
Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)**

**July 2018
Procedural**

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Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry¹

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended to assist sponsors, clinical investigators, contract research organizations, institutional review boards (IRBs), and other interested parties on the use of electronic health record data in FDA-regulated clinical investigations.² For the purposes of this guidance, *electronic health record (EHR) systems*³ are electronic platforms that contain individual health records for patients. EHR systems are generally maintained by health care providers, health care organizations, and health care institutions and are used to deliver care. EHR systems can be used to integrate real-time electronic health care information from medical devices and multiple health care providers involved in the care of patients.

For the purposes of this guidance, an *EHR* is an individual patient record contained within the EHR system. A typical individual EHR may include a patient's medical history, diagnoses, treatment plans, immunization dates, allergies, radiology images, pharmacy records, and laboratory and test results. This guidance uses broad definitions of EHRs and EHR systems to be inclusive of many different types of EHRs and EHR systems.⁴

¹ This guidance has been prepared by the Office of Medical Policy and the Office of Translational Sciences in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health at the Food and Drug Administration. This guidance was developed in consultation with the Office of the National Coordinator for Health Information Technology (ONC) at the Department of Health and Human Services (HHS).

² For FDA's regulatory definitions of a clinical investigation, see 21 CFR 50.3(c), 56.102(c), and 312.3(b). For FDA's regulatory definition of an investigation, see 21 CFR 812.3(h).

³ See the Glossary for definitions and usage of specific terms used throughout this guidance. Words and phrases in *bold italics* are defined in the Glossary.

⁴ We note that this definition of EHRs may not be consistent with the definition for EHRs published in other guidance documents.

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This guidance provides recommendations on:

- Deciding whether and how to use EHRs as a source of data in clinical investigations
- Using EHR systems that are interoperable with *electronic data capture (EDC) systems* in clinical investigations
- Ensuring the quality and integrity of EHR data collected and used as *electronic source data* in clinical investigations
- Ensuring that the use of EHR data collected and used as electronic source data in clinical investigations meets FDA's inspection, recordkeeping, and record retention requirements⁵

In an effort to modernize and streamline clinical investigations, the goals of this guidance are to:

- Facilitate the use of EHR data in clinical investigations
- Promote the interoperability of EHR and EDC systems

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. SCOPE

The recommendations outlined in this guidance apply to the use of EHR data in:

- Prospective clinical investigations of human drugs and biological products, medical devices, and combination products, including clinical investigations conducted in clinical practice settings⁶

⁵ For inspection requirements and principal recordkeeping requirements for clinical investigators who develop human drugs and biological products, see 21 CFR 312.62 and 312.68. For medical devices, see 21 CFR 812.140 and 812.145.

⁶Conclusions about the risks and benefits of medical products drawn from data, including EHR data, collected in routine clinical practice settings (i.e., outside of typical clinical research settings) are sometimes referred to as real world evidence. Such conclusions may be used to inform regulatory decision making, specifically in the approval of new indications for approved drugs and to satisfy post-approval study requirements. This guidance, which is intended to assist interested parties on the use of EHR data in FDA-regulated clinical investigations, satisfies, in part, the mandate under the 21st Century Cures Act (Cures Act) (Public Law 114-255) to issue guidance about the use of real world evidence in regulatory decision making. See Section 3022 of the Cures Act. See also 21 U.S.C.

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- Foreign clinical studies not conducted under an investigational new drug application (IND) or an investigational device exemption (IDE) that are submitted to FDA in support of an application for the marketing approval of a medical product⁷ (see 21 CFR 312.120, 314.106, and 814.15)

This guidance applies to data obtained from EHRs and EHR clinical data warehouses that store and integrate EHR data.

The Office of the National Coordinator for Health Information Technology (ONC) at the Department of Health and Human Services (HHS) has adopted use of the broader term *health IT* in the ONC Health Information Technology (Health IT) Certification Program that includes EHRs and other forms of health IT that provide electronic data.⁸ Other forms of health IT may include mobile and telehealth technology, medical devices and remote monitoring devices, assistive technologies, and sensors. This guidance does not apply to data from these other forms of health IT.

In addition, this guidance does not apply to the following:

- The use of EHR data in postmarketing observational pharmacoepidemiologic studies designed to assess adverse events and risks associated with drug exposure or designed to test prespecified hypotheses for such studies⁹
- The use of EHR data to evaluate feasibility of the trial design or as a recruitment tool for clinical investigations¹⁰
- Data collected for *registries* and natural history studies

355g. For more information on real world evidence, see Sherman RE, Anderson SA, Dal Pan GJ, et al., “Real-World Evidence – What is it and what can it tell us.” *N Engl J Med* 2016; 375:2293–2297.

⁷ For the purposes of this guidance, all references to medical products include human drugs and biological products, medical devices, and combination products that are regulated by CDER, CBER, or CDRH.

⁸ See the HHS final rule “2015 Edition Health Information Technology (Health IT) Certification Criteria, 2015 Edition Base Electronic Health Record (EHR) Definition, and ONC Health IT Certification Program Modifications,” published October 16, 2015 (80 FR 62602 at 62602). Also, see the Federal Health IT Strategic Plan (2015–2020) at <https://www.healthit.gov/policy-researchers-implementers/health-it-strategic-planning>.

⁹ When using EHR data for postmarketing observational pharmacoepidemiologic studies designed to assess the risks associated with a drug exposure, sponsors should follow the recommendations in the guidance for industry and FDA staff *Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data*. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

¹⁰ For more information on the use of EHR data as a recruitment tool for clinical investigations, see the guidance for institutional review boards and clinical investigators *Recruiting Study Subjects — Information Sheet*, available at <https://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm>.

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III. BACKGROUND

FDA issued guidance on electronic source data in clinical investigations (eSource guidance).¹¹ In the eSource guidance, FDA addresses attributes of *source data* used to fill predefined fields in an *electronic case report form (eCRF)* that would satisfy FDA's inspection, recordkeeping, and record retention requirements.¹² The guidance acknowledges that data entered into the sponsor's eCRF may be derived from a variety of sources, including EHRs.

In general, EHR systems are not under the control of FDA-regulated entities (e.g., sponsors, clinical investigators). In most instances, these systems belong to health care providers, health care organizations, and health care institutions. As provided in the eSource guidance, FDA does not intend to assess compliance of EHR systems with 21 CFR part 11.¹³ However, FDA's acceptance of data from clinical investigations for decision-making purposes depends on FDA's ability to verify the quality and integrity of the data during FDA inspections (see 21 CFR parts 312 and 812). This guidance clarifies FDA's expectations when EHRs are used as a source of data in clinical investigations.

Potential Advantages of the Use of EHRs in Clinical Investigations

With the widespread use of EHRs, there are opportunities to improve data accuracy and promote clinical trial efficiency when EHRs are used in clinical investigations. EHRs may enable clinical investigators and study personnel to have access to many types of data (e.g., clinical notes, physician orders, radiology, laboratory, and pharmacy records) that can be combined, aggregated, and analyzed. EHRs may have the potential to provide clinical investigators and study personnel access to real-time data for review and can facilitate post-trial follow-up on patients to assess long-term safety and effectiveness of medical products. In addition, there are opportunities for long-term follow up of large numbers of patients, which may be of particular importance in studies where the outcome of interest occurs rarely, such as in prophylaxis studies.

IV. INTEROPERABILITY AND INTEGRATION OF SYSTEMS

For the purposes of this guidance, *interoperability* refers to the ability of two or more products, technologies, or systems to exchange information and to use the information that has been exchanged without special effort on the part of the user. EHR and EDC systems may be noninteroperable, interoperable, or fully integrated, depending on supportive technologies and standards.

Noninteroperable systems, without the capability for electronic exchange of EHR data in clinical investigations, involve manual transcription of *data elements* from the EHR to the eCRF or to

¹¹ See the guidance for industry *Electronic Source Data in Clinical Investigations*.

¹² See footnote 5.

¹³ See footnote 11.

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the paper case report form, similar to the transcription performed with paper records. Such manual transcription procedures may introduce risks of data entry errors unless effective quality control systems are in place.

Interoperable systems allow electronic transmission of relevant EHR data to the EDC system. For example, data elements originating in an EHR (e.g., demographics, vital signs, laboratory data, medications) may automatically populate the eCRFs within an EDC system. In addition, an interoperable EHR and EDC system could provide access to additional patient information populated from other clinical information systems (e.g., radiology information systems, laboratory information systems). Interoperable systems may simplify data collection for a clinical investigation by enabling clinical investigators and study personnel to capture source data at the patient's point-of-care visit. Interoperable systems may also reduce errors in data transcription, allowing for the improvement in data accuracy and the quality and efficiency of the data collected in clinical investigations.

Fully integrated systems allow clinical investigators to enter research data directly into the EHR. This may involve, for example, use of research modules, use of research tabs built into the EHR system, or use of custom research fields within the EHR system for data that are entered for research purposes.

FDA encourages sponsors and clinical investigators to work with entities that control EHR systems, such as health care organizations, to use EHR and EDC systems that are interoperable or fully integrated. Moreover, diverse ownership of electronic systems and data may necessitate appropriate collaboration between the health care and clinical research communities. FDA encourages sponsors and health care organizations to work with EHR and EDC system vendors to further advance the interoperability and integration of these systems.

A. Data Standards

There may be practical challenges to the interoperability of EHR and EDC systems. These challenges may include the complex and diverse clinical data standards used by the health care and clinical research communities, which may hinder the exchange of information between different electronic systems. Many of these challenges are being addressed by the adoption of open data standards and through EHR data standardization requirements as part of the ONC Health IT Certification Program and ONC's Interoperability Standards Advisory.¹⁴ The data exchange between EHR and EDC systems should leverage the use of existing open data standards, when possible, while ensuring that the integrity and security of data are not compromised.

B. Structured and Unstructured Data

FDA encourages exchange of structured data (e.g., demographics, vital signs, laboratory data) between EHR and EDC systems so that data may be entered once at the point-of-care and used many times without manual re-entry or manual source data verification. Sponsors should ensure

¹⁴ The ONC Health IT Certification Program and their processes are discussed further in section V.A of this guidance. For more information on ONC's Interoperability Standards Advisory, see <https://www.healthit.gov/isa/>.

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that the structured data elements obtained from the EHR correspond with the protocol-defined data collection plan (e.g., time and method of measurement). In addition, for extraction of unstructured data, sponsors should consider the reliability and quality of unstructured EHR data and the appropriateness of using it as critical source data, such as study endpoints.

C. Validation

Sponsors should ensure that the interoperability of EHR and EDC systems (e.g., involving the automated electronic transmission of relevant EHR data to the EDC system) functions in the manner intended in a consistent and repeatable fashion and that the data are transmitted accurately, consistently, and completely. The sponsor's quality management plan (e.g., standard operating procedures, software development life cycle model, change control procedures) should address the interoperability of the EHR and EDC system and the automated electronic transmission of EHR data elements to the EDC system. Sponsors should ensure that software updates to the sponsor's EDC systems do not affect the integrity and security of EHR data transmitted to the sponsor's EDC systems. In addition, as part of the quality management plan, FDA encourages sponsors to periodically check a subset of the extracted data for accuracy, consistency, and completeness with the EHR source data and make appropriate changes to the interoperable system when problems with the automated data transfer are identified.

D. Data From Multiple EHR Systems

The EHR system at the clinical investigation site may be interoperable with multiple EHR systems from many different health care organizations or institutions that are not affiliated with the clinical investigation site. If data from multiple EHR systems from different health care organizations and institutions are integrated with EHR data at the clinical investigation site, data from another institution's EHR system may be used and transmitted to the sponsor's EDC system provided that data sharing agreements are in place.

V. BEST PRACTICES FOR USING EHRs IN CLINICAL INVESTIGATIONS

The use of EHRs as a source of data in clinical investigations may involve additional considerations, planning, and management as described in this section. Sponsors and clinical investigators should ensure that policies and processes for the use of EHRs at the clinical investigation site are in place and that there are appropriate security measures employed to protect the confidentiality and integrity of the study data.

Sponsors should also ensure that study monitors have suitable access to all relevant subject information pertaining to a clinical investigation, as appropriate. Such access must be described in the informed consent (see 21 CFR 50.25(a)(5)) (see section V.E). Furthermore, at any time during the course of a clinical investigation, sponsors should discuss with the relevant FDA review division any unique issues or challenges encountered relating to the data collection from the EHRs (see, e.g., 21 CFR 312.41).

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A. Use of Health Information Technology Certified by ONC

The Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH Act) (Title XIII of Division A and Title IV of Division B of the American Recovery and Reinvestment Act of 2009 (Public Law 111–5)) requires that ONC establish a voluntary certification program for health IT.¹⁵ Under the ONC Health IT Certification Program, certified EHR technology would be in compliance with applicable provisions under 45 CFR part 170. EHR technology with certified capabilities generally has clear advantages, because many of the certification requirements are aimed toward ensuring interoperable data sharing and enabling processes to keep electronic data confidential and secure. In particular, all EHR technology certified under the ONC Health IT Certification Program is required to meet certain privacy and security protection requirements for an individual’s health information (see 45 CFR 170.314(d)(1) through (8) and 45 CFR 170.315(d)(1) through (11)). FDA encourages the use of such certified EHR systems together with appropriate policies and procedures for their use.

Sponsors should include in their data management plan a list of EHR systems used by each clinical investigation site in the clinical investigation. Sponsors should document the manufacturer, model number, and version number of the EHR system and whether the EHR system is certified by ONC.¹⁶ If an EHR system is decertified during the course of the clinical investigation because the system no longer conforms to ONC’s certification criteria, sponsors should determine the nature or reasons for the nonconformity and determine whether it would affect the quality and integrity of data used in the clinical investigation.

B. Use of EHR Systems Not Certified by ONC

FDA recognizes the importance of data from foreign studies to support safety and efficacy claims for medical products and may accept data from clinical studies conducted outside the United States.¹⁷ EHR systems not certified by ONC, including EHR systems at foreign clinical sites, can provide adequate data to inform FDA’s regulatory decisions provided that adequate controls are in place to ensure the confidentiality, integrity, and security of data. Specifically, for EHR systems not certified by ONC, sponsors should consider whether such systems have the following privacy and security controls in place to ensure that the confidentiality, integrity, and security of data are preserved:

- Policies and processes for the use of EHR systems at the clinical investigation site are in place, and there are appropriate security measures employed to protect the study data.
- Access to electronic systems is limited to authorized users.

¹⁵ 80 FR 62602 at 62606. For information about the ONC Health IT Certification Program, see <https://www.healthit.gov/policy-researchers-implementers/onc-health-it-certification-program>.

¹⁶ Sponsors may check the certification status for EHR systems at <https://chpl.healthit.gov/#/search>.

¹⁷ See the guidance for industry and FDA staff *FDA Acceptance of Foreign Clinical Studies Not Conducted Under an IND — Frequently Asked Questions*.

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- Authors of records are identifiable.
- ***Audit trails*** are available to track changes to data.
- Records are available and retained for FDA inspection for as long as the records are required by applicable regulations (see section VI).

Sponsors should consider these factors when determining the suitability of EHR systems not certified by ONC for use in clinical investigations. If the clinical investigation site is using a system that does not contain the adequate controls previously described in the bulleted items, sponsors should consider the risks of employing such systems (e.g., the potential harm to research subjects, patient privacy rights, and data integrity of the clinical investigation and its regulatory implications).

The following information may be helpful to sponsors to determine the suitability of EHR systems not certified by ONC:

- Any EHR system certification information from other authorizing bodies outside the United States, including information about aspects of the EHR system that the authorizing body evaluated when certifying the EHR system
- Feature and product-specification information from the EHR system vendor

Sponsors should consult with the relevant FDA review divisions if any issues or challenges with the EHR system are identified.

C. eSource Principles for EHRs

As stated earlier in this guidance, FDA does not intend to assess EHR systems for compliance with 21 CFR part 11. However, part 11 applies to the sponsor's EDC system that extracts the EHR data for use in a clinical investigation, and FDA intends to assess the sponsor's EDC system for compliance with part 11, as provided in the guidance for industry *Part 11, Electronic Records; Electronic Signatures – Scope and Application*.

1. Data Originator

For the purposes of recordkeeping, audit trails, and inspection, each electronic data element should be associated with a ***data originator***. The EHR is identified as the data originator for EHR data elements gathered during the course of a clinical investigation.¹⁸ Identifying the EHR as the data originator may be sufficient because sponsors are not expected to know details about all users who contribute information to the patient's EHR.

¹⁸ See footnote 11.

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2. *Data Modifications*

After data are transmitted to the eCRF, the clinical investigator or delegated study personnel should be the only individuals authorized to make modifications or corrections to the data. Modified and corrected data elements should have data element identifiers that reflect the date, time, data originator, and the reason for the change. Modified and corrected data should not obscure previous entries. Clinical investigators should review and electronically sign the completed eCRF for each study participant before data are archived or submitted to FDA. If modifications are made to the eCRF after the clinical investigator has already signed the eCRF, the changes should be reviewed and approved by the clinical investigator. Use of electronic signatures for records that are subject to 21 CFR part 11 must comply with relevant requirements in that regulation (see 21 CFR 11.2).

D. *Blinded Study Designs*

When the study design is blinded, sponsors should consider whether the use of interoperable EHR and EDC systems has any potential to unblind the treatment allocation. If a potential for unblinding is identified, sponsors should determine whether the use of interoperable systems is appropriate or whether other appropriate controls should be in place to prevent unblinding.

E. *Informed Consent*

When informed consent is required, the consent must include a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (21 CFR 50.25(a)(5)) and should identify entities, such as health care providers, clinical investigators, sponsors, contract research organizations, study monitors, and regulatory agencies who may gain access to the patient's electronic health record relating to the clinical investigation.¹⁹ In addition, 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 (see 45 CFR 164.512). FDA may inspect study records, for example, to assess investigator compliance with the study protocol and validity of the data reported by the sponsor.

Under section 704(a)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(a)(1)), FDA may inspect and copy records relating to the clinical investigation (see 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 treat such information as confidential. On rare occasions, FDA may be required to disclose this information to third parties, such as to a court of law (see 21 CFR 20.63(a) and 20.83(a) and (b)). Therefore, the consent process should not promise or imply absolute confidentiality by FDA.

¹⁹ For more information, see the draft guidance for IRBs, clinical investigators, and sponsors *Informed Consent Information Sheet*. When final, this guidance will represent FDA's current thinking on this topic.

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For systems that are interoperable or fully integrated, sponsors and clinical investigators should have a detailed understanding of data flow and data visibility to allow for a clear description in the informed consent of the parties granted access to the patient's data.

VI. INSPECTION, RECORDKEEPING, AND RECORD RETENTION REQUIREMENTS

FDA must have access to records and may inspect and copy all records pertaining to a clinical investigation in accordance with 21 CFR 312.62, 312.68, 812.140, and 812.145. All relevant information in the EHR pertaining to the clinical investigation must be made available to FDA for review upon request (21 CFR 312.62(b), 312.68, 812.140(a), and 812.145).²⁰ This information should be made available and viewable to FDA as original records in the EHR or as *certified copies*. During an inspection, FDA may also request other paper or electronic records to support data in the eCRF (e.g., case histories, other data pertaining to the clinical investigation) (see 21 CFR 312.62(b), 312.68, 812.140(a)(3), and 812.145). In addition, FDA may request to review the EHR audit trail information during inspection.

Clinical investigators must retain all paper and electronic source documents (e.g., originals or certified copies) and records as required to be maintained in compliance with 21 CFR 312.62(c) and 812.140(d).

- For human drugs and biological products, clinical investigators must retain all records (e.g., including case histories and other EHR data pertaining to a clinical investigation), as required by 21 CFR part 312, for 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.
- For medical devices, an investigator or sponsor must maintain all records, including EHRs relating to the investigation, as required by 21 CFR 812.140(d), during the investigation and for 2 years after the latter of the following two dates:
 - The date on which the investigation is terminated or completed
 - The date that the records are no longer required for the purposes of supporting a premarket approval application or a notice of completion of a product development protocol

²⁰ If the necessary records are not available for a foreign clinical study that is not conducted under an IND, FDA may not accept the study data in support of an IND or an application for marketing approval. If the records exist but a sponsor or an applicant cannot disclose them to FDA because such disclosure is prohibited by applicable foreign law, the sponsor or applicant may seek a waiver of this requirement (21 CFR 312.120(c)). For FDA to rely on such data that cannot be disclosed, the sponsor and FDA would need to agree on an alternative validation procedure. For more information, see the guidance for industry and FDA staff *FDA Acceptance of Foreign Clinical Studies Not Conducted Under an IND — Frequently Asked Questions*.

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GLOSSARY

Audit Trail — Documentation that allows reconstruction of the course of events.

Certified Copy — A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

Data Element — A single observation associated with a subject in a clinical study. Examples include birth date, white blood cell count, pain severity measure, and other clinical observations made and documented during a study.

Data Originator — An origination type associated with each data element that identifies the source of the data element's capture in the eCRF. This could be a person, a computer system, a device, or an instrument that is authorized to enter, change, or transmit data elements into the eCRF (also, sometimes known as an author).

Electronic Case Report Form (eCRF) — An auditable electronic record of information that generally is reported to the sponsor on each trial subject, according to a clinical investigation protocol. The eCRF enables clinical investigation data to be systematically captured, reviewed, managed, stored, analyzed, and reported.

Electronic Data Capture (EDC) systems — Electronic systems designed to collect and manage clinical trial data in an electronic format.

Electronic Health Record (EHR) — An individual patient record contained within the EHR system. A typical individual EHR may include a patient's medical history, diagnoses, treatment plans, immunization dates, allergies, radiology images, pharmacy records, and laboratory and test results. This guidance uses a broad definition to be inclusive of many different types of EHRs and may not be consistent with the definition for EHRs published in other guidance documents.

Electronic Health Record (EHR) systems — Electronic platforms that contain individual health records for patients. EHR systems are generally maintained by health care providers, health care organizations, and health care institutions and are used to deliver care. EHR systems can be used to integrate real-time electronic health care information from medical devices and multiple health care providers involved in the care of patients.

Electronic Source Data — Data initially recorded in an electronic format.

Interoperability — The ability of two or more products, technologies, or systems to exchange information and to use the information that has been exchanged without special effort on the part of the user.

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Registries — Organized systems that use observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serve one or more predetermined scientific, clinical or policy purposes.²¹

Source Data — All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

²¹ For more information, see Registries for Evaluating Patient Outcomes: A User's Guide, available at <https://effectivehealthcare.ahrq.gov/topics/registries-guide-3rd-edition/research/>.