Seminar Series

REGULATORY AFFAIRS
ANIMAL HEALTH

Sponsor Perspectives on Effective Relationships with CROs

KANSAS STATE UNIVERSITY | Olathe

Sponsor and CRO Objectives

Sponsors produce a product (i.e. quality data) to make a profit.

- People
- Resources
- Expertise
- Time

CROs want to provide a service to make a profit.

CRO and Sponsor want to advance new product innovations to enhance animal health and well-being into the future

The Collaborative Consumer

- Sponsors are resource-limited and will depend on CROs to meet business objectives
- Successful partnership and collaboration is key to advance animal health innovation

This results in the Sponsor being the ***Collaborative Consumer*** of the CRO's services, creating a mutually beneficial partnership to advance animal health

Symbiotic relationship

Grow each other's knowledge and experience while enhancing the business

Types of CROs

- Exploratory/feasibility/pilot studies
  - Traditional animal laboratory (animal facility)
- Target animal safety/User safety
- Field effectiveness
  - Clinical CRO (all vs. bits and pieces)
  - Supporting lab for microbiology, biochemistry, and clinical pathology
  - Drug management
  - Regulatory
  - Data Management
- Environmental impact
- Chemistry manufacturing and controls
- Human food safety (metabolism residue, analytical methods)

Reasons to Use a CRO

- Limited or unavailable internal resources appropriate to meet study objectives
  - Lack of people
  - Lack of time
  - Lack of facilities
  - Lack of internal expertise
- Requirements for multi-site studies
- Utilizing experience and expertise of contractor
  - Especially if CRO is specialized

“A la carte vs entire study”

Hurdles in CRO/Sponsor Collaboration

1. Not in your physical location
2. Not part of all discussions (limited knowledge)
3. Multiple/competing priorities
4. Multiple projects with similar, but different requirements
5. Procedures different than CRO is used to
6. Language difference (in terms or in language)
7. Differences in perspectives (academia vs industry)
8. Communication needs

It is the responsibility of the Sponsor to bridge the gap where possible!!

Non-clinical Study CROs

Many different CRO requirements for non-clinical studies

- Early exploratory/POC
- Pivotal (FDA or EPA GLPs)
- All species

Tendency to “set it and forget it”

- Don’t assume what is written on paper (protocol) gets translated easily into the intended action – or results!
- Where do you draw the line between not enough involvement and too much involvement from both sides?

Non-clinical Study CROs

For novel models, molecules, hypotheses it is an especially important partnership -

Get CRO involved:

- Early discussions in the design phase
  - Investigate many CROs – what works best for both (experience, resources, timelines)
  - Show appreciation for their expertise, get them invested in the whole process = builds relationships
  - Encourage their honest feedback – don't take offense
- If they want your business…
  - Ask for the expert or the Study Director that has done it before
  - Don't be satisfied discussing with only Business Development

Non-clinical Study CROs

Let them know your needs up front and be very clear. This will allow them to prepare realistic timelines and quote accurately

- Set up the pilot as close to what the pivotal will look like (e.g. pilot DT, TAS, BE studies)
- If your study requires special dosing ask for the best administrator
- Let them know if special regulatory needs or reporting will be required – provide them examples
- If you have specific Final Study Report desires practice those on the pilot study – provide them examples, or use their template and make desired changes

Take a step back –

- Let them use their protocol template and forms
    - Your responsibility to make sure it meets all your needs
- Don't get in their "way" with minutia if not warranted (micro-managing)

Non-clinical Study CROs

Be willing to go the extra mile:

- Pre-study visits, QA audits/lab qualifications
- Don’t go with your favorite or cheapest CRO – you’re not doing either of you any favors
- Spend some money to do a practice run with one animal in order to work out all the kinks first
    - Most valuable piece of information I can give today!!
- Visit in-life phase
    - Don’t be overly critical but be willing to point out concerns
    - Let them do their job, encourage the animal techs to speak up
    - *THANK THEM, THANK THEM, THANK THEM!!*
    - Plan an exit discussion with the SD and their superior pointing out positives and negatives
- Report templates

Non-clinical CRO Lessons Learned

Biggest success –

- Did a practice run for a topical product that involved animal CRO and microbiology
  - Extremely involved application technique and sampling procedures
  - Identified numerous issues with the execution of the protocol as it was written
  - Invited others from the lab to weigh in on suggestions for improving specific procedures
  - Identified microbiology department procedure issues that were resolved
  - Instituted changes to final protocol, very successful study, excellent/solid results lead to our go/no-go decision
  - Lab really enjoyed themselves throughout the process and were invested in a very difficult project

Non-clinical CRO Lessons Learned

Biggest challenge –

- Trusting a CRO to perform “standard” feeding procedures (animals out of site of other animals eating/or around the food during fasting)
- Their lack of understanding of the molecule’s behavior in the gut, and the presence of food during fasting, lead to aberrant absorption and PK values – had to redo the study to confirm findings
- Sponsor should not have assumed anything regarding standard practices if the molecule was sensitive to gut pH and fully informed the CRO of special needs

Companion Animal Clinical Field Studies

Studies with client-owned animals

- Dogs, cats, horses
- Veterinary hospitals
  - Experienced sites have dedicated
  - Main business is running the hospital not clinical studies
- Specialty clinics or universities
  - May be teaching hospitals

Companion Animal Clinical Field Studies

- May need geographical diversity or may be multinational
- Types of studies
  - Small pilot
  - Larger pivotal studies (> 100 animals)
  - Post-marketing
- Enrollment
  - Dependent on indication
  - Number of sites

Clinical Field Study CROs

Size and complexity of the study needs to be considered.

Clinical Field Study CROs

25 cases/site

X 15 sites

X 3-4 monitors

X 4 countries

Clinical Field Study CROs

Standards for clinical field effectiveness studies (pilot or pivotal)

- USDA and EPA guidance for applicable studies
- FDA CVM expects adherence to **GFI #85 Good Clinical Practice**
- Adherence to Sponsor standards (Good Scientific Practices)
- Study protocol and SOPs
- Experience

What to use the CRO for?

- Entire study
- Parts of the study

Personnel	Tasks
Project Manager Trials Manager Monitoring Administrative Data Manager Data entry Statistician QA Regulatory Affairs	Central diagnostics Central laboratories Drug supply

Companion Animal Field Study CROs

- Establish relationships with the CRO early
  - Audit
    - Know how the CRO is structured
    - Know what you are getting into (CVs, SOPs)
  - Contracts
  - “Test” compatibility with your systems
  - Paper vs electronic
- Invest in the relationship
  - Best method for communication
  - Request inputs
- Set clear expectations (Transfer of Obligations)

Companion Animal Field Study Communications

Changes will occur - plan accordingly!

- Be deliberate and slow and about any changes in scope
- Follow proper communication channels
  - Asking CRO (sites) best communication channel
- Be up front about study history/knowledge
- Set appropriate expectations
- Frequent communications (especially when there is a question)
- Avoid the double standard of communication

Study Maintenance

Monitor the progress

- Never assume anything
- Do not wait until the end to check
- Participate in regular meetings
- Over communication from CRO is always preferred
- Ask for regular updates
- Ask specific questions

Lessons Learned

Problem: Format of dataset received

- Laboratory provided excel dataset in one format
- Statistician required data to be in a different format
- Formats were not compatible; required re-review of data

Lessons Learned:

- Understand what your data outputs are to reduce manipulation and review of data
- Handle the data as little as possible
- Make the process automatic with systematic checks along the way

Lessons Learned

Problem: Enrollment

- CRO hired to help increase enrollment and recruit new study sites
- CRO expected to use already established study sites

Lesson Learned:

- Be careful with assignment of sites
  - Mandating what sites the CRO uses vs Sponsor
  - Giving CRO the second tier sites
- Don’t expect that a CRO will magically do something you can’t do
  - Enrollment issues – “it’s me, not you”
  - Listen to CRO; ensure they are being heard
  - Be upfront in hurdles

Lessons Learned

Problem: CRO resource capacity

- Large CRO vs Small CRO
- Worked with a small CRO to monitor data and handle study drug
- CRO lost the majority of their staff in a three-week period

Lesson Learned:

- Discuss contingencies, particularly where resources are limited
- Be frank about deliverables and timing
- Be flexible

Food Animal Clinical CROs

How do we try to help ensure success in food animal clinical CROs (in addition to all points mentioned before)

- Does the CRO have a relationship with a supporting lab?
  - Open the lines of communication between support labs and the field investigator
- Does the CRO have a reliable source of animals to perform the studies? Will the investigator own the animals on their own farm or will these animals be owned by a private farm?
- Do the staff clearly understand data documentation requirements? Does the investigator and staff have the competency to follow the protocol?

Food Animal Clinical CROs

- What supplies can we provide to assist?
  - Protocol templates
    - Helps us to ensure all things are considered that may matter to QA and/or regulatory agencies
  - Premade shipping labels – especially to supporting labs
  - Investigational product available to the CRO well in advance of start of in-life
    - Personal Example: product shipped 2-weeks before start of in-life – the bottles arrived shattered! Getting them early allowed for this problem to occur and for us to correct it without delaying the study
  - Report templates

Food Animal Clinical CROs

- Check-in
- Check-in
- Check-in

Food Animal CROs

Many of the same rules apply regardless of the CRO, each with a different twist

Supporting labs (microbiology or other)

- How are data captured? Are any electronic systems Part 11 compliant?
- If not, are data controls described?

Microbial food safety (Risk Assessment and Hazard Characterization)

- Does the CRO understand the greater production system?
- Does the CRO understand where to find data to support assumptions for a Risk Assessment?

Other CROs

Metabolism/Residue (Pre-Clinical CRO)

- Is the CRO skilled at GLP studies?
- Is the analytical lab capable of implementing analytical methods and supporting documentation for results?
    - Example: Well performed POC efficacy and PK study. Methods required a plasma as well as a feed method to analyze in feed concentrations. Analytical lab stated they had done the feed method in the past and was comfortable with it… well they had done it once… a long time ago. Resulted in loss of these data from the study.

Lesson – Be forthcoming and do not assume!

Lessons Learned

CRO not accustomed to performing GCP (type) studies, biased by experience as academicians and working in a service based organization (not accustomed to dealing with regulated products)

- Study performed on commercial farms (not a problem)
- CRO accustomed to research (academic in style, not for regulatory agencies)
- Had systems in place to collect data
- What went wrong?
  - The assigned individual for the CRO to help oversee the study had NOT participated in research
  - The organization did not fully agree with the data collection rigor, nor understood what we were asking – but assured us that they would adjust and be okay

Lessons Learned

CRO not accustomed to performing GCP (type) studies, biased by experience as academicians and working in a service based organization (not accustomed to dealing with regulated products)

- What did we do?
  - Stuck it out because the marketing team believed there was a potential strategic partnership for the company and the product (which is why they were recommended to begin with)
- What happened?
  - Data quality, compliance, and CRO monitoring/control of the study were significantly lacking in quality
- What should we have done?
  - Identified an alternative provider

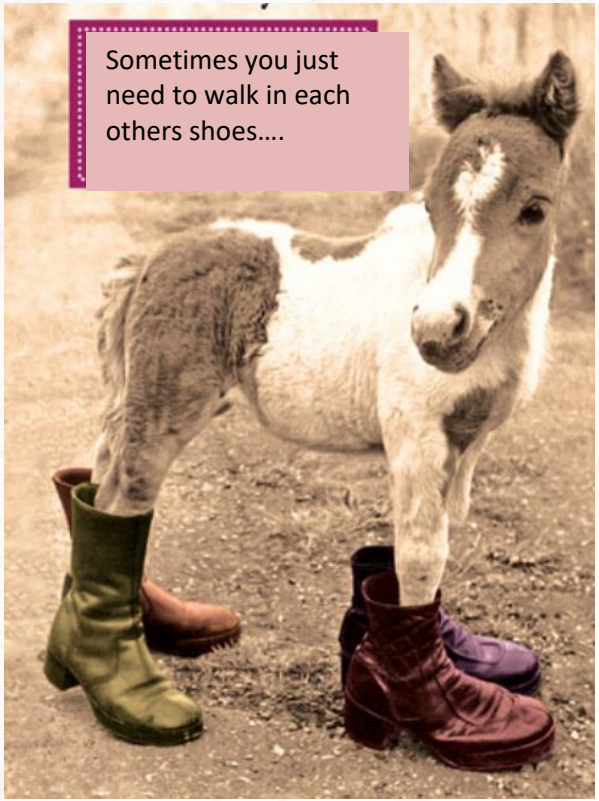
Identify red flags early and take them seriously

Sponsor Needs

- Sponsors frequently do not communicate their needs clearly to a CRO
- Many requirements are driven by regulatory authority demands
    - Sometimes seem excessive or illogical
    - Data may need to go to CVM for *all* studies
- Sponsors have timelines to meet

CRO Needs

- Frequently managing multiple projects at a time
- Have limited resources
- A study needs to fit within their systems
- More support from Sponsor



Take-Homes

- The Sponsor is a *Collaborative Consumer* of CRO services
- Mutually beneficial partnership to advance animal health
  - Involve CRO early in the plan
  - Integrate CRO personnel into the team and tap into their expertise
  - Determine communication style that works for both
  - Be prepared to change
  - Check in often
  - Be forthcoming with needs, what's working and what's not
- Identify red flags early (both Sponsors and CROs)

Any questions?

Non-clinical studies	Clinical companion animal field studies	Clinical food animal field studies
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Thanks for listening

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