

## Conversation Piece – The Pharmaceutical Medicine Doctor

**DR P.D. WELSBY:** Dr Bax, you are now a Senior Medical Adviser at ICI and are obviously having a very successful career. Do you think that working in industry can be considered to be a 'non-mainstream' career for doctors to pursue?

**DR R.P. BAX** (Senior Medical Adviser, ICI Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire. Formerly Hon. Lecturer in Microbiology, University of London):

The answer to the question is definitely no. A new Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of London, Edinburgh and Glasgow is shortly to be inaugurated: Pharmaceutical Medicine is thus now firmly recognized to be a speciality in its own right.

**PDW:** When did you decide to enter a career in the pharmaceutical industry?

**RPB:** I joined Glaxo in 1977 after spending five years in general practice. Obviously this was a major career decision.

**PDW:** Have you had any regrets?

**RPB:** None whatsoever – apart from a substantial drop in salary initially.

**PDW:** How did you embark on your new career?

**RPB:** After taking appropriate advice I entered the industry by replying to an advertisement in the *British Medical Journal*. There are recruitment agencies which will advise and place suitable candidates. At a senior level it is common for suitable candidates to be approached directly.

**PDW:** Do doctors in industry move around a lot?

**RPB:** Usually. Often a physician will have worked for two or three companies during a career. I worked for four (Glaxo, Roussel, Lilly, and ICI). I moved around to further my career and to work on exciting new compounds.

**PDW:** What are the career prospects for young doctors entering industry?

**RPB:** For enthusiastic committed doctors the prospects for promotion are good. The usual entering salary is equivalent to a first year National Health Service consultant's but a car and medical insurance cover are additional benefits. Higher up the career ladder a head of clinical research in a large company receives consultant scale pay plus a 'B' merit award and a medical director receives consultant scale pay plus an 'A' merit award. Job satisfaction is high and there are opportunities to become personally involved in producing a really useful drug or, occasionally, a significant therapeutic breakthrough.

**PDW:** What qualities do you look for in young doctors who express an interest in working in industry?

**RPB:** In general the pharmaceutical industry is looking for doctors with a solid grounding in *clinical* medicine; despite the conventional wisdom a 'good' research background without the clinical experience is less useful. The ability to work with multidisciplinary teams and sound judgement are essential. I am asked 'why' far more often than I ever was in general practice and the ability to accept all critical comment (no matter from what level) as constructive has to be learnt quickly. Like all competitive careers in medicine there has to be commitment to the speciality in question – in this case pharmaceutical medicine. It is certainly not a soft option: the scope is wide and ranges from the early phases of drug

research to post-marketing assessments. Many different skills are required.

**PDW:** Why do so few medical students consider a career in the pharmaceutical industry?

**RPB:** I suspect mostly lack of awareness. Most career advice is given by doctors who have not considered industry as a career themselves, and I suspect their advice is largely confined to careers in general practice, hospital medicine, or laboratory medicine, but not industry.

**PDW:** What are the stages that a new compound must go through before release?

**RPB:** New drugs are discovered by four main methods. Firstly empirically, secondly by chemical pathway modification (which may lead to numerous side-chain variations), thirdly by rational processes based upon mimicking or antagonizing known metabolic pathways, and fourthly serendipity. It is difficult to obtain prospective funding for the last method however!

The selection of a new drug often involves random screening of selected likely candidate substances, the accumulation of knowledge concerning the compound (often based on animal work), elucidation of mechanisms of action and interactions, and by assessment of the drug in humans.

**PDW:** What does a medical adviser do?

**RPB:** Many things. In Phase I and II studies he has to liaise with research personnel including toxicologists. In Phase II he has to be involved with the first administration of the drug to humans and to organize early clinical trials to assess efficacy and side effects. In Phase III large scale trials have to be initiated and completed; the product licence application has to be written (and this may take up to one year to be finalized); quality assurance checks have to be completed; results have to be presented and published; the company has to be advised about appropriate marketing of the drug. In Phase IV post-marketing studies have to be conducted and adverse reactions identified. In addition to the above advisers have to speak out on behalf of their companies and the industry in general – especially when answering questions such as these!

**PDW:** There is a feeling amongst the medical fraternity that there are too many 'me too' type drugs being marketed.

**RPB:** There is now a decline in the number of new compounds being evaluated in humans: there will therefore be less chance of unexpected benefits being realized. The reasons for this include the greater number of requirements before a new compound can be used and the increasing demand for a greater variety and complexity of pre-launch testing. Obviously the pharmaceutical industry must respond (and occasionally initiate) these measures.

**PDW:** What factors cause a new compound to be discarded?

**RPB:** For all new compounds the factors are (approximately) pharmacokinetic (40%), lack of efficacy (30%), animal toxicity (10%), adverse effects in man (10%), commercial reasons (5%), and miscellaneous (5%). Cox and Styles<sup>1</sup> estimated the probability of success in investigating a new compound was about 1.5:10,000.

**PDW:** How long does it take to develop a new drug?

**RPB:** Usually over 12 years. In the 1960s three years was typical. The development time usually takes about 7 to 8

years and includes preclinical research (synthesis and/or discovery to first human administration) usually two years or so, clinical evaluation (first given to man until product license application), and (in the UK) regulatory phases (including clinical trials). Regulatory phases take time: between application and approval for clinical trials may take about three months although the clinical trial exemption scheme (CTX) has improved the situation. The time taken to grant a product license is about two years.

PDW: This obviously represents a substantial investment. I gather that, worldwide, pharmaceutical sales are about £60 billion and research and development costs are in excess of £6 billion. How long do drug patents last so that the developing firm can recoup their investment?

RPB: The *effective* patent life of a new compound is the difference between the patent expiry date and the (UK) marketing date. In 1960 the patent life was 13 years: in 1986 it was less than five years and, allowing for License of Right extension, the average patent life is about seven years. Of course the chances of a firm recouping their investment depends on the success of a particular product in the market.

PDW: What is the breakdown of research and development expenditure?

RPB: This obviously varies depending on particular compounds. Typical figures would be for, firstly, *Research*, where synthesis/extraction and biological testing would cost about 10% and 20% respectively. *Development* costs would be taken up by toxicology, bioavailability and pharmacokinetic

studies and chemical development, each about 10%. Human volunteer studies and premarketing clinical studies would each cost rather less than 10%. Postmarketing studies come to about 5%, regulatory requirements to less than 5% and other miscellaneous costs to about 10%.

PDW: It seems obvious that a medical adviser must develop many skills, not all (a euphemism for 'hardly any') of which are taught to doctors. But to come back to an earlier point, why the plague of 'me-too' drugs?

RPB: If a drug company has invested large amounts of money in developing a drug to the point of marketing there may be a need to recover the investment, even if only partially, so that there is a pressure to market drugs that will not necessarily be market leaders. Drug companies are not static and future development of new drugs can only occur if companies do not make losses; indeed profits are necessary so that future investment can occur. Sir Derek Dunlop likened 'me-too drugs' to motor cars – just as the modern motor car has evolved via many small improvements so do drugs.

PDW: Finally the extra question that I am asking all participants no matter what their speciality or calling. 'I have it in mind to attempt to live forever. In the light of your knowledge are there any words of advice you could give me?'

RPB: Successful drugs emanating from a competitive market will be best. Our independently minded colleagues in clinical medicine will ensure that competition will be free and fair. So take and prescribe only these drugs!

#### Reference

1. Cox, J.S.G. & Styles, A.E.J. From lead compound to product. *R & D Management* 1979, 9: 123–127.