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*The Academia - Industry Symposium 2005*

**Medical Practice, Psychiatry and  
the Pharmaceutical Industry :  
And Ever the Trio Shall Meet**

**Ajai R. Singh, M.D.  
Shakuntala A. Singh, Ph. D.**



**Mens Sana Research Foundation**  
Mumbai, India  
2005

*The Academia - Industry Symposium*

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# **Medical Practice, Psychiatry and the Pharmaceutical Industry : And Ever the Trio Shall Meet**

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The Mens Sana Monographs provide a wide platform for serious discussion by psychiatrists, social scientists, philosophers, psychologists, sociologists and other thinkers interested in exploring social issues with scientific rigour.

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## **Medical Practice, Psychiatry and the Pharmaceutical Industry : And Ever the Trio Shall Meet**

One of the greatest happenings in the medical world today is the wide opportunity for collaboration between academic institutions, researchers and the pharmaceutical industry. While this holds great promise according to some, it portends equally great problems according to others. On the one hand is the growing commercialization of research with its effect on the ethical conduct of researchers. On the other are the advancements of scientific knowledge with their effect on the welfare or otherwise of patients. Both these are becoming areas of pressing concern. Connected to the growing clout of industry in institutions is concern about the commercialization of research and resolving the 'patient or product' loyalty. Issues related to conflict of interest, doctoring of data, control over publication, threats of legal tangles, patient or corporate welfare are vexing unresolved issues. The acceleration towards biological psychiatry at the expense of the psychosocial approach is another area of concern. Industry role in this is not insignificant. Gifts, sponsorships, pliant experts acting as industry spokespersons, journals and their ethical policies are no less. Guidelines, whether clinical practice or of journal editors, are also areas of increasing activity and equal concern.

This collection of two monographs (and two to follow) tackles these issues in the light of current research work done.

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Outer limit for a manuscript, including Preface, Abstract, Introduction, References and Questions Raised, is 10,000 words. Pertinent references alone should be quoted. Tables, figures and elaborate statistics should be avoided unless absolutely necessary. MSM is a viewpoint forum based on evidence, not necessarily statistical. Hence reviews, overviews, position statements are welcome, but they should be of a fundamental-foundational nature, not just a compilation of views. Conceptual analysis of evidential findings, and insightful analysis of epoch making writings of the past and present are welcome. Authors are advised to go through the Conceptual Foundations of the MSM on <http://mensanamonographs.tripod.com> to understand the four pillars of MSM: the middle path, comprehensivity, evidence and eclecticism

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Dedicated to

*Prof V.N. Bagadia*

A Life Time Devoted to Establishing the Relevance of  
Psychiatry in Medicine

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- The Eleventh Monograph: Medical Practice, Psychiatry And The Pharmaceutical Industry: And Ever The Trio Shall Meet-IV: Gifts and Samples, CMEs and ICMJE Revised guidelines
- All Four Monographs (Eighth To Eleventh) In One: Medical Practice, Psychiatry And The Pharmaceutical Industry: And Ever The Trio Shall Meet



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## **Introduction**

# **The Two Revolutions In Bio-Medical Research**

In the field of modern medical science, we can identify certain epochs. Some of these will be our concern here, for they offer important insights into the development of modern medicine and offer equally important predictors of where it is heading in the future. In fact they are so important that they qualify to be called nothing less than revolutions.

Till the early twentieth century, medicine was an activity dependent on a small privileged elite. This changed by the mid-twentieth century into a vast publicly owned enterprise with enlightened governmental approach, support and funding. One example of this was in the 1940s, sixty five years ago, when Vannever Bush in the US, for example, persuaded the government there to divert resources allocated for the then war effort (World War II) to fund basic research in academic institutions. Similarly, in India, what was earlier dependent on the benevolence of zamindars/philanthropists and some missionaries who set up charitable dispensaries/hospitals to serve certain sections of the population was supplemented, and then overtaken, by governmental funding after independence in 1947.

This major governmental support to medical science was an important development that led to great advances in medical research and facilities all over. Such funding and consequent blossoming of medical science was nothing less than a revolution, which we can legitimately consider the first revolution in modern medicine.

A second revolution was soon to follow four decades later. It was fuelled by a vast upsurge in medical research, training and therapy, with capital pouring in from private enterprise and philanthropy. This revolution is still on. It is aided by efforts like the Bayh-Dole Amendments of 1980 in the US, for example. This epoch making amendment conferred intellectual property rights to institutions and connected scientists even if they had developed their products/inventions with government funding. It was followed by incentives in tax laws that resulted in a massive inflow of venture capital into biomedical research. As a result, academia was suddenly besieged by profit seeking industry that saw immense vistas of opportunity opening up before them. Pharmaceutical majors, propped up with massive private funding by venture capital, were quick to seize the initiative.

Institutions realized their commercial potential and their vast possibilities for the first time, and were not averse to jump on to the bandwagon.

In India too, major foreign and indigenous pharmaceutical players were quick to cash in on the opportunity during this same time. As massive funds made new drug formulations available in the west, their Indian counterparts, and some enterprising wholly indigenous concerns, did not forget to latch on to the promising commercial opportunities opening up before them. They imported drugs wholesale, and/or their technology. And with glossy monographs, CMEs, sponsorships, and gifts thrown in, widened their commercial activities to greatly influence medical prescription and practice. Some amount of research in the form of clinical trials managed to get funds for departments and institutions, and researchers felt suitably rewarded. Some Indian drugs also entered the market, but they hardly captured world markets, except for a few Ayurvedic/herbal formulations that managed to hold attention abroad, but not on the basis of very sound scientific trials.

Alongside this, we also saw an interesting development in the last few decades in India. Private entrepreneurs, aided by political bigwigs, entered medical education to cater to a huge clientele of young people fresh after two years in college and desirous of making a career in medicine. Since reservations in government/municipal medical colleges for socially disadvantaged sections closed admission options in these institutions, many promising young people have gone in for costly private self-funding medical courses. As they come out of such institutions, they can be expected to want to recover their millions invested in medical education with some urgency. The institutions and research activities they get connected with will be quite keen to forward financial interests, for in so doing the financial interests of such individuals will be taken care of. At a time and phase when others (the free-seaters) are likely to be influenced by certain noble intentions of medicine, such high fees paying graduates and postgraduates can be expected to be keenly aware of the role money plays in medicine, right from its training to practice and research. And they can be further expected to forward the process of the corporate enterprise of medicine with some urgency and equal conviction. In other words, their role in commercialization of medical education and research can be expected to be substantial.

Another interesting development alongside this in India is the proliferation of a large number of corporate hospitals run as business enterprises with listing on stock exchanges, or owned by industrial/business barons, with foreign/NRI collaboration and entrepreneur input, both financial and intellectual. Such enterprises are profit oriented business concerns and market health care to interested clientele. Medical personnel involved in such institutions are likely to be heavily influenced by commercial interests and the profit motive, for they have targets to meet,

both for out-patient and indoor admissions. Else their contracts may get terminated. Also, they are vast repositories for influx of commercial influences from the institutions of the west that are their guiding stars. And as those are already on the course of rapid corporatisation, such institutions following suit is a foregone conclusion. So both medical education and research, in India and abroad, are bound to experience great upheavals in working methods and ethical concerns as commercially viable scientific inventions, and forwarding of commercial interests, hold center-stage in biomedical education and research in this century.

The massive entry of private enterprise into medical education and research heralds great changes in the mindset and set up of academia and is nothing less than a revolution of sorts.

If the *Academia-Government Connect* was the First Revolution, the *Academia-Industry Connect* is the Second. The first promised funds and legislative support for academia, the second provides funds and logistic support for academia. Hence, both these developments have been welcomed with some glee in academic circles. However, as is common with all such happenings, the flip side is getting uncovered by and by too.

All revolutions start with some noble objectives. But they are always in danger of being hijacked by vested interests that use the mass upsurge to fulfill private agendas. This second revolution hardly had any pretensions to great idealistic leanings anyway, and therefore has been hijacked to serve questionable interests right from day one. Unresolved issues related to conflict of interests, royalty, patents, practice guidelines, research publication are vexing enough. But fundamental questions about the ethical propriety of an academia-industry connect are being raised not just by the usual alarmists, but by concerned researchers who see disturbing portents in this connect.

Whether we want it or not, or like it or not, this second revolution is well and truly on. We can choose to be willing or unwilling participants. We cannot be uninvolved, much as some fence sitters would desire. It makes sense to be either willing participants, or unwilling protestors. Both these are possible only on an informed basis.

This *Academia-Industry Symposium* is an attempt to study the stand points of these participants, both willing and protesting. It also presents the viewpoint of some alarmists, whom we may dismiss to our own peril. And finally, it articulates also the small voice of the activists and advocates, which small voice is likely to become a uproar in the near future if academia and concerned industry do not wake up soon enough.

A conflict of epic dimensions is on the cards in the next few decades. Log in, and stay invested, gentlemen.

**ISBN 81-89753-09-6**

**The Eighth Monograph**

***The Academia - Industry Symposium***

Medical Practice, Psychiatry and the Pharmaceutical Industry:  
And Ever the Trio Shall Meet-I

**The Connection between Academia  
and Industry**

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# **Preface to the Eighth Monograph**

## **Second Anniversary**

The Mens Sana Monographs was started in May 2003. It is two years since we set on this course. During this time, we have tried to set a comprehensive agenda for the monographs, tackling issues in mental health, science, religion and public health. An Annual which compiled the first six monographs was published in October 2004, and released at the Annual Indian Psychiatric Society West Zone Conference in Oct 2004. It was dedicated to the memory of Dr. L.P. Shah, whose untimely demise robbed us of a dynamic torchbearer of mental health in India.

In February 2005, we were allotted an ISSN number (ISSN 0973-1229). On March 15, 2005, we started the *Mensanamonographs Group* on the internet, which is an active discussion group tackling a wide array of topics. The Monograph: *Resolution of the Polarisation of Ideologies and Approaches in Psychiatry* (Nov 2004-Feb 2005) has been listed in *JAMA*, May 18, 2005, 293, p2417-2418, *Books, Journals, New Media Received*.

A large number of senior clinicians and researchers in India look to the *Monographs* with expectations of making a difference where it matters. This present monograph series, which is an *Academia-Industry Symposium*, intends to study in some detail the pros and cons of the wide connections which academic and research institutions have with pharmaceutical and other medical ancillary industry. There is a great hope in this connect, and an equal measure of concern. This series of four monographs (this is the second in the series) intend to reflect this hope and concern to all who have the long term interests of the medical profession at heart:

### ***The Academia-Industry Symposium***

- The Eight Monograph: Medical Practice, Psychiatry And The Pharmaceutical Industry: And Ever The Trio Shall Meet-I: THE CONNECTION BETWEEN ACADEMIA AND INDUSTRY, *Mens Sana Monographs*, II-6, III-1 March-June, 2005.
- The Ninth Monograph: Medical Practice, Psychiatry And The Pharmaceutical Industry: And Ever The Trio Shall Meet-II: PUBLIC WELFARE AGENDA OR CORPORATE RESEARCH AGENDA? *Mens Sana Monographs*, III-2, 3, July-October, 2005.
- The Tenth Monograph: Medical Practice, Psychiatry, And The Pharmaceutical Industry: And Ever The Trio Shall Meet-III: GUIDELINES,



EDITORS, AND THE BIOLOGICAL PARADIGM SHIFT, *Mens Sana Monographs*, III-4,5, November 2005 -February, 2006.

- The Eleventh Monograph: Medical Practice, Psychiatry And The Pharmaceutical Industry: And Ever The Trio Shall Meet-IV: GIFTS AND SAMPLES, CMEs AND ICMJE REVISED GUIDELINES, *Mens Sana Monographs*, III-6, March-April, 2006.

Hope you enjoy reading them, and feel like remedying the situation.

Meanwhile, on this second anniversary, we rededicate ourselves to forwarding the conceptual foundations of the *Mens Sana Monographs* whose four pillars are *The Middle Path, Comprehensivity, Eclecticism* and *Evidence*.

Ajai R. Singh

Shakuntala A. Singh

*The Academia-Industry Symposium*

Medical Practice, Psychiatry and the Pharmaceutical Industry:  
And Ever the Trio Shall Meet-I

# **The Connection Between Academia and Industry**

*Ajai Singh  
Shakuntala Singh*

## **ABSTRACT**

*The growing commercialization of research with its effect on the ethical conduct of researchers, and the advancement of scientific knowledge with its effect on the welfare or otherwise of patients, are areas of pressing concern today and need a serious, thorough study. Biomedical research, and its forward march, is becoming increasingly dependent on industry-academia proximity, both commercial and geographic. A realization of the commercial value of academic biomedical research coupled with its rapid and efficient utilization by industry is the major propelling force here. A number of well-intentioned writers in the field look to the whole development with optimism. But this partnership is a double-edged sword, for it carries with it the potential of an exciting future as much as the prospect of misappropriation and malevolence. Moreover, such partnerships have sometimes eroded public trust in the research enterprise itself.*

*Connected to the growing clout of industry in institutions is concern about the commercialization of research and resolving the 'patient or product' loyalty.*

*There is ambivalence about industry funding and influence in academia, and a consequent 'approach-avoidance' conflict. If academia has to provide the patients and research talent, industry necessarily has to provide the finances and other facilities based on it. This is an invariable and essential agreement between the two parties that they can walk out of only at their own peril. The profound ethical concerns that industry funded research has brought center-stage need a close look, especially as they impact patients, research subjects, public trust, marketability of products, and research and professional credibility.*

*How can the intermediate goal of industry (patient welfare) serve the purpose of the final goal of academia is the basic struggle for conscientious research institutions/*

*associations. And how best the goal of maximizing profits can be best served, albeit suitably camouflaged as patient welfare throughout, is the concern of the pharmaceutical industry.*

*A very great potential conflict of interest lies in the fact that academia needs the sophisticated instruments that only big funding can provide, while at the same time resists the attempts of the fund provider to set the agenda of research, protocol, design, publication, the works. Conflicts arise at many steps and levels of functioning, and are related to the expectations, competing interests, and conflicting priorities of the different entities involved, whether they are the academic medical centers, the funding agencies, the patients and their families, or the investors and venture capitalists.*

*The public expects access to new treatments. Its appetite for innovation has been bolstered by the constant attention given by the press to new treatments and by the implicit promise from researchers of continuing advances. Similarly, patients demand privacy and control over information about themselves.*

*It makes greater sense for genuine researchers to associate with large long-term industry players who have a track record of genuine hard-core discoveries, even if the process is slow (maybe), and the funding less (may not be).*

*The element of control venture capitalists exert over the pharmaceutical industry is an under researched area for obvious reasons. But it needs further probing, for that will lay bare the pulls and pressures under which industry works.*

*It makes sense for ethically minded researchers and institutions not to fall in the trap of stocks and equity investments in industry, howsoever attractive they appear, and get rid of them as soon as possible if they have them. If at all they want, it makes more sense to own stocks of larger well established concerns, for the stock upheavals being less, the pressure of the market-place, and of venture sharks, is likely to be lower too.*

*While active participation by the researcher in the commercialization process may be greatly desired by industry, ostensibly in the name of creating value, academia must realize it is a bait it might find hard to swallow in the long run. It makes more sense for the researcher and institution to forego such temptations and/or walk out of such investments as soon as possible.*

*While mainstream medicine and research are booming, as is connected industry, concerns about professional commitment to patient welfare are growing too. Increasing corporate influence is challenging certain long held and fundamental values of patient care, which will have far reaching implications for biomedical care and the future progress of mainstream medicine.*

**KEY WORDS:** *Academia, Pharmaceutical Industry, Academia-Industry Proximity, Biomedical Research, Commercialization of Research, Pharmaceutical Funding, Public Accountability and Academic Freedom of Universities, Commercial Value of Academic Innovations, Ethical Issues, Venture Capital, Stocks and Equity, Patients and Public Interests, Large and Small Pharmaceutical Firms*

*It is possible to mentally resolve the issue for oneself rather well by the following argument. Academia-industry relationship is increasing and augurs well for the future growth of medical research and patient welfare. Well, there are some problems, as is inevitable with all such potentially controversial but useful relationships.*

## Introduction

A number of important areas of the connect between academia, the medical professional and the pharmaceutical industry have been highlighted by articles in the last decade, especially in the last five years, which have still to find place in textbooks of medicine or psychiatry. While this by itself can be considered alarming by some, for denial is a poor coping mechanism, if at all, what is of interest to us here is how the connect has

developed, what are the major areas of influence (and concern), what the remedies for the present, if any, and what the portents for the future. The growing commercialization of research with its effect on the ethical conduct of researchers, and the advancement of scientific knowledge with its effect on the welfare or otherwise of patients, are areas of pressing concern and need a serious, thorough study.

This monograph tries to address some of the issues in this connection.

Now it is possible to mentally resolve the issue for oneself rather well by the following argument. Academia-industry relationship is increasing and augurs well for the future growth of medical research and patient welfare. Well, there are some problems, as is inevitable with all such potentially controversial but useful relationships. Rather than concentrate on, and magnify, the faults, it makes more sense to accent the positive, and create an atmosphere whereby it continues to be maximized, while making the negative less attractive, and yet inevitable to an extent. There is negative fallout of everything. Instead of cribbing about it, we accept it and move on with optimizing the worthwhile.

This is a beautiful and useful rationalization, if the negative is to be put in its place and done away with. But it is a dangerous reasoning if it is meant to sweep certain ominous portents under the carpet. When it is the dust in our house that we have to take care of, we just brush it off right away, or sweep it under the carpet to be removed a little later. And do not bother any further. However, if the dust that flies is heralding an oncoming storm, we cannot brush it off, or sweep it under the carpet. For it retains the ability to sweep us off our feet, carpet and all. Here, damage control measures become mandatory, some after, but many more before, the storm erupts.

What is a saner option is to look at the dust today and prevent it from becoming a dust storm tomorrow. So, no glib rationalizations, only a serious look at the straws in the wind.

This monograph, and the ones that follow, looks at a bit of the dust raised and some of the straws floating around.

## Academia - Industry Proximity

Biomedical research, and its forward march, is becoming increasingly dependent on academia-industry proximity, both commercial and geographic. A number of well-intentioned writers in the field look to the whole development with optimism:

*We now have the potential to enter one of the most productive periods in biomedical research, the success of which will depend to no small degree on an increasingly close partnership between universities and industry (Nathan and Weatherall, 2002).*

*Economic partnerships between industry and academia accelerate medical innovation and enhance patient access to medical advances (Johns, Barnes and Florencio, 2003).*

*Most clinical studies that bring new drugs from bench to bedside are financed by pharmaceutical companies. Many of these drug trials are rigorously designed, employing the skills of outstanding clinical researchers at leading academic institutions (Bodenheimer, 2000).*

*Within many hundred years' time when people will reflect on history, the 19<sup>th</sup> century might well be written as the century of industry, the 20<sup>th</sup> century as the century of information and technology, and the 21<sup>st</sup> century as the century of biomedicines and healthcare (EFPIA, 2005).*

Industry funding is supposed to help disease prevention and treatment, improve clinical practice and result in useful products for patients. In this the profit motive acts as a spur:

*Without industry funding, important advances in disease prevention and treatment would not have occurred. In the words of Lee Goldman, chairman of the Department of Medicine, University of California at San Francisco, "companies translate biologic advances into useable products for patients. They do it for a profit motive, but they do it, and it needs to be done." ... many collaborations with pharmaceutical companies were conducted on a high professional level... The infusion of industry dollars into an industry-investigator partnership has clearly improved clinical practice (Bodenheimer, 2000).*

*Biomedical research, and its forward march, is becoming increasingly dependent on academia-industry proximity, both commercial and geographic. A number of well-intentioned writers in the field look to the whole development with optimism:*

*Already alarming portents from the activities of the recent past point to a rather roller-coaster ride for the academia - industry relationship, like the uneasy alliance or marriage of convenience it often turns out to be.*

But this partnership is a double-edged sword, for it carries with it the potential of an exciting future as much as the prospect of misappropriation and malevolence. Moreover, such partnerships have sometimes eroded public trust in the research enterprise (Johns, Barnes and Florencio, 2003). Links between academia and industry are of increasing concern to academics and to

society at large and the sectors involved must review and revise their policies in order to sustain the public accountability and academic freedom of universities (Nature, 2001). For, the selection of research topics, the freedom of the research process, the public perception of researchers' role and gains, and the extent of exploitation that industry can carry out of institutions and researchers—all these have come under close scrutiny that will increase in the years to come.

Already alarming portents from the activities of the recent past point to a rather roller-coaster ride for the academia-industry relationship, like the uneasy alliance or marriage of convenience it often turns out to be. Moreover, universities will have to decide on the extent to which they wish to become commercialized and will have to monitor the effect that such commercialization has on the pattern of their research, on public confidence in research, and on academic freedom (Nathan and Weatherall, 2002).

Writing an editorial in the NEJM, Angell (2000) makes the point rather piquantly:

*What is wrong with the current situation? Why shouldn't clinical researchers have close ties to industry? One obvious concern is that these ties will bias research, both the kind of work that is done and the way it is reported. Researchers might undertake studies on the basis of whether they can get industry funding, not whether the studies are scientifically important. That would mean more research on drugs and devices and less designed to gain insights into the causes and mechanisms of disease. It would also skew research toward finding trivial differences between drugs, because those differences can be exploited for marketing. Of even greater concern is the possibility that financial ties may influence the outcome of research studies.*

## **Increasing Connection**

The connection between academic institutions/research centers and private companies/pharmaceuticals is increasing for obvious reasons. A realization of the commercial value of academic biomedical research coupled with its rapid and efficient utilization by industry is the major propelling force here. An interesting offshoot of this is the close proximity of new major

laboratories to academic institutions all over the world. It makes sound business sense to have laboratories where academia can be easily accessed, and it makes equally sound business sense for academia to make itself accessible:

*The decision of several large pharmaceutical companies, and many biotechnology companies, to build major new laboratories near U.S., European, and Asian universities is just one example of the growing commercial value of academic innovation in biomedicine and the talent that produces it (Moses, Braunwald, Martin and Their, 2002).*

We may feel happy that this will add to the commercial value of academic innovations, and help sustain it in the long run, as well as provide great windows of opportunity to talent coming out of academia. But what we perhaps ignore is that the constant lure commercial interests provide may take away interest in any but such research as promotes industry's interest. While industry may innocently ask, 'So what's wrong with that', we all know precisely what's wrong with it, though may find it inconvenient to verbalize: namely, that so much that can be of patient welfare may not necessarily suit commercial interests of industry, and vice versa. And only that which can serve the latter will become research worthy in institutions. In other words, the research agenda will not be decided by academia, but by industry. More so in the future, if the present is any indication of portents. The wider and long-term implications of this process should be clearly understood, and agreed to only if found justified, not acquiesced in out of sheer ignorance, for inducement of profits, or other inappropriate gain.

## **'Patient or Product' Loyalty**

Connected to the growing clout of industry in institutions is concern about the commercialization of research and resolving the 'patient or product' loyalty:

*One of the major questions now is how to address potential conflicts of interest or commitment surrounding the commercialization of research — how to strike a balance between the need for investigators to act in the best interests of patients and their desire to serve the interests of the product they are developing (Kelch, 2002).*

This is what Kelch starts his paper with. But his conclusion is quite categorical:

*One cannot work simultaneously as an inventor-entrepreneur and a physician or other health care provider and maintain the trust of patients and the public. To attempt to do so is to challenge the primacy of the doctor-patient*

*What we perhaps ignore is that the constant lure commercial interests provide may take away interest in any but such research as promotes industry's interest.*

*There is the other belief that academia-industry proximity aids technology transfer beneficial to academia. But this claim is somewhat sustainable in basic research, though greatly exaggerated in clinical research, which is the mainstay of their proximity:*

*covenant. On the other hand, the system must allow enough flexibility for promising new approaches to be tested (Kelch, 2002).*

Which means the inventor-entrepreneur cannot also play the role of a treating physician, much though he may so desire, or feel competent about. At the same time, the system must continue to allow for him to prosper too, in so far as he demonstrates promise vis-à-vis patient welfare; and provide him an atmosphere whereby his experimental

approaches can be tested on research subjects supplied by academia.

There is the other belief that academia-industry proximity aids technology transfer beneficial to academia. But this claim is somewhat sustainable in basic research, though greatly exaggerated in clinical research, which is the mainstay of their proximity:

*I believe the claim that extensive ties between academic researchers and industry are necessary for technology transfer is greatly exaggerated, particularly with regard to clinical research. There may be some merit to the claim for basic research, but in most clinical research, including clinical trials, the “technology” is essentially already developed. Researchers are simply testing it. Furthermore, whether financial arrangements facilitate technology transfer depends crucially on what those arrangements are. Certainly grant support is constructive, if administered properly. But it is highly doubtful whether many of the other financial arrangements facilitate technology transfer or confer any other social benefit (Angell, 2000).*

In other words, grants facilitate technology transfer, other financial arrangements do not. We will have occasion to look into other financial arrangements when we study the effect of venture capital, stocks and equity, the pseudo-educational dollar etc. on the academia-industry connect.

## **Ambivalence About Industry Funding**

The discussion up till this point makes it very clear that there is ambivalence about industry funding and influence in academia, and the ‘approach-avoidance’ conflict is well summed up in the response of one of them quoted below:

*The infusion of industry dollars into an industry-investigator partnership has clearly improved clinical practice. Yet the medical literature contains many articles expressing concern about industrial funding of clinical research (Bodenheimer, 2000).*



And then he goes on to list a number of studies that voice this concern:

*Stelfox et al. (Stelfox, Chua, O'Rourke and Detsky, 1998) found that authors whose work supported the safety of calcium-channel antagonists had a higher frequency of financial relationships with the drugs' manufacturers than authors whose work did not support the safety of these medications. Davidson (1986) reported that results favoring a new therapy over a traditional one were more likely if the study was funded by the new therapy's manufacturer. Cho and Bero (1996) demonstrated that articles from symposiums sponsored by a single drug company were more likely than articles without company support to have outcomes favorable to the sponsor's drugs. Friedberg et al. (Friedberg, Saffran, Stinson, Nelson and Bennett, 1999) reported that 5 percent of industry-sponsored pharmacoeconomic studies of cancer drugs reached unfavorable conclusions about the company's products, as compared with 38 percent of studies with nonprofit funding that reached similar conclusions (Bodenheimer, 2000; parenthesis added)*

Financial support to research favours industry as regards safety and effectiveness of drugs, and favourable outcome of trials. Researchers, in other words, are not immune to financial considerations and extra-scientific considerations while pursuing so-called scientific goals.

In the case of the academia-industry connect, we are at a stage at which psychiatry was some decades ago. It had reams and reams written on psychopathology, with little to offer as treatment. Or medicine was half a century ago, when it, similarly, had volumes on signs and symptoms but little to offer as treatment (remember the sanatoria phase for tuberculosis?). Similarly, even here we have reams upon reams written about the desirability-undesirability of the academia-industry connect, but little about the methods to remedy it. Hopefully, this will change as more concerned with the long-term welfare of biomedical advance get conversant with the magnitude of the problem and girdle their loins to do something about it. As happened with medicine in this last fifty years. Or with psychiatry as a branch in the last two decades. Maybe the next two decades will see greater efforts at remedying this situation with regard to the academia-industry connect. A major step forward would be taken if the ambivalence could be taken care of, and more clarity and firmness demonstrated on both sides, whether academia or industry. In any case, events and activists will ensure this occurs, if the concerned parties continue to remain complacent. Which may not be a very pleasant state of affairs to be in for sure.

*Financial support to research favours industry as regards safety and effectiveness of drugs, and favourable outcome of trials. Researchers, in other words, are not immune to financial considerations and extra-scientific considerations while pursuing so-called scientific goals.*

*The need for large funds is, moreover, coupled with the desire to acquire it without making a dent in one's own pockets. The easiest way that can happen is getting an interested party to fund it, which has a big stake in the success of the entire venture. Hence, the pharmaceutical industry becomes a willing partner in the whole enterprise.*

## **Funds, Research Agendas, and Profit Maximization**

Where is the money coming from in medical research and related activities today? The reality is that academic institutions are becoming more and more dependent on pharmaceutical funding, as are the medical associations and conference organisers. The main reason for this is the need for large funds in the medical institutions and associations. This is no longer available to a significant degree from governmental agencies, or philanthropic foundations, except for a

fortunate few. This is from a May 2005 paper comparing industry and NIH funding in the US for psychotropic and other drugs:

*Clinical psychopharmacology has been and likely will remain heavily influenced, if not dominated by, the pharmaceutical industry, especially for compounds early in the product development sequence. Industry funding for clinical trials is many times larger than NIH (extramural, including NIMH) funding: \$4.1 billion, compared to \$850 million in 2000 (March, Silva, Compton, Shapiro, Califf and Krishnan, 2005).*

Even in 2003, Moynihan found:

*More than half the biomedical research being done in the United States is now privately funded, with sponsors able to set the research agenda (Moynihan, 2003).*

This need for large funds is, moreover, coupled with the desire to acquire it without making a dent in one's own pockets. The easiest way that can happen is getting an interested party to fund it, which has a big stake in the success of the entire venture. Hence, the pharmaceutical industry becomes a willing partner in the whole enterprise.

Now, this is fine as it goes, and academia may consider the issue beautifully resolved. The only spanner in the works is industry and its aspirations, which are not any idealized notions of research for patient welfare, but to run a profit making concern. And why not, if it cannot make the profits, it cannot survive. And if it cannot provide the funds that flow only if profitability is ensured, and maintained down the years, no academic institution would want to associate with it anyway.

The question we can ask is: why can patient welfare not maximize profit? To that the answer is the perpetual gap between *is* and *ought*. Patient welfare ought to optimize profit, however shrewd marketing in the name of

patient welfare does. Patient welfare is good to espouse and mouth, but profit is the name of the game for industry. So, profit always: if possible with, if necessary without, patient welfare. For academia, it ought to be patient welfare always: if possible with, if necessary without, industry sponsorship. Unfortunately, the reality seems to have gravitated to industry sponsorship always: if possible with, if necessary without, patient welfare.

So, if academia has to provide the patients and research talent, industry necessarily has to provide the finances and other facilities based on it. This is an invariable and essential agreement between the two parties that they can walk out of only at their own peril. What academia must continue to provide is necessarily a mass of compliant patients and a crop of compliant researchers and administrators to further industry goals. What industry must continue to provide is the ready finances to fund it all. Now, the issue fundamentally is that research has to continue, for so much is at stake for researchers, institutions, and even patients' expectations in it. The only way it can continue in the present scenario, so it seems, is by industry funding, and the only way that can be ensured is by research agendas maximizing industry profits. If anyone can suggest another way, well, we would all rise in our seats and applaud him. Well, actually Schafer (2004) does, when he boldly suggests doing away with industry support altogether, but one wonders whether he finds willing supporters amongst academia and researchers.

## **R and D in Pharmaceutical Companies**

While we present the flip side of industry funding, we must also note the way pharmaceuticals function with regard to research and development. It is not enough just to make them the whipping boys, and present academia as the holy cow led astray.

We must note that medicine costing is not only inclusive of R and D, marketing, infrastructure, raw material, manufacturing, regulatory authorities, trials and profits. Every new medicine carries the inbuilt cost of producing the next new medicine:

*Since the price of a new medicine carries within it a contribution towards the cost of discovering the next, the mainstay of the European pharmaceutical industry's long-term competitiveness is its ability to pay for research and development of future medicines (EFPIA, 2005).*

*If academia has to provide the patients and research talent, industry necessarily has to provide the finances and other facilities based on it. This is an invariable and essential agreement between the two parties that they can walk out of only at their own peril.*

*Out of 5000-10000 products studied, only one reaches the pharmacy shelf, and that too after 12-13 years, at a cost of approximately euro 895 million per product.*

Every new medicine is caught in an inevitable upward price spiral. Apart from other costs, it must pay for the development of the next new medicine. The pharmaceutical industry has to bear this in mind if it has to survive, and prosper, in the long run. So have the patients, and the medicine prescribers.

How can they expect newer medicines to come to them that are cheaper than the previous? Unless, of course, raw material is cheaper, and manufacturing/approval cost is lower? In other words, it is one thing to want new drugs, it is quite another to expect them to be cost effective. Activists and academia have to take note of this.

Pharmaceutical companies can take justified pride in the fact that many research-oriented pharmaceuticals spend more on R and D than most other industry sectors:

*Research-driven pharmaceutical companies invest about 20 % of their sales in R&D, which represents a higher percentage than any other industrial sector (incl. high-tech industries such as electronics, aerospace or automobiles) (EFPIA, 2005).*

However, money so invested needs to be recovered, if possible by patient welfare, if necessary without. It is absolutely necessary that recovery be ensured. Like the loan financing concerns run as much on how much they can finance as on how much is the recovery, you can trust the pharmaceuticals to go all out to recover their monumental investments. Being greater pals with prescribers and passing on the cost to the consumer are inevitable.

The next point is equally noteworthy here. We must know the difficulty of the pharmaceuticals to understand how they need to balance finance with patient welfare. Out of 5000-10000 products studied, only one reaches the pharmacy shelf, and that too after 12-13 years, at a cost of approximately euro 895 million per product:

*...it takes an average of 12 to 13 years to bring a new medicine from the laboratory to the pharmacy shelf... (And) on average, only one out of 5,000 to 10,000 promising substances will survive extensive testing in the R&D phase to become approved as a quality, safe and efficient marketable product. (Also) several studies put the cost of researching and developing a new chemical entity (NCE) at euro 895 million (EFPIA, 2005; 'And', 'Also' added in parenthesis).*

Hence, while costs are soaring, and pressures to reduce prices is on, individual companies find it difficult to survive, and are undergoing mergers and acquisitions so that overheads can reduce and profitability can be maximized:

*Soaring R&D costs - combined with downward pressure on prices - are making it harder and harder for many pharmaceutical companies to recoup their R&D expenditure before patents expire. Individual companies are therefore becoming highly vulnerable and are striving to consolidate their positions and to achieve critical mass, through an ongoing process of mergers and acquisitions (EFPIA, 2005).*

The greater pressures of soaring research and infrastructure costs, and added physician hospitality of various types, together with maintaining the great profitability of the pharmaceutical industry (one of the best amongst commercial enterprises today), and added litigation costs which are increasing and will increase in the future- all these point to a major cost escalation in the biomedical field, for which the already financially compromised patient will pay higher and higher sums, whether as actual sums or as insurance premium. Hence we can expect greater corporatisation of medicine in the future, and medicine becoming a business is a distinct possibility, if it is not already. However, there is a silver lining to it too. This is a fertile ground for greater preventive medicine, as also for complementary and alternative medicine (CAM). While some may have reservations about the latter, none can about the former. It also becomes clear why there is a greater thrust towards CAM we witness all over.

It makes sense for the critics of the academia-industry connect, as well as its proponents, to study the mechanics and compulsions of industry very closely if they wish to devise measures to remedy the ills that plague the relationship today, some of which we shall look into below. But it is equally important industry also carry out remedial measures to correct the anomaly at its end to ensure the future profitability of its enterprise, and justification for its continued presence.

## **Ethical Concerns and the Pseudo-Educational Dollar**

The profound ethical concerns that industry funded research has brought center-stage need a close look, especially as they impact patients, research subjects, public trust, marketability of products, and research and professional credibility. Here is what Boyd, Cho and Bero (2003) have to say:

*Clinical research involving human subjects and potentially marketable products carries with it unique ethical considerations. Human research subjects, the medical profession, and the public rely on clinical*

*It makes sense for the critics of the academia-industry connect, as well as its proponents, to study the mechanics and compulsions of industry very closely if they wish to devise measures to remedy the ills that plague the relationship today.*

*The evidence that financial ties affect outcome of trials is bound to undermine trust in clinical research and make all concerned question whether clinical research investigation is guided by considerations of patient welfare or personal gain.*

*investigators to make decisions based solely on professional judgment, without regard for personal gain (Blumenthal, 1996; Relman, 1989). However, growing evidence suggests that close financial ties between industry sponsors and clinical investigators may influence the quality and outcome of clinical studies (Bero and Rennie, 1996; Bodenheimer, 2000). Furthermore, these relationships may undermine the public's trust of clinical research (Weiss and Nelson, 2000; Angell, 2000.) (Boyd, Cho and Bero, 2003.*

*Parenthesis added.)*

The evidence that financial ties affect outcome of trials is bound to undermine trust in clinical research and make all concerned question whether clinical research investigation is guided by considerations of patient welfare or personal gain.

Moreover, there is evidence that drug-marketing techniques affect doctors' prescribing practices. This has ethical implications for doctors, as it affects the trust required in the doctor-patient relationship. Doctors need to recognise they are affected by drug marketing, and take steps to maintain their independence from the pharmaceutical industry (Breen, 2004). Some of the available evidence about doctors' prescribing habits points out that 80%–95% of doctors see industry representatives regularly (Moynihan, 2003). However that would not be a problem by itself without the other finding: more frequent contact is linked with unnecessary prescribing and increased use of new drugs (Wazana, 2000; Watkins, Moore and Harvey *et al*, 2003).

What is the evidence of the influence of attending sponsored conferences? Well, attendance at sponsored conferences is associated with increased prescribing of the sponsor's product. This increase can be seen for the next 6 months (Watkins, Moore and Harvey *et al*, 2003). And how much does the drug industry spend per physician? Hold your breath: it is estimated that industry spends about \$21 000 per year per practicing doctor on drug promotion (Jureidini and Mansfield, 2001) (See also Breen, 2004).

\$ 21,000 per year per practising physician? What are doctors? Some old time feudal lords who need to wallow in luxury?

Of course there are suggestions to reduce the impact of the industry dollar—by increasing government spending. In a letter as response to the Breen (2004) paper above, Woodruff (2004a), for example, suggests:

*...I suggest that the pharmaceutical pseudo-educational dollar be bypassed by a major expansion in government funding (Woodruff, 2004b). The provision of*

*regularly updated, easily accessible treatment guidelines integrated into prescribing software (which most general practitioners use daily) would go a long way to decreasing our reliance on the drug dollar for information on appropriate treatment. This requires government investment and professional college cooperation, but would lead to recurrent savings to the Pharmaceutical Benefits Scheme and better treatment (Woodruff, 2004a).*

Note the author considers the pharmaceutical financial support to be a pseudo-educational dollar. The suggestion of regularly updated easily accessible treatment guidelines is noteworthy, but who makes the treatment guidelines is very important. There is emerging proof of the influence of funding even there. We shall deal with this in the next monograph. (Nov. 2005-Feb2006).

He further points out:

*Currently, the federal government spends \$21 million on drug information to doctors (National Prescribing Service Limited, 2002–03), while the drug industry spends \$1 billion on marketing (Spending on drug promotion, July 2004). To partially redress this imbalance would, however, require both political will and pressure from the profession (Woodruff, 2004a; parenthesis added).*

The political will can be easily turned around, if it is not already. The professional will is already firmly turned towards the industry dollar. How practical Woodruff's approach will turn out to be only time can tell. But trust the well entrenched to resist it to the utmost, and do so in very persuasive ways. Well, if this sounds cynical, so be it. How can one hide the obvious?

But we would be most pleased to be proved wrong by events that follow.

## **Negative Implications of this Trend**

Many negative implications of this trend (the association between academic institutions and private companies) have been recognized. Concern of priority shift from public to corporate welfare and violation of the hallowed doctor-patient relationship is mounting:

*Articles in the popular and scientific press have discussed concerns about patient safety in clinical trials, issues related to privacy, conflicts of interest on the part of researchers and their institutions, a shift of priorities in academic research from the public good to*

*Many negative implications of this trend (the association between academic institutions and private companies) have been recognized. Concern of priority shift from public to corporate welfare and violation of the hallowed doctor-patient relationship is mounting.*

*How can the intermediate goal of industry serve the purpose of the final goal of academia is the basic struggle for conscientious research institutions/associations. And how best the goal of maximizing profits can be best served, albeit suitably camouflaged as patient welfare throughout, is the concern of the pharmaceutical industry.*

*private commercial gain, and the potential for disruption of the historical compact between physicians and their patients (Kelch, 2002)(Moses, Braunwald, Martin and Their, 2002).*

Concerns about patient safety, privacy, conflict of interest, and a shift of priorities in academic institutions are likely to be voiced all right, but essentially it is a losing battle for the institutions and associations as things stand today. This is because there is a fundamental dichotomy between the institutions/associations' professed principals and the pharmaceutical industry's goals and

objectives. While the former profess research for the sake of patient welfare and make their existence dependent on it, the latter researches for the sake of profits, patient welfare being only an intermediate goal. How can the intermediate goal of industry serve the purpose of the final goal of academia is the basic struggle for conscientious research institutions/associations. And how best the goal of maximizing profits can be best served, albeit suitably camouflaged as patient welfare throughout, is the concern of the pharmaceutical industry.

In this cat and mouse game, institutions/ associations may feel they are smart enough to utilize pharmaceutical industry for patient welfare, but often the case is otherwise. The pharmaceutical industry utilizes patients and willing doctors/researchers as accomplices, often without their awareness but sometimes as willing recruits, in their goal to maximize profits. And they are smart enough to do so with a massive ego-massage of the doctors/researchers concerned. And often the doctors/researchers concerned do not even realize it. Or even if they do, may continue to acquiesce in it.

If that is a tragedy according to you, well, it is one of epic proportions, and to which we see little hope of redress as things are proceeding at present.

## **Rationalizations abound**

The response of investigators to the influence of industry is pretty complex, and rationalizations abound. Investigators find many compelling reasons to continue accepting industry sponsorship. One of the most compelling is the belief that although the system can be abused, I am not one to do so, or one whom industry can manipulate.



According to one Stanford University researcher (Boyd, Cho and Bero, 2003), for example:

*It's a delicate thing. You have to decide for yourself. For example, I'm getting money from [a large pharmaceutical company] for a study I'm working on. They also have me on speakers' bureau. I feel comfortable with this arrangement as long as the slides I use are my own, and I'm speaking about my own research and opinions. I don't think the information I present has anything to do with what [the company] wants me to say. This system can be, and is, abused. Some people do give canned talks prepared by the companies that are paying them.*

*"I don't think the information I present has anything to do with what [the company] wants me to say".* Great. Will you be able to speak publicly about your negative findings of the sponsored research you are presently working on? Will you be able to say the drug is hopeless? Would you speak about the ill effects, or no effects, of the drugs your sponsor company is busy promoting all around? Or in the slides that you prepare? Those are the questions that need honest answers. It is not just a matter of not giving canned talks. It is a matter of loyalty to sponsors for future prospects.

Another rationalization is equally smart, and convenient too. For example, another Stanford University investigator (Boyd, Cho and Bero, 2003) stated:

*Obviously there is the potential for bad science, but I think that exists regardless of whether or not industry is involved. The issue fundamentally boils down to the sense of responsibility of individual investigators.*

Bad science existing regardless of industry is not the same as bad science existing because of industry involvement. The question is: is it there or not? And to leave it to individual investigators is fine. But it should not become a ploy to do nothing, lay down no parameters, offer no guidelines, and have no regulatory or redressal mechanisms in place.

Although the effectiveness of regulatory mechanisms in ensuring the ethical conduct of clinical research is limited (Miller, Rosenstein and DeRenzo, 1998), which means regulatory mechanisms may work poorly, if at all, it does not mean they are useless. All it means is they are being unheeded, or worked around. The situation can potentially change with greater awareness in all concerned.

*Bad science existing regardless of industry is not the same as bad science existing because of industry involvement. The question is: is it there or not? And to leave it to individual investigators is fine. But it should not become a ploy to do nothing, lay down no parameters, offer no guidelines, and have no regulatory or redressal mechanisms in place.*

*The academic biomedical and the industrial biomedical do not have similar needs. Their needs coincide only in so far as they both may need research fellows to work and senior investigators to guide. However, how the services of these research fellows and senior investigators have to be utilized is very different in both.*

Whether others work or not, one regulatory mechanism works for sure. The regulatory mechanism of the research career upswing - industry profit combine, and will continue to guide present and future efforts.

If you differ, we admire your feelings, but let us have proof that it is not so.

## **Needs of Academia and Industry**

Let us now take up the related issue of the needs of academia and industry.

Some researchers feel:

*Academic biomedical research and industrial biomedical research have similar needs. Both require ready access to specialized talent, from senior investigators through postdoctoral fellows (Moses, Braunwald, Martin and Their, 2002).*

This is one example of the naïve thinking so prevalent in academia, for which an antidote is urgently needed but will not be accepted as easily. The academic biomedical and the industrial biomedical do not have similar needs. Their needs coincide only in so far as they both may need research fellows to work and senior investigators to guide. However, how the services of these research fellows and senior investigators have to be utilized is very different in both. While the academic biomedical research professes to do so for patient welfare, the industrial one has to consider that only an intermediate goal in the ultimate one to maximize profits. This difference must be clearly understood and articulated, and academia has to seriously debate its ethical-pragmatic implications.

An important related issue is what researchers, both in academia and industry, seek, and how it is at variance with what industry and its needs can provide. Moses, Braunwald, Martin and Their (2002) believe:

*Researchers from both environments seek interactive, bidirectional relationships that involve the exchange of ideas, materials, and expertise, rather than relationships according to the terms dictated by corporate and university technology-transfer agreements, which emphasize confidentiality, ownership, and valuation of intellectual property.*

Indeed, and to good reason, and purpose, for they can survive, and prosper, only when they exchange ideas, materials and expertise, for those are their lifelines. And they are likely to see agreements as hindrances and irksome roadblocks in so doing. But their worth is immediately realized

when there are conflicts that need to be legally resolved, as happened in the recent Nancy Olivieri case (Downie, Thompson and Baird, 2001; Baylis, 2004; Schafer, 2004; Faunce, Bolsin and Chan, 2004) which we shall have occasion to discuss in a subsequent monograph (p53-55).

While, “Both groups of scientists often view the university’s technology-transfer office and the company’s legal staff as barriers to, rather than facilitators of, progress” (Moses, Braunwald, Martin and Their 2002), it maybe better for both sides to consider these as necessary processes, for the medical institution side to be careful about what it is going in for, and what are its rights if the whole project does not work out. As they say, a carefully worded and well-understood Dissolution Clause in any agreement is a necessary evil to prevent so much of potential bad blood entering in later, as did occur in the Olivieri case, for example (read a detailed exposition of the Olivieri case in Schafer, 2004). The need for full access to data, right to publish contrary findings, and ironclad protection for the researcher if the research contract between academia and industry goes bust is imperative. Moreover, institution and its researcher may have conflicting interests too, and that can be equally embarrassing to handle. As Drazen (2002) points out:

*Research performed under a contract that gives the investigators full access to the data and the right to publish their findings, without interference from the sponsor, lets the peer-review system and the scientific process of replication eventually get to the truth. Had Olivieri’s research been performed under such a contract, it is likely that the entire crisis could have been averted. Particular problems can arise when the contracting party — the institution — is both in a position to profit from the sale of the drug or device under study and the employer of the scientist doing the work. In such a case, there is even greater need for ironclad contractual protection for the investigator.*

## **Growing Scale of Research**

Another related and equally important issue is the growing scale of research, the sophisticated techniques and complex equipment needed for modern research, the high costs involved, and therefore the greater need for industry funding and collaboration:

*The growing scale of research is another important factor that favors collaboration. Basic research in normal biology and disease mechanisms is growing increasingly dependent on sophisticated techniques and complex equipment with high initial costs and high maintenance costs. These expenses are a substantial obstacle for many universities and make industry support or collaboration*

*The need for full access to data, right to publish contrary findings, and ironclad protection for the researcher if the research contract between academia and industry goes bust is imperative.*

*A realization of the differences in goals and motivations of academia and industry is an important step in increasing the ethical connectedness and reducing the ulteriority, while accepting that the connection has indeed been quite fruitful in some ways.*

*desirable (Moses, Braunwald, Martin and Their, 2002).*

But academia has something important to offer as well in the form of patients and controls, and the other backup material on which research can work:

*On the other hand, the critical task of genotype–phenotype correlation, on which pharmacogenomics, disease-predisposition testing, and early interventions depend,*

*requires access to well-characterized clinical populations and biologic material from normal and affected persons, as well as depth in bioinformatics and computational biology — resources that are the strength of the academic medical center (Moses, Braunwald, Martin and Their, 2002).*

So there is so much to complement in both these institutions that has the potential both for research maximization and exploitation:

*These complementary forces enhance the interdependence of industry and academic laboratories but also add to difficulties with regard to disclosure, ownership of intellectual property, and the interchange of researchers, information, and biologic materials (Moses, Braunwald, Martin and Their, 2002).*

A very great potential conflict of interest lies in the fact that academia needs the sophisticated instruments that only big funding can provide, while at the same time resists the attempts of the fund provider to set the agenda of research, protocol, design, publication, the works. The fund provider, similarly, has a conflict of interest insofar as he provides the funds ostensibly for research and patient welfare, but all the time seeks to maximize his commercial interests. And when there is a conflict between the two, he must firmly cater to the latter, if possible with academia's cooperation, if necessary with the courts'.

No clear-cut or worthwhile resolution of this situation appears in sight as yet. Which, in essence, means the academia-industry relationship is wide open to ulterior motivations as much as to ethical connectedness. However, a realization of the differences in goals and motivations of academia and industry is an important step in increasing the ethical connectedness and reducing the ulteriority, while accepting that the connection has indeed been quite fruitful in some ways:

*All of this is not to gainsay the importance of the spectacular advances in therapy and diagnosis made possible by new drugs and devices. Nor is it to deny the value of cooperation between academia and industry. But that cooperation should*

*be at arm's length, with both sides maintaining their own standards and ethical norms. The incentives of the marketplace should not become woven into the fabric of academic medicine. We need to remember that for-profit businesses are pledged to increase the value of their investors' stock. That is a very different goal from the mission of medical schools (Angell, 2000).*

Is academia ready to cooperate but at arm's length? Is it ready to forego incentives of the market place? Is it ready to maintain its own standards and ethical norms? Is it ready to understand that the mission of medical schools is very different from the values of for-profit businesses?

Let academia make up its mind. It talks of getting 'informed consent' from patients. Let it make a 'informed choice' here and then give an 'informed consent' if found appropriate. Or walk out of the procedure.

## **Conflict in Expectations, Competing Interests and Priorities**

Conflicts arise at many steps and levels of functioning, and they are related to the expectations, competing interests, and conflicting priorities of the different entities involved, whether they are the academic medical centers, the funding agencies, the patients and their families, or the investors and venture capitalists. Let us take up some of them here.

### **1. The Public**

*The public expects access to new treatments. Its appetite for innovation has been bolstered by the constant attention given by the press to new treatments and by the implicit promise from researchers of continuing advances. Direct-to-consumer advertising of drugs has increased the public's awareness of new developments in medicine, especially with respect to the treatment of common conditions, with the secondary effect of raising expectations (and health care spending) still further (Moses, Braunwald, Martin and Their, 2002).*

New treatments being continuously discussed in the media adds to the appetite, and expectations, of a novelty hungry public. And a whole mass of lip smacking industry and opportunistic academia may latch on to this want with glee. How best to articulate genuine aspirations and eschew ulterior motives is the prime intellectual task of concerned academia as much as of serious pharmaceutical players. For, even the latter, if they have to remain long term in

*Is academia ready to cooperate but at arm's length? Is it ready to forego incentives of the market place? Is it ready to maintain its own standards and ethical norms? Is it ready to understand that the mission of medical schools is very different from the values of for-profit businesses?*

*A healthy skepticism of the scientists' findings by the clinician, and a healthy respect for the needs of the practicing physician in the scientist may go a long way to bridge the gap, and increase connectedness all around.*

the field, will have to lay down certain ethical parameters that sustain their growth without hampering patient welfare. If they do otherwise, they may survive for a while, but will continuously be the target of justified malpractice suits and negative publicity, along with greater checks and balances being put in by governmental authorities and demanded by patient rights advocates, and a consumer-welfare aware, if sensation seeking, media.

Hardly a situation that fuels growth.

## 2. The Patients

*Patients demand privacy and control over information about themselves. Information about genetic predisposition is especially troublesome to patient groups and privacy advocates, not only because of the unknown implications for patients and their families, but also because of the fear that once the information proves to be commercially valuable, it will become more difficult to control. These issues led in part to the passage of such legislation as the Health Information Portability and Accountability Act of 1995 and weighed heavily as the act was subsequently modified (Kulynych and Korn, 2002) (Moses, Braunwald, Martin and Their, 2002).*

Genetic predisposition information as collected in research protocols is a real dilemma. Whilst knowing it is essential to enhance patients' interest, the advocacy groups nurse an apprehension not knowing how the information maybe utilized. How much of it will be considered and how much suppressed, especially when a commercially viable drug is at hand which can dramatically alter company balance sheets? Legislation is a necessary but often poor remedy. A clear protocol to reveal details of whether genetic predisposition impacts a certain drug is essential as a declaration in all drug research publications, just as conflict of interest at present is.

*Related also is the integration of roles that a researcher must carry out to minimize potential conflict between competing loyalties that may hamper optimal care of patients volunteering for research. The roles of clinician and scientist must be integrated to manage conscientiously the ethical complexity, ambiguity, and tensions between the potentially competing loyalties of science and care of volunteer patients (Miller, Rosenstein and DeRenzo, 1998).*

A healthy skepticism of the scientists' findings by the clinician, and a healthy respect for the needs of the practicing physician in the scientist may go a long way to bridge the gap, and increase connectedness all around.

### 3. Companies, large and small

A thought provoking insight into the way the size of a company affects its objectives in relation to academia is offered here:

*The objectives of companies in their relationships to academia often vary according to the size of the company. Large pharmaceutical companies see great value in access to academic talent, ideas, and research tools and de-emphasize the importance of discrete inventions and patentable discoveries. In contrast, smaller companies, especially those that develop devices and diagnostic techniques, see greater value in obtaining late-stage technology (i.e., products that are near clinical trial) that are closer to market. These companies derive considerable value from their association with reputable institutions and investigators, which validates their efforts to raise venture capital and the potential value of the company and its product (Moses, Braunwald, Martin and Their, 2002).*

This is an interesting observation about the differences in ways of functioning of large and small pharmaceutical companies. That the larger ones give greater value to continued access to academic talent, ideas, and research tools means they believe in long-term associations that sustain (probably ethically) over a longer period of time. That they de-emphasize the importance of discrete inventions and patentable discoveries means they may seek but are not obsessed with short term gains, which is but appropriate for long term players if they wish to sustain themselves over time. However, the smaller companies seek late-stage technology, and with ample justification. They are small players with limited capital, but an obsession to grow big and fast. That is possible only by palpable profits pouring in quickly, which late-stage technology provides very well indeed. Such companies woo venture capital armed with this technology, and understandably so. That they also woo researchers who have made a name for themselves to be part of their set-up in advisory/consultative capacity is equally understandable, for they have to continuously prove their credentials to others, as much as to themselves.

In this process, the Davids may make a killing at the expense of Goliaths of the pharmaceutical industry. It makes greater sense, therefore, for genuine researchers to associate with large long-term players who have a track record of genuine hard-core discoveries, even if the process is slow (maybe), and the funding less (may not be). Of course, if the researcher wants to grow fast, as much in wealth as in reach, he should know whom to approach, though be ready to be manipulated by

*However, the smaller companies seek late-stage technology, and with ample justification. They are small players with limited capital, but an obsession to grow big and fast. That is possible only by palpable profits pouring in quickly, which late-stage technology provides very well indeed.*

*The element of control venture capitalists exert over the pharmaceutical industry is an under researched area for obvious reasons. But it needs further probing, for that will lay bare the pulls and pressures under which industry works.*

market forces and shady operators in such companies who will maximize profits by side tracking him when it suits them, no explanations given. This is of course no guarantee that the large operators would not do likewise, but the risk is lesser, as is the frequency of such happenings. For they are used to a certain approach, and have a certain strong credibility to protect, and are hardly likely to indulge in petty deeds as a norm unless

someone treads too sharply on their toes. The smaller ones would have no qualms of taking such action. This, of course, does not mean exceptions do not exist in both categories.

#### **4. Venture capital**

The venture capitalists, especially in smaller companies, are the people who are in it mainly for profits. The pharmaceutical company, howsoever small, can be expected to have some qualms. Since they have to continuously interact with the medical profession, practicing doctors researchers or academia, they have to maintain at least a semblance of accountability to patient welfare. The venture capitalists, on the other hand, need have no such qualms at all. They can lay down their terms and conditions, and enforce them pretty ruthlessly. Their greater presence in industry is a new challenge to academia, to which an appropriate response is needed:

*Venture investors in these entities reinforce the importance of establishing the investigators' full commitment and making it public and visible (Moses, Braunwald, Martin and Their, 2002).*

Indeed, for any nexus between investigators and investors should be exposed, and any blurring of boundaries firmly resisted. But the presence of venture capital can become a good ploy to increase profitability for the pharmaceutical companies that depend on them, citing the former's pressures to suit their own profit motives too. In this whole game, if patient welfare can be served, great. If not, well, sorry, but that's the name of the game. Such games playing can also occur, which researchers and academia need to be aware of.

The element of control venture capitalists exert over the pharmaceutical industry is an under researched area for obvious reasons. But it needs further probing, for that will lay bare the pulls and pressures under which industry works. If there used to be a 'investor's lobby' in real estate which controlled the builders and the market rates, there seems to be a parallel



phenomena in pharmaceuticals which controls the manufacturers and the areas of research too. Some more probing in this area would make many skeletons tumble out of industry cupboards.

That venture capitalists should insist on researchers making financial stakes in their funded concerns is but plausible, for that ensures for them the researchers' total commitment to maximizing profit, even at the cost of ethical or patient considerations if need be. Hence, the insistence that researchers declare their financial stakes in companies whose products they research, as they do other data to declare conflict of interest, is an eminently worthy idea to implement.

## 5. Stocks and Equity

Let us also look at the other manner commitment to profits is ensured by industry:

*The most common vehicle used to assure such commitment is equity or stock options assigned to the investigator and, with increasing frequency, to the institution where the work is performed (Moses, Braunwald, Martin and Their, 2002).*

That investigators and even institutions should consider equity/stock options an attractive investment, especially as they have what could be considered 'insider-information', and maybe offered such options free or at substantially discounted rates, makes for potentially dangerous portents. While all may be fine if the products are really worthy, the problem comes if they bomb, or are found to have serious side-effects, or involve multiple legal cases or public interest litigations (PILs). In which case the company bottom-lines can go hopelessly in the red, especially if they are small companies mainly dependent on venture capitalists. Here researchers may be forced to toe the PRO line of the company involved.

In other words, it makes sense for ethically minded researchers and institutions not to fall in the trap of such investments, howsoever attractive they appear, and get rid of such stocks as soon as possible if they have them. If at all they want, it makes more sense to own stocks of larger well established concerns, for the stock upheavals being less, the pressure of the market-place, and of venture sharks, is likely to be lower too. They may also seriously consider whether owning stocks as a part of, or consequent to, research funding should be forsaken for long-term

*That venture capitalists should insist on researchers making financial stakes in their funded concerns is but plausible, for that ensures for them the researchers' total commitment to maximizing profit, even at the cost of ethical or patient considerations if need be.*

*While active participation by the researcher in the commercialization process may be greatly desired by industry, ostensibly in the name of creating value, academia must realize it is a bait it might find hard to swallow in the long run.*

peace of mind. In any case, there is no social benefit attached to researchers owning stocks:

*But it is highly doubtful whether many of the other financial arrangements facilitate technology transfer or confer any other social benefit. For example, there is no conceivable social benefit in researchers' having equity interest in companies whose products they are studying (Angell, 2000).*

As far as stocks of young companies go:

*Stock or options in young companies are relatively affordable, since they become valuable only if the company and product become successful. Active participation by the investigator in the commercialization process is viewed as essential in creating value. This engenders a powerful but controversial incentive for the investigator and has proved to be one of the most difficult issues for academic centers to manage (Moses, Braunwald, Martin and Their, 2002).*

While active participation by the researcher in the commercialization process may be greatly desired by industry, ostensibly in the name of creating value, academia must realize it is a bait it might find hard to swallow in the long run. It makes more sense for the researcher and institution to forego such temptations and/or walk out of such investments as soon as possible:

*Institutions and institutional decision makers should fully disclose industry-related financial interests and relationships. Without legitimate justification for such interests, individuals should divest themselves from these interests (Johns, Barnes and Florencio, 2003).*

However, considering the realities of the market place this may be easier said than done, especially for those investigators who depend on small/medium enterprises which themselves depend on venture capitalists, or heavily borrowed capital.

The intricacies of how economics plays a strong role in the whole process of research investigation is highly complex, and need detailed study on their own. Although one often feels one is better off being blissfully unaware of its intricacies. Which is probably the reason it is under probed, and may so remain. Both manifestations of our denial, which may prove costly in the long run.

A survey of the scenario yields certain mixed portents. While mainstream medicine and research are booming, as is connected industry, concerns about professional commitment to patient welfare are growing too. Increasing corporate influence is challenging certain long held and

fundamental values of patient care, which will have far reaching implications for biomedical care and the future progress of mainstream medicine. Events in the next two-three decades will decide the fate of modern medicine and connected industry.

The tug of war between commercial interests and ethical concerns promises to be a roller coaster one. Hold on to your seats, gentlemen.\*

*Increasing corporate influence is challenging certain long held and fundamental values of patient care, which will have far reaching implications for biomedical care and the future progress of mainstream medicine.*

## Concluding Remarks

1. Biomedical research, and its forward march, is becoming increasingly dependent on industry-academia proximity, both commercial and geographic. A realization of the commercial value of academic biomedical research coupled with its rapid and efficient utilization by industry is the major propelling force here.
2. Strengthening relationship between academic institutions and private companies has given rise to its fair share of problems.
3. Concerns about patient safety, privacy, conflict of interest, and shift of priorities in academic institutions are issues that need urgent redress.
4. Connected to the growing clout of industry in institutions is concern about the commercialization of research and resolving the 'patient or product' loyalty.
5. Academia needs sophisticated instruments/appliances that only big funding can provide, while at the same time resists the attempts of the fund provider to set the agenda of research, protocol, publication, the works.
6. Conflicts arise at many steps and levels of functioning, and are related to the expectations, competing interests, and conflicting priorities of the different entities involved, whether the academic medical centers, the funding agency, the patients and their families, or the investors or venture capitalists.
7. The profound ethical concerns that industry funded research has brought center-stage need a close look, especially as it impacts patients, research subjects, public trust, marketability of products, and research and professional credibility.

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\*Provided of course your seats remain, and you can still hold on to the rope.

8. How can the intermediate goal of industry (patient welfare) serve the purpose of the final goal of academia is the basic struggle for conscientious research institutions/associations. And how the goal of maximizing profits can be best served, albeit suitably camouflaged as patient welfare throughout, is the concern of the pharmaceutical industry
9. It makes greater sense for genuine researchers to associate with large long-term industry players who have a track record of genuine hard-core discoveries, even if the process is slow (maybe), and the funding less (may not be).
10. The element of control venture capitalists exert over the pharmaceutical industry is an under researched area for obvious reasons. But it needs further probing,
11. It makes sense for ethically minded researchers and institutions not to fall in the trap of stock and equity investments in industry, howsoever attractive they appear, and get rid of them as soon as possible if they have them.
12. The intricacies of how economics plays a strong role in the whole process of research investigation is highly complex, and need detailed study on their own.
13. While mainstream medicine and research are booming, as is connected industry, concerns about professional commitment to patient welfare are growing too. Increasing corporate influence is challenging certain long held and fundamental values of patient care, which will have far reaching implications for biomedical care and the future progress of mainstream medicine.

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## **Questions that this monograph raises**

1. Is the connection between academia and industry desirable?
2. Do we need the financial sponsorship to medical research on such a large scale?
3. Can medical conferences and associations work without industry sponsorship?
4. Is conflict of interest invariable in every academia-industry relationship? Can it be resolved?
5. Have you faced ethical problems in industry relationships, and how did you tackle it?
6. Do large and small pharmaceuticals really differ in their approach to research?
7. Can patient welfare be the final goal even of industry?
8. Does patient welfare guide medical research any longer, or has research become a handmaiden of commercial interests?
9. Is doing away with industry sponsorship a practical proposition?
10. Is industry sponsorship really the villain, or are smart operators in academia just painting it as such to carry on with their own questionable activities?
11. Is the academia-industry ethical problem unique, or only a manifestation of a wider malaise that afflicts society?
12. Where do we go from here?

## Readers Respond

*(You can read here some responses to the last issue of Mens Sana Monographs: Resolution of the Polarisation of Ideologies and Approaches in Psychiatry, Mens Sana Monographs, Mens Sana Research Foundation, 2004-2005, Vol II, No 4-5, Nov 2004- Feb 2005, ISSN 0973-1229.)\**

1. I read with interest and appreciation your Monograph *Resolution of the Polarisation of Ideologies and Approaches in Psychiatry*. When I was a medical student in CMC, Vellore, Dr. Stafford Clark from UK visited us and gave a public lecture. The main message was that all diseases are psychosomatic, in the sense that emotions are involved in all diseases, either in the causation or in the perpetuation. This is all the more true in Psychiatry. The so-called polarisation into biological and dynamic psychiatry is artificial and misleading. In all psychiatric conditions, both genetic and environmental factors are involved. The only difference is in the degree of involvement. In psychoses, genetic factors are more important than environmental factors and in neurotic and personality disorders, environmental factors are more important. We have to advocate integration and not polarisation. There should be only one school of psychiatry—biopsychosocial model as proposed by Engel.

**Dr. Abraham Verghese, Retd. Prof. of Psychiatry CMC, Vellore**

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2. The Monograph *Resolution of the Polarisation of Ideologies and Approaches in Psychiatry* is thought provoking. It has come out very well.

**Dr. J.K.Trivedi, Immediate Past President, Indian Psychiatric Society**

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\* This monograph has been listed for review by JAMA, May 18, 2005, 293, p2417 -2418. You may review it for the journal if you desire.

*Psychiatry, Science, Religion and Health*, our Annual 2004 issue, is also listed in JAMA, 20th July, 2005; 294,p377-378.



**ISBN 81-89753-10-X The Ninth Monograph**

***The Academia - Industry Symposium***

Medical Practice, Psychiatry and the Pharmaceutical Industry :  
And Ever the Trio Shall Meet - II

**Public Welfare Agenda or  
Corporate Research Agenda?**

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## Musings

### The Story of a Young Man

A bright young man decided he wanted to make the removal of suffering his mission. He also loved to understand human nature. So he chose psychiatry as his branch.

He studied hard. He mastered his textbooks, he attended the lectures and tutorials, he attended the ward rounds and grand rounds, he took and presented case histories, he admired his teachers, he looked up to the greats in his field with awe.

He wanted to do research and went about it in right earnest. But when the time came for publication, he was not the principal author. The Head of department was. He wanted to pursue further research, but his Head was interested in clinical trials that got money for the department, and free sponsored trips for him. The young man too got the sponsored trips to conferences to present papers. And since his Head was well known, his papers were appreciated, and got him further opportunities. The pharmaceutical companies took charge of financial matters, and he learnt the tricks of the trade quickly.

He wanted posts and publications, and his flexible nature and compliant attitude with his bosses ensured both. He got to know what was current coin in his field and starting mouthing it on suitable occasions in conferences, seminars and workshops to get approving nods from seniors. He started climbing the ropes first gradually, then with greater speed. He enjoyed the heady feel of success as he ascended up the ladder, knowing and learning quickly which side the bread was buttered. And also learned whose feathers not to ruffle, and whom to cozy with.

His publications list swelled, his invitations to CMEs and as speaker at other forums increased. All the time what he had learnt from his bosses served as a torchbearer.

He himself had bright students. They looked up to him in open-mouthed awe. He gave them research projects, got them stipends, but saw to it that he became the principal author. They quietly acquiesced, since they wanted to remain in favour. It served both parties very well indeed.

Awards, orations, posts, groupism, politics, became his major activity. Bright students handled research in any case, so that was taken care of. A cozy relationship with pharmaceutical companies looked after all expenses

of attending conferences, and even organising them. So Regional, then National and later even International ones followed one after the other, adding feathers to his cap.

Research done by his Department always kept up with current trends, and quoted extensively from numerous authorities abroad.

Name and fame were not far behind. It was fashionable to sound like a thinker so a couple of papers on ancient Indian concepts in mental health were written, while seeing to it no serious foray into any allied field occurred, for psychiatry had to always stress and re-stress its linkage with its parent branch— medicine.

One more psychiatrist made his mark in his field.

One more opportunity lost for Indian psychiatry to make its mark in the field of world psychiatry.

Ajai R. Singh

*The Academia-Industry Symposium*

Medical Practice, Psychiatry and the Pharmaceutical Industry:  
And Ever the Trio Shall Meet-II

## **Public Welfare Agenda or Corporate Research Agenda?**

*Ajai Singh  
Shakuntala Singh*

### **ABSTRACT**

*As things stand today, whether we like it or not, industry funding is on the upswing. The whole enterprise of medicine is booming, and it makes sense for industry to invest more and more of one's millions into it. The pharmaceutical industry has become the single largest direct funding agency of medical research in countries like Canada, the United Kingdom and the United States.*

*Since the goals of industry and academia differ, it seems that conflicts of interest are inevitable at times. The crucial decision is whether the public welfare agenda of academia, or the corporate research agenda of industry, should occupy center stage when they conflict.*

*There is enough evidence to show that funding by industry is very systematic, and results that are supportive of the safety and efficacy of sponsor's products alone get the funds. It is no surprise, therefore, that one finds very few negative drug trials reports published, and whatever are, are likely to be by rival companies to serve their commercial interests.*

*Renewed and continued funding by industry decides the future prospects of many academic researchers. At the same time there is now evidence that pharmaceutical companies attempt suppression of research findings, may be selective in publishing results, and may delay or stymie publication of unfavourable results. This is a major area of concern for all conscientious researchers and industry watchers.*

*Industry commonly decides which clinical research/trial gets done, not academia, much though the latter may wish to believe otherwise. It finds willing researchers to carry this out. This can be one area of concern. Another area of pressing concern is when industry decides to both design and control publication of research.*

*It makes sense for researchers to refuse to allow commercial interests to rule research reporting. Research having been reported, the commercial implications of such reporting is industry's concern. But, doctoring of findings to suit commerce is to be resisted at all costs. In this even pliant researchers need have no fear, for if they indeed publish what will work, the concerned sponsor will benefit in the long run. The only decision academia has to make is refuse to comply with predestined conclusions of sponsors for the 'thirty pieces of silver'. Instead do genuine research and make sixty for themselves.*

*The useful rule of thumb is: Keep the critical antenna on, especially with regard to drug trials, and more especially their methodology, and study closely the conflict of interest disclosed, and if possible undisclosed, before you jump on the band wagon to herald the next great wonder drug.*

*There are three important lessons to be learnt by academia in all academia-industry relationships:*

*i) Lesson number one: incorporate the right to publish contrary findings in the research contract itself. Which means, it makes great sense for academia to concentrate on the language and contractual provisions of sponsored research, to read the fine print very closely, and protect their research interests in case of conflict.*

*ii) Lesson number two: a number of lawsuits successfully brought up against industry recently reflect earnest attempts by patient welfare bodies and others to remedy the tilt. It will result in a newfound confidence in academia that augurs well for academia-industry relationship in the long run. Hence the second lesson for academia: do not get browbeaten by threats of legal action.*

*iii) Lesson number three: Academia should keep itself involved right from inception of the clinical trial through to ultimate publication. And this must be an integral part of the written contract.*

*The time to repeat clichés about the exciting future of the academia-industry connect is past. A concerted effort to lay a strong foundation of the relationship on practical ethical grounds has become mandatory.*

**KEY WORDS:** *Public Welfare or Corporate Research Agenda, The Olivieri Case, Doctoring of Research Findings, Selective publishing, Delay and Under reporting, Complete Disclosure, Multi-centred Trials, Ghost writing, Duplicate Publication, Access to Data, Control over Publication, Negative Drug Trials, The Porcupine Dance, Law Suits Against Industry, Design and Control of Publication, Connection between Funding and Positive Findings.*

*The advancements in medical symptomatology/diagnostics / therapeutics on the one hand, and the ancillaries needed for them on the other, kept pace with each other. And whilst the medical men and researchers excelled in one, the drug researchers, with the help of foundations, philanthropists, concerned governments and administrators, and now mainly organized industry, came to excel in the other.*

## Introduction

As medicine marched onwards from being only an art to becoming an art based on scientific inputs, great contributions were made in diagnostics as well as therapeutics from numerous quarters. In both these areas, medical research has played a great role, as has the education, training and acumen medical practitioners imbibe from institutions, dedicated medical teachers, research publications and other means of upgrading knowledge like CME, conferences, workshops, annual meets etc. An area of increasing activity is by organized industry, which supports and

funds major research and related ancillary/infrastructure development today. The pharmaceuticals have played a major role in organized industry, and their contribution cannot be ignored, nor sidelined, for they have been instrumental in placing at our disposal a huge arsenal of medications both effective and safe:

*One of the striking characteristics in the medical field in the 20th century has been the development of new drugs, usually by pharmaceutical companies. Until the end of the 19th century, the discovery of new drugs was largely a matter of chance. It was in that period that Paul Ehrlich, the German scientist, began to lay down the principles for modern pharmaceutical research that made possible the development of a vast array of safe and effective drugs (Encyclopaedia Britannica, 2005).*

The advancements in medical symptomatology/diagnostics/therapeutics on the one hand, and the ancillaries needed for them on the other, kept pace with each other. And whilst the medical men and researchers excelled in one, the drug researchers, with the help of foundations, philanthropists, concerned governments and administrators, and now mainly organized industry, came to excel in the other. This has resulted in a vast advancement in, and organization of, an institution called modern medicine, with its paraphernalia of practicing physicians, researchers, academia and related industry and its appendages\*.

Many in the pharmaceutical industry started with pioneering ideas of wanting to help mankind. (For example, Upjohn, the founder of the pharmaceutical by his name, began the use of true tablets/capsules,

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\* See also : *The Two Revolution in Bio-Medical Research, p vii-ix*

[Worthen, 2000]). So did academia, and the physicians it produced. Somewhere down the line, industry decided to make profit its major focus, and to good reason, for it was a commercial venture. And profit in an open market economy is the sweetest sound to the ears, whatever the others may say, or crib about.

Academic medical institutions, and the products from its precincts, had to balance their needs for gain with notions of patient welfare, since they could not make, or at least declare, profit their main motive. Probably, if they too had, things would have been less problematic ethically. What they did, however, was try and balance the ethics of a professional guided by patient welfare, with the needs of an entrepreneur who needed the patronage and investment that big funding could provide. So they started lobbying, first with government which was the major source of funding earlier, and later with industry. As the scale of investment increased, government found it easier to hand over funding to industry, which in any case was catching up with events and waiting for its chance. And its chance did come, as government found funding for medical advancement too hot to handle. Instead, it decided to play an overseer role, a role that both suited it and was within its capacity.

Industry and academia, both of which were in the meanwhile becoming commercial enterprises, welcomed this development. Industry with open arms, academia with folded ones, at least overtly. Over the decades, whilst government has settled in its legislative role, industry has settled in its commercial one. Academia has still to settle in any role, since it wants to settle in a professionals', but is compelled by the pulls and pressures of acting like an industry. The recent trend to run hospitals, and even academic institutions, along business lines is a step in the direction of seeing whether even medicine and medical research could become a business enterprise.

All said and done, it is a point worth serious consideration whether that may not be a worthy option to explore. Before a number of the well meaning get alarmed, let us clarify that this option may appear sacrilegious, but is very much in the offing, and prudence dictates either we resist it and know the implications, or accept it and enjoy the fruits. And when we do suggest prudence, we do not suggest no ethical parameters need be followed. But they will be as laid down in a business enterprise, not as in a profession. Meaning, thereby, profit will guide which

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*As things stand today, whether we like it or not, industry funding is on the upswing. The whole enterprise of medicine in booming, and it makes sense for industry to invest more and more of one's millions into it. Man, with the disturbed equilibrium/homeostasis of his internal and external environment, is giving the medical enterprise enough reasons to keep booming.*

patient welfare activities will be carried out, and not patient welfare decide where the profits will accrue from. Ultimately, market forces of a free economy, the great leveler, will decide which — profit or patient welfare, will prevail. If what profession feels today - that patient welfare alone will ensure long-term profits- is the truth, well, market forces will prove it. If, however, patient welfare is only an intermediate goal anyway (Singh and Singh, 2005), well, market forces will unravel that too. In any case, the ambivalence and confusion that prevails all around will at least disappear.

As things stand today, whether we like it or not, industry funding is on the upswing. The whole enterprise of medicine in booming, and it makes sense for industry to invest more and more of one's millions into it. Man, with the disturbed equilibrium/homeostasis of his internal and external environment, is giving the medical enterprise enough reasons to keep booming. This is hardly likely to go bust, at least in the near future.

So it makes sound business sense to stay invested in this enterprise, even increase ones stakes. This, the pharmaceutical industry realizes very well indeed. This the enterprising academics and connected researchers realize very well too. And both would like to make hay as the sun shines. And keep fresh stock of hay ready, and keep the sun shining, if possible indefinitely.

In this monograph, we shall see how both sides are making the hay, how wholesome it is, and who is chewing the cud.

The great role that the pharmaceutical industry is playing today, and will continue to play in the future, can be gauged from the fact that it is the single largest direct funding agency of medical research in Canada, the United Kingdom and the United States (Collier and Iheanacho, 2002). The major drug research activity is occurring in these countries, and the implications of this finding should be obvious. Those who pump in their millions do so mainly for profit, and only incidentally for patient welfare. And, as we saw above, this trend is not likely to get reversed, at least in the near future. Which means this is likely to become the trend in other countries as well, India included. If this appears alarming to some, it must be sweet music to some others.

All in all, as things stand today, the enterprise called medicine is booming, and industry is playing a major role in this boom, whatever the doomsday prophesiers may lament, or rant, about.

## Can Academia Call The Shots?

We mentioned earlier that the connect between academia and industry was a double-edged sword, and the prevailing ambivalence led to a typical 'approach-avoidance conflict' \*(Singh and Singh, 2005; see also Montaner, O'Shaughnessy and Schechter, 2001). Let us take another example of the ambivalence that pervades academia, not that we ourselves are immune to it:

*At its best, academic participation in the development of drugs leads to effective and safe new therapies (Baird, 2003). However, conflicts of interest are inevitable at times, because the goals of industry and of academia differ (Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis, 2001).*

Just saying that conflicts of interest between academia and industry are inevitable at times is acceptable as a *statement of fact* but not as a *state of affairs*. However the state of affairs can be remedied only if major leverage areas remain with academia. Evidence to that effect is sadly lacking at present. Whilst it is true that academia and industry must collaborate to develop newer and safer drugs, the problems come up when the so called newer drugs are just cosmetically different from the old, are not necessarily proven safe, but need to be hoisted on an unsuspecting patient population to keep proving the legitimacy of R and D departments, add to the impressive new drug tally of the company, and give a new potentially profit making tool to the marketing department, which can have another go at proving its legitimacy to those who matter.

The problem that comes up when boundary lines between academia and industry get blurred is well brought out by Angell (2000) below:

*When the boundaries between industry and academic medicine become as blurred as*

*Whilst it is true that academia and industry must collaborate to develop newer and safer drugs, the problems come up when the so called newer drugs are just cosmetically different from the old, are not necessarily proven safe, but need to be hoisted on an unsuspecting patient population to keep proving the legitimacy of R and D departments, add to the impressive new drug tally of the company, and give a new potentially profit making tool to the marketing department, which can have another go at proving its legitimacy to those who matter.*

\* See page 11.

*Granted, the ground realities are that if academia decides to call the shots, the money may go to the smart operators who do not mind cozying up to industry. Granted, that funds may not come that easily. But whoever thought the straight and narrow path was ever easy. It always was difficult. Because insofar as it was straight, it was easy; but insofar as it was narrow, it always ran the risk of the person falling off.*

*they now are, the business goals of industry influence the mission of the medical schools in multiple ways. In terms of education, medical students and house officers, under the constant tutelage of industry representatives, learn to rely on drugs and devices more than they probably should. As the critics of medicine so often charge, young physicians learn that for every problem, there is a pill (and a drug company representative to explain it). They also become accustomed to receiving gifts and favors from an industry that uses these courtesies to influence their continuing education. The academic medical centers, in allowing themselves to become research outposts for industry, contribute to the overemphasis on drugs and devices. Finally, there is the issue of conflicts of commitment.*

*Faculty members who do extensive work for industry may be distracted from their commitment to the school's educational mission (Angell, 2000).*

The crucial point is that the goals of academia and industry differ. And we purposely mention *academia* and *industry*, and not vice versa, to highlight what should be the state of affairs. It is academia which has to call the shots, it is industry which has to play second fiddle, and make its millions playing it. But it cannot be that in making its millions, it decides to also call the shots and decide what academia does or does not do. How does academia ensure this is a crucial issue. This, in spite of the analysis we presented in the introduction. Because, the analysis presents trends, which if understood, can either be forwarded or reversed. This thought supports the latter, and we shall see further how academia can really call the shots.

Granted, the ground realities are that if academia decides to do so, the money may go to the smart operators who do not mind cozying up to industry. Granted, that funds may not come that easily. But whoever thought the straight and narrow path was ever easy. It always was difficult. Because insofar as it was straight, it was easy; but insofar as it was narrow, it always ran the risk of the person falling off.

How things are accepted by pragmatic researchers is obvious from a recent paper in which the authors expect practical clinical trials in psychiatry, which they consider important, *not* to be funded by industry. This is not because they are not useful (even to industry), but because they may not serve their interests; in fact, may go against it:

*Although a compelling scientific argument can be made for practical clinical trials funded by industry (fewer negative findings and more definitive answers to safety questions, among other reasons), it is unlikely, although not inevitably so, that pharmaceutical companies will pursue a practical clinical trials agenda in psychiatry if doing so will, in their perception, put profits at risk, even when the answers would be of substantial public health importance. Particularly when comparing newer to older off-patent treatments, the risk of an adverse outcome (including a true tie) would be too great (March, Silva, Compton, Shapiro, Califf and Krishnan, 2005).*

In other words, industry plays not a patient welfare but a profit welfare game, whatever academia may desire. In other words, academia realizes which research project will get the finances, and so will be guided accordingly. What are the implications of this trend in the future is anybody's guess.

## **Corporate Research Agenda Center Stage**

Conflicts between the differing goals of academia and industry “put pressure on researchers to stretch — occasionally to the point of breaking — fundamental principles of ethical and scientific behaviour, and they may result in corporate research agendas, rather than the broader public agenda, being placed centre stage” (Baird, 2003).

There is no problem if all is hunky dory. The problem is that academia accepts that the public welfare agenda is hardly likely to motivate industry, and agrees to play ball accordingly:

*... industry-sponsored research often fails to address broad public health needs or the needs of individual practitioners seeking to make good clinical decisions for individual patients. This shortcoming of industry-sponsored research is especially pertinent for decisions regarding risk, use of adjunctive treatments to improve partial response, maintenance and discontinuation of treatment, and transportability of treatments from the research to the clinical setting (March, Silva, Compton, Shapiro, Califf and Krishnan, 2005).*

Issues like risk, adjuncts, maintenance, discontinuation and transfer to clinical use concern practitioners, but are not likely to motivate industry-sponsored research. What does it mean? It means research agendas of

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*The crucial decision is whether the public welfare agenda, or the corporate research agenda, should occupy center stage when they conflict. We cannot but note here that the former should be possible for academia only if it keeps vantage bargaining points to itself. But this is only if academia is more aware both of its clout and also how it is getting minimized by subtle pressures, often unrealized.*

industry are out of tune with needs of clinicians and patients, but still manage to determine what research gets done. Which also brings to the fore the schism between research developed in academia and practice done by clinicians. That, however, is a topic by itself. But what needs to be noted here is that industry and academia collaborate to produce much that has poor genuine clinical relevance to practitioners, although that does not at all mean new drugs do not get into the market, and sell well enough to produce industry dollars. Or research does not occupy center stage in academia and publications.

Well, if that is a paradox, it is one of the greatest unresolved paradoxes of our times in the field of medicine.

## **Public Welfare, or Corporate**

The crucial decision is whether the public welfare agenda, or the corporate research agenda, should occupy center stage when they conflict. We cannot but note here that the former should be possible for academia only if it keeps vantage bargaining points to itself. But this is only if academia is more aware both of its clout and also how it is getting minimized by subtle pressures, often unrealized.

*Many researchers profess that they are outraged by the very notion that their financial ties to industry could affect their work. They insist that, as scientists, they can remain objective, no matter what the blandishments. In short, they cannot be bought. What is at issue is not whether researchers can be "bought," in the sense of a quid pro quo. It is that close and remunerative collaboration with a company naturally creates goodwill on the part of researchers and the hope that the largesse will continue. This attitude can subtly influence scientific judgment in ways that may be difficult to discern. Can we really believe that clinical researchers are more immune to self-interest than other people? (Angell, 2000).*

Evidence that academia intends to keep vantage bargaining points to itself is sadly lacking at present. In fact as Boyd, Cho and Bero (2003) point out: faculty members are poorly informed even about campus conflict-of-interest or other institutional policies, in spite of it being on web sites, and staff meant to enforce it. This is the ostrich attitude at its best, or rather, worst. This is the result of the Boyd, Cho and Bero (2003) study:

*Based on our interviews, it seems likely that faculty are poorly informed regarding their campus' conflict-of-interest policies. Fewer than half of the faculty we interviewed could accurately state their institution's policy, even though the policies are posted on universities' Web sites and staff at each institution are devoted to enforcing the policies (Boyd, Cho and Bero, 2003).*

Now, if someone is ignorant of policy, he can hardly be expected to know its repercussions, or the problems he and others face because of this ignorance. That is a matter of obvious concern:

*Because administrators depend on faculty to consistently disclose their relationships and because disclosure requires knowing when and what to disclose, these findings are of concern. If some investigators believe that they have no need to know the policy because they are not in conflict, then more must be done to educate investigators about both the specifics of relevant policies, as well as the nature of conflicts of interest (Boyd, Cho and Bero, 2003).*

Educating them as to why it is essential is of course necessary, but some concrete steps so that they cannot get away with ignorance in this matter are necessary. A compulsory crash course highlighting academia-industry problem areas and how to resolve them is necessary before grants or projects get sanctioned. And matter on institution web sites should be regularly updated and become important reference source for such a course.

As awareness increases, investigators' apprehensions, justified or otherwise, would be allayed, ensuring greater compliance, because ignorance today manifests both as a feeling of discrimination and skepticism, and they increase chances of noncompliance:

*Furthermore, some faculty we interviewed perceived that the policies are inequitable because they are not consistently applied to all faculty. Such (mis)perceptions could also lead to noncompliance (Boyd, Cho and Bero, 2003).*

Awareness of increase in academia-industry conflicts of interest by education, remedial steps and an element of compulsion like a crash course (at least initially, to shrug off the lethargy), are urgent steps needed by academia if it desires the equation skewed against it at present to be set right.

## **Academia's naiveté**

As we see the reality, academia is pretty naïve in this regard, only too eager to hand over the initiative in conflict

*A compulsory crash course highlighting academia-industry problem areas and how to resolve them is necessary before grants or projects get sanctioned. And matter on institution web sites should be regularly updated and become important reference source for such a course.*

*The signing over, the money for research in, the future prospects for rising up the academic ladder ensured, academia thinks all is well. And industry, with the power of money, the need for profits, and the smartness of legal expertise, manages to create for itself an almost fool proof means of survival in conflict situations.*

situations to industry, almost accepting that the sponsor can be tough and the recipient cannot:

*... when results are disappointing for a company, conflicts may develop. Dr. Furberg, with years of experience in industry-funded drug trials, stated: "Companies can play hardball, and many investigators can't play hardball back. You send the paper to the company for comments, and that's the danger. Can you handle the changes the company wants? Will you give in a little, a little more, then capitulate? It's tricky for those who need money for more studies" (Bodenheimer, 2000).*

This is obvious as much in the disinclination to fight back as in the bored resignation academics show in reading agreement documents with industry, as well as in not consulting lawyers who will protect their interest, and in being too eager to sign on the dotted line for the carrot of the sponsorship cheque dangling so invitingly in front. It is essential to note that academia-industry transactions are like any business deal wherein the agreement contract is to be carefully perused to ensure ones interests. As Drazen (2002) points out:

*No matter how altruistic the motive, investigators must recognize that research performed under these contracts is a business transaction. It is imperative that the terms of such contracts guarantee the safety and confidentiality of patients while preserving the academic independence of participating investigators.*

However, academia can be quite complacent in this matter. The signing over, the money for research in, the future prospects for rising up the academic ladder ensured, academia thinks all is well. And industry, with the power of money, the need for profits, and the smartness of legal expertise, manages to create for itself an almost fool proof means of survival in conflict situations. This is aided no end by academia's strong belief still that it can recognize and handle conflict of interest situations, and regulate its behaviour, even in the face of evidence that they may be underestimating the risks to the integrity of research. As Boyd, Cho, and Bero, (2003) point out:

*Although most clinical investigators in our study recognized that financial relationships with industry sponsors pose possible conflicts of interest, many believed strongly in their own ability to recognize these conflicts, avoid bias, and regulate their own behavior.*

Going on to analyse this attitude, they describe the peculiar denial academia manifests:

*Investigators have this attitude despite the publicity that has been given to a few high-profile cases involving the suppression of research by investigators with financial ties to companies (Nathan and Weatherall, 2002; Rennie, 1997). The investigators' expressed belief that risks of conflict of interest do not apply to themselves, a viewpoint that is consistent with their support for self-regulation. (Parenthesis added).*

Their caution that follows is worth more than a cursory look :

*However, the well-publicized risks, mentioned above, and the data on the association of funding and financial ties with outcomes of research (Cho and Bero, 1996; Barnes and Bero, 1997; Barnes and Bero, 1998) suggest that investigators may be underestimating the risks to the integrity of their research. Furthermore, these views may ultimately undermine the effectiveness of institutional policies. (Parenthesis added).*

And the concluding remarks make eminent sense, for they recommend that potential for bias, conflict and pressure be seriously recognized in all academia-industry ties:

*Insofar as investigators believe in their own abilities to "handle" conflicts of interest, policies may be perceived (and perhaps treated) as irrelevant. Thus, a fundamental challenge facing administrators and policymakers is to demonstrate to all investigators, both clinical and nonclinical, that the potential for bias, pressure, and conflict is relevant to all investigators with industry relationships (Boyd, Cho and Bero, 2003. Parenthesis added.).*

This situation needs some measure of urgency from academia, which is in the know of things but resists acting on it. Let us see the other manifestation of denial pointed out by another recent paper:

*Although industry sponsors provide approximately 70 percent of the funding for clinical drug trials in the United States, little is known about the legal agreements that exist between industry sponsors and academic investigators (Mello, Clarridge, Studdert, May, 2005).*

Little is known about the legal agreements. This in May, 2005. Why? What's the reason? What's there to conceal? Who is concealing it, and why? Will serious academics deliberate over this state of affairs?

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*But the situation is not necessarily that bad, for the soul searching that the Olivieri case has brought about in academia is a promising fall out of the murky events that led to, and also followed, the whole affair. The Olivieri Symposium in the Journal of Applied Ethics is a welcome addition*

## Contrary Findings and The Olivieri Case

The need to protect its right to publish finding even if contrary to industry interests is a crucial determining factor with regard to forwarding the public welfare agenda. How many from academia can stand up and ask for it is a crucial factor. How many remain ever vigilant not to allow research agendas to be hijacked by industry is another crucial factor. How many have the nerve to support colleagues who stand by public welfare and are hauled to court for it, or smeared as to their credentials for it, is still another crucial factor.

The way in which many from academia played into the hands of industry in the recent Nancy Olivieri case (see Baylis, 2004; Schafer, 2004) is a sad commentary on how money and grants rule the minds of academia at the cost of patient welfare. In so far as that is happening, the earlier situation of conflict between academia and industry has been wonderfully well resolved. For it no longer obtains, academia having submitted tamely to industry's demands. How usefully is the issue resolved for society and patients is for many, well, an embarrassment better swept under the carpet.

But the situation is not necessarily that bad, for the soul searching that the Olivieri case has brought about in academia is a promising fall out of the murky events that led to, and also followed, the whole affair. The Olivieri Symposium in the *Journal of Applied Ethics* is a welcome addition (three articles from there worth a close look are Baylis, 2004; Schafer, 2004; Faunce, Bolsin, Chan, 2004), as is the discussion in various forums and research journals of its pros and cons.

The Schafer (2004) comment in which he takes a close look not only at haematologist Nancy Olivieri's case but even the equally alarming one of psychiatrist David Healy is worth a close look here. He talks about the common elements in both episodes, and the shady role that well known pharmaceuticals played. This is a gist of what he says:

*Not coincidentally, the Olivieri and Healy scandals share in common a number of key elements:*

- *Wealthy and powerful drug companies hover in the background of both, and sometimes occupy a good deal of the foreground, as well: Apotex in the case of Olivieri, Eli Lilly in the case of Healy.*
- *These drug companies not only fund university and hospital researchers, they are also major donors to the institutions within which researchers carry out their clinical studies.*

- *Neither Apotex nor Eli Lilly was happy to have adverse information about their drugs publicized (Schafer, 2004)*

Talking of the negative consequences the two experienced for promoting the patient welfare agenda, he mentions how both industry and academic institutions ganged up to discredit the two researchers:

- *Both Olivieri and Healy personally experienced serious negative consequences from their willingness to speak publicly about potential dangers to patients.*
- *Each of them appealed for assistance, unavailingly, to the senior administrators of the University of Toronto and its Faculty of Medicine. Although there had been a changeover of university presidents and medical faculty deans in the interval between these two scandals, personnel changes made very little difference to the university's official response.*
- *In both scandals, university and hospital officials failed to recognise that there had been a fundamental violation of the principle of academic freedom at the affiliated hospitals (Schafer, 2004).*

The way institutions where the researchers worked (Olivieri), or were to get connected (Healy), behaved is straight out of a movie thriller:

- *In both cases, the whistleblowing physicians found themselves removed from their positions: Olivieri was fired from her position as director of the Hemoglobinopathy Research Program at Sick Kids' Hospital; Healy's employment contract with both CAMH and the University of Toronto's Department of Psychiatry was terminated.*
- *Both hospitals and the university denied strenuously that these "firings" were in any way related to the whistleblowing (Schafer, 2004).*

And to ensure the movie would be a sure hit:

- *Damaging rumours were circulated among Olivieri's colleagues, including allegations that she was scientifically incompetent, guilty of stealing money from her research grants, unethical in her patient care and sleeping with some of the scientists who looked favourably on her research findings; damaging rumours were circulated about Healy that he was a bad clinician, and both a racist, and a member of a cult known as Scientology. A journalist who telephoned me for an interview at the height of the Healy controversy asked whether I knew that Healy was a prominent Scientologist. Her*

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*What happened with the bioethicists was not an isolated phenomenon. What the medical academic community did was equally reprehensible. Schafer's paper (2004) describes it in uncomfortable detail. If this does not open the eyes of academia, one wonders what will. Or is it that academia has decided to lie back and enjoy it, for the lure of lucre rules?*

*previous interviewee had been a hospital spokesperson who was circulating that piece of disinformation among the media, presumably in an effort to discredit Dr Healy.*

- *The perpetrators of these false but damaging accusations against Olivieri and Healy mostly preferred to remain anonymous (Schafer, 2004).*

How much further will academia bow down to, and ingratiate itself, for a few pieces of silver? How often would Judas' stories get repeated, and Christs crucified?

And the Baylis (2004) comment on fellow bioethicists who maintained a stony silence while the Olivieri episode raged is equally unsparing:

*Bioethicists in Canada failed Dr Olivieri and her colleagues at HSC. Why? Did they fear losing their jobs? There are few bioethicists who have the security of tenure. Did they fear being sued? Many of the individuals and organisations involved in this case had shown themselves willing to engage in litigation. Did they fear loss of reputation? Again, many involved in this case had shown themselves willing to make damaging public comments. Did they fear retribution and consequent damage to their careers? After all, bioethics in Canada is a very small and fractured community. I do not know the reason(s) for the ensuing silence. I do know, however, that by and large Canadian bioethicists failed to speak up when there was ample time and opportunity. As a responsible community, we must ask ourselves whether we could and should have done more.*

What happened with the bioethicists was not an isolated phenomenon. What the medical academic community did was equally reprehensible. Schafer's paper (2004) describes it in uncomfortable detail. If this does not open the eyes of academia, one wonders what will. Or is it that academia has decided to lie back and enjoy it, for the lure of lucre rules?

Decide. It's a trifle urgent.

## **Doctoring of Research Findings**

Let us move on to the way suppression of findings contrary to a company's interests occurs. "It is an area of increasing concern that when clinical research results are contrary to a company's interests, conflicts are more likely to develop, and there are numerous documented instances in recent years in Canada of attempted suppression of research findings by

pharmaceutical companies” (Skolnick, 1998; Downie, Thompson and Baird, 2001). (Baird, 2003).

The recent paper by Mello, Clarridge, Studdert (May, 2005) makes the point equally clearly in the case of the AIDS vaccine, Remune, about which the researchers concerned filed negative reports and had to face legal action by the sponsor:

*In September 2000, Immune Response, a biopharmaceutical company, filed a \$7 million legal action against the University of California at San Francisco after researchers published negative findings from a clinical trial of the company’s experimental acquired immunodeficiency syndrome (AIDS) vaccine, Remune. The investigators had refused to allow the company to insert its own statistical analyses into the manuscript (Saltus, 2000). Immune Response demanded that the researchers not publish the article and withheld some of the data in an effort to dampen their publication prospects (Hilts, 2000). The investigators succeeded in publishing (Kahn, Cherng, Mayer, Murray and Lagakos, 2000) but subsequently faced a legal battle that ended only after the university filed a counterclaim alleging that the contract between the parties gave the researchers permission to publish (Lee, 2001) (Mello, Clarridge and Studdert, 2005. Parenthesis added.)*

What was interesting was that the permission to publish was, fortunately, part of the agreement. And, equally fortunately, the academic institute stood by the researchers, not the sponsors, regardless of consequences. A few more researchers of this ilk, and a few more institutions which support them, and the problem may not remain that grave at all. The time to give weak-kneed responses to sponsors is past.

*The Remune case, other high-profile clashes between academic researchers and pharmaceutical sponsors (Rennie, 1997; Shuchman, 1998; Hailey, 2000): and recent controversies concerning the disclosure of unfavorable findings in studies of antidepressants in children (Meier, 2004) and rofecoxib (Topol, 2004) have elevated concerns about industry-sponsored trials (Angell, 2004; Drazen, 2002; Bodenheimer, 2000; Nathan and Weatherall, 2002). Because conflicts often turn on the language of the clinical-trial agreement, they illuminate the potential consequences of contractual provisions that restrict academic investigators’ control over trials (Mello, Clarridge and Studdert, 2005. Parenthesis added.)*

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*Lesson number one in academia-industry relationship: incorporate the right to publish contrary findings in the research contract itself.*

*The second lesson to be learnt by academia: do not get browbeaten by threats of legal action.*

Which means, it makes great sense for academia to concentrate on the language and contractual provisions of sponsored research, to read the fine print very clearly, and protect their research interests in case of conflict. In particular, a provision to publish contrary findings must be inbuilt in any academia-industry contract. This is so as to avoid pressures that may not allow the investigator to publish them later, and in general retain control over the trial results. If only the agreement had no clause to publish

contrary findings, the researchers and the academic institution in the Remune case would have landed themselves in a big soup by acting in patient welfare. Since it was, sponsors had to back track after showing the customary legal scare.

Hence, lesson number one in academia-industry relationship: incorporate the right to publish contrary findings in the research contract itself.

The Remune case is only one in a succession of many others. Skolnick, (1998), in an earlier paper, for example, talks of a pharmaceutical firm suing a statutory body in Canada so as to prevent publication of findings about its cholesterol-lowering statin drug called Pravachol:

*A CANADIAN appeals court has upheld a lower court's decision denying a pharmaceutical company's motion to block publication of a health technology report that the company contends may damage its commercial interests.*

*In December 1997, Bristol-Myers Squibb Canada Inc sued the Canadian Coordinating Office of Health Technology Assessment (CCOHTA) to prevent the release of its summary report on cholesterol-lowering statin drugs. The company contends that the report contains "negligent misstatements" that could negatively affect the sale of its drug Pravachol (pravastatin) (Skolnick, 1998).*

Malignant misstatements! What do not suit commercial interests become malignant misstatements. The bluff was exposed soon after:

*When the Ontario Court denied Bristol-Myers Squibb's motion for an injunction to suppress the report in March, the company appealed. On May 6, an appeals court upheld the lower court's decision and CCOHTA promptly published the report, A Clinical and Economic Review of HMG-CoA Reductase Inhibitors in Coronary Heart Disease, which was based on a technical review of published clinical trials and pharmacoeconomic evaluations (Skolnick, 1998).*

So, the contrary findings were published. The legal threat was exposed for what it was: an attempt to intimidate.

The second lesson to be learnt by academia: do not get browbeaten by threats of legal action.

If lesson number one is learnt well, lesson number two is easy to implement.

## Selective publishing, delay

Legal threat is not the only method industry adopts to ensure compliance. In the case of those researchers who depend on industry to decide about publication, or hand over their work to them because of whatever compulsions, they had better note another mechanism used by them. Companies may be selective in publishing results, and they may delay or not publish unfavourable results at all (Stelfox, Chua, O'Rourke and Detsky, 1998; Chalmers, 1990; and Stern and Simes, whose 1997 paper in the *BMJ* is titled: *Publication bias: evidence of delayed publication in a cohort study of clinical research projects*). Which, in essence, means publish and rise as long as you publish what suits me. If not, well, I can stymie your publication, your research and even your future. Academia will have to decide how far will it go in this regard, and take suitable corrective steps with some alacrity. The two lessons learnt earlier should help academia in this direction.

The moot point also is to note the above statement: Companies may be selective in publishing results, and they may delay or not publish unfavourable results at all. Companies? Do companies decide publication? What do researchers do? Only do the trial, report the finding to the company, and wait for them to use it whatever way they desire? Well, if that is how it is to go, why should academia crib about doctoring of research findings? Rather, it should expect it, maybe even welcome it. For, handing over findings so obediently, or rather professionally, ensures continued industry sponsorship but also ensures continued doctoring. Why does academia abdicate its responsibility in this regard?

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*Hence lesson number three: Academia should keep itself involved right from inception of the clinical trial through to ultimate publication. And this must be an integral part of the written contract.*

This calls for some soul searching. The remedy which comes to mind is for academia not to hand over findings, but to insist on working over the research right from methodology through to statistical analysis and eventual publication, not handing over charge at any stage. Well, does that ensure funds to academia? It does, because if what are legitimate findings are published, the concerned sponsor will know whether the

product indeed has business potential, or is just a red herring. And will be on the right track to pump in his millions to market it.

Hence lesson number three: Academia should keep itself involved right from inception of the clinical trial through to ultimate publication. And this must be an integral part of the written contract.

## Under Reporting

Let us come to another scientific impropriety. Chalmers (1990), for example, points out that under reporting of clinical trials is a form of scientific misconduct:

*Substantial numbers of clinical trials are never reported in print, and among those that are, many are not reported in sufficient detail to enable judgments to be made about the validity of their results. Failure to publish an adequate account of a well-designed clinical trial is a form of scientific misconduct that can lead those caring for patients to make inappropriate treatment decisions (Chalmers, 1990).*

Publishing only positive findings, fudging with figures or reporting incomplete figures to suit predestined conclusions, making convenient conclusions from insufficient data are some related forms of scientific misconduct that serious researchers have to keep away from, much though market forces may try to convince academia to do otherwise.

The above author enjoins upon all concerned to take concerted steps to prevent underreporting by prospective registration of trials, amongst other things:

*Investigators, research ethics committees, funding bodies, and scientific editors all have responsibilities to reduce underreporting of clinical trials. An extended use of prospective registration of trials at inception, as well as benefiting clinical research in other ways, could help people to play their respective roles in reducing underreporting of clinical trials (Chalmers, 1990).*

As regards other related forms of scientific misconduct, it makes sense for researchers to refuse to allow commercial interests to rule research

reporting. Research having been reported, the commercial implications of such reporting is industry's concern. But, doctoring of findings to suit commerce is to be resisted at all costs. In this even pliant researchers need have no fear, for if they indeed publish what will work, the concerned sponsor will benefit in the long run. The only decision academia has to make is refuse to comply with predestined conclusions of sponsors for the 'thirty pieces of silver'. Instead do genuine research and make sixty for themselves.

## Complete Disclosure

Another area that maybe a sore point for some on both sides is what and how much to make public in the academia-industry relationship. Stelfox, Chua, O'Rourke and Detsky, (1998) are categorical when they support complete disclosure of industry relationships after their study found positive correlation between author's opinion and financial relationship with the industry concerned:

*Our results demonstrate a strong association between authors' published positions on the safety of calcium-channel antagonists and their financial relationships with pharmaceutical manufacturers (Stelfox, Chua, O'Rourke and Detsky, 1998).*

Their suggestion of a more effective conflict of interest policy and complete disclosure of industry relations is worthy of implementation:

*The medical profession needs to develop a more effective policy on conflict of interest. We support complete disclosure of relationships with pharmaceutical manufacturers for clinicians and researchers who write articles examining pharmaceutical products (Stelfox, Chua, O'Rourke and Detsky, 1998).*

Well, if someone has objections, let him ask himself what that means.

## Multi-centred Trials

Another area of concern, especially in multi-centred trials or collaborative studies, is that industry sources often analyse the data collected from different centres, and the authors may not have access to the complete data, neither may they have control over what data is likely to be utilized, and what findings published. "Clinical trials now often include many centres, and potential for bias is clear, as the company often collates and analyzes the data. The listed authors may not have seen the complete data set" (Bevan, 2002). (Baird, 2003)

*The medical profession needs to develop a more effective policy on conflict of interest. We support complete disclosure of relationships with pharmaceutical manufacturers for clinicians and researchers who write articles examining pharmaceutical products (Stelfox, Chua, O'Rourke and Detsky, 1998).*



*Though greater finesse and expertise may help bring larger number of leads in scientific research from elsewhere, it is in their confirmation and their universal relevance, or denial, that centers in the developing countries can help. And let us not forget that often corroboration is the bedrock on which many a fancied scientific hypothesis or theory stands, or falls (Singh and Singh, 2004).*

It is essential for all researchers to beware the trap of the easy way out: handing over of research findings to be worked over by the glib talking research departments of industry. The ease of getting things done may please be forsaken for the welfare of their own research credentials, if nothing else. For doctored writing based on fudged results are hardly likely to stand the scientific scrutiny of peers and replicative studies. Here, well-planned corroborative research can play a major role, even if it is not original. And centers in developing countries can have an important role to play here:

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## **Ghost Writing, Duplicate Publication and Industry**

Ghost writing is another area worth a look. Bevan (2002) says, "Biomedical journals communicate new information that changes health-care decisions. If authors ignore the fundamental values of honesty and trust, that information becomes flawed, and society or patients may be harmed". He describes something very interesting, and equally alarming, when he discusses two cases, one of duplicate publication, another of ghost writing, both representing the soft under belly of research. He touches, we suspect, the tip of an iceberg. By describing two cases of unethical behaviour by authors, and using them as a focus to review acceptable ethics in publication, he aims to educate readers who have not considered the ethical implications of writing manuscripts for biomedical journals :

*Two cases of unethical behaviour by authors occurred when the results of new drug trials were reported. They were discovered after publication in a biomedical journal, and in the review process after the submission of a manuscript for publication respectively. In the first case, duplicate publication was identified because the same control data were used, but not acknowledged, in three publications by the same investigators. In the second, ghost writing by a pharmaceutical company writer was suspected because of the atypical presentation of a senior author's work (Bevan, 2002).*

The result was interesting:

*The editor consulted with the authors of both reports. In the first case, the authors concurred about the duplication, and the editors of the three journals wrote editorials to record the duplicate publications. The second case of ghost writing was unconfirmed by the authors, but the submission was withdrawn, and the article was later published in another journal (Bevan, 2002).*

What they conclude needs deliberation:

*These cases draw attention to recently recognized types of scientific misconduct that influence the perception of scientific work. Duplicate publication and ghost writing not only deceive the reader, but may also conceal flawed study design and conflict of interest (Bevan, 2002).*

Duplicate publication and ghost writing need to be acknowledged and exposed for what they are. Forms of scientific misconduct. And no amount of cynicism about its inevitability should be allowed to cloud ones judgment here.

## **Access to Data and Control Over Publication**

Another area of concern we briefly touched upon earlier was access to clinical trial data, especially in multicenter trials, by site researchers. A relatively recent survey from November 2001 through January 2002 (Schulman, Seils, Timbie, Sugarman, Dame, Weinfurt, Mark, and Califf, 2002) of 108 medical schools in the United States showed that only 1% of the site researchers surveyed had access to all of the trial data and only 10% had control over plan for data collection and monitoring. And these were medical schools and members of the Association of American Medical Colleges, which is supposed to adhere to the new ICMJE guidelines. This is what Schulman *et al* (2002) did:

*From November 2001 through January 2002, we interviewed officials at U.S. medical schools about provisions in their institutions' agreements with industry sponsors of multicenter clinical trials. A subgroup of the respondents were also asked about coordinating-center agreements for such trials.*

And this is what they found:

*Of the 122 medical schools that are members of the Association of American Medical Colleges, 108 participated in the*

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*This means, out of around ten thousand trials, investigators had access to all trial data in hardly a hundred. And they were involved in planning how to collect and monitor data in just a thousand. Now, if you do not have access to data, you cannot control how to collect and monitor it, and yet want to call yourself a researcher, and get another publication to your name in a peer-reviewed indexed research journal, well, what are you?*

*survey. The median number of site-level agreements executed per institution in the previous year was 103 (interquartile range, 50 to 210). Scores for compliance with a wide range of provisions — from ensuring that authors of reports on multicenter trials have access to all trial data (1 percent [interquartile range, 0 to 21]) to addressing the plan for data collection and monitoring (10 percent [interquartile range, 1 to 50]) — demonstrated limited adherence to the standards embodied in the new ICMJE guidelines. Scores for coordinating-center agreements were somewhat higher for most survey items (Schulman, Seils, Timbie, Sugarman, Dame, Weinfurt, Mark, and Califf, 2002).*

Site-level agreements: 103. Access to trial data: 1%. Plan for data collection and monitoring: 10%. Number of clinical trials:  $108 \times 103 = 10,024$ .

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## **Negative Drug Trials and the Porcupine Dance**

It is no surprise, therefore, that one finds very few negative drug trials reports published, and whatever are, are likely to be by rival companies to serve *their* commercial interests.

Academic researchers are caught in an unenviable position. They want the funds but do not want the accountability and hassles that follow utilization of someone's money. They want to keep their accountability towards patients, while the sponsor wants it towards his welfare. They want the funds to continue to flow for their research depends on it, as does their career, but they want the freedom to report contrary findings. They want to listen to the voice of their conscience and go ahead and publish those findings contrary to industry interests, but they do not want legal hassles, and the reputation of a difficult guy to manage, that must invariably follow. And the temporary, and sometimes even permanent, brakes that may get applied to an otherwise promising career by such conscientious reporting.

So the smart guys learn to play the game pretty fast. They either avoid ruffling feathers or learn to ‘dance with the porcupines’ (Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis, 2001; Wager, 2003). Like the porcupine’s quills, drug companies’ interactions with doctors are numerous and can be harmful if approached the wrong way (Wager, 2003).

Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis (2001) warn to dance carefully with the porcupine if the precious commodity called intellectual integrity is to be protected by academia. While proposing certain guidelines, they expressly warn against allowing industry to dictate what to investigate, which methodology to use, and how to express results:

*Not infrequently, universities encounter challenges, veiled in the language of increased accountability, to their freedom of inquiry and expression. The claim that proposed constraints would be fatal to the academic mission becomes hypocrisy if universities allow industry to define the nature of inquiry, dictate methods and shackle expression. An industry–university contract is a transaction, and our proposed rules are designed principally to protect the university’s most precious commodity: intellectual integrity (Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis, 2001).*

So, the academia-industry transaction can never be at the cost of intellectual integrity of academia. And academia knows precisely well what that means.

This does not mean all academia-industry contact be forsaken, or condemned. It only means protecting it from nefarious influence and leaving no loopholes for pliant researchers, and manipulative sponsors, to get away with research impropriety. And if loopholes are not plugged, it does not take long for the list of pliant researchers and manipulative sponsors to swell, with fresh recruits coming from the ranks of erstwhile conscientious researchers. Such guidelines ensure improved industry behaviour and minimize research misconduct by academia. Moreover, they also help reduce the atmosphere of paranoia and consequent aggressive names calling that can result as a sequelae from both quarters:

*This does not mean all academia-industry contact be forsaken, or condemned. It only means protecting it from nefarious influence and leaving no loopholes for pliant researchers, and manipulative sponsors, to get away with research impropriety. And if loopholes are not plugged, it does not take long for the list of pliant researchers and manipulative sponsors to swell, with fresh recruits coming from the ranks of erstwhile conscientious researchers.*

*We are not asking academic researchers to forswear all interactions with industry. We are merely proposing rules for exercising due*

*The academia-industry relationship is indeed like a porcupine dance which academia takes part in at its own peril if it is not forearmed. And it can seriously harm itself if the 'industry porcupine' is approached unprotected. For the quills of commercial interests can hurt when least expected, and when one is most proximal.*

*diligence to protect the essence of academic inquiry. A positive effect of the proposed rules would be voluntarily improved industry behaviour, with enlightened companies adopting honourable codes of conduct that in time may mitigate the wariness and cynicism that recent aggressions have doubtless engendered (Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis, 2001).*

And a relationship based on mutual respect, which is professional enough to work but at arms length enough not to get sullied, is but appropriate:

*All of this is not to gainsay the importance of the spectacular advances in therapy and diagnosis made possible by new drugs and devices. Nor is it to deny the value of cooperation between academia and industry. But that cooperation should be at arm's length, with both sides maintaining their own standards and ethical norms. The incentives of the marketplace should not become woven into the fabric of academic medicine. We need to remember that for-profit businesses are pledged to increase the value of their investors' stock. That is a very different goal from the mission of medical schools (Angell, 2000).*

The academia-industry relationship is indeed like a porcupine dance which academia takes part in at its own peril if it is not forearmed. And it can seriously harm itself if the 'industry porcupine' is approached unprotected. For the quills of commercial interests can hurt when least expected, and when one is most proximal. So dance carefully with the porcupine:

*Some bargains are Faustian, and some horses are Trojan. Dance carefully with the porcupine, and know in advance the price of intimacy (Lewis, Baird, Evans, Ghali, Wright, Gibsons and Baylis, 2001)\*.*

Faustian, indeed. For one need not, but may, run into a pact with the Devil\*. And the struggle between the higher and lower nature in man that academia-industry connect arouse may even make Goethe squirm in his grave.\*\*

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Note :

\*1. *The basis of the Faust story is that he sold his soul to the Devil in return for twenty-four years of further life during which he is to have every pleasure and all knowledge at his command. The climax comes when the Devil claims him as his own (p418).*

\*\*2. *Goethe's Faust (1772-1831) is founded on Dr. Johann Faust, or Faustus, a magician and astrologer, who was born in Wurttemberg and died in 1538, and about whom many stories soon began to circulate crediting him with supernatural gifts and evil living....It was Goethe who was responsible for transforming the necromancer into a personification of the struggle between the higher and lower natures in man (p417).*

*All page numbers from Evans (1981).*

The Trojan horses are implanted in academia's midst all the time\*\*\*. And it behoves academia to ferret such out. As it also behoves some amongst them to become Trojans themselves!\*\*\*\*

Wager (2003) has her own views on how to 'choreograph' the porcupine dance. She suggests guidelines developed jointly by medical men both in academia and industry so that misapprehensions and misunderstandings on both sides can clear and wider acceptance of guidelines prevail:

*What can we conclude about regulations designed to choreograph the porcupine dance? Most were developed only recently, and many are still evolving. They come from many organisations with different aims and are therefore scattered and occasionally conflicting, although consensus seems to exist on the broad principles. From my own experience of more than a decade of working closely with the industry and with doctors, misapprehensions and misunderstandings persist on both sides. I would therefore urge proper dialogue between the parties before any more guidelines or regulations are drawn up or revised. Guidelines developed jointly by doctors working both inside and outside the industry might be more widely accepted than those from a single constituency (Wager (2003)).*

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She opines further that the dance is complex, it cannot exclude any party, it is necessary for it is useful, and it is improper to smear all of industry:

*Drug companies, like porcupines, come in a range of shapes and sizes; some are fiercer than others, and this diversity must be recognised. The relationships between doctors, academic institutions, pharmaceutical companies, and medical journals will always be complex and interdependent, but we should not forget that the dance*

Note :

\*\*\*3. **The Wooden Horse of Troy:** VIRGIL tells us that, after the death of HECTOR, ULYSSES had a monster horse made by Epios and gave it out that it was an offering to the gods to secure a prosperous voyage back to Greece. The Trojans dragged the horse within their city, but it was full of Grecian soldiers, including MENELAUS, who stole out at night, slew the guards, opened the city gates, and set fire to TROY (p568).

\*\*\*\*4. **He is a regular Trojan:** A fine fellow, with courage and spirit, who works very hard at some un congenial task, indeed, doing more than could be expected of him. The Trojans in Homer's ILLIAD and Virgil's AENID are described as truthful, brave, patriotic, and confiding (p1138).

All page numbers from Evans (1981).

*It is interesting that 50% disallowed insertion of sponsor's statistics, 40% disallowed drafting of manuscript, 34% (that is one third) disallowed sharing of data after trial was over. What is interesting to note is that a sizeable number stuck to ethical parameters. This is a heartening sign.*

*has produced some remarkable collaborations that have enabled the discovery and development of the medicines we all rely on (Wager, 2003).*

A reasoned response that looks for the silver lining. Hopefully it is not an illusion. But more of that in the next monograph.

## **Remedial measures**

Attempts to remedy this situation have begun as more awareness seeps in.

For example in a recent study of Mello, Clarridge, Studdert, (May, 2005) in which 107 institutions participated, growing awareness of institutions that disallowed industry sponsors to revise manuscripts or decide about results to be published was clearly manifest (85%), although other data was not that unequivocal:

*Of 122 institutions approached, 107 participated. There was a high degree of consensus among administrators about the acceptability of several contractual provisions relating to publications. For example, more than 85 percent reported that their office would not approve provisions giving industry sponsors the authority to revise manuscripts or decide whether results should be published (Mello, Clarridge and Studdert, 2005).*

As regards other important issues like allowing sponsors to insert their own statistical analysis, drafting manuscript, and sharing data with third parties after trial was over, administrators were equivocal:

*There was considerable disagreement about the acceptability of provisions allowing the sponsor to insert its own statistical analyses in manuscripts (24 percent allowed them, 47 percent disallowed them, and 29 percent were not sure whether they should allow them), draft the manuscript (50 percent allowed it, 40 percent disallowed it, and 11 percent were not sure whether they should allow it), and prohibit investigators from sharing data with third parties after the trial is over (41 percent allowed it, 34 percent disallowed it, and 24 percent were not sure whether they should allow it) (Mello, Clarridge and Studdert, 2005).*

It is interesting that 50% disallowed insertion of sponsor's statistics, 40% disallowed drafting of manuscript, 34% (that is one third) disallowed sharing of data after trial was over. What is interesting to note is that a sizeable number stuck to ethical parameters. This is a heartening sign. Although, 50% allowing drafting of manuscript is an ominous sign indeed, as is 24%+ 29%= 53% allowing or ambivalent about sponsors analysis being inserted. In other words half the researchers allowed manuscripts to

be written, and half allowed or were confused about allowing statistical insertion by sponsors. Well, some eye opening study data for academia to ponder over.

The other issue they studied were areas of dispute. As expected, payment problems were on top, followed by issues of intellectual property and last by control over data issues:

*Disputes were common after the agreements had been signed and most frequently centered on payment (75 percent of administrators reported at least one such dispute in the previous year), intellectual property (30 percent), and control of or access to data (17 percent) (Mello, Clarridge and Studdert, 2005).*

It is interesting that disputes over payment far over-shadowed issues more germane to research like intellectual property or control over data. What does that mean? That payment matters were left unresolved by academia and industry? Hardly likely. It was more likely it was of greater import to both parties, rather than issues like intellectual property or control over data. So, while you and we may cry us hoarse over such issues, we cannot but know what dominates researchers' minds in sponsored research. Exactly the same as dominates the sponsor's.

## Legal action

An issue that needs a close look now is legal hassles in academia-industry conflict situations. Industry is routinely found to suppress unfavourable data, and threaten legal action, termination of trial and contract, and future non-availability of funds for those who continue to persist in embarrassing them:

*Cases of suppression of data and intimidation by industry are troubling, but they are likely only the visible tip of a bigger iceberg. For many academic researchers, the future prospects of their laboratories and careers depend on renewed industry funding. They also may be understandably reluctant to speak out: if they trigger a legal action, it is time consuming and expensive, and it disrupts work and harms reputations (Baird, 2003).*

The threat of legal action, and the hassles it involves, coupled with a widespread abhorrence for legal tangles that pervades academia, and for fighting to protect their rights, or for a careful reading of the fine print of academia-industry agreements almost always skewed in industry's favour, is a ripe situation for them to buckle under pressure. Those who wish to persist with

*Industry is routinely found to suppress unfavourable data, and threaten legal action, termination of trial and contract, and future non-availability of funds for those who continue to persist in embarrassing them:*



*Moreover, for industry, legal hassles are part of the day's work, and lawyers are paid retainer ships to handle cases. They hardly mind the legal hassles, in fact may welcome it, for it justifies their initial decision to retain legal counsel as retainers in the first place.*

their obligations to society at the cost of industry welfare get their contracts terminated, their publication delayed, or their papers rejected by the better known journals for obvious reasons. For others, it may involve an intellectual stranglehold and oblivion, or at least a setback by a decade or two, which essentially amounts to the same thing. The message is clear: know-tow, or perish. A balancing of interests is necessary, for which academia needs to pull up its socks.

Moreover, for industry, legal hassles are part of the day's work, and lawyers are paid retainer ships to handle cases. They hardly mind the legal hassles, in fact may welcome it, for it justifies their initial decision to retain legal counsel as retainers in the first place. And it suits the lawyers very well too to fight with vigour for their industry client, for it justifies their presence for industry, and makes them inevitable partners in industry's enterprise, almost like insurance. A pain when you pay, but essential relief when you need it. Hence, "Large pharmaceutical companies, on the other hand, may see such legal expenses as a 'cost of doing business'" (Baird, 2003; Generic gadfly, 2002). And the icing on the cake for industry is that, "Even if a company ultimately loses an action, in effect they win by delaying publication of adverse findings for lengthy periods, and the case serves as a deterrent to others from acting independently" (Baird, 2003).

Appropriate legal counsel by academia on a regular basis and a close study of legal documents before signing is necessary. And a clear understanding of rights of researchers, and the implications of sponsorship, is mandatory.

In other words, have your own lawyer who will take no nonsense from sponsors, and do not allow the patient welfare agenda to be high jacked under any circumstance.

## **Law Suits against Industry**

Efforts to remedy this situation are not entirely absent. A number of lawsuits have been successfully brought up against some pharmaceutical companies. As Studdert, Mello and Brennan (2004) point out about the Lupron case involving TAP Pharmaceuticals and some urologists who connived with them:

*In 1997, government investigators began to probe relationships between TAP Pharmaceuticals, a joint venture of Takeda Chemical Industries and Abbott*

*Laboratories, and various urologists for the marketing of Lupron, a potent gonadotropin-releasing hormone agonist used in the treatment of prostate cancer (United States v. TAP Pharmaceuticals, Dec. 14, 2001). The government determined that TAP encouraged the urologists to bill Medicare at the average wholesale price for Lupron, which they received free or at discounted prices. This arbitrage netted the urologists a substantial profit. Federal prosecutors charged TAP with criminal violations of the Prescription Drug Marketing Act. TAP entered into a settlement with the government in which it agreed to pay \$290 million in criminal fines plus \$585 million in civil penalties. The whistle-blowers received nearly \$100 million of the total damages. TAP also faces a series of private class-action lawsuits brought by insurers and patients for unnecessary and costly services.*

That the medical people connived and were exposed is as important as the prosecution of the industry player. The Hebrew Faustian story in action.

The pharmaceutical paid fines and penalties of such large sums. What is interesting is that the whistle-blowers too received \$ 100 million out of the total amount of \$ 875 million. Well, a cool amount for helping enforce ethical conduct. Whoever thought ethics did not pay!

The same authors go on to point out the cascading effect (Studdert, Mello and Brennan, 2004):

*The successful prosecution of TAP has spawned a series of other cases. In 2003, AstraZeneca settled criminal-fraud charges of \$355 million in a case dealing with the drug Zoladex, a case that involved not only arbitrage issues but also marketing inducements similar to those in the Lupron litigation (Petersen, 2003). On July 14, 2004, Schering-Plough pleaded guilty and paid a fine of \$350 million, in part for providing grants private to physicians to conduct educational programs, which prosecutors characterized as kickbacks (Harris, July 16, 2004). Schering-Plough faces an ongoing investigation into whether it used sham consulting arrangements and clinical trials to remunerate physicians for prescribing its hepatitis drug, Intron A (Harris, June 27, 2004). Prosecutors' momentum is unlikely to be slowed by the unsuccessful criminal prosecution of certain TAP employees by the U.S. attorney in Massachusetts. Moreover, the prosecution of specific physicians in this case may add a potent dimension to enforcement (Dembner and Murphy, March 5, 2004; parenthesis added.).*

The number of recent lawsuits successfully brought up against industry reflects earnest attempts by patient welfare bodies and others to remedy the tilt. It will result in a newfound confidence in academia that augurs well for academia-industry relationship in the long run. Although one must be careful not to

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*“ It has been estimated that, on average, a manufacturer loses over a US\$1 million for each day’s delay in obtaining US Food and Drug Administration approval of a new drug” (Baird, 2003).*

Which, in effect, means industry would not want anything to go wrong with approval by regulatory authorities later.

overbalance the other way too. For it is naïve to believe that all academia-governmental victory is necessarily beneficial to patient welfare. And the cost of litigation is bound to be passed on to patients.

## **Design and Control of Publication**

Another area of pressing concern is when industry decides to both design and control publication of research. “Although particular instances of outright suppression are of concern, much more worrying (although less visible) is the well-documented increasing control

by industry over design and publication of clinical trials (Baird, 2003). This is so obviously because “it makes commercial sense for large drug companies to create their own study designs” (Baird, 2003). The financial burden on a company for delay in approval by regulatory authorities has been studied. For example, “ It has been estimated that, on average, a manufacturer loses over a US\$1 million for each day’s delay in obtaining US Food and Drug Administration approval of a new drug” (Baird, 2003). A recent paper reiterates the same when it emphasizes the need for industry to comply with FDA requirements rather than effectiveness of products:

*It is important to note that although industry-sponsored research is critical to new product development, its emphasis is on meeting U.S. Food and Drug Administration (FDA) regulatory requirements and on obtaining expanded marketing claims, not on evaluating the effectiveness of products as used in the general population. As a result, industry-sponsored research often fails to address broad public health needs or the needs of individual practitioners seeking to make good clinical decisions for individual patients (March, Silva, Compton, Shapiro, Califf and Krishnan, 2005).*

Which, in effect means industry would not want anything to go wrong with approval by regulatory authorities later. Therefore, we should not be surprised at moves by industry to try to take more control of research, (Baird, 2003), all the way from design and methods, through analysis, data presentation and publication vehicle (Montaner, O’Shaughnessy and Schechter, 2001). (Baird, 2003)

## Connection between Funding and Positive Findings

Another area worth touching over here is how industry funding decides what sorts of findings get published. There is a strong connection between funding and positive findings for the sponsoring company's product. Numerous studies and literature reviews show the systemic influence of industry funding, with a correlation between funding by the manufacturers and findings that show results supportive in terms of efficacy and safety of the sponsor's products (Davidson, 1986; Rennie, 1999; Deyo, Psaty, Simon, Wagner and Omenn, 1997; Friedberg, Saffran, Stinson, Nebon and Bennett, 1999; Bekelman, Li and Gross, 2003; Stelfox, Chua, O'Rourke and Detsky, 1998). (Baird, 2003)

Which, in effect means, better find positive correlation between my product and your findings, if you want funding renewal and continued support later. And fund seekers are quick on the uptake here, for a pariah from one pharmaceutical company for this reason is hardly likely to be welcome in any other. In this matter, common interests of industry barons help close the ranks even amongst sworn rivals.

How the intellectual dishonesty is carried out to suit sponsor's interest maybe by some rather ingenious means. "A sponsor's drug at high doses may be compared with lower doses of a competing product, or with a poorly absorbed preparation, or it may be tested in patients who are younger and healthier than patients who typically have the disease, thus reducing the likelihood of adverse events." (Bero and Rennie, 1996; Bodenheimer, 2000; Gotzsche, 1989). (Baird, 2003)

Such dishonesty may easily pass off as genuine research, and can get exposed only if we are vigilant about the material and methods reported by researchers, and question them very closely on such issues. This is as applicable to peer reviewers as to editors, and readers too. The useful rule of thumb is: keep the critical antenna on, especially with regard to drug trials, and more especially their methodology, and study closely the conflict of interest disclosed, and if possible undisclosed, before you jump on the band wagon to herald the next great wonder drug. While this should not become a reason to debunk all drug trials, it is necessary to avoid getting taken for a ride; and only a healthy skepticism always, coupled with a cautious optimism, can ensure it.

*Which, in effect means, better find positive correlation between my product and your findings, if you want funding renewal and continued support later. And fund seekers are quick on the uptake here, for a pariah from one pharmaceutical company for this reason is hardly likely to be welcome in any other. In this matter, common interests of industry barons help close the ranks even amongst sworn rivals.*

*The time to repeat clichés about the exciting future of the academia-industry connect is past. A concerted effort to lay a strong foundation of the relationship on practical ethical grounds is mandatory today if the ominous portents detailed here are not to initiate a storm that engulfs us all.*

As we end this monograph, the feelings are mixed. The nefarious influences we detail leave a bad taste, but certain remedial steps taken promise hope for the future. The time to repeat clichés about the exciting future of the academia-industry connect is past. A concerted effort to lay a strong foundation of the relationship on practical ethical grounds is mandatory today if the ominous portents detailed here are not to initiate a storm that engulfs us all.

## Concluding Remarks

1. As things stand today, whether we like it or not, industry funding is on the upswing. The whole enterprise of medicine is booming, and it makes sense for industry to invest more and more of one's millions into it. The great role that the pharmaceutical industry is playing today, and will continue to play in the future, can be gauged from the fact that it is the single largest direct funding agency of medical research in Canada, the United Kingdom and the United States.
2. Conflicts of interest between academia and industry are inevitable at times is acceptable as a statement of fact but not as a state of affairs. The crucial point is that the goals of academia and industry differ. It is academia which has to call the shots, it is industry which has to play second fiddle, and make its millions playing it. Issues like risk, adjuncts, maintenance, discontinuation and transfer to clinical use concern practitioners, but are not likely to motivate industry-sponsored research. It means research agendas of industry are out of tune with needs of clinicians and patients, but still manage to determine what research gets done.
3. The crucial decision is whether the public welfare agenda of academia, or the corporate research agenda of industry, should occupy center stage when they conflict. The need to protect its right to publish finding even if contrary to industry interests is a crucial determining factor with regard to forwarding the public welfare agenda. In fact, lesson number one in academia-industry relationship is: incorporate the right to publish contrary findings in the research contract itself. Which means, it makes great sense for academia to concentrate on the language and contractual provisions of sponsored research, to read the fine print very closely, and protect their research interests in case of conflict.

4. There is enough evidence to show that funding by industry is very systematic, and results that are supportive of the safety and efficacy of sponsor's products alone get the funds. It is no surprise, therefore, that very few negative drug trials reports get published, and whatever do, are likely to be by rival companies to serve their commercial interests.
5. Legal hassles are becoming all too common. A recent paper makes the point clearly in the case of the AIDS vaccine, Remune, in which the researchers concerned filed negative reports and had to face legal action by the sponsor. The way in which many from academia played into the hands of industry in the recent Nancy Olivieri case who had to face legal hassles for whistle blowing on industry is a sad commentary on how money and grants rule the minds of academia at the cost of patient welfare.
6. However, a number of lawsuits successfully brought up against industry recently reflect earnest attempts by patient welfare bodies and others to remedy the tilt. It will result in a newfound confidence in academia that augurs well for academia-industry relationship in the long run. Hence the second lesson for academia: do not get browbeaten by threats of legal action.
7. Industry commonly decides which clinical research/trial gets done, not academia, much though the latter may wish to believe otherwise. It finds willing researchers to carry this out. This can be one area of concern. Another area of pressing concern is when industry decides to both design and control publication of research.
8. Companies may be selective in publishing results, and they may delay or not publish unfavourable results at all. The remedy that comes to mind is for academia not to hand over findings, but to insist on working over the research right from methodology through to statistical analysis and eventual publication. Well, does that ensure funds to academia? It does, because if what are legitimate findings are published, the concerned sponsor will know whether the product indeed has business potential, or is just a red herring. And will be on the right track to pump in his millions to market it.
9. Hence lesson number three: Academia should keep itself involved right from inception of the clinical trial through to ultimate publication. And this must be an integral part of the written contract.
10. Publishing only positive findings, fudging with figures or reporting incomplete figures to suit predestined conclusions, making convenient conclusions from insufficient data are some related forms of scientific misconduct that serious researchers have to keep away from. Another area of pressing concern is when industry decides to both design and control publication of research. Which, is usually because industry

would not want anything to go wrong with approval by regulatory authorities later.

11. As regards other related forms of scientific misconduct, it makes sense for researchers to refuse to allow commercial interests to rule research reporting. Research having been reported, the commercial implications of such reporting is industry's concern. But, doctoring of findings to suit commerce is to be resisted at all costs.
12. The negative consequence of promoting the patient welfare agenda is that both industry and academic institutions may gang up to discredit researchers. The suggestion of a more effective conflict of interest policy and complete disclosure of industry relations is worthy of implementation.
13. The academia-industry relationship is indeed like a porcupine dance which academia takes part in to its own peril if it is not forearmed. And it can seriously harm itself if the industry porcupine is approached unprotected. For the quills of commercial interests can hurt when least expected, and when one is most proximal. So dance carefully with the porcupine.
14. Appropriate legal counsel by academia on a regular basis and a close study of legal documents before signing, is necessary. And a clear understanding of rights of researchers, and the implications of sponsorship, is mandatory. In other words, have your own lawyer, and do not allow the patient welfare agenda to be high jacked under any circumstance.
15. Industry is routinely found to suppress unfavourable data, and threaten legal action, termination of trial and contract, and future non-availability of funds for those who continue to persist in embarrassing them.
16. There is a strong connection between funding and positive findings for the sponsoring company's product. Numerous studies and literature reviews show the systemic influence of industry funding, with a correlation between funding by the manufacturers and findings that show results supportive in terms of efficacy and safety of the sponsor's products.
17. The useful rule of thumb is: Keep the critical antenna on, especially with regard to drug trials, and more especially their methodology, and study closely the conflict of interest disclosed, and if possible undisclosed, before you jump on the band wagon to herald the next great wonder drug
18. The time to repeat clichés about the exciting future of the academia-industry connect is past. A concerted effort to lay a strong foundation of the relationship on practical ethical grounds has become mandatory.

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## Questions that this monograph raises

1. Do the goals of academia and industry really differ? Can they be one?
2. It is fine to say the public welfare agenda of academia and not the corporate research agenda of industry, should occupy center stage when they conflict. How do we ensure it?
3. If funding by industry is very systematic, and results that are supportive of the safety and efficacy of sponsor's products alone get the funds, what can academia do to get the funds and yet not be bullied into publishing only supportive evidence?
4. What can be done so that even negative drug trials reports get published?
5. Legal hassles are becoming all too common. This happened recently in the case of the AIDS vaccine, Remune, in which the researchers concerned filed negative reports and had to face legal action by the sponsor. What can academia do so as not to get browbeaten by threats of legal action?
6. How can academia decide to both design and control publication of research?
7. If academia decides not to hand over findings, and insists on working over the research right from methodology through to statistical analysis and eventual publication, will it still manage to get the finds it seeks from industry?
8. Publishing only positive findings, fudging with figures or reporting incomplete figures to suit predestined conclusions, making convenient conclusions from insufficient data are some related forms of scientific misconduct that serious researchers have to keep away from. What measures will ensure this happens?
9. If researchers refuse to allow commercial interests to rule research reporting, and insist that the commercial implications of such reporting is industry's concern only after research has been reported, will it be a viable option?
10. The academia-industry relationship is indeed like a porcupine dance which academia takes part in to its own peril if it is not forearmed. And it can seriously harm itself if the industry porcupine is approached unprotected. Can academia decide not to dance with the porcupine, or should it continue to do so with due precautions?

11. Can academia ensure the patient welfare agenda is not high jacked under any circumstances?
12. Can academia ensure that cases like the Olivieri and Healy cases do not recur? How?
13. What can be done so that academia takes appropriate legal counsel on a regular basis and does a close study of legal documents before signing?
14. Industry is routinely found to suppress unfavourable data, and threaten legal action, termination of trial and contract, and future non-availability of funds for those who continue to persist in embarrassing them. Can academia still embarrass them for patient welfare? How do they do so without jeopardizing future research grants?
15. Numerous studies and literature reviews show the systemic influence of industry funding, with a correlation between funding by the manufacturers and findings that show results supportive in terms of efficacy and safety of the sponsor's products. What does academia do to publish findings at variance with these objectives? Should it at all do so, or remain loyal to its sponsors?
16. It is true readers must keep the critical antenna on, especially with regard to drug trials, and more especially their methodology, and study closely the conflict of interest disclosed, and if possible undisclosed. But do they really have a choice not to be influenced by an academia-industry connect so well accepted and espoused all over?
17. Is there another way of looking at this problem?

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