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July 6, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane,
Rockville, MD 20852,

Re. Docket No: 2004N-0133 Electronic Record; Electronic Signatures FDA Public Meeting (69 Federal Register 18591-18593; April 8, 2004)

Dear Sir/Madam:

The following comments on the above-captioned Notice of Public Meeting concerning FDA's re-examination of regulations on electronic records and electronic signatures (21 CFR Part 11) are submitted on behalf of Pfizer Inc. Pfizer discovers, develops, manufactures and markets leading prescription medicines for humans and animals and many of the world's best-known consumer brands. Our innovative, value-added products improve the quality of life of people around the world and help them enjoy longer, healthier and more productive lives. The company has three business segments: health care, animal health and consumer health care. Our products are available in more than 150 countries.

Pfizer supports the premise that electronic records and electronic signatures represent an important advance in information management in pre- and post-approval drug development. Further, we endorse use of electronic signatures and electronic records as tools in a comprehensive approach to ensuring availability of and access to safe and effective medicines by those who need them. We commend the Agency for recognizing concerns that some interpretations of the Part 11 requirements could, as summarized in the above-captioned Federal Register Notice (Notice): "(1) Unnecessarily restrict the use of electronic technology in a manner inconsistent with FDA's stated intent in issuing the rule; (2) Significantly increase the costs of compliance to an extent that was not contemplated at the time the rule was drafted; and (3) Discourage innovation and technological advances without providing a significant public health benefit."

Particular areas of concern are the requirements for validation, audit trails, record retention, record copying and legacy systems. Thus, we concur with FDA's proposal to

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re-examine the scope, interpretation and implementation of Part 11, along with stakeholders and we also agree with the objectives outlined in Section III of the Notice:

1. "To prevent unnecessary controls and costs, yet retain the objectives of the rule;
2. "To clarify the scope of Part 11 (e.g., how it relates to other FDA regulations);
3. "To ensure that Part 11 provides an adequate level of record security, authenticity and integrity and encourages innovation and technological advances."

Further, we encourage FDA to work together with Pfizer and other stakeholders to identify areas where Part 11 could be less proscriptive and also to clarify the relationship between Part 11 and other FDA regulations. Pfizer believes both FDA and industry stakeholders can more successfully find solutions for managing electronic records and electronic signatures when there is an on-going dialogue between all parties, including discussions of actual case studies and acceptable practices. FDA should consider how to include such a dialogue in future activities.

We appreciate the opportunity to provide comments and we would like the Agency to consider the following:

Part 11 Subpart A—General Provisions (reference Section IV.A. of the Notice)

Pfizer supports the clarification and narrowing of scope as outlined the FDA's guidance for industry "Part 11, Electronic Records; Electronic Signatures—Scope and Application" (Guidance), issued on September 5, 2003 (68 Federal Register 52779). Additionally, we have the following comments regarding clarification and scope of Part 11:

(1) Section 11.1(b) of Part 11 presently states that Part 11 applies to records "that are created, modified, maintained, archived, retrieved, or transmitted" if such records are required by a predicate rule. This section should be revised to reflect the FDA's current thinking as outlined in the Guidance issued on Sept 5, 2003.

(2) Section 1.1(b) of Part 11 indicates that the rule applies to any electronic records submitted to FDA, even if the records are not identified in agency regulations. Since Part 11 was issued, FDA has consistently referenced predicate rules as a basis for interpretation and application of Part 11. In non-regulated areas, such as early-phased discovery research, there are no FDA predicate regulations. As such, we recommend FDA clarify its intent as to whether Part 11 applies to all records submitted to the agency or only those records and signatures required by predicate rules.

(3) With the exception of the definition of legacy systems, we do not believe that revisions to the definitions now included in Section 11.3 of Part 11 are necessary.

However, we would like to suggest the following definition be used to clarify the term legacy system.

Legacy system - Computer based systems that were in production prior to the effective date of 21 CFR Part 11. To maintain legacy status the system must meet the following conditions:

- The System was installed and operational prior to August 20 1997, and that it met all applicable GXP requirements at that time.
- The system has been maintained in a validated state (if required) or in accordance with software quality assurance practices.
- The system currently meets all predicate rule requirements.
- Changes to the application software or configuration, operating system software, database software and/or all associated hardware for a given system has in no way altered the intended purpose of the system on or after August 20 1997.

There is documented evidence and justification that the system is fit for its intended use.

(4) In order to make the requirements of Part 11 transparent, FDA should identify the relevant predicate rules that Part 11 incorporates. We have attached a non-exhaustive listing of what we believe to be the predicate rules. However, we believe specific guidance from FDA on this topic is necessary. (Attachment A)

(5) The predicate rule basis for APIs is also unclear. API's fall under ICH Q7A, identified as guidance for industry rather than regulation. It would be extremely helpful if the Agency could clarify the basis for predicate rule record keeping requirements for API.

Part 11 Subpart B-Electronic Records (reference Section IV.B. of the Notice)

We believe there are numerous opportunities for additional clarity in this section of Part 11, specifically:

(1) GMP and GLP predicate regulations explicitly address validation requirements for computerized systems. GCP predicate regulations do not.

We recommend that FDA clarify whether validation is required for computerized systems that are used to capture and maintain electronic records and/or electronic signatures related to clinical activities.

We also recommend that the scope of validation be commensurate with the need to protect the confidentiality, integrity, and availability of electronic records and/or signatures that are required by predicate rule.

(2) We agree that the extent of validation required for electronic record and electronic signature solutions should be based upon a documented risk assessment. Decisions regarding the system design, construction, validation, maintenance and extent of testing for computerized systems should be based on how the system supports the business processes or regulatory information that impact product safety, efficacy, and quality. The determination of risk may be used to justify decisions regarding the depth of controls and testing applied to the system. Risk-based assessments related to computerized systems should also incorporate an understanding of the supported business processes and the regulatory information they contain.

(3) As noted in your discussion of the Proposed Rule (Federal Register Docket No. 92N-0251), the proposed list of system controls included in Section 11.10 of Part 11 was "not intended to be all inclusive of what may be needed for a given electronic records system, and that some controls may not be necessary in all types of systems".

In present form, however, Part 11 lists specific controls in Section 11.10 for copies (b), retrieval (c), access (d), audit trails (e), operational checks (f), authority checks (g), and device checks (h). This specificity in Part 11 without the context provided in your discussion of the rule has led to considerable confusion and expense. Industry has expended tremendous effort and resources to implement these controls in systems where they may not be technically feasible or appropriate relative to the underlying risk to information confidentiality, integrity and/or availability. Furthermore, the level of detail provided in Section 11.10 is proscriptive and may serve to inhibit future innovation in the approach to risk-based controls.

Instead of listing specific controls, we recommend that FDA recognize that information security controls should vary based on the purpose and use of the system. In that regard, the Draft NIST SP 800-53, specifies the following Security Controls for Federal Information Systems to include:

- "Periodic assessments of risk, including the magnitude of harm that could result from the unauthorized access, use, disclosure, disruption, modification, or destruction of information and information systems that support the operations and assets of the organization;
- "Policies and procedures that are based on risk assessments, cost-effectively reduce information security risks to an acceptable level, and ensure that information security is addressed throughout the life cycle of each organizational information system;
- "Security plans for providing adequate information security for networks, facilities, information systems, or groups of information systems, as appropriate;

- "Security awareness training to inform personnel of the information security risks associated with their activities and their responsibilities in complying with organizational policies and procedures designed to reduce these risks;
- "Periodic testing and evaluation of the effectiveness of information security policies, procedures, and practices to be performed with a frequency depending on risk, but no less than annually;
- "A process for planning, implementing, evaluating, and documenting remedial action to address any deficiencies in the information security policies, procedures, and practices of the organization and its information systems;
- "Procedures for detecting, reporting, and responding to security incidents; and
- "Plans and procedures to ensure continuity of operations for information systems that support the operations and assets of the organization."

Recognizing or adopting this approach would provide necessary flexibility in the application of Part 11 by allowing the selection of specific technical and procedural controls based on a documented assessment of risk to electronic record/signature confidentiality, integrity and availability.

(4) A well-defined information security program should mandate use of appropriate technical and procedural controls when transmitting electronic information. We recommend removing the distinction between open versus closed systems, as it is not helpful in this regard.

(5) We believe that the requirement for control over system documentation as stated in Part 11 Section 11.10(k) is appropriate as written and any discussion of specific solutions such as configuration and document management would be too proscriptive and could serve to inhibit future innovation.

(6) With respect to source code, 21 CFR 211.68 identifies a requirement to maintain a written record of the program, i.e., Source Code. The new rule could provide clarity with respect to source code as an electronic record. Perhaps an approach similar to CPG 7132a.15 e.g.: Product specific source code (e.g., recipe) is subject to Part 11; generic source code is not; distinguishing between source code generally and source code that represents Master Record content (i.e., contains manufacturing instructions).

(7) With respect to audit trail requirements we believe that the requirements should include safeguards designed and implemented to deter, prevent and document unauthorized record creation, modification and deletion. If an electronic system cannot provide the audit trail or if it is not practical to implement and maintain, then a manual log should be acceptable. In the absence of the technical capability to record an audit trail, a manual process should be allowed for many types of systems. Other means can be used to assure the quality of the records. There are also situations whereby a combination of the electronic and manual audit trails can be applied for the same business process without unduly compromising security.

**Title: Predicate Rule Requirements****21 CFR 211 Good Manufacturing Practice (cGMP) for Finished Pharmaceuticals: Predicate Regulation Record/Signature Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
Sub Part B - Organization and Personnel			
Responsibilities of the quality control unit 211.22 (a)	Quality Control Unit (QCU) shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company	Record of rejection or approval	Signature not specifically stated
211.22 (c)	Quality Control Unit shall have the responsible for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product	Record of rejection or approval	Signature not specifically stated
211.22 (d)	The responsibilities and procedures applicable to the quality control unit shall be in writing: such written procedures shall be followed.	QC procedures required	
Personnel qualifications 211.25 (a)	Each person engaged in manufacture, processing, packing, or holding of a drug shall have the education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions.	Training records not specifically required.	
211.34 Consultants	Consultants advising on the manufacture, processing, packing, or holding of a drug shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject they are retained. Records shall be	Consultant qualification records	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	maintained stating the name, address, and qualifications of any consultants and the type of service they provide.		
211.56 (a) Sanitation.	Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a clean and sanitary condition, Any such building shall be free of infestation by rodents, birds, insects, and other vermin (other than laboratory animals). Trash and organic waste matter shall be held and disposed of in a timely and sanitary manner	Procedure required	
211.56 (b)	There shall be written procedures assigning responsibility for sanitation and describing in sufficient detail the cleaning schedules, methods, equipment, and materials to be used in cleaning the buildings and facilities; such written procedures shall be followed.	Procedure required	
211.56 (c)	There shall be written procedures for use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents. Such written procedures shall be designed to prevent the contamination of equipment, components, drug product containers, closures, packaging, labeling materials, or drug products	Procedure required	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	and shall be followed. Rodenticides, insecticides, and fungicides shall not be used unless registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 135).		
211.56 (d)	Sanitation procedures shall apply to work performed by contractors or temporary employees as well as work performed by full-time employees during the ordinary course of operations	Procedure required	
Subpart C - Buildings and Facilities (NO Records Stated or implied)			
Subpart D - Equipment			
Equipment cleaning and maintenance 211.67 (b)(c)	<p>(b) Written procedures shall be established and followed for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product. These procedures shall include, but are not necessarily limited to, the following:</p> <p>(1) Assignment of responsibility for cleaning and maintaining equipment;</p> <p>(2) Maintenance and cleaning schedules, including, where appropriate, sanitizing schedules;</p> <p>(3) A description in sufficient detail of the methods, equipment, and materials used in cleaning and maintenance operations,</p>	Equipment maintenance procedures Records shall be kept of maintenance, cleaning, sanitizing, and inspection as specified in 211.180 and 211.182	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>and the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance;</p> <p>(4) Removal or obliteration of previous batch identification;</p> <p>(5) Protection of clean equipment from contamination prior to use;</p> <p>(6) Inspection of equipment for cleanliness immediately before use.</p> <p>(c) Records shall be kept of maintenance, cleaning, sanitizing, and inspection as specified in 211.180 and 211.182</p>		
<p>Automatic, mechanical, and electronic equipment.</p> <p>211.68 (a)</p>	<p>(a) Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product. If such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance. Written records of those calibration checks and inspections</p>	<p>Equipment checks based on written program. Written records of those calibration checks and inspections shall be maintained</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	shall be maintained.		
211.68 (b)	(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss	A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	shall be maintained.	that it is secure from alteration, inadvertent erasures, or loss shall be maintained.	
Subpart E Control of Components and Drug Product Containers and Closures			
General Requirements 211.80 (a) (d)	211.80 General requirements. (a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures; such written procedures shall be followed. (d) Each container or grouping of containers for components or drug product containers, or closures shall be identified with a distinctive code for each lot in each shipment received. This code shall be used in recording the disposition of each lot. Each lot shall be appropriately identified as to its status (i.e., quarantined, approved, or rejected).	Procedures required Specific lot code required used in the recording of lot disposition.	
Testing and approval or rejection of components, drug product containers, and closures 211.84 (v) (5-6)	(5) Sample containers shall be identified so that the following information can be determined: name of the material sampled, the lot	Specific records required for sample containers.	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>number, the container from which the sample was taken, the date on which the sample was taken, and the name of the person who collected the sample.</p> <p>(6) Containers from which samples have been taken shall be marked to show that samples have been removed from them.</p>		
211.84 (d)	<p>(d) Samples shall be examined and tested as follows:</p> <p>(2) Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity test is conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.</p> <p>(3) Containers and closures shall be tested for conformance with all</p>	Written specifications required	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>appropriate written procedures. In lieu of such testing by the manufacturer, a certificate of testing may be accepted from the supplier, provided that at least a visual identification is conducted on such containers/closures by the manufacturer and provided that the manufacturer establishes the reliability of the supplier's test results through appropriate validation of the supplier's test results at appropriate intervals.</p> <p>(5) Each lot of a component, drug product container, or closure that is liable to contamination with filth, insect infestation, or other extraneous adulterant shall be examined against established specifications for such contamination.</p> <p>(e) Any lot of components, drug product containers, or closures that meets the appropriate written specifications of identity, strength, quality, and purity and related tests under paragraph (d) of this section may be approved and released for use. Any lot of such material that does not meet such specifications shall be rejected.</p>		
Rejected components,	Rejected components, drug	Record of	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
drug product containers, and closures 211.89	product containers, and closures shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable	rejected components, quarantine system required.	
211.94 (d)	(d) Standards or specifications, methods of testing, and, where indicated, methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures.	Written standards and specifications required.	
Subpart F – Production and Process Controls			
Written procedures; deviations 211.100 (a) (b)	(a) There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit. (b) Written production and process control procedures	Execution of the various production and process control functions and shall be documented at the time of performance. Any deviation from the written procedures shall be recorded and justified. Documented evidence of process execution and	Signature not specifically stated, production procedures must be approved by both the organizational unit and quality control unit

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	shall be followed in the execution of the various production and process control functions and shall be documented at the time of performance. Any deviation from the written procedures shall be recorded and justified.	deviations required.	
Charge-in of components 211.101	Written production and control procedures shall include the following, which are designed to assure that the drug products produced have the identity, strength, quality, and purity they purport or are represented to possess: (a) The batch shall be formulated with the intent to provide not less than 100 percent of the labeled or established amount of active ingredient. (b) Components for drug product manufacturing shall be weighed, measured, or subdivided as appropriate. If a component is removed from the original container to another, the new container shall be identified with the following information: (1) Component name or item code; (2) Receiving or control number;	Specific production and control procedures required. Specific records required for container identification Specific verification requirements identified	Signature not specifically stated, verification required

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>(3) Weight or measure in new container;</p> <p>(4) Batch for which component was dispensed, including its product name, strength, and lot number.</p> <p>(c) Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person to assure that:</p> <p>(1) The component was released by the quality control unit;</p> <p>(2) The weight or measure is correct as stated in the batch production records;</p> <p>(3) The containers are properly identified.</p> <p>(d) Each component shall be added to the batch by one person and verified by a second person.</p>		
Calculation of yield. 211.103	Actual yields and percentages of theoretical yield shall be determined at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product. Such calculations shall be	Actual yields and percentages of theoretical yield	Signature not specifically stated, verification required

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	performed by one person and independently verified by a second person.		
Equipment identification 211.105 (b)	(b) Major equipment shall be identified by a distinctive identification number or code that shall be recorded in the batch production record to show the specific equipment used in the manufacture of each batch of a drug product. In cases where only one of a particular type of equipment exists in a manufacturing facility, the name of the equipment may be used in lieu of a distinctive identification number or code.	Distinctive identification number or code shall be recorded in the batch production record.	
Sampling and testing of in-process materials and drug products. 211.110 (a)	(a) To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in process	(1) Tablet or capsule weight variation; (2) Disintegration time; (3) Adequacy of mixing to assure uniformity and homogeneity; (4) Dissolution time and rate; (5) Clarity, completeness, or pH of	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	material and the drug product. Such control procedures shall include, but are not limited to, the following, where appropriate:	solutions.	
211.110 (c)	(c) In-process materials shall be tested for identity, strength, quality, and purity as appropriate, and approved or rejected by the quality control unit, during the production process , e.g., at commencement or completion of significant phases or after storage for long periods. (d) omitted N/A Written procedures for sampling and testing of in-process materials and drug products	Tests must be approved or rejected by the quality control unit. Written procedures for sampling and testing of in-process materials and drug products	Signature not specifically stated, approval or rejection required
Time limitations on production 211.111	When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product. Deviation from established time limits may be acceptable if such deviation does not compromise the quality of the drug product. Such deviation shall be justified and documented.	Deviation from established time limits shall be justified and documented.	
Control of microbiological contamination	(a) Appropriate written procedures , designed to prevent objectionable microorganisms in drug	Written procedures required.	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
211.113	products not required to be sterile, shall be established and followed. (b) Appropriate written procedures , designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of any sterilization process.		
Reprocessing 211.115 (a) (b)	(a) Written procedures shall be established and followed prescribing a system for reprocessing batches that do not conform to standards or specifications and the steps to be taken to insure that the reprocessed batches will conform with all established standards, specifications, and characteristics.(b) Reprocessing shall not be performed without the review and approval of the quality control unit.	Written procedures for reprocessing required. Review and approval by the quality control unit.	Signature not specifically stated, or review and approval required by the quality unit
Subpart G -- Packaging and Labeling Control			
Materials examination and usage criteria. 211.122 (a)	(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials; such written	Written procedures required.	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	procedures shall be followed. Labeling and packaging materials shall be representatively sampled, and examined or tested upon receipt and before use in packaging or labeling of a drug product.		
211.122 (b)	(b) Any labeling or packaging materials meeting appropriate written specifications may be approved and released for use. Any labeling or packaging materials that do not meet such specifications shall be rejected to prevent their use in operations for which they are unsuitable.	Approval or rejection required	Signature not specifically stated, or rejection or approval required
211.122(c)	(c) Records shall be maintained for each shipment received of each different labeling and packaging material indicating receipt, examination or testing, and whether accepted or rejected	Records covering receipt, examination or testing and status accepted or rejected are required	
211.122 (g)(3) (h)	(g) If cut labeling is used, packaging and labeling operations shall include one of the following special control procedures: (3) Use of visual inspection to conduct a 100- percent examination for correct labeling during or after completion of finishing operations for hand-applied labeling. Such examination shall be performed by one person and independently verified by a	Cut label hand-applied labeling visual inspection, examination shall be performed by one person and independently verified by a second person. Monitoring required for printing	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	second person. (h) Printing devices on, or associated with, manufacturing lines used to imprint labeling upon the drug product unit label or case shall be monitored to assure that all imprinting conforms to the print specified in the batch production record.	devices used to imprint labeling upon the drug product unit label or case.	
Labeling issuance 211.125 (f)	(f) Procedures shall be written describing in sufficient detail the control procedures employed for the issuance of labeling; such written procedures shall be followed.	Procedures for labeling issuance and compliance to specifications required.	
Packaging and labeling operations 211.130 (d) (e)	There shall be written procedures designed to assure that correct labels, labeling, and packaging materials are used for drug products; such written procedures shall be followed. These procedures shall incorporate the following features: (d) Examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production record. (e) Inspection of the packaging and labeling facilities immediately before use to assure that all drug products have been removed from previous operations. Inspection shall also be made to assure that	Procedures for correct labeling – examination records, inspection records; compliance records Results of inspection shall be documented in the batch production records.	

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GMP Reference	Description	Records Required	Signatures/ Initials Required
	packaging and labeling materials not suitable for subsequent operations have been removed. Results of inspection shall be documented in the batch production records.		
Drug product inspection 211.134 (c)	(a) Packaged and labeled products shall be examined during finishing operations to provide assurance that containers and packages in the lot have the correct label. (b) A representative sample of units shall be collected at the completion of finishing operations and shall be visually examined for correct labeling. (c) Results of these examinations shall be recorded in the batch production or control records.	Results of these examinations shall be recorded in the batch production or control records.	
Subpart H – Holding and Distribution			
Warehousing procedures 211.142	Written procedures describing the warehousing of drug products shall be established and followed. They shall include:	Quarantine and storage procedures	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
Distribution procedures 211.150	Written procedures shall be established, and followed, describing the distribution of drug products. They shall include: (a) A procedure whereby the oldest approved stock of a drug product is distributed first. Deviation from this requirement is permitted if such deviation is temporary and appropriate. (b) A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary.	A procedure whereby the oldest approved stock of a drug product is distributed first. A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary.	
Subpart I – Laboratory Controls			
211.160	General requirements. (a) The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit.	Documents written and approved: specifications standards sampling plans test procedures laboratory control mechanisms calibration program any change in such Determination of Conformance required. Any	Signature not specifically stated, procedures must be approved by both the organizational unit and quality control unit

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GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.</p> <p>(4) The calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used.</p>	deviation from written procedures shall be recorded and justified.	
<p>Testing and release for distribution</p> <p>211.165</p>	<p>(a) For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release</p>	<p>Determination of conformance</p> <p>Any sampling and testing plans shall be described in written procedures</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>(c) Any sampling and testing plans shall be described in written procedures that shall include the method of sampling and the number of units per batch to be tested; such written procedure shall be followed.</p> <p>(e) The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented.</p>	<p>Test methods employed by the firm shall be established and documented</p> <p>The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented.</p>	
211.166	<p>Stability testing.</p> <p>(a) There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates. The written program shall be followed and shall include:</p>	<p>Written stability test program required.</p>	
<p>Special testing requirements</p> <p>211.167</p>	<p>(a) For each batch of drug product purporting to be sterile and/or pyrogen-free, there shall be appropriate laboratory testing to determine conformance to such requirements. The test procedures shall be in</p>	<p>Written Test procedure required</p> <p>Conformance to appropriate laboratory testing.</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>writing and shall be followed.</p> <p>(b) For each batch of ophthalmic ointment, there shall be appropriate testing to determine conformance to specifications regarding the presence of foreign particles and harsh or abrasive substances. The test procedures shall be in writing and shall be followed.</p> <p>(c) For each batch of controlled-release dosage form, there shall be appropriate laboratory testing to determine conformance to the specifications for the rate of release of each active ingredient. The test procedures shall be in writing and shall be followed.</p>		
Reserve Samples 211.170 (3)(b)	Reserve Samples – retained for each lot Any evidence of reserve sample deterioration shall be investigated in accordance with 211.192. The results of examination shall be recorded and maintained with other stability data on the drug product.	Reserve Sample inspection results must be recorded and maintained with stability data.	
Laboratory Animals 211.173	Animals used in testing components, in-process	Adequate records required to be	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	materials, or drug products for compliance with established specifications shall be maintained and controlled in a manner that assures their suitability for their intended use. They shall be identified, and adequate records shall be maintained showing the history of their use.	maintained showing history of use.	
Subpart J - Records and Reports			
211.180 (a)	Any production, control, or distribution record that is required to be maintained in compliance with this part and is specifically associated with a batch of a drug product shall be retained for at least 1 year after the expiration date of the batch or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under 211.137, 3 years after distribution of the batch.	Maintenance of required records associated with a batch of drug product.	
211.180 (b)	Records shall be maintained for all components, drug product containers, closures, and labeling for at least 1 year after the expiration date or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for	Maintenance of all components, drug product containers, closures, and labeling records associated with	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	exemption under 211.137, 3 years after distribution of the last lot of drug product incorporating the component or using the container, closure, or labeling.	a batch of drug product.	
211.180 (c) (d)	<p>(c) All records required under this part, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection. Records that can be immediately retrieved from another location by computer or other electronic means shall be considered as meeting the requirements of this paragraph.</p> <p>(d) Records required under this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records. Where reduction techniques, such as microfilming, are used, suitable reader and photocopying equipment shall be readily available.</p>	Records required by this Part must be available for review and copying.	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
211.180 (e)	<p>(e) Written records required by this part shall be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures. Written procedures shall be established and followed for such evaluations and shall include provisions for:</p> <p>(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.</p> <p>(2) A review of complaints, recalls, returned or salvaged drug products, and investigations conducted under 211.192 for each drug product.</p> <p>(f) Procedures shall be established to assure that the responsible officials of the firm, if they are not personally involved in or immediately aware of such actions, are notified in writing of any investigations conducted under 211.198, 211.204, or</p>	<p>Written records maintained for the purpose of drug product evaluation.</p> <p>Written procedures shall be established and followed for such evaluations.</p> <p>Procedures shall be established to assure that the responsible officials of the firm, if they are not personally involved in or immediately aware of such actions, are notified in writing of any investigations conducted</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	211.208 of these regulations , any recalls, reports of inspectional observations issued by the Food and Drug Administration, or any regulatory actions relating to good manufacturing practices brought by the Food and Drug Administration.		
Equipment cleaning and use logs 211.182	A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed. If equipment is dedicated to manufacture of one product, then individual equipment logs are not required, provided that lots or batches of such product follow in numerical order and are manufactured in numerical sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record. The persons performing and double-checking the cleaning and maintenance shall date and sign or initial the log indicating that the work was performed. Entries in	A written record of major equipment cleaning, maintenance and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed.	The persons performing and double-checking the cleaning and maintenance shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	the log shall be in chronological order.		
Component, drug product container, closure, and labeling records. 211.184	These records shall include the following: (a) The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labeling; the name of the supplier; the supplier's lot number(s) if known; the receiving code as specified in 211.180; and the date of receipt. The name and location of the prime manufacturer, if different from the supplier, shall be listed if known. (b) The results of any test or examination performed (including those performed as required 211.84(a) 211.84(d), or 211.122(a) and the conclusions derived therefrom. (c) An individual inventory record of each component, drug product container, and closure and, for each component, a reconciliation of the use of each lot of such component. The inventory record shall contain sufficient information to allow determination of any batch or lot of drug product associated with the use of	Component, container, closure, labeling records include: Identity and quantity of each shipment, name of supplier, supplier's lot number, receiving code, receipt date, name/location of prime manufacturer; Results of test or examination; Individual inventory record; Documentation of review of labels and labeling; Disposition of rejected items	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>each component, drug product container, and closure.</p> <p>(d) Documentation of the examination and review of labels and labeling for conformity with established specifications in accord with 211.122(c) and 211.130(c).</p> <p>(e) The disposition of rejected components, drug product containers, closure, and labeling.</p>		
<p>Master production and control records.</p> <p>211.186</p>	<p>(a) To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.</p> <p>(b) Master production and control records shall include:</p> <p>(1) The name and strength of the product and a description of the dosage</p>	<p>Master production and control records</p> <p>To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person.</p>	<p>Full handwritten signature required. For master production and control records.</p> <p>Labeling signed and dated.</p>

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>form;</p> <p>(2) The name and weight or measure of each active ingredient per dosage unit or per unit of weight or measure of the drug product, and a statement of the total weight or measure of any dosage unit;</p> <p>(3) A complete list of components designated by names or codes sufficiently specific to indicate any special quality characteristic;</p> <p>(4) An accurate statement of the weight or measure of each component, using the same weight system (metric, avoirdupois, or apothecary) for each component. Reasonable variations may be permitted, however, in the amount of components necessary for the preparation in the dosage form, provided they are justified in the master production and control records;</p> <p>(5) A statement concerning any calculated excess of component;</p> <p>(6) A statement of theoretical weight or measure at appropriate phases of processing;</p> <p>(7) A statement of</p>	<p>The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.</p> <p>Specimen or copy of each label and all other labeling signed and dated by the person or persons responsible for approval of such labeling</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>theoretical yield, including the maximum and minimum percentages of theoretical yield beyond which investigation according to 211.192 is required;</p> <p>(8) A description of the drug product containers, closures, and packaging materials, including a specimen or copy of each label and all other labeling signed and dated by the person or persons responsible for approval of such labeling;</p> <p>(9) Complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed.</p>		
<p>Batch production and control records. 211.188</p>	<p>Batch production and control records shall be prepared for each batch of drug product produced and shall include complete information relating to the production and control of each batch. These records shall include:</p> <p>(a) An accurate reproduction of the appropriate master production or control record, checked for accuracy, dated, and signed;</p> <p>(b) Documentation that each</p>	<p>Batch production and control records required for each batch of drug product.</p> <p>An accurate reproduction of the appropriate master production or control record, checked for accuracy, dated, and signed;</p>	<p>Reproduction of master signed/dated by person checking for accuracy to original</p>

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including:</p> <ul style="list-style-type: none">(1) Dates;(2) Identity of individual major equipment and lines used;(3) Specific identification of each batch of component or in-process material used;(4) Weights and measures of components used in the course of processing;(5) In-process and laboratory control results;(6) Inspection of the packaging and labeling area before and after use;(7) A statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;(8) Complete labeling control records, including specimens or copies of all labeling used;(9) Description of drug product containers and closures;(10) Any sampling performed;		

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>(11) Identification of the persons performing and directly supervising or checking each significant step in the operation;</p> <p>(12) Any investigation made according to 211.192.</p> <p>(13) Results of examinations made in accordance with 211.134.</p>		
<p>Production record review. 211.192</p>	<p>All drug product production and control records, including those for packaging and labeling, shall be reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed. Any unexplained discrepancy (including a percentage of theoretical yield exceeding the maximum or minimum percentages established in master production and control records) or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated, whether or not the batch has already been distributed. The investigation shall extend to other batches of the same drug product and other drug products that may</p>	<p>Production Record review by QCU required.</p> <p>A written record of any investigation.</p>	<p>Signature of QCU (implied)</p>

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and followup.		
211.194	Laboratory records. (a) Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays, as follows: (1) A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing. (2) A statement of each method used in the testing of the sample. The statement shall indicate the location of data that establish that the	Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays	Initials or signatures (with date) of person who performs each test Initials or signatures of second person (with date) reviewing records

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested The suitability of all testing methods used shall be verified under actual conditions of use.</p> <p>(3) A statement of the weight or measure of sample used for each test, where appropriate.</p> <p>(4) A complete record of all data secured in the course of each test, including all graphs, charts, and spectra from laboratory instrumentation, properly identified to show the specific component, drug product container, closure, in-process material, or drug product, and lot tested.</p> <p>(5) A record of all calculations performed in connection with the test, including units of measure, conversion factors, and equivalency factors.</p> <p>(6) A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, drug product container, closure, in-process material, or drug</p>		

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>product tested.</p> <p>(7) The initials or signature of the person who performs each test and the date(s) the tests were performed.</p> <p>(8) The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.</p> <p>(b) Complete records shall be maintained of any modification of an established method employed in testing. Such records shall include the reason for the modification and data to verify that the modification produced results that are at least as accurate and reliable for the material being tested as the established method.</p> <p>(c) Complete records shall be maintained of any testing and standardization of laboratory reference standards, reagents, and standard solutions.</p> <p>(d) Complete records shall be maintained of the periodic calibration of laboratory instruments, apparatus, gauges, and recording devices required</p>		

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	by 211.160(b)(4) (e) Complete records shall be maintained of all stability testing performed in accordance with 211.166.		
Distribution records 211.196	Distribution records shall contain the name and strength of the product and description of the dosage form, name and address of the consignee, date and quantity shipped, and lot or control number of the drug product. For compressed medical gas products, distribution records are not required to contain lot or control numbers.	Distribution Records retained	
211.198 (a)	Complaint files. (a) Written procedures describing the handling of all written and oral complaints regarding a drug product shall be established and followed. Such procedures shall include provisions for review by the quality control unit, of any complaint involving the possible failure of a drug product to meet any of its specifications and, for such drug products, a determination as to the need for an investigation in accordance with 211.192. Such procedures shall include provisions for	Written procedures describing the handling of all written and oral complaints regarding a drug product shall be established and followed. A written record of each complaint shall be maintained in a file designated for drug product complaints. The compliant	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>review to determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to the Food and Drug Administration in accordance with § 310.305 of this chapter.</p> <p>(b) A written record of each complaint shall be maintained in a file designated for drug product complaints. The file regarding such drug product complaints shall be maintained at the establishment where the drug product involved was manufactured, processed, or packed, or such file may be maintained at another facility if the written records in such files are readily available for inspection at that other facility. Written records involving a drug product shall be maintained until at least 1 year after the expiration date of the drug product, or 1 year after the date that the complaint was received, whichever is longer. In the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under 211.137, such written records shall be maintained for 3 years after distribution of the drug</p>	<p>file must be readily available for inspection at the manufacturing facility.</p> <p>The record or copy of the record of the (Production record review) investigation shall be maintained at the establishment where the investigation occurred.</p> <p>Where an investigation under 211.192 (production record review) is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>product.</p> <p>(1) The written record shall include the following information, where known: the name and strength of the drug product, lot number, name of complainant, nature of complaint, and reply to complainant.</p> <p>(2) Where an investigation under 211.192 is conducted, the written record shall include the findings of the investigation and followup. The record or copy of the record of the investigation shall be maintained at the establishment where the investigation occurred in accordance with 211.180(c).</p> <p>(3) Where an investigation under 211.192 is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.</p>		
Subpart K – Returned and Salvaged Drug Products			
Returned drug products. 211.204	Returned drug products shall be identified as such and held. If the conditions under which returned drug products have been held, stored, or shipped	Returned drug products: Name and label potency of drug product dosage form Lot number	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
	<p>before or during their return, or if the condition of the drug product, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality or purity of the drug product, the returned drug product shall be destroyed unless examination, testing, or other investigations prove the drug product meets appropriate standards of safety, identity, strength, quality, or purity. A drug product may be reprocessed provided the subsequent drug product meets appropriate standards, specifications, and characteristics. Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product. If the reason for a drug product being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of 211.192. Procedures for the holding, testing, and reprocessing of returned drug products shall be in writing and shall be followed.</p>	<p>Reason for return</p> <p>Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product.</p> <p>Procedures for the holding, testing, and reprocessing of returned drug products shall be in writing</p>	

**Title: Predicate Rule Requirements**

GMP Reference	Description	Records Required	Signatures/ Initials Required
Drug product salvaging. 211.208	Drug products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether drug products have been subjected to such conditions, salvaging operations may be conducted only if there is (a) evidence from laboratory tests and assays (including animal feeding studies where applicable) that the drug products meet all applicable standards of identity, strength, quality, and purity and (b) evidence from inspection of the premises that the drug products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Organoleptic examinations shall be acceptable only as supplemental evidence that the drug products meet appropriate standards of identity, strength, quality, and purity. Records including name, lot number, and disposition shall be maintained for drug products subject to this section.	Records including name, lot number, and disposition shall be maintained for drug products subject to this section.	

**Title: Predicate Rule Requirements****21 CFR 58 Good Laboratory Practice (cGLP): Predicate Regulation
Record/Signature Requirements**

GLP Reference	Description	Records Required	Signatures/ Initials Required
Subpart A 58.3 (k)	Raw data – exact transcripts of raw data...verified accurate by signature and date	(see 58.190)	Signature of person creating copy of raw data
Subpart B 58.29	Personnel - Each testing facility shall maintain a current summary of training and experience, and a job description for each individual engaged in or supervising a nonclinical laboratory study	Training/experience records; Job descriptions	
58.33	Study Director Recordkeeping Responsibilities	Protocol Experimental data Deviations and corrective actions	
58.35 (b1)	Quality Assurance Unit: Maintain master schedule sheet	Master schedule sheet: Test system Nature of study Study initiation date Current study status Sponsor Study director	
58.35 (b3)	Quality Assurance Unit: Maintain written and signed inspection records	Inspection Records: Inspection Date Study inspected Phase or segment inspected Inspector Name Findings/problems Action Recommended Scheduled date for reinspection	QA Signature (of inspector implied)
58.35(b4)	QA unit: Submit written status reports to management and study director	Written study status reports: Problems and corrective actions	
58.35 (b7)	QA unit: Prepare and sign statement to	Study Inspection Statement: Dates inspections made	QA signature

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/ Initials Required
	include with final study report to specify inspections and findings	Findings	
58.35 (c)	QA unit: Responsibilities, procedures, records, indexing of records shall be in writing and maintained and available to FDA.	QA responsibilities and procedures QA records Inspection dates Study inspected Phase or segment of study Inspector Method of indexing records	
58.35 (d)	QA unit: Written procedures	Procedures for handling inspections	
Subpart D 58.63 (b)	SOP for maintenance and calibration of equipment	Equipment SOP details: Methods, materials, and schedules used in routine inspection, cleaning, maintenance, testing, calibration, standardization of equipment Remedial action in event of failure or malfunction Person responsible for performance of operations	
58.63 (c)	Written records for maintenance and calibration of equipment	Equipment records: Inspections Maintenance Testing Calibration and/or standardizing Date of operation Routine or non-routine For Non-routine repairs: Nature of defect How/when defect discovered Remedial action taken	
Subpart E 58.81 (a)	Testing Facilities Operation: Written SOPs required for nonclinical laboratory study methods to insure quality and	Testing Facilities SOPs Deviations from SOPS Changes in SOPS	Study director signature for deviations

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/Initials Required
	integrity of study data. Deviation from SOPs shall be authorized by study director and documented in raw data. Changes in SOPs shall be authorized by management.		from SOPs (implied) Management signature for change in SOPs
58.81 (b)	Testing Facility SOPs	SOPS: Animal room preparation Animal care Receipt, id, storage, handling, mixing, method of sampling of test and control articles Test system observations Laboratory tests Handling of dead or moribund animals Necropsy or postmortem exams Collection and identification of specimens Histopathology Data handling, storage, and retrieval Maintenance and calibration of equipment Transfer, proper placement, and identification of animals	
58.81 (c)	Testing Facility SOPs	Laboratory manuals; laboratory procedure SOPs	
58.81 (d)	Historical file of SOPS	SOP history Revision history of SOP Dates of revisions	
58.83	Reagents and solutions: labels	Labels	
58.90 (c)	Documentation of treatment of diseased animals in study	Diseased animal records: Diagnosis Authorizations of treatment Description of treatment Date of treatment	
58.90 (g)	Analyses of feed and water	Feed and water analysis	

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/ Initials Required
	periodically done and documented.	Maintained as raw data	
58.90 (i)	Documentation of pest control materials	Pest control materials used	
Subpart F 58.105 (a)	Test and control article characterization shall be documented	Test and control article characterization: Identify Strength Purity Composition Other characterization to define test/control article Methods of synthesis, fabrication, or derivation of test/control articles	
58.107 (d)	Test and control article handling – receipt and distribution of each batch shall be documented	Test and control articles: Date and quantity of batch distributed or returned	
Subpart G 58.120 (a)	Study Protocol: Each study shall have an approved written protocol that indicates objectives and methods for study	Study Protocol includes: Descriptive title and purpose Test and Control Articles Name Chemical abstract number Code number Name of sponsor Name/ address of testing facility Test system: Number Body weight range Sex Source of supply Species Strain Substrain Age Procedure for identification of test system Description of experimental	Study Sponsor Signature Study Director Signature

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/Initials Required
		design Methods for control of bias Description/identification of diet Materials used to solubilize or suspend test/control articles Specifications for acceptable levels of contaminants Dosage level of test/control article Method and frequency of administration of test/control articles Type and frequency of tests, analyses, measurements Records to be maintained Date of protocol approval by sponsor Dated signature of study director Statement of proposed statistical methods	
58.120 (b)	Documentation of changes in protocol	Protocol changes: Changes/revisions Reasons for change Approval date	Study Director signature
58.130 (d)	Nonclinical laboratory study: Records of gross findings for a specimen from postmortem observations	Gross findings from postmortem observations	
58.130 (e)	Nonclinical laboratory study: All data generated during the conduct of a study, except those generated by automated collection systems, shall be recorded directly, promptly, and legibly in ink	All data generated during a study Include study date Changes to data Reason for change Date of change Automated collection systems data	Signature or initials of person entering data Signature of person making change to data

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/ Initials Required
	For automated data collection systems, individual responsible for collection shall be identified. Changes to automated data entries must be made without obscuring original entry.	Person responsible for changes, reason and date of change, original entry	
Subpart J 58.185	Reports: A final report shall be issued, and signed and dated by the study director Corrections to the final report shall be in the form of an amendment.	Final Report: Name/address of facility performing study Dates study initiated and completed Objectives/procedures in protocol, changes in original protocol Statistical methods Test and control articles Name, chemical abstracts number/ code number, strength, purity, composition Stability of test/control articles Description of methods Description of test system: Number of animals, Sex, body weight range, source of supply, species, strain and substrain, age, procedure for identification Description of dosage, dosage regimen, route of administration, duration Description of circumstances affecting the quality and integrity of data Study director, other scientists, supervisory personnel Description of transformations,	Signature of each scientist on individual reports Signature of study director on final report Signature of person responsible for final report amendment

**Title: Predicate Rule Requirements**

GLP Reference	Description	Records Required	Signatures/ Initials Required
		calculations, operations on data; summary and analysis of data; statement of conclusions Signed and dated reports of individual scientists/professionals Locations of specimens, raw data, final report QA prepared statement Signature/date of study director Corrections/additions amendment: Part of final report to amend Reasons for correction Signature/date of person responsible	
58.190	Storage and retention of records and data	Nonclinical study records to be retained: All raw data Documentation Protocols Final reports Specimens (except mutagenicity tests and wet specimens) Person responsible for archives Index of material archived	
58.195 (c)	Retention of records	Documentation of expired samples	
58.195 (h)	Retention of records	Notification of move	
58.217	Suspension or termination of a testing facility by a sponsor	Notice of termination	



Attachment A

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Title: Predicate Rule Requirements

**21 CFR 50 Protection of Human Subjects - Good Clinical Practice (cGCP):
Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
50.27	General Requirements for Informed Consent	Written consent form	Signed and dated by the subject or the subject's legally authorized rep

**Title: Predicate Rule Requirements****21 CFR 54 Financial Disclosure by Clinical Investigators - Good Clinical Practice (cGCP): Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
54.4	Certification and Disclosure Requirements	Certification (FDA form 3454) or disclosure (FDA form 3455) for each clinical investigator	FDA form 3454 must be dated and signed by the chief financial officer or other responsible corporate rep
54.6	Recordkeeping and Record Retention	Complete records showing any financial interest or arrangement paid to clinical investigators by sponsor Complete records showing significant payments of other sorts Complete records showing any financial interests held by investigators	

**Title: Predicate Rule Requirements****21 CFR 56 Institutional Review Boards- Good Clinical Practice (cGCP):
Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
56.108	IRB Functions and Operations	Written procedures	
56.109	IRB Review of Research	Informed consent Written notification to investigator Written notification to sponsor	
56.115	IRB Records	Research proposals reviewed Approved sample consents Investigator progress reports Subject injury reports IRB minutes Continuing review activities Correspondence with investigators IRB member list Written IRB procedures Statements of significant new findings given to subjects	

**Title: Predicate Rule Requirements****21 CFR 312 Investigational New Drug Application- Good Clinical Practice (cGCP): Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
312.23	IND Format and Content	IND application	(1) Sponsor signature on FDA form 1571 (2) Information submitted to the agency by a person other than the sponsor is required to contain a written statement that authorizes the reference and that is signed by the person who submitted the information.
312.30	Protocol Amendments	Protocols and amendments	
312.31	Information Amendments	Information amendments essential to IND that are not in the scope of a protocol amendment	
312.32	IND Safety Reports	Adverse experience reports	
312.33	Annual Reports	IND annual report	
312.35	Submissions for Treatment Use	Treatment protocol	
312.38	Withdrawal of IND	Notification of IND withdrawal	
312.52	Transfer of Obligations to a Contract Research Organization	Written transfer of obligations from sponsor to contract research organization	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
312.53	Selecting Investigators and Monitors	Sponsor to obtain the following from an investigator: (1) Statement of Investigator (FDA 1572) (2) Curriculum Vitae (3) Clinical protocol (4) Financial disclosure	Investigator signature on FDA form 1572
312.55	Informing Investigators	Investigator brochures and updates	
312.57	Recordkeeping and Record Retention (Sponsor)	(1) Drug shipment, receipt and disposition records (2) Financial interest and payments	
312.62	Recordkeeping and Record Retention (Investigator)	(1) Drug disposition (2) Case histories	Signed and dated informed consent forms
312.64	Investigator Reports	(1) Progress (2) Safety (3) Final report (4) Financial disclosure	
312.110	Import and Export Requirements	Request to export drug	
312.120	Foreign Clinical Studies Not Conducted Under an IND	Data submissions	
312.160	Drugs for Investigational Use in Laboratory Research Animals or In Vitro Tests	Drug shipment and disposition records	

**Title: Predicate Rule Requirements****21 CFR 314 Applications for FDA Approval to Market a New Drug - Good Clinical Practice (cGCP): Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
Subpart B – Applications 314.50	Content and Format of an Application	Application form Index Summary Technical sections Samples and labeling Case report forms and tabulations Patent information Claimed exclusivity Financial certification or disclosure statement	Applicant or attorney or authorized agent must sign the application
314.52	Notice of Certification of Invalidity or Noninfringement of a Patent	Notice	
314.53	Submission of Patent Information	Patent reporting requirements	Authorized signature by applicant or patent owner or applicant's or patent owner's attorney or agent
314.54	Procedure for Submission of an Application Requiring Investigations for Approval of a New Indication for, or Other Change From a Listed Drug	Submission records	
314.55	Pediatric Use Information	Submission records	
314.60	Amendments to an Approved Application	Submission records	
314.65	Withdrawal by Applicant of an Unapproved Application	Withdrawal letter	
314.70	Supplements and Other Changes to an Unapproved Application	Submission records	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
314.71	Procedures for Submission of a Supplement to an Approved Application	Submission records	
314.72	Change in Ownership of an Application	Letters New application form	Signature of new owner on application form
314.80	Postmarketing Reporting of Adverse Drug Experiences	Submission records	
314.81	Other Postmarketing Reports	Submission records	
Abbreviated Applications 314.94	Content and Format of an Abbreviated Application	Application form Table of Contents Basis for submission Conditions of use Active Ingredients Route/dose/strength Bioequivalence Labeling Chemistry manufacturing and controls Samples Patent certification Financial certification or disclosure statement	Applicant must sign the application
314.95	Notice of Certification of Invalidity or Noninfringement of a Patent	Notice	
314.96	Amendments to an Unapproved Abbreviated Application	Submission records	
314.97	Postmarketing Reports	Submission records	

**Title: Predicate Rule Requirements****ICH Good Clinical Practice (cGCP): Predicate Regulation Record/Signature Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
1.17	Contract: A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract.	Contract	Signature of involved parties
3.3	The IRB/IEC should have documented, written procedures	Written procedures for: its composition; scheduling, notifying its members of, and conducting meetings; conducting initial and continuing review of trials; determining the frequency of continuing review; providing expedited review and approval of minor changes in ongoing trials; specifying that no subject admitted to trials before their written approval of the trial; specifying that they approve protocol amendments before use, except in extreme circumstances; specifying that the investigator promptly report deviations, changes, ADRs, and new information that may adversely affect subjects or trial conduct; ensuring that they promptly notify investigator/institution concerning its trial related decisions, reasons for	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
		decisions, and procedures for appeal of decisions	
3.4	Relevant records of IRB/IEC activities	Applicable written documentation, such as: Written procedures Membership lists Lists of occupations/affiliations of members Submitted documents Minutes of meetings Correspondence	
4.1.1	Evidence of investigator's qualifications	Up-to-date curriculum vitae and other relevant documentation	
4.5.1 5.6 8.2.2	Investigator/institution should conduct the trial in compliance with the protocol...approved by IRB/IEC	Approved protocol	Signature of Sponsor Signature of Investigator / Institution
5.1	Sponsor SOPs for implementing and maintaining quality assurance and quality control systems	Applicable, written SOPs	
5.5.2	Documentation for the IDMC (Independent Data Monitoring Committee), if established by the sponsor	Written SOPs Written meeting records	
5.5.3	Obligations of sponsor regarding documentation for electronic trial data handling systems	System validation documentation, including system's ability to maintain an audit trail SOPs for system use Security system that prevents unauthorized use of the system List of individuals authorized to make data changes Maintain adequate backup	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
		of the system's data Safeguard the blinding, if any, of the trial	
5.6.3	Sponsor obtains investigator's / institution's agreement to: conduct trial in compliance with GCP, regulatory requirements, protocol agreed to by sponsor and approved by IRB/IEC; comply with data recording/reporting procedures; permit monitoring, auditing, and inspection; and retain essential documents until informed otherwise by sponsor	Document confirming this agreement, which may be the protocol	Signature of Sponsor Signature of Investigator / Institution
5.11	Sponsor confirmation of review by IRB/IEC	Sponsor obtains name/address of IRB/IEC, statement that IRB/IEC organized according to GCP and applicable laws and regulations, documented IRB/IEC approvals and other related trial documents	
5.14.3	Supplying and handling investigational products	Written procedures for the handling and storage of investigational products for a trial	
5.18.5	Monitoring procedures	Sponsor's general and specific written SOPs for trial monitoring	
5.19	Auditing of trials conducted by sponsor	Documentation of observations and findings of auditor(s)	
7.1 8.2.1	Documentation of relevant and current scientific information about the investigational product provided to the investigator Medically qualified person	Investigator's brochure	Signature (implied) of discipline(s) that generated the data in the brochure

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
	should generally participate in the editing of the documentation		
8.2.2	Documentation of agreement to the protocol/amendment(s) and Case Report Form (CRF) by the investigator and sponsor	Signed protocol and amendment(s) along with sample CRF	Signature of Investigator and Sponsor
1.28 4.8.8 4.8.9 4.8.12 8.2.3	Documentation <ul style="list-style-type: none">- to show that recruitment measures are appropriate and not coercive- of information given to trial subjects to support their ability to give fully informed consent	<ul style="list-style-type: none">- Any other written information- Advertisement for subject recruitment (if used)- Informed consent form (including all applicable translations)	Signature and personal dating of person giving consent If required, signature of witness to informed consent discussion Signature of person conducting informed consent discussion (See also section 4.8.12 for signature requirements for minors, patients with severe dementia, etc.)
8.2.4	Documentation of financial agreement between the investigator/institution and the sponsor for the trial	Financial aspects of the trial	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
8.2.5	Documentation that compensation to subject(s) for trial-related injury will be available	Insurance statement (where required)	
8.2.6	Documentation of agreement between involved parties	Signed agreements (where relevant): <ul style="list-style-type: none">- Investigator/institution and sponsor- Investigator/institution and Clinical Research organization (CRO)- Sponsor and CRO- Investigator/institution and authority(ies) (where required)	Signatures of involved parties
8.2.7	Documentation that the trial has been subject to Institutional Review Board (IRB) / (Independent Ethics Committee (IEC) review and been given approval/favorable opinion. Document(s) identified by version number and date	Dated, documented approval/favorable opinion of IRB/IEC of the following: <ul style="list-style-type: none">- Protocol and any amendment(s)- CRF (if applicable)- Informed consent form(s)- Any other written information provided to the subject(s)- Advertisement for subject recruitment (if used)- Subject compensation (if any)- Any other documents given approval/favorable opinion	Signature of IRB/IEC (implied)
8.2.8	Documentation that the IRB/IEC is constituted in agreement with Good Clinical Practices (GCP)	Document stating composition of the IRB/IEC	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
8.2.9	Documentation that appropriate authorization/approval/notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s)	Regulatory authority(ies) authorization/approval/notification of protocol (where required)	
8.2.10	Documentation of qualifications and eligibility of personnel to conduct the trial and/or provide medical supervision of subjects	Curriculum vitae and/or other relevant documents evidencing qualifications of investigator(s) and sub-investigator(s)	
8.2.11	Documentation of normal value(s) and/or range(s) for medical/laboratory/technical procedure(s) and/or test(s) included in the protocol	Normal value(s) and/or range(s) for medical/laboratory/technical procedure(s) and/or test(s) included in the protocol	
8.2.12	Documentation of competence of facility to perform required test(s) and support reliability of results	Medical/laboratory/technical procedures/tests <ul style="list-style-type: none">- Certification or- Accreditation or- Established quality control and/or external quality assessment or- Other validation (where required)	
8.2.13	Documentation of compliance with applicable labeling regulations and appropriateness of instructions provided to the subjects	Sample of label(s) attached to investigational product container(s)	
8.2.14	Documentation of instructions needed to ensure proper storage, packaging, dispensing, and disposition of investigational products and trial-related materials	Instructions for handling of investigational product(s) and trial-related materials (if not included in the protocol or the Investigator's Brochure)	
8.2.15	Documentation of shipment dates, batch numbers, and method of shipment of investigational product(s) and	Shipping records for investigational product(s) and trial-related materials	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
	trial-related materials; and of allowing for tracking of product batch, review of shipping conditions, and accountability		
8.2.16	Documentation of identity, purity, and strength of investigational products to be used in the trial.	Certificate(s) of analysis of investigational product(s) shipped	
8.2.17	Documentation of how, in case of an emergency, the identity of blinded investigational product can be revealed without breaking the blind for the remaining subjects' treatment.	Decoding procedures for blinded trials.	
8.2.18	Documentation of method of randomization of the trial population	Master randomization list	
8.2.19	Documentation stating that the site is suitable for the trial (may be combined with 8.2.20)	Pre-trial monitoring report	
8.2.20	Documentation that the trial procedures were reviewed with the investigator and the investigator's trial staff (may be combined with 8.2.19)	Trial initiation monitoring report	
8.3.1	Documentation that investigator is informed in a timely manner of relevant information as it becomes available	Investigator's brochure updates	
8.3.2	Documentation of revisions of trial-related documents that take effect during the trial	Any revision to <ul style="list-style-type: none">- Protocol/amendment(s) and CRF- Informed consent form- Any other written information to be provided to the subject- Advertisement for subject recruitment (if used)	
8.3.3	Documentation that the amendment(s) and/or	Dated, documented approval/favorable opinion	Signature of IRB/IEC

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
	revision(s) have been subject to IRB/IEC review, were given approval/favorable opinion, and are identified by version number and date	of IRB/IEC of the following <ul style="list-style-type: none">- Protocol amendment(s)- Revision(s) of<ul style="list-style-type: none">- Informed consent form- Any other written information to be provided to the subject- Advertisement for subject recruitment (if used)- Any other documents given- Approval/favorable opinion- Continuing review of the trial (where required)	(implied)
8.3.4	Documentation of compliance with applicable regulatory requirements	Regulatory authority(ies) authorizations/approvals/notifications where required for <ul style="list-style-type: none">- Protocol amendment(s) and other documents	
8.3.5	Documentation of qualifications and eligibility to conduct trials and/or provide medical supervision of subjects (see 8.2.10)	Curriculum vitae for new investigator(s) and/or sub-investigator(s)	
8.3.6	Documentation of normal values and ranges that are revised during the trial (see 8.2.11)	Updates to normal value(s)/range(s) for medical/laboratory/technical procedures(s)/test(s) included in the protocol	
8.3.7	Documentation that tests remain adequate throughout the trial period (see 8.2.12)	Updates of medical/laboratory/technical procedures/tests <ul style="list-style-type: none">- Certification or- Accreditation or- Established quality	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
		control and/or external quality assessment or – Other validation (where required)	
8.3.8	Documentation of shipment dates, batch numbers, and method of shipment of investigational product(s) and trial related materials (see 8.2.15)	Shipping records for investigational product(s) and trial-related materials	
8.3.9	Documentation of identity, purity, and strength of investigational product(s) to be used in the trial (see 8.2.16)	Certificate(s) of analysis for new batches of investigational products	
1.38 8.3.10	Documentation of site visits by, and findings of, the monitor, including act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and the applicable regulatory requirement(s).	Monitoring Reports	
8.3.11	Documentation of any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting	Relevant communications other than site visits – Letters – Meeting notes – Notes of telephone calls	
8.3.12	Documentation showing that consent is obtained in accordance with the GCPs and the protocol, and dated prior to participation of each subject in the trial. Also documents direct access permission (see 8.2.3)	Signed informed consent forms	Signature of person providing consent
8.3.13	Documentation of existence of the subject and substantiation of integrity of trial data collected. To include original documents related to the trial, to medical	Source documents	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
	treatment, and to history of subject		
8.3.14	Documentation that the investigator or authorized member of the investigator's staff confirms the observations recorded	Signed, dated, and completed case report forms (CRFs)	Signature of investigator or authorized designee
4.9.3 8.3.15	Documentation of all changes, additions or corrections made to the CRF after initial data were recorded maintaining an audit trail of the data information changed	Documentation of CRF corrections	Initials of individual making corrections
8.3.16	Notification by originating investigator to sponsor of serious adverse events and related reports in accordance with 4.11	Notification by originating investigator to sponsor of serious adverse events and related reports	
8.3.17	Notification by sponsor and/or investigator, where applicable, to regulatory authority(ies) and IRB(s)/IEC(s) of unexpected serious adverse drug reactions in accordance with 5.17 and 4.11.1 and of other safety information in accordance with 5.16.2 and 4.11.2	Notification by sponsor and/or investigator, where applicable, to regulatory authority(ies) and IRB(s)/IEC(s) of unexpected serious adverse drug reactions and of other safety information	
8.3.18	Notification by sponsor to investigators of safety information in accordance with 5.16.2	Notification by sponsor to investigators of safety information	
8.3.19	Interim or annual reports provided to IRB/IEC in accordance with 4.10 and to authority(ies) in accordance with 5.17.3	Interim or annual reports to IRB/IEC and authority(ies)	
8.3.20	Documentation of identification of subjects who entered pre-trial screening	Subject screening log	
8.3.21	Documentation that investigator/institution keeps a	Subject enrollment log	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/ Initials Required
	confidential list of names of all subjects allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any subject		
8.3.23	Documentation that investigational product(s) have been used according to the protocol	Investigational product(s) accountability at the site	
8.3.24	Documentation of signatures and initials of all persons authorized to make entries and/or corrections on CRFs	Signature sheet	Signatures and Initials of all individuals authorized to make entries on CRFs
8.3.25	Documentation of location and identification of retained samples if assays need to be repeated	Record of retained body fluids/tissue samples (if any)	
8.4.1	Documentation that the investigational product(s) have been used according to the protocol. Documentation of the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by subjects, and returned to sponsor	Investigational product(s) accountability at the site	
8.4.2	Documentation of destruction of unused investigational products by sponsor or at the site	Documentation of investigational product destruction	
8.4.3	Documentation of identification of all subjects enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for an agreed upon time	Completed subject identification code list	
8.4.4	Documentation that an audit	Audit certificate (if	

**Title: Predicate Rule Requirements**

GCP Reference	Description	Records Required	Signatures/Initials Required
	was performed	available)	
8.4.5	Documentation that all activities required for trial close-out are completed, and copies of essential documents are held in the appropriate files	Final trial close-out monitoring report	
8.4.6	Documentation to be returned to sponsor to document any decoding that may have occurred	Treatment allocation and decoding documentation	
8.4.7	Documentation of completion of the trial	Final report by investigator to IRB/IEC where required, and where applicable, to the regulatory authority(ies)	
8.4.8	Documentation of results and interpretation of the trial	Clinical study report	