# Medical specialists and pharmaceutical industry-sponsored research: a survey of the Australian experience

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## ABSTRACT

**Objectives:** To characterise research relationships between medical specialists and the pharmaceutical industry in Australia.

**Design and setting:** Questionnaire survey of medical specialists listed in the *Medical Directory of Australia* and believed to be in active practice, conducted in 2002 and 2003.

**Main outcome measures:** Details of medical specialists' involvement in pharmaceutical industry-sponsored research, and reports of potentially undesirable research outcomes.

**Results:** Of 2120 specialists approached, 823 (39%) responded. Participation in pharmaceutical industry-sponsored research was more commonly reported by those in salaried practice (49%) than those in private practice (33%); $P < 0.001$. 216 reported that industry had made initial contact, compared with 117 who had initiated contact with industry. 14.0% of respondents reported premature termination of industry-sponsored trials, which they considered appropriate when in response to concerns about adverse drug effects. 12.3% of respondents reported that industry staff had written first drafts of reports, which they viewed as an acceptable practice for "internal" documents only. Of greatest concern to respondents were instances of delayed publication or non-publication of key negative findings (reported by 6.7% and 5.1% of respondents, respectively), and concealment of results (2.2%). Overall, 71 respondents (8.6%) had experienced at least one event that could represent breaches of research integrity.

**Conclusions:** These data indicate a high level of engagement in research between the pharmaceutical industry and medical specialists, including those in private practice. Examples of possibly serious research misconduct were reported by 8.6% of respondents, equivalent to 21% of those with an active research relationship with industry.

MJA 2005; 182: 557–560

There are extensive ties between pharmaceutical manufacturers and clinical researchers.[1] While engagement with industry is inevitable and has positive features, there is concern that these interactions may lead to a dependence on commercial funding for clinical research, which might influence the research agenda, the conduct of studies and the reporting of their results.[2,3] Incomplete or biased reporting of the results of clinical studies is a particular concern, and has been highlighted by the recent controversies surrounding the harms of selective serotonin reuptake inhibitors in treating childhood and adolescent depression, and of cardiovascular toxicity with the selective cyclooxygenase-2 inhibitor, rofecoxib.[4,5]

Studies of the relationships between the medical profession and industry have tended to focus on academic medical centres in the United States (rather than on individual practising clinicians) or on the experience from other countries.[6] There is evidence that the relationship between industry and researchers has changed in recent years, with commercially-sponsored clinical research increasingly being performed by contract research organisations (CROs) rather than academic medical centres, and with physicians in private practice playing a more prominent role in research.[2,3]

Despite interest in this important topic, few Australian data have been published.[3] However, there have been calls locally for more public investment in clinical trials.[7] As part of a study of relationships between Australian medical specialists and the pharmaceutical industry, we sought to characterise the extent, nature and consequences of their research collaboration.

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## METHODS

Our methods were approved by the Human Research Ethics Committee of the University of Newcastle. We obtained 5000 names of medical specialists from an electronic file extracted from the 2002 edition of the *Medical Directory of Australia* (MDA),[8] and stratified these by clinical subspecialty and geographical location. Specialists with minimal prescribing responsibility (eg, surgeons, anaesthetists) were excluded; general practitioners were not included.

We surveyed participants by means of a questionnaire developed in collaboration with three advisory groups — medical specialists, consumers, and staff from pharmaceutical companies. The questionnaire had 46 questions seeking information on all aspects of relationships between medical specialists and pharmaceutical companies. Topics covered included: the frequency and nature of interactions with the pharmaceutical industry; descriptions of industry-spon-

**1 Respondents compared with the original study sample**

| Speciality | Sample | Respondents |
|---|---|---|
| Psychiatry | 330 (14.7%) | 112 (16.4)% |
| Paediatric medicine | 221 (9.8%) | 79 (11.6)% |
| Cardiology | 239 (10.6%) | 63 (9.2%) |
| Gastroenterology | 192 (8.5%) | 53 (7.8%) |
| Rheumatology | 109 (4.8%) | 49 (7.2%) |
| Neurology | 141 (6.3%) | 45 (6.6%) |
| General medicine | 233 (10.3%) | 40 (5.9%) |
| Geriatric medicine | 93 (4.1%) | 44 (6.4%) |
| Dermatology | 132 (5.9%) | 39 (5.7%) |
| Endocrinology | 110 (4.9%) | 39 (5.7%) |
| Respiratory medicine | 121 (5.4%) | 36 (5.3%) |
| Medical oncology | 81 (3.6%) | 31 (4.5%) |
| Infectious diseases/Microbiology | 79 (3.5%) | 23 (3.4%) |
| Immunology/Allergy | 42 (1.9%) | 12 (1.8%) |
| Renal medicine | 75 (3.3%) | 11 (1.6%) |
| Clinical haematology | 45 (2.0%) | 7 (1.0%) |
| Others | 10 (0.4%) | |
| Total | 2253 (100%) | 683 (100%)* |
| **State of practice address** | | |
| New South Wales/Australian Capital Territory | 497 (22.1%) | 150 (19.2%) |
| South Australia | 436 (19.4%) | 158 (20.2%) |
| Victoria | 430 (19.1%) | 163 (20.8%) |
| Queensland | 389 (17.3%) | 131 (16.7%) |
| Western Australia | 384 (17.0%) | 137 (17.5%) |
| Tasmania | 90 (4.0%) | 30 (3.8%) |
| Northern Territory | 27 (1.2%) | 14 (1.8%) |
| Total | 2253 (100%) | 783 (100%)† |

* Not all respondents provided information on their main clinical specialty. † Not all respondents provided information on the state in which they practiced.

**2 Frequency of pharmaceutical industry-sponsored research activity by salaried or private clinical practice**

| | Involved in industry-sponsored research in the past 12 months | |
|---|---|---|
| Practice type | Yes | No |
| Full-time salaried | 66 (40%) | 99 (60%) |
| Mostly salaried | 101 (58%) | 73 (42%) |
| Equal or neither | 50 (43%) | 66 (57%) |
| Mostly private | 85 (41%) | 121 (59%) |
| Full-time private | 36 (22%) | 126 (78%) |

$\chi^2$ (linear trend) = 18.4; $df = 1$; $P < 0.0001$.

sored activities and gifts; the extent and nature of research funding (see below); details of advisory panel and consultancy roles; personal views and opinions on the value of these interactions; and personal demographic, professional and practice details. The sections covering industry research funding comprised 11 questions that allowed up to 43 response categories, including: who initiated the activities; the source of funding (company or CRO); the reasons for working with industry; the type of research (including stage of drug development); negative experiences, including drafting of reports by company staff rather than investigators, alteration of data (beyond the normal process of cleaning), concealment of relevant findings, inappropriate editing of reports, major changes to protocols, delay in publication of data, failure to publish key findings, and premature termination of trials. After answering these questions, respondents were invited to provide a brief account of the events that they had reported (without naming companies or products). This article will focus on the nature and outcomes of research collaborations with industry.

The questionnaire was mailed to 2253 specialists in September 2002.

Data were analysed with SAS statistical software.[9] Conventional descriptive analyses (means and standard deviations [SDs], proportions, and 95% CIs) were calculated when relevant. We compared proportions using $\chi^2$ analysis; means were compared using $t$ tests.

## RESULTS

Of the 2253 specialists, 133 were unable to participate (for reasons such as having died or having changed professional role). Of the remaining 2120, 823 completed and returned the survey instrument (overall response rate, 39%). Respondents were fairly similar to the original sample in terms of geographical location and clinical specialty (Box 1). The average age of the respondents was 48 years (95% CI, 32–69 years), and, on average, they were 27 years (95% CI, 10–45 years) from graduation. Most (79%; 95% CI, 76%–82%) were male. We do not have data on the sex distribution of the mail-out sample, but data provided separately by the publishers of the MDA indicate that 4960 of 6422 doctors listed as practising internal medicine specialties (77%) were male. Respondents spent an average of 46% of their time in salaried hospital practice and 47% in private practice, and, on average, saw 20 patients and wrote 20 prescriptions daily.

### Research relationships and types of research

Three hundred and thirty-eight specialists (41% of respondents; 95% CI, 38%–45%), reported engaging in pharmaceutical industry-sponsored research in the previous 12 months. These specialists were younger than the others (47.8 v 50.6 years; $P = 0.001$ for difference in means), and more likely to be male (83% v 76%; $P = 0.02$ for difference in proportions).

Of specialists who described themselves as being in full-time (or predominantly) salaried clinical practice, 49% had engaged in industry-sponsored research in the previous 12 months, significantly more than those in private practice (Box 2). Nonetheless, 33% of those in exclusively or substantially private practice reported engaging in industry-sponsored research.

Industry funding was sought by 117 respondents for 160 research projects — 103 approached a manufacturer, and 18 approached a CRO or other source (Box 3). Two hundred and sixteen specialists reported being approached by industry on 272 occasions to participate in 373 research projects. On 156 occasions, the initial approach was by manufacturers, and on 116 it was by a CRO. Industry-initiated research projects

**3 Type of research by initiator of approach**

| Type of research | Approach by: Specialist | Industry |
|---|---|---|
| Preclinical | 18 (11.3%) | 6 (1.6%) |
| Phase I | 7 (4.4%) | 24 (6.4%) |
| Phase II | 23 (14.4%) | 81 (21.7%) |
| Phase III | 48 (30.0%) | 149 (39.9%) |
| Phase IV | 24 (15.0%) | 84 (22.5%) |
| Other* | 40 (25.0%) | 29 (7.8%) |
| Total projects | 160 | 373 |

* Such as epidemiology.

were more likely than investigator-initiated projects to involve phase II, III and IV clinical trials, and less likely to involve preclinical or other studies ($P < 0.001$; Box 3). The relevance of the research to the company and the robustness of research design were most commonly cited as reasons for seeking pharmaceutical company research funding, while anticipated or actual failure of competitive grant applications were among the least common (Box 4).

## Potentially undesirable outcomes of commercially funded research

One hundred and ninety-six respondents (24%) reported 374 potentially undesirable outcomes of their research collaboration (Box 5). The most frequently reported outcome was premature termination of trials, reported by 114 (14%) of the medical specialists. Eighteen respondents volunteered additional comments, including statements that premature termination of trials was justified when the reason was adverse events experienced by participants, adverse events experienced in trials overseas, or safety concerns raised by preclinical studies. Respondents also reported premature termination because of slow recruitment, lack of clinical benefit and commercial considerations. The next most frequent occurrence — reported by 100 respondents (12%) — was the first draft of a report being written by staff in a company or CRO. Eleven provided additional comments, including statements that the drafts were well-written, accurate and balanced; investigator input was sought and changes incorporated into the report; and report drafting by the company was "standard practice under good clinical research practice guidelines". Underlying this was the sense that companies should be responsible for writing internal reports. One respondent noted that if the questionnaire had specifically referred to papers for publication then it would be unacceptable for company staff to draft the first report.

"Unreasonable delay" in presentation or publication of results was reported by 55 participants (6.7%) and failure to publish key research findings from industry-sponsored research studies was reported by 41 respondents (5%). Eleven provided additional comments, with five referring to lack of benefit (null results) as the reason for delayed or non-publication. In one case, a negative outcome (increased mortality) was reported as a factor. One respondent noted that unpublished data were omitted from the company's literature on the drug, and another reported being discouraged from presenting adverse reaction data from an unpublished study.

Editing of a report to make a drug look better, concealment of findings relevant to the study's conclusions, and alteration of patient data or statistics were also reported. Respondents provided additional detail, describing omission of findings from company literature, a favourable report being written about a drug that "didn't work" and underreporting of adverse events. One respondent wrote: "It is common for adverse event data to be favourably analysed and selectively reported". However, another described an episode where concealment of findings was initiated by a senior researcher, not the pharmaceutical company.

Changes to study protocols while trials were under way were reported by 17 respondents (2.1%). One described not knowing who had changed the protocol, and another pointed out that investigators may change entry criteria if recruitment is slow, but that this may lead to a "substantial weakening of focus".

We categorised 143 reports from 71 (8.6%) respondents as being potentially serious breaches of research integrity (Box 5).

**4 Reasons given by 115 respondents for seeking pharmaceutical industry funding**

| Reason | Number* |
|---|---|
| Research questions relevant to the company | 85 |
| Design robust irrespective of funding | 80 |
| Efficient way to obtain funds | 76 |
| Project important . . . regardless of funds | 69 |
| Previously successful with pharmaceutical funding | 46 |
| Competitive grant unlikely to be successful | 42 |
| Access to particular expertise | 32 |
| Unsuccessful in securing competitive grant | 15 |

* More than one reason was provided by most respondents.

**5 Breakdown of 374 reports of potentially negative research outcomes**

| Outcome | No. of respondents (%) |
|---|---|
| Premature termination of a study by a company | 114 (14.0%) |
| First draft of a report written by pharmaceutical company or contract research organisation | 100 (12.3%) |
| Delay in presentation or publication of key findings unrelated to data integrity* | 55 (6.7%) |
| Failure to publish key findings* | 41 (5.1%) |
| Editing of report to make drug appear better than was justified by the study results* | 22 (2.7%) |
| Concealment of relevant findings* | 18 (2.2%) |
| Major protocol changes while study in progress (excludes changes mandated by independent committees) | 17 (2.1%) |
| Alteration of patient data or statistics (excluding the normal processes of data editing)* | 7 (0.9%) |

* Potentially serious misdemeanours.

## DISCUSSION

Collaborative research between medical specialists and pharmaceutical companies has been responsible for many significant advances in clinical practice. In Australia, there are widespread research ties between the pharmaceutical industry and medical specialists, including those working largely or exclusively in private practice. This is in line with experience in the US, where there has been a shift from involvement of established researchers in academic centres to private research organisations.[1,2] Our data also show the complexity of relationships between researchers and the pharmaceutical industry, with collaboration sometimes initiated by medical specialists, rather than the industry, and management often in the hands of CROs rather than the manufacturing companies themselves.

Most respondents in this study did not believe they had made ethical compromises during their research collaboration, and

many expressed positive views of their relationships with industry. However, instances of questionable practice were reported. The two most frequent — premature discontinuation of trials and preparation of first drafts of research reports by industry staff — were considered appropriate when termination was in response to safety concerns and the first drafts of reports were generally meant primarily for internal circulation. More serious instances of possible research misconduct included delayed or non-publication of results and modification or concealment of data that negatively reflected on a drug product. Overall, 8.6% of respondents (equivalent to 21% of those with an active research relationship with industry) reported experiencing one or more episodes of potentially serious research misconduct. This finding is similar to the 19.8% of researchers at life sciences faculties in the US who reported delaying publication of results for (largely) commercial reasons.[10] These results are consistent with abundant literature that has examined the risks of collaborations between industry and researchers, including conclusions biased in favour of products, restrictions on publication and data sharing, and financial interests that conflict with primary professional responsibilities.[11] In our analysis, we did not categorise protocol changes as serious research misdemeanours, reflecting the comments of some of our respondents. However, other researchers have shown that in over 60% of trials one or more primary outcomes were changed, introduced, or omitted while the research was under way.[12] Such changes may bias the reporting of results in favour of the drug being tested. As noted earlier, our respondents were generally tolerant of industry staff drafting reports for internal use, but others have pointed to the undesirability of ghost-writing of manuscripts for publication in journals, and editors have introduced guidelines designed to discourage this practice.[2,13]

Our findings have limitations. One is the low response rate (39%), although it should be noted that data in the MDA are updated voluntarily by practitioners, so it is likely that a number of the non-respondents had left active clinical practice.

Other limitations include reliance on self-report and our focus on a specific population. The views of non-respondents may also have differed from the views of respondents. In terms of demographic characteristics and clinical specialty, our respondents were fairly similar to all medical specialists listed in the original sampling frame, and the sample size was large (more than 800 respondents), giving us some confidence in the precision of our estimates. However, our reliance on self-report leaves open the possibility of selective or inaccurate recall; given the need to maintain anonymity, we could not independently assess the reliability of respondents' disclosures. The study was restricted to medical specialists, limiting any generalisations that can be made about other medical populations, such as general practitioners.

Our data do not allow us to make an overall evaluation of industry-sponsored research; we accept that our questionnaire concentrated on the negative consequences of such studies, and did not ask respondents to describe their positive experiences. There are clear benefits from such research collaborations with industry, but to quantify those was beyond the scope of this study.

Our results raise some significant concerns. The first is the apparent high level of industry-supported research being conducted by medical specialists working substantially or exclusively in private practice. We don't have data on whether the involvement of private specialists has increased in recent years, but hard questions are now being asked about who oversees clinical research and the integrity of research publications and their authorship.[13] We believe that professional organisations, institutions, and practitioners themselves, need to ensure that mechanisms are in place to ensure appropriate governance of clinical research when it is conducted substantially in the private arena.

The second issue concerns the examples of possible research malpractice, particularly delayed publication or failure to publish the results of clinical research. This clearly troubled some of our respondents, and has been the subject of widespread comment and action by the editors of major medical journals.[13]

Our findings underscore the necessity for ethics committees to oversee not only the conduct of research, but also the analysis and reporting of results, to ensure that the public has access to accurate data on the benefits and harms of modern medical treatments. However, it is doubtful that ethics committees have the resources to act alone in policing these activities. It is essential that clinical trials are registered at their inception and that pharmaceutical companies and researchers themselves adopt and adhere to guidelines for good publication practices.[14,15]

## ACKNOWLEDGEMENTS

The study was supported by a grant from the National Health and Medical Research Council of Australia. We are extremely grateful to the medical specialists who responded to our survey.

## COMPETING INTERESTS

David Henry has, in the last 3 years, held a contract with Wyeth to review the toxicity of non-steroidal anti-inflammatory drugs. He has not worked as an advisor or consultant to industry and does not own shares in pharmaceutical companies. Graham MacDonald is employed by Merck Sharp & Dohme (Australia). Richard Day serves as an Advisory Board member for Merck Sharp & Dohme (Australia) (rofecoxib, etoricoxib), Merck Sharp & Dohme (Asia) (rofecoxib), Abbott Australia (adalimumab), Schering-Plough Australia (infliximab), Amgen Australia (anakinra), GlaxoSmithKline Consumer Australia (paracetamol) and, previously, Pfizer Australia (celecoxib). Any honoraria for these activities are placed in audited trust funds of St Vincent's Hospital, Sydney, to be used to support academic activities within the Department of Clinical Pharmacology.

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*(Received 11 Nov 2004, accepted 17 Feb 2005)* ❑