
Data Integrity and Compliance With Drug CGMP Questions and Answers 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 Veterinary Medicine (CVM)**

**December 2018
Pharmaceutical Quality/Manufacturing Standards (CGMP)**

Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry

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Data Integrity and Compliance With Drug CGMP Questions and Answers 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

The purpose of this guidance is to clarify the role of data integrity in current good manufacturing practice (CGMP) for drugs, as required in 21 CFR parts 210, 211, and 212. Unless otherwise noted, the term *CGMP* in this guidance refers to CGMPs for drugs (including biologics). FDA's authority for CGMP comes from section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). Part 210 covers Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General; part 211 covers Current Good Manufacturing Practice for Finished Pharmaceuticals; and part 212 covers Current Good Manufacturing Practice for Positron Emission Tomography (PET) Drugs. All citations to parts 211 and 212 in this document pertain to finished pharmaceuticals and PET drugs, but these requirements are also consistent with Agency guidance on CGMP for active pharmaceutical ingredients with respect to data integrity.² This guidance provides the Agency's current thinking on the creation and handling of data in accordance with CGMP requirements.

FDA expects that all data be reliable and accurate (see the "Background" section). CGMP regulations and guidance allow for flexible and risk-based strategies to prevent and detect data integrity issues. Firms should implement meaningful and effective strategies to manage their data integrity risks based on their process understanding and knowledge management of technologies and business models.³

Meaningful and effective strategies should consider the design, operation, and monitoring of systems and controls based on risk to patient, process, and product. Management's involvement

¹ This guidance has been prepared by the Office of Pharmaceutical Quality and the Office of Compliance in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research, the Center for Veterinary Medicine, and the Office of Regulatory Affairs at the Food and Drug Administration.

² See the International Council for Harmonisation (ICH) guidance for industry *Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients*. We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

³ See ICH guidance for industry *Q9 Quality Risk Management*.

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in and influence on these strategies is essential in preventing and correcting conditions that can lead to data integrity problems. It is the role of management with executive responsibility to create a quality culture where employees understand that data integrity is an organizational core value and employees are encouraged to identify and promptly report data integrity issues. In the absence of management support of a quality culture, quality systems can break down and lead to CGMP noncompliance.

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. BACKGROUND

In recent years, FDA has increasingly observed CGMP violations involving data integrity during CGMP inspections. This is troubling because ensuring data integrity is an important component of industry's responsibility to ensure the safety, efficacy, and quality of drugs, and of FDA's ability to protect the public health. These data integrity-related CGMP violations have led to numerous regulatory actions, including warning letters, import alerts, and consent decrees. The underlying premise in §§ 210.1 and 212.2 is that CGMP sets forth minimum requirements to assure that drugs meet the standards of the FD&C Act regarding safety, identity, strength, quality, and purity.⁴ Requirements with respect to data integrity in parts 211 and 212 include, among other things:

- § 211.68 (requiring that “backup data are exact and complete” and “secure from alteration, inadvertent erasures, or loss” and that “output from the computer ... be checked for accuracy”).
- § 212.110(b) (requiring that data be “stored to prevent deterioration or loss”).
- §§ 211.100 and 211.160 (requiring that certain activities be “documented at the time of performance” and that laboratory controls be “scientifically sound”).
- § 211.180 (requiring that records be retained as “original records,” or “true copies,” or other “accurate reproductions of the original records”).
- §§ 211.188, 211.194, and 212.60(g) (requiring “complete information,” “complete data derived from all tests,” “complete record of all data,” and “complete records of all tests performed”).

⁴ According to section 501(a)(2)(B) of the FD&C Act, a drug shall be deemed adulterated if “the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirement of the act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.”

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- §§ 211.22, 211.192, and 211.194(a) (requiring that production and control records be “reviewed” and that laboratory records be “reviewed for accuracy, completeness, and compliance with established standards”).
- §§ 211.182, 211.186(a), 211.188(b)(11), and 211.194(a)(8) (requiring that records be “checked,” “verified,” or “reviewed”).

When considering how to meet many of these regulatory requirements, it may be useful to ask the following questions:

- Are controls in place to ensure that data is complete?
- Are activities documented at the time of performance?
- Are activities attributable to a specific individual?
- Can only authorized individuals make changes to records?
- Is there a record of changes to data?
- Are records reviewed for accuracy, completeness, and compliance with established standards?
- Are data maintained securely from data creation through disposition after the record’s retention period?

This guidance helps answer these questions and enables an understanding of key concepts behind the regulatory requirements.

While not in the scope of this guidance, data integrity-related CGMP violations can also impact or be directly linked to application filing, review, and regulatory actions.

Electronic signature and record-keeping requirements are laid out in 21 CFR part 11 and apply to certain records subject to records requirements set forth in Agency regulations, including parts 210, 211, and 212. For more information, see guidance for industry *Part 11, Electronic Records; Electronic Signatures—Scope and Application*, which outlines FDA’s current thinking regarding the scope and application of part 11 pending FDA’s reexamination of part 11 as it applies to all FDA-regulated products.

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III. QUESTIONS AND ANSWERS

1. Please clarify the following terms as they relate to CGMP records:

a. What is “data integrity”?

For the purposes of this guidance, *data integrity* refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).⁵

Data integrity is critical throughout the CGMP data life cycle, including in the creation, modification, processing, maintenance, archival, retrieval, transmission, and disposition of data after the record’s retention period ends.⁶ System design and controls should enable easy detection of errors, omissions, and aberrant results throughout the data’s life cycle.

b. What is “metadata”?

Metadata is the contextual information required to understand data. A data value is by itself meaningless without additional information about the data. Metadata is often described as data about data. Metadata is structured information that describes, explains, or otherwise makes it easier to retrieve, use, or manage data. For example, the number “23” is meaningless without metadata, such as an indication of the unit “mg.” Among other things, metadata for a particular piece of data could include a date/time stamp documenting when the data were acquired, a user ID of the person who conducted the test or analysis that generated the data, the instrument ID used to acquire the data, material status data, the material identification number, and audit trails.

Data should be maintained throughout the record’s retention period with all associated metadata required to reconstruct the CGMP activity (e.g., §§ 211.188 and 211.194). The relationships between data and their metadata should be preserved in a secure and traceable manner.

c. What is an “audit trail”?

For purposes of this guidance, *audit trail* means a secure, computer-generated, time-stamped electronic record that allows for reconstruction of the course of events relating to the creation, modification, or deletion of an electronic record. For example, the audit trail for a high performance liquid chromatography (HPLC) run should include the user name, date/time of the run, the integration parameters used, and details of a reprocessing, if any. Documentation should include change justification for the reprocessing.

⁵ These characteristics are important to ensuring data integrity and are addressed throughout the CGMP regulations for drugs. For *attributable*, see §§ 211.101(d), 211.122, 211.186, 211.188(b)(11), and 212.50(c)(10); for *legible*, see §§ 211.180(e) and 212.110(b); for *contemporaneously recorded* (at the time of performance), see §§ 211.100(b) and 211.160(a); for *original or a true copy*, see §§ 211.180 and 211.194(a); and for *accurate*, see §§ 211.22(a), 211.68, 211.188, and 212.60(g).

⁶ For examples of record retention periods, see §§ 211.180 and 212.110(c).

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Audit trails include those that track creation, modification, or deletion of data (such as processing parameters and results) and those that track actions at the record or system level (such as attempts to access the system or rename or delete a file).

CGMP-compliant record-keeping practices prevent data from being lost or obscured and ensure that activities are documented at the time of performance (see §§ 211.68, 211.100, 211.160(a), 211.188, and 211.194). Electronic record-keeping systems, which include audit trails, can support these CGMP requirements.

d. How does FDA use the terms “static” and “dynamic” as they relate to record formats?

For the purposes of this guidance, *static* is used to indicate a fixed-data record such as a paper record or an electronic image, and *dynamic* means that the record format allows interaction between the user and the record content. For example, a dynamic chromatographic record may allow the user to change the baseline and reprocess chromatographic data so that the resulting peaks may appear smaller or larger. It also may allow the user to modify formulas or entries in a spreadsheet used to compute test results or other information such as calculated yield.

e. How does FDA use the term “backup” in § 211.68(b)?

FDA uses the term *backup* in § 211.68(b) to refer to a true copy of the original record that is maintained securely throughout the record retention period (e.g., § 211.180). Backup data must be exact, complete, and secure from alteration, inadvertent erasures, or loss (§ 211.68(b)). The backup file should contain the data (which includes associated metadata) and should be in the original format or in a format compatible with the original format.

FDA’s use of the term *backup* is consistent with the term *archive* as used in guidance for industry and FDA staff *General Principles of Software Validation*.

Temporary backup copies (e.g., in case of a computer crash or other interruption) would not satisfy the requirement in § 211.68(b) to maintain a backup file of data.

f. What are the “systems” in “computer or related systems” in § 211.68?

The American National Standards Institute (ANSI) defines systems as people, machines, and methods organized to accomplish a set of specific functions.⁷ *Computer or related systems* can refer to computer hardware, software, peripheral devices, networks, cloud infrastructure, personnel, and associated documents (e.g., user manuals and standard operating procedures).⁸

⁷ American National Standard for Information Systems, *Dictionary for Information Systems*, American National Standards Institute, 1991.

⁸ See guidance for industry and FDA staff *General Principles of Software Validation*.

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2. When is it permissible to invalidate a CGMP result and exclude it from the determination of batch conformance?

Data created as part of a CGMP record must be evaluated by the quality unit as part of release criteria (see §§ 211.22 and 212.70) and maintained for CGMP purposes (e.g., § 211.180).⁹ Electronic data generated to fulfill CGMP requirements include relevant metadata required to reconstruct the CGMP activity captured in the record. Invalidating test results to exclude them from quality unit decisions about conformance to a specification requires a valid, documented, scientifically sound justification. See, for example, §§ 211.160(b), 211.188, 211.192, and 212.71(b) and the guidance for industry *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production*. Even if test results are legitimately invalidated on the basis of a scientifically sound investigation, the full CGMP batch record provided to the quality unit would include the original (invalidated) data, along with the investigation report that justifies invalidating the result. The requirements for record retention and review do not differ depending on the data format; paper-based and electronic data record-keeping systems are subject to the same requirements.

3. Does each CGMP workflow on a computer system need to be validated?

Yes, a CGMP workflow, such as creation of an electronic master production and control record (MPCR), is an intended use of a computer system to be checked through validation (see §§ 211.63, 211.68(b), and 211.110(a)). The extent of validation studies should be commensurate with the risk posed by the automated system. When the same system is used to perform both CGMP and non-CGMP functions, the potential for non-CGMP functions to affect CGMP operations should be assessed and mitigated appropriately.¹⁰

If you validate the computer system but you do not validate it for its intended use, you cannot know if your workflow runs correctly.¹¹ For example, qualifying the Manufacturing Execution System (MES) platform, a computer system, ensures that it meets its relevant requirements and specifications; however, it does not demonstrate that a given MPCR generated by the MES contains the correct calculations. In this example, validating the workflow ensures that the intended steps, requirements, and calculations in the MPCR are accurate and perform properly. This is similar to reviewing a paper MPCR and ensuring all supporting procedures are in place before the MPCR is implemented in production (see §§ 211.100, 211.186, and 212.50(b) and the guidance for industry *PET Drugs—Current Good Manufacturing Practice (CGMP)*).

⁹ For purposes of this guidance, the term *quality unit* is synonymous with the term *quality control unit*. For the definition of *quality control unit*, see § 210.3(b)(15).

¹⁰ See note 8.

¹¹ In computer science, *validation* refers to ensuring that software meets its requirements. However, this may not meet the definition of *process validation* as found in guidance for industry *Process Validation: General Principles and Practices*: “The collection and evaluation of data ... which establishes scientific evidence that a process is capable of consistently delivering quality products.” See also ICH guidance for industry *Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients*, which defines *validation* as providing assurance that a specific process, method, or system will consistently produce a result meeting predetermined acceptance criteria. For purposes of this guidance, *validation* is being used in a manner consistent with the above guidance documents.

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FDA recommends you implement appropriate controls to manage risks associated with each element of the system. Controls that are appropriately designed to validate a system for its intended use address software, hardware, personnel, and documentation.

4. How should access to CGMP computer systems be restricted?

You must exercise appropriate controls to assure that changes to computerized MPCRs or other CGMP records or input of laboratory data into computerized records can be made only by authorized personnel (§ 211.68(b)). Other examples of records for which control should be restricted to authorized personnel include automated visual inspection records, electronic materials management system records, and automated dispensing system weighing records. FDA recommends that you restrict the ability to alter specifications, process parameters, data, or manufacturing or testing methods by technical means where possible (e.g., by limiting permissions to change settings or data).

The system administrator role, including any rights to alter files and settings, should be assigned to personnel independent from those responsible for the record content. To assist in controlling access, it is important that manufacturers establish and implement a method for documenting authorized personnel's access privileges for each CGMP computer system in use (e.g., by maintaining a list of authorized individuals) (see § 211.68(b)).

5. Why is FDA concerned with the use of shared login accounts for computer systems?

When login credentials are shared, a unique individual cannot be identified through the login and the system would not conform to the CGMP requirements in parts 211 and 212. FDA requires that system controls, including documentation controls, be designed in accordance with CGMP to assure product quality (e.g., §§ 211.100 and 212.50). For example, you must implement documentation controls that ensure that the actions as described in question 4 are attributable to a specific individual (see §§ 211.68(b), 211.188(b)(11), 211.194(a)(7) and (8), and 212.50(c)(10)).

Shared, read-only user accounts that do not allow the user to modify data or settings are acceptable for viewing data, but they do not conform with the part 211 and 212 requirements for actions, such as second person review, to be attributable to a specific individual.

6. How should blank forms be controlled?

There must be document controls in place to assure product quality (see §§ 211.100, 211.160(a), 211.186, 212.20(d), and 212.60(g)). For example, bound paginated notebooks, stamped for official use by a document control group, provide good document control because they allow easy detection of unofficial notebooks as well as any gaps in notebook pages. If used, blank forms (e.g., electronic worksheets, laboratory notebooks, and MPCRs) should be controlled by the quality unit or by another document control method. As appropriate, numbered sets of blank forms may be issued and should be reconciled upon completion of all issued forms. Incomplete or erroneous forms should be kept as part of the permanent record along with written justification for their replacement (see, e.g., §§ 211.192, 211.194, 212.50(a), and

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212.70(f)(1)(vi)). All data required to recreate a CGMP activity should be maintained as part of the complete record.

7. Who should review audit trails?

Audit trail review is similar to assessing cross-outs on paper when reviewing data. Personnel responsible for record review under CGMP should review the audit trails that capture changes to data associated with the record as they review the rest of the record (e.g., §§ 211.22(a), 211.101(c) and (d), 211.103, 211.182, 211.186(a), 211.192, 211.194(a)(8), and 212.20(d)). For example, all production and control records, which includes audit trails, must be reviewed and approved by the quality unit (§ 211.192). The regulations provide flexibility to have some activities reviewed by a person directly supervising or checking information (e.g., § 211.188). FDA recommends a quality system approach to implementing oversight and review of CGMP records.¹²

8. How often should audit trails be reviewed?

If the review frequency for the data is specified in CGMP regulations, adhere to that frequency for the audit trail review. For example, § 211.188(b) requires review after each significant step in manufacture, processing, packing, or holding, and § 211.22 requires data review before batch release. In these cases, you would apply the same review frequency for the audit trail.

If the review frequency for the data is not specified in CGMP regulations, you should determine the review frequency for the audit trail using knowledge of your processes and risk assessment tools. The risk assessment should include evaluation of data criticality, control mechanisms, and impact on product quality.¹³

Your approach to audit trail review and the frequency with which you conduct it should ensure that CGMP requirements are met, appropriate controls are implemented, and the reliability of the review is proven.

See the audit trail definition in 1.c. above for further information on audit trails.

9. Can electronic copies be used as accurate reproductions of paper or electronic records?

Yes. Electronic copies can be used as true copies of paper or electronic records, provided the copies preserve the content and meaning of the original record, which includes all metadata

¹² See guidance for industry *Quality Systems Approach to Pharmaceutical CGMP Regulations*. See also guidance for industry *Contract Manufacturing Arrangements for Drugs: Quality Agreements* for information about auditing as it relates to contract facilities.

¹³ Risks to data include, but are not limited to, the potential to be deleted, amended, or excluded without authorization or without detection. Examples of audit trails that may be appropriate to review on a risk-based frequency include audit trails that capture instrument operational status, instrument communication logs, and alert records.

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required to reconstruct the CGMP activity and the static or dynamic nature of the original records.

True copies of dynamic electronic records may be made and maintained in the format of the original records or in a format that allows for the content and meaning of the original records to be preserved if a suitable reader and copying equipment (e.g., software and hardware, including media readers) are readily available (§§ 211.180(d) and 212.110).

10. Is it acceptable to retain paper printouts or static records instead of original electronic records from stand-alone computerized laboratory instruments, such as an FT-IR instrument?

A paper printout or static record may satisfy retention requirements if it is the original record or a true copy of the original record (see §§ 211.68(b), 211.188, 211.194, and 212.60). During data acquisition, for example, pH meters and balances may create a paper printout or static record as the original record. In this case, the paper printout or static record, or a true copy, must be retained (§ 211.180).

However, electronic records from certain types of laboratory instruments—whether stand-alone or networked—are dynamic, and a printout or a static record does not preserve the dynamic record format that is part of the complete original record. For example, the spectral file created by FT-IR (Fourier transform infrared spectroscopy) is dynamic and can be reprocessed. However, a static record or printout is fixed and would not satisfy CGMP requirements to retain original records or true copies (§ 211.180(d)). Also, if the full spectrum is not displayed in the printout, contaminants may be excluded.

You must ensure that original laboratory records, including paper and electronic records, are subject to second-person review (§ 211.194(a)(8)) to make certain that all test results and associated information are appropriately reported. Similarly, in microbiology, a contemporaneous written record is maintained of the colony counts of a petri dish, and the record is then subject to second-person review.

Document control requirements in § 211.180 pertain only to CGMP records.

For more information on static and dynamic records, see 1.d. in this guidance. For PET drugs, see the guidance for industry *PET Drugs—Current Good Manufacturing Practice (CGMP)* for discussion of equipment and laboratory controls, including regulatory requirements for records.

11. Can electronic signatures be used instead of handwritten signatures for master production and control records?

Yes, electronic signatures with the appropriate controls can be used instead of handwritten signatures or initials in any CGMP required record. Although § 211.186(a) specifies a “full signature, handwritten,” an electronic signature with the appropriate controls to securely link the signature with the associated record fulfills this requirement (21 CFR 11.2(a)). See part 11, which establishes criteria for when electronic signatures are considered the legally binding

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equivalent of handwritten signatures. Firms using electronic signatures should document the controls used to ensure that they are able to identify the specific person who signed the records electronically.

There is no requirement for a handwritten signature for the MPCR in the PET CGMP regulations (21 CFR part 212).

12. When does electronic data become a CGMP record?

When generated to satisfy a CGMP requirement, all data become a CGMP record.¹⁴ You must document, or save, the data at the time of performance to create a record in compliance with CGMP requirements, including, but not limited to, §§ 211.100(b) and 211.160(a).

FDA expects processes to be designed so that data required to be created and maintained cannot be modified without a record of the modification. For example, chromatographic data should be saved to durable media upon completion of each step or injection (e.g., peak integration or processing steps; finished, incomplete, or aborted injections) instead of at the end of an injection set, and changes to the chromatographic data or injection sequence should be documented in an audit trail. Aborted or incomplete injections should be captured in audit trails and should be investigated and justified.

It is not acceptable to record data on pieces of paper that will be discarded after the data are transcribed to a permanent laboratory notebook (see §§ 211.100(b), 211.160(a), and 211.180(d)). Similarly, it is not acceptable to store electronic records in a manner that allows for manipulation without creating a permanent record.

You may employ a combination of technical and procedural controls to meet CGMP documentation practices for electronic systems. For example, a computer system, such as a Laboratory Information Management System (LIMS) or an Electronic Batch Record (EBR) system, can be designed to automatically save after each entry. This would be similar to indelibly recording each entry contemporaneously on a paper batch record to satisfy CGMP requirements. The computer system described above could be combined with a procedure requiring data be keyed in or otherwise entered immediately when generated.

For PET drugs, see the “Laboratory Controls” section of the guidance for industry *PET Drugs—Current Good Manufacturing Practice (CGMP)*.

¹⁴ Under section 704(a) of the FD&C Act, FDA inspections of manufacturing facilities “shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs [and] nonprescription drugs intended for human use ... are adulterated or misbranded ... or otherwise bearing on violation of this chapter.” Accordingly, FDA routinely requests and reviews records not intended to satisfy a CGMP requirement but which nonetheless contain CGMP information (e.g., shipping or other records that may be used to reconstruct an activity).

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13. Why has FDA cited use of actual samples during “system suitability” or test, prep, or equilibration runs in warning letters?

FDA prohibits sampling and testing with the goal of achieving a specific result or to overcome an unacceptable result (e.g., testing different samples until the desired passing result is obtained). This practice, also referred to as *testing into compliance*, is not consistent with CGMP (see the guidance for industry *Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production*). In some situations, use of actual samples to perform system suitability testing has been used as a means of testing into compliance. FDA considers it a violative practice to use an actual sample in *test, prep, or equilibration* runs as a means of disguising testing into compliance.

According to the United States Pharmacopeia (USP), system suitability tests must include replicate injections of a standard preparation or other standard solutions to determine if requirements for precision are satisfied (see USP General Chapter <621> *Chromatography*). System suitability tests should be performed according to the firm’s established written procedures—which should include the identity of the preparation to be injected and the rationale for its selection—and the approved application or applicable compendial monograph (§§ 211.160 and 212.60).

If an actual sample is to be used for system suitability testing, it should be a properly characterized secondary standard, written procedures should be established and followed, and the sample should be from a different batch than the sample(s) being tested (§§ 211.160, 211.165, and 212.60). CGMP original records must be complete (e.g., §§ 211.68(b), 211.188, 211.194) and subjected to adequate review (§§ 211.68(b), 211.186(a), 211.192, and 211.194(a)(8)). Transparency is necessary. All data—including obvious errors and failing, passing, and suspect data—must be in the CGMP records that are retained and subject to review and oversight. An investigation with documented, scientifically sound justification is necessary for data to be invalidated and not used in determining conformance to specification for a batch (see §§ 211.160, 211.165, 211.188, and 211.192).

For more information, see the ICH guidance for industry *Q2(R1) Validation of Analytical Procedures: Text and Methodology* and VICH guidances for industry *GL1 Validation of Analytical Procedures: Definition and Terminology* and *GL2 Validation of Analytical Procedures: Methodology*.¹⁵

14. Is it acceptable to only save the final results from reprocessed laboratory chromatography?

No. Analytical methods should be accurate and precise.¹⁶ For most lab analyses, reprocessing data should not be regularly needed. If chromatography is reprocessed, written procedures must be established and followed and each result retained for review (see §§ 211.160, 211.165(c), 211.194(a)(4), and 212.60(a)). FDA requires complete data in laboratory records, which includes

¹⁵ VICH=Veterinary International Conference on Harmonisation.

¹⁶ See ICH guidance for industry *Q2(R1) Validation of Analytical Procedures: Text and Methodology*.

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but is not limited to notebooks, worksheets, graphs, charts, spectra, and other types of data from laboratory instruments (§§ 211.194(a) and 212.60(g)(3)).

15. Can an internal tip or information regarding a quality issue, such as potential data falsification, be handled informally outside of the documented CGMP quality system?

No. Regardless of intent or how or from whom the information was received, suspected or known falsification or alteration of records required under parts 210, 211, and 212 must be fully investigated under the CGMP quality system to determine the effect of the event on patient safety, product quality, and data reliability; to determine the root cause; and to ensure the necessary corrective actions are taken (see §§ 211.22(a), 211.125(c), 211.192, 211.198, 211.204, and 212.100).

FDA invites individuals to report suspected data integrity issues that may affect the safety, identity, strength, quality, or purity of drug products at DrugInfo@fda.hhs.gov. “CGMP data integrity” should be included in the subject line of the email. This reporting method is not intended to supersede other FDA reports (e.g., field alert reports or biological product deviation reports that help identify drug products that pose potential safety threats).

16. Should personnel be trained in preventing and detecting data integrity issues as part of a routine CGMP training program?

Yes. Training personnel to prevent and detect data integrity issues is consistent with the personnel requirements under §§ 211.25 and 212.10, which state that personnel must have the education, training, and experience, or any combination thereof, to perform their assigned duties.

17. Is FDA allowed to look at electronic records?

Yes. All records required under CGMP are subject to FDA inspection. This applies to records generated and maintained on computerized systems, including electronic communications that support CGMP activities. For example, an email to authorize batch release is a CGMP record that FDA may review.

You must allow authorized inspection, review, and copying of records, which includes copying of electronic data (§§ 211.180(c) and 212.110(a) and (b)). See also the guidance for industry *Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection* and section 704 of the FD&C Act. Procedures governing the review of electronic records are described in chapter 5 of the *Investigations Operations Manual* (IOM) at <https://www.fda.gov/iceci/inspections/iom/default.htm>.

18. How does FDA recommend data integrity problems be addressed?

FDA encourages you to demonstrate that you have effectively remediated your problems by investigating to determine the problem’s scope and root causes, conducting a scientifically sound risk assessment of its potential effects (including impact on data used to support submissions to

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FDA), and implementing a management strategy, including a global corrective action plan that addresses the root causes. This may include retaining a third-party auditor and removing individuals responsible for data integrity lapses from positions where they can influence CGMP-related or drug application data at your firm. It also may include improvements in quality oversight, enhanced computer systems, and creation of mechanisms to prevent recurrences and address data integrity breaches (e.g., anonymous reporting system, data governance officials and guidelines).

These expectations mirror those developed for the Application Integrity Policy. For more detailed information, see *Points To Consider for Internal Reviews and Corrective Action Operating Plans* at <http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/ucm134744.htm>.