

Clinical Trial Grant Applications: How to succeed by really trying.

John KOLBE

Department of Medicine



THE UNIVERSITY
OF AUCKLAND


FACULTY OF MEDICAL
AND HEALTH SCIENCES

Outline.

- NOT a comprehensive review of grant application
- Preparation for application
- What is assessed in application
 - Common pitfalls.

- Personal Opinion
 - not as HRC representative
 - avoid specific examples
 - full application vs EOI

ON TRACK Network.

- Congratulations on the initiative.
- cf ANZICS Clinical Trials group
 - Collaborative approach across A'asia to
 - address “big questions”
 - internal review process that is more rigorous than any external process
 -  high quality, successful applications

Preparation.

- A good (original) idea (vs a great proposal)!
- SPIRIT 3013 Statement.
- CONSORT guidelines.
- Review HRC guidelines
- Review HRC Scoring Criteria
- Write application
- Review HRC Scoring Criteria again
 - all criteria addressed; including Maori responsiveness, health delivery (!)
 - EOI comments addressed

General Issues: 4 Cs.

- **Clarity**
 - spare a thought for the reviewer!
 - layout
- **Concise.....**
- **Comprehensible, by**
- **Complete**



Mission Australia

AN OPEN LETTER TO ALL OUR SUPPORTERS

After a recent and thorough review of our financial practices, we are forced to publicly admit, that every cent of the money you have donated **has gone....**

To all the right places.

Yours faithfully

Toby Hall, CEO

COMPASSION

INTEGRITY

RESPECT

PERSISTENCE

CELEBRATION

Our Vision is to see a fairer Australia by enabling people in need to find pathways to a better life

General Issues: 4 Cs.

- **Clear**
- **Concise**
- **Comprehensible, by**
 - reviewers
 - committee members
- **Complete**

"If I can't understand it, the management probably doesn't want me to understand it.

And if management doesn't want me to understand it, there is probably something wrong going on."

Warren Buffett

2003 Berkshire Hathaway
Annual Meeting.

"If I can't understand it, the management probably doesn't want me to understand it.

And if management doesn't want me to understand it, there is probably something wrong going on."

Warren Buffett

2003 Berkshire Hathaway
Annual Meeting.

.....but is also a major disincentive to try to decipher.

General Issues: 4 Cs.

- **Clear**
- **Concise**
- **Comprehensible, by**
- **Complete**
 - assessment based solely on application.

References.

- Accurate/correct
- Complete
- Available
- Appropriately cited
-often reviewed by reviewers and

“Very few people, including authors willing to commit to paper, ever really read primary sources – certainly not in necessary depth and completion and often not at all.”

“..... no longer surprised when the study of a neglected original shows that later interpretations departed from an author’s own intentions. “

Stephen Jay Gould

“Leonardo’s Mountain of Clams and Diet of Worms.”

Rationale.

- **Justify the need for the trial**
 - Not just an important health issue
 - Present existing knowledge (eg systematic review)
...and gaps
 - Argue clinical equipoise
 - Preliminary data
 - Link to Aim(s) and primary outcome

Aim(s)/Hypothesis.

- Clarity
 - In a single sentence, define purpose, scope, design, population, intervention and analysis.

(Primary) Outcome(s).

- Consistency with Aim/Hypothesis
-and with Rationale
- Valid, reproducible, relevant, responsive.....
- **Explain and justify**
- Composite outcomes
 - Benefits vs Drawbacks
- Limited (vs plethora of) secondary outcomes

Re the Primary Outcome.

“When the right thing can only be measured poorly, it tends to cause the wrong thing to be measured only because it can be measured well. And it is often much worse to have good measurement of the wrong thing - especially when, as is so often the case, the wrong thing will *in fact* be used as an indicator of the right thing - than to have poor measurements of the right thing.”

Tukey, JW. 1979. J Am Stat Assoc

(Primary) Outcome(s).

- Consistency with Aim/Hypothesis
- Valid, reproducible, relevant, responsive.....
- Explain and justify
- **Composite outcomes**
 - May be necessary and appropriate
 - Justify use of ..
 - Benefits vs Drawbacks
- **Limited (vs plethora of) secondary outcomes**

Methods.

- Address the Aim/Hypothesis
 - eg benefits and risks
- Is comparator “active”/standard of care
- Address feasibility (...of recruitment, etc)
- Assignment of intervention, data management and monitoring; important but seldom an issue .
- Appropriate management of patient safety issues – not just a DSMB.
- Acknowledge and address any weaknesses eg lack of blinding.

Statistics.

- Carefully reviewed
- Bio-statistician on committee
- Demonstrate “involvement” of bio-statistician
- Power calculation
 - all information
 - 90% power
- Justify (effect size, non-inferiority margin....)

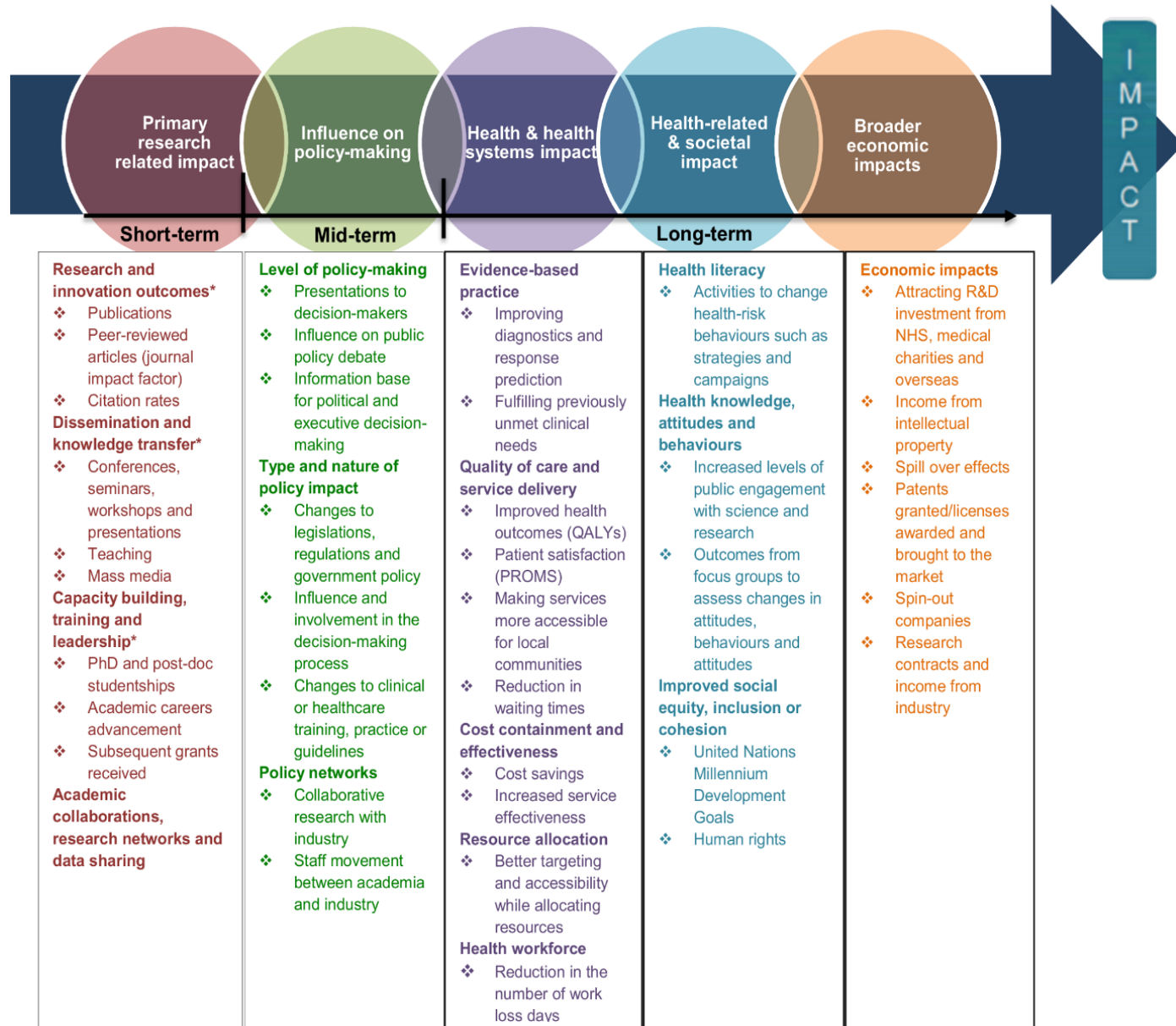
Maori Responsiveness/ Maori Health Advancement.

- Guidelines under review
- Will vary with type of application
- As and where applicable, the application (and methodology) demonstrates and understanding of, and respect for, Maori culture.
- Relationship with Maori health stakeholders; appropriate level of consultation....but not token
- Development of Maori (bio-medical) scientific workforce
- Addressed under multiple sections: rationale, design and methods, research impact....

Research Impact.

- Address HRC Investment Signal Goals, but....
- Take a broad approach
- ...to improve human health and quality of life, and generate economic and other societal benefits in New Zealand.
- “add value,make a difference”
- Scalability, feasibility, “buy in”,
- Pathways for knowledge “mobilisation”
- Dissemination, uptake and implementation of research results
- See MBIE criteria !

MBIE's Pathways to Research Impact.



Key: [Bold, [impact categories]; Diamond, [impact subgroups]; *top three metrics]

“Track Record”.

- Depth and breadth (mix) of personnel and other requirements , to complete the proposed study.
 - bio-statistics, health economics, bio-informatics, etc
 - Not just track record of PI
 - Realistic FTE allocations
 - Appropriate networks and research environment
 - History of productivity and delivery.
-
- “.....if we wish our civilization to survive we break with the habit of deference to great men.”

Karl Popper.

Outline.

- NOT a comprehensive review of grant application
- Preparation for application
- What is assessed in application
 - Common pitfalls.

"Things cannot always go your way. Learn to accept in silence the minor aggravations, cultivate the gift of taciturnity, and consume your own smoke with an extra draft of hard work, so that those about you may not be annoyed with the dust and soot of your complaints."

Sir William Osler.

- The three key questions to ask about a healthcare intervention:
 - "Can it work?"
 - "Does it work in practice?" and
 - "Is it worth it?"

Archie Cochrane
British Epidemiologist

- It isn't that they can't see the solution. It is that they can't see the problem.

G K Chesterton

“The Scandal of Father Brown”: 1935.