A Financial Conflicts of Interest Checklist for Clinical Research Studies

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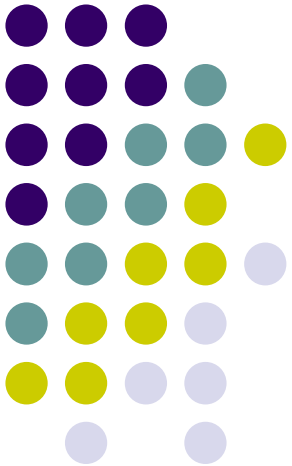

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November 21, 2017

Objectives

1. Why a Financial Conflicts of Interest Checklist is needed
2. Development of the Checklist
3. Current and Future Opportunities

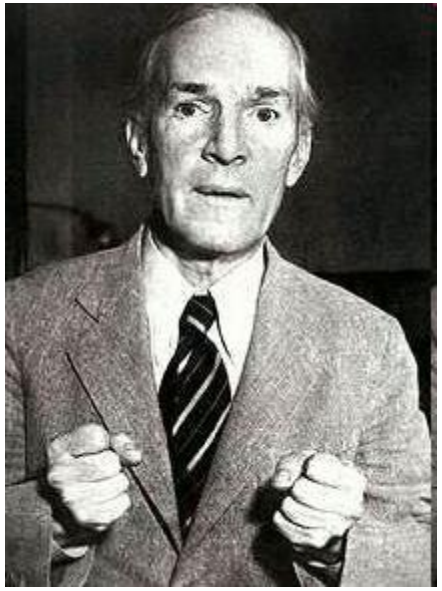
Disclosure

Presenter: Paula A. Rochon

- Financial support of this work has been made possible by the following grant:
  - CIHR Operating Grant “Evaluation of the Integrity of Clinical Research in Canada EIC-77338”
- Relationships with commercial interests:
  - None
- Potential for conflict(s) of interest:
  - None

"You can't make somebody understand something if their salary depends upon them not understanding it."

Upton Sinclair
1878-1968



- Read many NSAID trials
- No conflicts of interest reported
  - The question asked: Is there an association between drug performance and manufacturer sponsorship?

ARCHIVES OF
INTERNAL MEDICINE

A Study of Manufacturer-Supported Trials of Nonsteroidal Anti-inflammatory Drugs in the Treatment of Arthritis

Paula A. Rochon, MD, MPH, FRCPC; Jerry H. Gurwitz, MD; Robert W. Simms, MD; Paul R. Fortin, MD, MPH, FRCPC; David T. Felson, MD, MPH; Kenneth L. Minaker, MD, FRCPC; Thomas C. Chalmers, MD. Jan 1994.

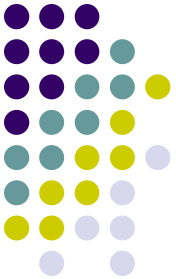
- Was this a manufacturer sponsored trial?
  - Work address
  - Contracts
  - Supply of medications
  - Published in journal supplement (one-third)

Which drug was linked to the manufacturer?

- Identify drug
- Identify manufacturer sponsoring the trial
- Determine which drug was produced by the manufacturer (using texts)
- Identify manufacturer supported drug

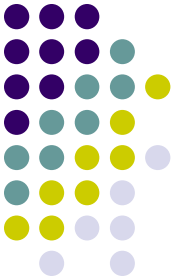
- Almost all trials were manufacturer sponsored trials
- 56 trials included
- Compared manufacturer sponsored drug and comparison drug on:
  - Dose
  - Efficacy
  - Toxicity

Key Findings



- Manufacturer-associated drug almost always superior in efficacy and less toxic
- **One of first papers to show this association**
- Claims often not supported by data
- Doses of drugs chosen to optimize the efficacy performance of the manufacture's drug
- Manufacturer support not documented

Our Recommendations



- Include structured information in articles to help reader objectively interpret trial findings
- If study was published in association with a manufacturer
  - Name of the manufacturer
  - Name of the manufacturer-associated drug
  - Type of manufacturer sponsorship
- **This paper was cited in over 40 books and more than 200 peer-reviewed publications**

To maintain public trust in research, it is important that financial conflicts of interest are disclosed and steps are taken to manage them.

Toward Effective Canadian public-private partnerships in health research

- CIHR committed to launch an RFA examining the integrity of clinical research in Canada
- Announced in CMAJ commentary

Alan Bernstein

In a recent editorial on researcher–university–industry research contracts, *CMAJ* calls for further study and guidance on issues affecting clinical research in this country.[1] Indeed, it recognizes the need for leadership in promoting and monitoring "ethical behaviour in research."

As Canada's lead federal health research agency, the Canadian Institutes of Health Research (CIHR) has a responsibility to promote and ensure ethical conduct in research, a responsibility that it has vigorously embraced since its establishment. The significant growth in industry support for research over the past 10–20 years has greatly strengthened health research efforts in this country, as well as our potential to translate research findings into improved health for Canadians. At the same time, all partnerships bring with them their own challenges of establishing shared vision, goals and standards of research.

In early 2001, CIHR's Governing Council established a national Working Group on Partnerships co-chaired by Dr. Matthew Spence, President and CEO of the Alberta Heritage Foundation for Medical Research, and Dr. Michel Bureau, Président and CEO, Fonds de recherches en santé du Québec, and including representatives of other agencies and, importantly, of industry.[2] That working

quiry, dissemination of research results, integrity of research, sensitivity to conflict-of-interest issues, accountability and transparency, and the paramount importance of the public interest as an essential element of publicly supported research. CIHR and *CMAJ* also co-sponsored a meeting of editors of Canadian peer-reviewed health sciences journals in November 2001 to promote and enhance discourse regarding the ethical issues involved in research, dissemination of results, editing and publication.[3]

These activities complement the ongoing consideration of ethical issues within each of CIHR's 13 institutes, its entire research portfolio and its Governing Council, and reflect the foundational values and framework driving our approach to partnerships within the larger health research community. CIHR is committed to building on these initiatives in order to develop a robust program of research on ethics, the objectives of which are to achieve greater clarity and consistency in the ethical principles governing health research practices.

Looking forward, and as advocated by *CMAJ*, CIHR is planning to support an analysis of Canadian practices following a recent US study that surveyed investigator independence and subject protection in contracts between

Development of the Checklist

- Funded by CIHR award EIC-77338; “Evaluation of the Integrity of Clinical Research in Canada”
- We proposed a comprehensive Checklist that investigators can use to describe their study and provide a structured report of the potential fCOI situations they may have related to their role in the study.

CIHR IRSC

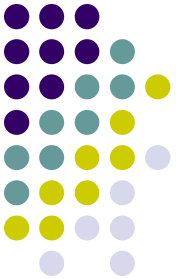
Purpose

- To create a *uniform* structured report than can be reviewed by *multiple* stakeholders as part of the research review process.
- The Checklist could be used by :
  - Research Ethics Boards
  - Funding agencies
  - Institutions
  - Journal editors

The Process

- A team of 35 experts from across Canada, US and Europe
  - Research team
  - External experts (n=19)
  - Research support staff (n=4)
  - Combined expertise in
    - trial registration
    - research guideline development (CONSORT, EQUATOR)
    - ethics review
    - policy
    - health law
    - medical journals
    - media

Three Phase Checklist Development Process



Pre-Meeting
Item Generation

Consensus
Meeting

Post Meeting
Consolidation

Pre-meeting item generation

Checklist **version 1**

15 items, 92 sub-items

Rating of all items using a 5-point scale

(1 = least important, 5 = most important) by 29 reviewers:

Mean score 3.1–4.8 points

71/92 (77%) items with mean score ≥ 4.0

Checklist **version 2**

13 items, 65 sub-items

Rating of all items using a 5-point scale

(1 = least important, 5 = most important) by 24 reviewers:

Mean score 3.1–5.0 points

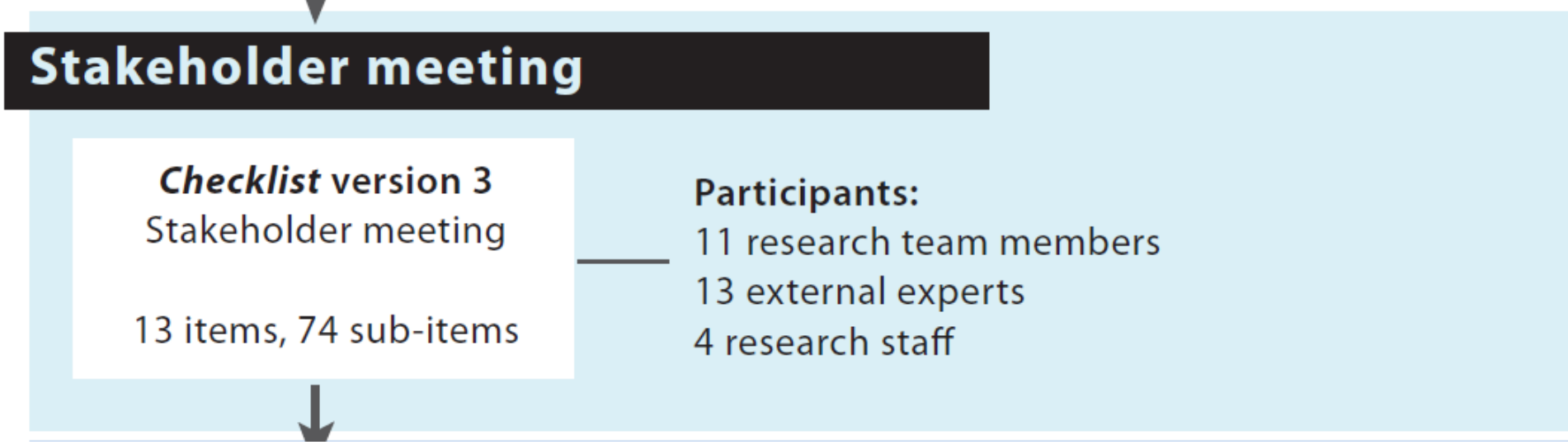
60/65 (92%) items with mean score ≥ 4.0

Pre-Meeting Item Generation

No.	Checklist Item	Expert Panelist Rating of Item
4.0	**Who is the sponsor/funding source?** *(include all sources)*	**(1 - Not important 5 - Very important)**
4.1	Industry	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Cannot Answer ☐
4.2	Peer reviewed funding agency (e.g. CIHR, NIH)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Cannot Answer ☐
4.3	Other (please specify source)	1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ Cannot Answer ☐

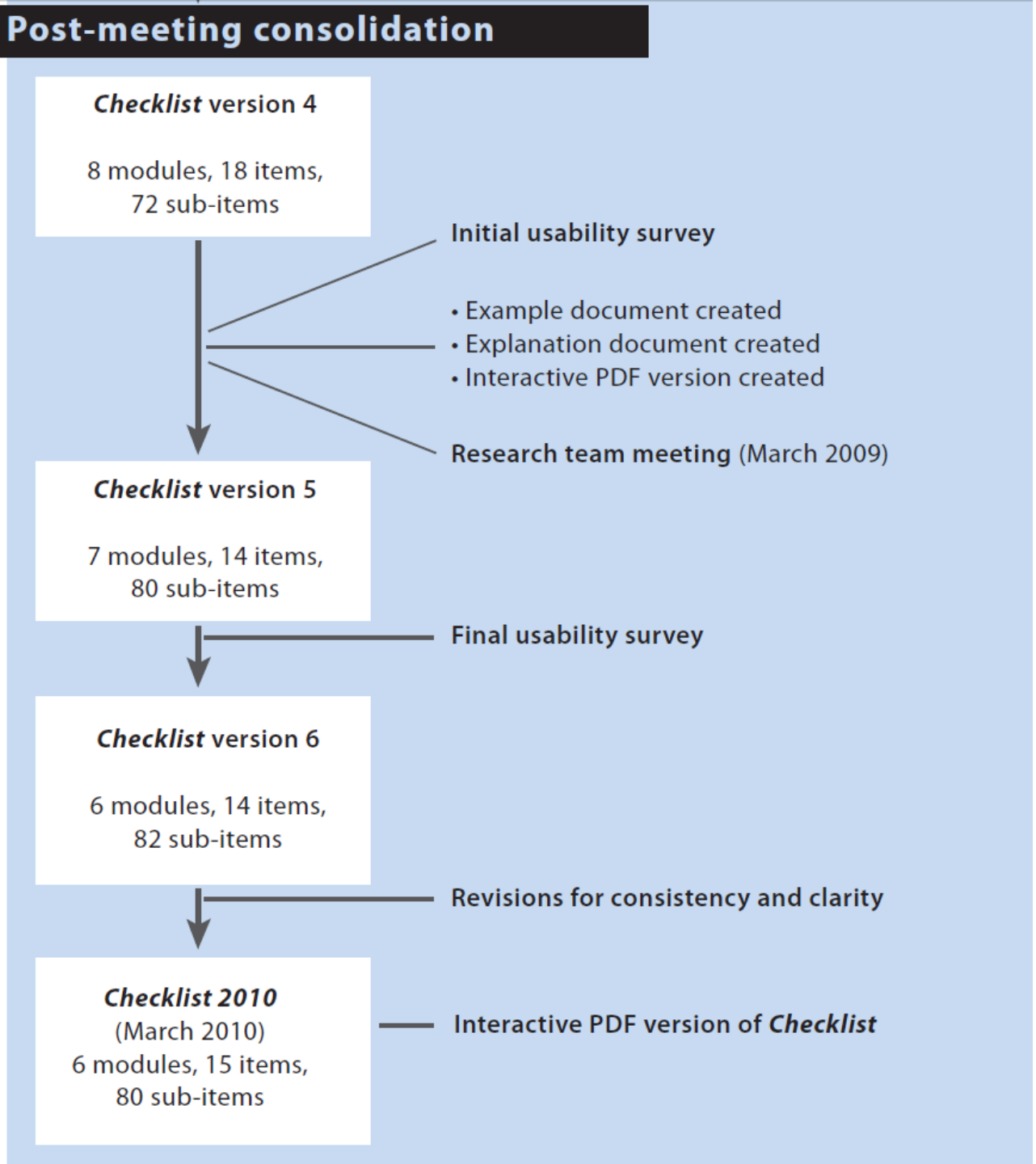
Please add your comments, suggested revisions, or additional items for Section 4:

This process was modelled after CONSORT

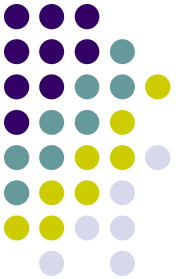


- Four panel discussions
- Invited experts were solicited for feedback and facilitated discussion
  - Registry users
  - Funders and Policy Makers
  - Legal / Ethics / REB
  - Medical journal editors
    - Representatives from *Annals of Internal Medicine*, *The Council of Science Editors*, *BMJ* and *JAMA*

Post-meeting consolidation



The Checklist: Structure



Four sections with six modules:

- Section 1: Administrative Information section
  - Module A: Administrative Profile
    - Study information
    - Investigator information
    - Dates of checklist initiation & completion
- Section 2: Study Information section
  - Module B: Funder Profile
  - Module C: Contract Profile
  - Module D: Study Team and Funder Relationship
- Section 3: Personal Financial Information section
  - Module E: Financial Profile
- Section 4: Authorship section
  - Module F: Authorship Profile

SECTION 1: ADMINISTRATIVE INFORMATION

This section is completed at the study's initiation and updated as necessary.

MODULE A: ADMINISTRATIVE PROFILE

ITEM	DESCRIPTOR	RESPONSE
A.1.0	**Study**	
A.1.1	Study name	_____
A.1.2	❑ Single site or ❑ multi-site	
A.1.3	Countries in which the data will be collected	_____
A.1.4	Is this a clinical trial?	❑ Yes ❑ No
A.1.4a	If you answered yes to item A.1.4:	
	Is the study registered in a primary clinical trial registry that follows international standards developed by the World Health Organization and endorsed by the International Committee of Medical Journal Editors?	❑ Yes ❑ No ❑ Don't know
	A list of approved registries can be found at http://www.who.int/ictrp/network/primary/en/index.html	
A.1.4b	What is the primary registry name and the registration number?	_____
A.1.5	Name of the institution from which the study will be coordinated	_____
A.1.6	Is any part of the study to be conducted by a contract research organization?	❑ Yes ❑ No
A.2.0	**Investigator**	
A.2.1	Name of the overall study official	_____
A.2.2	Name of the investigator completing the checklist	_____
A.2.3	What is your role in this research study? (check all that apply)	
A.2.3a	Principal investigator for the entire study	❑ Yes ❑ No
A.2.3b	Principal investigator for a site or region	❑ Yes ❑ No
A.2.3c	Co-investigator for the study	❑ Yes ❑ No
A.2.3d	Paid consultant for the study	❑ Yes ❑ No
A.2.3e	Member of steering committee	❑ Yes ❑ No
A.2.3f	Participant recruiter	❑ Yes ❑ No
A.2.3g	Other (please specify)	_____

Date the checklist section 1 was first completed (day/month/year) _____

Date(s) the checklist section 1 was updated (day/month/year) _____

SECTION 2: STUDY INFORMATION

This section is completed at the study's initiation and updated as necessary.

MODULE B: FUNDER PROFILE

ITEM	DESCRIPTOR	RESPONSE
B.1.0	**Is this study funded?**	❑ Yes ❑ No ❑ Don't know
B.1.1	If you answered yes to item B.1.0, identify the type of funding support: ❑ Financial ❑ Equipment ❑ Test kit ❑ Drug ❑ Device ❑ Other (please specify: _____)	
B.1.2	List the funder(s)	_____
B.1.3	To which categories do/does the funder(s) belong? (check all that apply):	
B.1.3a	Industry (e.g., pharmaceutical company, test or medical device company, biotech company)	❑ Yes ❑ No
B.1.3b	Government funding agency (e.g., National Institutes of Health, Canadian Institutes of Health Research, Medical Research Council)	❑ Yes ❑ No
B.1.3c	National or regional government body (e.g., National Health Service, Ministry of Health, Department of Defense)	❑ Yes ❑ No
B.1.3d	Charitable foundation (e.g., American Heart Association, The Bill & Melinda Gates Foundation, Wellcome Trust)	❑ Yes ❑ No
B.1.3e	Other(s) (please specify: _____)	❑ Yes ❑ No

MODULE C: CONTRACT PROFILE

ITEM	DESCRIPTOR	RESPONSE
C.1.0	**Is there a <u>contract</u> with the funder(s)?**	❑ Yes ❑ No ❑ Don't know
	(If you answered no or don't know, skip to module D)	
	If you answered yes to item C.1.0, does your contract:	
C.1.1	include someone signing on behalf of your institution?	❑ Yes ❑ No
C.1.2	require you to obtain additional funds for this research study from other sources?	❑ Yes ❑ No
C.1.3	contain a clause that prohibits you from disclosing certain aspects about the study without the permission of the funder?	❑ Yes ❑ No
C.1.4	specify the maximum allowable time for pre-publication review by the funder?	❑ Yes ❑ No
C.1.4a	If you answered yes to item C.1.4, what is that time?	_____ days

MODULE D: STUDY TEAM AND FUNDER RELATIONSHIP PROFILE

ITEM	DESCRIPTOR	RESPONSE			
D.1.0	**Who bears final responsibility for and/or has ultimate authority over the following areas of the study?**				
D.1.1	Conceptualizing and designing the study *†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.2	Approving the final design†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.3	Approving the final data analysis plan	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.4	Recruiting participants	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.5	Collecting or assembling data*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.6	Analyzing the data*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.7	Interpreting the data*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.8	Supervising or coordinating the study	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.9	Deciding on the dissemination plan related to study results	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10	If the study is published, who bears final responsibility for and/or has ultimate authority over the following areas of the manuscript development?				
D.1.10a	Drafting all or parts of the manuscript(s)*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10b	Revising the manuscript(s) for important intellectual content*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10c	Giving final approval of the version to be published*†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10d	Deciding where the manuscript(s) will be submitted for publication†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10e	Deciding the timing of the manuscript(s) submission for publication†	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10f	Deciding authorship	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10g	Deciding authorship order‡	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10h	Acting as the study guarantor‡	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know
D.1.10i	Providing administrative, technical or logistic support	❑ Study team	❑ Funder	❑ Shared§	❑ Don't know

SECTION 3: PERSONAL FINANCIAL INFORMATION

This section is completed at the study's initiation and updated as necessary.

MODULE E: FINANCIAL PROFILE

ITEM	DESCRIPTOR	RESPONSE
E.1.0	**Does this study provide you with salary support?**	❑ Yes ❑ No
E.1.1	If you answered yes to item E.1.0, what percentage of your annual salary do you estimate will be obtained from the funder(s)?	_____ %
E.2.0	**Will you personally receive direct or indirect financial benefit for your role in this study?**	❑ Yes ❑ No ❑ Don't know
E.2.1	If you answered yes to item E.2.0, what is the amount?	$ _____
E.3.0	**Will your department or institution receive or has it received financial benefit (e.g., direct funding, gifts, general use or discretionary funds or any other payment above your institution's standard administrative overhead rate) from the study funder(s)? (check all that apply)**	❑ Yes, it does now ❑ Yes, it has in the past ❑ Yes, it will in the future ❑ No ❑ Don't know
E.3.1	If you answered yes to item E.3.0, please specify the financial benefit:	_____
E.4.0	**Does this study involve the commercialization of intellectual property (e.g., through patents, copyrights or royalties from such rights)?**	❑ Yes ❑ No ❑ Don't know
E.4.1	If you answered yes to item E.4.0, who receives the financial benefit from this commercialization?	_____
E.4.2	If you answered yes to item E.4.0, how is the intellectual property commercialized (e.g., through patents, copyrights or royalties from such rights)?	_____
E.5.0	**Do you have any financial interests related to competitor(s) of the funder(s) of your study?**	❑ Yes ❑ No
E.5.1	If you answered yes to item E.5.0, please specify:	_____
E.6.0	**Do you currently have or expect to have any financial interests related to the study funder(s)?**	❑ Yes ❑ No ❑ Don't know
E.6.1	If you answered yes to item E.6.0, please specify:	_____
E.7.0	**Do any of your immediate family members (spouse or spouse equivalent, dependent child) currently have or expect to have any financial interests related to the study funder(s)?**	❑ Yes ❑ No ❑ Don't know
E.7.1	If you answered yes to item E.7.0, please specify:	_____

SECTION 4: AUTHORSHIP INFORMATION

This section is completed when a manuscript is being submitted for publication.

MODULE F: AUTHORSHIP PROFILE

ITEM	DESCRIPTOR	RESPONSE
F.1.0	**Is there a manuscript submitted for publication?**	❑ Yes ❑ No
F.1.1	If you answered yes to item F.1.0, what is the title of the manuscript?	_____
F.2.0	**Are you an author on this manuscript?**	❑ Yes ❑ No
F.2.1	To which aspects of the study and the manuscript development did you make a substantial contribution?	
F.2.1a	Obtaining funding‡	❑ Yes ❑ No
F.2.1b	Conceptualizing and designing the study*	❑ Yes ❑ No
F.2.1c	Providing study materials and/or recruiting participants‡	❑ Yes ❑ No
F.2.1d	Collecting or assembling data*	❑ Yes ❑ No
F.2.1e	Analyzing and interpreting data*	❑ Yes ❑ No
F.2.1f	Providing statistical expertise‡	❑ Yes ❑ No
F.2.1g	Supervising or coordinating the study‡	❑ Yes ❑ No
F.2.1h	Drafting all or part of the manuscript*	❑ Yes ❑ No
F.2.1i	Revising the manuscript for important intellectual content*	❑ Yes ❑ No
F.2.1j	Giving final approval of the version to be published*	❑ Yes ❑ No
F.2.1k	Providing administrative, technical or logistic support‡	❑ Yes ❑ No
F.2.2	Are you the study guarantor?†	❑ Yes ❑ No
F.3.0	**Are you aware of the involvement of a guest or ghost author?†**	❑ Yes ❑ No

The Checklist

Advantages and Features

- Fillable form
- Built-in logic
- Integrated glossary of terms

GLOSSARY

Authorship

"An 'author' is generally considered to be someone who has made substantive intellectual contributions to a published study."

– *International Committee of Medical Journal Editors*[1]

Authorship order

"Many different ways of determining order of authorship exist across disciplines, research groups, and countries. Examples of authorship policies include descending order of contribution, placing the person who took the lead in writing the manuscript or doing the research first and the most experienced contributor last, and alphabetical or random order. While the significance of a particular order may be understood in a given setting, order of authorship has no generally agreed upon meaning."

– *Faculty of Medicine Harvard Medical School*[4]

Clinical trial

"Research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes"

– *World Health Organization*[5]

Clinical trial registry

"The [online] entity that houses the clinical trial register. It is responsible for ensuring the completeness and accuracy of the information the register contains, and that the registered information [can be] used to inform health care decision making."

– *World Health Organization*[5]

Contract

"A document, dated and signed by the investigator, institution and sponsor, that sets out any agreements on financial matters and delegation/distribution of responsibilities. The protocol may also serve as a contract when it contains such information and is signed."

– *Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products*[6]

Contract research organization

"A scientific organization (commercial, academic or other) to which a sponsor may transfer some of its tasks and obligations [related to a clinical trial]. Any such transfer should be defined in writing."

– *Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products*[6]

Dissemination plan

"Specific details on how information or knowledge gained from a project is distributed and shared. Project dissemination can occur through presentations, conferences, publications and web sites."

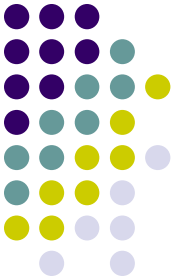
– *Human Resources and Skills Development Canada*[7]

Use in Practice

The Checklist

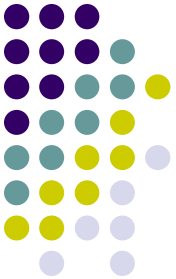
- Completed by each investigator
- Is a ‘living document’
  - Modules completed at different study transition points.
    - Modules A to E at study inception
    - Module F upon study completion

Why a fCOI Checklist?



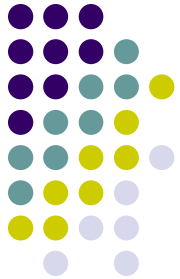
- Promotes transparency and accountability
- Provides a standardized set of questions to be completed individually by each investigator.
- Allows investigators to be sensitized to information they should know about their study

Advantages of this Checklist



1. Prospective
2. Places disclosure in context of study
3. Single document for multiple stakeholders
4. Evolves over the project
5. Allows opportunities for early management of fCOI
6. Standardized tool
7. Comprehensive
8. Provides information on potential areas of the study where bias can be introduced
9. Links financial relationships with the opportunity to introduce bias
10. Easy to complete

Current and Future Opportunities



Education

- Alerts users to potential conflicts
  - Identifies opportunities for early interventions

Communication

- Facilitates communication among investigators

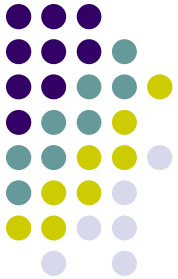
Integration

- Relate to institutional requirements
- Encourage Checklist completion for institutional sign off for clinical research grant submissions
- Include as part of REB review package

Recognition of importance of disclosure

- Operationalize required COI policy disclosures

TAHSN COI Policy Development



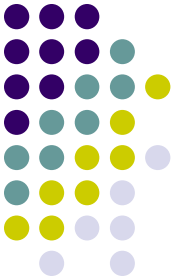
Relationship Attestation and Disclosure Policy drafted

- Focus is on disclosure

Circulated for TAHSN feedback in summer 2017

- Feedback obtained
- How to operationalize
- Ongoing revision

In Summary



1. Early research indicated need for Conflicts of Interest reporting
2. Financial Conflicts of Interest Checklist facilitates disclosure
3. Opportunities for harmonized approach

Research Team

Principal Applicant:

- Paula Rochon MD, MPH — Academics

Co-applicants:

- An-Wen Chan MD, DPhil — Academics
- Lorraine Ferris PHD, LLM — Research Ethics
- Jennifer Gold LLB — Legal
- John Hoey MD — Journal Editor
- Joel Lexchin MD, MSC — Academics
- James Maskalyk MD — Journal Editor
- David Moher PHD — CONSORT
- David Streiner PHD — Statistics
- Nathan Taback PHD — Statistics
- Marleen Van Laethem MSC — Research Ethics

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Finding the Checklist:

FCOI Checklist
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3116675/

Interactive/Fillable PDF fCOI Checklist
https://goo.gl/tNdy5H

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