Conflicts of Interest in Research: The Clinician Scientist’s Perspective

Pierce K.H Chow  FRCSE  PhD
Professor, Duke-NUS Graduate Medical School, Singapore
Senior Clinician-Scientist, National Medical Research Council Singapore
Senior Consultant Surgeon, National Cancer Center Singapore
Senior Consultant Surgeon, Singapore General Hospital

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What does Society expect from (biomedical) research?

Why do we do research?

The primary purpose of biomedical research are to:

- understand the causes, development, and effects of a disease
- improve preventive, diagnostic, and therapeutic interventions
- develop improved methods, procedures and treatments
Why should (bio)medical research be conflicted?
Biomedical research is essentially conflicted

**Institution**
Bottom line
Growth
Diversification

**Researcher**
Increase funding
Increase income
Improve profile

**Sponsor**
Growth /Profit
(industry)
Win votes
(government)

**Purpose of Research**

*Understand the causes, development, and effects of a disease*

*Improve preventive, diagnostic, and therapeutic interventions*

*Develop improved methods, procedures and treatments*

*SGH – Surgery*
A clinician who also engages in clinical and translational research

Doctor

Most practical, cheapest, & most immediate diagnosis and treatment

Service clinical needs

Institutional bottom line

Fiduciary interests

Minimal potential patient risk

Scientist

Data for the most scientifically based diagnosis and treatment

Scientific confirmation

Intellectual bottom line

Scientific judgement

Maximal potential patient benefit

...plays a dual role that is contradictory at its very constitution....

SGH – Surgery
• Is this conflicted existence of biomedical research necessarily unchangeable?
  – *Can the aims of selected institutions and individuals be aligned to the purpose of research?*

• What are conflicts of interests in biomedical research and how can these be mitigated?
  – *such that its negative impact be minimized*
philosophy aside
definition of conflict of interest (coi) in biomedical research

“Circumstances that adversely affect impartiality, objectivity and independence, and encapsulates both actual and potential conflicts”

Singapore Bioethics Advisory Committee, 2004
Definitions of COI in Biomedical Research

“When a personal or institutional interest/relationship interferes with the ability of the individual or institution to act in the interest of another party, when the individual or institution has an ethical or legal obligation to act in that other party's interest.”

Boatright J, 2001

“COI is a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.”

Institute of Medicine (US) Committee on Conflict of Interest in Medical Research, Education, and Practice
Components of COI in Biomedical Research

• **Primary Interests:**
  • promoting and protecting the integrity of research
    • the public and research participants need to trust physicians and researchers to act and make judgments in ways that are consistent with these primary interests

• **Secondary interests:**
  • The interests of the physician/researcher, institution, sponsor
    • Financial gain
    • Professional/ institutional advancement,
    • Personal/ institutional recognition
    • Favours to friends and family and allies etc
Components of COI in Biomedical Research

Conflict itself:

NOT an occurrence where primary interests are necessarily compromised but rather, circumstances/relationships that create or increase the risk of neglecting the primary interests, as a result of the pursuit of secondary interests.

A COI exists whether or not an individual/institution is actually influenced by the secondary interest.

Resolution of COI requires that the primary interest should take precedence over a secondary interest.
Not all relationships represent conflicts

But the potential for COI an exists whether the clinician/researcher believes that relationship affects their scientific judgment.
Overt and Covert COI

“Conflicts of interest are a special concern in biomedical research because they have the potential to influence the outcome of study results or clinical trials, leading to results that favour certain products or unnecessary risks for patients”

SOURCE: Magazine of Wall Street

Overt: e.g. a direct financial interest in a facility
Covert: e.g. patients suffer no actual physical or financial harm

physician may not even being aware
no actual adverse outcome may occur

SGH – Surgery

Greenberg RD, 2012
Conflict of Interest in Biomedical Research can occur at the level of:

**Individual (Researcher)**  
**Institution**  
**Sponsor/ Funder**
# Types of (personal) Conflicts of Interests

<table>
<thead>
<tr>
<th>Financial</th>
<th>Non-financial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Incentives e.g.:</strong></td>
<td><strong>Professional e.g.:</strong></td>
</tr>
<tr>
<td>• Incentives for patient recruitment</td>
<td>• <strong>Scientific advancement</strong>, influence, recognition</td>
</tr>
<tr>
<td>• Financial stakes in outcome of trial</td>
<td>• <strong>Undue interest to attain positive results</strong>, pressure to publish</td>
</tr>
<tr>
<td>• research grants</td>
<td>• <strong>Disregarding</strong> or under-reporting AEs</td>
</tr>
<tr>
<td><strong>Financial gains e.g.:</strong></td>
<td><strong>Personal e.g.:</strong></td>
</tr>
<tr>
<td>• Travel, meals, lodging, personal expenses, &amp;</td>
<td>• <strong>Nepotism</strong>- bias for family &amp; friends</td>
</tr>
<tr>
<td>payment for professional services e.g. talks,</td>
<td>• <strong>Vigilante desire</strong> – recruitment of patients into</td>
</tr>
<tr>
<td>sponsored consultancy, gifts, equity interest,</td>
<td>trial for free medication/treatment</td>
</tr>
<tr>
<td>personal funds</td>
<td></td>
</tr>
<tr>
<td><strong>Intellectual Property e.g.:</strong></td>
<td><strong>Intellectual e.g.:</strong></td>
</tr>
<tr>
<td>• Monetary benefits from patents and technology transfer, new venture formation, royalties</td>
<td>• <strong>Prejudice</strong> against or towards certain therapy/drug due to any reasons not purely for patient benefit</td>
</tr>
</tbody>
</table>
COIs: Fiduciary & More

• **Financial relationships:**
  – More societal focus on FCOIs does NOT indicate they are more corrupting, but because they are more objective & quantifiable than others
  – Most likely to undermine credibility: employment, consultancies, stock ownership, honoraria, and paid expert testimony

• **Others:** personal relationships, academic competition, and intellectual passion – difficult to define

*International Committee of Medical Journal Editors (ICMJE)*
Financial COIs

Financial relationships with the industry has been the focus of public, institutional, and regulatory scrutiny. It is relatively more measurable and objectifiable than non-financial relationships.

United States: 18.3% of respondents said they received reimbursement for their costs of travel, time, meals, lodging, and personal expenses for attending meetings sponsored by drug companies, and 14.1% reported that they received payments to give talks, do consulting, or enrol patients in clinical trials.

Campbell EG. Arch Inter Med 2010
Non-Financial COIs

<table>
<thead>
<tr>
<th>Non-financial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Professional e.g.:</strong></td>
</tr>
<tr>
<td>• <strong>Scientific advancement</strong>, influence, recognition</td>
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<tr>
<td>• <strong>Undue interest to attain positive results</strong>, &amp; pressure to publish</td>
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<tr>
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</tr>
<tr>
<td><strong>Intellectual e.g.:</strong></td>
</tr>
<tr>
<td>• <strong>Prejudice</strong> against or towards certain therapy/drug due to any reasons not purely for patient benefit</td>
</tr>
</tbody>
</table>

Even more pervasive

Difficult to define and regulate

Requires undisputed violation of research ethic
Trends and Changing Practices: The Rise in Industry Control

1980s
- Industry $\rightarrow$ Fund studies
- Academic researchers $\rightarrow$ full control of study design & conduct, collection & analysis of data, reporting of results

Today
- Industry $\rightarrow$ Partakes in what used to be PI’s decision
  - Design multicenter trials, control study design, data analysis, make publication writing & decisions

Greenberg, R. D., 2012
The relationship of Academia with Industry

- **Conflict is relevant to all relationships with industry**

- **The good:**
  - Results produced from interactions between academic research and industry support have so far been *significantly positive*
  - **Funding** allows continual production of promising new diagnostics and therapeutics to enter industrial development

- **The Bad:**
  - Undue influence on primary interest
  - Society’s perception of relationships with industry: *that industry funding adversely affects the validity of the research by producing a pro-industry result or conclusion* (Lundh et al., 2012)
COIs in Clinical Trials

- Common now for pharmas to prefer to run trials as the only industry sponsor/only owner
- Co-sponsorship typically reflected co-ownership of the same intervention
- Pharmas becoming specialized in medical fields where they face little competition

\[(D. N. Lathyris, Eur J Clin Invest 2010)\]
All 15 companies strongly preferred to run trials where they were the only industry sponsor or even the only owner of the assessed interventions.
COIs in Clinical Trials

• Industry sponsored trials tend to have a better chance of positive results, perhaps due to decision to only conducting potentially positive trials

• Serious implications on medical research:
  – Progressively dependant on financial and commercial criteria, and less on scientific ones
  – Diminishes understanding of relative merits of different interventions for the same condition

(D. N. Lathyris, Eur J Clin Invest 2010)
High-Dose Tamoxifen in the Treatment of Inoperable Hepatocellular Carcinoma: A Multicenter Randomized Controlled Trial

Pierce K. H. Chow,1,2 Dee-Choo Tai,1 Chee-Kiat Tan,1 David Machin,2 Kin Mun Win,1 Phillip J. Johnson,7 and Kee-Choo Soo3,1,2 for the Asia-Pacific Hepatocellular Carcinoma Trials Group

In the Asia-Pacific region and elsewhere, almost 85% of patients with hepatocellular carcinoma (HCC) are inoperable at diagnosis and have a dismal prognosis. Tamoxifen (TMX) is believed to inhibit HCC growth in vivo but has not been evaluated for its effect in clinical trials. Results of previous phase 3 trials in inoperable HCC have been conflicting and inconclusive. At higher doses, however, TMX inhibits HCC through ER-independent mechanisms.

A multicenter randomized controlled trial was performed to assess the role of high-dose TMX versus placebo (P) in the treatment of patients with inoperable HCC with respect to survival and quality of life (QoL). A total of 329 patients from 10 centers in 9 countries in the Asia-Pacific region enrolled in a double-blind randomized controlled trial of TMX 120 mg/d (TMX120) against P as a control arm with an intermediate dosage of TMX 60 mg/d (TMX60) to assess possible dose response. An independent data monitoring committee reviewed all aspects of the trial. QoL was assessed using the European Organization for Research and Treatment of Cancer QiL-Q30 questionnaire. Median survival rates for the P, TMX60, and TMX120 groups were 44%, 41%, and 35%, respectively, with a statistically significant trend difference in survival across the 3 treatment regimens (P = .011).

There was a significantly higher risk of death in the TMX120 group compared with the P group. A subset analysis identified that patients with hepatitis B virus infection had a better survival outcome than patients with hepatitis C virus infection. A subset analysis identified that patients with hepatitis B virus infection had a better survival outcome than patients with hepatitis C virus infection.
Negative trials that impacted practice: Asia-Pacific Hepatocellular Carcinoma Trials Group

Chow PK et al Hepatology 2002
329 patients 132 placebo

Chow PK et al Br J Cancer 2011
204 patients 69 placebo

HR = 1.25, 95% CI = 0.92–1.71, P = 0.16
The huge debate:
Pro-industry bias in Medical Publishing

• **Cochrane analysis, 2012** suggested that in industry sponsored studies:
  
  – There was less agreement between the results and the conclusions than in non-industry sponsored studies
  
  – Often more favourable to the sponsor’s products than non-industry sponsored drug and device studies due to biases that cannot be explained by standard “Risk of bias” assessment tools

* (Lundh et al. Cochrane Database Syst Rev 2012)
Industrial Collaborations & Publishing

- A systematic review on the impact of trial sponsorship on study interpretation demonstrated a statistically significant association between industry sponsorship and pro-industry conclusions (OR 3.60; 95% CI, 2.63–4.91) OR (OR 4.05; 95% CI, 2.98–5.51)

### Analysis 3.1. Comparison 3 Conclusions: Industry sponsored versus non-industry sponsored studies, Outcome 1 Number of studies with favorable conclusions.

#### Review: Industry sponsorship and research outcome.

**Comparison:** 3 Conclusions: industry sponsored versus non-industry sponsored studies

**Outcome:** 1 Number of studies with favorable conclusions

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Industry n/M</th>
<th>Non-Industry n/N</th>
<th>Risk Ratio (Random 95% CI)</th>
<th>Weight</th>
<th>Risk Ratio (Random 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Armer 2006</td>
<td>125/138</td>
<td>39/50</td>
<td></td>
<td>6.1%</td>
<td>1.16 [0.99, 1.36]</td>
</tr>
<tr>
<td>Aasebak 2009</td>
<td>26/39</td>
<td>2/10</td>
<td></td>
<td>0.5%</td>
<td>4.48 [1.29, 15.58]</td>
</tr>
<tr>
<td>Aas-Nielsen 2003</td>
<td>92/197</td>
<td>42/73</td>
<td></td>
<td>4.2%</td>
<td>1.88 [1.39, 2.53]</td>
</tr>
<tr>
<td>Bero 2007</td>
<td>66/94</td>
<td>39/97</td>
<td></td>
<td>4.5%</td>
<td>1.75 [1.32, 2.30]</td>
</tr>
<tr>
<td>Booth 2008</td>
<td>66/118</td>
<td>55/153</td>
<td></td>
<td>4.6%</td>
<td>1.56 [1.19, 2.03]</td>
</tr>
<tr>
<td>Buchlowsky 2004</td>
<td>138/181</td>
<td>224/319</td>
<td></td>
<td>6.7%</td>
<td>1.09 [0.97, 1.21]</td>
</tr>
<tr>
<td>Chard 2000</td>
<td>106/108</td>
<td>372/383</td>
<td></td>
<td>7.3%</td>
<td>1.01 [0.98, 1.04]</td>
</tr>
<tr>
<td>Cho 1996</td>
<td>39/40</td>
<td>89/112</td>
<td></td>
<td>6.7%</td>
<td>1.23 [1.10, 1.36]</td>
</tr>
<tr>
<td>Davidson 1986</td>
<td>32/36</td>
<td>31/49</td>
<td></td>
<td>4.9%</td>
<td>1.41 [1.10, 1.79]</td>
</tr>
<tr>
<td>Djulbegovic 2000</td>
<td>26/35</td>
<td>50/95</td>
<td></td>
<td>4.5%</td>
<td>1.41 [1.07, 1.85]</td>
</tr>
<tr>
<td>Finucane 2004</td>
<td>30/30</td>
<td>12/18</td>
<td></td>
<td>3.9%</td>
<td>1.50 [1.08, 2.07]</td>
</tr>
<tr>
<td>Jefferson 2009</td>
<td>64/176</td>
<td>13/194</td>
<td></td>
<td>6.3%</td>
<td>1.25 [1.09, 1.43]</td>
</tr>
<tr>
<td>Kjaergard 2002</td>
<td>28/38</td>
<td>16/22</td>
<td></td>
<td>4.0%</td>
<td>1.01 [0.74, 1.29]</td>
</tr>
<tr>
<td>Liss 2006</td>
<td>62/63</td>
<td>12/37</td>
<td></td>
<td>2.6%</td>
<td>2.02 [1.50, 2.48]</td>
</tr>
<tr>
<td>Lynch 2007</td>
<td>26/34</td>
<td>49/65</td>
<td></td>
<td>5.0%</td>
<td>1.01 [0.80, 1.28]</td>
</tr>
<tr>
<td>Pepperman 2007</td>
<td>52/67</td>
<td>48/73</td>
<td></td>
<td>5.4%</td>
<td>1.18 [0.96, 1.46]</td>
</tr>
<tr>
<td>Perlis 2005a</td>
<td>87/102</td>
<td>47/77</td>
<td></td>
<td>5.5%</td>
<td>1.40 [1.15, 1.70]</td>
</tr>
<tr>
<td>Rasmussen 2009</td>
<td>83/90</td>
<td>15/28</td>
<td></td>
<td>3.5%</td>
<td>1.42 [0.99, 2.04]</td>
</tr>
<tr>
<td>Rattinger 2009</td>
<td>31/36</td>
<td>21/25</td>
<td></td>
<td>5.3%</td>
<td>1.03 [0.83, 1.27]</td>
</tr>
<tr>
<td>Reker 2006</td>
<td>121/189</td>
<td>21/151</td>
<td></td>
<td>3.7%</td>
<td>1.55 [1.10, 2.20]</td>
</tr>
<tr>
<td>Tinganaka 2007</td>
<td>124/146</td>
<td>28/44</td>
<td></td>
<td>5.0%</td>
<td>1.33 [1.06, 1.69]</td>
</tr>
</tbody>
</table>

**Total (95% CI):** 1866 / 2075

Total events: 1+24 (Industry), 1345 (Non-Industry)

*Heterogeneity Test:* $I^2 = 2.01$, $Q = 1.1575$, df $= 20$ ($P < 0.0001$), $I^2 = 83%$

Test for overall effect: $Z = 5.70$ ($P < 0.0001$)

Test for subgroup differences: Not applicable

- P < 0.05: Industry less favorable
- P > 0.05: Industry more favorable

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Influence of industry-supported RCTs on JIF & revenue

• A study involving six major medical journals demonstrated that industry-supported trials were more frequently cited than trials with other types of support, and omitting them from the impact factor calculation decreased journal impact factors of up to 15% for NEJM in 2007.

• Income from the sales of reprints for The Lancet contributed to 41% of the total income in 2005–2006

### Table 1. Description of support of randomised controlled trials published in major general medical journals.

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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n trials (%)</td>
<td>71 (16)</td>
<td>58 (17)</td>
<td>67 (13)</td>
<td>80 (13)</td>
<td>91 (6)</td>
<td>116 (16)</td>
<td>76 (7)</td>
<td>113 (19)</td>
<td>186 (12)</td>
<td>129 (20)</td>
<td>160 (20)</td>
<td>206 (34)</td>
</tr>
<tr>
<td>Total n citable papers</td>
<td>458</td>
<td>339</td>
<td>519</td>
<td>593</td>
<td>1624</td>
<td>745</td>
<td>1120</td>
<td>590</td>
<td>1515</td>
<td>661</td>
<td>785</td>
<td>611</td>
</tr>
<tr>
<td>Industry support (%)</td>
<td>19 (27)</td>
<td>11 (19)</td>
<td>22 (33)</td>
<td>12 (15)</td>
<td>12 (13)</td>
<td>8 (7)</td>
<td>23 (30)</td>
<td>29 (26)</td>
<td>47 (25)</td>
<td>28 (22)</td>
<td>51 (32)</td>
<td>66 (32)</td>
</tr>
<tr>
<td>Mixed support (%)</td>
<td>27 (38)</td>
<td>20 (34)</td>
<td>14 (21)</td>
<td>23 (29)</td>
<td>19 (21)</td>
<td>23 (20)</td>
<td>21 (28)</td>
<td>33 (29)</td>
<td>46 (25)</td>
<td>46 (36)</td>
<td>54 (34)</td>
<td>95 (46)</td>
</tr>
<tr>
<td>Nonindustry support (%)</td>
<td>19 (27)</td>
<td>27 (47)</td>
<td>24 (36)</td>
<td>37 (46)</td>
<td>52 (57)</td>
<td>82 (71)</td>
<td>26 (34)</td>
<td>50 (44)</td>
<td>61 (33)</td>
<td>55 (43)</td>
<td>42 (26)</td>
<td>41 (20)</td>
</tr>
<tr>
<td>Not stated (%)</td>
<td>6 (8)</td>
<td>0 (0)</td>
<td>7 (10)</td>
<td>8 (10)</td>
<td>8 (9)</td>
<td>3 (3)</td>
<td>6 (8)</td>
<td>1 (1)</td>
<td>32 (17)</td>
<td>0 (0)</td>
<td>13 (8)</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Change in support (p-value)*</td>
<td>—</td>
<td>0.047</td>
<td>—</td>
<td>0.041</td>
<td>—</td>
<td>0.101</td>
<td>—</td>
<td>0.255</td>
<td>—</td>
<td>0.251</td>
<td>—</td>
<td>0.498</td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pmed.1000354.t001

### Table 2. Citations for randomised trials published in major general medical journals and change in impact factors when industry-supported trials are excluded.

<table>
<thead>
<tr>
<th>Citation and Impact Factor</th>
<th>Annals</th>
<th>Archives</th>
<th>BMJ</th>
<th>JAMA</th>
<th>Lancet</th>
<th>NEJM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean n citations&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Industry support</td>
<td>13.3</td>
<td>27.7</td>
<td>6.5</td>
<td>14.4</td>
<td>7.6</td>
<td>9.9</td>
</tr>
<tr>
<td>Mixed support</td>
<td>18.7</td>
<td>17.1</td>
<td>9.4</td>
<td>11.8</td>
<td>7.3</td>
<td>11.3</td>
</tr>
<tr>
<td>Nonindustry support</td>
<td>9.3</td>
<td>12.0</td>
<td>5.5</td>
<td>6.5</td>
<td>7.3</td>
<td>5.7</td>
</tr>
<tr>
<td>Not stated</td>
<td>10.8</td>
<td>—</td>
<td>10.9</td>
<td>8.3</td>
<td>8.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Difference in citations (p-value)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.186</td>
<td>&lt;0.001</td>
<td>0.237</td>
<td>&lt;0.001</td>
<td>0.949</td>
<td>0.033</td>
</tr>
</tbody>
</table>

### Change in impact factor

| Without trials with industry support (%) | −1 | 0 | −1 | −2 | 0 | 0 | −3 | −3 | −5 | −4 | −7 | −7 |
| Without trials with industry and mixed support (%) | −6 | −4 | −3 | −4 | −1 | −1 | −5 | −5 | −11 | −6 | −13 | −15 |

<sup>a</sup>For each journal citations are reported for their impact factor year (i.e., citations in 1998 to trials published in 1996–1997 and in 2007 to trials published in 2005–2006).

<sup>b</sup>Difference in citations depending on type of support using Jonckheere-Terpstra test for trend (two-sided, support not stated excluded from the analysis).

doi:10.1371/journal.pmed.1000354.t002

Industrial Collaborations & Publishing

- **IP protection**
  - lead to deliberate delay in publishing
- **Withholding negative results**
- **Publication in unreliable & dubious journals**
- **Gift authorships & Ghost authorships**
  - Authors (Industry/Academic) not stated as author
  - Incentives given to academics ghost authors
  - Pharma writers as ghost authors controls writing
- **Expert opinions from paid scientific advisors**
  - In reality are campaigns to promote company products

Ghost Writing & Guest Authorship

Guest authorship
• Publishing studies prepared by hired medical writers but signed by academic “guest authors” who are invited to add their names without fulfilling authorship criteria

Ghost writing
• Published article fails to acknowledge contributions of original writer
• Raises serious ethical and legal concerns

Dadhich JP., 2012
“Once a conflict is declared, it needs to be managed”
Managing COIs- A Fundamental Tenet of a Clinician Scientist’s Professionalism

- Public trust and the credibility depends in part on how well conflict of interest is handled *(International Committee of Medical Journal Editors, ICJME)*

- The reality: patients and the public benefit when physicians and researchers collaborate with industry

- The conflict: relationship to industry has been shown extensively to influence professional judgment
Managing COIs- A Fundamental Tenet of a Clinician Scientist’s Professionalism

• A clinician scientist plays a multi-faceted role - unavoidable COI

• Recognize that organizations like Academic Medical Centers, which include both medical services and medical research have, by the nature of their structure, built-in conflicts

• Prevention & Management of COIs
# Types of COI Mitigation

<table>
<thead>
<tr>
<th>5 types of COI mitigation</th>
<th>General theme of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recognize</strong></td>
<td>Recognise and remove any potential COI before it happens</td>
</tr>
<tr>
<td><strong>Disclosure</strong></td>
<td>Disclose all potential COIs. Be aware of the threshold levels established by government, regulatory authorities, academic institute</td>
</tr>
<tr>
<td><strong>Recusal</strong></td>
<td>Institute prevents participation in activities that may lead to COI</td>
</tr>
<tr>
<td><strong>Third party independent review</strong></td>
<td>Independent up-front investigation through outside organization e.g. DMC, IRB, HSA (Singapore), FDA (US)</td>
</tr>
<tr>
<td><strong>Codes of ethics</strong></td>
<td>Set standards of conduct</td>
</tr>
</tbody>
</table>

Table adapted with modifications from: Conflict of evidence or conflict of interest? Evid Based Spine Care J, 3 (1), 5-7.
Managing COIs: Organization & Above

Institutional level
Develop detailed COI policies to help investigators assess severity of conflicts

Government level
Industry to report financial support given to researchers and doctors
Research Integrity

Faculty, staff and student of the University community engaging in research should adhere to the highest standard of ethics and Research Integrity. This is to ensure that the reputation of the University for scholarly integrity is preserved.

Research Integrity includes the rigour, care and accountability that are the hallmarks of good scholarship and is not merely the avoidance of wrongdoing. Research Misconduct by the University community, defined as fabrication, falsification, plagiarism or other wrongdoing in proposing, designing, performing, recording, supervising or reviewing research, or in reporting research results is unacceptable and is grounds for disciplinary action.

Research Integrity Officers appointed by the University are responsible for assessing allegations of Research Misconduct and determining when such allegations warrant inquiries, and for overseeing formal inquiries. Allegations of Research Misconduct can be made by an individual in person, or in writing in a sealed envelope, signed and marked “strictly confidential” to the Office of the Deputy President (Research & Technology) who will assign a Research Integrity Officer to look into the allegations.

Please refer to the website of NUS Institutional Review Board for more information.

Policy Governing the Use of Human Subjects in Research and Teaching

All NUS activities related to research involving human subjects, regardless of funding sources, will be guided by the Declaration of Helsinki, The Belmont Report and all relevant laws and regulations in Singapore.

All NUS activities related to US federally conducted or supported human subject research will comply with both:

- The Terms of the Federalwide Assurance (FWA) for International (Non-U.S.) Institutions as stated in the US Department of Health and Human Services (DHHS) website, and
- ICH E6 Good Clinical Practice.

Please refer to the website of NUS Institutional Review Board for more information.
Managing COIs:
At the Investigator Level

Investigator level
1. Recognise potential COIs ✓
2. Disclose conflicts ✓
3. Manage COIs
The First Step: Recognise & Disclose

Disclosure of individual and institutional financial relationships is a critical but limited first step in the process of identifying and responding to conflicts of interest

(Resnik, Account Res 2010)

"Under disclosure rules, I'm required to tell you I own stock in the company whose drug I'm prescribing."
Disclosure of COIs

The International Committee of Medical Journal Editors (ICMJE) requires information from researchers about work under consideration for publication:

- Receiving grant, consulting fee/honorarium, payment for writing/reviewing manuscript

- Relevant financial activities outside submitted work including board membership, consultancy, payment for lectures

(International Committee of Medical Journal Editors, ICJME)
Why should we Discloses?

• Some researchers worry that:
  – reporting COI may be intrusive
  – it suggests an unproven tie between industry fees and research findings

• But disclosure is the first and best defence against bias charges, and not disclosing information evokes suspicion

Collaborating with Industry

- Having a COI is not necessarily a negative

- The relationships that should exist between industry and investigators is long-term and mutually beneficial, and should continue to be so

- Institutions need a robust strategy to manage COIs in order not to lose research investment from industry

Importance of COI management in Asia

• Increasing number of clinical trials and related research in Asia underscores the importance of good COI management.

• Introduction of a proper system for COI declaration and management will in turn encourage academic research whilst breeding appropriate research values.
  – In line with Asia’s vision of becoming the next medical/research center of gravity.
Investigator-Initiated Trials: 
*The Asia-Pacific Hepatocellular Carcinoma Trials Group Model*

Structure introduces accountability and reduces potential conflict
## Summary of Recommendations

| **Recognise** | • Assess potential fCOI i.e. any gifts, speaking fees, meals & travel  
• Assess *advantages vs disadvantages* of attending industry-sponsored events, attendee or speaker  
• Consider whether serving on an industry board poses a conflict before accepting |
| **Disclose** | • Familiarize with reporting rules & disclosure limits of your institution & government  
• When unsure, contact office in your institution that handles financial disclosures to determine if the need to declare & what to file  
• Consider whether bias could be introduced into your research & guard against those threats e.g. *industry funding should be declared, no matter the results*  
• Disclose financial relationships in all reports, presentations & speeches to ensure transparency |
| **Decline** | • Decline industry offers to ghostwrite papers, articles or presentations |
| **Others** | • Attend seminars offered by institution or government to learn more about the reporting process |
Disclosure Statement

Relevant financial activities related to this presentation:

– None

Financial Activities outside this presentation: *(Money paid for services rendered, generally honoraria, royalties, or fees for consulting, lectures, speakers bureaus, expert testimony, employment, or other affiliations)*

– Pierce Chow has received honoraria & grant funding for research studies from Sirtex Medical Limited, GlaxoSmithKline (GSK), MSK, Bayer HealthCare, NMRC, BMRC, NRF, SingHealth

Non-Financial Support outside this presentation: *(Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc)*

– Pierce Chow has received paid travel for independent lectures and talks from Sirtex, Bayer, Novartis, MSK, Special Conference Benefit from Singapore General Hospital
Disclosure Statement

Intellectual Property Licensed:

1. PCT Number PCT/AU02/00558; WIPO Number WO2002/090580NIL 3 May 2002.


Thank You!

“The value and benefits of research are vitally dependent on the integrity of research. While there can be and are national and disciplinary differences in the way research is organised and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken.” (Singapore Statement on Research Integrity, World Conference on Research Integrity 2010)
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