Designing a Field Trial

The Devil is in the Details

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Study Design

- Appropriate controls
- Masked (AKA blinded) to avoid bias
- Strong data analysis plan (statistics)
- Powered to get statistically significant results
- Defined enrollment criteria
- Clear end points
- Well defined study schedule

Write it Down!

- Develop a detailed protocol
- Include “Case report forms” – pages where everything you want to record has a place.
- Data – the lifeblood of a study – if you didn’t write it down, it didn’t happen.

What is in a protocol?

- Everything! (see list)
- Think of everything that could go wrong and plan for it
  - Wrong treatment given
  - Lost to follow up
  - Mix up in animal ID
  - Missing data points
Changing the protocol and deviations

- No matter how well you plan, “...happens”!
- Amendments – planned changes
- When a deviation from the protocol (AKA mistake) happens, document it and evaluate its impact on the integrity of the study

Training

- Everyone involved in the study should be trained on the protocol and forms
- Document the training – who did it and when
- Train on amendments

Data

- Make an effort to record who collected the data and when
- Signatures and dates on forms
- Keep it safe! Originals are important.

Final Report

- Study final report is different from a research publication
- Include all details – helps with analysis later
- Journal publications can be ‘extracted’ from final study report
Getting Involved in Field Testing of Non-surgical Contraceptives: Lessons Learned, and what Organizations and Veterinarians Should Consider when Getting Involved

Ethical & Welfare Considerations in Field Trials for Products Destined for Underprivileged Populations

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The need for research in the developing world and among disadvantaged populations

• “Each year £35-40 billion is spent on healthcare research worldwide
• Only 10 percent of this is devoted to the health problems of 90 percent of the world’s population
• Developing countries urgently need research to help prevent and treat diseases such as TB and malaria
• Many countries have limited funds and a lack of trained staff to conduct their own research”
What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research

- Poverty, limited health-care services, illiteracy, cultural and linguistic differences, and limited understanding of the nature of scientific research increases risk
- Local regulatory infrastructure may be inadequate to protect participants
- Participants and communities should both benefit from research during and after the trial

Whose standards of care?

<table>
<thead>
<tr>
<th>Sponsor’s standards or local standards</th>
<th>Review and informed consent</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Control groups</td>
<td>• External review</td>
</tr>
<tr>
<td>- Placebo?</td>
<td>- IACUC (animals)</td>
</tr>
<tr>
<td>- Best local standard?</td>
<td>- IRB (people)</td>
</tr>
<tr>
<td>- Best known standard?</td>
<td>- Home institution and study site if different</td>
</tr>
<tr>
<td>• Treatment of adverse events</td>
<td>- Informed consent</td>
</tr>
<tr>
<td>• Post-trial definitive treatment</td>
<td>- Pet owner</td>
</tr>
<tr>
<td>• Post-trial ongoing care and disposition</td>
<td>- Who consents for community animals?</td>
</tr>
</tbody>
</table>

American veterinary students performing surgery in Latin America in compliance with the local standard of care

Good enough?
• Field trial team must be prepared to adapt to unexpected events
• Example: Neutersol reactions in the Galapagos 2004
  – Suspended product use
  – Surgical treatment for effected dogs
  – House-to-house visits to examine dogs
  – Findings published
  – Re-think approach, refine procedures, more work in dogs in USA

• Field trials are necessary to demonstrate safety and efficacy in populations targeted for treatment
• Animals, like children, are particularly vulnerable, particularly if they lack effective guardians or live in under-resourced communities
• Investigators are obligated to protect their animal subjects both during and after clinical trials, including management of adverse events
• Results of clinical trials should be shared transparently with regulators, colleagues, and communities