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The Antidote

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The Antidote

Welcome to our latest edition of The Antidote. Our newsletter begins with a look at the new Market Abuse Regulation (MAR) which comes in to effect on 3 July. We look at the changes the regulation brings to how quoted companies deal with inside information, such as confidential drug trial results, and how senior employees in possession of inside information can deal in company shares.

We also examine the European General Court's judgement in an important appeal case between Teva Pharmaceuticals and the European Medicines Agency on generic entry into the EU orphan medicines market.

We then look at the out-licensing of technology in the lifesciences sector and how licensors can use diligence obligations to effectively protect their position by imposing performance requirements on licensees.

Finally we consider the impact of new procurement rules on lifesciences organisations and how companies in the sector can engage with public health authorities in order to influence how the rules and procedures should be applied.

If you would like to discuss any of these topics in more detail, please get in touch with me or the authors of the articles.

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Market abuse regulation

23 June may be the key day that is in most people's minds over the next few weeks, but quoted companies and their company secretaries, brokers and NOMADs are equally focussed on 3 July, which is when the Market Abuse Regulation (MAR) comes into effect.

MAR makes major changes to the way in which all quoted companies (both Main Market and Alternative Investment Market (AIM)) deal with inside information, for example, confidential drug trial results. It also makes changes to rules governing when directors and other senior employees (known as PDMRs), who often have inside information, can deal in company shares and how those transactions are reported. MAR is an EU-wide regulatory framework and, because it is a regulation, takes direct effect in the UK. This has led to the Financial Conduct Authority (FCA) and AIM having to remove many existing UK provisions in these areas from their rulebooks (including the Model Code), although in many cases the underlying law will remain the same.

Inside information

Both Main Market and AIM already have a general rule that inside information must be publicly announced by companies without delay. Although there are subtleties, MAR continues this requirement but requires all companies to keep all announcements of inside information on their website in chronological order, in a clearly identifiable section and for five years.

Both Main Market and AIM companies have, however, always been able to delay announcing information in certain cases. The MAR rules are not significantly different and allow a delay where immediate disclosure is likely to prejuduce the legitimate interests of the issuer, the delay is not likely to mislead the public and the issuer is able to ensure that the inside information remains confidential. A change though is that the FCA must also be told of any delay, once the announcement has later been made, using a FCA-prescribed form. Extensive new company record-keeping requirements are also being introduced on the process of identifying and controlling the delay of the release of the information over the course of the project eg a large licensing deal being negotiated.

New rules are also being introduced on insider lists, which are lists of those people working for a company with access to inside information either on a permanent or project basis. This is a big change for AIM companies who have not to date been required to keep insider lists. However, all companies should use the introduction of new rules as a reason for an overall review of their compliance and procedures in this area. More than many other companies, life science companies are particularly subject to sudden developments, whether it is raising money, related to science or regulatory approval, or licensing deals or M&A activity and so these rules are particularly important to them.

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‘AIM companies are most affected by these new changes and have most to do to make changes to their procedures’.

PDMR transactions

All Main List companies will have been used to announcing transactions in their own shares by PDMRs, but AIM companies must now also announce dealings not just by their directors but also other senior employees. Moreover, all companies must now make the announcements not just to the market via a Regulatory Information Service announcement but also to the FCA itself, and notifications must be made on a prescribed electronic form.

Periods when PDMRs cannot deal

These are known as black-out periods in the US. The Model Code currently requires Main Market companies to make sure all PDMRs obtain clearance to deal from someone at the company, and generally blocks deals completely in the two months before annual and half-yearly results or at other times when the company has inside information. Deals also include the grant of most employee share plan awards and the receipt of shares under them. AIM companies normally have similar rules. The pre-results periods can be predicted in advance, but the inside information periods can crop up at any time, without warning.

The law is being liberalised going forward. There will be no requirement for PDMRs to obtain clearance (other than in certain limited respects). PDMR dealings are just restricted in the 30 days before results (as opposed to two months beforehand as currently) and the only PDMR restriction outside those pre-results periods is to stop actual trading on the basis of inside information (which is unlikely in the case of receiving pre-arranged share awards or vestings, or selling shares to pay tax liabilities, where there is little choice other than to sell shares to meet tax liabilities). However, whether the market is ready for these changes still remains to be seen. From our discussions with companies, many of them do not seem ready to let their PDMRs deal without clearance (and AIM is still proposing at the time of writing to have some kind of dealing and clearance code), sell shares say 31 days before results or sell shares when the board is considering a major contract but that particular PDMR does not know about it. It is hoped some codes may emerge which set out the market views of new best practice, but until then companies will need to consider what their own dealing rules will be after 3 July.

In conclusion, AIM companies are most affected by these new changes and have most to do to make changes to their procedures: their position is made more complicated by AIM still consulting on its proposed post-3 July 2016 rulebook. However, all quoted companies are likely to need to make some changes to their systems – whatever the result of the vote on 23 June!

European Court decides on generic market entry relative to orphan medicinal products

The European General Court gave judgment in March 2016 in an important appeal case on generic entry into the EU orphan medicines market.

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The judgment came a day after the Commission published the responses to a public consultation on a proposed replacement for its 2003 Communication on orphan medicines (2003/C 178/02) which provides guidance on certain aspects of the legislation and a possible revision of its implementing regulation 847/2000, which defines many of the key terms for the EU regulation of orphan medicines. The EU orphan medicines regulation (EC Reg 141/2000) was of course introduced to incentivise development of innovative medicines for treatment of rare but severe conditions, or which, when sold on the market, would not generate sufficient returns to justify investment in their development and which in either case would provide a significant benefit over other existing available treatments. The appeal focussed on the key incentive, which is a 10-year market exclusivity period for the product with the orphan indication and the circumstances in which a marketing authorisation (**MA**) may nonetheless also be granted for the same therapeutic indication to a similar medicinal product (**similar product**).

The Teva appeal case

The appeal concerned a dispute between Teva Pharma (**Teva**) and the European Medicines Agency[1] (**EMA**) concerning the EMA's refusal to grant a MA to its generic version of Novartis' then orphan medicine, Glivec (imatinib). Glivec was one of the first designated orphan medicines after the introduction of the EU orphans legislation and had been granted a MA as an orphan product for several chronic myeloid leukaemia (**CML**) indications as well as certain non-CML cancer indications from 12 January 2001 onwards. Teva's MA application, for authorisation of a generic version (imatinib mesylate), for certain of the CML indications and for Glivec's non-CML cancer indications, was made on 5 January 2011, shortly prior to the expiry of Glivec's 10-year market exclusivity period for the original CML indications.

‘The appeal focussed on the key incentive, which is a 10-year market exclusivity period’.

Teva’s MA application had been rejected by the EMA, to the extent that the indications of its generic imatinib overlapped with those of Novartis’ own similar orphan product, Tasigna (nilotinib). Tasigna was designed to address imanitib resistance in some CML patients and, like Glivec, is a tyrosine kinase inhibitor and is itself a similar product to Glivec within the meaning of the orphans legislation. Tasigna was authorised between November 2007 and December 2010 for certain CML-related orphan indications and its 10-year orphan market exclusivity period for the CML indications was therefore still current at the date of Teva’s MA application. The EMA also argued that the non-cancer indications for Glivec were also still protected by market exclusivity, having been authorised later than January 2001.

The MA for Tasigna had been granted under the consent-based derogation from the general rule in the EU orphan medicines legislation prohibiting the granting or consideration of any MA (or extension) for a similar product in respect of an existing orphan indication for the duration of the 10-year orphan market exclusivity period. As Novartis was the holder of the MA for Glivec and also the MA applicant for Tasigna, it had been able to consent to its own Tasigna MA application.

Teva’s application to annul the EMA’s refusal decision failed at first instance (see judgment in Care T-14/12 dated 22 January 2015). Teva then appealed on grounds of misinterpretation of the legislation and distortion by the court of Teva’s first instance arguments on the basis that:

a. a similar product, which is granted an MA under the derogation provisions, cannot benefit from the 10-year market exclusivity in the same way as the original orphan, because this would contradict the very notion of market *exclusivity*, which implies a status enjoyed by a single product only. It would moreover frustrate the objective of the EU orphans legislation which, Teva argued, was intended to provide a reward for the first orphan authorised for a particular indication (a concept developed in the Commission’ Communication of 2003 which foresaw latecomer similar products merely sharing the remaining period of original 10-year market exclusivity in what was referred to colloquially as the ‘race for exclusivity’); and

b. granting the full 10-year period of market exclusivity to a similar product by consent of the MA holder for the original orphan product, who also owns the similar product in question, would perversely incentivise companies to develop a series of slightly different, but nevertheless similar, orphan products, thereby benefiting from a prolongation of the normal 10-year market exclusivity period.

The appeal judgment of 3 March 2016 accepted the first instance court’s assessment of the objectives of the EU orphan legislation, namely as the encouragement of investment in the research, development and marketing of orphan medicinal products. The court pointed out that although the 10-years market exclusivity is reserved for orphan products, the derogations (including consent) apply to any similar products, irrespective of whether those products are orphan products or not. The appeal court also endorsed the conclusion of the first instance court that the EU orphans legislation does not contain any provision to justify not granting a full 10-year market exclusivity to an orphan product which has been designated an orphan and subsequently granted a MA, provided it continues to meets the criteria for orphan status. Consequently, a similar product, which is also an orphan and which receives a MA will automatically enjoy its own full 10-year market exclusivity period.

It is interesting that the notion of ‘global marketing authorisation’ and the associated data exclusivity rules for non-orphan medicines (essentially allowing a single period of protection per manufacturer, per active substance) do not translate into the orphan medicines area. Rather, the judgments underline the point that the key market exclusivity incentive is there to provide the pharmaceutical industry with an incentive to sponsor research, development and marketing of these orphan products and that those efforts will be rewarded, also where they result in similar products.

[1] *Teva Pharma BV and another v European Medicines Agency*, C-138/15 P - Court of Justice of the European Union (Sixth Chamber)

Diligence obligations in licence agreements

In out-licensing technology within the lifesciences sector there is the potential for the original rights' holder to relinquish control (at least in part and in some cases absolutely) of the development and commercialisation of a key asset.

Consequently, it is imperative (particularly where technology is licensed exclusively), that the licence agreement sets out the diligence obligations that are expected of the licensee. Without a contractual commitment the licensee could refrain from exploiting the licensed rights sufficiently and the licensor may be left without a remedy. The licensor will want to protect its position by imposing performance obligations and the licensee will want to ensure that such obligations are reasonable and not unduly onerous. For example, the licensee will not want to be forced to continue investing in the development of a pharmaceutical product or medical device if unanticipated hurdles or barriers to development arise which make further development commercially unviable.

General obligation

Acknowledging that it is unreasonable for a licensee to be bound by an absolute commitment to develop and commercialise in-licensed technology, the parties to a licence agreement may agree to qualify the extent to which a licensee is required to do so by reference to an 'endeavours' obligation. Whilst often used and, on the face of it, a sensible approach, the recognised meanings of the terms 'reasonable endeavours', 'all reasonable endeavours' and 'best endeavours' are far from certain and often debated. Although generally the phrases are to be assessed at the date the agreement was entered into, the circumstances in existence at the time the obligation was, or ought to have been performed, are to be taken into account when deciding whether or not the obligation has been fulfilled. In the context of a licence agreement, this means that the phrases will need to be applied to a broad range of activities that arise during the lifecycle of a product, exacerbating the potential for disagreement between the parties as to their meaning. Consequently, the parties to a licence agreement will often define exactly what they mean by 'Commercially Reasonable Efforts'.

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'…it is imperative (particularly where technology is licensed exclusively), that the licence agreement sets out the diligence obligations that are expected of the licensee'.

Commercially reasonable efforts

In defining 'Commercially Reasonable Efforts' the parties can either look to the licensee's own activities (an 'Inward Facing' definition) or to the activities of the industry in which the licensee operates (an 'Outward Facing' definition). An 'Inward Facing' definition is generally viewed as more favourable to the licensee; it applies the licensee's own standards for carrying out research, development and commercialisation and in evidencing performance the licensee would be able to refer to its internal decision processes, risk appetite and investment thresholds. In applying industry-standard requirements an 'Outward Facing' definition, on the other hand, is generally considered to be more favourable to a licensor since its construction draws on the activities of other industry players, some of which may have taken steps beyond those taken by the licensee in developing or commercialising the licensed technology.

Additional measurable objectives

An alternative, or additional, solution is to establish objective, numerical obligations with the licensor such as making a minimum financial investment or achieving key milestones by determined dates. The licensee's obligations can be combined with a means for the licensor to monitor performance (for example, by the licensee providing detailed disclosure) and exercise a right to recourse in the event that the objectives are not met, for example the reversion of an exclusive licence to non-exclusive, grant-backs of rights, or liquidated damages. Whilst not removing the possibility of dispute in relation to the licensee's diligence entirely, including clearly defined milestones will mean that there can be no subsequent argument about their meaning. Examples of typical regulatory, development or commercial milestones include:

— committing an agreed amount of financial resource to the development of the licensed technology;

— initiation of Phase I, II or III clinical trials regarding the licensed technology with respect to specified jurisdiction(s) within an agreed time after the effective date of the licence;

— securing all required regulatory approvals, pricing and reimbursement approvals in specified jurisdiction(s) within an agreed time after following completion of all appropriate trials; and

— making the first commercial sale of a licensed product in specified jurisdiction(s) within an agreed time following the issuance of the regulatory approvals and pricing and reimbursement approvals.

Influencing government procurements in a time of austerity

The procurement of effective healthcare solutions is one of the most pressing public policy issues in the EU and globally, yet the procurement of healthcare products and services in many countries faces a stark dilemma in a climate of austerity. On the one hand, rapidly evolving innovation has raised societal expectations, given aging populations and an increasing demand for high-calibre healthcare services. On the other, health and finance ministries must achieve sustainable health systems against a background of limited budgets and dwindling public resources.

Procurement law regulates how public health authorities purchase products from the lifesciences sector, whether medicines, medical devices, diagnostic or other medical equipment, or the services linked to any of these products. In this article, we set out how lifesciences companies can engage with public health authorities in order to influence how the rules and procedures should be applied, with a particular focus on the importance of maintaining a dialogue with the authorities outside the context of a tender process.

In addition, recent critical developments in EU procurement law are highly relevant to how governments might achieve a balance between procuring valuable products whilst spending wisely and procuring smartly.

A new Public Procurement Directive came into force on 17 April 2014, requiring national implementation by 18 April 2016. A number of EU Member States failed to implement by the set date, but most are expected to do so shortly.

The UK (without Scotland) was the first to introduce new national legislation with the Public Contracts Regulations 2015, in force since February 2015. The UK therefore already has active experience of operating under these new rules, although all issues are likely to be relevant to current and future practice in other Member States.

Before the tender: the critical importance of explaining market needs to healthcare authorities

The procurement reforms introduce new rules which explicitly allow contracting authorities to consult with industry to assist in the preparation of tenders on condition that the authorities ensure that the outcomes of specific tenders are not distorted by such consultations.

Pre-tender engagement is the most important stage of procurements. Informed prior research is now actively encouraged in many jurisdictions as an essential tool in the allocation of public resources to healthcare procurement:

— Market testing allows both the health authorities and the supplier base to understand how market offerings, including product pipelines, can be aligned to healthcare requirements.

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‘There is an increasing tendency for lifesciences companies to take a proactive stance against perceived bad procurement practice’.

— In advance, officials can be better assured that companies asked to provide products and services can meet the stated needs within appropriate timescales and to a suitable level of quality.

— For pharmaceuticals, pre-tender engagement represents an opportunity to ensure the procurement of a suitably broad range of safe and effective medicines; for devices, there is the added dimension of how to structure a managed service model where the hospital may be able to achieve efficiencies through the appointment of a supplier to manage a particular commercial function within a hospital.

— Consultation with the marketplace allows both private and public sectors a forum in which they can discuss lessons learnt from previous procurements and create a virtuous circle for future procurements. Suppliers should beware of unduly influencing the conduct of specific, ongoing tenders, but should not hesitate to provide authorities with their general views on what has previously failed to work in tenders.

Procuring for value

In a time of austerity, there is a temptation for government procurement teams to opt for lower-cost products, which may lead to a focus on short-term commodity purchasing without due regard to the long-term value of medicines or devices which, even if they are priced higher, may be safer and ultimately more effective. The new EU regime requires a value-based approach, in that awards must be based on the “most economically advantageous tender” or “MEAT”. On the face of it, this removes the option for price as a definitive award criterion. Yet, price is still one of the permitted factors in determining a MEAT award, so a price-based award remains a possibility.

It may therefore be advisable to consider arguing to contracting authorities that procuring for value means looking at all aspects of relevant products. Even where the acquisition price seems high, the effect on health outcomes and general cost-effectiveness may yield net gains in broad value terms.

An expanded range of available procedures

The rules now allow for a competitive procedure with negotiation, which entails a staged and more sophisticated assessment of bids and therefore has some similarities to the existing competitive dialogue procedure (although the latter still applies where the authority is unable to state its needs from the outset).

There is also a wholly new procedure, innovation partnerships, which contemplate the award of a phased contract to cover all stages of product development, including R&D. An innovation partnership may cover R&D only or both R&D and the commercialisation stage.

Going by the UK experience so far, take-up of these new procedures has been limited. However, it may in some cases be helpful to make representations to government about the relevance of staged or dialogue-based procedures.

A further significant point regarding procedure under the new regime is that procuring authorities are now encouraged to split contracts into smaller contracts or “lots” to stimulate greater competition from smaller or new market players. A lotting structure may be particularly appropriate in a managed service context where many services are provided.

Conclusion: an increasing awareness of procurement issues

The procedure for challenging tender outcomes, and the remedies available, are unchanged in the new regime. However, there is an increasing tendency for lifesciences companies to take a proactive stance against perceived bad procurement practice in the implementation of all the rules described in this article. It is critical to remember that, in addition to launching formal challenges, companies may raise issues with healthcare authorities through informal approaches, such as pre-tender engagement.

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