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Good pharma? Bad pharma? Better pharma

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INTRODUCTION

Despite having good intentions – 'developing better, safer medicines for patients' – the pharmaceutical industry has often been criticised for the way it works, and its reputation has been tarnished.

The reasons for the criticisms are varied but include: an inherent disquiet from some members of the public about profit-making and medicines' development; a lack of understanding of the medicines' development process; a small number of examples of behaviours which are unacceptable; lack of access to individual patient data from clinical trials; and the complexity of medicines' development in third world countries, to name but a few. These have fuelled the flames of mistrust and have therefore led to an ever-increasing demand for greater transparency.

The industry can improve its reputation by listening carefully to criticisms, trying to understand the underlying concerns and responding in a way that demonstrates that, where possible, these concerns have been addressed. This will be a continuous process, especially as science advances and the demands for information in an increasingly patient-focused healthcare service will change.

However, some things will not change. These include the need for better, safer medicines despite the increasing pharmaceutical armamentarium; financial incentives to support an innovation culture; the confidentiality of individual patient data; the requirements for more sophisticated benefit/risk assessments (especially with stratified medicines), based on real-life data as well as on randomised clinical trials; the challenges of poly-pharmacy in an ageing population; and the inequalities of healthcare around the world.

Improving the perception of the pharmaceutical industry's contribution in the complex environment of medicines development needs a collaborative approach from all stakeholders including the industry, the trade associations, the UK Regulatory Authority, the UK Government, the EU and the public.

WHAT HAS THE PHARMACEUTICAL INDUSTRY DONE TO ADDRESS THE RECENT CONCERNS?

Clinical trial data

One of the criticisms was related to clinical trial data. It was felt that some clinical trial results were not made available and it was possible that 'negative' results were being suppressed. Without a complete picture of all the available data the true benefit/risk profile could not be assessed. Furthermore, the patients who participated in clinical trials were not informed of the trial results and individual patient data were not routinely available for further research.

This has been addressed in the joint European Federation for Pharmaceutical Industry and Associates (EFPIA) and Pharmaceutical Research and Manufacturers of America *Principles for Responsible Clinical Trial Data Sharing*.[1]

The principles are:

- Safeguarding the privacy of patients
- Respecting the integrity of national regulatory systems
- Maintaining incentives for investment in biomedical research

The document addresses:

1. **Enhancing data sharing with researchers** – Biopharmaceutical companies commit to sharing, on request from qualified scientific and medical research workers, patient-level clinical trial data, study-level clinical trial data and protocols from clinical trials in patients for medicines and indications approved in the US and in the EU, as necessary for conducting legitimate research.
2. **Enhancing public access to clinical study information** – Following approval of a new medicine or new indication for an approved medicine in the US and EU, biopharmaceutical companies will make publicly available the synopses of clinical reports for clinical trials in patients submitted to the Food and Drugs Administration, European Medicines Agency or national competent authorities of EU Member States.
3. **Sharing results with patients who participate in clinical trials** – Biopharmaceutical companies will work with regulators to adopt mechanisms for providing a factual summary of clinical trials results and make the summaries available for research participants.
4. **Certifying processes for clinical trial information** – Companies following the Principles for Responsible Clinical Trials Data Sharing will certify on a publicly available website that they have established policies and procedures to implement these data sharing commitments.
5. **Reaffirming commitment to publishing clinical trials results** – All company-sponsored clinical trials should be considered for publication in the scientific literature irrespective of whether the results of the sponsors' clinical trials are positive or negative.

Payments or transfers of value to healthcare professionals

Another area of criticism was the lack of transparency in relation to the payments or transfers of value to healthcare professionals. It was felt that the industry might be providing inappropriate levels of compensation to healthcare professionals involved in medicines development or company sales representatives might be providing inappropriate 'gifts' when visiting healthcare professionals, and that there may be conflicts of interest.

This topic has been addressed in the *EFPIA Code on Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organisations*[2] and in the USA Physician Payments Sunshine Act.[3] Both of these will result in open databases disclosing payments from the pharmaceutical industry to healthcare professionals.

The USA Physicians Payment Sunshine Act has implemented the most stringent rules. In compliance with the Act, 'drug and device makers must now collect and disclose payments exceeding $10 (£6.50; €7.60) to physicians and teaching hospitals and, starting in September 2014, the data will be posted on a publicly accessible website that will be administered by the Centers for Medicare & Medicaid Services. The data must also include all ownership or investment interests held by a doctor or family member'.[4]

In the case of the EFPIA Code, this was adopted by the EFPIA Statutory General Assembly of 24 June 2013, and required implementation in national codes by 31 December 2013. The EFPIA code has been incorparated in the Association of the British Pharmaceutical Industry *Code of Practice for the Pharmaceutical Industry 2014,* together with the Prescription Medicines Code of Practice Authority Constitution and Procedures.[5] The principles are similar to those of the USA Physician Payments Sunshine Act but some of the details vary.

THE UK GOVERNMENT RESPONSE

The Patent Box legislation

There are some areas where the response to the challenges of medicines development had to be addressed at a national government level. One example of this is the 'Patent Box' legislation which has been introduced to encourage innovation by providing an incentive for companies to 'locate their high-value jobs associated with the development, manufacture and exploitation of patents in the UK and maintain the UK's position as a world leader in patented technologies'.[6] The Patent Box enables companies to apply a lower rate of Corporation Tax to profits earned after 1 April 2013 from its patented inventions and certain other innovations. The relief has been phased in from 1 April 2013 and the lower rate of Corporation Tax to be applied will be 10%.[7]

The Cancer Drug Fund

In England, another example is the Cancer Drugs Fund (CDF). The CDF provides an additional £200m each year to enable patients to access drugs that are not routinely funded by the NHS. It was established in 2010 and will run until the end of March 2016.[8] This is another mechanism to remove a barrier to the development and introduction of innovative medicines resulting in a win-win for the patients and for the pharmaceutical industry. There is now a single, national list of drugs and indications that the CDF will routinely fund and standard operating procedures for administration of the fund.

The list of drugs and indications has been compiled by the NHS England Clinical Reference Group (CRG) for Chemotherapy working with the local clinician leads who oversaw the administration of the 10 regional

TABLE 1 R&D as a percentage of sales in key UK manufacturing industry sectors, 2010–2012

Product group	R&D expenditure (£million)			R&D as a % of sales		
	2010	2011	2012	2010	2011	2012
Pharmaceuticals	4,673	4,933	4,206	31.7	35.5	33.8
Aerospace	1,437	1,438	1,518	8.0	7.7	7.5
Electrical equipment	513	509	466	4.2	3.9	3.7
Chemicals	666	523	591	3.0	2.2	2.6
Motor vehicles and parts	1,237	1,525	1,732	3.4	4.0	4.4
Other manufactured goods	136	146	139	0.9	0.9	0.9
Manufacturing total (inc all of the above + all other manufactured goods)	11,585	12,466	12,235	3.3	3.6	3.4

Source: ONS Business Enterprise Research and Development, 2013

CDFs. The CRG for Chemotherapy will continue to play a key role in the management of the CDF. The Chair will make recommendations to NHS England as to how the list should be developed and the group will adopt a formal process of horizon-scanning for new treatments which could have potential benefits for specific groups (cohorts) of patients.

On 1 April 2013, NHS England took on responsibility for the operational management of the CDF.[8]

THE REGULATORY AGENCY RESPONSE

The Medicines and Healthcare Products Regulatory Agency (MHRA) announced the new Early Access to Medicines Scheme (EAMS), which took effect from April 2014. The scheme is intended to 'give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorisation'. This could include patients with severe forms of rare genetic diseases as well as advanced forms of cancer.[9] Under the scheme, the MHRA will provide a scientific opinion on the benefit/risk balance of the medicine, based on the data available at the time of the EAMS submission. The opinion lasts for a year and can be renewed.

EU LEGISLATION

EU legislation has led to the development of the non-publicly accessible EudraCT, which holds information on all EU trials dating back to 2004, and the public-facing EU Clinical Trials Register. Registration with EudraCT is necessary to obtain a EudraCT number, a prerequisite for conducting clinical trials within the EU. Updated guidance from the European Commission in 2012 has also driven the development of a publicly accessible site that will provide access to trial results and data. Version 10 of EudraCT[10] is due to be launched in 2014. Posting of results will be the responsibility of trial sponsors and individual member states – in the UK's case the MHRA will be responsible for policing adherence. Guidelines are currently being drafted on what constitutes commercially sensitive information and can be withheld. The MHRA anticipates making these available by the end of 2014.

The new European Clinical Trials Regulation is due to come into force in 2016 and will supersede the European Clinical Trials directive. It contains additional requirements for clinical trial transparency including the need to post all clinical trial summary results within one year of trial completion and a lay summary of the results.

GREATER COLLABORATION BETWEEN THE ACADEMIC COMMUNITY AND THE PHARMACEUTICAL INDUSTRY

Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) is a public-private initiative which aims to speed up the development of better and safer medicines for patients and is a shared undertaking between the EU and EFPIA. In IMI 1 (2008–2013) there was a total budget of €2 billion (50% from each partner) which funded around 50 projects. Both the EU and the pharmaceutical industry agreed to continue the collaboration and IMI 2 (2014–2024) was launched in July 2014 with a budget of €3.2 billion.[11]

One of the IMI projects is the European Patients' Academy for Therapeutic Innovation,[12] which provides scientifically reliable, objective, comprehensive information to patients on medicines research and development. This project will increase the capacity of well-informed patients to be effective in medicines' research but will also dispel some of the myths and misunderstandings that have contributed to the tarnished reputation of the pharmaceutical industry.

Medical Research Council collaborations

In July 2014 the UK Business Secretary announced that researchers will be granted access to a 'virtual library' of deprioritised pharmaceutical compounds through a new partnership between the Medical Research Council (MRC) and seven global drug companies.[13] The compounds have undergone a degree of industry development, but have all been discontinued at some point in early testing – often because they are not sufficiently effective against the disease in question. However, they may still be useful against other diseases with shared biological pathways.

These compounds can now be used by academic researchers, to understand disease biology and how it might be stopped or slowed down. It is hoped that re-purposing such compounds could lead to the development of new medicines for many debilitating conditions. And, because the compounds have already undergone some preliminary development such as safety testing, any new treatments arising from the research could reach patients much faster.

Medicines for the third world – WIPO Re:Search

In October 2011, the World Intellectual Property Organization (WIPO), in collaboration with leading pharmaceutical companies and BIO Ventures for Global Health, launched WIPO Re:Search, a consortium where public and private sector organisations share valuable intellectual property and expertise with the health research community to promote the development of new drugs, vaccines, and diagnostics to treat neglected tropical diseases, malaria and tuberculosis.[14]

UK ECONOMY

For those not familiar with the industry's contribution to the UK economy perhaps the following facts and Table 1 will be useful.[15]

- The pharmaceutical industry is one of Britain's leading manufacturing sectors and brought in a trade surplus of £2.8 billion in 2013. The value of UK pharmaceutical exports in 2013 was £21.3 billion, more than £292,275 per employee.
- Research and development lie at the core of the pharmaceutical industry, which invests more than any other industrial sector in the UK, with approximately £11.5 million spent every day.
- An analysis of the world's top 100 medicines reveals that Britain's pharmaceutical companies' market share places the UK in the group of the top 10 most important sources of new medicines in the world.
- It takes over 12 years to develop a new medicine to the standards of quality, efficacy and safety laid down by legislation. It typically costs £1.15 billion to do the necessary research and development before a new medicine can be licensed for use.

SUMMARY

This broad combination of improvements, demonstrates that the pharmaceutical industry has listened to its critics, and has tried to understand and address their concerns. It has also worked with other stakeholders to create a more supportive environment for medicines research and development, marketing authorisation and funding in the UK. This will help to redress the balance and hopefully the next YouGov report on British attitudes to the pharmaceutical industry will be more favourable.[16]

We've found a way to do it better – but the improvement cycle continues.

Disclaimer

The views expressed in this article are those of the author and do not represent the views of AstraZeneca PLC.

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