:

FDA Warning Letters, Form 483 Observations and Establishment Inspection Reports – Preview

FDA 警告文字，来自 483 观测资料和预先检查报告。

Important: Warning letters and other FDA inspection documentation should be interpreted in the context of full content. Just looking at extracts may be misleading. And sometimes they include good advice from the FDA not mentioned in the extracts.

重要性：警告文字和其他的 FDA 检查文件必须说明，根据上下文包括全部内容。仅是看摘录可能被误解。并且有时要包括从 FDA 那里征求好的建议，而不是只提到摘录。

FDA 483 Inspectional Observations, EIRs & Warning Letters - Preview keywords and excerpts

Type	Content&deviations
	Keywords, selected examples (not complete).
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FDA 检查报告，EIRS 和警告文字-预览关键词和摘录。

类型　　内容和目录

关键词，选择事例（不用完整）

尽力画出“D”来观察、印刷和/或下载所有文件的全部内容 。

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483 85 items

Keywords: Water systems, diagrams, process validation, cleaning validation, batch record review, training, instrument calibration, reserve samples, testing, product specification, distribution records, analytical method, USP standard, failure investigation, labeling, SOPs

- 483 关键词：水系统，图表，过程确认，清洁确认，一批记录：有回顾，培训，仪表校正，储备样本，检测，制品技术规格，分析方法，USP 标准，故障调查，标签，SOPS。

W-156

- **Primary deviations:** missing diagrams, no installation qualification, no operation qualification, no batch record review, inadequate GMP training, inadequate equipment calibration, inadequate storage of reserve samples, SOPs not approved, inadequate procedures for sampling and testing
- **Examples:**
  -There was no diagram of the water system

- Batch records not reviewed by QC,
- Routine calibration not performed according to a written program
- Conductivity meters not calibrated to an NIST traceable device
- Batch records lack a description of name of the equipment
- No reference in analytical method to recognized standard method.
- Current SOPs not reviewed and approved by QCU

W—156 。**主要错误：**缺少图表，无安装资格，无操作资格，无回顾记录，GMP 培训不充分，设备刻度不清楚，储备事例不充分，SOP 没被证明，取样和检测程序不充分。

事例：

-水系统没有图表

-大批记录没有被质控回顾

-常规表格没有根据书面程序执行

-电导计没有根据 NIST 可追踪装置校准

-大批记录缺少设备描述名字

-没有根据分析方法涉及可识别的标准方法

-当前 SOPS 没有被 QCU 回顾和验证

483 **Keywords: Electronic records, electronic signatures, Part 11, Equipment calibration, equipment qualification, certificate of analysis, review of records** D

关键词：电子记录，电子信号，设备刻度，分析证书，回顾记录。

W-155

- **Primary deviations:** missing Certificate of Analysis, inadequate equipment calibration, failure to review production and control records by QA, no recalibration after equipment move.

W-155 。**主要错误** ：缺少分析证书，设备刻度不适当，缺少质保的产品回顾和控制记录。当设备移动后没有校准。

- **Examples:**
  - Failure to establish laboratory controls which include 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 remedial action in the event the accuracy and/or precision limits are not met [21 CFR 211.160(b)(4)].
  - Specifically, your firm does not have a Certificate of Analysis (COA) for ...
  - The procedure is unclear and is inconsistent with the manufacturer's recommendation which advises to calibrate the **[redacted]** Oxygen Analyzer each time the analyzer is moved.
  - Failure to routinely calibrate, inspect, or check automatic, mechanical, or electronic equipment according to a written program designed to assure proper performance [21 CFR 211.68(a)]. Specifically, your firm has not performed any equipment qualification on the "mobile" cryogenic pumping system.
- **事例：**
- -缺少建立实验控制，包括器械刻度、规格、记录装置在适当的距离，根据建立的书面表格：有特殊方向、时间表、限制的精确度、当重大事件发生时的矫正措施和/或精确度，所有这些都要满足。[21CFR211。160（b）（4）]
- -特殊性，你的公司没有分析证明书（COA）为了….
- -程序不清晰和没包括制造商推荐信，氧分析器的每次移动没有校准。
- -缺乏常规校准、检查、或自动核对、机械核对，或根据书面程序设计电子设备来确保正确的执行。[21CFR211.68（a）]
- 特殊性，你的公司还没有执行设备资格在可移动的低抽吸泵系统中。

Warning Letter **Keywords: Equipment calibration, equipment qualification, certificate of analysis, review of records** D

警告关键词：设备刻度，设备规格，分析证书，记录回顾

W-154

- **Primary deviations:** missing Certificate of Analysis, inadequate equipment calibration, failure to review production and control records by QA, no recalibration after equipment move.
- **主要错误：** 缺少分析证书，设备刻度缺少，缺少质保的回顾生产记录和控制记录，设备移动后没有校准。
-

- Failure to establish laboratory controls which include 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 remedial action in the event the accuracy and/or precision limits are not met [21 CFR 211.160(b)(4)].
- Specifically, your firm does not have a Certificate of Analysis (COA) for ...
- The procedure is unclear and is inconsistent with the manufacturer's recommendation which advises to calibrate the **[redacted]** Oxygen Analyzer each time the analyzer is moved.
- Failure to routinely calibrate, inspect, or check automatic, mechanical, or electronic equipment according to a written program designed to assure proper performance [21 CFR 211.68(a)]. Specifically, your firm has not performed any equipment qualification on the "mobile" cryogenic pumping system.

- **事例：**

- **事例：**
- -缺少建立实验控制，包括器械刻度、规格、记录装置在适当的距离，根据建立的书面表格：有特殊方向、时间表、限制的精确度、当重大事件发生时的矫正措施和/或精确度，所有这些都要满足。[21CFR211。160（b）（4）]
- -特殊性，你的公司没有分析证明书（COA）为了….
- -程序不清晰和没包括制造商推荐信，氧分析器的每次移动没有校准。
- -缺乏常规校准、检查、或自动核对、机械核对，或根据书面程序设计电子设备来确保正确的执行。[21CFR211.68（a）]

- 特殊性，你的公司还没有执行设备资格在可移动的低抽吸泵系统中。-

Warning Letter
警告信

Keywords: capa, process validation, change control, quality systems

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- 关键词：过程确认，变更控制，质量系统

W-153

Primary deviations: inadequate corrective and preventive actions, inadequate process validation, inadequate change control procedure

主要错误：缺少足够的矫正和预防措施、过程确认、变更控制程序。

- **Examples:**
  -Failure to establish and maintain an adequate corrective and

preventive action procedure which ensures identification of actions needed to correct and prevent the recurrence of nonconforming product and other quality problems, as required by 21 CFR 820.100(a)(3).

- Failure to validate changes to your manufacturing process with a high degree of assurance to ensure that specified requirements are met as required by 21 CFR 820.75(c).

- Validation did not include verification assurance that the changes did not affect the device

-Failure to identify the acceptance status of product throughout manufacturing, packaging, labeling, and servicing of the product to ensure that only product which has passed the required acceptance activities is distributed or used.

- **事例：**
- -缺少建立和维持足够的矫正和预防程序，这能保证统一行为所需纠正 和预防非一致性的产品和其他质量问题再次发生，正如 21 CFR 820.100(a)(3).所需的。
- -对于你的产品生产过程缺乏有效的变更保证来保证特殊需求，正如 21 CFR 820.75(c).所需。
- -确认没有包括确认保证，这些改变是否会影响装置。
- -缺乏贯穿于生产、包装、标签、和产品服务的统一可接受的标准，来确保只有产品通过所需要的可接受的行为才被分发和应用。

Warning Letter
警告信

Keywords: root cause, capa, compliant handling, management responsibility
关键词：根本原因，CAPA，抱怨处理，操作责任。

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W-152

- **Primary deviations:** no root cause analysis, insufficient complaint handling
- **主要错误：**没有分析根本原因，不足的抱怨的处理。
- **Examples:**

- You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action of your quality system. Failure to promptly correct these deviations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. Additionally, no premarket submissions for Class III devices to which QSR deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

- - You have failed to establish complaint handling procedures sufficient to ensure that all complaints are documented and processed in a uniform and timely manner, as required by 21 CFR 820.198(a).
  - Management with executive responsibility has failed to ensure that an adequate and effective quality system has been fully implemented and maintained at all levels, as required by 21 CFR 820.20
  - You have also failed to establish a policy of overall intentions and direction of your firm with respect to quality
- **事例：**
- -你有责任调查和决定这些违反 FDA 的一致性原因。对于你的质量系统你也必须迅速的发起持久的纠正和预防行动。缺乏迅速的纠正这些错误可能导致调整的行为开始没有被 FDA 进一步发现。这些行为包括，但不限于，没收、命令，和/或全民的处罚。[，**另外, premarket 提议为 QSR 缺乏是合理地相关的类 III 设备不会被清除直到侵害被改正了**]同样，没有要求证明对外国政府批准直到侵害与附属的设备被改正了
- -你已缺乏建立足够的抱怨操作程序来确保所有的抱怨是有一致和及时操作的文件证明和处理，正如 21 CFR 820.198(a).所需。
- -缺乏以行政责任处理来确保足够的和有效的质量系统，而这个系统需要贯彻和保持在所有水平，正如 21 CFR 820.20 所需。
- -你也缺少建立关于公司质量的全面的意图和指导的政策。

Warning Letter
警告信

Keywords: stability testing, failure investigation, batch reprocessing, missing records
关键词：稳定性实验，故障调查，批物料的回收，丢失的记录

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W-151

- **Primary deviations:** No adequate stability test program, missing failure investigation, missing procedure for the reprocessing of batches, missing records regarding unexplained discrepancies
- **主要错误：**没有足够的稳定性实验，故障调查，批物料回收丢失的手续，关于无法解释的差异缺失手续。
- **Examples:**
  - You have failed to establish an adequate stability testing program to determine appropriate expiration dates for all your drug products (21 CFR 211.166(a) and (b)
  - You have failed to investigate failures of a batch or any of its components to meet their specifications (21 CFR 211.192).
  - You do not maintain any written records regarding unexplained discrepancies and batch failures as required by 21 CFR 211.192
  - Batches are routinely reprocessed when initial release specifications fail.
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- -
  - None of the stability failures, described above, were the subject of an investigation as required by 21 CFR 211.192
  - You have not established written procedures for the reprocessing of batches to ensure that they will conform to all established specifications (21 CFR 211.115).
- **事例：**
- -对于药物生产缺乏建立足够的稳定性实验来解释生产中的数据。（21 CFR 211.166(a) and (b)
- 一批物料或其中的一部分缺乏失误调查来满足他们的特殊性。(21 CFR 211.192).
- -关于无法解释的差异和和批物料没有记录下来，正如 21 CFR 211.192 所提。
- -当开始发布的说明错误时没有例行公事的修改
- -没有稳定性的错误，就向上文所描述的，也是一种客观的调查，正如 21 CFR 211.192 所提
- -对于所有回收的物料没有建立书面程序来符合所有建立的说明。(21 CFR 211.115).

Warning Letter **Keywords: CAPA, complaints, audits, document control, quality system, training**

警告信 关键词：CAPA ，抱怨，文件控制，质量系统，培训

W-150

- **Primary deviations:** No or inadequate CAPA system, inadequate complaint handling procedures, no quality audits, inadequate organizational structure, inadequate document control, failure to review effectiveness of quality system by management with executive responsibility, insufficient personnel with necessary education.
- **主要错误：**没有或缺乏足够的 CAPA 系统、不适当的抱怨处理系统，没有质量审核，缺乏足够的组织结构，缺乏足够的文件控制，没有通过行政责任来回顾有效的质量系统，个人缺乏足够的必需教育。
- **Examples:**
  Significant deviations include, but are not limited to, the following
  - Analyzing processes, work operations, complaints, returned product and other sources of quality data to identify existing and potential causes of nonconforming product
  - Investigating the cause of nonconformities relating to product, processes, and the quality system
  - Identifying the actions needed to correct and prevent recurrence of nonconforming product and other quality problems
  - Verifying or validating the CAPA to ensure that such action is effective and does not adversely affect the finished device

- **事例：**
- 有意义的错误包括，但不是仅限于以下方面：
- -分析方法，工作业务，抱怨，返回产品和其他来源，有通过质量数据识别不合格的产品存在的和潜在的错误。
- -调查相关产品、程序、和其他质量系统不一致的原因。
- -检验和确认 CAPA 来确保这样的做法是有效的而不是由于已完成的装置产生相反的作用。

Warning Letter
警告信

W-149

Keywords: API, testing, impurity testing, supplier testing, certificate of analysis, solvent recovery, labeling system
关键词：API，测试，混合物测试，厂商测试，证书分析，溶解性恢复，标签系统。

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- **Primary deviations:** Insufficient testing of individual batches, supplier testing not verified, no procedures for solvent recovery, inadequate proof of incoming labels.
- **主要错误：**个别产品没有足够测试，供应商测试没有校验，没有程序恢溶解性，引入的标签没有足够的证据。
-
- **Examples:**
  - The laboratory did not have an adequate impurity profile that identifies organic, inorganic and solvent impurities to monitor unidentified and apparent impurities in the API
  - The microbiological laboratory fails to document the lot number and expiry date of xx
  - The reliability of the supplier's certificate of analysis (COA) was not established in that a complete analysis was not performed with the COA at the appropriate intervals.
  - Procedures for solvent recovery have not been established to ensure that solvents are controlled and monitored
  - Incoming labels received from the vendor are not proofed against the master label
- **事例：**
- -实验室没有杂质分布图分辨有机物，无机物，溶解混合物来监控未经确认的和外观杂质。
- -分析提供者证书的的可靠性不是建立在已完成的分析基础上，在适当的时间间隔是否符合 COA。
- -溶解能力的恢复程序还没有建立来确保溶剂可控制和监控。
- 收到的引入标签没很好的控制。

Warning Letter **警告信**

Keywords: API, testing, raw data, failure investigations, equipment design, English language, equipment maintenance

关键词：API，测试，原始数据，失误调查，设备设计，英语，设备维护

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W-148

- **Primary deviations:** Insufficient testing of individual batches, insufficient recording of raw data, inadequate failure investigation, inadequate equipment design, inadequate equipment maintenance
- **主要错误：**单独一批货物没有足够测试，原始数据记录不足，错误调查不足，设备设计不足，设备维护不足
- **Examples:**
  - The individual batches are not tested for residual solvents
  - Laboratory records do not include all raw data. For example, weights determined during the preparation of standard solutions were not recorded
  - Critical production deviations may not have been investigated and documented.
  - Production equipment was not designed to minimize contamination
  - Equipment was not maintained in an adequate state of repair.
  - If you whish to to continue to ship APIs to the United states, you should evaluate all equipment and written procedures and your employees adherence to written procedures, for compliance with this standards.
  - Failure to promptly correct these deficiencies may result in the refusal to permit entry of these APIs or finished products made from these APIs into the United States.
  - Please submit documentation, with English translation, of these corrections.
- **举例：**
- -单独一批货物没有经残留溶剂检验。
- -实验记录没有包括所有所有原始数据。例如，重量设计在解决标准准备时没有记录。
- -重要生产装置没有调查和备有证明文件。
- -设备在完好维修状态下没有很好的维护。
- -如果你希望继续装运 APIS 到美国，为了适应许多标准，你必须估计所有设备和书面手续和雇员坚持书面手续。
- 如果没有迅速的改正这些不足可能会导致拒绝接受这些 APIS 或产品完成，这会使这些 APIS 进入美国。
- -请提交改正的英语文件，
- -

Warning Letter **警告信**

Keywords: audits, CAPA, risk assessment, complaint handling, validation, test equipment, training

关键词：审核，CAPA，风险评估，抱怨处理，设备测试，培训

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W-147

- **Primary deviations:** no audits of records, inadequate validation of workstation test equipment, inadequate compliant handling, inadequate procedures for CAPA, inadequate risk assessment.
- **主要错误：**没有审核记录，没有充分确认工作站测试设备，没有完全处理好抱怨，对于 CAPA 没有充足的手续，没有充分的风险评估
- **Examples:**
  - There is no indication that your firm conducted periodic checks or audits of the records during this time to assure the validity of the data.
  - Failure to establish and maintain procedures for implementing corrective and preventive actions (CAPA) to include requirements for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a)(1)
  - For example, your firm performed risk assessments for product failures without documenting how the severity or likelihood of occurrence used in the assessment was determined, in violation of your own procedures.
  - For example, the validation of the workstation test equipment used as part of the final device testing system; did not include a process capability challenge, did not ensure that the test equipment used was capable of functioning as necessary to capture results at both the high and low ends of the test specifications, and did not include challenges with known failures to ensure the equipment detected fault conditions
- **事例：**
- -没有迹象表明你的公司进行定期检查或审计这些记录，来确保数据的有效性。
- -缺乏建立和保持程序，这需要改正和预防措施的工具，这包括维修的分析程序，工作操作，让步，返修品，或其他的质量数据资源，以此来鉴别现在和潜在的不合格产品存在的原因，或其他质量问题，正如. 21 CFR 820.100(a)(1)
  -例如，确认工作站测试设备作为最后测试系统的一部分；不包括性能测试，不能保证过去的测试设备有能力发挥作用，来获得所有高水平和低水平测试规格的结果，不包括熟知的错误，来确保设备察觉错误情况。

Warning Letter 警告信

Keywords: risk analysis, design validation, change control, software testing, acceptance criteria, quality control, installation qualification, inspection, supplier assessment

关键词：风险评估，设计确认，变更控制，软件测试，接受标准，质量控制，安装控制，检查，厂商评估

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W-146

- **Primary deviations:** no procedures for validating the device design, no formal risk analysis for software changes, no procedures for finished device acceptance, inadequate installation, inadequate inspection, no procedures for supplier assessment.
- **主要错误：**没有装置设计的确认手续，对于软件变更没有正式的风险评估，没有完成的可接受装置的程序，没有充分的检查，供应商没有评估手续。
- **Examples:**

  - Failure to establish and maintain adequate procedures for validating the device design to ensure that the device conforms to user needs and intended uses and include risk analysis, as required by 21 CFR 820.30(g) (FDA 483, Item 151.
- **事例：**
- -

  - For example, a formal risk analysis of the original system design and software changes to correct software bugs that caused incorrect functionality or performance problems, and to enhance the product, has not been documented. Although your software release notes briefly describe the nature of unresolved software bugs in a particular software version, they do not explain the impact of these software bugs on user needs and intended uses. For example, in the workflow release notes, dated 6/24/04, software version 2.Otr17 described that "the scores for the left eye and right eye was reversed, and the macular edema value used previously was confusing."
- 例如：一个对原始系统设计的正式的风险分析没有证明文件，改变软件以修补那些会引起错误功能和行为的软件漏洞的行为也没有文件证明，以及改变软件以增强生产的行为也没有文件证明。虽然你的软件

  - Status of design changes was not documented to explain why certain design changes were not implemented to correct Software bugs
  - The "Workflow Release Notes by xxx has no status information or discussion of the test releases of software versions v2.xx36 through v2.xx40
  - Failure to establish and maintain procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices is not released for distribution until all the requirements are completed as required by 21 CFR 820.80(d) [FDA 483 item 3]. For example, your firm has not documented the signature(s) of approval

needed to release xxx for distribution
- Failure to establish and maintain procedures for adequate installation and inspection, as required by 21 CFR 820.170(a) and document the installation activities and inspection results, as required by 21 CFR 820.170(b) [FDA 483 Item 5]. For example, your firm's device installation procedure was in the draft form at the time of our inspection, and your firm has not maintained records of installation activities and inspection results of the retinal image acquisition subsystem of the 3DT system at the clinical sites.
- Failure to establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50 [FDA 483, Items 10, 11, 12, and 13). For example, your firm has not (a) evaluated the suppliers for their ability to meet your firm's requirements; (b) defined the quality requirements that each supplier must meet; (c) defined the frequency of supplier evaluations; and (d) documented supplier evaluations.

Warning Letter

Keywords: part11, electronic records, electronic medical record (EMR) system, computer validation, audit trail, accurate and complete copies, invalid and altered records

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W-145

- **Primary deviations:** missing documentation for validation and other part 11 requirements
- **Examples:**
  Our review of the inspection results also noted that you use an electronic medical record (EMR) system to maintain medical and other clinical data for your patients, including study subjects . You told Mr. xxx that data obtained during study visits are entered directly into the EMR, and no paper records are used. A follow-up letter from you to Mr. xxx, dated January 31, 2005, detailed the name of the EMR system and the means by which study subject information is entered Please note that Title 21, Code of Federal Regulations, Part 11, "Electronic Records; Electronic Signatures" outlines specific requirements that must be met for any system that is being used to maintain required records . In addition to the information requested above, please submit the following:
  - documentation of the validation of your EMR system to ensure accuracy, reliability, and the ability to detect invalid or altered records;
  - documentation of the ability to generate accurate and complete copies of records suitable for inspection, review, and copying by the agency;
  - documentation of a secure, computer-generated, time-stamped audit

trail that can independently record the date and time of operator entries and actions that create, modify, or delete electronic records, and to verify that record changes do not obscure previously recorded information.

Warning Letter W-144

Keywords: complaints, suppliers, contractors, software validation, change control

D

- **Primary deviations:** no or inadequate software validation, no quality requirements for suppliers, contractors and consultants, no supplier audits, inadequate change control
- **Examples:**
  - Failure to perform software validation, as required by xxx. Specifically, the xxx controller unit, software version xxx was changed to xxx. The change in the software allowed for adjustment in the speed of the water pump, and inverse pulsing from the A valve to the B valve when the speculum was clogged. Your firm did not have any documentation showing that the current software version was validated.
  - Failure to establish and maintain the requirements, including quality requirements, that must be met by suppliers, contractors, and consultants, as required by xxx. Specifically, your firm did not have any documentation showing audits of the contract manufacturer responsible for manufacturing the disposable xxx which is used with the xxx. Your firm also did not define the type and extent of control to be exercised over the product, suppliers, and contractors.
  - Failure of management with executive responsibility to ensure that an adequate and effective quality system has been fully implemented and maintained at all levels of the organization, as required by 21 CFR 820.20(a). Specifically, management with executive responsibility has failed to ensure that an adequate and effective quality system has been established. There was no management oversight for employees responsible for manufacturing, finished device release, distribution, and for maintaining quality system records.

483 **Keywords: System suitability testing, process validation, part 11, method validation, OOS, laboratory controls, impurities, QA procedures, training, vendor qualification, refractive index detector, electronic records, stability testing** D

W-143

- **Primary deviations:** no or inadequate failure investigation, inadequate process validation, inadequate method validation, inadequate instruction for testing, insufficient justification for impurity specifications, QA procedures not followed, insufficient training on cGMP and operations, failure to establish controls and procedures to establish authenticity, integrity and security of all electronic records, failure to qualify suppliers, IQ/OQ or equipment not performed or data not reviewed, no records for refractive index detector qualification, incomplete laboratory records, inadequate stability
- **Examples:**
  - Drug products failing to meet established specifications are not rejected
  - The xxx solution used in the xxx assay test did not meet USP suitability test specification during the analysis of Sample lot...
  - Control procedures are not established which validate the performance of those manufacturing process that may be responsible for causing variability in the characteristics of in-process material and the drug product.
  - Initial OOS results for accuracy and intermediate precision were retested with no laboratory investigation conducted; a revised analytical method was developed, the samples retested, and only the passing results reported.
  - The analytical method report was not signed off as approved until it had been used to test released batches
  - Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.
  - The firm has failed to establish controls and procedures to assure authenticity, integrity and security of all electronic records including data generated in the QC laboratory.
  - All laboratory analysts and supervisors have system administration privileges in the firm's HPLC and GC acquisition systems which allow them overwrite original raw data files.
  - Refractive Index Detector used for component testing , sugars, there is no record that the equipment has been qualified

Warning Letter **Keywords: SOPs, complaints, annual product reviews, failure investigations, laboratory controls** D

W-142

- **Primary deviations:** missing SOP to handle drug quality complaints, missing labels, not following written procedures, inadequate corrective actions regarding failure investigations, failure to follow laboratory procedures
- **Examples:**
  - Your QCU also failed to extend the investigation into other similar lots
  - Laboratory failed to properly label sample preparations in your laboratory refrigerator and workbench areas
  - Failure to follow written procedures for Annual Product Reviews
  - Failure to follow established Standard Operating Procedures regarding the handling of written and oral drug product quality complaints
  - Failure to follow established laboratory control procedures

Warning Letter **Keywords: bioequivalence study, contamination, procedures, policy, failure investigation** D

W-141

- **Primary deviations:** equivalency of analytical method not demonstrated, inadequate approach to investigating sources of contamination, lack of procedures and policies
- **Examples:**
  - You failed to demonstrate that the analytical method used in this in vivo bioavailability study was accurate to measure the accurate concentration of loratadine and its metabolite
  - Your approach to investigating sources of contamination in bioequivalence studies is inadequate and has resulted in the submission of invalid data to the agency. You should have conducted a systematic and thorough evaluation to identify and correct the source of contamination when it was first observed.
  - The manner in which (company name) investigated the contamination problem in this study causes FDA to have concerns with the validity of other bioequivalence data generated by (company name).

Warning Letter W-140

Keywords: number of people, stability testing, laboratory records, data integrity, equipment maintenance

D

- **Primary deviations:** no adequate number of trained people, laboratory records missing, inadequate change of raw data, no adequate equipment maintenance
- **Examples:**
  -Written control procedures not always followed when changes were made to test methods and validated system
  - No positive control has been used while conducting the USP test since December 2002
  -The inappropriate change to test method was made without Quality Control unit review. as a result, batches of product were released for export to the US based on invalid USP test results
  - Written procedures for investigating deviations were not followed on at least six occasions in 2004, when recording charts showed malfunctions
  - no adequate number of trained people to carry out the responsibilities of your quality assurance department, ... only one person conducted the dual functions of quality control and quality assurance.
  - Maintenance performed on the xxx in September and October 2003 was not correctly recorded

Warning Letter W-139

Keywords: quality control unit, training, stability testing, water purification, batch production and control records, batch record review

D

- **Primary deviations:** QC unit did not follow written responsibilities, employees not trained on CGMP, no microbial analyses/or preserve analysis on finished drug products, water qualification, no batch record review
- **Examples:**
  - SOPS have not been approved by the quality control unit, and the review of any complaints involving the possible failure of a drug product to meet any of its specifications has not been performed per SOP.
  - According to the Executive Director of the firm, the employees have never received any type of CGMP training
  - Your firm failed to conduct microbial analysis and/or preservative assays on finished drug products as a criteria for release.
  - The firm does not have a sampling and test procedures designed to assure that the water from the purification system conforms to appropriate standards
  - Failure to have all drug product production and control records

reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed.

Warning Letter

Keywords: computer validation, data integrity, acceptance levels, method validation, process validation, revalidation, OOS

关键词：计算机检验，数据完整，容纳水平，方法检验，过程检验，再检验，无库存

D

W-138

- **Primary deviations:** No acceptance and/or rejection levels for theoretical and actual batch yields, no test method validation, lab computer software not validated, no process revalidation, no OOS investigation
- **主要错误：**没有理论上和实际上的批产量接受或、及拒绝的标准，实验室的计算机软件无效，没有再检验过程，没有无库存调查
- **Examples: 例如**

  -The process validation for the product Syncro-Mate-B Implants is inadequate in that your firm's 1994 retrospective validation report evaluated batches that were manufactured and tested at a different manufacturing facility. Your firm failed to perform any new process validation or revalidate the manufacturing process, at your current site. Additionally, your firm failed to validate the testing methods used to analyze the batches in your retrospective validation report and the equipment used to manufacture and test the validation batches was never qualified.
- 生产 Syncro-Mate-B Implants 的再检验过程不恰当，您的公司的 1994 回顾检验报告评估不同的生产设备生产及测试的批次。您的公司没有执行人任何新的过程检验或生产过程检验，在您的目前的位置上，加之，您的公司没有检验用于分析在您的回顾检验报告中的批次的测试方法以及用于生产和测试批次的检验设备不够资格。

  - The firm's computer software programs which operate all of the lab during the analysis of raw materials and xxx finished product, have not been qualified and/or validated. The software programs do not secure files from accidental alteration or losses of data. The functions that modify and delete partial or whole data files are available for use by all analysts. In addition, the firm has not established any security

procedures for the laboratory computer systems. There are no procedures for backing-up data files and no levels of security access established.

- 在原材料分析和某某总产品分析期间，公司运行在所有实验室的计算机软件程序不够资格或未被检验，软件程序无法保证数据以外修改和丢失后的安全性。所有的分析家都可使用部分或全体数据文件的修改和删除功能。另外，公司没有任何的实验室计算机系统的安全程序，没有回投数据文件的程序以及已定的安全标准。

Warning **关键词：安全性，计算机验证，QA 规程，设备清洗，HVAC,无菌罐** D

- **主要偏差：**QA 单元不符合规程，自动化设备没有进行验证，对审核人员没有限制，对设备的清洗与维护没有规程可循

W-109

- **例子**

-QA 部门没有很好的遵循书面规程，应该对工作中的疏忽与审核负责

- 没有保证自动化设备能满足制药所需的运行标准[21 CFR 211.68].

例如：

- 过程控制所用的计算机没有进行确认
- 设备没有进行确认（HVAC,无菌罐，纯化水系统）
- 没有限制一些非授权人员进入限制区

Warning **关键词：质量体系，管理，纠偏，预防** D

- **主要偏差：**没有管理规程，没有纠偏与预防措施，没有质量体系
- **例子：**

W-108

- 没有建立对质量体系的稳定性与有效性的审核负责的管理体系
- 没有建立与保存关于纠偏与维护措施的规程
- 没有建立与保存有关质量体系的规程

Warning 关键词：电子数据表的验证，数据积分，中间介质与电子文档的长期保存，电子文档的消除，清洗的验证，方法验证，过程验证，OOS，事故调查，培训 107 106

W-107 105

现在应采用充分的检查报告(EIRs),

W-106 063

完整的过程是从 483 (W-105)开始，遵循初检的充分检查报告（W－106），警告信(W-063)，以及后续检查的 EIR (W107)。**后续检查报告是对为了使其达到 FDA 要求而进行的纠偏过程的详细描述。**

W-105

EIRs：详细描述了怎样检查，应该检查什么，应该问些什么问题以及公司应该为什么负责。应该对 EIRs 进行审核，例如：由总办公室负责决定是否发送警告信。一般有 483，EIR，以及来自此部门的警告信。通读这些信息有利于很好的准备检查。有利于公司了解检查中的提问类型以很好的回答那些问题，这样不仅可以避免收到 FDA 的警告信，还可以减少自己重做的概率。

Warning 关键词：胃肠外给药的无菌制剂的生产操作，part 11,追踪审查，完整的纠偏计划，环境验证 D

W-104

- **主要偏差：**缺少电子追踪审查，对第 11 部分没有计划，对无菌填充器没有作环境验证
- **例子：**
  - 此外，较高要求是将有关步骤记录到电子版 cGMP 记录中（应满足 21 CFR Part 11 的要求，电子记录，电子标志。Part 11 的建立应满足电子记录的要求，且电子标志应可靠，并与常用的书面标志和传统的手写标志相统一。电子记录与电子标志用于会议记录和 Part 11 要求的 21CFR 的 210，211 部分标志。
  - .在给缺陷通知的回复中应出具公司的全面纠偏计划，包括纠偏周期，记录到 Part 11 中
  - 检查应对实验室电子控制体系中的不足进行公开，这个体系主要是对色谱仪的维护和追踪审核。
  - 没有根据验证计划收集足够的样品来评估特定的材料
  - 没有对 XXX 无菌填充器进行环境验证
  - 对使用方法与容器的清洗没有详细的描述

Warning 关键词： 人员培训与资格，计算机系统，安装记录，验证 D

W-103

- **主要偏差：**缺乏或没有对员工关于计算机系统的培训，计算机系统的安装记录不完整，计算机系统的验证不完整
- **例子：**
  - 对员工关于用于原料筛选和生产过程的新的计算机系统的使用培训不够完整
  - 中心主管人员没有进行过任何培训，尽管他保留了输入到计算机系统中的安全性很高的数据记录
  - 计算机系统的验证与安装记录不完整。系统的安装参照 11/1

7/2000，但验证研究直至 4/1 9/2001 才会被正式批准。测试范围有以下方面：

Warning **关键词：API，OOS,文件，过程验证，方法验证，过程参数的纠偏变更控制** D

W-102

- **主要偏差：**OOS 没有文件记录，生产过程没有验证，分析方法没有作稳定性检查，对分析方法没有进行变更控制，关键的过程参数没有进行确认
- **例子**
  -没有文件记录对纠偏过程和实验结果 OOS 的调查
  -在检查过程中，我们的调查应参照纠偏过程的调查与实验室结果 OOS 的调查。这些只能作为指导，但不能作为文件
  -方案没有对关键步骤、关键的过程参数、在线测试和说明进行确定

483 **关键词：网络，WAN,LAN，变更控制的验证，图表，IT 人员的培训，修订控制，变更控制** D

W-101

- **主要偏差：**对网络系统的安装与升级的验证失败，对 IS 人员关于 GMP 的培训失败
- **例子**
  - 该程序没有通过修订号进行控制
  - 整个软件结构设计没有维护内容的描述和关于最初设计说明的校正
  - 完整的表格和文字描述应能用 XXX 确定所有其他的网络程序的界面，详细说明 XXX 和其他哪些没有被维护或没有对原始设计说明进行校正的数据可以进行改变
  - 广域网（WAN）表格应附有适当的说明文件使用 XXX 来识别网络上的公共网站，在任何的 XXX 验证文件中都没有对他进行描述
  - 这些表格没有表明日期，没有文件控制号，没有审核与批准指示
  - 公司对 9.8 版本的配置的修订控制体系没有达到一体化
  - 没有文件记录信息技术（IT）人员接受过包括 cGMP 规程与该规程涉及的一些书面文件的培训

Warning 关键词：设备条件，临界试验，CAPA，人员培训，统计分析，第 11 部分 D

W-100

- **主要偏差：**没有将不一致性进行适当的追究调查，设备没有对所有的参数进行测试，没有临界试验，对不一致性的潜在原因没有进行评价，对人员的培训不够充分，统计分析
- **例子**

-没有记录证明操作参数（最大值，最小值，对照参数）核对无误，没有文件证明采样与样品的检测符合验证方案

-公司没有分析、确定和文件描述产品不一致性的潜在原因何其他质量问题，如…要求

-对产品和质量的统计和非统计分析没有制定程序可以遵循

-公司没有对足够的人员进行充分的培训以确保所有活动能按照…要求进行正确的执行

Warning 关键词：网络系统，环境监测，记录维护，结构和功能设计，代码审核，绝对代码，代码注释，第 11 部分 D

W-099

- **主要偏差：**对计算机系统没有进行足够的回顾性验证，软件版本控制不恰当，代码审核不完善，没有结构和功能设计，环境监测不够完善，维护记录不完善，对代码没有注释，代码包括绝对代码和不使用的代码
- **例子**

- 对计算机系统没有进行足够的回顾性验证，这些系统涉及到质量保证／质量控制，原材料的控制与发放，中间材料与成品，例如：
- 对程序的验证中没有包括结构和功能设计
- 每个程序只有一小部分进行了详细的审核
- 软件修订控制不完善

Warning 关键词：过程验证，OOS，微生物试验，API，方法验证，稳定性测试，记录维护 D

W-098

- **主要偏差：**对生产过程没有进行验证，没有建立和保存关于不能解释的矛盾的调查的书面记录，没有成功制定 API 的发放标准，没有成功的对操作和测试方法的稳定性进行验证，没有很好的对校正检查和自动化设备的检查的相关记录进行很好的维护
- **例子：**

- 例如：对药品生产过程与药品生产相关设备没有进行验证
- 对产品的微生物测试没有文件记录可查，使其不具备回顾性，也就没有结果和依据可循
- 对校正检查和自动设备，机械或电子设备的检查的记录的维护失败

Warning 关键词：API，稳定性测试，原始数据，HPLC，线性检测仪，管式加热器的温度精度，线性积分仪 D

W-097

- **主要偏差**：稳定性测试不能追朔到在生产地点进行的批生产过程，缺少原始数据，没有对线性检测仪进行测试，没有对管式加热器和检测仪所设置的温度的精度进行检测，没有对 GC 和 GC 顶部单元进行恰当的校正，没有第二个分析者或监督者对原始数据和从经质量合格的分析仪器所获的结果的验证进行精确性与完整性的检查。
- **例子**：
  - 对…样品的稳定性进行测试但不能向 DMF97－001 提供稳定性数据来回顾批生产过程

-对原料药与成品药没有区分，没能很好的遵循 cGMP，没有符合 Act 的要求
- 在设备检查过程中不能提供稳定批的现有记录的原始数据
- 对 HOLC 的校正不恰当，没有对线性检测仪与积分仪、注射器的选择、管式加热器与检测仪进行校正
- 如果直至 FDA 进行第二次检查时还没有根据 cGMPs 对这些缺陷进行相应改进，将被扣留新药应用清单和原料药(APIs)制造等设施的批准书。如果不能迅速的解决这些问题将失去这些产品进入美国市场的机会

Warning 关键词：API,清洗验证，微生物规程，HOLC，方法验证，稳定性试验，输入警告 D

W-096

- **主要偏差**：API 的生产不符合 cGMP 的要求，没能很好的建立微生物规程，HPLC 的分析方法没有进行，对取样的时间间隔的稳定行测试失败
- **例子**：
  - 这封信是关于 FDA 对在…原料药生产设施的检查的。在我们的检查中我们发现你们对原料药(API)的生产与 cGMP 的要求有较大的偏离。
  - 对用于原料药 APIs 和中间产物生产所用的非反应容器、盛装容器、重结晶器、离心分离器和干燥器的清洗过程没有进行验证

Warning 关键词：无菌生产，无菌过程，消毒设备，微生物污染，输入警告 D

W-095

- **主要偏差**：关键设备没有进行重新灭菌，对消毒设备表面的限制不恰当，监测时间间隔过长
- **例子**：
  - 对无菌粉末的填充过程在一些关键问题上没有作恰当的处理，如：工作时间长短，关键设备长时间没有进行再次灭菌。
  - 对消毒设备表面的限制不恰当使其对无菌生产的环境没有保证
  - 如果你希望自己的产品能进入美国市场，你必须保证能遵循美国的 cGMPs 标准

- 将扣留无菌产品的生产商的任何新的申请

483 关键词：销售资格，实验室条例，退回的产品，成品的储存，变更控制 D

W-094

- **主要偏差：** 对销售资格和实验室条例没有制定 SOP，销售资格没有文件记录，没有对实验室条例进行审核，对退回的产品没有进行确认，对文件和生产过程的 SOP 没有进行变更控制
- **例子：**
  - 对销售资格和实验室条例没有制定 SOP，也没有文件对其进行管理
  - 对纯化水的测试没有根据实验室条例进行审核

Warning 关键词：GCP,会议记录，研究审核 D

W-093

- **主要偏差：**对研究过程没有从头到尾进行审核，没有报告研究过程中的一些变化，没有对 FDA 所没有预料到的一些问题进行报告，没有保存会议记录
- **例子：**
  - 没有及时向 IRB、其他有关部门、FDA 报告一些他们所没有预料到的对人类存在威胁或与相关规则与要求不符的问题
  - 如果在会议的参会人员中有一个非科学领域的成员，IRB 会拒绝对所提交的研究进行审核

Warning 关键词：管理职责，管理审核，CAPA,验证 D

W-092

- **主要偏差：**没有明确管理职责，没有管理审核程序，没有对改正与预防措施制定程序
- **例子：**
  - 没能指出或证明指定的管理人员（不对其他责任负责）的明确职责和其确保质量体系进行有效维修并报告对质量体系的管理职责
  -没能很好的建立和执行管理审核程序
  -对出现不一致性的产品的现有原因和潜在原因的原始数据的分析的预防和改正措施的执行的程序的建立失败。
  -对检查、测量和检测设备是否能达到特定的目的和达到所需的生产

结果的证明失败

Warning 关键词：API，原始数据，数据的维护，培训 D

W-091

- **主要偏差：**APIs 没有按照 cGMP 的要求进行生产，没有原始数据，对数据的维护没有 SOP 文件，没有对 GMP 进行培训
- **例子：**

-这封信是关于…的设施的检查的。在我们的检查中我们发现你们对原料药(API)的生产与 cGMP 的要求有较大的偏离。

- 对人员的培训不够，没有涉及对 cGMP 的培训

Warning 关键词：原始数据，API，方法验证，缺陷对其他过程的影响，地方 SOPs，微生物污染，微生物检测 D

W-090

- **主要偏差：**没有记录原始数据，杂质标准没有进行恰当的确定，内部标准已经有四个月没有数据对其在此期间的稳定行进行保证，没有很好的执行在线检测，对缺陷对其他过程的影响没有进行评估，方法验证不恰当，只有中文版的验证方案和最终验证报告。
- **例子：**

-在实验过程中没有恰当记录原始记录

-回复中没有证明对其他实验过程中的类似缺陷进行审核，并已经执行新的 SOPs

-对化验与杂质的实验室检测没有根据单独的药品主控文件(DMF)（USP 指定的方法）中的相关描述进行

-直到设施符合 cGMP，公司仍会被拒绝作为 API 的供应商，或对 API 进行进口警告或拒绝进入美国市场。

483 **关键词：生物分析检测实验室，校正标准，承诺标准，分析天平，冷冻器，冷藏库，吸液管，吸液管微机管理器** D

W-089

- **主要偏差：**SOP 允许删除校正标准，标准中没有包含准确数据，QC 部门没有达到承诺标准，承诺标准不够详细，分析证明书中的数据不恰当，分析天平的使用超过了其量程，数据终止不恰当，色谱仪的重现性只是在运行初期进行了检查，对冷冻器和冷藏库的温度没有进行监测，使用已经出现偏差的吸液管进行分析，对多探头型吸液管微机管理器的验证没有制定 SOP.
- **例子：**
  -SOP #F-00“分析执行承诺标准”的目的并不是允许删除校正标准以至于 QC 评价不能处在可接受的限度之中。
  -公司采用的分析参考标准不当，或在任何地方都使用此标准，尽管它符合分析标准，但在某些特定的分析中它可能达不到所要求的纯度或效力
  - 校验记录表明在一些场合所使用的吸液管出现了偏差。但没有方法证明这些吸液管在用以分析的什么时候出现了偏差。

Warning **关键词：GLP，主进度表，QAU** D

W-088

- **主要偏差：**由 QAU 制定的 GLP 文件没有进行审核，主进度表的复印件没有进行保存
- **例子：**
  -没有对所有非临床实验研究的主进度表的复印件进行保存
  -没有确保 QAU 对 GLP 研究的组织学准备过程进行监测

Warning **关键词：OOS，电子数据表，时间标记，HPLC 溶剂的再生，追踪审核，电子记录，原始数据的书面记录，第 11 部分** D

W-087

- **主要偏差：**对 HPLC 溶剂的再生没有进行测试，没有进行追踪审核，没有恰当的密码保护措施，删除电子记录
- **例子：**
  -由两个不同的人进行三次再测试，第三个分析者只是获得了数据并进行报告后，这批产品就被放行
  -不能证明 HPLC 溶剂进行再生后是否能达到报告中所提到的纯度，效力
  -没有对涉及数据计算的数字模板进行追踪审核
  -密码保护可通过系统旁路进行
  -数据档案在被拷贝后自动删除
  -没有要求对分析和对电子数据表的时间日期标记进行确认
  -改变方法将其作为工作标准使用，但不能证明它能等价于 USP 中的方法，例如：

Warning 关键词：活性成分，稳定性实验，设备的清洗，记录，校正数据 D

- **主要偏差：**测试不完整，稳定性测试不恰当，对校正数据没有进行记录，没有器具清洗规程

W-086

- **例子：**

-没能做到对每批药品进行实验室测试后的优先放行，以确定成品在活性成分的均一性与有效性等方面均能满足要求[21 CFR 211.165 (a)]。尤其，你不能…

-没能做到用可靠有效的方法对药品稳定性的书面测试计划进行执行[21 CFR 2 11.166 (a)(3)]。特别是…

-对实验室器具的定期检查的所有数据的没有进行验证，记录对 FTIR 分光镜和 HPLC 分析仪的使用有关，这些仪器用于对产品和人用药品的检测

- 没能做到对设备和器具进行恰当的定期清洗与维护

Warning 关键词：验证，再验证，临界实验，破坏性实验，原始数据，实验记录 D

- **主要偏差：**主要过程没有进行验证，验证前对每批的分配不完善，没有对 OOS 的原因进行调查，实验记录中没有原始数据

W-085

- **例子：**

-实验记录中没有包括实验测试过程中出现的所有原始数据

-药品的样品在整批中的分配不合理或不具代表性，如…

-没有对最大的一批或主要的复杂的生产工序进行再验证

Warning 关键词：软件的验证，电子记录表，CAPA,OOS,培训，自检，设计审核 D

- **主要偏差：**软件的验证不恰当，对设计在执行前的变更的审核不恰当，质量检查过程不恰当

W-084

- **例子：**

-没有作恰当的改正和维护措施（CAPA），例如分析数据以确定产生不均一产品和其他质量问题的现存原因和潜在原因

-软件的验证没有涉及到电子记录表的数据输入设备

-没能对程序进行恰当维护和对环境进行控制

483 关键词：GLP，毒理学，生物学研究监测，研究指导，测试，研究报告 D

- **主要偏差：**对测试项目的测试不恰当，没有完整的测试记录，研究报告不完整，没有及时更换研究主管

W-083

- **例子：**

-不能保证研究中的测试项目和给药方式#224 和 #323 对均一性、有效性和稳定性进行恰当的测试

-在测试初期与周期性测试中使用不同的方法，记录不完整或对方法不能进行验证，不能将它用于色谱分析的光谱中，以及环境和用于校正的有关原料的数量中

-不能证明更换后的研究主管对方案偏差和 QAU 关于研究的检查报告进行了评估。

Warning 关键词：自动化系统的验证，设备的检查与测试，偶然性事件计划书，偏差 (OOS) D

- **主要偏差：**对自动化系统的验证失败

W-082

- **例子：**

对连接生产和质量体系的自动化系统的验证失败

不能对所有检查和测试设备是否适用于此目的和是否能满足产品的追踪要求进行证明。检查发现所采用的自动化模拟实验没有根据硬件和软件 C2000 版的改变作相应的更新

Warning 关键词；质量保证部门，方法验证，实验室记录，分析设备的质量电子数据表，数据审核，色谱峰值的重叠，第 11 部分 D

- **主要偏差：**没有程序或程序不充分，有关培训的文件，工作表不完整，缺少设计与控制，第 11 部分

W-081

- **例子：**

- 对以上违规的补充，调查员发现实验室所使用的生产过程的电子版记录与原子吸收和 HPLC 的数据的保存缺少对其安全性与数据完整性的控制，这是因为没有对系统进行保密控制，没有系统备份预防措施，没有对系统的性能进行最终检查。发现系统的设计与控制与 21CFR,第 11 部分，电子记录的要求不符。

- 不能证明对实验室人员进行药品检测的特殊方法、设备的使用方法和有关…的 cGMP 等内容进行了培训。

Warning and 483

W-075 to W-080

关键词：质量单位不合格，过程验证，再验证，软件验证，安全性验证，验证方案，验证标准，设备的 IQ 与 OQ，方法验证，操作范围没有进行评价，清洗验证，HVAC 系统不合格，预防性维护，实验数据，计算机验证，资料变更后的验证,变更控制，测试的审核与批准，主验证计划不恰当，第 11 部分

D1 D2 D3 D4 D5 D6

FDA 明确表示将继续执行

在出现了很多 GMP 问题后 Schering-Plough 在 1998 年同意 FDA 的裁决并赔款 5000 万美元。这是对 FDA 所管制的公司的最大的一次评定。这份裁决涉及到 100 多条不同的规定而且包括了非处方药的内容，并且公司还同意了停止生产 73 种其他产品（验证时间，2002 年 5 月 21 日）。Schering 收到了 5 封警告信和 483 条款。你可以下载 5 封警告信（D2 至 D6）和 18 页 483 检查报告（D1）.这份 483 条款非常全面，可以作为检查清单来准备 FDA 检查。

Warning

警告信

W-074

Keywords: Process validation, revalidation, external auditor

关键词:检验过程,再检验,外聘审计员

- **Primary deviations:** quality system, no or insufficient process validation, no revalidation after changes 主要的错误:质量系统,没有检验过程和及检验过程不完善,没有更改后的再检验.

Example:例如

Your firm failed to demonstrate adequate documentation that justifies the decision for not revalidating the ...process after making these changes;

In order to facilitate FDA in making the determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance for class III devices for which a 5 1 O(k) premarket notification or Premarket Approval application (PMA) has been submitted, and Certificates to Foreign Governments for products manufactured at your Billerica and Burlington, MA facilities, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirement of the device Quality System regulations (21 CFR Part 820).

- 您的公司没有提供恰当的文件来证明做了改变却不进行此流程再检验的理由.为了有利于 FDA 作出决定,已经作了这种修订,以便于 FDA 可以收回给其他的联盟代理商关于政府契约奖励的咨询工作,**,还可以恢复 3 级设备的市场清除,此决议已经提交了一个 510(K)的预说明或预说**明批准申请(PMA),以及授权给外国政府可以使用柏林敦，Billerica，摩络哥的设施进行产品生产，我们要求你必须服从此机构的下述进度表，并有一个外部的专家顾问进行验证，此专家应指导过你公司符合设备质量

体系规则（21 CFR Part 820).的生产和质量检测体系。

Warning

警告信

W-073

Keywords: Validation, Spreadsheet, Excel, MS Access, Excel, Word, part11
关键词：检验，电子数据表，**Excel, MS Access, Excel, Word** 软件

- **Primary deviations:** no validation of Excel, Access, Word 主要的错误；缺少对 Excel, Access, Word 软件的检验
- **Example:** 例如
  Failure to validate computer software used as part of the quality system for its intended use according to an established protocol as required by 21 CFR 820.70(i). For example: Software such as Excel, Access, and Word used to create and maintain data bases (rejects, complaints, and concessions) and electronic documents, is not validated.
  In their response dated April 3, 2000, your firm stated that by May 31st, they will have identified what software is used for data processing, and identified a method or methods for validation and/or verification of the software. This response is not adequate since ...
- 没有检验作为质量体系的一部分的计算机软件是否满足 21 CFR 820.70(i)的协议制定的应用要求。例如：用于创建和维护数据库（或者拒绝，抱怨和妥协）的 Excel, Access, Word 软件以及电子文件都没被检验。在他们 2000 年 4 月 3 号做出的回复中，您的公司声称截至到 5 月 31 号，他们要确定哪个软件用于数据的处理，以及确定一种或几种软件的检验和查证方法。这种回复是不恰当的，因为

Warning

警告信

W-072

Keywords: Validation, Spreadsheet, MS Access, Excel, effect on other program, part11
关键词：检验，电子数据表, MS Access 和 Excel 软件，对其他程序的影响

- **Primary deviations:** insufficient validation of Access, no validation of impact on other software 主要的问题：对 Access 软件的检验不充分，没有检验对其他软件的影响

Example: 例如
You failed to investigate the failure of the ... when operating in MS

Access. The system locks up at random and it is unknown whether the software which controls the .... during off of MS Excel, could be similarly affected. 当运行 MS Access 软件时您没有调查某某的失败原因。此系统会胡乱锁住，以及当脱离 MS Excel 软件时，不明确控制``````的软件是否也会受到类似的影响。

Warning

Keywords: Spreadsheet, validation, change control, validation of corrective action, part11

关键词：电子数据表，检验，控制更改，修订行为的验证

警告信

W-071

- **Primary deviations:** no validation of spreadsheet, no validation of corrective action, no documentation of changes 主要错误：缺少对电子数据表的检验，缺少对修订行为的检验，没有修订文件
- **Examples:** 例如

  - Failure to validate computer software used as part of the quality system for its intended use according to an established protocol as required by 21 CFR 820.70(i). For example, the data in the Excel spreadsheet identified as a "Hit List" of top non-conforming components contains 16 record counts for part number 8601618 DC converter failures compared to 18 record counts for part number 860168 DC converter failures in the dbase database. The spreadsheet is used for management review of component suppliers for all components.
  - Failure to verify or validate corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example, ...
  - Failure to maintain records of changes to documents as required by 21 CFR 820.40(b). For example, ... 没有检验作为质量系统的一部分的计算机软件是否满足 21 CFR 820.70(i)的协议制定的要求。例如：**在 Excel 电子数据表中的数据被认为是头等的不一致部分的“暗杀清单”，包括使数据库中 16 记录的部分数字 8601618 DC 转换失败以及使 18 记录的 860168 DC 转换失败。这种电子数据表被用于对所有单元提供的组分的检测**。没有对修订行为和预防性行为的核实和检验以保证此行为有效以及此行为对精巧的设备无反作用，正如 21 CFR 820.100(a)(4)所述，例如：
    没有进行对文件更改记录的维护，正如 21 CFR 820.40(b)中所要求的，例如：

Warning

Keywords: Spreadsheet, validation, part11

关键词：电子数据库，检验

警告信

W-070

- **Primary deviations:** no validation of spreadsheets 主要错误：缺少对电子数据库的检验
- **Example:** 例如：

  Your response indicated that Braun is currently changing the complaint handling system from tracking complaint information on an ... spreadsheet to using an

off-the-shelf database system, ... Tracker. As required by 21 CFR 820.70(i), Automated Processes, this off-the-shelf software shall be validated for its intended use if Braun has not already done so. 你的回复表明目前布劳恩正在更改抱怨操作系统，从通过一个　　数据库来追踪抱怨信息到使用一种不用定制的　　数据库系统　　的追踪者。正如 21 CFR 820.70(i)所要求的自动化过程，假如布劳恩不是已经这样作了，这种不用定制的软件应被检验是否满足对它的预定应用。

Warning **Keywords: Excel, documentation, protection of electronic records, back-up, part11**

关键词：Excel 软件,文件，电子记录的保护，备份

W-069

- **Primary deviations:** no documentation of Excel application software, no protection of electronic records 主要错误；没有关于 Excel 应用软件的文件，没有对电子记录的保护
- **Example:** 例如
  There is no documentation covering Excel application software, or any procedures instituted covering the protection of electronic records or an established back-up system 没有文件涉及到了 Excel 应用软件，或者没有任何涉及到电子记录的保护程序及一个确定了的备份系统。

Warning **Keywords: validation, accurate and complete copies, limited access, part11**
关键词：检验，正确完善的拷贝，限制入口

W-068

- **Primary deviations:** inadequate validation, inaccurate and incomplete copies, no limited access to the system, 主要的错误：不恰当的检验，不正确和不完善的拷贝，没有限制系统入口
- **Examples:**例如
  - review of your electronic complaint files reveals they have not been properly validated, there is no ability to generate accurate and complete copies of records in human readable and electronic form, there is no protection of records to enable their accurate and ready retrieval, access to your system has not been limited, as well as other significant deficiencies.
  - We strongly encourage you to perform a thorough and complete evaluation of all your electronic records in accordance with 21 CFR Part 11 as well as any guidance generated by FDA to assure conformance to our requirements. Do not limit your evaluation solely to the examples cited above. Only electronic records and electronic signatures that meet 21 CFR Part 11 may be used to satisfy the requirements of 21 CFR 820.198, Complaint Files.

您的电子抱怨文件的审查表明它们没有被恰当的检验，没有能力创建书面形式和电子表格形式的正确完善的记录拷贝，没有确保正确迅速的索回的记录

保护，使用系统的权利未受限制，以及其他一些重大的不足。我们非常鼓励你们进行一个对所有的电子记录的正确完善的评估，可以参考 21 CFR 中第 11 部分的要求或者任何来源于 FDA 的且与我们的要求一致的指南，不要将你的评估仅限于上述例子。只有符合 21 CFR 中第 11 部分要求的电子记录和电子签名才满足 21 CFR 820.198 中对抱怨文件的要求。

Warning

Keywords: networks, testing, critical test, part11

关键词：网路，测试，严格的测试

W-067

- **Primary deviations:** design not suitable for intended use, insufficient performance testing
- The network ... module design limitations, which can only support up to four chromatographic acquisition systems, had up to five chromatographic systems connected. There was no validation showing this configuration to be acceptable
- 主要错误：设计不适合预定的应用，性能测试不足
- 某某网路模块设计了限制性，限制仅能达到支持四个层离法的获得系统，而此网路必须要达到五个层离法体系相关连。没有检验表明这种构造是可接受的。
- **Examples:** 例如

  - The network ... module design limitations, which can only support up to four chromatographic acquisition systems, had up to five chromatographic systems connected. There was no validation showing this configuration to be acceptable
  - System testing was not conducted to ensure that each system as configured could handle high sample rates.
  - Validation of the system did not include critical system tests such as volume, stress, performance, boundary, and compatibility

某某网路模块设计了限制性，限制仅能达到支持四个层离法的获得系统，此模块必须要达到五个层离法体系相关连。没有检验表明此构造可以接受。系统测试不能确保已成型的每个系统都可以处理高样本率系统检验不包括系统临界测试，例如；容积，压力，性能，边界以及兼容性

Warning **Keywords: internal quality audits, quality policy, management reviews, compiler, structural validation, part11**

关键词：内部质量审计，质量政策，管理审核，编译器，结构验证

W-066

- **Primary deviations:** inadequate quality unit, inadequate number of qualified people, missing batch production and control records, incomplete laboratory records, inadequate stability program

主要错误：不恰当的质量单元，合格的人才不足，缺少批生产和控制记录，不恰当的稳定性程序

- **Examples:** 例如
  - Failure to have, and/or to follow, laboratory controls which include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality and purity, as required by 21 CFR 211.160
  - Failure to maintain laboratory records that include complete data from all tests necessary to assure compliance with established specifications and standards, as required by 21 CFR 211.194.

没有（及、或没有遵守）实验室的控制，包括明确科学性和恰当的规格，标准，取样方法，和测试程序，此测试程序要能确保成分，药物生产仪器，阀门，中间产品，，标签及药物生产要符合强度，质量，纯度标准，正如 21 CFR 211.160 要求的那样。
缺少对实验室记录的维护，包括对所有必须测试的完整的测试数据要满足已定标准和规格，正如 21 CFR 211.194 所要求的那样。

Warning **Keywords: internal quality audits, quality policy, management reviews, compiler, structural validation, part11**

关键词：内部质量审计，质量政策，管理审核，编译器，结构验证

W-065

- **Primary deviations:** incomplete structural software validation, compilers were not validated, inadequate internal quality audits, inadequate quality policy, no ESD reduction procedures, inadequate corrective and preventive action plan, training needs not established, training not documented
- 主要错误：对结构软件的检验不完善，没有检验编译器，内部质量审计不恰当，不恰当的质量政策，没有 ESD 降低程序，纠错性的和防御性的行为计划不恰当，培训没被确定，培训没有文件支持。
- **Examples:** Your firm failed to adequately validate software integral to the IVD, IVD wireless and ...devices as required by 21 CFR 820.75. For example, structural testing o the software is not completed or documented, there are no

software validation protocols available, and the compilers were not validated

- Failure to have a quality control unit adequate to perform its functions and responsibilities. Your failure to have an adequate quality control unit is demonstrated by the number and types of inspectional observations made during this inspection
- Failure to have an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of a drug product
- Failure to ensure that each person engaged in such activities has the education, training, and experience, or any combination thereof, to enable them to perform their assigned functions, as required by 21 CFR 211.25. Your failure to have a staff adequate perform their assigned functions, is the number and types of inspectional during this inspection.
- Failure to maintain adequate control over air handling and exhaust systems

例如：您的公司没有恰当的检验软件来完善 IVD，无线 IVD 以及某某设备正如 21 CFR 820.75.所要求那样。例如：结构测试软件不完善或无文件支持，软件检验协议没有生效，以及没有检验编译器。缺少能恰当执行功能和责任的质量控制单元。在检验期间做出的检验资料中的数字和拷贝不能恰当的证明你的质量控制单元

没有恰当数量的合格人员来实施或监管加工，处理，包装，或成品药的储存工作。

不能确保每个参与此工作的人都受过教育，培训，或者任何上述内容的结合，以保证他们能执行他们的指定工作，正如 21 CFR 211.25.所要求的那样。没有恰当的人员来实施他们指派的工作，在审核期间你的失败体现在所做审核的数目和拷贝。

对空气处理和空气排放系统的控制不足

Warning

Keywords: limited access, accurate and complete copies, protection of records, computer validation, change control, quality audit, complaint handling, environmental monitoring, part11

关键词：限制入口，正确完善的拷贝，记录保护，计算机检验，控制更改，质量审核，抱怨处理，环境监控

W-064

- For example, drawing .... collection set is considered an electronic record. There is no documentation to establish that the system by which these records were produced has been properly validated.
- There is no ability to generate accurate and complete copies of records in human readable and electronic form. There is no protection of records to enable their accurate and ready retrieval. Access to your system has not been limited and there are other significant deficiencies as well. Do not limit your evaluation solely to the example cited above. Only electronic records and electronic signatures that meet part 11 requirements may be used to satisfy record and signature requirements of 21 CFR $820.30(d), Design Output.
- During the FDA inspection it was discoveredthat electronic records are used to establish portions of your design output, 21 CFR 820.30(d). However, there is no documentation to establish that these records meet the requirements of 21 CFR Part 11, Electronic Records; Electronic Signatures. The requirements of 21 CFR Part 11 are designed to ensure that electronic records are trustworthy, reliable, and generally equivalent to paper records.
- Failure to validate computer software for its intended use according to an established protocol to when computers or automated data processing systems are used as part of production or the quality system as required by 21 CFR 820.70(i). For example: your firm's ... is computer-controlled. It uses software programs to record data from measurements of the radius of curvature and corneal refraction of the eye. However, your firm has not validated the software and computer system used to record this data for its intended uses. Your firm has no documentation to assure that they perform as intended.
- Also, there is no validation and documentation of subsequent changes to the software
- Quality audits are inadequate to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system, as required by 21 CFR 820.22. For example, your firm's quality audits did not document or justify your failure to validate the ... software and the ... process.
- Failure to establish and maintain complaint handling procedures that ensure that all complaints are evaluated to determine whether a complaint represents an event which is required to be reported to FDA under Medical Device Reporting (MDR), as required by 21 CFR part 820.198(a)(3). For example...

例如：某某制图收集装置可以看做是一个电子记录，没有文件来支持记录产生系统已经受到适当的检验。无法以书面和电子表格的形式生成正确完整的

记录拷贝。没有保证可以正确并迅速取回的记录保护。系统的使用权没受限制以及类似的一些其他的不足。不要把你的评估仅限于上述举例，只有符合第 11 部分要求的电子记录和电子标记可被用于满足 21 CFR $820.30(d)中对记录和标记的要求，设计输出。

在 FDA 审查期间，发现电子记录被用在了建立部分的设计产量，正如 21 CFR 820.30(d)。然而，没有文件支持这种记录满足 21 CFR 中的 11 部分中关于电子记录和电子标记的要求，21 CFR 中第 11 部分的要求被设计成可保证电子记录是可信的，可靠的，与书面记录简单匹配

当计算机和自动数据处理系统 被当做生产的一部分使用时或当做 21 CFR820.70(i).中要求的质量体系的一部分时，没有检验计算机软件是否符合协议要求的预定应用。例如；您公司的某某是由计算机控制的，它使用软件程序记录曲率半径和眼角膜折光的测定数据，然而，您的公司没有验证用于记录这些数据的某某软件系统和计算机系统，您的公司没有文件可以保证他们能按要求完成任务。

而且，没有检验以及软件后续更改的文件

质量审核不能确保质量系统遵从已定的质量系统的要求和决定质量系统的效力，正如 21 CFR 820.22.所要求的。例如：你公司的质量审核没有某文件支持或验证你检验某软件和某工序的失败。没有建立或维持抱怨处理程序以确保所有的抱怨都被评估决定是否此抱怨提出了一个需上报给 FDA 的并在医疗设备报告支持下的事件，正如 21 CFR part 820.198(a)(3).所述那样，例如：

Warning

Keywords: validation of spreadsheets, data integrity, deletion of e-records, cleaning validation, method validation, process validation, OOS, failure investigation, part11

W-063

关键词：电子数据表的检验，数据的完整性，电子记录的删除，清除检验，方法检验，过程检验，无库存，审核失败

- Failure to have an adequate validation procedure for computerized spreadsheets used for in-process and finished product analytical calculations. The current validation procedure uses only the values that result in within specification findings, aberrant high findings, and aberrant low findings [21 CFR211. 165(e)]. For example, SOP 644.00, QA/QC Spreadsheet Validation, is deficient in that only a small range of values are being used to challenge computerized spreadsheet mathematical calculations.
- Failure to use fully validated computer spreadsheets to calculate analytical results for in-process and finished product testing [21 CFR 211.165(e)]. For example, the computer spreadsheets used to calculate analytical results for... have not been validated.
- Failure to have appropriate controls over computerized laboratory systems to

assure that changes in or deletions of records are instituted only by authorized personnel [21 CFR211. 165(e)]. For example, instrumentation where data is stored on the interfacing computer hard drive up to thirty days prior to being written on a compact disk for storage is available to all analysts. While the data exists on the hard drives, any analyst can access, print, or delete the data.

- Products were manufactured and shipped in interstate commerce before process validation was successfully completed.
- Batch records do not accurately reflect the actual manufacturing process. For example, there was no documentation, in the batch record that powder blend was reclaimed from the vacuum system of the - Encapsulator and added back into the virgin blend for process validation batches was successfully completed [21 CFR211.110(a)].
- The investigation of OOS data for validation batch 0000498 Q-Capsules was not extended to batch 98058190 capsules that was also manufactured using ….

对于用于中间和最终生产分析计算的计算机化的电子数据表缺少恰当的检验程序。目前的检验程序仅用于评估结果中符合标准的发现量，异常的高频率发现量，和异常的低频率发现量[21 CFR211. 165(e)]，例如：SOP 644.00, QA/QC 电子数据表的检验不足，由于仅仅一个小范围的评估会挑战计算机化的电子数据表的精确性计算.

没有全面有效的计算机电子数据表来计算中间和最终产品测试的分析结果[21 CFR 211.165(e)]，例如：计算机电子数据表用于计算某某的还未被检验的分析结果

- 没有对计算机化的实验室系统进行恰当的控制以确保记录的加入或删除都是由权威人士进行的 [21 CFR211. 165(e)]。例如：可**将数据储存在界面连接计算机上的仪器很难达到三十天** 。同时，储存在硬盘驱动器上的数据，任何的分析家都能进入，打印或删除数据。
- 在工序检验被成功完成之前，产品已进行生产或洲际贸易的运输。
- 批记录没能正确的反映出真实的生产工序，例如：没有文件，粉末混合的批记录重复了胶囊形成的真空系统以及为了批过程检验成功通过而加回到原始的混合[21 CFR211.110(a)]

0000498 Q-C 胶囊的批检验的缺货日的调查不能延伸至也被应用的 98058190 胶囊的批次

Warning

Keywords: corrective and preventive action procedures, missing non conformity evaluation, process validation

关键词：修正性程序和预防性程序，缺少不一致的评估，过程评估

W-062

- Failure to control your firm's corrective and preventive actions procedures to ensure that all data from quality data sources are analyzed to identify existing and potential causes of nonconforming product and other quality problems
- … and there was no documentation describing any evaluations of the returned goods or their quality problems as they related to your customer complaints
- Failure to ensure that a process whose results cannot be fully verified by subsequent inspection and testing, has been validated and approved according to established procedures
- Specifically, your firm has no documented evidence that provides a high degree of assurance that the manufacturing specifications and processing controls used in the automated and software controlled …operations of your … will consistently produce a product meeting its pre-determined specifications and quality attributes (traditionally termed validation).

没有控制贵公司的修正程序和预防性程序以确保所有来自于质量资源数据系统的数据被分析了现存的和潜在的造成不合格产品和其他质量问题的原因。

以及没有文件描述任何的对于涉及到消费者抱怨的退货和质量问题的评估。

不能确保一个程序可被规定程序检验或证明，此程序的结果无法被后来的检验和测试充分查证。

尤其是，您的公司没有文件化的证据可提供一个高水平的保证，使用于自动化和某软件控制程序的生产规格和过程控制将生产出一个满足预定规格和质量特性的产品

Warning

Keywords: cleaning validation, method validation,

关键词：清洗检验，方法检验

W-061

- Adequate cleaning procedures have not been established in that FPL has not conducted cleaning validation studies for non-dedicated manufacturing equipment. For example, the cleaning procedures have not been validated to demonstrate removal of API residues, cleaning agents, and impurities in buildings 1,2 & 7.
- Cleaning verification testing methods for Ammonium Lactate, Inulin, and Decitabine are not validated.
- Manufacturing processes have not been validated for several products.
- Investigations are not completed in a thorough and timely manner. For example,

investigations were not completed for several incidents of Purified Water not meeting specifications for microbial contamination and endotoxin levels during...

- Representative samples of components are not collected for testing and examination. For example, the inspection revealed that the microbiological samples of Purified Water collected at the points of use are not drawn through the same equipment as water used in product.

在 FPL 中未确定恰当的清洗方法，恰当的清洗方法不受非专业生产设备作出的清洗检验的指导。例如：清洗过程没被检验，从而无法论证 API 残渣的除去，清洗剂，以及混合物 1,2 & 7 中的杂质。

乳酸胺，菊粉和 Decitabine 的清洗确认的测试方法没有被检验。

若干产品的生产过程没被检验。

调查没有以一种彻底的适时的方式完成，例如，若干纯化水的事件调查没有完成，在某某期间，此纯化水不符合微生物污染水平规格和内毒素水平规格。

没有收集成分的代表性样品用于了测试和考核。例如：检查显示在使用点上收集的纯化水的微生物样本不是抽提自同样的用于生产用水的设备。

Warning

Keywords: electronic records, data base, audit trail, training, part11

关键词：电子记录，数据库，查账索引，培训

W-060

- It is also noted in the inspection report that you do not have adequate control over the receipt of study data and its subsequent input into the database.
- There are no records to show when study data is received and when it is entered into the database.
- There is also no audit trail for changes made to the database. No data queries or clarifications have ever been generated and sent to the sites to verify missing information or to clarify discrepancies...
- Electronic records, the subject of SOP-100-720, Electronic Database Maintenance, are subject to 21 CFR Part 11- Electronic Records; Electronic Signatures, as well as to the record keeping regulations found in 21 CFR 812.140, a guidance document regarding this regulation, Computerized Systems Used in Clinical Trials, dated April 1999.
- There is no documentation to show that investigators or their personnel were trained in the use of the ... regarding the investigational plan, or in how to complete the CRFs
- There is no documentation of the number on the number of ...and ... the number manufactured and distributed, the number of copies of the controlling software made, or the disposition of each copy of the software. There are no records showing to which sites the device was shipped or whether the required software was supplied.
- 在检验报告中也指明了您没有适当的控制收到的研究数据和以及后来再将它们输

入数据库。

- 没有记录显示什么时候收到了研究数据，什么时候把它们输入了数据库。
- 也没有更改数据库的查帐索引，没有产生任何的数据质疑和澄清以及发到指定地点核实丢失的信息或澄清差异。
- 主题为 SOP-100-720,的电子记录，电子数据库的维护要遵从 21 CFR 中第 11 部分的电子记录。Electronic Signatures, as well as to the record keeping regulations found in 21 CFR 812.140, a guidance document regarding this regulation, Computerized Systems Used in Clinical Trials, dated April 1999.

没有文件表明调查员或者他的下属要训练使用关于调查计划的某某或者以何种方法来完成 CRF。

没有关于某某数目的数字文件，关于生产分配数目，控制性软件作出的拷贝数目或者每个拷贝软件的部署的数字性文件。没有记录表明设备的出处或者是否提供了要求的软件。

Warning

Keywords: Data back-up and archiving, laboratory tests, method validation, change control, part11

关键词：数据备份和存档，实验室测试，方法检验

W-059

- Failure to maintain complete data from all laboratory tests as required by 21 CFR 211.94 (a).
- 没有对实验室测试数据进行维护，正如 21 CFR 211.94 (a)所述那样
- There is no back-up file for laboratory UV spectrophotometer test results for some tests. The spectrophotometer does not automatically back-up data and the analyst is required to assign an identification number to each individual chromatogram in order for it to be saved. In some cases, original data was lost and the tests had to be performed again to determine final distribution of the lots
- 对于一些测试所进行的实验室的紫外分光光度计的测试结果没有备份文件。分光光度计不能自动的备份数据以及分析者应对每个单独的色谱设计鉴证数据以便保留，在一些事件中，原始资料丢失了，测试必须要再次进行以确定对丢失部分的最终分类。
- Failure to have documentation of Method Validation for the stability assay method for ... Injection.
- 没有对某某注射济的稳定性化验方法进行检验的文件
- Failure to document changes to written specifications and to have the changes approved before implementation as required by 21 CFR 211.160 (a). For example...
- 在执行 21 CFR 211.160 (a)的要求之前，文件没有，变成书面规格和已被核准的更改，例如

Warning

Keywords: Software validation, security, audit trail, data integrity, failure investigation, laboratory records, training, part11

关键词：软件检验，安全，查账索引，数据完整，失败调查，实验室记录，培训

W-058

- The computer software your firm uses to determine metals analysis is deficient. It has no security measures to prevent unauthorized access of the software, no audit trails, and data can be copied or changed at will, with no documentation of the copying or changes.

您的公司用于金属分析的计算机软件不足，没有安全措施来防止未经认可的软件通路，没有查帐索引，以及数据不能按意志拷贝或更改，没有拷贝或更改的文件。

- Your procedures do not require the documentation of calculation or entry errors.

您的程序不要求计算的文件或者进入的错误。

- There is no documentation to indicate that analysts are trained in the software and its applications.

没有文件显示分析者要培训软件和它的应用。

- You or your employees performed repeat testing on products without first conducting an investigation. No explanation into the reason for repeat testing and invalidating the previous results was documented. Further, the initial results were not communicated to your customers; only the repeated and passing results were communicated. Specific examples include.....

你和你的雇员实施没有没有引导一个调查的产品的重复测试，没有解释重复测试的原因以及使有文件证明的先前文件的失效，更进一步说，最初的结果没有传达给你的客户，只有重复的和过期的结果被传达，特殊的例子有

- You (specifically) are not documenting raw data when you perform inductively coupled plasma emission spectrograph or high-pressure liquid chromatography analyses. This raw data includes....
- 当您使用诱导连接血浆散发声谱仪或高压液体套色版分析时，您没有证明原始数据。这种原始数据包括
- Following flood damage in September, 1999 to your facility and equipment, you or your employees failed to evaluate the raw data storage conditions, recalibrate or re-qualify repairable analytical equipment, or implement any procedures or changes to existing procedures to alleviate future damages.
- 在 1999 年九月对您的设备和仪器造成的流体损伤，您或您的雇员没有检验原始数据的储藏条件，校准或再证可修理的分析仪，或执行任何的程序或对现存程序的更改用以减轻未来的损伤。

- Your firm does not have a quality assurance program in place to: *a)* qualify analytical equipment prior to their use, and b) calibrate and maintain analytical equipment according to manufacturers' specifications.
- 您的公司没有对下述的质量确保程序：（1）质量分析仪使用之前，（2）根据生产规格校准和维修分析设备
- Your firm has no system for the receipt and storage of standards and analytical chemicals. Expired standards were used in the calibration of equipment. Working solutions were not properly labeled or documented in laboratory notebooks or other records in that the data did not bear complete information, including the analyst or preparer's identity, solution designation, strength, and expiry dates.
- 您的公司没有标准的分析化学药品的接受和储藏系统。终止的标准还被用于设备的校准。正在使用的溶液没有贴上合适的标签或者记录在实验室的笔记本上或者其它数据不全的记录，包括分析者和制备者一致，溶液名称，浓度和有效日期
- The integrity of raw data produced by various laboratory instrumentation is questionable. For individual pieces of equipment, including ...either no equipment qualification was performed, no calibration was performed prior to their use, audit trail exists for data collection and entry, or their inclusion in method or system validation was not made.
- 来自多方的实验仪器的原始数据的完整性很可疑，对于单独的设备，包括某某既没有执行设备规格，也没有执行设备使用前的校准以及数据收集和输入的审核，或者没做对于方法和程序的内含成分的检验。
- Your firm's laboratory records and recordkeeping are deficient. corrections to laboratory raw data were noted to be obscured with white correction fluid or improperly voided (no initials, date, reason or explanation of change). Laboratory worksheets did not contain information of the analytical method used to perform the analysis in question. Analytical calculations were not recorded in laboratory notebooks. There is no other demonstrable record of said calculations.
- 您的公司实验记录和保存记录不足，实验原始数据的修正使用了白色的修正液或者存在不应有的缺失（缺少词首，数据，更改的原因和解释），实验室工作表不含有用于问题分析的分析方法的相关信息，实验室笔记本中没有记录分析计算方法，以及没有其它上述考虑的可论证记录
- Laboratory records did not contain documentation of a second individual's review and verification of the original data.
- 实验室记录中没有第二人做的检查文件以及对原始数据的查证
- You and your employees performing analyses of drug products are not trained in Current Good Manufacturing Practices applicable to your operation. Further, your supervisory employees have not documented any of their subordinates as being qualified to execute the analytical work to which they have been assigned.
- 您和您的执行药物生产分析的雇员没有培训目前较好的可用于生产的生产实践，更进一步，您的监管人员没有证明任何雇员都

收集数据

Warning

Keywords: Data integrity, authorized changes, manufacturing deviations, part11
关键词：数据完整，授权更改，生产错误

W-057

- Your firm failed to implement appropriate controls over your High Performance Liquid Chromatography (HPLC) to assure that only authorized changes can be made. It was noted during the inspection that there is an option on the HPLC that allows analysts to delete results after they are processed.
- 您的公司没有适当的控制您的高性能流体套色版（HPLC）以确保所做的都是权威性的更改，在检查期间有一个对 HPLC 的选择，HPLC 允许分析者删除处理后的结果。
- There is no assurance that all manufacturing deviations are recorded and justified. It was noted that ...
- 不能保证所有的生产错误都记录下来并被检验，而不是

Warning

Keywords: Data integrity, unauthorized access, out of specifications, director of quality control, part11
关键词：数据完整，未授权的入口，超出规格，质量控制主管

W-056

- Failure to maintain the integrity and adequacy of the laboratory's computer systems used by the Quality Control Unit in the analysis and processing of test data. 没有维护实验室的计算机系统的完整性和恰当性，此系统用于分析处理测试数据的质量控制单元
- For example a) There was a lack of a secure system to prevent unauthorized entry in restricted data systems. 例如（1）缺少一个安全的系统来防止未经确认进入保密数据系统
- Data edit authorization rights were available to all unauthorized user not only the system administrator
- 数据编辑权对于所有权威的使用者都有效，不仅仅是系统管理员
- The firm ignored initial out-of-specification results, performed retesting, and released product for distribution without conducting adequate laboratory investigations. In one instance, the Director of Quality Control crossed out the analyst's statement of true results and determined the low results were due to laboratory error without any evidence or investigation of the results.
- 公司忽视了最初的不合格结果，实施再测试，以及未经恰当的实验室调查就发放产品，在一个例子中，质量控制主管删除了分析者对真实结果的称述，以及认为低度的结果是由于实验室的错误造成，而不做任何的对结果的证明和检测
- The Director of Quality Control crossed out the analyst's statement "This proves that there was not an analyst error." The Director concluded....
- 质量控制主管删除了分析者的申明“这证明不存在分析错误”，这主管包括
- Laboratory controls are deficient in that the firm established a written procedure, which allowed for the averaging of out-of-specification and within-specification analytical test data results, as was done with ...

- 实验室的控制在公司确定的书面程序方面不足，此程序允许合格的和不合格的分析测试的数据结果的平均，像

Warning

Keywords: Statistics, quality problems, investigating non-conformities, complaint procedure

关键词：统计表，质量问题，调查不一致，抱怨程序

W-055

- Not analyzing all significant sources of quality data, and using appropriate statistical methodology where necessary to detect recurring quality problems, as required by 21 CFR 820. 10O(a)(I). For example, your firm does not conduct ....
- 没有分析所有的重要的质量数据的来源，以及使用一个恰当的统计方法，此方法对于测试重复出现的质量问题很有必要，正如 21 CFR 820. 10O(a)(I). 中所要求的，例如，你的公司不能指导
- Not investigating the cause of nonconformities relating to product, processes and the quality systems, as required by 21 CFR 820. 10O(a)(2). For example, ... 没有调查关于产品，过程，质量系统的不合格原因，正如 21 CFR 820. 10O(a)(2)所述，例如
- Failure to adequately evaluate and document complaints, as requiredby21 CFR 820.198. Our inspection revealed that the PIR's are considered to be customer complaints and are handled via your sales/distribution personnel, RMA's are considered to be product returns, including defective goods that are handled by your customer service department. Review of your records
- 没有恰当的评估文件，正如 21 CFR 820.198.所述，我们的检查显示 PIR's 被当作是客户的抱怨以及被销售分配人员掌控，RMA's 被看作是产品利润，包括你的客户服务部的次品，回顾你的记录

Warning

Keywords: Batch production record, training, calibration procedures, certificate of analysis

关键词：批生产记录，培训，校准程序，分析证明

W-054

- There is no documentation of the Batch Production Records being reviewed and approved by the Quality Control Unit since January 1, 2001 [21 CFR 211. 192].
- 没有经质量控制单元审核及证明批生产记录文件，2001 年 1 月日[21 CFR 211. 192].
- There is no documentation that members of the Quality Control Unit possess the education, training and/or experience to perform this function [21 CFR 211.25(b)].
- 没有文件支持质量控制单元的成员受过教育，培训及工作经历[21 CFR 211.25(b)].
- The calibration procedures and documentation for the ... Analyzer are inadequate in that the frequency for calibration to be performed is not specified and the standards used for calibration are not certified cylinders of nitrogen and oxygen as specified in your procedures [21 CFR 211.68(a)]. 对于某某分析仪的检验程序和文件不恰当，校准的频率和标准没有被详细说明 sed for calibration are not certified cylinders of nitrogen and oxygen as specified in your procedures [21 CFR 211.68(a)
- There is no documentation that you receive a Certificate of Analysisyou're your procedures indicate, upon receipt of each cylinder of incoming source oxygen [21 CFR 21 1.84(d)(2)].没有文件证明收到了分析证明，你的程序表明 upon receipt of each cylinder of incoming source oxygen [21 CFR 21 1.84(d)(2)].
- There is no documentation of a complaint received regarding released product [21 CFR211.198(b)].没有收到发放产品的抱怨文件 [21 CFR211.198(b)]

Warning

Keywords: Method validation, effectiveness testing, stability testing

关键词：方法检验，效力测试，稳定性测试

W-053

- Your firm has not validated the analytical methods used for in-process, stability and product testing 您的公司没有检验用于中间测试，稳定性测试和产品测试的计算方法
- Your firm does not perform preservative effectiveness testing as part of your release testing and stability program for dl prescription and OTC drug preparations.
- 您的公司没有将防腐效力测试作为你的处方药和非处方药的免除测试和 稳定性计划 的一部分
- Failure to follow the Standard Operating Procedure ... "Acceptable Testing Time Intends", which states stability samples are to be tested within 60 days of their scheduled pull date. Your Stability Testing Log documented total of 67 out of 378 stability samples that did not meet the 60-day testing time frames since August2000. 没有遵守操作程序的标准 "可接受的测试时间计划"，申明了稳定性的样本将在预定日期的 60 天内被测试，你的稳定性测

试日志有文件支持的

Warning

Keywords: Scientifically sound specifications, stability characteristics, verification of calculations by a second person

关键词：科学可靠的规格，稳定性，由第二人进行的计算查证

W-052

- Failure to establish scientifically sound and appropriate specifications for raw material and finished product testing.
- 没有建立对原材料和终产品的科学恰当的测试规格
- Failure to have a written testing program to assess the stability characteristics of the .... products.
- 没有评估　产品稳定性的书面测试计划
- Failure to determine theoretical and actual yields, and failure to have the calculations performed by one person and independently verified by a second individual.
- 没有确定实际利润和理论利润，以及没有一个人作的计算和第二个人作的独立查证。

Warning

Keywords: Quality control unit, drug manufacturing records, SOPs, identity and purity tests, cGMP training

关键词：质量控制单元，药生产记录，SOP，一致性和纯度测试，**cGMP 培训**

W-051

- Failure to establish and operate an effective quality control unit in conformity with requirements of 21 CFR 211.22. There re no written procedures concerning individual responsibility for quality control operations.
- 没有确定和运行有效的质量控制单元，如 21 CFR 211.22. 所述，没有关于质量控制中个人责任的书面程序
- Drug manufacturing records (...) contained numerous errors and omissions, although they had undergone quality control review.
- 药物生产记录有数字错误且很长，虽然经过了质量控制审核
- Written standard operating procedures covering .... were inaccurate, incomplete, and contained no documentation of origin, review or approval.
- 关于某某的书面的标准操作程序是错误的，不完整的，没有原始文件，回顾及证明
- Failure to follow written production and process control procedures as required by 21CFR 211.100. A significant example is the failure to conduct identity and purity testing of some .... as required by SOPS.

- 没有遵守 21CFR 211.100 要求的生产和过程控制程序，一个重要的例子是没有指导一致性和纯度测试 SOPS.
- Failure to establish and implement an effective employee cGMP training program. Employee training records contain no reference to cGMP
- 没有建立及执行对雇员的一个有效的 cGMP 培训计划，雇员培训计划没有涉及到 cGMP，
- There or e no cGMP training SOPs in place and at least one employee denied knowledge of cGMP regulations.
- cGMP 中有或无恰当的 SOP 培训，至少一个雇员否认 cGMP 章程的规定

Warning

Keywords: Management reviews, quality audits, destruction of records

关键词：生产审核，质量审计，记录销毁

W-050

- Failure to conduct *management reviews* as required by21 CFR 820, 2O(c) and as called for in your procedure QOO1 "Quality System", to assure that the your firm is in compliance with the regulations.
- 没有指导 21 CFR 820, 2O(c 中要求的管理审核以及
- Failure to conduct quality audits requiredby21 CFR 820.22, and in your procedure QO02, "Audits" to assure your firm is operating in compliance with the regulations.
-
- Your procedure QO02, "Audits", Section 3,3.2, provides for the destruction of the audit reports when corrective action is completed. This represents a failure to document the dates and results of the quality audits as required by 21 CFR 820.22.

Warning

Keywords: Software validation, cleaning and maintenance of equipment, part11

关键词：软件检验，清洗和维修设备

W-049

- Failure to validate computer software used to control the ... to ensure the software will perform for its intended use. 21 CFR 820.70(i).
- 没检验用于控制　的计算机软件，以确保软件按要求运行，正如 21 CFR 820.70(i).
- Failure to adequately validate processes which cannot be fully verified by subsequent inspection and test, 21 CFR 820.75, for example, the ....
- 没充分检验工序
- Other deficiencies found during the inspection include failure to follow procedures for the cleaning and maintenance of manufacturing equipment, and failure to report Medical Device Regulation (MDR) reportable events in a timely manner.

FDA 的警告	**关键词：遗漏会议纪录，品质监查，供应商资格，预防和惩治行为。**	D
W-048	。疏忽建立管理审核规程和疏忽证明管理审核[21 CFR 820.20(c) 的] 日期和结果。 例如，您的企业召开管理会议谈论产品质量但未保留会议的文献记录。 。疏忽证明质量监查的日期和结果。 例如，您的企业有... 。 • 疏忽建立和维护要求,包括供应商[21 CFR 820.50]必须遇见的质量要求。例如，您的企业未指定供应商的质量要求，维护被批准的供应商的名单，以及建立的书面规程应该描述评估供应商怎样才能达到质量采纳要求。 • 疏忽建立和维护为实施矫正和预防措施[21 CFR 820.100]的规程。例如，您的企业没有.... 。.	
FDA 的警告	**关键词: QA 审核，雇员能力审计，人资格，超出范围价值**	D
W-047	• 疏忽执行 QA 审核.... 从 2/2/01 至 7/26/01 实验室申请书测试形式的结果？ • 疏忽审核处理失败(错误和事故)的形式。 • 疏忽执行雇员能力的审计。 • 疏忽执行每日折射计记录的 QA 审核，冰箱冷冻机记录，主文件和重要的单位日志; • 疏忽执行每年主医师重认证和医师替代。 • 疏忽记录最初超出范围价值在....	
FDA 的警告	**关键词:代理采样和测试，供应商分析的验证,微生物的污染。**	D
W-046	• 包括在检查期间 CGMP 偏差的记录，但不限制：活跃药物成份(API)作为包装产品不需要以代表性方式在用途上做测试抽样[21 CFR 211.84(b)] 。 • 供应商分析的可靠的支持药物组分被采纳并不适合确认为所有组分[21 CFR 211.84(d)(2)] 。 • 不能确定和遵循适合书面规程从而防止厌恶微生物污染环境来源 [21 CFR 211 。 113(a)] 。	

FDA 的警告 W-045	**关键词：供应链审计， 稳定性测试，方法验证，清洁验证** • 接受 (未加工的) 材料只根据进口文件审核，譬如托运人的声明和来料证明。供应链的审计无需核实证明。在 2001 年 3 月 29 日为新材料承诺审计供应链直到 2001 年底,但是不要 写出已经生产的材料的地址。 • 对没有包括准确演示，特异性，范围,险峻性 ,耐用性和系统适用性的批验证释放和分析用的试样及杂质稳定性测试比较适当。 • 为多使用处理设备清洗验证研究还很不足是由于清洁规程没有指定漂洗的数量和时间...因此机器组分任何被发现的有机残渣无法被定量。拖把采样不能代总表面...，拖把样品回采数据是不可利用的。	D
FDA 的警告 W-044	**关键词：QC 单位的职责，失败的调查，不符合规范** • 疏忽一些描述适用 QC 单位责任和规程的文件。 [21.CFR 21 1.22(d)] • 疏忽充分地调查批没有符合规格的批。 [21 CFR 211.192] • 疏忽不符合规范的规程，像找不到要记录在经过测试的过失处分的数据或者实验室调查非结论性。 [21.CFR 21 1.165]	D
FDA 的警告 W-043	**关键词：验证，实验室数据系统， 培训, QC 单位的职责，清洗验证, 11 部分** • 例如，还没有确定和说明 QC 单位当局设计保证药品质量和纯净各批药品职责。(21 CFR 211.22) • 没有训练雇员在药品生产方面与工作职能相关的 CGMPS 的一些内容。 [21 CFR 211.25(a)] 。 • 您还未验证，例如，药物生产过程(21 CFR 211.100)；为维护实验室数据和药品发行信息的计算机化的控制系统(21 CFR 21 1.68)；以及药物清洗过程的同设备和化妆用品生产过程(21 CFR 21 1.67) 。	D

FDA 的警告	**关键词：稳定性测试，软件更改控制，方法验证，实验室纪录，实验室， 演算，设备校准, 11 部分**	D
W-042	• 有不充分的实验室规程和记录 APIs 的恰当的质量和净化的保证。 检查报告缺乏关于以下实验室规程和记录: 分析方法验证, 系统适用性测试，不完整的实验室记录，不精确的实验室演算, 实验室设备不足的校准。 • 生产, 程序控制, 和实验室操作的书面规程要求保证 APIs 有相当的质量和纯度。检验报告了许多关于不需要书面规程的一般实践操作的示例: 稳定测试,检疫和易分解释放的物质的存贮， 软件更改, 完成干燥的 API	
FDA 的警告	**关键词：调查失败，更改行为，过滤，清洗验证**	D
W-041	• 疏忽仔细地调查任何未经说明的差误或批或达到它的任何规格的任何组分[21 CFR211 。 192], 如下.... • .疏忽对设备清洗和维护所要建立和遵循的书面规程, 包括用来制造的器物, 处理, 包装,或者药品器皿 [21 CFR211 67(b)] 由于.... • 超过滤/diafiltration (UF/DF)的清洗单元使用在制造... 还未充分地验证。 • 由于支持再加工白蛋白的 proteinaceous 材料（PM）没有书面规程和检验数据和潜在的玻璃碎片。从而疏忽了要保证再加工批产品所要遵循的所有确立的标准, 规格, 和特征[21 CFR 211.115(a)] • 疏忽维护和/或遵循生产和程序控制的书面规程，设计确保药品的力度, 质量, 和纯度，他们声称或代表团队并且保证这样规程, 包括规程的任何更改, 起草, 审核, 和批准合适的组织单位和质量管理的审核和批准。 例如...	
FDA 的警告	**关键词：验证方案，11 部分**	D
W-040	• 由于在这检验期间雇员找到并运用了其他人的计算机通入... 计算机的记录系统，疏忽了建立和充分实施计算机安全性和数据完整性。 审核 21 CFR 第 11 部分对电子附属记录和签名, 和两个附属安全控制。 • 偏差包括: 缺乏验证方案和执行验证方案完整的维护和准	

确的文献以及计算机系统的结果分析。

FDA 的警告 W-039	**关键词：实验室试验规程，方法验证，原始数据，第 11 部分** • 由于实验室试验方法并不表示所有批（ ）实验室试验和规程不够充分，由于使用的方法不科学适当，所以要遵循适当的规范。 具体地说，使用的方法与当前在描述的纲要有着极大的不同。 使用方法未被证明与当前的纲要方法是等效的，而决定产品遇见当前的纲要极限。 此外，（ ）设备所需要的适当的分析方法是不可行的。 • 稳定性测试( )分析使用的方法，还未证实是稳定性指示方法。 另外，稳定性样品未在受控情况下存放。 • 原始数据是为标准参照物和试剂的准备的，样品重量，和稀释因素总未被记录；实验室的工作表总得不到复检，并且工作表上已被注销的数据也没人经常观察，就被更改数据的人签上名字和日期。 • 此外，没有关于分析员训练的执行实验室分析。 • （ ）系统还未验证。 。 没有记录表明（ ）有这设施制造或者从某个供应商那购买，微生物测试的说明书。	D
FDA 的警告 W-038	**关键词：管理职责，身机，软件验证，更改措施 。** • 疏忽了适合您公司制造的精确的装置实施和操作的质量系统 • .负责的管理代表没有审核审计报告。 • 没有建立设计计划和发展计划。 • 尽管装置已经更改但是没备有证明来支持设计更改的验证。 • No procedures for the development of software used to control devices. 没有用来控制装置的发展软件的规程。 • The software used for the operation of the ( ) system was not properly validated. 用来操作（ ）系统的软件没有得到完全的验证。 • Failure to establish and control procedures for implementing corrective and preventive actions. For example... 疏忽了建立和控制用来实现更正性和预防性措施的规程。例如……	D

Warning **Keywords: Corrective actions, preventive actions, trend analysis** 关键词：更正措施，预防措施，倾向分析 D

W-037

- Failure to establish and maintain adequate corrective and preventive action procedures. Not all sources of quality data are analyzed to identify existing and potential causes of nonconforming product and other quality problems. For example,... 疏忽了建立和威势足够的更正性和预防性的规程。不是所有的质量数据都用来分析识别是已经存在和潜在的原因导致了不合格产品和其它质量问题。例如……
- Other failures/problems noted in the complaint system such as （ ） are not evaluated/analyzed and processed through your firm's corrective and preventive action system. 其它记录在抱怨系统的失误/问题像（ ）在您公司的更正性和预防性措施系统中并没有得到评估/分析和处理。
- There is no rationale why other events are not trended and analyzed 对为何其他 结果没有倾向和分析的问题没有基本原理说明。
- Failure to establish and maintain an adequate complaint handling program. Complaints received by your firm are not processed in accordance with your firm's SOP in that there was missing information on the complaint form 疏忽了建立和维持一个适当的抱怨处理程序。由于在抱怨形式上失去了信息，您公司受到的抱怨和您公司的 SOP 并不相一致。
- Also, in your firm's response to the FDA 483, you stated that your firm consistently files MDR reports within 30 days of becoming aware that an event is reportable. FDA generally considers that a manufacturer becomes aware of an adverse event whenever an employee becomes aware of an adverse event. The 30-day time frame begins ..... 还有，在您公司回应 FDA483 条款中，申明您公司一直都提出 MDR 报告持续 30 天，意识到了一项结果的可报告性。FDA 一般认为只要一个雇员知道了不好的结果，制造商就回知道了不好的结果。30 天的期限开始……

Warning **Keywords: Legacy systems, retrospective evaluation, software validation, analytical equipment, calibration stickers, part11** **关键词：旧系统，回顾性评估，分析设备，货物标度，11 部分** D

W-036

- The software programs have not been verified or validated".软件程序还未校验或者验证。
- You indicate that you will develop a complex software validation schedule in cooperation with the software vendor by December 31. However, the validation schedule will not be approved until January 21, 2001, and the software validation exercise will not be completed until June 30, 2001. It appears that you are proposing to continue to use these … systems for testing of … without having completed the calibration of … or validation of its software. This is unacceptable". 指出您将与软件商协作 在 12 月 31 日制定一个综合的软件验证进度表。 然而，验证进度表要知道 2001 年 1 月 21 日才能批准，并且要在 2001 年 1 月 30 日完成验证演习。这就表示你将未经过完成……校准就用软件继续用用这些……系统测试……
- Written procedures had not been established for the calibration of analytical instruments and equipment in quality control laboratories used for ..... 校准和分析仪表以及设备在质量控制的实验室用于……的书面规程还未得到建立。
- Furthermore, calibration data and results provided by an outside contractor were not checked, reviewed and approved by... 此外，外部的承包人提供的校准数据和结果没有得到……人的核对，审核和批准。
- Most instruments lacked calibration stickers indicating ... 大多数的仪表缺少货物标度表明……

Warning **Keywords: Networks, WAN, LAN, LIMS, computer validation, retrospective evaluation, documentation, part11** **关键词：网络，广域网，局域网，LIMS，计算机验证，第 11 部分。** D

W-035

- The network program lacked adequate validation and/or documentation controls 网络程序缺少足够的验证和/或文件控制。
- System design documentation has not been maintained or updated throughout of the software dating back to 1985 despite significant changes and modification that have taken place. These include program code, functional/structural design, diagrams, specifications and text descriptions of other programs that interfere with (this program) 尽管已经发生了重大的更改和修正，系统设计文件还未得到维护和更新还贯穿于软件，这追溯到了 1985 年。

- The program was not controlled by revision numbers to discriminate one revision from the other 程序不是由修订号控制来区分一个修订与其它修订。
- There was no assurance that complete functional testing had been performed in the ... system. For example you failed to assess all historical testing and compare it with current functionality to ensure that all ... functionality has been adequately evaluated 还不确定在……系统中执行的完全的功能测试。
- The software validation documentation failed to adequately define, update and control significant elements customized to configure the system for specific needs of operation. 软件验证文件不能充分的定义，更新和控制重要的用户化的元件使形成特殊操作系统。
- You make no commitment to retrospectively put historical documentation together 没有拟订委托事项来回顾性地把历史文件收集起来。
- Validation documentation failed to include complete and updated design documentation, and complete wiring/network diagrams to identify all computers and devices connected to the ... system 验证文件没有包括完全的和最新的设计文件以及全部的配线/网络图表来识别所有的电脑和连接……系统的装置。
- The Quality Control Unit failed to ensure that adequate procedures where put in place to define and control computerized production operations, equipment qualifications, documentation review and laboratory operations. 质量控制部门眉宇确保足够的到位的规程来说明和操作用计算机处理的产品操作，设备条件，文件审核和实验室操作。

Warning **Keywords: Database, networks, audit trail, computer validation, retrospective evaluation, documentation, part11** 关键词：数据库，网络，查帐索引，计算机验证，回顾性评估，文件，第 11 部分。 D

W-034

- Lack of audit trail function of the database to ensure against possible deletion and lost of records 缺少对数据库的查帐索引功能来确保避免可能的删除和失去的记录。
- Absence of of documentation defining the database, operating system, location of files and security access to database 缺乏定义数据库的文件，操作系统，文件的位置和数据库的安全使用。
- Validation documentation did not address signal lines between detection devices and computer 验证文件没有在发生装置和电脑间标出显眼的单线。
- Documentation control deficiencies were reported such as review, approval, and maintenance of records 文件控制的不足是报告，

像审核，批准，和文件的养护。

- The ... network program lacked adequate validation and/or documentation controls. ……的网络程序缺少足够的验证和/或文件控制。
- The following had not been maintained or updated from original release/design specification back to approximately
  - revision control system
  - validation records
  - structural and functional diagrams and design descriptions
  - complete diagrams with text description identifying other network programs which interface with ... 以下是从原始版本/设计说明书后面大概的没有得到维护和更新的内容。
- -修订控制系统
- -记录验证
- -结构图，操作图和设计说明书
- -完成识别其他网络带有正文说明的图表
- Inadequate standard operating procedures to ensure that records are included with validation documentation, maintained and updated when changes are 当要更改时，不充分的 SOP 保证记录，那些记录包括文件验证，养护和更新。
- Your response fails to trace back to source code, and the related document cycle which establish evidence that all software requirements have been implemented correctly and completely and are traceable back to system requirements 您的回应未能追溯到原码，和那些所有的已经正确完全实施以及追溯系统需求的软件要求的相关文件整套。
- Your response fails to discuss extending the retrospective evaluation to other elements of the system needing to be defined and controlled as part of the overall configuration management. 您的回应未能讨论伸张回顾性地评估到需要定义的系统和作为全部结构管理一部分控制的基本原理。

Warning **Keywords: Action plan for part 11, environment validation, cleaning validation, part11 关键词：第 11 部分的运作计划，环境验证，清洗验证，第 11 部分** D

W-033

- No action plan to correct for deficiency of 21 CFR Part 11 for a record keeping system, which is used for maintaining chromatography and audit trails.没有运作计划对用来养护套色版和查帐索引的维护系统来更正 21CFR 第 11 部分的不足。
- Insufficient environment validation 环境验证的不足。
- Inadequate cleaning validation 清洗验证的不充分。

Warning **Keywords: Computer validation, security, modem access, data review, change control, part11** 关键词：计算机的验证，安全，调制调解器的接口，数据审核，更改控制。 D

W-032

- Lack of proper validation of computer software. 缺少对计算机软件的正确验证。
- Failure to establish and implement adequate security in allowing the software vendor unrestricted modem access and not consistently documenting this access 疏忽建立和实施足够的安全措施来按照软件商无限制的调制调解器的接口以及没有始终如一地记录这种接口。
- Not conducting a secondary review of software modification 没有对软件修正引导第二次审核。
- Lack of computer hardware and software change control SOP 缺少计算机硬件和软件的更新来控制 SOP。
- Lack of verification that software modifications validated on the 'test' system are identical to the modifications implemented later in the 'live' system 缺少‘测试系统的验证’的软件修正验证，对运作着的系统而言同样也会导致修正执行的滞后。

Warning **Keywords: Laboratory records, electronic records, failure investigation, security procedures, part11 关键词：实验室记录，电子记录，调查的失误，安全规程。** D

W-031

- Failure to maintain laboratory records to include complete data derived from all tests necessary to assure compliance with established specifications and standards 疏忽了养护实验室记录，包括来自所有测试中的完整数据，保证依从已制定的说明与标准。
- Specifically, your firm failed to properly maintain electronic files containing data secured in the course of tests from 20 HPLCs and 3 GLCs. 确切地说，您的公司未能适当地维护电子文件，包括来自于 20HPLCs 和 3GLCs 的安全数据。
- Additionally, no investigation was conducted by your company to determine the cause of missing data and no corrective measures were implemented to prevent the recurrence of this event.另外，您公司没有调查来引导决定数据丢失的原因和经济调整措施的实施来防止这种事情的复发。
- Additionally, please provide copies of your written procedures describing system security, system maintenance, and data file backup procedures for assuring backed up automated laboratory files are retrievable. 另外，请提供您的书面规程的副本来说明系统

的安全性，系统的养护，和用来保证支持实验室自动化文件的数据文件备份规程是可获得的。

- Failure to establish procedures to assure equipment and utensils are sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of drugs beyond the official or other established requirements *(more specifics to follow)* 疏忽建立规程来保证设备和器具的清洁要在合适的距离从而防止可能导致改变药物安全性，均一性，强度，质量或者纯度的污染，这些污染会超过官方或者其它确定的要求（更多的细节需要遵循）

Warning **Keywords: Computer system validation, maintenance, data review, laboratory notebook entries, LIMS, autoclave validation 关键词：计算机系统的验证，维护，数据审核，实验室笔记本条目，LIMS，高压灭菌器的验证** D

W-030

- The computer system, used to monitor and maintain critical systems has not been validated. The computer system is used to monitor temperature, conductivity, water pressure and time (in hours) Additionally, this system monitors the differential pressure between... *(examples follow)* 用来监控和维护鉴定系统的计算机系统还未得到验证。计算机系统是用来监控温度，传导率，水压和时间（小时）。另外，这个系统监督在……之间的微分压力（示例如下）
- The unit, used to compare the computer line's air pressure measurement readings with equipment air pressure measurements, has not been calibrated. 这个单元，用来比较计算机线路风压的测量和设备风压的测量并未校准。
- There has been no periodic maintenance to assure that the unit is operating appropriately.没有定期维修来保证这个单元准确的运行。
- Failure of the Quality Control Unit to establish a system for reviewing microbiological laboratory data to assure completeness and accuracy. 忽视了要 QC 部门来建立一个可以审核微生物实验室数据的系统从而保证它的完善性和准确性。
- Reviews of multiple entries in microbiology laboratory notebooks were not performed in a timely manner. For example…微生物实验室的笔记本中多条目的审核没有快速及时地得到执行。例如……
- Data (from this testing) was entered into the Laboratory Information Management System (LIMS) prior to the documented review of the data. 数据（来自测试）在数据审核记录前就记录在了实验室信息管理系统（LIMS）。

- Validation of the autoclave, used to sterilize equipment, stoppers and filled syringes, is inadequate in that:高温灭菌器的验证，不适合用来设备，塞子和满的鸣管消毒。
  a. The worst case load configuration has not been established. *(other examples follow)* a.最糟糕的病例数的构型还没有建立。（其它的例子如下）

483 D

W-029

Keywords: Client/server system, chromatography data system, user requirement specifications, change control, audit trail, file security and integrity, system security, back-up and recovery, WAN backup 关键词：客户/服务器系统，套色版数据系统，用户要求说明书，更改控制，查帐索引，文件安全和诚信，安全系统，备份以及恢复，广域网支持。

- Data transfer of a (chromatographic) client server system not validated 客户服务器系统的数据输送（色析法）没有得到验证。
- No documented evidence of validation of user requirement specifications 没有备有用户要求说明书的证明文件。
- No validation after hardware and software upgrades and configuration changes 硬件和软件改良和结构更改后没有进行验证。
- Insufficient security controls to prevent analysts from submitting modified data 提交的经过修正的数据缺少安全控制而阻碍分析。
- User can select programmable functions without record or documentation in the QC network system that could circumvent system and data integrity 客户可以不需要记录或者在网络 QC 系统中的文件中挑选有编程的功能，保持系统的完善性及数据的完整性。
- Each analyst has access to read/write, purge, copy, rename files 每个分析员都有权阅读/写，清除，拷贝重新命名的文件。
- Audit trail was intentionally disabled 查帐索引散失功能。
- Client/server passwords to access the system never expired and had only four characters 进入系统的客户/服务器的密码从没终止并且只包括四个字符。
- Authorized LAN access through corporate WAN users was not validated 经授权的局域网访问进入法人广域网用户没有经过验证。
- No documented evidence to demonstrate the WAN was capable of properly performing backup and recovery of

data on the QC server 没有证明文件来证明广域网在 QC 服务器上有足够的能力来完成做文件备份和恢复。

Warning **Keywords: Computer maintenance, computer validation, worst case testing, change control 关键词：计算机的维护，计算机的验证，最坏情况的测试，更改控制** D

W-028

- Failure to maintain a computer system with validated program capabilities 忽视了用验证程序性能来维护计算机系统。
- No testing of the computer system after installation at the operating site. 安装计算机系统后在操作的地方没有进行测试。
- No testing under worst case conditions 没有进行在最坏条件下的测试。
- The protocol mentions without explanation or supportive documentation, "historic experience" with terminals, but doesn't specifically identify the terminals 方案没有论及说明或者支持的文件，‘历史经验’的接线端，但是不能准确地识别接线端。
- The protocol lacks change control procedures 方案缺少更改控制的规程。

Warning **Keywords: Laboratory records, data integrity, equipment maintenance, part11 关键词：实验室记录，完整的数据，设备的维护** D

W-027

- Laboratory records are incomplete and inadequate. Data in numerous records were altered, erased, not recorded, recorded in pencil, or covered with white-out material. For example….实验室记录是不完整不充分的。许多记录的数据更改了，删掉了，没有记录上，用铅笔记录，或者被改正液覆盖。例如……
- Altered values were written under computer generated values. Review of electronic data confirmed the incorrect values 更改的评估记在计算机引起的评估中。电子数据的审核证实了不正确的评估。
- Two pages of laboratory notebook written in pencil were erased 实验室笔记本中用铅笔写的两页被擦掉了。
- Typewritten dates were pasted over computer generated dates 打字机打出的数据输出计算机里面的数据。
- The use log has no entries from Aug to Dec 17, 日志中没

有从 1999 年 8 月到 12 月 17 日 的条目。

- It is not possible to trace computer generated xxxx because they were not stamped 追踪计算机引起了 xxxx 是不可能的，因为他们未被盖印
- Equipment was nor properly maintained (explanation is given) 设备没有得到较好的维护（已经给出过说明）
- The qualification and maintenance of equipment used in, and the process validation of the xxxx system is inadequate. 用于 XXXX 系统性能验证和生产设备的限定和维护这些方面做得不够。

Warning **Keywords: security, data integrity, audit trail, equipment calibration, part11 关键词：安全性，数据完整性，查帐索引，设备校准。** D

W-026

- An employee user name and computer password were publicly posted for other employees to 'access the xxxx data management.雇员用户名和计算机密码公开地张贴，让其它雇员通入 xxxx 数据管理。
- Unauthorized access to a running system 对一个运行系统未经批准的通入。
- Access of previous employees to critical Data Management System functions 老雇员进入重要数据管理系统起作用
- Changes made to critical data base entries not electronically recorded or controlled by procedures 对没有电子记录或者由规程控制的重要数据库词条的更改。
- The RPM calibration and timer check of the centrifuge was not performed every 60 days as required in the written procedure and operator's manual. 可靠性能测定和离心分离机的时间校验没有像书面规程和操作人员手册里所要求的那样每 60 天执行一次。

Warning **Keywords: security, data integrity, database access, file privileges, equipment validation, training, part11** 关键词：安全性，数据完整性， 数据库存取，文件特权，设备验证，培训，第 11 部分 D

W-025

- Inadequate controls over computers and related systems to assure that changes in the master production and control records or other records are instituted only by authorized personnel 计算机和相关系统控制的不充分，保

证主要产品的改变和控制记录或其它纪录只由授权人员制定。

- No current listing of individuals who have access to the database program or to what level of access each individual has;当前还没有关于个人有权使用数据库程序或者个人有什么进入数据库程序的水平的列表。
- No procedure in place to grant, modify or remove access privileges to software 对软件没有规程到位准予，修改或去除访问权限
- There is no audit trail within the computer that identifies how many worksheets have been generated for a given sample number 计算机内没有查帐索引来辨认为一个特定的样品号产生了多少工作单。
- Worksheets and logs used to record raw data were available in the appropriate laboratories without any mechanism controlling their use 用来记录原始数据的工作单和日志可以在没有任何机械装置的适当实验室条件下获得。
- Procedures allow for managers to approve their own work. Work they perform and approve does not require the initials and signature of a second person showing that the work has been reviewed for accuracy, completeness and compliance with standards 规程考虑到管理人员来批准他们自己的工作，他们执行和批准不需要第一签字人和第二签字人的签名来说明他们的工作已经准确地，完整地符合了标准。
- There were no raw data indicating that cold spot mapping as part of steam sterilization autoclave revalidation was ever performed 没有原始数据表明，冷点映射出作为蒸汽灭菌器重新生效的一部分，曾经执行过。
- The validation of the Biotech Suite was inadequate in that there were no pre-defined criteria describing what the requirements of the suite, other than that of environmental monitoring, were to be, nor were there any pre-defined criteria describing what the requirements for the equipment of this suite were to be. Biotech　Suite 检验是不充分的，是因为没有预先确定的标准描述什么是组的要求，除了环境监测是之外，没有任何预先确定的标准来描述设备组的要求。
- There are no procedures defining training, qualification, disqualification and re-qualification of sterility suite operators when they exceed the microbial limits defined 没有规程定义的训练，有资格，没有资格和当通过微生物

限定定义重新恢复资格的操作人员。

Warning **Keywords: scientifically sound methods, cleaning validation Keywords 关键词：科学合理的方法，清洗验证** D

W-024

- Laboratory controls have not established that the test method for assay of xxxx content of xxxx 'is scientifically sound to assure that this product conforms to specifications of strength, quality and purity (examples: insufficient separation, no verification of method suitability under actual conditions etc) 实验室控制未建立，化验为 xxxx 内容为 xxxx 的科学合理的测试方法保证这个产品依照浓度的说明，质量和纯净(例子：分离不彻底,，在实际条件下没有适当的验证方法等)
- The calculation for assay fails to include a correction factor for the actual purity of the reference standard 化验演算未能包括实际纯度参考标准的修正因素。
- Cleaning procedures for process equipment used interchangeably to manufacture pharmaceuticals, including cosmetics, and invitro diagnostic solution. lack sufficient detail to assure contamination will not occur that could alter the safety. quality or purity of pharmaceutical products. *(examples follow)* ?用来更改生产药物的设备的清洗规程，包括化妆用品，和体内诊断解答的药物。 缺乏详尽的细节保证不会发生改变药物产品安全，质量和纯度的污染。 (下面是例子)
- There is no provision to document what cleaning chemicals are actually used. 文件中没有对化学用品的正确使用做规定。

Warning **Keywords: Clinical investigation, FDA access control** D

W-023

- You failed to permit an FDA officer to have access to and copy and verify records and reports relating to a clinical investigation conducted under Part 312. [21 *CFR 312.58(a)].* 您没有允许 FDA 得以进入复制和核实与在 312 部分指导下的临床调查有关的记录和报告。 [21 CFR 312.58(a)] 。
- You failed to provide access to the records for each subject you described in your Investigational New Drug Applications (INDs). 您没有对每次的描述新药调查应用（IND）中提供记录访问。

- You failed to provide a copy of the protocol to the Immunogenetics' Investigational Review Board during their review of your study, citing concerns about proprietary information. 您没有提供方案的拷贝还要修改！！！！！！！！！！！！
- You failed to withhold administration of an investigational new drug until an IND is in effect. 您没有制止一种正在调查的新药物的管理直到 IND 生效。

Warning **Keywords: out of specification results, cleaning validation** D

主题词: 不符合设计说明书的结果, 清洗验证

W-022

- Investigations and follow-up of out of specification results inadequate or incomplete and are inadequate or incomplete. 调查和跟踪不符合设计说明书的结果，不充分或者不完善，意见不充分或者不完善。
- Equipment cleaning procedures used for cleaning multiple use been validated. 验证用来清洗多种用途的设备的清洗规程。
- The computer systems used to control and/or monitor production, reconcile raw materials, assign batch numbers, and control solvents, have not been validated。用来控制和/或监控产品，调停原材料, 选定批号, 和控制溶剂的计算机系统还未得到确认。.
- Qualification of processing equipment has not been completed. 生产设备的限定条件还没得到完善。

Warning **Keywords: failure investigation. Retesting, OOS, cleaning validation 关键词：调查失误，再测验，不符合设计说明书，清洗验证** D

W-021

- Failure to perform a thorough investigation, including conclusions and follow-up, when your drug products do not meet their finished product specifications. 当您的药品不符合成品药的设计说明书时，疏忽了要进行一次彻底的调查, 包括结论和后续,
- There is no documentation available to demonstrate that an appropriate investigation is conducted to determine the root cause of batch failures. 没有可获得的文件来显示引导一种适当的调查来断定批失败的原因。

- Failure to follow your own SOP, "04-003 – Retesting 00S Results" for the investigation of out of specification results for your drug products. 未能遵循自己的 SOP，按“04-003-重新测试 OOS 结果”调查药品不符合计划说明书的原因。
- Failure to establish procedures for the cleaning of your drug manufacturing equipment that include a description, in sufficient detail, of the methods, equipment, and materials used to assure that the equipment is adequately cleaned. For example, ….. 疏忽建立一个药物生产设备清洗的规程，这个规程包括描述说明足够的细节，方法，设备，和用过的原料,确设备得到了充分的清洗。 例如，…..
- Failure to have written master production records that include complete manufacturing and control instructions, and sampling and testing procedures. For example *(examples follow)* 未能记录包括主产品完整生产和控制的说明，采样及试验过程。 例如(示例如下)

医课汇
公众号
专业医疗器械资讯平台
WECHAT OF
HLONGMED

hlongmed.com
医疗器械咨询服务
MEDICAL DEVICE
CONSULTING
SERVICES

医课培训平台
医疗器械任职培训
WEB TRAINING
CENTER

医械宝
医疗器械知识平台
KNOWLEDG
ECENTEROF
MEDICAL DEVICE

MDCPP.COM
医械云专业平台
KNOWLEDG
ECENTEROF MEDICAL
DEVICE