

# Protecting the Scientific Integrity of the *IARC Monographs*



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*The presenter has no conflicting interests to declare.  
This presentation does not necessarily reflect the views of OEHHA, CalEPA, or the State of California.*

# Disclosure

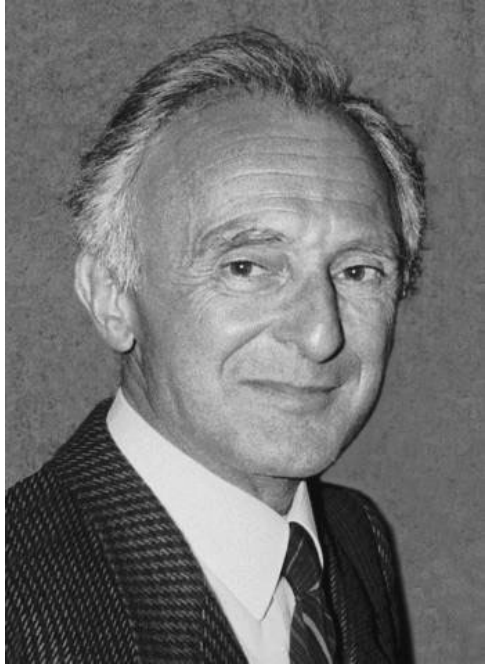
- The presenter's only professional compensation is from the State of California, but this presentation was developed outside of official time.
- The principles and processes discussed in this presentation were developed as part of the presenter's previous employment at the International Agency for Research on Cancer.
- There are no other relationships to disclose.



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# The *IARC Monographs*: “The encyclopaedia of carcinogens”



**Dr Lorenzo Tomatis**  
1929-2007  
Founder of the *IARC Monographs*

- The *IARC Monographs* are a series of scientific reviews that identify environmental factors that can increase the risk of human cancer
- The *IARC Monographs* are developed by experts who conducted the original research
- National and international health agencies use the *Monographs*
  - as a source of scientific information on known or suspected carcinogens
  - as scientific support for their actions to prevent exposure to these agents



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# THE LANCET

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## Transparency at IARC

The appointment in mid May of the next Director of the International Agency for Research on Cancer (IARC) parallels that of the next Director-General of WHO, to be announced next week. IARC was formed in 1945 as part of WHO, is based in Lyon, France, and is most noted for its influential series of monographs on definite, probable, and possible carcinogens. IARC also does original research, especially on cancer epidemiology and laboratory carcinogenesis. Starting last September, *The Lancet* sought to create public discussion about the appointment of the next WHO Director-General (see pages 184 and 231), and some of the issues about that appointment also apply to the next IARC Director, especially about conflicts of interest, accountability, and transparency.

IARC relies on the expertise of its staff and external on-epidemic scientific advisers and, like all public bodies, must be seen to be free of bias, especially from pressure by industry given IARC's important role in pronouncing on the carcinogenic potential of substances in manufacturing, use, or consumption. There is no escaping the fact that expert advisers often have links with industry, either through funding of their research or in previous employment. But there have been instances in which IARC may have come under undue influences, especially commercial ones.

The January, 2003, edition of *The Lancet Oncology* reports accusations of industry influence on IARC, especially when carcinogens are downgraded to a lower category of risk, and the difficulties faced by non-industry observers in attending IARC meetings. Paul Kleihues and Gert Hainken Brandtland, the outgoing heads of IARC and WHO, respectively, denied any such influence. Brandtland told *The Lancet Oncology* that she had commissioned a report which showed that financial disclosure is working properly at IARC. But, for full credibility, the report should be available publicly.

Lorenzo Tomatis was IARC's Director from 1982 to 1993. Last year, in the *International Journal of Occupational and Environmental Health*, he summarised IARC's monograph programme. Tomatis describes political rivalry when scientific values clashed with other influences, especially pressure from industry, and how the monograph

programme had to learn to resist pressure. The monographs use only peer-reviewed and published data, yet, according to Tomatis, industry often tried to slip in their unpublished data on the condition that such data remained confidential. In the same journal, also last year, James Huff, chief of an earlier monograph programme, reported that in volumes 62-79 nearly a third of about 250 monograph authors were "aligned" to industry, as were eight of 19 chairpersons or vice-chairpersons.

How publicly funded organisations such as WHO, and then IARC, should not operate was highlighted last week by the leaking of a report, commissioned and paid for by WHO, to a health journalist. As done for passive smoking by the tobacco industry, this report (according to *The Guardian*, Jan 9), highlights infiltration of, and pressure against, WHO by scientists in the pay of or sympathetic to the food industry. WHO responded that the report is really about the tobacco industry. Several tobacco companies are allied to food industries commercially, and both have major interests in safety and regulation of their products. In response to the newspaper article, Derek Yach, Executive Director for non-communicable disease at WHO, welcomed "the increasingly open and transparent debate on the issue of diet and its effect on the growing burden of chronic disease", although the report's author told *The Lancet* that he would not release the report without WHO's permission.

It only needs the perception, let alone the reality, of financial conflict and commercial pressures to destroy the credibility of important organisations such as IARC and its parent, WHO. Keeping reports confidential, reports that are funded by public monies, is not the way to maintain or restore credibility and only fuels sceptic's suspicions. The new IARC Director could make a good start by opting for full public transparency and access by non-industry third parties. A first step should be to launch an independent external audit into IARC—that would allay any suspicion that discredited and long-established practices are being eliminated under a new regime.

*The Lancet*

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## Transparency at IARC

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*The Lancet* 361: 189 (2003)

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# A Range of Approaches for Addressing Conflicting Interests

- Ignore the issue (fewer organizations are doing this)
- Disclosure only
- Disclosure only, but check that not too many experts have conflicts
- Balance experts with a conflicting interest with other experts who have no conflicting interests
- Balance experts with a conflicting interest with other experts who have opposing interests
- Strive to avoid conflicting interests



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# Tension Between Competing Ideals

Evaluations developed by the most-qualified experts

— VERSUS —

Evaluations whose impartiality is beyond question

*Can the public be confident that experts with a conflicting interest have put the public interest ahead of the conflicting interest?*



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# Most-Qualified Experts or Impartial Experts?

- A difficulty arises when an expert with relevant knowledge and experience also has a real or apparent conflict of interests
- This issue has become more visible in recent years, as interested parties increasingly sponsor epidemiological and experimental studies, or re-analyses of earlier studies
- The selection of experts with real or apparent conflicts of interests can erode confidence in the integrity and impartiality of the results
- On the other hand, the omission of prominent experts can create a perception of reduced scientific quality

# Most-Qualified Experts or Impartial Experts?

- IARC strives to achieve both ideals, by creating a new category of participant known as the “Invited Specialist”
- An Invited Specialist is an expert with critical knowledge and experience who is recused from certain activities because of a conflicting interest
- Invited Specialists may be invited to IARC meetings in limited numbers to contribute their unique knowledge and experience





# IARC's Invited Specialists

- Invited Specialists
  - **do not** chair a meeting or subgroup
  - **do not** draft text that summarizes or interprets cancer data
  - **do not** participate in developing conclusions
- Thus, IARC meetings can include the best-qualified experts while the *Monographs* are developed by experts with no conflicting interests
- The Invited Specialist role also protects the integrity of scientists affiliated with interested parties—they are present as a resource, not to influence the outcome



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# Selection of *IARC Monographs* Experts

- Literature searches are used to identify most experts
  - There are also public nominations via a *Call for Experts*
- A *Declaration of Interests* is required from all potential participants
  - If there is no conflicting interest, the expert may be invited
  - If there is a conflicting interest, look for a comparable expert
  - If necessary (an expert's knowledge and experience is unique) the expert may participate in a limited capacity as an Invited Specialist
- All *Declarations* are updated and reviewed again at the meeting



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# ***Declaration of Interests***

- Employment and consulting (past 4 years or anticipated)
  - Employment by an interested party
  - Consulting, especially expert testimony on matters before a court or government agency
- Research support (past 4 years or anticipated)
  - Support for an expert's own research, includes equipment/supplies
  - Support for others in the expert's research unit or organization
- Financial interests (current interests)
  - Stock, other securities, and business interests
  - Intellectual property (for example, patent rights)



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# Beyond the *Declaration of Interests*

- Ask specific, objective questions
  - *Have you served as an expert witness on this topic in court?*
  - *Have you prepared remarks on this topic for a government review?*
- Look for a pattern of activities that suggests an ongoing relationship
- Verify the absence of conflicting interests
  - Check recent papers for acknowledgments of research support
  - Search the internet for links to special interests
  - Review what constitutes a conflict at the meeting





## **Speculative question**

If this committee activity were to provide the basis for government regulatory action, could the research funding and support for you or your close research colleagues and collaborators be directly affected?

## **Objective question**

Please declare financial interests, employment and consulting, and research support derived from commercial entities whose operations or products result in human exposure to 1,3-butadiene, ethylene oxide, or vinyl chloride.



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# Beyond the *Declaration of Interests*

Experts have said:

"Just get all the experts together and let them fight it out"

"I didn't disclose it because the money doesn't affect my views"

"I'll get paid no matter which side wins" [on expert testimony]

"Vaccines and drugs save lives" [on support from Pharma]

"I have the final say in what gets published"

"I'm just telling the truth"

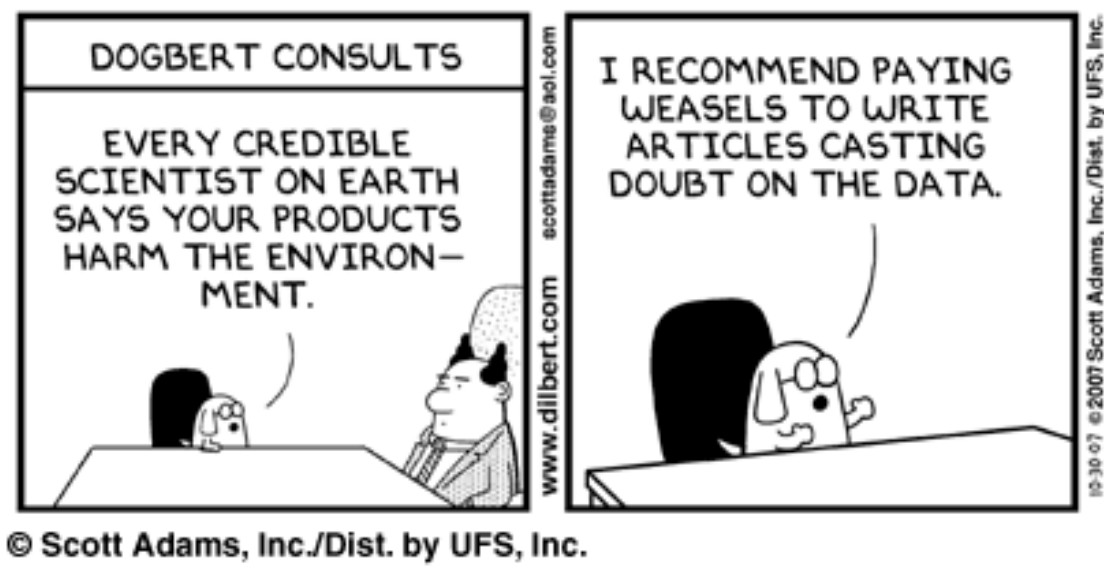


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# Beyond the *Declaration of Interests*

- Late-breaking reanalyses to counter positive studies
- *Ad-hoc* conferences and journal supplements related to a *Monograph*
- Honoraria disguised as travel reimbursements
- Staff of an interested organization sent to Lyon to monitor a meeting, communicating through an Observer or Invited Specialist



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# Using an Invitation To Solicit Work

"Last month, I was contacted by Dr. \_\_\_\_\_ of EPA's Office of Research and Development regarding my availability to attend a conference on EPA's Exposure Factors Handbook. The conference will provide a significant opportunity to present \_\_\_\_\_'s positions on fish consumption and other exposure parameters relevant to the [Superfund site].

"As we discussed last winter at the [Superfund site] strategy meeting, there are excellent technical arguments that justify levels of fish consumption of 1-3 gm/day.

"We anticipate that the cost for this revision [Task 1] will be approximately \$15,000.

"\_\_\_\_\_ believes that . . . [Task 1 and Task 2] . . . will be effective in obtaining a revision of the current estimate of 30 grams per day in the Exposure Factors Handbook."



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# Independent Reporting of Conflicting Interests by a Third Party

- IARC identifies experts, reviews their *Declarations*, then invites experts to a meeting
- At the meeting, IARC asks experts to update their Declarations and also to complete the conflict-of-interest form used by *The Lancet Oncology*
- The editor of *The Lancet Oncology* independently reviews the conflict-of-interest statements and reports any conflicting interests alongside a published summary of the IARC meeting
  - Cogliano et al, *Lancet Oncology* 6(10): 747 (2005)



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# Freedom from Interference

Before a meeting, IARC posts a list of committee members on its website and advises,

“IARC requests that you do not contact or lobby meeting participants, send them written materials, or offer favours that could appear to be linked to their participation . . . IARC will ask participants to report all such contacts and will publicly reveal any attempt to influence the meeting.”

• *Lancet Oncology* 6(10): 747 (2005)



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# Freedom from Interference

IARC reminds committee members to safeguard the integrity of everyone's work by resisting and reporting all attempts at interference

- in the invitation letters
- during the meeting

"It is not acceptable for Observers or third parties to contact other participants before a meeting or to lobby them at any time."

- Preamble to the *IARC Monographs*



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# Summary of IARC's Processes

- IARC invites the most-qualified experts
- IARC also ensures that its committees are not influenced by conflicting interests
  - The “Invited Specialist” role balances the tension between most-qualified experts and impartial experts
- IARC provides for independent reporting of conflicting interests by a third party
- IARC takes additional steps to keep meetings free from interference



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## One Reaction

" . . . an important step towards restoring trust in the way that results of studies done by publicly funded agencies are both prepared and reported. The issues encountered by IARC are certainly not unique and we hope that this joint initiative will serve as a model for other health agencies."

- *Lancet Oncology* 6(10): 735 (2005)



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# IARC's Process Has Been Used As a Model

## U.S. EPA process for contractor-managed peer reviews

- Contractor selects experts who adhere to conflict-of-interest criteria
- Contractor meets with the EPA Science Advisor, who determines whether conflicting interests are adequately addressed

- EPA posts the list of peer reviewers, including the language,

EPA requests that no individual or organization contact in any way its contractor or the subcontractor panel members . . . written materials . . . offers . . .

- Re-sign conflict-of-interest forms at the meeting

- [https://www.epa.gov/sites/default/files/2015-01/documents/epa-process-for-contractor\\_0.pdf](https://www.epa.gov/sites/default/files/2015-01/documents/epa-process-for-contractor_0.pdf)



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# Good Studies Are Not Enough . . .

We also need review committees

- Composed of knowledgeable experts
- Who are free from conflicting interests
- And who can work free from interference

*Not only must we reach an appropriate conclusion, we must do so in a transparent manner that promotes public confidence*

