY

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

AMERICAN SOCIETY OF NUCLEAR CARDIOLOGY

AMERICAN SOCIETY OF PLASTIC SURGEONS

AMERICAN SOCIETY FOR RADIATION ONCOLOGY

AMERICAN UROLOGICAL ASSOCIATION

CALIFORNIA JOINT REPLACEMENT REGISTRY

NORTH AMERICAN SPINE SOCIETY

SOCIETY OF INTERVENTIONAL RADIOLOGY

SOCIETY OF THORACIC SURGEONS

SOCIETY FOR VASCULAR SURGERY