Data protection for pharmaceuticals in the European Union

The first pharmaceutical legislation in the European Union (EU) came into force in 1965 (Directive 65/65). It required all member states to implement an assessment and approvals system for new pharmaceuticals within a time frame of 15 years. This article examines the development of EU pharmaceutical legislation since then.

Background

This first significant pharmaceutical directive was followed by two major directives in 1975 (Directives 75/318 and 319), which laid down the basic contents of a registration dossier and the basic principles of community procedures for the registration of new drugs. They also gave instructions as to how and when all drugs on the market at that time should be assessed and approved (or rejected) based on these new rules. In 1993 a regulation came into force establishing the European Agency for the Evaluation of Medicinal Products (EMEA) and the centralised registration procedure.


These new pieces of legislation define the approvals procedures for all new medicinal products in the EU. Furthermore, they describe in detail the role of the European Medicines Agency and the EMEA, and define timelines on when generics may enter the community market.

EU data protection

EU data protection as defined in the pharmaceutical legislation does not interfere with intellectual property protection via patents or supplementary protection certificates. It is a protection against referencing of a generic medicinal product to the clinical and pre-clinical data generated by the originator of a new medicinal product. The relevant article in the legislation (Directive 2004/27) states: “...without prejudice to the law relating to the protection of industrial and commercial property, the applicant shall not be required to provide the results of pre-clinical tests and of clinical trials if he can demonstrate that the medicinal product is a generic of a reference medicinal product which is or has been authorised … for not less than eight years in a Member State or in the Community.”

This legislation effectively protects an originator (the person bringing a product onto the EU market for the first time) from generic competition for exactly ten years, even if other means of protection, a patent or a supplementary protection certificate, have already expired. In this respect it is important that the name generic has now been officially defined in the EU legislation for the first time.

This ten years of protection time starts after the first approval of a medicinal product somewhere in the EU. If a product has not been approved using the centralised procedure where an approval is effective throughout the EU in all member states with immediate effect, but using a national approval procedure first which is then followed by utilising the mutual recognition procedure, the ten years' protection time starts with this first approval.

If, for example, Denmark was used as the first approving country (Denmark being the reference member state for a later mutual recognition procedure), this marketing authorisation date would automatically determine the protection period for the entire 27 member states of the EU.

This fact makes the choice of the right registration procedure and, if the choice is the mutual recognition procedure, the right reference member state, crucial.

The situation has become less difficult for originators since the introduction of the decentralised procedure, where an applicant can choose its reference member state as well as all concerned member states. Here, the main (decentralised) procedure will be finalised by all member states involved at the very same time. As the decentralised procedure is eventually concluded after the international part is finalised by the granting of national marketing authorisations, there is still some risk that one of the commercially less viable countries grants a marketing authorisation earlier than those with more commercial importance and, in doing so, starts the clock for the protection time. Figure 1 summarises how this data protection fits together with intellectual property protection via patents or SPCs.
The data protection coming with the EU pharma legislation provides additional protection against generic competition only for those products that have had a development and approval cycle of more than 25 years. Otherwise, patent protection and supplementary protection certificates will not be expired and the launch of a generic would be a breach of the patent and SPC legislation.

Figure 1: Duration of protection: how the different measures fit together

Other means of protection

There are three more important factors to be taken into consideration when discussing data protection: orphan protection, protection due to investment in children, and supplementary protection certificates.

Orphan protection

If a disease has a prevalence in the EU of less than five patients in 10,000 persons, it can obtain an orphan drug designation. Once approved, such a product obtains market exclusivity. Market exclusivity means that no other medicinal product with a comparable mechanism of action can receive a marketing authorisation unless it has shown superiority, i.e. a significant advantage against the first approved product in clinical comparison. This is a significant hurdle, and so this market exclusivity can be seen as a rather robust protection against competition.

Generation of significant new data

If a medicinal product is being developed further within the first eight years after its first approval in the community, the European Commission can grant one year of additional data protection. This means that a generic product must not be launched in the EU in the first 11 years following the first approval in the EU. It should be noted that to date no solid and accepted definition exists as to what a significant new development might be, but as seen in the current political discussion it becomes apparent that the granting of such a one-year addition will be difficult to achieve for a pharmaceutical company.

Paediatric medicines

If a company provides a paediatric investigation plan for a compound that is still data protected, it can obtain an additional six months of data protection for the entire medicinal product, not just for the paediatric indication, thus providing a commercial benefit for developing a medicinal product for use in children. In cases where the medicinal product is an ‘orphan’, this additional data protection prolongs the data exclusivity period by two more years to a total of 12 years.

Conclusion

EU data protection is an important instrument for the pharmaceutical industry to provide a benefit scheme for the development of new pharmaceuticals with a limited patent or SPC protection period but which have not previously been approved in the EU. In addition, it is a system that encourages pharmaceutical companies to develop new indications for already widely used and thus better-known drugs. This limits the potential risks for the patients as they will receive a drug in a new indication with an already well-known side-effects profile.

The new orphan and paediatric legislation encourages the pharmaceutical industry to develop new medicines for children and for neglected diseases.

Notes

1. A ‘generic medicinal product’ (GMP) shall mean a medicinal product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product, and whose bioequivalence with the reference medicinal product has been demonstrated.
2. A ‘paediatric investigation plan’ (PIP) is a company’s proposal on how to investigate a medicinal product in children. This PIP will be submitted to the EMEA, and approved by the paediatric committee.

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Data protection regulations in Canada

by Joan Chypyha, Barrier Therapeutics

Recent changes to regulations in Canada, now provide patentees with eight years of data exclusivity for the first product incorporating a new medicinal ingredient. This means that once an innovator receives the first approval to market a novel product, the regulations will prevent a generic manufacturer from filing for and receiving approval on its ANDS (abbreviated new drug submission) for eight years. The generic company is also prevented from filing its ANDS for a period of six years within that eight year period.

Another change to the regulations involves granting an additional six months of exclusivity when the innovator completes paediatric research. This change is in line with current data protection regulations in the EU.

This exclusivity will apply to all current submissions for new chemical entities that had been filed with Health Canada, but not yet approved, as of 17 June 2006.

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‘Mind the gap’: how to negotiate with innovators and scientists

Business development executives often describe, and frequently complain about in vivid terms, the difficulties they have encountered when negotiating with innovators and scientists. From these conversations, two sets of linked concerns emerge: those about planning for negotiations and those about the management of the negotiating process itself.

The specific context of these conversations was usually an individual who was in the process of taking ideas to the commercial market from not-for-profit organisations, or who had recently done so. In other cases they were ‘infant’ organisations with minimal resources seeking to grow, and in the most extreme cases they were struggling to avoid a short-term catastrophe or collapse. I am going to use the words ‘innovator’ and ‘scientist’ as generic terms to describe these individuals without regard to the life science involved. I am also going to apply the term to those engaged in the process of commercialisation of ideas irrespective of where they are positioned in the process itself, ie initial exploratory talks with potential investors or within ‘new’ organisations that are variously labelled ‘start-ups’.

However, before we can move forward to address the issues, we must step back in order to create a different and perhaps more robust perspective.

The gap

Any passenger on the London Underground will be familiar with the warning painted in large white letters, at frequent intervals on the platform, asking passengers to ‘mind the gap’. This safety warning appears to work for travellers but is ignored by business development negotiators far more frequently than we realise.

Identifying the gap between the two parties – the business development executive and the innovator or scientist – is a critical activity for both effective planning and in the management of the negotiations themselves. Table 1 lists some of the elements of the structural and psychological gap that requires to be bridged to conclude an agreement.

Visible differences in age, education and gender between the executive and the scientist appear either to be minimal or at least relatively easy to resolve during the negotiating process. However the items listed in Table 1 form a significant and obvious gap that drifts to build an unconscious chasm. In popular parlance the word ‘mad’ is so often attached or implied when we use the word ‘scientist’ that we can also become victims of social stereotyping. To compound this stereotyping process we regard universities as organisations that provide secure environments for their ‘madness’.

Table 1: Differences between business development executives and innovators/scientists

<table>
<thead>
<tr>
<th>Business development executives</th>
<th>Innovators / scientists</th>
</tr>
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<tbody>
<tr>
<td>Lower ego involvement</td>
<td>High / very high ego involvement</td>
</tr>
<tr>
<td>Portfolio of potential projects</td>
<td>Single project or ‘concept’</td>
</tr>
<tr>
<td>Partial and intermittent commitment</td>
<td>Total commitment</td>
</tr>
<tr>
<td>Managed risk</td>
<td>Unmanaged total risk</td>
</tr>
<tr>
<td>Salaried</td>
<td>Entrepreneur (living on capital or debt)</td>
</tr>
<tr>
<td>Planned career</td>
<td>No career, seeking recognition</td>
</tr>
<tr>
<td>Access to resources</td>
<td>Excluded from / competing for resources</td>
</tr>
<tr>
<td>Represents an organisation / investors</td>
<td>Represent themselves and a dependent group</td>
</tr>
<tr>
<td>Team members / players</td>
<td>Team leaders or isolated individualists</td>
</tr>
<tr>
<td>Know and use management English</td>
<td>Distrust ‘management speak’</td>
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The business development executives are the ‘sane’ salaried professionals living in the real world. The financial and marketing criteria they apply in the negotiations represent the ‘real God’ of the pharmaceutical marketplace. The scientists’ unwillingness to grovel before this marketplace is a clear indicator of their ‘insanity’ or worse, their naivety. Like children they need to be guided and corrected in order to achieve full adult status. But seen from the other side of the line the scientists are the real entrepreneurs, the intellectual risk-takers. Their personal, emotional and intellectual investment in ideas and innovation is total and it is often difficult to separate individual egos from their ideas. For the entrepreneurial scientist the business development manager may represent the administrative and bureaucratic processes that have squashed innovation and squandered money. In psychological terms they seem incapable of treating the scientist as an ‘adult’. Negotiating as a process can bridge this gap but we must recognise its existence in order to close it.

Planning for rationality and irrationality

In our planning, this structural gap will have an impact on the issues that we need to resolve, the common ground between the parties, and the assumptions that the parties bring to the table.

Most negotiations contain five or six key issues or bundles of issues that can be linked both logically and for tactical reasons. For example, a deal for the US market will be more expensive to negotiate than one for the UK market, the logic being that actual market size or its potential drives the potential income and therefore its cost/value. An example of a tactical linkage would be if either negotiator insists that the USA is excluded until the price for the UK is perceived to be satisfactory.

During the negotiations both parties will be required to manage these linkages. To describe the counterparty’s linkages as an indicator of ‘insanity’ is totally unhelpful and may cause insurmountable problems. The philosopher Wittgenstein observed that thinking about a line requires one to think about two sides. More critically, if either negotiator invests a psychologically disproportionate amount in one specific issue before the negotiations begin we may be building in failure before we start. Negotiating may be a route to meeting our ego needs but we know there are better and quicker alternatives (therapy)!

Both experience and research indicate that effective negotiators devote considerable thought and time identifying the common ground that exists between the parties. This common ground can exist at many levels and must take into account the psychological needs of the scientist. The Maslow needs hierarchy is not an exclusive concept! For example, when preparing to negotiate intellectual property rights we must recognise that we are also negotiating a psychological contract that contains three elements: equity, control and flexibility. Transferring ownership is like an adoption process: it entails anxiety, hope and guilt. The executive has to show how his proposals will address these concerns, a task that is facilitated or impeded by organisational factors. Who can predict, let alone guarantee, pharmaceutical new product development strategies over a 20-year period?

We expect our counterparty to bring different assumptions to the negotiations. Yet business development executives continue to express surprise that the gap is so wide between them and their counterparty, the scientist. They have a significant shared educational experience and now find it hard to comprehend that employment can create a psychological chasm. For example, the parties have very different perceptions and judgements about organisational structures, decision-making processes and time-scales. The requirement for risk assessment procedures is a corporate fact of life that is virtually meaningless to the entrepreneurial scientist. Equally, decision making is always too slow and burdensome. From the perspective of the scientist, what is simple becomes unnecessarily complex, what should be accomplished in a timely fashion is lost in an all-consuming organisational black hole.

From this depressing litany one might be forgiven the conclusion that many negotiations are doomed to failure. If we recognise this we can start to take corrective action during the planning phase. The business development executive is employed on the boundary of the organisation to negotiate both inside the organisation and outside, with a wide range of actual and potential partners. Given constant exposure to negotiating, the business development executive should insist that the entrepreneurial scientist has effective and active negotiating support throughout the deal-making process. The existence of technology transfer groups, licensing executives and independent consultants who can act as guides, mentors, shop stewards and midwives to the deal is vital. Don’t start without them, because without them rational negotiating is less likely.

Managing the negotiating process

Let us assume that when the entrepreneurial scientist has effective negotiating support in place, there can be a transition from relationship building to talking about talks. This pre-negotiation activity is critical, but is often rushed, or even ignored, because the parties are caught in a dynamic which they believe requires a systematic progression to ‘yes’. Experience tells us that failure to invest in pre-talks will result in deadlock, failure and recrimination. Talks about talks allow both parties to review their expectations and aspirations. How will both parties manage time? The executive’s working life is regulated by an organisational calendar that may be incapable of synchronisation with the needs of the scientist. The effective reconciliation of different timelines may be the first, and critical, indicator of the acceptance of bounded rationality by both parties.
Sooner rather than later the representatives have to ‘talk money’. What is the range of values that have characterised ideas in this area? The executive may anticipate that the counterparty, driven by high ego needs, will arrive at the start of the negotiation process with totally unrealistically high expectations. In some instances this happens. Equally however, anxiety and current events may cause a desperation that could result in unrealistically low aspirations. To attempt to take advantage of this situation is the equivalent of skydiving without a parachute. Irrespective of any exclusivity arrangements that may exist, the scientist can, and will, end the negotiations once they recognise their mistake.

Once both parties are ready to make the transition from talks about talks to the negotiations themselves, it is vital that they confirm a shared vision of their interdependent future, both in the negotiations and in the implementation of the agreement. What are the features of success? Which obstacles could they encounter and what are the signs of problems/failure? If we know what data and events might mean to both parties we can respond more effectively. Joint problem solving is more effective than mutual recrimination as problems occur.

As the negotiations develop, both parties recognise that negotiating power is a reality that has to be managed constructively in the search for an agreement. Power in a negotiation is the ability to say ‘no’. Our ability to create, retain and manage realistic alternatives is fundamental to achieving our negotiating objectives. It is equally important to identify our counterparty’s alternatives and examine their robustness. In the highly personalised negotiations that we are discussing, the risks and rewards are even more pronounced.

The entrepreneurial scientist may make the mistake of saying ‘no’ too frequently on consequential issues that thus undermine their credibility completely. An equal but different danger is avoiding ‘no’ out of fear of its consequence. Critically, the executive must hear and question the ‘no’ for clarification. Is it highly specific or general and all-embracing? Is it temporary or permanent and, if the former, when and how will it be reviewed? Only an in-depth understanding of the counterparty’s alternative will give us the confidence to quietly challenge what we hear. We must avoid being swept away by tantrums driven by ego needs and short-term fears. As an aside, we must remember there are many ways of saying ‘no’ and that native English speakers are more adept at hinting at ‘no’ than any other nationality!

From time to time negotiators use or encounter the use of attrition as a technique. It only works if, in a specific meeting or on a specific issue, we have an expectation about ‘making progress’ or reaching an interim agreement on a time-scale that is understood by both parties. It is a legitimate ploy even if its use appears disruptive. Perhaps it is appropriate to ask why it is being used at this point in the negotiations. This question can be posed to both oneself and the counterparty. Usually the answer can be found in the internal dynamics: the ghost at the table (eg the bank or critical shareholders), although if we are driven by anxiety we create the apparition of a competing party.

Experience suggests you should provide feedback to your counterparty: explain how you feel about the situation and question to identify the causes. Procrastination and delays are a fact of life but for the negotiator they are drivers of increased anxiety because of the psychological investment being made in the relationship and the anticipated agreement. The objectives of the party using the tactic of attrition can be varied but there is one response that must be avoided at all costs. Do not under any circumstance consider making a concession – or even worse, actually make a concession. The correct response is to match their behaviour.

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**Conclusion**

If we admit that negotiating is the component of our work that we enjoy most, we may also admit that it generates a disproportionate amount of anxiety and frustration. We all know who is an easy person to negotiate with – we see them in the mirror many times a day. Unfortunately, negotiating with a counterparty who is both so like and so unlike ourselves will always remain an unpredictable situation. Given our wish for success we should derive some comfort from two observations: when in doubt predict the trend will continue; and, a trend is a trend but when will it bend?

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