

# Key Opinion Leaders - Understanding Physician-Pharmaceutical Industry Relationships Conference

## Day one, September 29th, London 2008

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### Conference Report

The use of key opinion leaders (KOLs) by pharmaceutical companies is a hot potato. Talk to ten different people and you will hear ten different views, all strongly expressed and equally certain of their 'facts'. For instance, 'Pharma is manipulative and KOLs are little more than covert drug reps' is typical of one extreme. 'Pharma nurtures academics and their research, filling gaps left by the deficiencies in government funding' represents its antipode.

There is perhaps no more polarised issue in medicine today. Conspicuously absent from such views is any sense of balance, of perspective even. Recent articles in the BMJ and elsewhere have focused on presenting two sides of a debate. But this falls short of dialogue. Positions are entrenched and there is little meaningful discussion.

It seems obvious but any discussion is best conducted with all parties in the same room, talking to each other as well as to an audience. "Key Opinion Leaders – Understanding Physician-Pharmaceutical Relationships" in London on 29th and 30th September 2008 sought to achieve precisely this – dialogue between all relevant parties. As well as the KOLs, there were regulators, academics and pharmaceutical and agency representatives.

### David Gillen asks 'How did it get to this?'

After a brief introduction, Dr David Gillen, UK Medical Director for Pfizer, provided the context of the discussion: Medicine is being challenged by the media and the focus of much of this debate is the relation between pharma and opinion leaders. By way of illustration, he cited Alexander Fleming. Although instrumental in the discovery of penicillin, Fleming needed input from Howard Florey in Oxford and assistance from Pfizer to turn an unusual petri dish into a mass-produced, lifesaving medicine.

How did the relationship between academia and pharma sour? How did it slip from such positive beginnings to its present low point, where a recent issue of the BMJ resorted to caricatures of puppets to illustrate an article on opinion leaders? More important still, Gillen asked, what impact is this deterioration of relations having on human health?

Gillen's position is clear. Without a private independent pharmaceutical industry, there would be no drugs. State-owned pharmaceuticals, such as the model developed in Russia in the past have not been effective. 'In 30 years I think that they developed about one medicine Gillen said. He sees industry-funded research as pivotal to the reductions in many common diseases over the last 40 years and reminded the audience of George Merck's maxim that profit is a follower not a leader of innovation.

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KOLs are a part of that research and come from many sources. Gillen lists medics, scientists, government representatives, patients, and the media as possible KOLs, but does not subscribe to the ‘Orwellian view of an opinion leader as a drug representative in disguise’. He attributes the poor public perception of pharma to two main reasons – institutional short termism and a failure of the current industry R&D model.

Short-termism is driven by shorter patent lives and the need to support investors. Drugs need to make money more rapidly. Higher regulatory hurdles and increasingly complex disease conditions have led to a failure of industrial R&D to deliver. Despite increased year-on-year research spending, the number of new FDA drug approvals continues to fall. Collectively, these factors have engendered suspicion of the motives of the pharmaceutical industry.

Placing doctor-industry relations in a historical context, Gillen illustrated the decline in relations from the mutual respect of the 1940s to the current position of mistrust and the need for rebuilding. Key landmarks were the erosion of trust by the thalidomide disaster and a perception of manipulative marketing, leading ultimately to the present nadir where all academic-industry relations are viewed with suspicion. ‘The media absolutely hound all of us’ Gillen says ‘ all they want to talk about is a miracle drug or a killer drug’.

Gillen is nonetheless optimistic – he sees the present standoff as an opportunity to redress the balance and re-establish a proper distance between academia and industry but emphasises that this requires action by physicians as well as pharma to rebuild a mutual and respectful working relationship based on transparency and regulation as necessary

## Key points

- The erosion of trust in the pharmaceutical industry has been fuelled by press moulding of public perceptions.
- The pharmaceutical industry and its research is instrumental in the reduction in the prevalence of many illnesses over the last 40 years.
- There is a need to regain patient trust by transparent, regulated, respectful relationships between academia and industry.

## Emma D’Arcy frames the debate

Finishing his presentation, David Gillen asked the group to consider a range of issues posed by the co-chair **Emma D’Arcy**, Scientific Leader of myPHID:

- What value do these interactions give to benefit medical science and patient care?
- What key transitions in thinking need to prompt everyday changes in relationship management?
- What are the everyday improvements and new methodologies that will underpin future interactions?
- How are companies striving today to achieve a better sense of alignment and transparency surrounding the nature of their interactions for tomorrow?

## Rapid regulator decision making

The second presentation of the day was given by **Keith Tolley**, a health economist working with the Scottish Medicines Consortium (SMC) who gave a detailed insight into the workings of the SMC in assessing new drugs and the role of external experts. Despite geographical constraints, the influence of the SMC extends beyond Scotland and Tolley mentioned instances where SMC rulings have been used to inform access decisions in the UK, in the absence of NICE guidance.

The SMC is one of three health technology appraisal boards. Although broadly analogous to NICE, the SMC differs from NICE in its scope of interest and the speed of its decision making. Unlike NICE, which is selective in its appraisals, the SMC covers all new pharmaceuticals, new formulations and new indications. The SMC aims to provide guidance as close as possible to product launch.

The principal distinction of the SMC is the speed of its assessment process, with decisions typically reached within 4 months of submission. Three possible decisions are used – accepted for use, restricted use or not accepted for use. Restricted use can encompass limitations of dosage, or restrictions to second-line usage for instance. In the last couple of years about 20% were accepted, 30% given limited use and 50% were not accepted for use

Submissions have a 2-part process comprising assessment and appraisal. The assessment team mainly examines the manufacturer’s data for clinical and cost effectiveness evidence. The assessors provide a draft advice document which is then submitted for appraisal. At this stage, unmet needs and patient perspectives are incorporated and a final guidance is issued.

The critical step in all this is the New Drug Committee (NDC) at which expert opinions are solicited. Key individuals are the economic assessor and the committee chair who sets the tone. Cost effectiveness is pivotal. The committee also comprises clinical assessors, internal experts and external experts. The external expert corps contains mainly pharmacists, with very few physicians, and the occasional pharmacologist.

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External experts are typically NHS experts but are not necessarily KOLs. Tolley emphasised that few nurses are used and that they would like to see this group better represented.

External experts are selected by a series of 6 generic questions that address current guidelines, unmet needs, disease prevalence, and current treatment practice. The experts are important to the process, especially at the NDC stage. Tolley emphasised that decisions were not influenced by KOLs writing to the committee and that media ‘noise’ has a minimal effect beyond emphasising the need for media training of experts.

## Key points

- External experts are central to the assessment of new medicines by the SMC.
- The SMC uses experts from wider healthcare groups than is commonplace amongst the pharmaceutical industry.

## ‘Honest brokers’ – an agency perspective

The interface between opinion leaders and the pharmaceutical industry is often the medical education agency. In addition to many other roles, agencies take care of the housekeeping elements of the KOL-pharma relationship, allowing dialogue between both parties to be conducted at a scientific level. Agencies may also act as intermediaries, initiating and facilitating communications, brokers of the relationship.

In her presentation ‘Redefining expert relationships – balancing expert aspirations with brand needs’ **Sue Wright**, Director of Business Communications for Adelphi Communications, gave an overview of the agency role and the extent to which Adelphi have tried to reassess the relationship.

There are two guiding principles, says Wright. Firstly, conduct yourself in such a way that anything written about you on a bus shelter would not offend. Secondly, always remember the man on the Clapham omnibus and how he might view the evidence.

The key is balance – between the needs and aspirations of the experts and industry goals and objectives. ‘There’s nothing wrong with profit’ says Wright ‘we should be proud that. It’s profit that goes on development and innovation’. Alongside the experts and pharma, she went on to describe a third important stakeholder – society at large, with its concerns that current alignments are too close and that patients are not best served.

These concerns inevitably mean change engendered by scrutiny. Wright shared the Adelphi vision of the future, a consensual relation between experts and industry based on transparency, the furtherance of medicine, better mutual understanding and fair reward. She illustrated her point with an example of an anti-infective agent that was used mainly as a last ditch therapy. The perception of practising clinicians differed and by facilitating open trust-based discussion between the company and the experts, a different treatment sequence emerged. This is at the same time the hardest and yet most rewarding aspect of an agency's brokerage.

Wright concluded by outlining Adelphi's approach to relationship alignments. The first step is understanding of the area, based on wide consultation. Then follows primary and secondary research to identify experts. The final part is the alignment of experts with the pharmaceutical clients, to find a relationship that is equitable to all.

## Key points

- The relationship between the KOL reflects a balance between the needs and aspirations of the experts and industry goals and objectives.
- The role of the medical education agency is to broker the KOL-pharma to the benefit of both parties.

## What makes an opinion leader?

Having heard from David Gillen and Sue Wright on behalf of the pharmaceutical industry and medical education agencies, **Iain Macdougall**, a consultant nephrologist at King's College Hospital presented a KOL perspective.

After a brief but diverting googling of the KOL acronym, Macdougall introduced the idea of opinion leaders, thought leaders and key experts. Are they all the same? Is there an identikit KOL? Macdougall draws some recognisable stereotypes – the 'extreme' KOL with strong links to pharma such as stocks and shares, regular consultancies, patents and so on. Much more common are the 'occasionals' who participate on an infrequent ad hoc basis, receive research grants and occasional consultancies for modest honoraria. At worst a KOL may be 'a company rep in disguise' says Macdougall, quoting Professor Spiers's recent letter to the BMJ 'easy to spot – his expenses and remunerations are shamelessly high and he uses proprietary names and drug company slides.'

Moving on, Macdougall went on to address four main areas – how he became a KOL, the advantages and drawbacks of a relationship with industry and the need for regulation. Speaking from his own experience, Macdougall cited his early research on erythropoietin (Macdougall et al., Lancet 1990; 335: 489-493) as the first step on his path to becoming a KOL. Despite such a high profile publication, Macdougall is disarmingly honest about the process 'It wasn't rocket science' he says 'it was a case of being in the right place at the right time'. Significantly, Macdougall was approached by the pharmaceutical industry rather than courting their involvement.

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Macdougall sees several clear advantages of being a KOL. Firstly it brings kudos to the KOL's department, university and even the nation. This helps the department to recruit high quality, research-orientated staff and he was upfront enough to admit that it boosts the ego! There are financial benefits too, both personal (honoraria) and general (research support and event sponsorship).

The main drawback of being a KOL is maintaining scientific credibility. 'I regard myself first and foremost as a clinical scientist' says Macdougall 'I do not want to be known as a drug rep'. He stressed the need to do research in collaboration with industry.

In a frank assessment of agency writers, Macdougall felt that their role was unhelpful and too often too clearly linked to industrial sponsorship than the needs of the KOL and a potential conflict of interest. Although perhaps a personal viewpoint rather than the symptom of a general malaise, this clearly is an area in need of attention.

Macdougall also had concerns about the misrepresentation of data and gave examples such as rofecoxib, the use of SSRIs in children and alleged publication bias in antidepressant studies. He too has experienced difficulty agreeing manuscript contents with industrial sponsors and is sensitive to the need to avoid data selection for publication.

Finally, he posed the question of regulation. Is it necessary? The strongest case for regulation is protection of the KOL, of industry and, above all, Macdougall says, of the patient. In a clear illustration of the need for regulation he gave an example of a KOL who had spoken at two back to back satellite symposia, sponsored by rival pharmaceutical companies and gave two different messages. 'That just makes you lose credibility' says Macdougall 'as a clinical scientist, know what your message is and stick to it'. Sound advice.

## Key points

- Medicine and industry can only realise their true value in synergy
- The interests of pharmaceutical companies are best served when their drugs are used in the right patients at the right dose
- KOLs have a duty to act responsibly as educators, providing analysis, critique, and guidance

## Regulation, regulation, regulation

Taking his lead from Iain Macdougall's call for regulation, the next speaker was **Richard Tiner**, Medical Director of the Association of the British Pharmaceutical Industry (ABPI).

Fresh from chairing a previous evening's fringe meeting on risk-benefit analysis of medicines at a party conference in Birmingham, Tiner outlined the role of the ABPI in the regulation of KOL-industry relationships, starting with a description of several different types of KOL. These include lead clinician in a therapeutic area, principal investigator in a clinical trial, the senior author on a paper, invited speakers and advisory board participants.

Turning his attention to the June BMJ issue and its more contentious views of KOLs, Tiner painted a vivid picture of being interviewed by Roy Moynihan in the middle of the night to provide a sentence in an anti-pharma article. He counterpointed this with Charlie Buckwell's statement in the same issue that it was 'not in the interest of industry to have its products used incorrectly or in the wrong patients'. Tiner reiterated Buckwell's view of an ethical imperative for pharma to work with the best health care professionals and emphasised that, in his view, the pharmaceutical industry is populated by high-minded individuals.

On publication bias engendered by KOLs reviewing for journals and blocking dissemination of data that may conflict with their special interests, Tiner is unconvinced. 'Actually there are very few people who have no conflicts'. The key point is that any such conflicts are disclosed. Ultimately, journals need to sell and the peer review process should be seen against that backdrop.

Tiner addressed the subject of KOLs influencing prescribing, citing the BMJ correspondence by Hamish McAllister Williams that this should not be a cause for concern so much as celebration, resulting in better healthcare. Like Iain Macdougall, he reiterated oft-expressed views surrounding the shortcomings of 'infomercial' company slides.

So what is the role of the ABPI? Tiner took time to remind us that the ABPI code is 50 years old and, moreover, that this is Code Awareness Week! Tiner drew the conference's attention to new clauses effective from November 2008. Most germane is Clause 20 which pertains to the use of consultants and stipulates inter alia that arrangements must have a written contract, a legitimate need for the services and documented records of the contract must be kept. Most importantly, there must be no inducement to prescribe and any payments must be made at fair market value. Fair market value is contentious in the absence of any readily usable guidelines. The BMA, which might normally be expected to provide such figures, is constrained by the UK's Office of Fair Trading.

While the ABPI takes care of the pharmaceutical industry's practices, the GMC in the UK is the main regulator of physician practices. The Probity section of their Good Medical Practice document mirrors the ABPI's position. Paragraphs 74 and 75 specifically proscribe inducements that might affect or be seen to affect prescribing habits, and prevent financial or commercial influences on prescribing. Tiner pointed out that, when revalidation comes into effect, probity will form one of the 7 domains appraised annually. Notably, since 2000, the NHS has mandated that trusts have a duty to record doctors' interests above £25 in a register. This does not appear to exist.

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A role of the ABPI is to provide spokesmen for the pharmaceutical industry, often on radio programmes, mostly when things have gone wrong. Tiner concluded by asking participants to help keep him off the radio!

## Key points

- KOLs can be a force for good and bad interactions are over-reported.
- Pharma-KOL relations must be transparent and governed by a written contract.
- The ABPI code provides a transparent modus operandi for pharma and it is vital that the code and is understood and implemented.

## Small pharma, small problems?

In any media demonisation of the KOL-industry relationship, the emphasis is upon 'Big Pharma'. Somehow smaller companies, 'Little Pharma' if you will, slip through under the radar. As a counterpoint to David Gillen's testament, **Malcolm Allison**, Head of Strategic Marketing at Actelion opened the door on a more Lilliputian pharmaceutical world.

Allison outlined the history of the company from modest beginnings with an orphan Roche drug for pulmonary artery hypertension (PAH), a rare condition most commonly diagnosed at post mortem. Over 10 years they have grown to 2000 people. 'We are the third largest pharmaceutical company in Basel' Allison laughed, acknowledging that Roche and Novartis were numbers 1 and 2.

The rarity and severity of PAH pose unusual problems. There are few patients, they are commonly misdiagnosed and the condition is rapidly fatal. This poses unique problems for a company with a drug for this condition. How can one reach the patients? As expected KOLs play a vital role but in a way quite different from most conditions. Rather than pick and choose from a long list of suitable KOLs, Actelion engaged with all the KOLs worldwide. All 4 of them.

Not surprisingly, the relationship between these KOLs and the company is very close. 'These people are our friends' says Allison. The KOLs conduct clinical trials, and have helped build reference and referral centres. Whilst the relationship might seem cosy to the outsider, Allison is forthright in its defence. 'How could we possibly have done anything differently? There are people alive today who wouldn't be if we had not gone that way'.

Nonetheless, as the company expands, Allison recognises that the company needs to respond to the call for regularisation of relations and applauds the steps that Pfizer and Lilly have taken in compliance. Allison sounds a warning bell that, in a small field such as PAH, enforcing a more distant KOL-industry relationship may actually be detrimental to patient care.

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The key is documentation and audit. Despite its modest size, Allison acknowledges that the rules are the same as for the pharmaceutical giants. Actelion is developing an in-house tracking system that will allow all aspects of the relations to be monitored transparently. Transparency – that word again.

### Key points

- The KOL-industry relationship for a rare condition is closer and more mutually beneficial than in a larger therapeutic area.
- The proximity of this relationship has positive benefits for patients that are the direct result of this familiarity.
- The need for transparent working practices applies to small and large companies alike

### Can our laptops save us?

Just like an alcoholic holding his hand up to speak, accepting the need for transparency is a first step on the road to reform. Central to any efforts toward transparency in expert-industry interactions is the concept of audit. In the final presentation of the day, **Sanjay Singhvi**, Director of System Analytic described the use of technology to both regulate and enhance the KOL-industry relationship.

Among many areas, Singhvi identified tracking remuneration, specific compliance needs, grants audit trails, market value justification, KOL extranets, speakers bureaux, KOL profiling, social network analysis, and internal activity tracking. In many respects, these are simple uses of technology if also, by Singhvi's own admission, rather dull.

What about other applications? Taking as his cue the leitmotif of the meeting – transparency – Singhvi explored 3 case studies using limited or negligible technology. Analysis of publication databases can provide information not only about fields of interest but also about scientific networks. Citing the US experience of 'teller towers', where customers and bank teller see the same information, Singhvi described its application to KOL databases to encourage KOL ownership and thus contribution to their own database. KOLs sign off their own data.

In a second example, Singhvi addressed compliance. The onus to comply is for both parties and ignorance is no defence. The solution, applicable to any KOL activity, is to move the presentation and acknowledgement of regulations closer to the activity itself. Singhvi cited the example of off-label usage discussions. The third example addressed a sea of interactions that prevail at international meetings. The solution is to impose a meeting management tool to mediate between KOLs and brand teams.

In conclusion, Singhvi focussed on five 5 Ts – transparency, trust, tenancy, totality and truth. Singhvi saw these less as a hurdle and more about opportunities to boost collaboration using agile, integrated solutions.

### Key points

- The value of data is enhanced by looking at interactions between data rather than datapoints alone.
  - Engagement of KOLs with the data enhances its value and stimulates transparency.
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