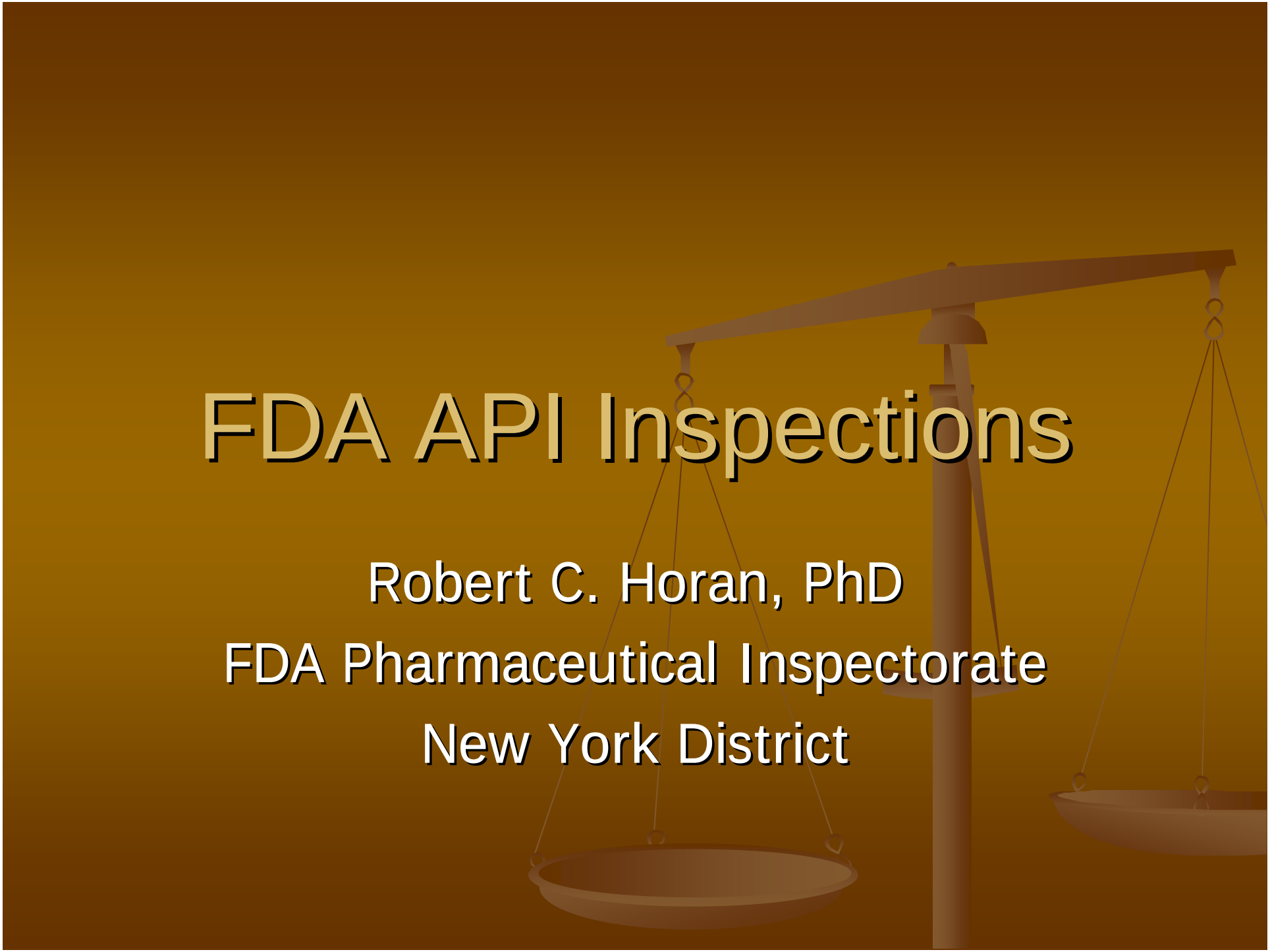

FDA API Inspections

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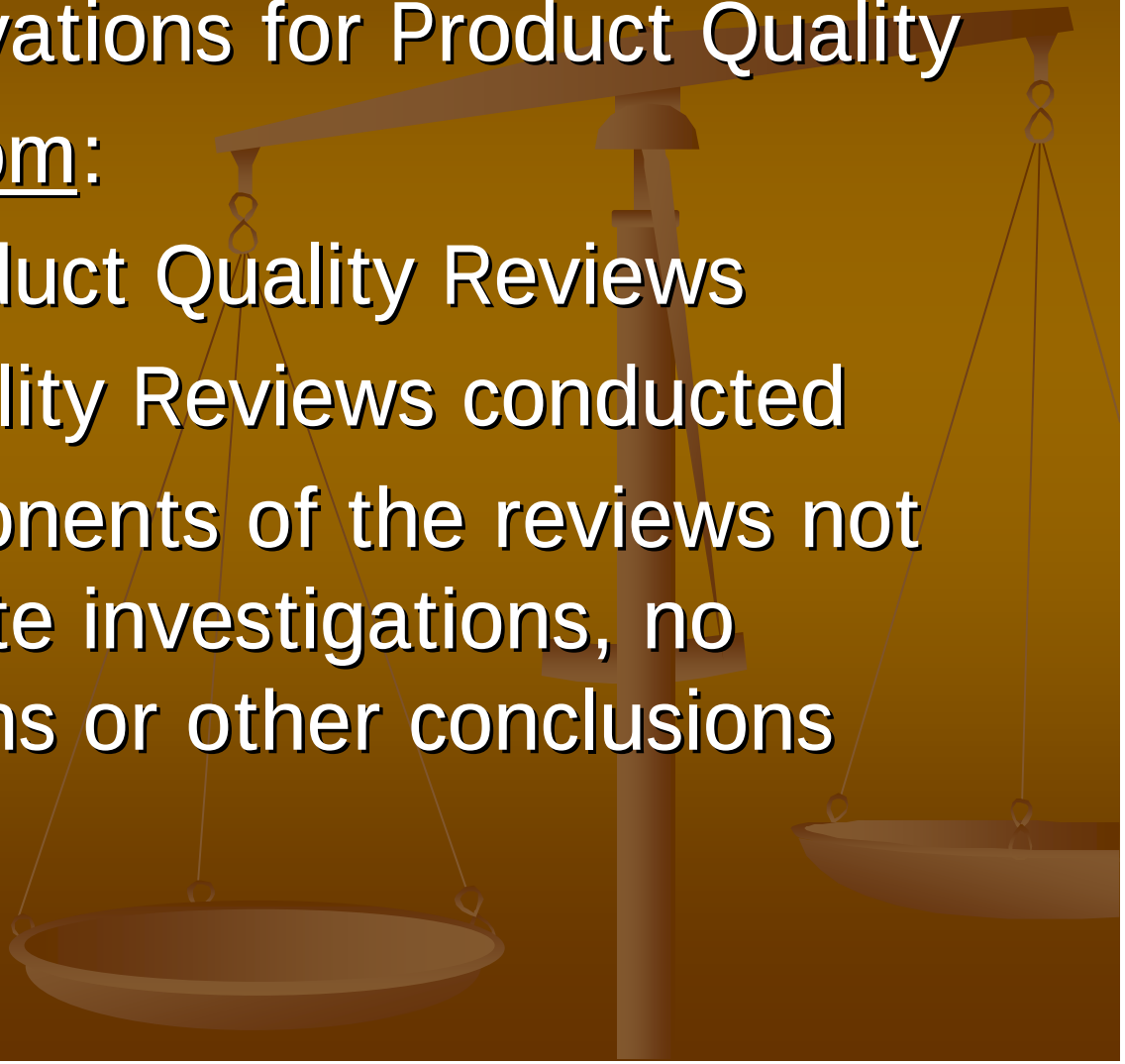
New York District

Quality System observations

FDA 483 Observations for Product Quality Reviews range from:

- No SOP for Product Quality Reviews
- No Product Quality Reviews conducted

to: Various components of the reviews not done, inadequate investigations, no corrective actions or other conclusions



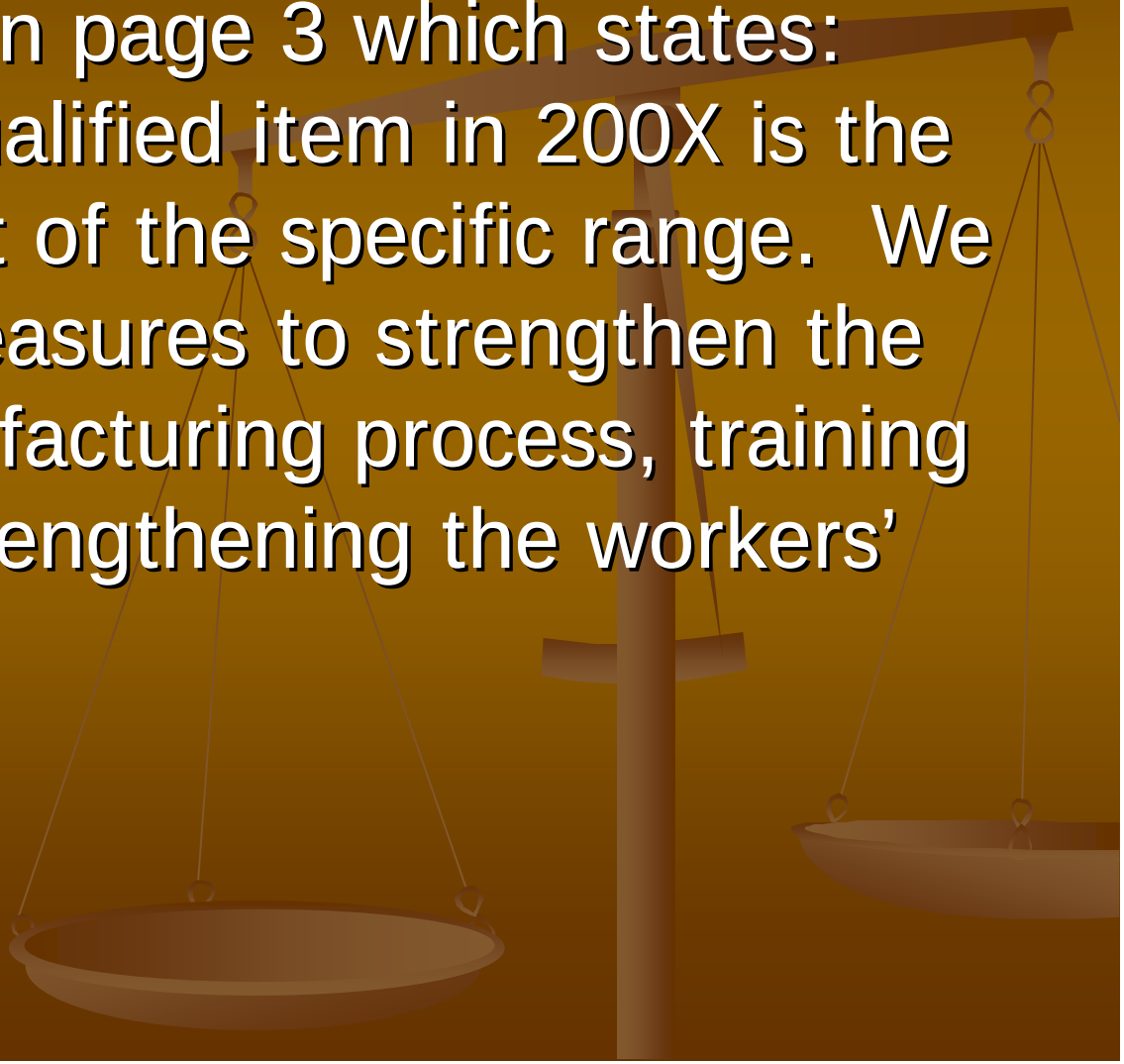
Quality System observations

Regarding the annual product reviews:

- The reports do not identify the specific batches which were covered by the review period and there is no evaluation of specific data from the batches covered.
- The annual report from 200X was found to contain some conclusions regarding out of specification data and corrective actions without providing specific information such as batch numbers, actual events, specific data, conclusions and any specific corrections made.

Quality System observations

An example is on page 3 which states: “The main unqualified item in 200X is the XXX content out of the specific range. We take relative measures to strengthen the control of manufacturing process, training the workers, strengthening the workers’ quality sense”.



Quality System observations

Many of the firm's written procedures (SOPs) have not been periodically reviewed and revised where needed to ensure that they accurately describe current procedures at the firm and are in compliance with cGMPs. Some of the SOPs were found to have approval dates as far back as 1994. Examples include but not limited to:

a) **********, revision 1, approved 10 Jan 1994

b) XXXXXXXXX, revision 1, approved 23 March 1998

Further, review of SOP XX found that it describes equipment which had been removed two years ago and the attachments "C" and "D" are no longer used for documentation and were replaced by other forms which were not attached to the SOP.

Quality System observations

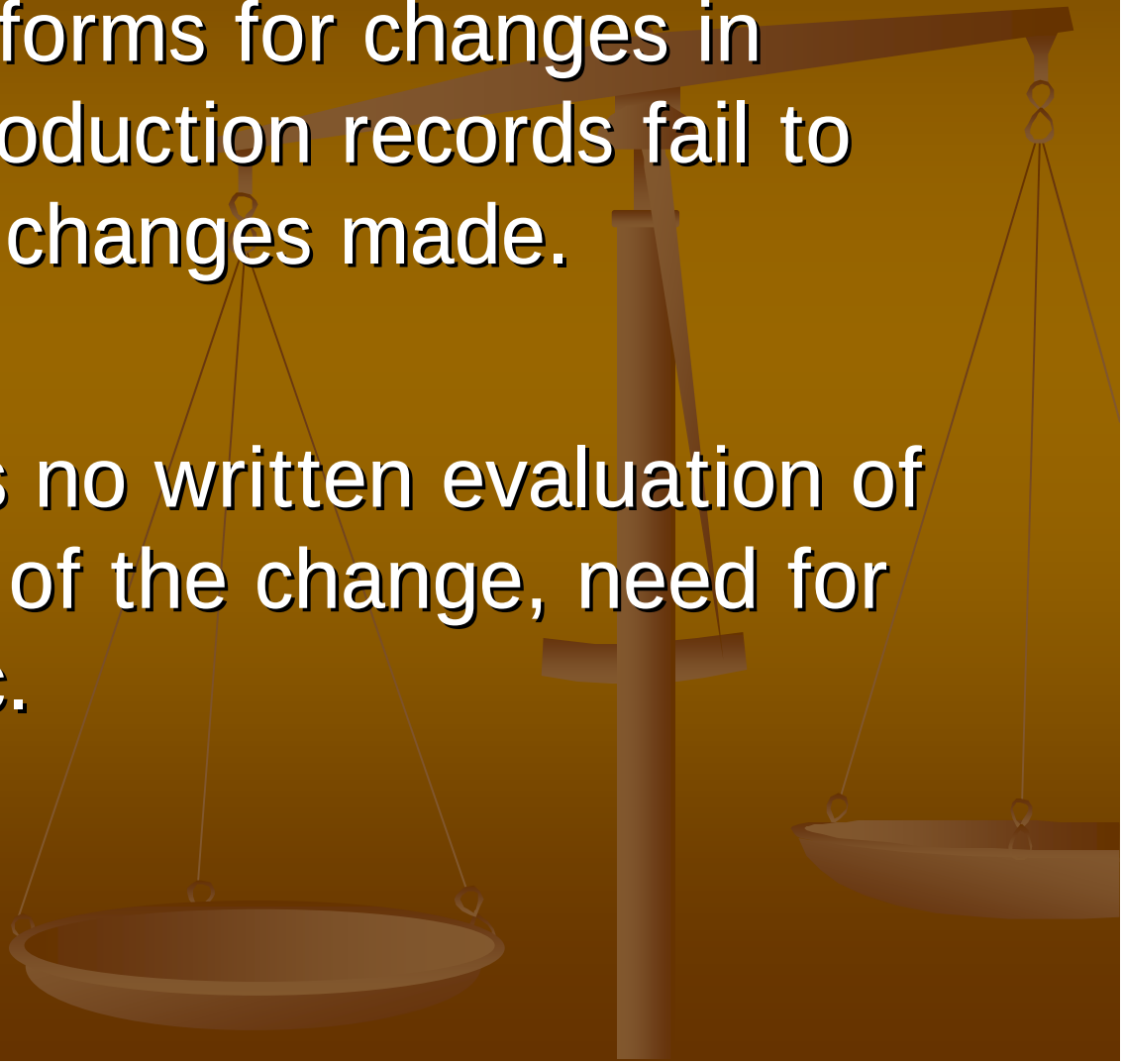
From a Warning Letter:

“Failure to establish corrective and preventive actions (CAPA) procedures for investigating the cause of non-conformities relating to product, processes and the quality system.

Specifically, the firm received – complaints related to..... You failed to follow SOP # -- in that investigations were inadequate and no CAPAs were implemented.

Quality System observations

- Change control forms for changes in Master Batch Production records fail to identify specific changes made.
- Further, there is no written evaluation of the significance of the change, need for re-validation etc.

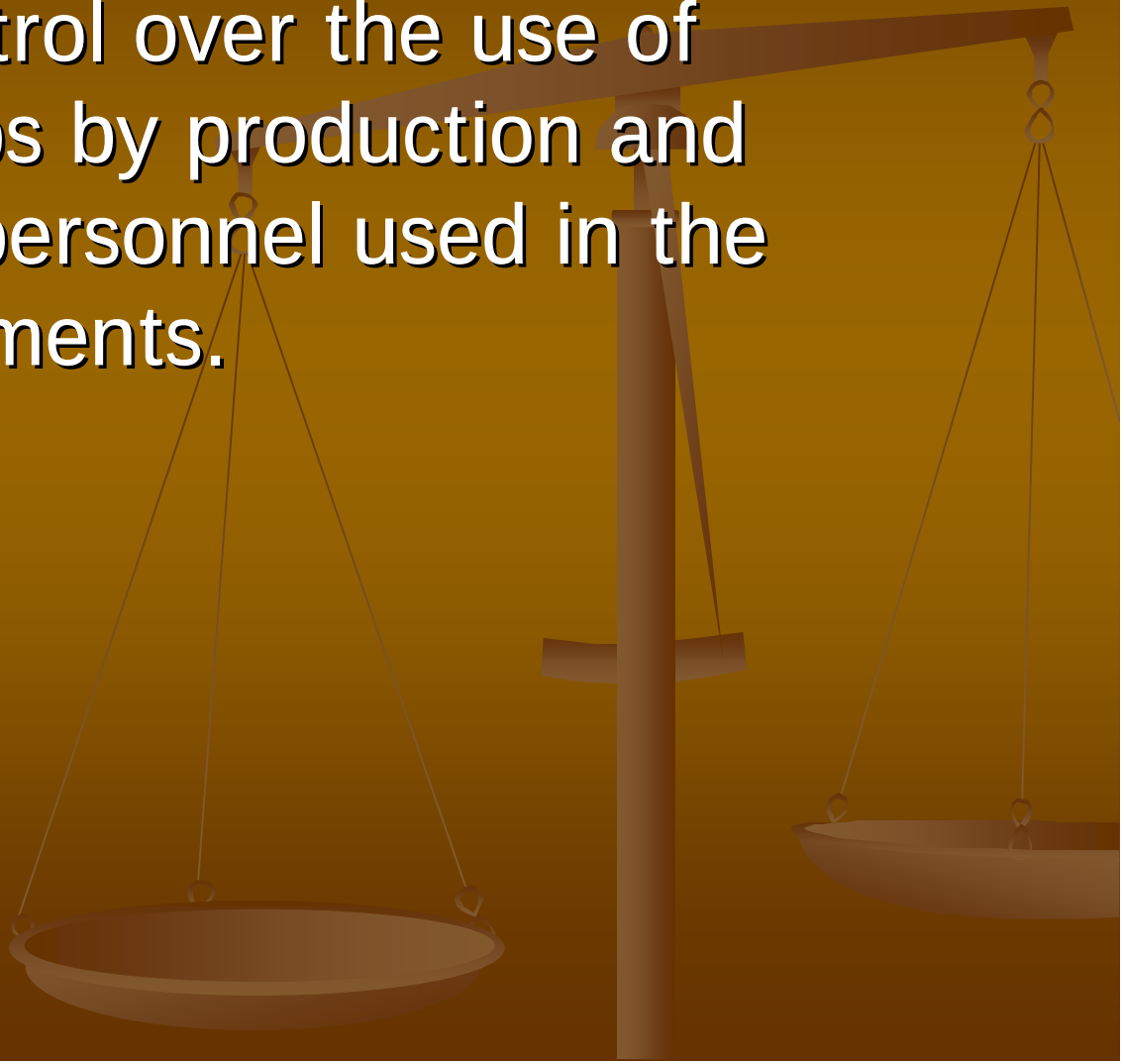


Quality System observations

Software change control reports were found to have multiple text changes made by means of “white-out” rather than by following the firm’s written procedure of crossing out the original text and initialing (stamp) the correction. Further, there were no written explanations given for the specific changes made.

Quality System observations

- There is no control over the use of signature stamps by production and quality control personnel used in the signing of documents.



Quality System observations

Process validation reports for API *** did not have criteria for acceptable reduction of the two specified impurities “eimp” and “fimp”. Batch record review (20 consecutive batches) found that post-validation batches showed typical levels of both impurities were much higher than in the validation batches. A number of batches exhibited “eimp” values that were more than double that in validation batches and approached the limit of 1.0%.

Quality System observations

SOP “QA Inspector in the Workshop” describes a twice daily check of equipment readings versus data recorded in batch records. Examination of several entries in the QA inspector’s log and corresponding batch records from those same dates/times found discrepancies between the QA inspector’s record and batch record data.

Quality System observations

Further, on (date), the QA inspector recorded a temperature of 0 C for the critical **** reaction step ------for batch ***, however, my examination of the batch record found that for that step which lasts 5 hours, the temperature never reached 0 C. In fact, the critical temperature range is 12 to 20 C and examination of 25 batch records close to dates for batch *** found

1) Examples of temperature exceed upper limit
2) No batches recorded a temperature of 0C.

Cited on warning letter

The firm's procedures for identifying and documenting problems that occur in manufacturing are deficient. For example, 235 "minor" deviations were logged year-to-date, of which only one was fully documented as a deviation investigation. Minor deviations that were not fully investigated and documented included:

Quality System observations

1) API ^^^ production lot *** failed to form final product crystals. The cause was attributed to an operator error and the charging of excess solvent. Non-validated measures were used to attempt to force the formation of crystals. The in-process lot was subsequently divided into thirds and blended into three other production lots that became finished API ^^^ lots ***, *** and ***. This was listed as a minor deviation and a full investigation was not performed.

continued

2) API ^^^ production lot *** yielded only 57%. The yield was approximately 30% below average. The cause was attributed to an initial high processing temperature caused by the computer system. No additional information or justification was provided; this was listed as a minor deviation and a full investigation was not performed.

Quality System observations

Review of a number of “oos” for potency in API ***, it was found that this was attributed to failure of temperature sensors on manufacturing equipment XXX and that the temperature had been out of the critical control range. In reviewing other deviation reports, it was found that following earlier episodes of “oos” potency values, there were corrective actions recommended including one to increase the frequency of calibrations of the sensing devices. Examination of the applicable SOPs found these recommended had not been implemented and no other corrective action taken.

Quality System observations

Action limits for testing of Purified Water have been exceeded several times without any investigations or completion of non-conformance reports. The test results were included in the Purified Water System Qualification report dated (date). For example, Use Point XX sampled on (date), results were “Unsatisfactory” for absence of clinically significant organisms (pathogens), User Point YY sampled on (date, three months earlier) had Total Viable Counts which were more than 10 times the action limit of X cfu/mL. This data was recorded in the final report signed by quality management.

Quality System observations

The written procedure (SOP XX-Y) for training of employees does not address the conduct of job specific, performance based training and there is no documented record of such training for quality control laboratory and production personnel.

Inspection found many production deviations where the cause was reported to be operator error and retraining was conducted. SOP XX-Y does not address the retraining of personnel and there is no documentation of retraining.

There are no individual training records for personnel.

Laboratory observations

- Calibration of pH meter #__ is done using buffers at pH 4.0, 7.0 and 9.0, however, it is used to measure the pH of *** which has an expected pH around 12.
- Balance # ___ used in the testing of *** is calibrated at ___ intervals using weights in the range *-*, however, sample weights as per the method for testing of *** are considerably below the lower end of the calibration.

Laboratory observations

- The identification test used for XX@-Na by FTIR compared the spectrum of XX@-Na against the spectrum for USP XX@. These spectra are not equivalent and are in fact quite different.

- Identification testing of API *** batches ...,...,...,...,... using IR was not actually done. The analyst simply used a previous spectrum and changed the batch number each time.

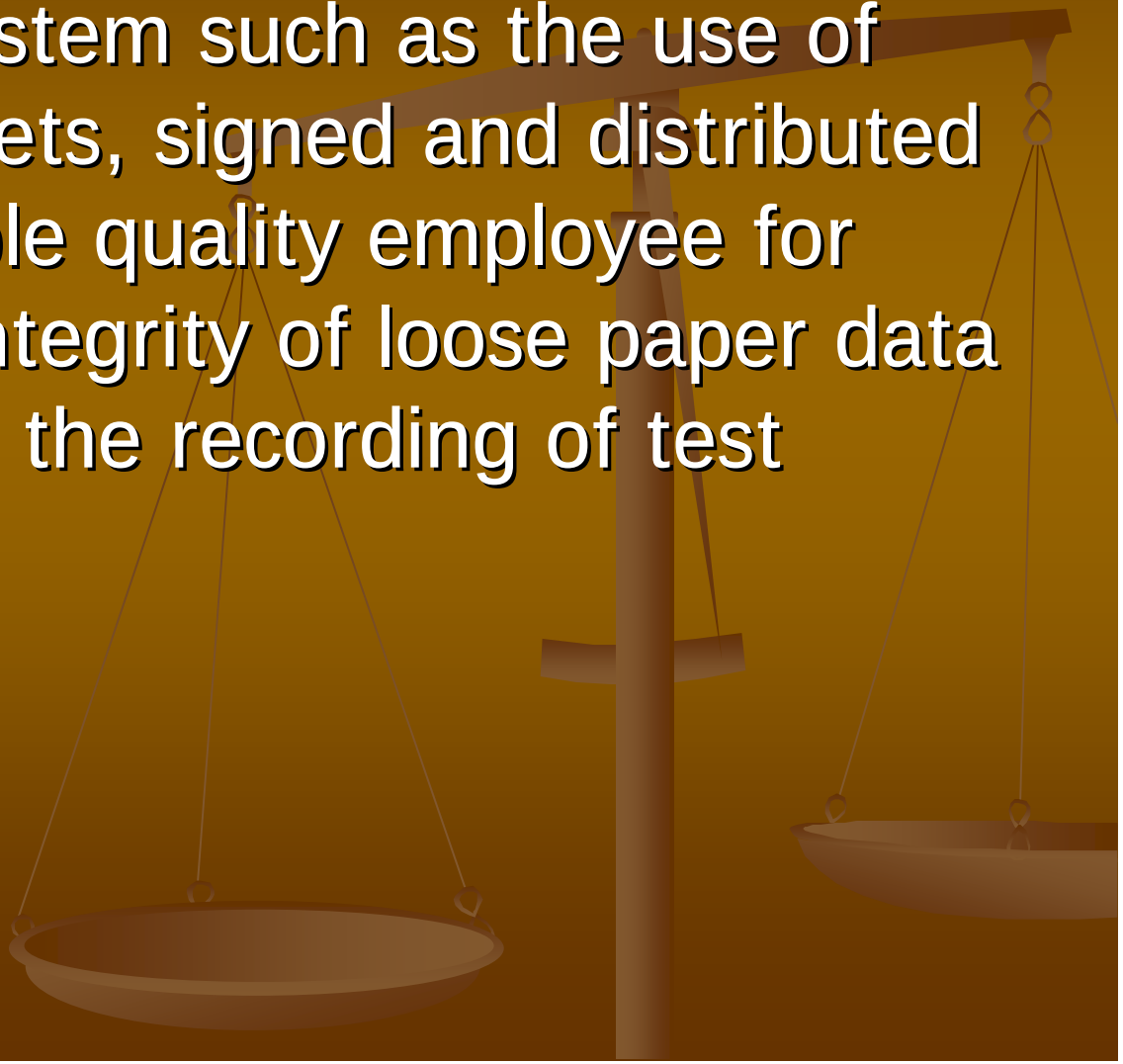
Laboratory observations

Regarding the computerized and paper systems used in the recording of quality control testing data for chemistry, microbiology and in-process production testing the following was observed:

a) The computerized (LIMS) system is not secure in that it is possible for data to be changed. This was observed following a request during inspection for a challenge to be performed. In performing the requested challenge, the analyst was able to change previously recorded input including sample gross and net weights resulting in changed assay results.

Laboratory observations

b) There is no system such as the use of pre-coded sheets, signed and distributed by a responsible quality employee for assuring the integrity of loose paper data sheets used in the recording of test results



Laboratory observations

Inspection of the QC and Microbiology laboratories found that analysts use loose printed sheets for recording raw data, there were stacks or pads of blank pages readily available.

In the microbiology laboratory, in response to a question about how the name of the product is stamped on the data page, an analyst took out a stamp and ink pad and demonstrated how it would be done. There is no procedure in place to insure the integrity of data sheets used in the QC laboratory.

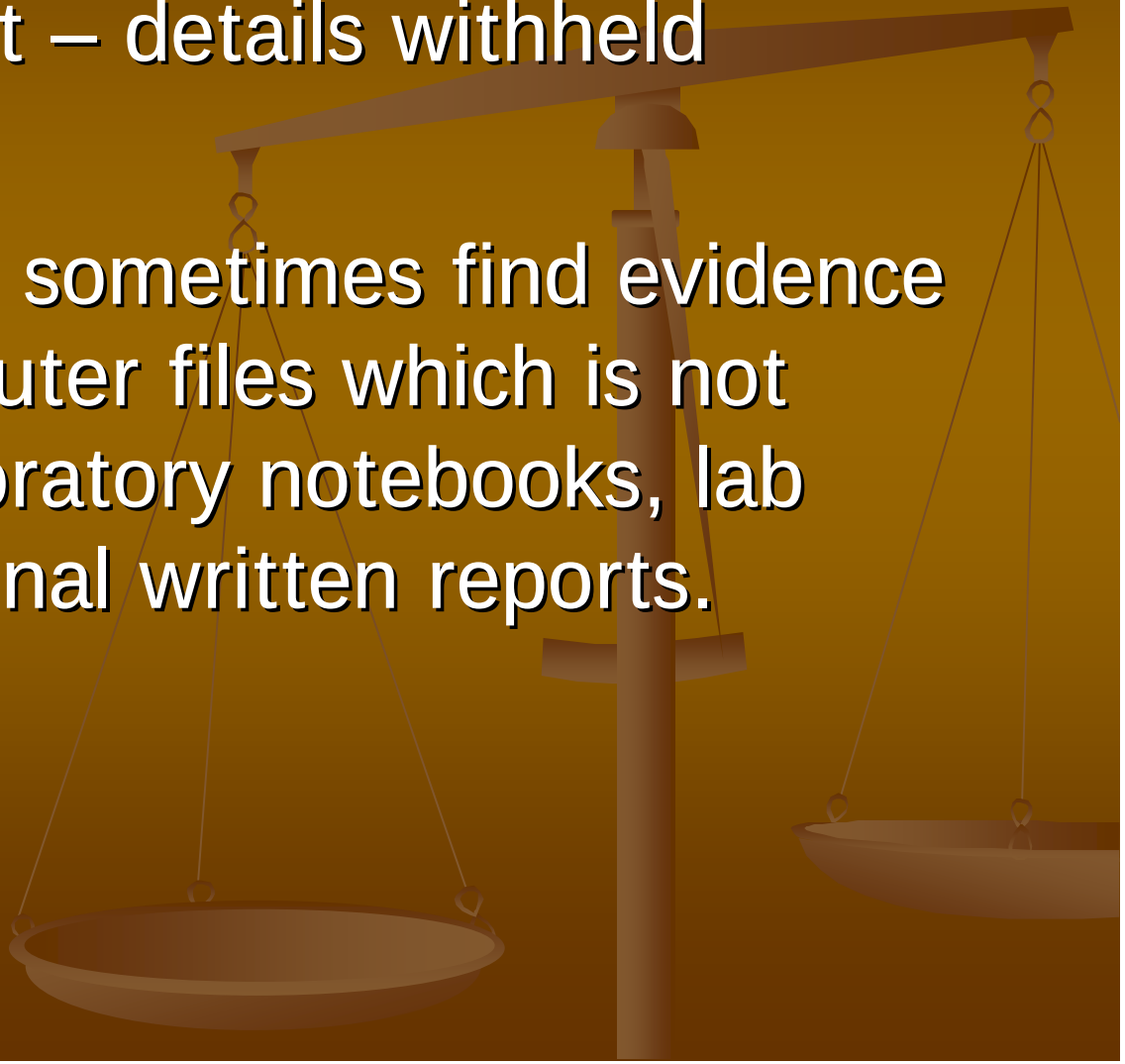
Laboratory observations

- Examination of the HPLC systems in the API testing laboratory found that for the *** systems, the audit trail function was not enabled.
- For the *** HPLCs, the audit trail function was enabled, however, the laboratory management has never conducted an examination of the audit trail on any of these instruments.
- No training of analysts regarding audit trail.

Laboratory observations

Generic Statement – details withheld

FDA inspections sometimes find evidence of data in computer files which is not recorded in laboratory notebooks, lab worksheets or final written reports.



Laboratory observations

The firm's QC chemistry laboratory has three HPLC systems and reportedly tests about 2000 samples per year, however, the calibration is done only once every two years (by government agency).

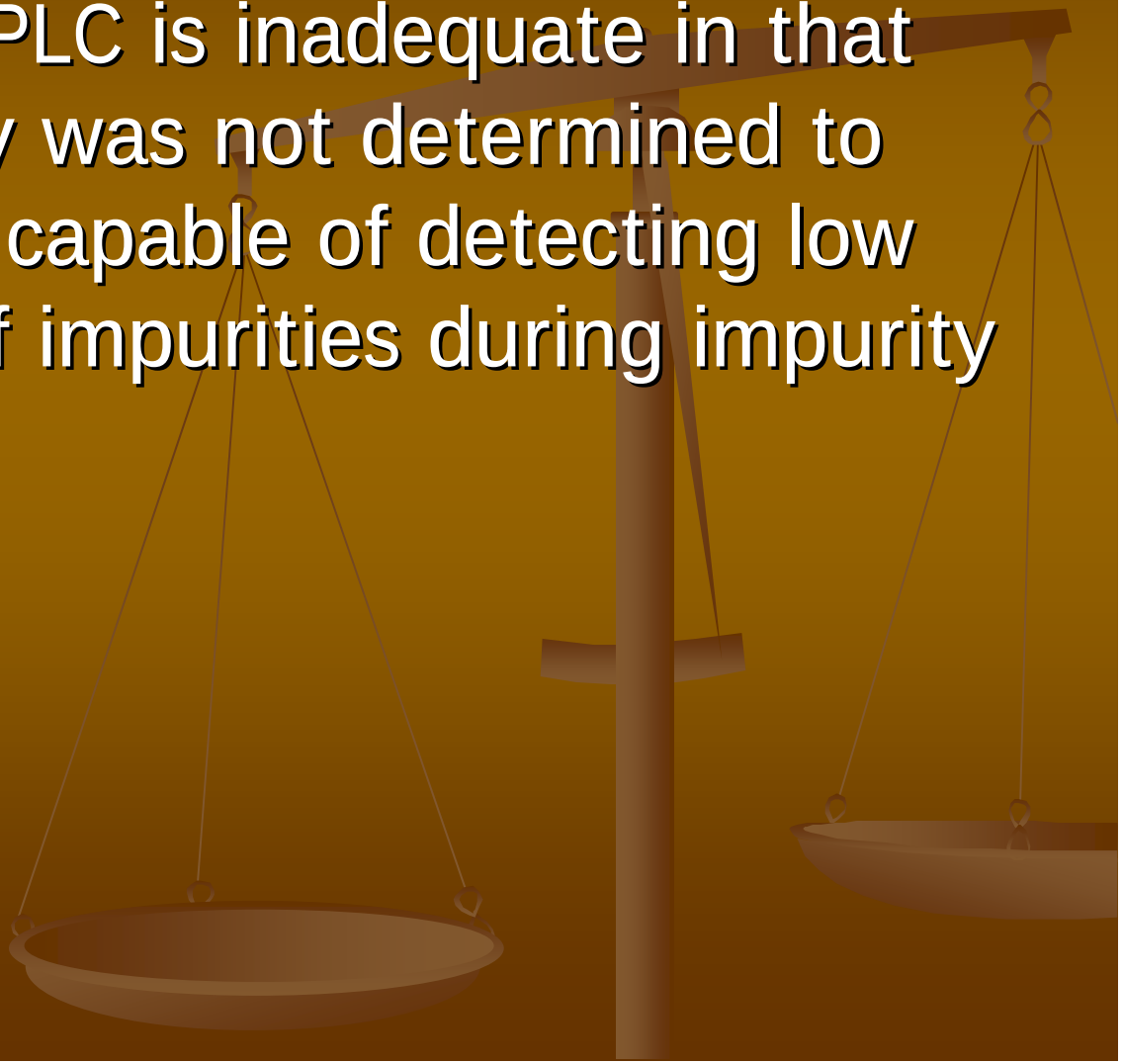
There is no established basis for not conducting more frequent full equipment calibration related to the high equipment usage.

Laboratory observations

Note: At least several FDA 483s have cited observations regarding incomplete information provided on certificates following their calibrations. It has also been cited several times that the factories receive no other information and that it is not possible for an adequate review to be done of the instrument calibration – either by the factory or outside auditor - such as FDA).

Laboratory observations

- Calibration of HPLC is inadequate in that the lamp energy was not determined to assure that it is capable of detecting low concentration of impurities during impurity determination.



Laboratory observations

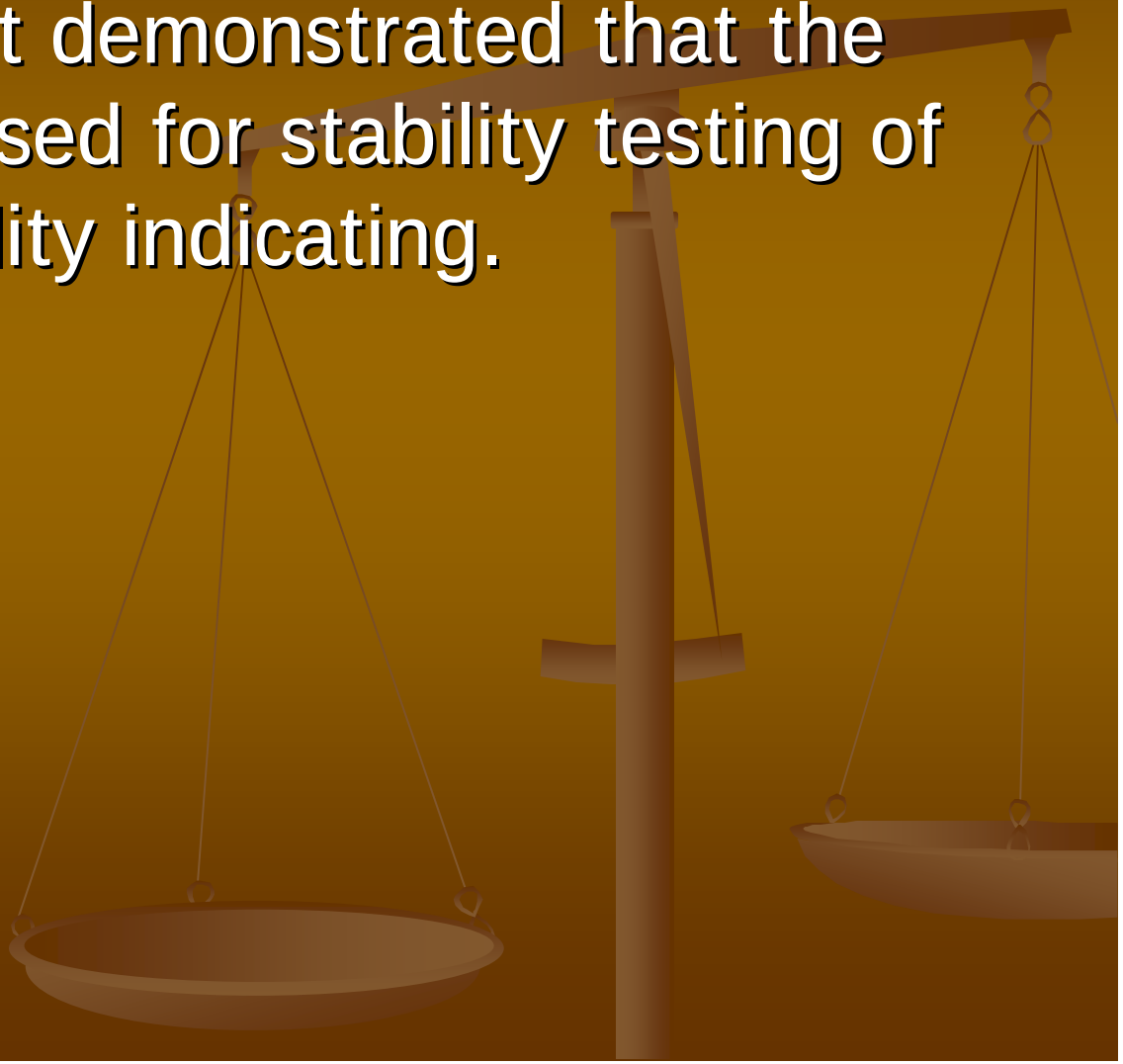
System suitability is not performed each time the HPLC assay method is run.

The firm has conducted system suitability only once in the history of testing API***.

The firm does no conduct system suitability each time testing is done as per USP.

Laboratory observations

- The firm has not demonstrated that the assay method used for stability testing of API *** is stability indicating.



Laboratory observations

There is no data available from the forced degradation studies which serve as the basis for demonstrating that the stability test method for testing of API stability samples is stability-indicating.

The management stated that at the time the studies were conducted in 200X, the factory was not retaining raw data.

(continued)

Laboratory observations

Further, there is no record of preparation of samples, sample stress treatments or the actual testing.

Finally, there is no record of the sub-dividing of stressed samples to prepare a sub-sample to be sent to a contract laboratory for the peak purity studies.

Laboratory observations

- For the related compounds methods for *** API, the procedure states to run the chromatogram for NLT 2.5 times the retention time of the API. Review of earlier test data shows that a significant recurring impurity elutes at approximately five times the retention time of the API, which could go undetected when following the instructions for chromatographic run time.

Laboratory observations

For several tests from the USP monograph for API ^^^, USP, the firm either did not perform the test or did not conduct it as per USP. For example, the UV identity test was not done and the IR identity scan in the batch records was simply a copy of a “representative” batch run previously; “the test for the specified impurity 4-XXXXX was not conducted for any of the batches examined (batches ***, *** and ***) and the “Crystallinity” test was not done.

Laboratory observations

- The firm's "out of trend" ("OOT") investigation for stability testing on three consecutive validation batches ****1, ****2 and ****3 concluded that the "OOT" result was due to analyses being conducted by different analysts on different instruments. The following is noted:
- The analysts were also reportedly trained and the instruments calibrated and deemed acceptable for the testing
- There is no documented basis for the investigation conclusion
- The conclusion suggests the method is not robust, however, the investigation did not address the significance for all other previous testing

Laboratory observations

- For the related compounds method for ***, several errors exist in the procedure that were not detected during the review process. These include the incorrect concentration listed for the stock standard and the incorrect dilution for the low level standard preparation.

Laboratory observations

- Following an out of specification result for *** in the 6 month stability sample of ***, lot ***, the analyst reported that the "Test FAILED" on the report sheet and forwarded this to the group leader, however, no action was taken. According to the laboratory manager, the sheet must have been missed and was not discovered for more than two months.

Laboratory observations

- There is no written procedure which requires the investigation, review and trending of laboratory deviations not covered by “oos” investigations.
- Inspection of product *** found that there were HPLC assays discontinued when an outdated reference standard solution introduced unknown peaks. The firm has stability data for 15 days use of *** reference standard solution and supervisor stated “We would not normally use such an old solution. It was done because standard is expensive”.

“oos”

The firm’s investigation of “oos’ test results for assay,, related substances and residual solvents for the two consecutive batches *** and *** of API ^^^ was limited to verifying that there was no laboratory error and the results were valid.

There was no evaluation to determine the root cause of the multiple critical specification failure, no extension of the investigation to consider the potential significance for other batches. The only further action taken was to reprocess the batches and sell them to the local market instead of U.S.

"OOS"

The firm received complaint of batches **** and *** of the API product ^^^ failing the related substances test for the single largest related substance. The API manufacturer investigated the original test records from (date) and found that the analyst had selected the wrong peak as the largest related substance peak.

The investigation was not extended to other batches. Review during the current inspection of test results from other batches found that the same analyst made the same mistake for several other batches. This had not been discovered by the API manufactuer's investigation.

“oos”

Inspection found that an “oos” for potency of API ^^^, lot *** was invalidated based solely on the testing of a new sample. Examination of the firm’s SOP PP-T, found the following regarding the procedure for “oos” investigations:

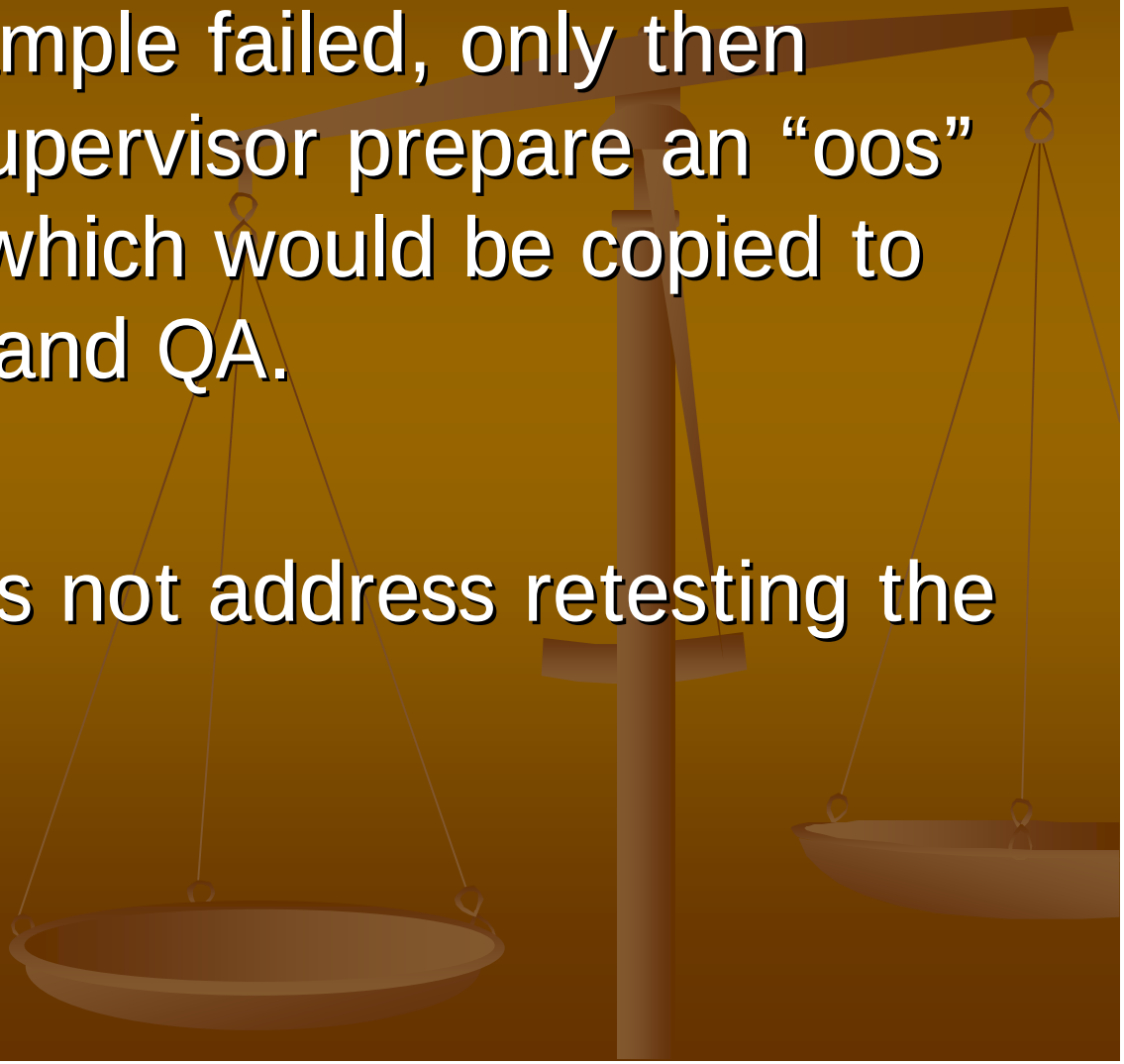
a) If an identified cause for the “oos” is not determined or not confirmed, then a second analyst will test a new sample.

b) If the second sample meets specification, the conclusion is made that the original sampling was flawed. (continued next slide)

“OOS”

c) If the new sample failed, only then would the lab supervisor prepare an “oos” reporting form which would be copied to production, QC and QA.

d) The SOP does not address retesting the original sample.



“oos”

Regarding the firm’s procedure for investigation of “oos” test results:

a) There is no log, file or other cumulative record of the firm’s “oos” investigations.

b) The annual product reviews do not include review of these investigations.

c) There is no time frame identified in the SOP for completion of “oos” investigations.

"oos"

(From an FDA letter sent to factory to indicate inadequate written response to FDA 483):

Specifically, we remain concerned regarding the consistency of the manufacturing process and/or analytical procedures.

The inspection revealed numerous "oos" assay results in different samples from batch *** as well as "oos" for two other batches within the same campaign. Some of the "oos" values were attributed to analytical error but the cause of others remain undetermined.
(continued next slide)

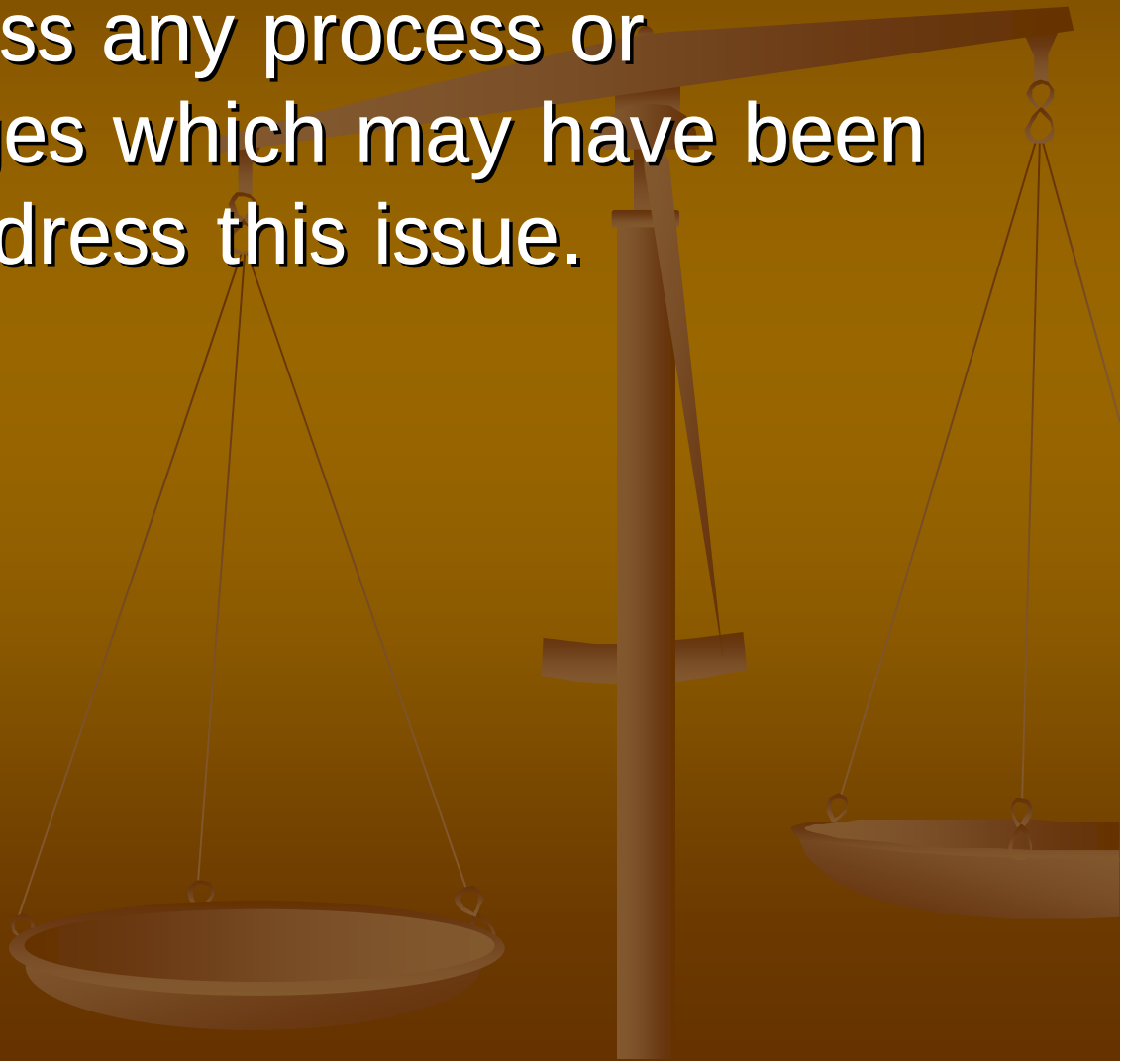
"oos"

Your written response indicates that the "oos" investigations will be closed out within 30 days and that new laboratory SOPs have been written, training has been provided to laboratory personnel, and additional laboratory personnel have been recruited.

Please provide the documentation that the "oos" investigations have been completed and that the cause of the "oos" assay results have been identified as either process related or analysis related. (continued next slide)

“OOS”

Please address any process or analytical changes which may have been necessary to address this issue.



Facilites & Equipment

- The firm's written procedures for preventive maintenance (PM) do not include examination and evaluation of all equipment components or schedule for replacement of parts. In this regard, there were three batches (***, *** and ***) which were reported in the annual product review to be contaminated with particles from a shredded Teflon gasket associated with the --- mixer. Inspection found: (continued.....)

Facilites & Equipment

a) There was no extension of the investigation to determine if previous batches may have been contaminated. In addition, the investigation does not document the identification of the contamination being consistent with Teflon particles.

b) The engineering management stated that while they are responsible for equipment maintenance, they have no PM procedures and stated PM should be the responsibility of production.

Facilites & Equipment

c) There are no PM SOPs in the production department.

d) The production department has a machine log for each piece of equipment, however, review of the machine log for the mixer found no record of the Teflon gasket replacement in the period following the reported contamination.

Facilites & Equipment

The investigation into lots of API ^ ^ ^ returned due to the presence of metallic particles does not include a measure to prevent future recurrence.

Please note: The following two slides list other observations on that same FDA 483.

Facilites & Equipment

Facilities & equipment in which crude APIs are exposed during processing are not maintained in a clean and sanitary manner and are not designed to prevent contamination of the crude APIs from foreign particles like dirt, rust, dust, paint chips and metal.

Facilites & Equipment

Then 483 lists a number of examples.....transfer of crude API from ----- reactor to centrifuge is performed underneath a metal platform in a building which is open to the outside; transfer to the multimill is performed in a room with peeling and flaking paint on walls/ ceiling; inside of the multimill granulator is corroded toward the bottom of the chute and was missing knives; interior of the vacuum dryer for crude API is rusted; transfer room of API to drums has peeling/ flaking paint on wall/ceilings.

Facilites & Equipment

In the warehouse for storage of replacement parts such as valves for the process water system and reverse osmosis membranes, there were numerous pigeons observed flying above the equipment parts and evidence of bird droppings. This included in the locked cage which contained the stored reverse osmosis membranes.

Facilites & Equipment

There are no piping or instrument drawings of the incoming source water, deionized water or Ultrafiltration Water systems to show current “as-built” components, treatment or distribution systems of water, for the purpose of system maintenance, monitoring and operation.

Facilites & Equipment

Welds used in the initial installation or replacement of critical equipment components are not examined, not electropolished or in any other manner evaluated against acceptance criteria.

Several investigations of microbial contamination implicated residual weld material as a principal contributing factor.

Facilites & Equipment

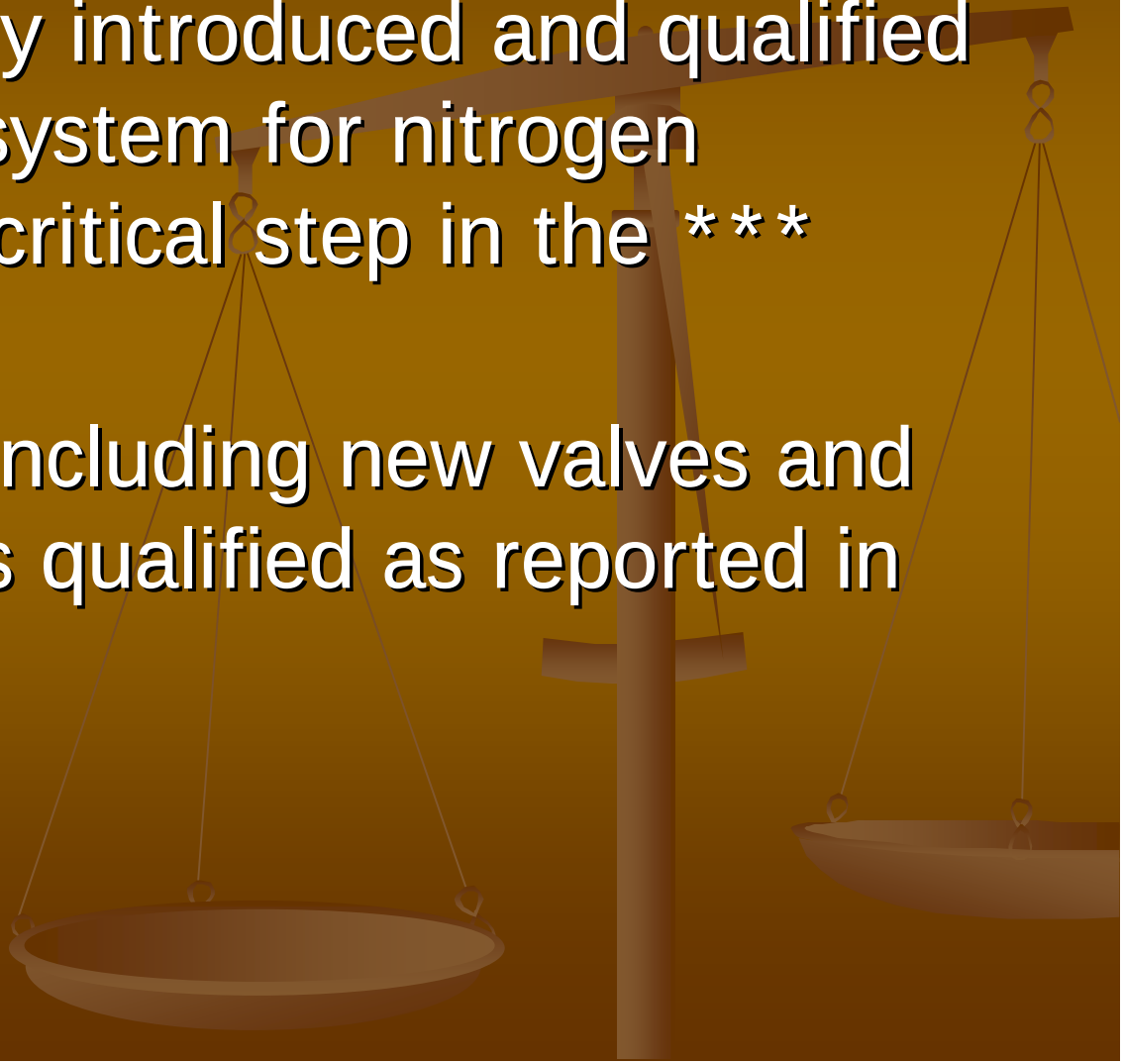
There is a dead leg of at least 1 foot in length between the crystallization vessel XX (for purified API) and the centrifuge.

(Note: This was from a previously used connection to another piece of equipment – no longer is use – now capped)

Facilites & Equipment

The firm recently introduced and qualified a new delivery system for nitrogen blanketing of a critical step in the *** process.

The system including new valves and flow meters was qualified as reported in IQ, OQ reports.



Facilites & Equipment

- Inspection on (date) found that although the replacement valves associated with lines X and Y were closed, the nitrogen flow meter display indicated a significant nitrogen flow to line X.

- (NOTE: The initial change was made to deal with intermittent flow problem. Following the inspection, the firm determined that the new valve design was faulty/ not appropriate for the intended use and replaced all of the valves).

Facilites & Equipment

Equipment cleaning deficiencies include:

a) Product residues were visible in numerous pieces of equipment labeled as clean (including fluid bed dryers, centrifuges; one vessel which was stated to have not been used in several weeks had yellow-brown residue, no status label)

Facilites & Equipment

- b) Tape on discharge chutes of centrifuges and other surfaces with potential for product contact.
- c) There were rough welds on the product contact surface of the hopper used to charge purified product to the dryer.

- (Risk for next batch ? Degradants ?)

Facilites & Equipment

According to the firm's written procedure (SOP XX-Y), the cleaning of Sparkler filters requires that at the completion of a campaign, the equipment is dismantled and all components thoroughly cleaned. Examination of Sparkler filters #s *** and *** found the bolts to be worn/ stripped.

Facilites & Equipment

The firm's maintenance employees in the presence of the plant manager and the FDA investigator were unable to remove the bolts using dedicated tools. The firm has no individual equipment cleaning record and the batch documentation records only that all equipment in the "train" was cleaned.

Facilites & Equipment

The Ultra-Filtered (UF) Water system which produces water used in the critical steps of API production was observed to have ball-type valves at numerous locations including in the finishing area for the final API ******. These valves are potential “dead-legs” in the UF Water system. (API ****** is intended to further processing to manufacture sterile products for injection.)

Facilites & Equipment

The piping throughout the purified/UF water system is ABS plastic pipe and elbows and the line leading to the stainless steel holding tank (ABS) attaches to a stainless steel line by means of a flange. It was stated that the water in the line before the storage tank is drained at times when the system is not producing water, however, it was noted that the ABS line to the flange slopes in a manner which would not promote adequate drainage and, therefore, could promote biofilm production.

Production observations

The firm's SOP XX states that batch production records for use in production are photocopied from the master record, however, examination of executed batches found that:

- Batch production records are not an accurate reproduction of the master.
- The following steps lacked instruction details given in the master records:

  (6 examples listed on FDA 483)

Production observations

This observation was on FDA 483 and then cited in a letter from FDQ CDER to firm:

"The master production and batch production records for APIs ***, ^^^ and +++ are deficient in that they do not require documentation of all significant steps and in many cases are unclear. (Ten examples given on FDA 483)."

Production observations

From an FDA 483:

Stage IV master production record does not specify the mill speed nor the screen to be used during milling and this information is not recorded in the batch record. Additionally, the master record does not specify the screen to be used during seiving.

Production observations

From Regulatory Letter:

We also have concerns regarding particle size specifications in which all four prospective validation batches failed to meet the release specification.

(Note: The letter then reports the fact that inspection found that firm actually used different equipment from that described in manufacturing instructions and validation protocol).

Production observations

In the crystallization step to obtain crude ***, the manufacturing instructions state to add 100 Liters of xxx dropwise within 5 to 10 minutes. When it was pointed out that this would be more than 3000 drops per second (in 10 minutes) and that the same instruction is given in the (original language version), the firm's (management title) stated that discussion with the production personnel found that this is accomplished "roughly" in the time period mentioned in the batch record by means of a valve.

Production observations

- It was noted that, in contrast to other manufacturing steps which provide details, there is no instruction regarding use of valves or other means of controlling the flow.

  (Note: There was suggestion at one point that the word “dropwise” came from pilot scale batches but no documented evaluation of the criticality of the rate of addition and how “dropwise” should have been converted to an accurate instruction for the scaled-up batches).

Production observations

- Inspection of first batches of new product *** found that the first batch failed specification for --- and this was related to a critical step. Batch rejected. Corrective action, change critical process step time from 20 minutes to 30 minutes.

(see next slide)

Production observations

- Examination of batch records for product +++ which has similar critical step states in the manufacturing instruction:

“ Perform operation --- for twenty (30) minutes”.

- There is no record of the actual time it took for the operation, yet every batch record has two signatures verifying step done as described.

Production observations

From Warning Letter ("****" from FDA not by RCH)

Several batches of API are *** in a *** to produce one large batch. The individual batches are not tested for residual solvents and found to meet appropriate specifications prior to ***. This process has not been validated for *** of the combined batch. The *** is tested for residual solvents, but the sampling method, one composite sample, does not provide evidence of ***.

Production observations

- Inspection of the manufacturing facility on (date) at (time) found that while the two batches of ***, lots ----- and ----- had just begun the XXXXX step, the BPRs were signed by two operators verifying that the 9 step process had been completed.
- Further, the production QA employee signed the sheet stating that the above was reviewed and approved.

Production observations

Examination of reactor GLR # XXX in use for the ****** step (critical step) for batch $$$$$ of the API ***** found that the thermometer which extends into the reaction mass could not be read. The QA Manager who was accompanying the inspection examined the batch record for that batch, then leaned forward, examined the thermometer and stated that the temperature was XX C which she stated was “right on target”. (continued)

Production observations

I asked for the production manager to examine the thermometer and it was determined that not only could it not be read, the thermometer bulb was broken and the fluid had emptied. It could not be determined when the thermometer had broken nor where the contents of the thermometer had gone.

Production observations

- Inspection found that the initial production deviation report # D-XX stated that batches ##### and +++++ of the product *** from a campaign in (time period) were rejected due to failing potency results. An amended deviation report prepared just the week before the current inspection reported that operators admitted to not adequately monitoring the critical step X.00Y and simply recorded results typical of previous batches. (continued)

Production observations

The amended deviation report:

a) Failed to explain how the workshop supervisor was able to sign the batch record stating that he had observed the monitoring of the batches and that it had been done as per written instructions

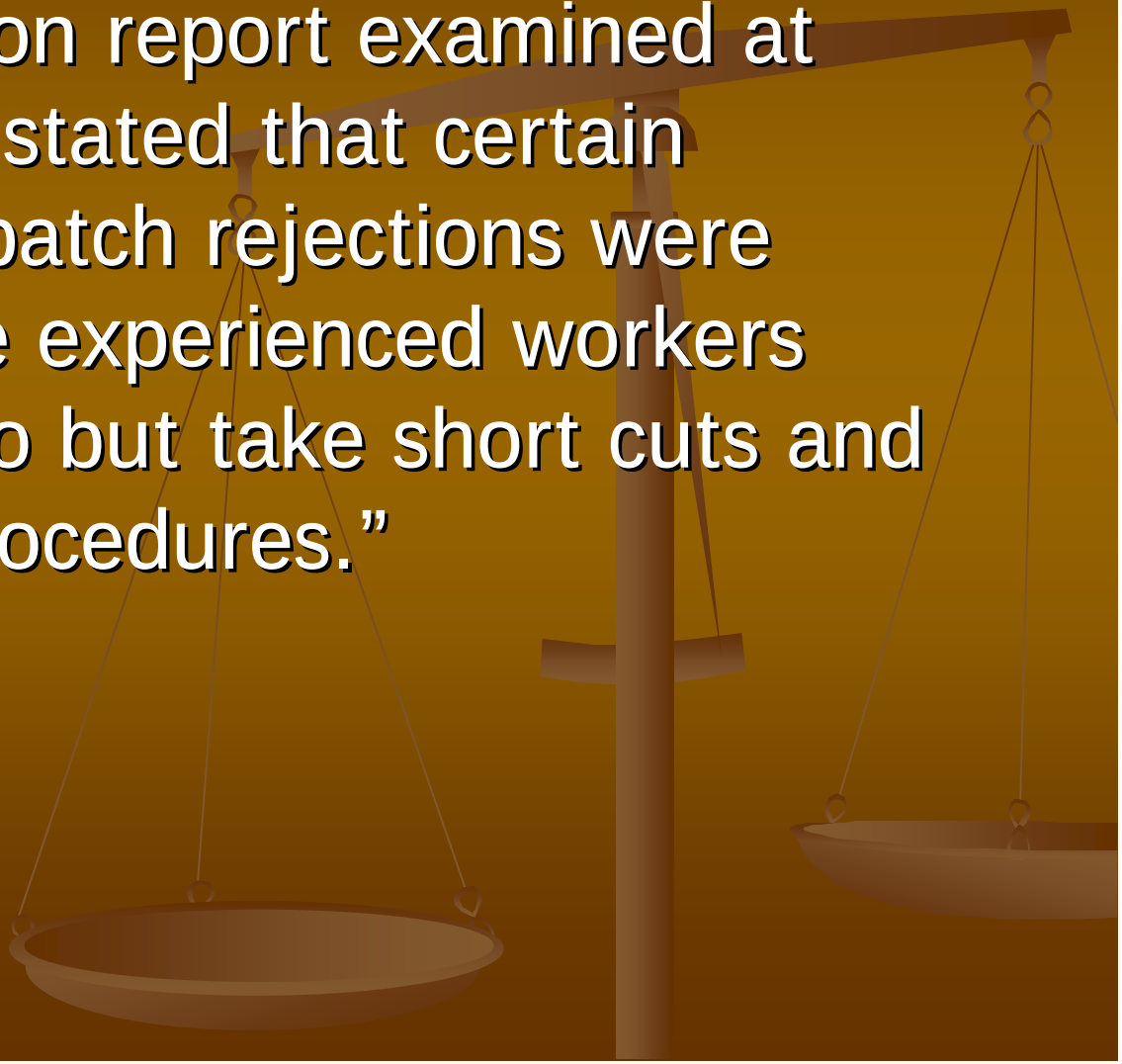
b) Failed to document an extension of the investigation to determine if there were other batches for which the operators had not properly monitored and documented the reaction progress.

Production observations

Related to the previous observation, a production employee from that shift who was reprimanded reported that for a previous batch ***, there was a spill of the final product blend from the blender onto the floor of production room XX and the employees swept the batch with broom and with scoops and reloaded the material back into the blender. According to the investigation report written five months after the event, the team leader was confronted and acknowledged this had happened. This incident had not been documented or reported at the time it occurred.

Production observations

Note: A deviation report examined at another factory stated that certain deviations and batch rejections were related to “More experienced workers know what to do but take short cuts and do not follow procedures.”



Materials observations

(From a Warning Letter) Sampling and Testing of incoming xxx used in the manufacture of API *** were inadequate:

- At least one specific identity test to verify the identity of the incoming material was not conducted.
- The reliability of the supplier's certificate of analysis (COA) was not established in that a complete analysis was not performed and compared with the COA at appropriate intervals.

Materials observations

(From a Warning Letter) Procedures for the recovery of solvents were inadequate:

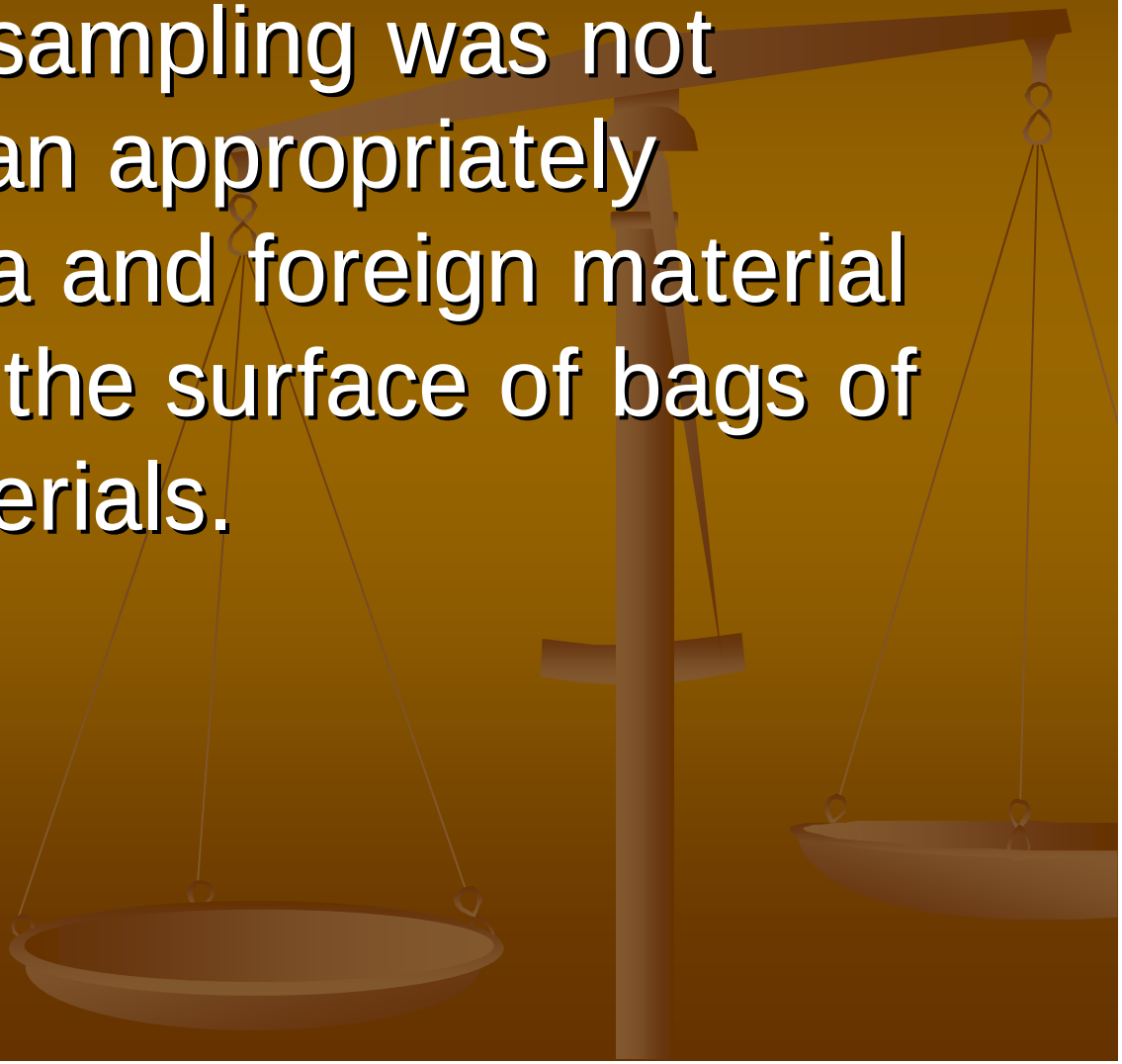
Procedures for solvent recovery had not been established to ensure that solvents are controlled and monitored to assure they meet appropriate standards before reuse or commingling with other approved materials. (FDA 483 observation concerned co-mingling recovered solvent with fresh solvent before testing of the recovered solvent).

Materials observations

Recovered solvents were not adequately controlled in that a drum of recovered chloroform was observed stored in the area identified for storage of recovered ethyl acetate. (From a Warning Letter; the actual FDA 483 observation also pointed out that the recovered chloroform was in the middle of several drums of the other solvent).

Materials observations

Raw material sampling was not performed in an appropriately controlled area and foreign material was noted on the surface of bags of approved materials.



Materials observations

Sterile PE film used during production to form sterile bags for the finished product is gamma irradiated in a validated sterilization at another firm, however, the integrity of this film may potentially be compromised prior to use due to the practice employed in sampling for release for production. The PE film is transferred to the production area (class 100), sampled, resealed and transferred back to the warehouse with “Release” stickers place of the original cardboard boxes in which the rolls of PE film are stored.

Materials observations

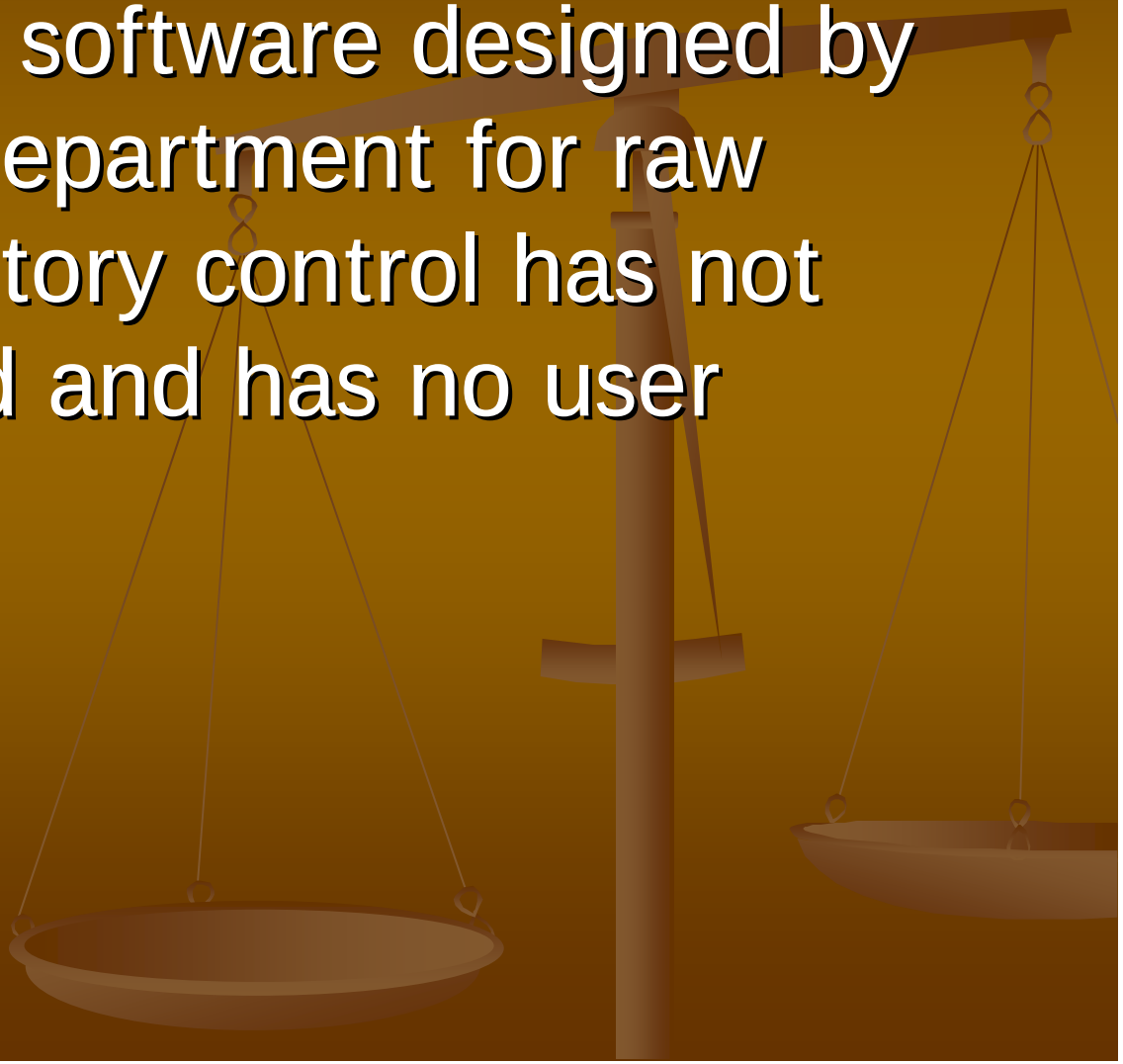
The firm has out-sourced the testing of API ^ ^ ^ for residual solvents and does not request testing of residual solvent for every batch of product manufactured. In addition, review of two test reports from the contract laboratory, selected at random, found that despite the fact that the firm's batch records and the DMF show ethanol to be the only solvent used in the process, the test results showed benzene to be present at levels more than 20 PPM. (continued)

Materials observations

Finally, the firm reportedly sends recovered solvent to a contract firm which performs further purification, however, there were no records present to support this arrangement and in response to my inquiry, it was stated the factory has never audited the contract firm which purifies the solvents.

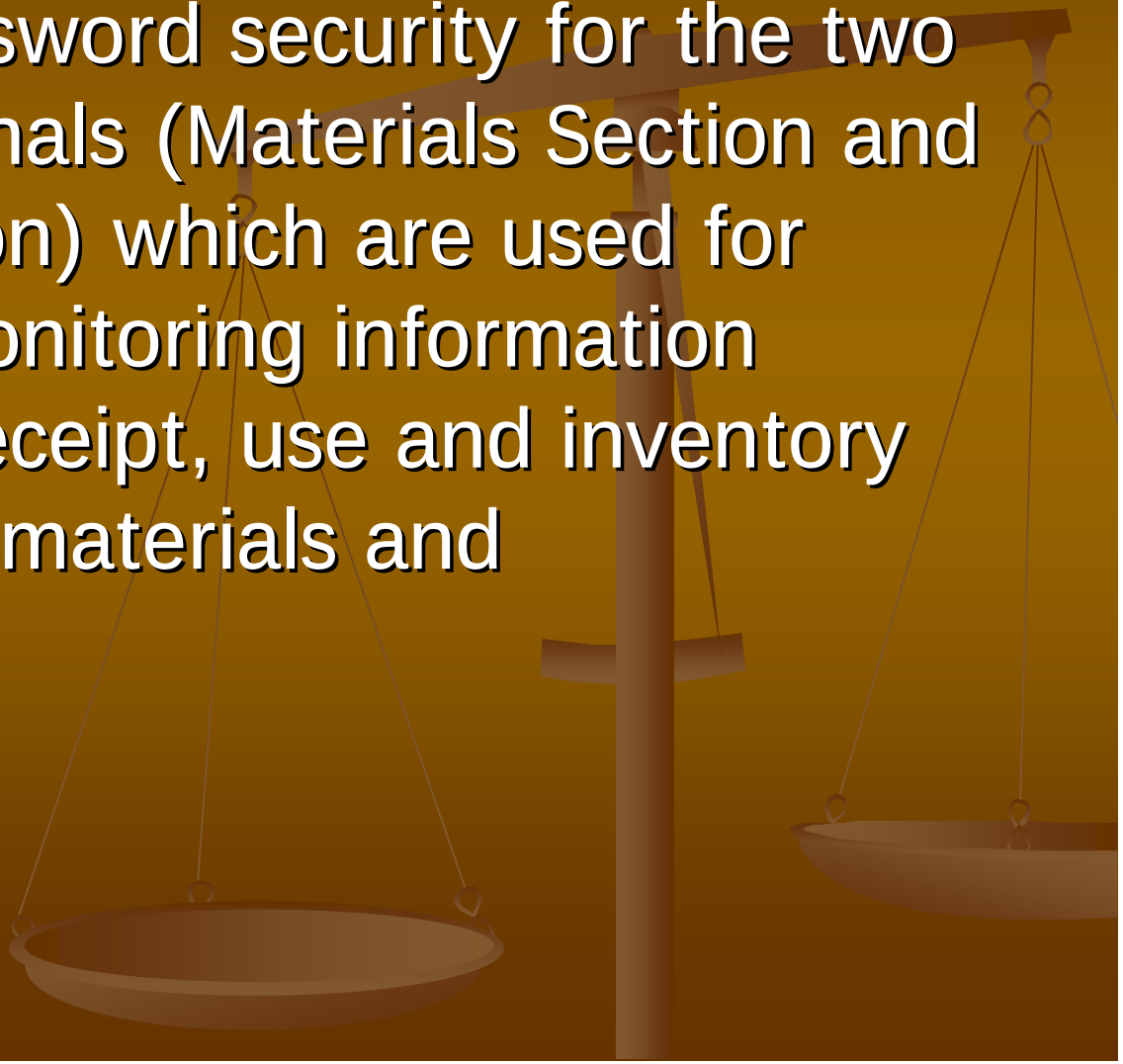
Materials observations

The computer software designed by the firm’s IT department for raw material inventory control has not been validated and has no user controls.



Materials observations

There is no password security for the two computer terminals (Materials Section and Synthesis Section) which are used for entering and monitoring information regarding the receipt, use and inventory records for raw materials and intermediates.



Packaging & Labeling observations

- Failure to have a written procedure for receipt, identification, quarantine, sampling, release and handling of labels
- Incoming labels are not proofed against a master label.
- There is no specimen labels placed in the executed batch records.

Packaging & Labeling observations

- There is no procedure to reconcile the quantities of labels issued and returned or destroyed.
- Final product labeling for API *** lacks retest date and storage temperature.
- Labels on drums of finished API not sticking. (Note: Inspection found solution employed was use two labels – hope one sticks).

Packaging & Labeling observations

The written procedure (SOP) covering labeling of finished product, i.e., printed bags stamped with lot number does not address the details of label issuance or reconciliation following the labeling operation.

(Inspection found printed bags with two API batch numbers in packaging staged for use in packaging of those batches. The accompanying paperwork recorded numbers of bags issued and returned even though operation not yet started.)