Introduction of Electronic Data Capture Systems (EDC) in Animal Health VICH GCP Clinical Studies – Impact of Change for the Animal Health Sector

PEER REVIEWED

The last few years have seen some dramatic changes in the method of collecting data in animal health VICH GCP clinical studies. Electronic data capture (EDC) has been in the human clinical study arena for a number of years; however, this technology has only recently been introduced to animal health clinical VICH GCP studies. EDC has been a constant learning curve for all the individuals affected by the changes in using an EDC system. Although there are numerous guidance documents and information available related to EDC for human GCP studies, using EDC in animal health VICH GCP studies does have unique challenges based on the logistics of running small and large animal field studies.

Introduction of EDC impacts on all levels across an organisation and in the investigator study sites. These include organisational decisions on choosing an EDC vendor, to provide a study-specific database or to build the EDC database in-house, the training of industry professionals in the related disciplines i.e. data management, quality assurance and monitoring roles, and the way in which we select and train study site personnel at the veterinary clinics or on farms. It is a fundamental change to how we have worked up to now, and the key is to adapt as smoothly as possible with the overall goal of maintaining data integrity and compliance with the study protocol and relevant guidelines.

Change always has an impact, and what we are seeing is how animal health professionals are rising to the challenge of this change. We have "interviewed" three of the roles that have been impacted directly by the introduction of EDC in animal health and asked for their opinions on any positives and negatives, and any comments related to using EDC systems. The implementation of EDC has many advantages; however there is a cost to these "potential" advantages in terms of organisation restructuring, development of new procedures, staff re-training, time required prior to study start, etc. Is it all worthwhile? Well, read on and see some of the opinions to date!

Interview with a Study Monitor - by Jo McKelvie, Evita Services

1. What concerned you most about EDC before you had an opportunity to use it to capture data?
My biggest concern was the availability of reliable connectivity in the field and being able to find 'computer-literate' investigators. In fact, I was pleasantly surprised to realise that most veterinary practices, even those in rural areas, now have some form of internet connection. Admittedly, connectivity can still be an issue: on occasions internet connections have been lost or are frustratingly slow. However, this has been the exception, and providing that a paper alternative is available, it has not greatly hampered the conduct of a study. Also, despite the occasional 'older' veterinarian who is uncomfortable with recording their data electronically, most investigators actually embrace this form of technology, and find it easy to use!

2. What are the key planning differences in comparison to using a paper-based system?
The first time with any new process is the most challenging! Further, if you are using an external vendor to provide the system, you will have an additional member of your team. The biggest difference when comparing EDC and paper-based systems is the need for more up-front planning when using EDC to allow for the design and testing of the system. I would recommend that a data management plan and the database are developed in tandem with the study protocol, rather than subsequent to the protocol, and that CRFs are designed primarily as electronic, with paper intended to be only a back-up version. Therefore, enough time must be available to prepare adequately for the EDC study, bearing in mind that significant time will be saved at study close-out.

3. How has EDC changed your study site selection criteria?
Admittedly, I think EDC is currently more suited to the set-up of small animal practice-based studies rather than for farm-based studies. However for companion animal studies, it has not changed my site selection criteria too much! Finding an enthusiastic and conscientious investigator with the right clinical expertise, time and access to the suitable cases is still most important. Ideally the practice will already have a secure and reliable internet connection wherever the study investigations will occur. However, there are solutions to many potential issues, such as providing tablet computers for mobility within the practice.

4. How has EDC changed the way you monitor studies?
For me, the positives definitely outweigh the negatives! With EDC I can monitor the data almost in real time, and quickly provide feedback to the investigator. It also allows me to rapidly identify and report the adverse events, although there is a temptation to be constantly online, just in case! This can be managed if email alerts are set up to inform you of relevant events within the system (e.g. randomisation or AEs). As most of the data review can be conducted from the office, site visits have a different dynamic. I find I can be more prepared for what I want to review in advance (e.g. owner consent forms and drug accountability). This allows for more face-to-face time to discuss the study with the investigator and facilitate the management of any other non-data-related study issues (e.g. increasing case recruitment).

Interview with Study Investigators – by Janice Sarasola, Ondax Scientific
A selection of Spanish investigators and dispensers were interviewed recently with regards to the hands-on use of EDC systems at their clinics. They were asked to comment on

the perceived advantages and disadvantages of EDC versus paper-based data recording systems. These investigators/ dispensers had recently completed VICH GCP small animal studies using three different EDC systems. Computer expertise at the study sites ranged from minimum to competent users.

1. What were the main advantages you found when using EDC systems compared to paper when recording the study data?

- The lack of paper!!! Also the reduction in the number of folders to store the study documentation.
- NOT having to fax all the completed CRFs to the monitors on each study day.
- Data entry much easier than on paper and more difficult to forget to add data or enter incorrect format of data *(obviously this depends on the level of edit checks that have been built into the system!)*.
- Data corrections and answering queries are much easier on EDC as the system clearly documents when all the corrections are made and by whom. Less "messy" than paper-based CRFs.
- Randomisation and dosing calculations on EDC saves time and potential errors.
- Receiving notifications of study activities, i.e. queries pending etc., really helps keep on top of all the study activities to be performed.

2. What would you say were the some of the disadvantages of an EDC system versus paper systems?

- Having to learn how to use the different EDC systems for different studies.
- Although the EDC systems have the CRFs translated into the local language, in certain cases the menus are in English, therefore we need to have a clear understanding of what they actually mean.
- Remembering to "save" the data, as some systems used do not save automatically after each field is entered and the page has to be manually saved – and if the system gets "stuck" before the page has been saved, then potentially you can lose the data entered on that page.
- Remembering to NEVER use the internet browser back arrow as data will be lost if the page had not been saved.
- When more than one animal has to be enrolled, for example when enrolling several dogs within one household, then it can take longer than using the paper CRFs.
- It does take longer to review electronic data than on paper as there are several electronic "clicks" required for the equivalent of turning a paper page.

3. What would you say has helped you make the transition from performing clinical studies using EDC compared to paper systems?

Without any doubt, being able to contact the monitor at any time with any query on how to use the EDC system, and who can explain it in the local language. Veterinary practices are open routinely until 8 or 9pm and therefore being able to talk to the monitor at any time is a huge advantage.

4. Given the choice, what method of collecting study data would you like to use in future clinical studies and what improvements would you make to the systems?

Definitely EDC; the overall experience of recording data on an EDC system rather than paper appears much more straightforward and less time-consuming.

Improvements could be made in the design of the systems, for example to clearly identify the animal name together with the animal study ID, as we remember animals' names easily, however animal study IDs are more difficult to associate with the animal. In addition the ability to "view" several pages of the same animal at the same time would also be a nice optional feature.

Interview with Quality Assurance - EDC for Animal Health Applications - a QA perspective on validation by Iain McPhee, Novartis Animal Health

The recent explosion of interest in EDC within animal health for the collection and management of clinical study data has meant that EDC vendor companies are showing interest in the animal health market and its unique challenges. Some of these animal health-specific challenges include lack of computer bandwidth during a sheep study in rural Northumbria, or coping with hardware that cannot withstand the driving rain on a hillside while recording clinical assessment scores. The movement from paper to e-records is also a challenge for the QA unit. How to effectively focus resources in a changing environment? The QA challenge starts with the introduction of the system to the sponsor company. QA in this context may be a specialist department within the quality department of a company depending on company size and structure.
VICH GL9 GCP expects that the computer systems we use in clinical studies are validated. How else can there be a comparable level of confidence to a paper record?

> 8.3.6. …….. A computerized system should ensure that the methods for record keeping and retention afford at least the same degree of confidence as that provided with paper systems. For example, each entry, including any change, should be made under the electronic signature of the individual making the entry, and any changes that are made to data stored on electronic media should be maintained in an audit trail to protect the authenticity and integrity of the electronic records.

For EDC systems there are at least three configurations of sponsor and vendor software that can be considered:

1. Outright purchase of an EDC system and internal sponsor validation with or without leveraging the vendor's information for the validation
2. Software as a service (SAAS): the system is owned and run by the service provider, data are captured at the vendor's data centres, and the vendor carries the system risk

3. Some hybrid of the two above; variations on purchase, siting of software and computer servers, data capture and validation responsibility

Each has different challenges for QA's assessment of systems compliance. Outright purchase of EDC software to run on the sponsor company's computer infrastructure is a traditional option. QA may audit the vendor company to ensure their systems and processes for software development are adequate; the audit outcome will moderate the depth of in-house validation. QA will be involved in the validation, reviewing and approving the high-level validation document deliverables and the validation plans and reports, and approving test scripts for the installation, operational and performance qualification steps (IQ, OQ & PQ), etc., in the development of a validated system.

Because of internal resource and computer systems expertise constraints, SAAS may appear to be an obvious choice. The vendor has responsibility for the system and system validation, but remember, 'the ultimate responsibility for the quality and integrity of the study data always resides with the sponsor'. Sponsor QA resource requirement may be lower, but greater care is required in assurance of the vendor, their systems, processes and system validation. Computer vendors do not work to the quality systems of the pharmaceutical industry, though many are ISO certified. Carefully structured vendor audit is required during vendor selection to provide the assurance that the vendor can provide a validated system within a secured environment. The vendor will need to be on the sponsor's routine audit programme as a qualified supplier.

The third choice of a hybrid system is perhaps the most difficult from the QA viewpoint. There must be absolute clarity in the contractual agreements with regard to who is responsible for what parts of the system and its validation. QA can then develop an auditing plan to adequately test the compliance of the system during procurement and installation. QA should be involved at an early stage. Hybrid systems most readily fail at the interface between the sponsor and vendor.

QA need to reflect on their study-related activities. The database design by skilled IT staff, including study-specific user requirements, design of e-CRFs, security and data controls etc., all require structured testing (PQ), and QA oversight will also be required for these activities. On the other hand, the many issues that may occur with paper CRF are removed, e.g., no transcription errors, hence saving QA audit time. The requirements for investigator site audits will not change significantly; a minor adjustment to the new technology is needed. At final study reporting, QA can have greater confidence in the data sets provided, assessment of CRF against the database provides no added value, leaving time to concentrate on risk areas like adverse event reporting when IVP is a medicinal product.

With an EDC system, QA has an important role to assure compliance and validation of the system that will protect the sponsor's technology investment. The QA practitioners study-related activities in Animal Health will change, and the focus of study-related review, particularly at the beginning and end of a clinical study, will change.

Janice Sarasola: Born and bred in Glasgow, Janice graduated with a BSc. in Biology followed by a PhD in Veterinary Medicine at Glasgow University (1993). Janice continued her post doctoral research at Glasgow in swine diseases. On completion of her postdoctoral studies Janice joined Pfizer Research at Sandwich where she held different positions within Human Clinical Development (R&D) involved mainly in European Phase III anti-infective clinical trials.
Following her career in the pharmaceutical industry, Janice jointly set-up ONDAX Scientific, a contract research organisation (CRO) located in the UK and Northern Spain. Since the year 2000, ONDAX has been providing clinical development services to the pharmaceutical industry including set-up and monitoring of multinational VICH GCP clinical trials in livestock and companion animals, Data Management, Statistics, Quality Assurance and Training in VICH GCP.
Janice is responsible for the Quality Assurance department within ONDAX Scientific whose activities include the auditing of the VICH GCP clinical trials and the related Data Management activities including database design and validation audits for both paper and Electronic Data Capture (EDC) database systems.
Janice has been a member of RQA since 2000, becoming a member of the Animal Health Committee in 2008.

Jo McKelvie: After graduating from Glasgow Vet School (1992), Jo started her career as a clinician in mixed veterinary practice in Scotland before moving south to the RVC, London. There she studied for her PhD on veterinary immunopharmacology and enhanced her clinical skills whilst working in the equine hospital. Upon completion of her PhD in 1998, Jo joined Pfizer Animal Health, Kent. As an Associate Director, Jo's duties at Pfizer Animal Health included Global Team Leadership for multifunctional product development teams and the design and execution of clinical trials compliant with predominantly VICH GCP. Jo has contributed significantly to several successful novel product marketing authorisations for both farm and companion animals. Currently, Jo is based in Ireland providing independent consultancy services in the field of clinical trials, technical and medical writing, project management and quality assurance, as EVITA Services. Jo has been a member of RQA since 2007.

Iain McPhee: From a nutrition/biochemistry background as Study Director developing trace element medications for ruminants, he became involved in quality with the impending EU requirement for GLP in veterinary pre-clinical safety studies. The facility in which he became Quality Manager was the first exclusively veterinary medicinal development laboratory to come into the GLP compliance programme. He was a member of QAG, the precursor to RQA, and a founder member of the RQA Scottish and Northern Regional Group. Iain has sat on a number of committees both in RQA and allied areas to promote veterinary research quality assurance. Currently working for Novartis Animal Health as a specialist in Quality Assurance he is concerned with Veterinary GCP and GMP, having been involved in the globalisation of VICH GCP throughout the company.