Ethics Review – bottle – necks and pre-review

How to be more efficient?

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WHO

World Health Organization

- Protocol -Complete, coherent, and scientifically sound
- Protocol - Ethically appropriate
- Acceptance by multiple ethics committees
- Research or no?
- Pre –approved protocols and templates

All that I wanted to know in life – I learnt in Kindergarten….

- Nothing new
- Basic, home truths

- “we know everything, the protocol is just a formality, so lets just get on with it…..”

- The protocol is everything…. If it is not written, it doesn’t exist….

Operating a high quality clinical trial is science not an administrative fu

Turning a protocol into reliable evidence needs strong operational deliv

Good operations staff know how to answer the question whilst mitigati
participant and community safety, rights and ethics and reliable data

Excellent clinical trials need clinical research nurses, doctors, pharmacist
ab staff, fieldworkers..... Who understand the protocol and can apply it
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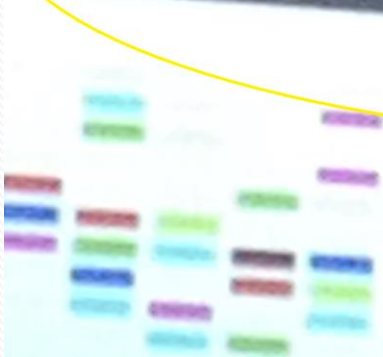
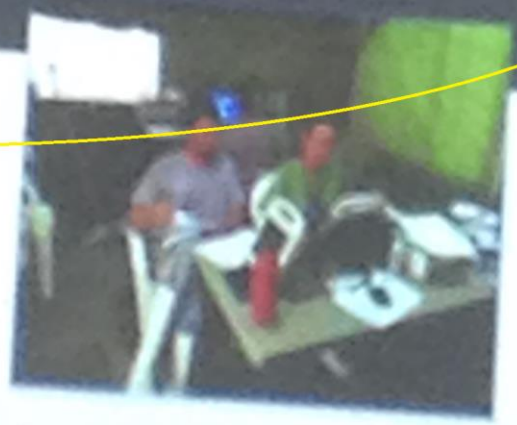


THE GLOBAL HEALTH NETWORK



Complete, coherent and scientifically sound

- Complete information on the intervention
- Complete information on the populations in which the intervention is proposed
- All that we know about the intervention and the populations in literature
- All sections of the protocol are consistent, and saying the same thing (the dose of the drug is correctly written, and is the same in all sections, the age group does not change from the inclusion criteria to the analysis, to the questionnaires, the protocol is implemented in the same site throughout….)
- Data collection and analysis is fully described, with justifications for the sample size
- Investigators have thought through feasibility and completion issues etc. etc.

What we see very often

- Incomplete background sections
- Interventions and data collection methods don't match objectives
- Study design is not appropriate for the study
- Sample size is not justified – sample size calculations are not described
- No consistency in inclusion/exclusion criteria, drug dosage, timing of interventions etc.

Often we are told that the protocol has been approved by a scientific peer review group

Scientific Peer Review

- Need guidance for peer reviewers
- Scientific Committees often approve proposals/ concept notes
- Ethics Committees review the protocols.
- There is a gap…….

Ethically appropriate…

- Is this the right populations to test the intervention?
- Is there enough justification for testing the intervention?
- Is the sample size appropriate?
- Will the study be feasible? What if the sample size is not achieved?
- Will the study be independently monitored? And self-corrections made mid-way if required?
- Are there stopping Rules? Enough safeguards to protect participants from un-necessary harm
- Where appropriate has a DSMB been established?

Ethically appropriate…. (2)

- Fair selection of participants – people are not excluded because they are difficult to reach or monitor.
- Kept informed about the research process and modifications and at the end of the study
- Collection, storage and use of samples….
- Benefits sharing….

If you have done both these,
then review should not be time consuming

Is it research?

- Collection and analysis of data that should have been collected as part of clinical care – with outputs supporting clinical management of the patient
- Collection of additional data
- The ISARIC data collection form (including various body samples)

- Hypothesis driven analysis and outputs
- Use of samples for purposes other than clinical care

Multiple ethics review…

Sponsor Ethics Committee

Ethics Committee 1

Ethics Committee 2

Ethics Committee 3

World Health Organization

Multiple ethics review -

Advantages

- Multiple perspectives - Adds value
- Local ownership

Disadvantages

- Logistically cumbersome
- Ethics Committees may have had no prior engagement
- Local and some international ethics committees are over-burdened during the emergency
- Local Committees influenced by political leadership
- No or little learning

- Local Ethics Committees used to reviewing less than a dozen protocols in a year
- Usually not clinical trials
- Usually not complex trials

In less than 5 months, 47 **registered trials** in ICTRP, of which 17 are on treatment, 28 on prevention and 2 on diagnostics

In one of the affected countries, the numbers went upto 60 in a 6 month period

- All ethics Committees defer review to a Central Committee with caveats
- CC includes a core group of experts from the global community (membership time limited)
- Ad-hoc membership of 2 members of each participating ethics committee
- CC reviews all comments from each committee, and everyone agrees to the final set of recommendations
- Sponsor receives a single set of comments
- Responds to the Central Ethics Committee
- Response shared with all ethics committees, but decision made by CC
- Advantage of being independent

Template protocols and consent forms

- In principle a good idea for pre-reviewing
- Need more guidance on development and use
- Template protocols for one type of epidemic may not work for others.
- Difficult to imagine what specific situations may be – so review of the actual protocol may not necessarily be expedited – expectations of PIs must be tempered….

What else can be done

- Community Engagement - should begin in 'peacetime'
  - One of the oft-repeated 'bottlenecks' is that communities do not understand research
  - We should begin NOW…. Engage with experts thinking about CE and see how to loop in
- Capacity strengthening – not only of committees but also of their secretariats and researchers
- Capacity strengthening to go beyond clinical trials – epidemiological studies, risk factors, socio-behavioral studies etc.