From: OC GCP Questions
To: [redacted]
Subject: Subject protected health information + independent review
Date: Thursday, November 12, 2015 7:23:35 AM

Good morning –

FDA regulations do not prohibit sponsors and or CROs to have subject names and identifiers. FDA regulations do not prohibit patient (subject) identifiers or names on study documents. 21 CFR 312.68 Inspection of investigator's records and reports states –

An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.

You may wish to consult the Health Insurance Portability and Accountability Act (HIPPA) For questions regarding issues pertaining to HIPAA, you may contact OCR directly at OCRPrivacy@hhs.gov . Here also is a link to OCR's general website for HIPAA http://www.hhs.gov/ocr/privacy/ , and OCR also has HIPAA Frequently Asked Questions that can be accessed at http://www.hhs.gov/ocr/privacy/hipaa/faq/index.html. You may also wish to discuss your question with other in-house legal staff, including any Privacy Officer, within your sponsor organization

Below is a link to our new draft guidance on informed consent.

http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM405006.pdf It states --

5. Confidentiality
A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records. (21 CFR 50.25(a)(5).) The consent process must describe the extent to which confidentiality of records identifying subjects will be maintained (21 CFR 50.25(a)(5)) and should identify all entities, for example, the study sponsor, who may gain access to the records relating to the clinical investigation. The consent process must also note the possibility that FDA may inspect records (21 CFR 50.25(a)(5)), and should not state or imply that FDA needs permission from the subject for access to the records. Please note that under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, FDA does not need permission to inspect records containing health information (45 CFR 164.512). FDA may inspect study records, for example, to assess investigator compliance with the study protocol and the validity of the data reported by the sponsor. Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA may inspect and copy all records relating to the clinical investigation. 21 U.S.C. § 374(a)(1). See also 21 CFR 312.58(a), 312.68, and 812.145(b). FDA generally will not copy records that include the subject's name unless there is reason to believe the records do not represent the actual cases studied or results obtained. When FDA requires subject names, FDA will generally treat such information as confidential, but on rare occasions, FDA may be required to disclose this information to third parties, for example, to a court of law. See 21 CFR 20.63(a) and 20.83(a)-(b). Therefore, the consent process should not promise or imply absolute confidentiality by FDA.

Additionally, there should be adequate provisions in place to protect the privacy of subjects and to maintain the confidentiality of data. Note that neither the regulations or even guidance do not specifically address the methods used to maintain the confidentiality of records identifying the subject nor do they prohibit sponsors/CROs from receiving subject information, even with identifiers. Typically, study sponsors, CROs, and sites usually follow their own Standard Operating Procedures (SOPs) that direct document handling and maintaining confidentiality.

The ICH GCP E6 Good Clinical Practice: Consolidated Guidance, (which is recognized as official FDA guidance) mentions in section 6.10 that the sponsor should ensure the protocol or other written agreement specifies who has access to source data/documents (you can access this guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073122.pdf). I've copied below section 6.10 and other relevant sections of the ICH GCP E6 guidance for your

consideration.

6.10 Direct Access to Source Data/Documents

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s) by providing direct access to source data/documents.

Direct access is defined as:

1.21 Direct Access: Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information.

Additionally below is the Office of Regulatory Affairs (ORA) said regarding subject records during a FDA inspection.

Although sometimes challenging, ideally FDA would like to see and get copies of, original unchanged records. If not possible, the de-identification of records should be done as to not obliterate the required info necessary to identify the subject and the evidence of his/her participation in the study. Usually a combination of subject initials and subject number on study records will suffice this requirement.

The Privacy Rule also indicates the following: "…the Privacy Rule provides that, unless the use or disclosure is otherwise permitted or required by the rule, the use or disclosure of the protected health information of an individual, such as a research subject, is permitted only if the individual signs an authorization for the use or disclosure (45 CFR 164.508)."

One of the required elements of an Informed Consent Form is a statement describing the extent to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA may inspect the records. By signing the ICF the study subject is, in part, authorizing the disclosure of study info to FDA.

You might be interested in FDA's guidance document on Protecting the Rights, Safety, and Welfare of Study Subjects. Link below.
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM187772.pdf

I cannot specifically answer your second question. I recommend that you contact the FDA project manager of the study to obtain guidance on how to handle correcting and documenting radiology reading errors to ensure that the data collected and or changed is not compromised. I assume documentation for imaging, testing, and reviewing radiology films would have to comply with state and local laws for medical licensure and medical practice. I cannot advise you on contractual language as well.

I hope this information is helpful. Please contact us again at gcp.questions@fda.hhs.gov should you have additional questions.

Kind regards,

Doreen M. Kezer, MSN
Senior Health Policy Analyst
Office of Good Clinical Practice
Office of the Commissioner, FDA

-----Original Message-----

From: [redacted]
Sent: Tuesday, November 10, 2015 5:27 PM
To: OC GCP Questions
Subject: Subject protected health information + independent review

Hi-

I work for a CRO and have two questions--

1. Subject confidentiality breach: we receive high volume data from site with subject name, social security, MRN, address via study email inbox. The data is then placed in our network folder for QC and then blinded. Are we in violation of a regulation for keeping the unblinded PHI data in our network folder?

2. Independent review: when a sponsor asks us to investigate a possible error with a read and our radiologist confirms the error. Does changing our data compromise the independent nature of the our radiologists review? What contactual language do we need to avoid risk of introducing bias? Is it bad practice to change our data per sponsors request once the error is internally confirmed?

Thanks,

[redacted]