VALIDATION OF A DSI / NOTOCORD HEM 3.5 TELEMETRY SYSTEM FOR USE IN DOGS

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ABSTRACT

The validation of a DSI / Notocord telemetry system was conducted in order to confirm its function and performance with respect to data integrity, accuracy and reproducibility as per FDA GLP Regulations and the Electronic Records; Electronic Signatures (21 CFR Part 11). The intended use of the system is to collect electronic data records, with electronic signatures, based upon ITR's interpretation of the rule. The validation was assembled from Installation (IQ), Operational (OQ), Performance (PQ) Qualification Test Scripts (TS) and from the results obtained by the conduct of a study with conscious Beagle dogs implanted with telemetry transmitters. All test scripts were designed at ITR by members of the validation team (including pharmacology (scientific and technical), IT, QA and senior management). Following the IQ and OQ testing and as part of a PQ testing, positive controls were administered to the dogs and the cardiovascular effects were monitored for long periods without human intervention or contact. The system was able to detect the expected increases of both pulse rate and heart rate following the administration of Isoproterenol. The second positive control substance, L-NAME, induced the expected sustained increase in blood pressure in the four treated dogs. The results obtained from this validation study showed that reporting values over a period of 5 minutes for parameters acquired by telemetry, allows measurement over several heart beats and provides accurate results. The validation also included a retraceable Excel reporting workbook that links data in a flexible but secure manner.

VALIDATION APPROACH

- According to an internal SOP (Computer System Validation)
- Qualification of the system with series of test scripts for Installation, Operation and Performance of the system
- Coverage of the Functional Requirements Specifications

VALIDATION TEAM

A good collaboration between each group for a successful validation approach

End users:	define and document user requirements, develop test plans, co-provide resource for qualification, methods for usability and practicability, system performance, system training
MIS/IT:	informatics infrastructure, installation and maintenance, co-provide resource for qualification, develops test plans, tools for data security/back-up/archiving, system change control, networks training
QA:	provides quality assurance expertise for the plan and deliverables, monitors compliance with regulations, audits, training for application of regulations
Management:	provides sufficient resources, oversees validation

QUALIFICATION

Using Test Scripts written at ITR, with the software user manual and in collaboration with the vendor

IQ: by vendor and MIS/IT
OQ: by end users and MIS/IT

- Access manager
- Functionality (with a simulator = controlled tool)
- Reporting
- Audit trail
- Configuration, connection and channel activation
- Security

PQ: by end users and MIS/IT

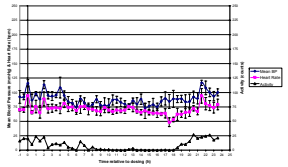
- Challenge
- Recording with instrumented animals
- Monitoring of positive control substances
- Virus check
- Backup
- Power failure

All audited by QA

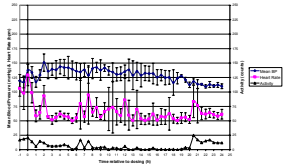
PERFORMANCE QUALIFICATION

Monitoring of positive control substance effect on blood pressure and heart rate:

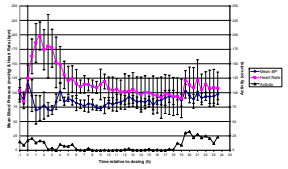
Empty capsule (p.o.)



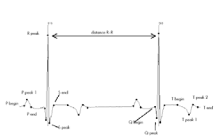
L-NAME 40 mg/kg (p.o.)

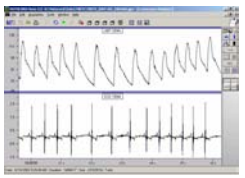


Isoproterenol 5 mg/kg (p.o.)



ECG: AUTOMATIC ANALYSIS BY THE SOFTWARE





DELIVERABLES

- Test results
- Any incidents are reported with workaround and resolution
- SOP
- Training
- Maintenance / Change control
- Validation Report

21 CFR PART 11

Approach:

- Checklist already in place which had been used for assessment of existing systems
- Checklist included a direct transcript of the requirements of the rule
- These were expanded upon to describe the company's interpretation of each requirement

Assessment:

- Was made in relation to the system
- Justification was provided on the checklist for each requirement
- Assessment based on results of the validation process
- Assessment was made by and agreed upon by all members of the validation team

Claim of Compliance:

- From the assessment it appeared that the system was compliant with the requirements of part 11
- Decision to claim full compliance made and agreed upon by all members of the validation team
- A milestone for the company (paper less system and electronic signatures)

REPORTING WORKBOOK DESIGN

- Retraceable workbook (Excel audit trail/sharing track changes)
- Workbook protection for structure
- Validated link with acquired telemetry data
- Flexibility: duration and intervals to report
- Automatization of graphical data representation
- Change control procedure

Ex.:

LESSONS LEARNED

- Define & document user requirements
  - User requirements from the basis of the user acceptance testing
- Good understanding of the system prior to validation
- Collaboration and good communication of all parties (including vendor)
- Maximize use of different expertise
- Close monitoring of validation schedule to ensure all parties keep to timelines
- In house designed test scripts
- Test scripts that include not only expected results but tests to stress the system
- Training, SOPs
- Time and effort (pays off in the end)
- Improvements to the part 11 checklist
- Valuable experience gained for future validations

CONCLUSION

From the Performance Qualification:

- The Notocord-hem 3.5 telemetry system monitors cardiovascular functions, locomotor activity and body temperature in conscious freely moving dogs, unanesthetized and unrestrained, for long periods without human intervention or contact while the animal remains in its home cage.
- The system senses, measures, digitizes and transmits the information of interest by radio telemetry transmitters.
- Following the administration of Isoproterenol, a catecholamine, the system could detect a strong increase of both the pulse rate and the heart rate. The expected results were observed in the four treated animals.
- The second positive control substance administered, L-NAME, induced the expected increase of blood pressure in the four treated dogs. The effect of the latter substance was sustained and could be easily monitored by the telemetry system.
- The results obtained from this validation study showed that the reporting method using average values calculated over a period of 5 minutes for parameters acquired by telemetry allows measurement over several heart beats and therefore, provides accurate results.

GLP and 21 CFR Part 11 compliance:

The Notocord-hem 3.5 telemetry system is compliant, through the software and SOP restrictions, with the Good Laboratory Practice regulations of the United States Food and Drug Administration (21 CFR Part 58 and subsequent amendments) and the GLP Requirements for computerized systems, electronic records and electronic signatures (21 CFR Part 11).

In summary, the results from this study confirmed that the system functioned according to the predefined expectations and as such, is considered validated for use in this laboratory.