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Business Development and Licensing Journal

For the Pharmaceutical Licensing Groups

Maximising value through out-licensing & divestment

The future is now: negotiating in post Brexit Europe

Actavis vs Eli Lilly: UK Supreme Court introduces Doctrine of Equivalents in patent law

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The Right Place to do Business

Welcome

As we move into 2018 there seems to be some small respite from the political instability which was a key feature in the economic landscape during 2017 as the tax reforms progress in the USA. The much anticipated impact of this in terms of deal and acquisition activity is reviewed in the December Deal Watch article from Roger Davies.

With a short pause for the Christmas break, there is, maybe, hope that Brexit will now not continue its domination of the UK headlines. Although there is still no certainty over what exactly Brexit will bring, our contracts need to be able to adapt to cover new commercial circumstances; Andrew Gottschalk takes a look at the negotiation landscape in the article "The Future is Now".

Also reflecting on the fact that we may in the future need to report on different perspectives from Europe and the UK, Alisa Carter from Gowling WLG has provided insight into the landmark case Actavis v Lilly on the doctrine of equivalents explaining the infringement ruling of the UK Supreme Court.

Staying with changes to current practice, updates to the original Lambert agreements are reviewed in our article on the Lambert toolkit. Introduced back in 2004 the Lambert agreements were seen as a means of simplifying negotiations between industry and academia. Finally, focusing on operational aspects, this issue is completed by some insights from AstraZeneca on successful out-licensing and divestments.

I hope that you enjoy reading Issue 26, sending best wishes for a successful and prosperous New Year from all here at the PLG!

Sharon Finch

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2018 European PLG events

Swiss HLG Winter Conference *Reset Partnering - Step out of the Box!* **28th - 30th January** | Flueli Ranft, Switzerland	www.swisshlg.com
11th Annual PLG Business Development Awards *"Best Newcomer and AZ Executive of the Year"* **8th February** | The Law Society, London, UK	www.plg-uk.com
3rd OTCToolbox/PLG OTC Conference *Capitalising on Change Through OTC Innovation & Business Development* **1st - 2nd March** | Hilton London Tower Bridge, London, UK	www.plg-uk.com
PLG UK Introduction Training *In Healthcare Business Development & Licensing* **26th - 28th March** | Marriott Lingfield Park, UK	www.plg-uk.com
PLCD-Basis-Seminar 2018 *In Licensing & Business Development* **28th - 30th May** | Gendarmenmarkt, Berlin	www.plcd.de
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Maximising Value Through Out-licensing & Divestments

Leveraging the core Alliance Management skill sets to effect a smooth and efficient asset transfer

By Steven E. Twait, CSAP and Emma Barton PhD, AstraZeneca

Out-licensing activities are becoming an increasingly important aspect in the business development strategy of many medium to large pharmaceutical companies. However, as with all other deal types, signing the contract is just the first step in the path to maximising the value from the deal. A smooth and efficient transfer of assets is essential to ensure that neither the asset nor the patients it serves, are put at risk.

About the Author

Steven Twait is responsible to shape AstraZeneca's alliance and integration management (AIM) strategy in line with more diverse and varied externalisation deals and to further enhance AZ's AIM capability. Steve is a well published author in Pharmaceutical Executive, PLG's Business Development & Licensing Journal, and Strategic Alliance Magazine and is a board member and treasurer of the Association of Strategic Alliance Professionals.

Emma Barton's key focus within the AstraZeneca Alliance and Integration Management team is divestment transitions, building divestment transition capability and promoting best practice across the enterprise.
Emma joined AstraZeneca in 2000 and has spent over ten years in business development where she had experiences of diverse and varied externalisation deals including: mergers and acquisitions, spin outs, divestments, late stage licensing, early scientific led alliances and collaborations.

Whilst asset transfer between companies is complex and involves activities not commonly encountered by Alliance Managers when managing traditional co-development alliances; the key skill sets and capabilities that underpin the role make them ideally placed to execute transitions and ensure maximum value is achieved for both parties.

A Changing Deal Landscape

At AstraZeneca, business development and partnering forms the bedrock that supports our three strategic priorities of achieving scientific leadership, returning to growth and being a great place to work. We are committed to building strong and strategic partnerships that expedite the availability of innovative and life changing medicines to patients. Through this activity our Alliance and Integration Management (AIM) team has a strong tradition of managing long term collaborations which bring innovation into our business. As AstraZeneca, like many of our peers, has narrowed its therapeutic focus to three core areas, we have found ourselves with a wealth of innovation and important marketed brands that we are no longer best placed to bring most effectively to patients. Externalisation activity has therefore become a vital part of the AstraZeneca business development strategy.

Externalising innovation can be done to great effect through long term collaborative partnerships, especially in the case of medicines which are still in development and where fundamental expertise still resides in the company.

> There may be a significant emotional attachment

Leveraging the capabilities and expertise of multiple partners to share risk and rewards can be a powerful way to accelerate medicines to market, allowing a business to retain an interest and equity in a therapeutic area outside its direct interest. In some cases, the strategy and portfolio of a business can change to the extent that some established or emerging brands would be better served by another company with specialised sales forces or relationships with particular patient groups. The advantages of divesting a product in this way are multiple. Not only can the divested product be brought to a wider patient group and the brand value maximised, the divestment generates upfront revenues that can be reinvested in the seller's core business and also releases personnel and internal resources to focus on priority projects. Both out-licensing and divestment deals therefore have a role to play in any externalisation strategy.

Balancing the clear and significant advantages of out-licensing and divestment deals, however, poses a unique set of challenges. The transfer of assets between company portfolios is complex, and it can take several years to fully achieve the handover, which can include Marketing Authorisations, packaging and manufacturing activity.

The availability or accessibility of asset information can be a substantial challenge, especially for a mature asset where many of the original personnel who worked on it have moved on. Information may be embedded in data systems that have been upgraded several times. For larger organisations which operate in many countries across the globe, information may be held by local company entities. Pulling all the pertinent information and data together to share with the partner can be an immense, time-consuming task.

Adapting to Change

Human risk is a challenge that is often overlooked with externalisation deals – handing over control to a partner, whether it be of single assets or entire business units, is of poignancy for personnel working on the asset(s).

There may be significant emotional attachment to an asset or franchise: the asset may represent a career's worth of research; there may be mixed reaction and response to a deal sparked by a shift in strategic direction, and uncertainty and concern for personal job security with the transfer of assets from a business. In instances where the transfer of personnel or potential redundancies are involved, the sense of insecurity and uncertainty is heightened. Even simple, general uncertainties stemming from first time involvement in transitioning work can potentially spark points of misunderstanding between the out-licensing and in-licensing companies. By its very nature, the process of transitioning a product out of a business successfully will rely on the company's product or franchise experts – those who are personally affected by the change at the point where they are experiencing most uncertainty.

Cultural and operational fit between the two organisations involved is also important. Very often - with divestments, the corporate culture of the buyer and seller is very different. Frequently, the attraction of an asset to the other party is a chance to expand a portfolio or geographic presence and so the two companies are likely to be different from each other in terms of size and operational focus, origin of business and geographical location. All of this raises potential challenges when transferring assets between the businesses. There is also a high likelihood of a key priority discrepancy between the organisations with regard to the asset(s) under consideration. For the buyer, frequently the asset in question will be transformational for their business and rightly afforded highest priority; a new asset entering a company generates a lot of excitement and enthusiasm and has high visibility

with the senior management. For the seller, particularly if it is one with a large portfolio or the asset is a mature product, the asset represents one of a number that the product or franchise experts usually manage; enthusiasm and focus for working on a brand that no longer belongs to the business, or that a partner will be leading on, can wane over time and needs to be carefully managed throughout the transfer.

An Enterprise-wide Approach

People are key to all successful transactions and transitions, and alliance managers are ideally positioned to optimise the experts within their business to maximum effect; not only to add value to the transition activities post-deal closure, but also as a crucial member of the deal team. Alliance teams have an enterprise-wide network. The nature of managing complex collaborations and driving projects with partner organisations ensures that alliance teams are the central hub for the key functional areas across their business and will have strong relationships with foremost figures within those functions.

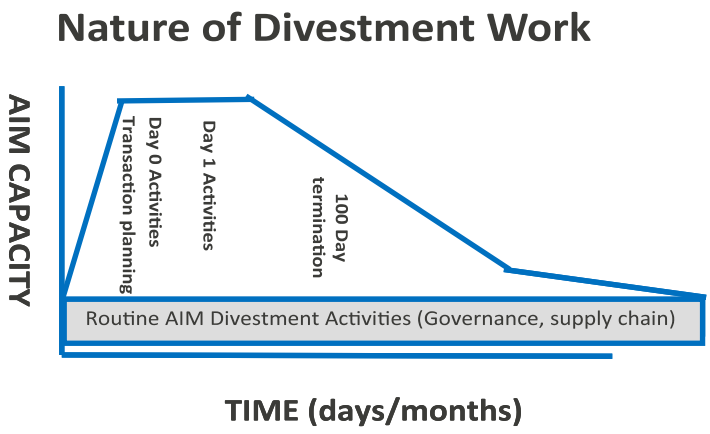
A clear understanding of the asset(s) to be transferred, their strengths and challenges and the likely complexity this will bring to any transition between company portfolios is vital to planning a successful transition and also to influencing early deal documents.

Alliance professionals are strong people managers and typically have a high emotional intellect. This fundamental capability when coupled with an enterprise network makes the alliance manager ideally skilled and well placed to anticipate internal sensitivities across the organisation and to identify and thus mitigate potential human risks for the externalisation.

Alliance professionals have strong internal networks, because they have spent their careers building long-term partnerships with other companies and institutions. This extensive experience of working with different organisations, very often spanning peer pharma, biotech, academic institutions, charitable organisations and governmental interactions means that they are exceptionally experienced to assess the cultural and operational fit between out- and in-licensing organisations. They are able to understand the potential challenges that may occur and plan to mitigate these.

As an alliance manager, one of the key ways to leverage skills and add value to externalisation agreements is to engage early in the deal process. Externalisation activities typically ramp up at a measured pace as transition planning begins, and complete with the maximum level of activity occurring through the first 100 days as the plans are effected and early transitioning begins. As time passes and more activities are handed over to the purchaser, the alliance management workload starts to reduce, tailing off as the last markets transfer and only the manufacturing supply remains.

When an asset is to be transferred from a company portfolio, the timing and pace of activity is within the control of the out-licensing company. Very often a competitive process is initiated which runs to a pre-determined timetable. For the company that owns the asset(s) the target signing and completion date for the deal are therefore generally understood in advance. For the transition manager this is a perfect opportunity to front-load preparation activities and use the time during the deal process to work closely with the deal team. This ensures key planning activities are completed, information transfer activities are started and transition can begin as soon as the deal closes to minimise the time it takes to transfer the business.



Alliance Management from the Outset

The experience, skills and capabilities of the alliance professional have much to offer the deal team, and at AstraZeneca we advocate the **involvement of the transition manager as an active participant in the deal team from the outset**. Thus, they are positioned advantageously to leverage their internal enterprise-wide network to identify the correct functional experts and to coordinate them to understand the product differentiation, competitive advantages and limitations in order to optimise the deal scope and timing of a transaction. The alliance professional as manager for the transition of the asset will need to anticipate the challenges that will arise for the transition team during the planning phase.

Early engagement to make this assessment benefits the transition team by front-loading the activities and the business as a whole by removing duplication of efforts by the deal and transition teams.

Simultaneously, the transition manager is able to advise on deal scope and design, and provide insight to the key issues that need to be addressed in the transitional service and supply agreements, such as complex manufacturing processes or specific country regulatory restrictions.

The alliance manager's in-depth understanding of the interconnectivity between functions, the cross-functional dependency and constraints across those functions, is inherent from managing collaborative alliances. This insight is a rich source of information to a deal team as it is useful for informing the timings and contractual content in order to avoid contractual ambiguity. This is especially true for the **Transitional Service Agreement** where clear and accurate description of the activities that will be carried out by the out-licensing company and the duration of that service is crucial for an efficient post-close execution of the deal.

As with all well-run strategic alliances, governance design is also key to the smooth transition, providing a defined route by which issues can be raised, escalated and resolved between the two organisations. The alliance professional is versed in a variety of governance designs and also experienced in running long term partnerships with organisations of various backgrounds; and therefore is able to ensure a process is adopted which is both robust and practical to execute.

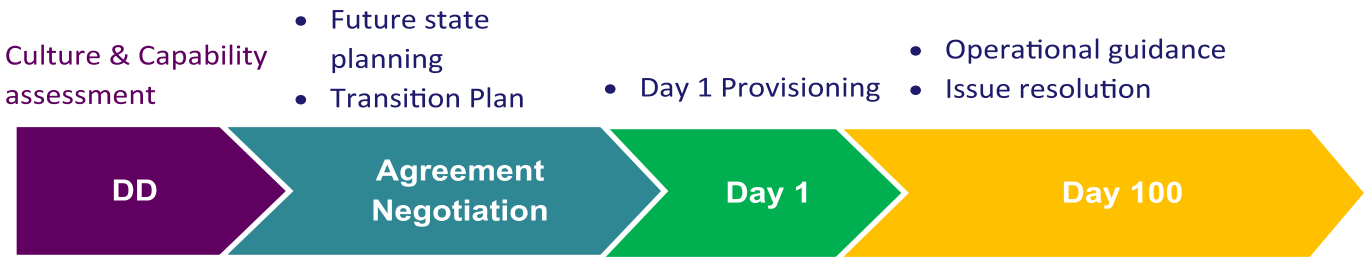
Exposure of the alliance manager to the partner organisation early in the deal process and alongside the deal team is another opportunity to leverage the complimentary expertise of deal and transition experts. They contribute to an understanding of the other party's capabilities. This provides insight for the organisation to allow them to anticipate and plan across the

functions within their business for the resource and support they will need to provide in order to effect the transfer of the asset. It will also further inform the likely duration and scope of the transitional services that will be required. Where multiple companies are in a competitive process for an asset, understanding the relative capabilities of the potential acquirers - and the full impact of this on the seller organisation against its own priorities - can be an insightful differentiator between bidders.

The presence of the alliance manager during early interactions can also add significant value to the transaction process. It can provide the other party with reassurance of the expertise and capability of the organisation to deliver the asset(s) with minimal impact and disruption. This is especially true when an in-licensing organisation is using the asset to significantly increase its geographical footprint.

The value of externalising products can be realised fully by ensuring a well planned and executed transition of assets between companies. This can only be achieved with strong collaborative and active management of the transition by alliance professionals in both organisations.

Ensuring a smooth handover



Building Lasting Relationships

Transition team on-boarding, a core activity familiar to any alliance manager, is an important first step to reducing the human risk of an externalisation deal. It is key that the company strategy and decision-making leading to the externalisation are well understood. Roles and responsibilities must be clear and there should be a good understanding among all involved of the complexity of the agreement, cross functional dependencies, likely challenges to overcome and duration of involvement so that functional planning can begin across the wider organisation.

Engagement with the buyer transition team is essential to the planning process and as deal negotiations progress, transition managers from both organisations can use the time to align on principles for transfer, agree rules of engagement between their teams and confirm governance design.

At AstraZeneca we consider a face-to-face kick-off meeting between transition teams an essential starting point and the single most effective way the alliance professional can mitigate the human risk of the deal. A meeting held over two days removes time pressures, allowing ample opportunity for joint briefing and alignment of transition teams, functional breakout sessions and wider cross-functional discussion between teams. It also allows for some social interaction. The

> “Communication is at the heart”

time is formally used for high-level cross-company planning to pave the way for more detailed plans through subsequent regular functional meetings between companies.

The single most important objective though, is to **allow the functional team members to start to build a close relationship with their counterparts**. It is essential to a smooth transition of assets that when issues and challenges arise, our functional colleagues feel comfortable engaging in open and frank dialogue to find resolutions collaboratively. Again, early engagement is critical to maximising the impact of the activity and something we seek to do ahead of deal closure to ensure that when day 1 arrives, the transition teams have completed as much of the planning as possible and can start to act on those plans immediately.

As time progresses beyond day 1, the role of the transition manager moves from operational guidance to ensuring that the teams remain aligned and focused on their deliverables and timings, tracking the progress of the transfer against the TSA timings. Not all organisations have the benefit of an alliance management capability and one of the necessary value-adds that an alliance management professional can bring is flexibility and a collaborative approach to driving results. A good alliance manager will spot the gap in alignment within their partner organisation. They will then use their own expertise and a fair and balanced approach to galvanise both company transition teams into a collaborative approach to transition. By driving key cross-functional and cross company alignment, they ensure that transition occurs smoothly and at the optimal times.

Communication is at the heart of alliance management and is no less important in the externalisation arena; the transition manager can play an important role in issue resolution, representing the first stage in the escalation process. Their internal and external networks can serve well to leverage the learnings of others and help inform of potential solutions or propose alternative options. In this position they can play a useful role in briefing senior management and stakeholders, ensuring that they are updated on progress and achievements of the transitioning team. This communication leverages the senior management to help remove any internal barriers or to hold high-level cross company discussion to promote resolution if required.

Winding Down with Purpose

It can be difficult to determine where a transition ends; different functions across the business will hand over their activities supporting the transferring asset at different times. For some, the involvement is an intensive few months; for others, dependent on market authorisation transfer or manufacturing set up, involvement can be several years. So when the transition is finally complete, for how long should specific functional contacts remain in place to answer any arising queries?

Practices common to long-term partnerships and alliances sign-off translate well to the transition wrap up scenario, differing predominantly in timing of the wrap up. In the alliance setting, wrap up typically happens for differing functions in parallel; with an externalisation agreement, the timing of handover varies so widely that a formal sign-off on a function by function basis giving an appropriate time for final wrap up questions is most effective.

This guarantees that both parties are certain of the deadline to ensure everything has transferred and follow up on any queries; the externalisation functional lead can formally hand over and redeploy their time to other

projects; and both parties are clear on the circumstances under which further information requests are appropriate and how to do so if required.

One of the many benefits to specifying a wrap up and formal sign-off on a function by function basis is that it allows for a timely review of the transition for that function, a chance to capture lessons learned and to memorialise them in a central corporate 'memory' within the alliance management and integration team. It is also an important chance to recognise that success and reward personal achievement. One of the challenges for the alliance professional managing an outbound transition is the level of enthusiasm in their organisation for working on an asset that is no longer managed by their organisation.

At AstraZeneca we have worked hard to ensure that the value externalisation work brings to the business is clearly understood throughout the organisation, and that individuals who contribute positively and are instrumental to the smooth transitioning of assets are recognised at senior management level. We try to affirm that the experience of working on a transition is valued as an opportunity for personal development and make the experience a positive one. Through this approach we have cultivated an enthusiasm for externalisation work with many people willing to work on subsequent externalisation projects. This has allowed us to embed transitioning capability across our organisation and to generate a community of functional transitioning experts which will allow us to execute future externalisation agreements, learning and improving with every deal.

AstraZeneca

11th Annual PLG Workshop, Dinner and Business Development Awards Evening

8th February 2018

The Law Society, London

Event Highlights :

The **Medius Deal Watch Team** - "The 2017 Deal Watch Environment", review and insights plus an outlook into 2018 and beyond.

Andrew Dean - "Cheques & Drugs and Change of Control", an interesting look at Divestment case histories.

Dr Paul-Peter Tak, Senior Vice President R&D Pipeline, Global Development Leader and Chief Immunology Officer at GSK - As the after-dinner speaker, Dr Tak will be enlightening the audience with his vast industry experience and time presenting on Dutch TV!

Finishing the evening in style - the **PLG Business Development Awards 2017** :

Categories : **AstraZeneca Business Development Executive of the Year -** nominate **here**

The PLG Best Business Development Newcomer of the Year - nominate **here**

If you are interested in attending this event, please contact Adam Collins **admin@plg-uk.com** or visit the website - **www.plg-uk.com/awards**

The Future is now:

Negotiating in Post-Brexit Europe

By Andrew Gottschalk, Group AG

In the UK we are, for good reason, consumed by the politics of Brexit. Our attention is locked onto the management of the exit process and specifically the terms on which we leave the European Union. Different visions of our national economic and political future clash in the media. For those engaged in pharmaceutical business development this torrent of words and print may appear both irrelevant and threatening. National and international politics are somehow "out there". Within our organisations projects are starting, being developed or nearing completion so what are the negotiating impacts?

About the Author

Andrew Gottschalk (Group AG) works as a negotiator, consultant and educator. His clients include governments, state agencies, corporations and not for profit organisations. His practice is Europe, North America and in Asia having been based in Singapore.

He wrote the PLG University of Manchester module on Negotiating. At Partnership Capital, with Greg Watson, he works with companies that have innovative technology platforms.

Linking macro and micro behaviour is not a task for the faint hearted. Yet the negotiator, both implicitly and explicitly, inhabits both environments. As a social psychologist working on negotiating and culture I am now deliberately extending the envelope of my ideas. I will be locating the negotiating process, national and organisational culture within the context and dynamics of a specific international political negotiation, Brexit.

Here is the rationale:

> "Overall, the impact on pharmaceutical research in the UK would be immediate and adverse. In practice, large pharmaceutical companies would have to plan well in advance for such an eventuality, which would presumably mean moving some or all of their research and development activities"
>
> (*Cost of No Deal: The UK in a Changing Europe*, King's College & ESRC, London 2017, p17)

This is our world of pharmaceutical business development. We are part of it. We know it, own it and live it. It is happening now! As practitioners of the dark arts and science of negotiating we will have developed our own perspectives but on a day-to-day basis we need to "keep calm and carry on".

In order to place some boundaries on this review a number of countries were selected by reference to The Pharmaceutical Industry in Figures published annually by EFPIA. Three criteria were used: R&D, employment and production. Denmark, France, Germany, Italy and the United Kingdom emerged. Switzerland, although not a member of the European Union was added because of its obvious significance.

We will begin with a perspective on Brexit itself and the description of the process being "a divorce" albeit complex. This will be followed by a behavioural analysis at an organisational level that is the more specific context for our negotiations. We will end with some observations on the national negotiating cultures of the six countries listed earlier.

Brexit is not a divorce: its politics stupid!

As individuals and citizens we often know more than we wish to acknowledge, in public or in private, about relationships and divorce. "Using the divorce analogy can at best be distracting and potentially very harmful because it glosses over both the short and long-term consequences".

In a divorce the interaction between the parties is often driven by a denial of what we know from our professional lives. Negotiate over interests not positions, identify and negotiate multiple issues simultaneously, understand the other party's interests and constraints, analyse the negotiating space and finally don't try to beat the counterparty. From our negotiating encounters we know how to avoid irritators. "Constructive ambiguity" is not constructive.

Brexit is not a divorce and the analogy is unhelpful. Family relationships are different because they embody biology and continuity not democracy. Long-standing relationships have ingrained paterns. Individuals develop and play certain roles within a family that become fixed and also limit current and future interaction. Power and social norms derives from these roles. A divorce transforms and redefines this power. Brexit will redefine the political and economic power of the UK.

Brexit is, not will be

We need to start from a stark and contrary perspective. Brexit has already taken place. Talking and writing about Brexit as a future event or process is not only wrong but naive and dangerous. Brexit has happened. March 2019 will be an explicit milestone in the redefinition of UK's relationship with the European Union and the larger global economy.

The Brexit vote has broken the key psychological contract that underpinned many of our previous agreements. They have been replaced in a referendum that demands total obedience to its outcome. The 52:48 outcome has acquired the significance of a statement of unquestionable faith. It is a dogma. To doubt or question its legitimacy is to invite the opprobrium that meets the unrepentant sinner. This single act, a referendum vote, has irrevocably transformed a complex network of business relations and agreements.

The psychological contract, as a concept is a trade-off between three equally significant factors: flexibility, equity and control. As we construct agreements in our personal and public domains most frequently we are unaware of the dynamics of this contract for the very obvious reason that it is implicit. It is rarely written but always referred to in the event of the deal failing. Brexit redefines the content of deals and questions the value of existing relationships.

Brexit, as a process is a series of linked negotiations where the carry-over of unresolved items and the spillage of psychological hurt will limit the quality of the succeeding outcomes at multiple levels. This is a very real trickle down!

Fear and loathing

We are now in a world of fear and consequent loathing. Extreme words perhaps but they serve to identify the psychodynamic context of our present and future negotiating environment. The business development negotiator may be a "remainer" or have been excluded from voting because of nationality but as a representative of a UK based company they are now a member of the out-group having previously been "one of us". We have decisively moved away from merely being semi-detached to being independent or at worst isolated.

Brexit, for a negotiator, can be experienced in many ways. From our experience of sour deals we can see, hear and feel some of the signals:

- Deal optimism is replaced by doubt, cynicism and anger
- Problem solving and trust is replaced by literal interpretation, unilateral risk management and legalism
- Open flexible communication is stranded by a tide of formalization
- We hear the language of defend-attack spirals and blame
- Social distance and social barriers re-emerge through agendas, formal minutes and over-zealous time management
- Organizational processes and the re-emerging cult of privacy block enthusiasm, our sense of ownership and identification with project success
- Second and third generation transactions that were being explored have been delayed of, even worse, disappeared
- Individuals with whom we had established a robust relationship and trust are now required to explore and build alternatives. They are required to disengage without appearing to abandon us.

The bigger challenge for us, as individual negotiators, will be recalibrating our previous relationships. At worst, finding new partners and constructing new relationships. There may be ideologues and optimists amongst us who will welcome the new commercial environment post March 2019 with enthusiasm. However for the majority our concern will be to identify, protect and promote the agreements and the relationships that we have built.

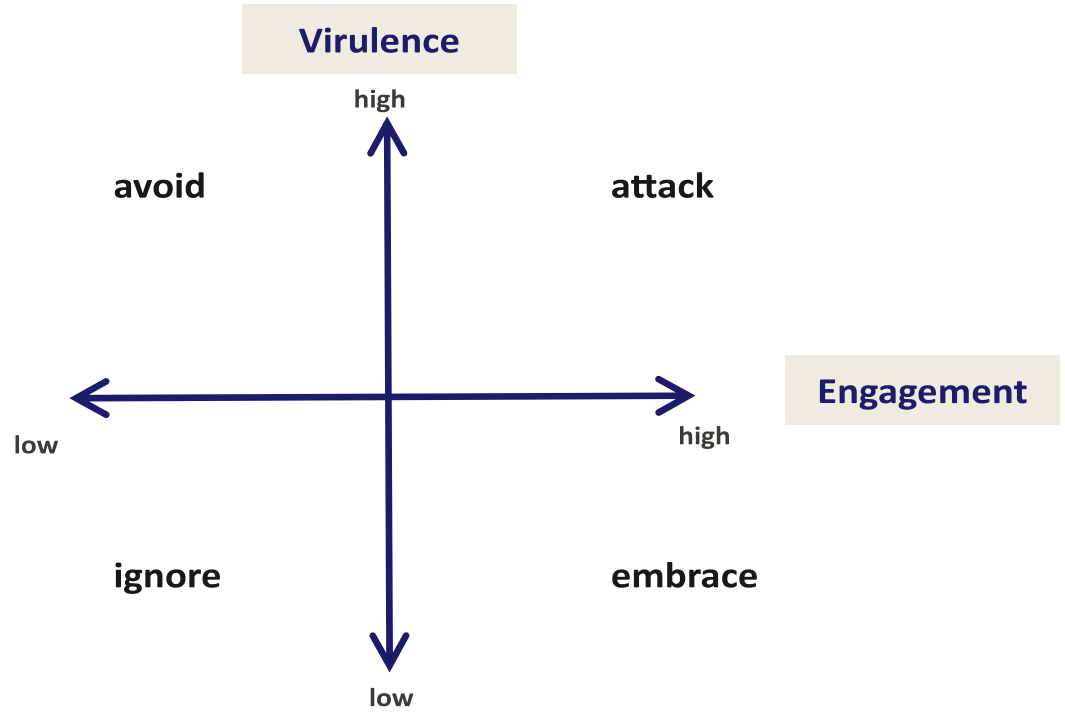
Before we can explore the cross-cultural negotiating impacts and implications of Brexit we need to design a simple and robust typology that we can use in planning for our upcoming post-Brexit encounters.

The Psychological Responses: from different to not one of us

Both at the national macro and the micro organisational level we can expect to encounter these four clusters of behaviour. For the UK political representative or the civil servant they are perhaps less obvious because the European Union is represented by the Commission. Their Agent (Michel Barnier) has a decisive impact in mediating or disguising the " behavioural" responses of national governments.

The UK government wish to circumvent the Agency role but will continue to be blocked because intra-party unity between the Commission, the President (Jean-Claude Juncker), the Council President (Donald Tusk), the European Parliament and the national capitals is a critical one-time strategic and process asset that cannot easily be rebuilt.

A two dimensional model of counterparty psychological responses to Brexit*



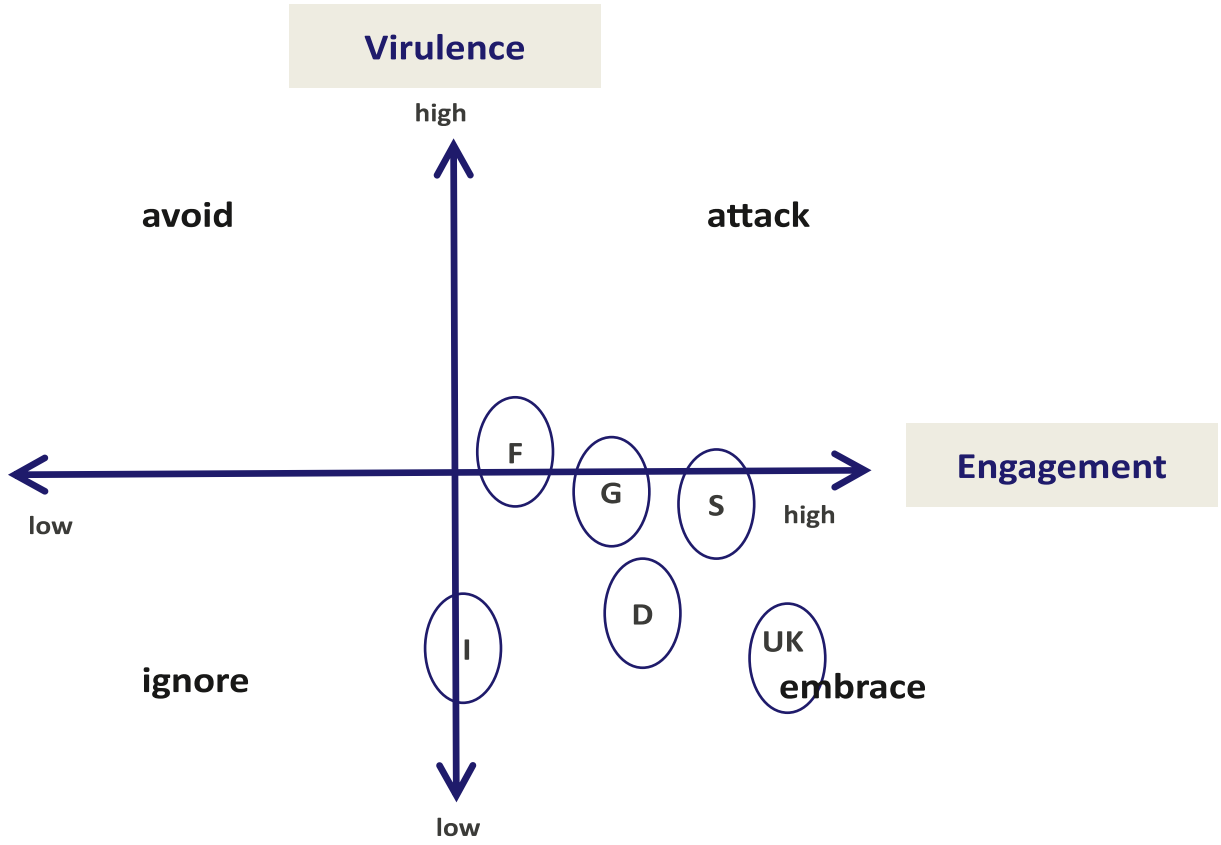
** adapted from Burns CT & Rempel JK, Me, myself and us, 2008*

In our business development encounters there is no Agent to protect us from ire and frustration of the counterparty. We are the representatives from that Brexit voting country and now we are the problem! In many situations since June 2016 it has become increasingly legitimate in psychological terms to project most, if not all, negative feelings on "the Brits." It is a remarkably short journey from being a valued contributing member to becoming the scapegoat. We have moved from being different to "not one of us"

Locating the national actors

Using managed information, such as government position papers and secondary sources we will "place" the six national actors within our two dimensional model.

There is an elephant in the room! The European Commission and mandate given to Mr Barnier suggests that they are firmly in the Attack quadrant because they are the Secretariat. They are the disciples who now must negotiate with the new out group of one (sinners?). The reality is that public posture and private negotiating are the reality. However they can and will shift to the Embrace quadrant once the political stars are aligned. Money talks!



The challenge facing the UK based negotiator is how to move from the "political" to the commercial in one step. The response to our counterparty cannot be "please don't blame me". Guilt by association is a universal psychological trait. Our challenge will be to identify where the agreements that underpinned our working relationship require adjustment to a new reality. For example, at a strategic level where will the partners undertake Phase 3 trials within the new EU framework. The intended transfer of *acquis* into UK law is promised but it remains in the legislative process. Uncertainty is dynamic and impacts both parties differentially.

Developing our Negotiating Options

How do we respond? There are two equally unattractive options. In some instances we can appeal to an authority figure (corporate head office) or plead mitigating circumstances. However it is unlikely that we can easily design and develop an integrative, win-win outcome given that the options for mutual gain have been so severely constrained by uncertainty.

The second option is to identify an external opportunity or threat that should justify a shift away from these attacks. For example, the continuing needs to manage relations with the FDA or EMA. We know that Brexit will adversely impact clinical trials including cross-border clinical trials currently in progress.

Some indicative counterparty Brexit response behaviours

	Ignore	Embrace	Attack	Avoid
Emotions	apathy	empathy	anger	fear
Behavioural intent	evasive	stay calm	fight	flight
New information demands	no	yes	yes	no
Engagement	avoid	active / strategic	tactical / positional	avoid
Established scientific criteria	continue	review	enhance	continue
Operating financial criteria / rules	slow drift	planned review	improve	continue
Governance	inactive	active	variable	informal
Stakeholders	ignored	engaged	political	reactive

A test of a good agreement is that both parties would want to repeat the deal. We should have confidence in, and be committed to, what we have achieved.

Brexit provides us with an opportunity to review our existing agreements and identify areas for improvement. For example the governance clauses of many agreements are often "tagged on" during a period of exhaustion as the final details are settled. Boilerplate clauses were included as a substitute for an investment in understanding the needs of our counterparty. Experience reminds us that transactions take longer than planned and are usually late!

Our existing agreements are a source of information about our negotiated relationships. Starting with an internal review that identifies areas that require no change alongside those items for potential change. This exercise must encourage us to "think both sides of the line" as Brexit has consequences for both parties. They are not always equal.

We must not allow the Brussels dance to paralyse either our thinking or constrain our negotiating planning. Now is the time to begin the talks about talks. Herding cats will become a required skill. For the representative from a young cash constrained innovator the threats are almost immediate. For the established national champion or global operator Brexit could be either an irritant or the trigger for a strategic review that is outside our personal remit or above our pay grade. This process of attitudinal structuring can begin to prevent a drift to zero sum outcomes.

The Attack response may indicate that your counterparty negotiator is under internal organisational pressure from opportunist or disaffected stakeholders. We need to know and understand their stakeholders if they are to develop a mandate that will survive for the duration of the negotiations. That stakeholders' perceptions may shift or that new stakeholders will emerge is something that has to be understood by both parties. For example the often silent or excluded representatives from operations and the supply chain management.

An open discussion may also reveal that future negotiations need to give more attention to the intra-organisational dynamics than was previously needed. Their internal communication processes and the demands for accountability exert continuous pressure on them as representatives of their parties. The naive optimism of the internal audiences who chant "they need us" has to be transformed into the art of the possible and the practical.

DADA

What follows is not a discussion about the German art movement of the Twenties but a mnemonic that we should use in thinking through how we will deal with the involuntary sour deals created by Brexit.
We will need to work through four stages:

- from **D**enial that we have a problem
- to **A**cceptance that we have a problem
- to **D**ecide on strategic action
- to taking **A**ction

At work Brexit either dominates conversations or it is studiously avoided. Leavers suppress buyer's remorse. Remainers, struggle to avoid exposing anxiety. Denial must be confronted. A frequent response is delay. The dynamics of the political situation justify inaction however we know that our counterparties are experiencing anxiety. The destruction of our psychological contract impacts both parties but a problem delayed is not a problem solved. We have to open talks and indicate a willingness to renegotiate now because a failure damages our credibility.

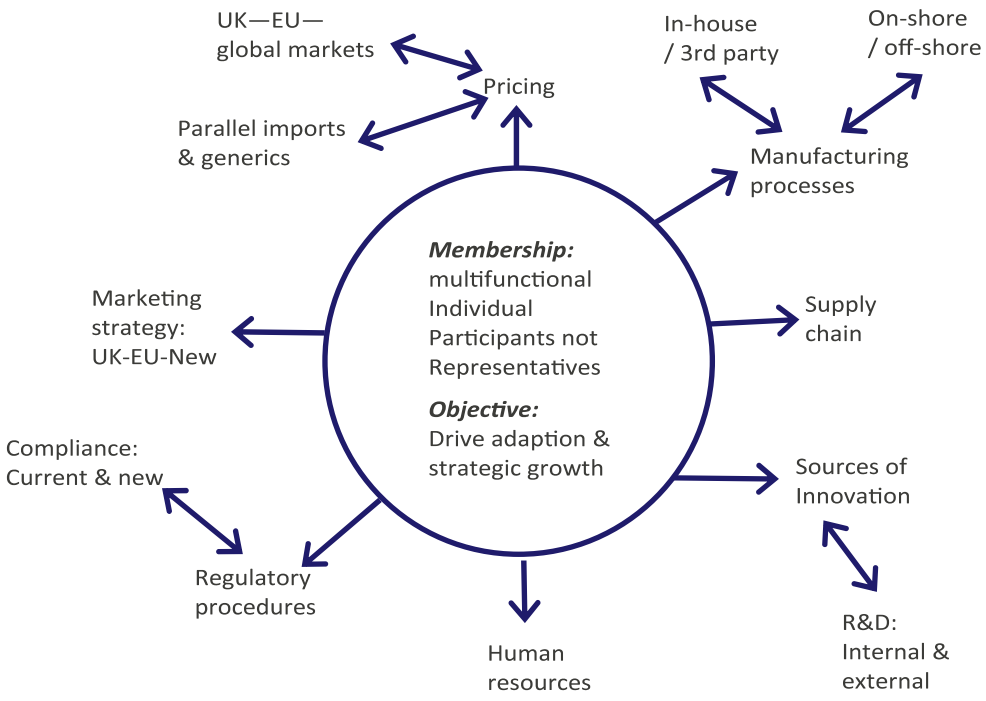
We have to build acceptance within our function, business development and within the totality of our organisation. A model for the mobilisation of our organisation to respond to Brexit comes from Quality Circles and Toyota Lean Production. Many organisations continue to engage groups in the task of improving organisation performance. Brexit requires a similar response: Brexit Circles (see below). They can drive culture change and build commitments that cannot be achieved by edicts and plans generated in the C-suite.

One benefit from Brexit Circles is that as negotiators we can have greater confidence that we have surfaced and explored most of our internal organisational issues. Intra-organisational bargaining and stakeholder management should now be less of a problem going forward.

The use of Brexit Circles does not absolve us from the requirement to design and implement the strategy but a process based on inclusive discussions and consensus is attractive internally. It also demonstrates to our counterparty that as an organisation we are accepting and processing the consequences of our responsibilities in the unilateral destruction of the psychological contract.

Action for the negotiator, as a representative, means that we must avoid rancour and recrimination. The review of our new situation, characterised by bilateral uncertainty and ambiguity, suggests we must focus on building the common ground between the two parties. Our previous agreements were effective and delivering benefits to both parties.

The Brexit Circle: Membership & Issues

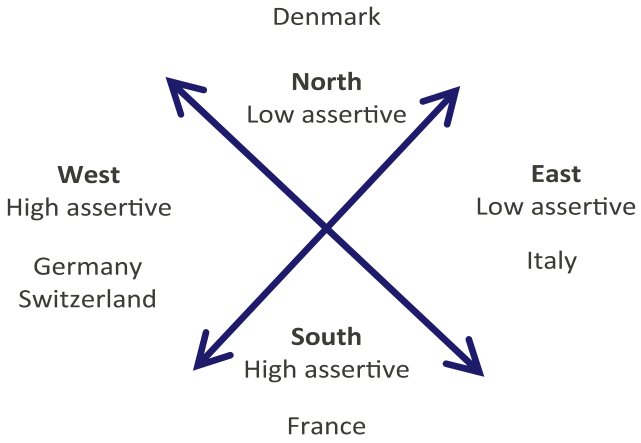


Brexit is a learning opportunity! For learning to occur we need, initially, to unlearn previously correct responses. This is a discovery process and could be a joint activity. This could be an early stage in reconstructing a broken psychological contract.

The Company Culture Context: using the Compass Model

In her monograph *Managing Cultures: making strategic relationships work* Wendy Hall presents an elegant model that is particularly appropriate to developing our negotiating response in the context of our post-Brexit negotiating environment. Using two dimensions of assertiveness and responsiveness we are able to comfortably locate five of our six national counterparties. For Denmark there was less data available so there is an element of a force fit. The particular strength of Wendy Hall's work is that it s based primarily on extensive work within individual European companies or the European affiliates of US and Japanese companies.

The Compass Model (W. Hall 1995)



Having provided a location tool Hall provides additional behavioural indicators that we can identify from our encounters.

The Social Behaviours of the our Cultural Styles in the Compass Model

North cultural style	**South cultural style**
more quantitative	move boldly ahead
more cautious / indecisive	more challenging targets
more factual	intense pace of action
more precise	more unpredictable
more task focus	quick moving
more consistent	individualistic
West cultural style	**East cultural style**
factual	sensitive
individualistic	loyal
demanding not giving	compromising
taking control & pushy	trusting
authoritative	value harmony
unpredictable	group / team players

Before transitioning from the corporate cultural environment in which our negotiations take place to national negotiating cultures we should remind ourselves of some of the cultural factors that an integral component of our encounters.

Negotiating is cognitive decision-making. We bring our biases to the table:

- fixed pie, with the assumption that interests are diametrically opposed
- self-serving perceptions of fairness & competitive behaviour
- dispositional attribution biases & errors
- group serving biases & hyper-competition between groups

Brexit is and will continue to be a major disrupter in the evolution of the European pharmaceutical sector. In a previous article on individual negotiating styles our data showed that this sector shares many characteristics with the oil and gas sector. The negotiating style profile of two science based innovative industries, with long lead times, similar major capital requirements and risk profiles suggests the mix of competitive and collaborative relationships will accommodate the structural political and economic turbulence that is our present negotiating environment.

Actavis vs. Eli Lilly: UK Supreme Court introduces Doctrine of Equivalents in Patent Law

By Pat Duxbury, Partner, and Ailsa Carter, Professional Support Lawyer, IP at Gowling WLG

In a landmark decision, *Actavis v Eli Lilly* [2017] UKSC 48, the UK Supreme Court has re-steered the law of patent infringement in the UK, stating that there is a doctrine of equivalents, and expressly permitting recourse by the courts to the prosecution file in appropriate limited circumstances.

As a result of the Supreme Court's ruling, Actavis' proposed pemetrexed medicines were found to infringe, directly and indirectly, Eli Lilly's European patent no. 1,313,508 ("EP '508"), which has claims directed to pemetrexed disodium in combination with vitamin B12 for cancer treatment.

About the Authors

Patrick Duxbury helps clients to research, develop, manufacture and sell pharmaceutical, biotech and medical device products, using his extensive experience of structuring and executing transactions in the life sciences sector. He specialises in all aspects of transactional work in the life sciences sector.

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Background to the claim

Actavis sought from the UK court a declaration of non-infringement in respect of a number of pemetrexed compounds used together with vitamin B12 for cancer treatment. The pemetrexed active ingredient in those products ("the Actavis products") was (a) pemetrexed **diacid**, (b) pemetrexed **ditromethamine**, or (c) pemetrexed **dipotassium**.

EP '508 contained the following claim:

> *"1. Use of **pemetrexed disodium** in the manufacture of a medicament for use in combination therapy for inhibiting tumour growth in mammals wherein said medicament is to be administered in combination with vitamin B12 or a pharmaceutical derivative thereof [which it then specifies]."*

Claim 1 was in Swiss form (i.e. use of X in the manufacture of a medicament for the treatment of Y). Claim 12 was, essentially, to the same subject matter but in purpose-limited product form (i.e. X for use in the treatment of Y). The form of the claim language was not material to the outcome of the dispute and the Supreme Court's reasoning focused upon claim 1.

Direct infringement

Three famous decisions have developed and defined the law on patent infringement in the UK in recent decades: *Catnic Components Ltd v Hill & Smith Ltd* [1982] RPC 183, *Improver Corpn v Remington Consumer Products Ltd* [1990] FSR 181 and *Kirin-Amgen Inc v Hoechst Marion Roussel Ltd* [2005] RPC 9.

For the last decade, the most influential decision has been that of the House of Lords in *Kirin-Amgen*, in which Lord Hoffmann said, essentially, that issues of infringement could be resolved by adopting a 'purposive' construction to the language of the patent claim, so giving effect to "what the person skilled in the art would have understood the patentee to be claiming".

The role of the House of Lords as the highest appeal court has since ended; the Supreme Court of the UK has, since 1 October 2009, been the highest court of appeal for all civil law cases in the UK. Now, in *Actavis UK Limited & Ors v Eli Lilly and Company* [2017] UKSC 48 (12 July 2017), the leading Justice of the current generation, Lord Neuberger (with the agreement of the other four Justices), respectfully rowed back from Lord Hoffmann's judgment in *Kirin-Amgen*.

In the Supreme Court, Lord Neuberger went back to first principles, beginning with the legislative provisions, the critical text being that of Article 69 of the European Patent Convention (EPC) and the Protocol on its interpretation.

This, said Lord Neuberger, meant that ([54]):

> *"…a problem of infringement is best approached by addressing two issues, each of which is to be considered through the eyes of the notional addressee of the patent in suit, i.e. the person skilled in the relevant art. Those issues are: (i) does the variant infringe any of the claims as a matter of normal interpretation; and, if not, (ii) does the variant nonetheless infringe because it varies from the invention in a way or ways which is or are immaterial? If the answer to either issue is "yes", there is an infringement; otherwise, there is not."*

Lord Neuberger explained that issue (i) self-evidently raises a question of interpretation, whereas issue (ii) raises a question which would normally have to be answered by reference to the facts and expert evidence. The difficulty with Lord Hoffmann's approach in *Kirin-Amgen* was that it conflated the two issues. This was wrong in principle and, therefore, could lead to error. Issue (ii) involves not merely identifying what the words of a claim would mean in their context to the notional addressee, but also considering the extent if any to which the scope of protection afforded by the claim should extend beyond that meaning.

Lord Neuberger explained that issue (i), the question of whether the variant infringes any of the claims as a matter of normal interpretation, requires the application of the normal principles of interpreting documents. In the UK these were recently affirmed by Lord Hodge in the Supreme Court in *Wood v Capita Insurance Services Ltd* [2017] UKSC 24 (paragraphs 8 to 15).

The authors note that the court is required to establish the skilled addressee's understanding of what the author of the patent meant by using the words of the claim in the context of the specification. However, and importantly, this does not involve consideration of the *Improver* questions, either as originally phrased or as re-formulated by Lord Neuberger.

Issue (ii) poses more difficulties of principle: what is it that makes a variation “immaterial"? In this context, Lord Neuberger considered that the three questions formulated by Hoffmann J (as he then was) in *Improver* (which pre-dated Kirin-Amgen), provide helpful assistance but needed some reformulation. He proceeded to undertake the reformulation, saying that the reformulated questions remain only guidelines, not strict rules, and that they may also sometimes have to be adapted to apply more aptly to the specific facts of a particular case. The reformulated questions are:

1. Notwithstanding that it is not within the literal meaning of the relevant claim(s) of the patent, does the variant achieve substantially the same result in substantially the same way as the invention, i.e. the inventive concept revealed by the patent?
2. Would it be obvious to the person skilled in the art, reading the patent at the priority date, but knowing that the variant achieves substantially the same result as the invention, that it does so in substantially the same way as the invention?
3. Would such a reader of the patent have concluded that the patentee nonetheless intended that strict compliance with the literal meaning of the relevant claim(s) of the patent was an essential requirement of the invention?

Lord Neuberger clarified:

> *"In order to establish infringement in a case where there is no literal infringement, a patentee would have to establish that the answer to the first two questions was "yes" and that the answer to the third question was "no"."*

Lord Neuberger explained that in the **first reformulated question**, the emphasis is on how "the invention" works. The court should focus on "the problem underlying the invention", the "inventive core" or "the inventive concept" as it has been variously termed in other jurisdictions.

Compared with the original first *Improver* question, Lord Neuberger's re-wording crucially shifts the focus away from assessing the invention as set out in the claims towards identifying the inventive concept of the patent.

Lord Neuberger explained that the **second reformulated question** should be asked on the assumption that the notional addressee knows that the variant works to the extent that it actually does work. He considered this a fair basis on which to proceed in light of the factors identified in article 1 of the Protocol and the fact that the notional addressee is told (in the patent itself) what the invention does. Lord Neuberger noted that this approach was consistent with that taken by the German, Italian and Dutch courts.

> no reason why the variant should not infringe the original patent

Compared with the original second *Improver* question, this is a lowering of the burden on the patentee seeking to establish infringement. In the original question the patentee needed to establish that it would have been obvious, at the date of the publication of the patent to a reader skilled in the art, "that the variant has no material effect". This required the addressee to figure out *whether* the variant would work.

Lord Neuberger said that the facts of the *Actavis v Eli Lilly* case illustrated why this was too strict a test: because a chemist would not be able to predict the effect of a substitution for the sodium counter-ion without testing at least the solubility of the active ingredient in the Actavis products, it was not possible to predict in advance whether any particular counter-ion would work. However, salt screening was a routine exercise in determining suitability, and the chemist would be reasonably confident that he would come up with a substitute for the sodium counter-ion. In those circumstances, given that the inventive concept of the patent was the manufacture of a medicament which enabled the pemetrexed anion to be administered with vitamin B12, the application of the original second *Improver* question failed to accord "a fair protection for the patent proprietor" as required by article 1 of the Protocol.

Lord Neuberger also said that the reformulated second question should apply to variants which rely on, or are based on, developments that have occurred since the priority date, even though the skilled addressee is treated as considering the second question as at the priority date. There is also no requirement for the variant *not* to be inventive – it may be that the infringer is entitled to a new patent, but that is "no reason why the variant should not infringe the original patent".

Regarding the **third reformulated question**, Lord Neuberger made a number of points:

- Although the language of the claim is important, consideration is not excluded of the specification of the patent and all the knowledge and expertise which the notional addressee is assumed to have.
- The fact that the language of the claim does not on any sensible reading cover the variant is not enough to justify holding that the patentee does not satisfy the third question. In other words, the fact that the variant is not within the "normal interpretation" of the claim and so does not infringe pursuant to limb (i) does not prevent the skilled reader of the patent from concluding that the patentee did not intend that strict compliance with the literal meaning of the claim was necessary, and therefore from concluding that the variant infringes pursuant to the doctrine of equivalents.

  (The authors note that this is common sense; if it were otherwise, it is difficult to imagine any scenario in which the doctrine of equivalents might be found to apply).
- It is appropriate to ask if the component at issue is an "essential" part of the invention, but that is not the same thing as asking if it is an "essential" part of the overall product or process of which the inventive concept is part. In Lord Neuberger's view, in the *Improver* case, Hoffmann J "may" have wrongly considered the latter question.
- When one is considering a variant which would have been obvious at the date of infringement rather than at the priority date, it is necessary to imbue the notional addressee with rather more information than he might have had at the priority date.

Proceeding to consider whether the Actavis products would infringe EP '508 pursuant to limb (ii), Lord Neuberger tentatively concluded that the doctrine of equivalents did indeed apply. However, before deciding the point conclusively, he turned to the issues in the case regarding the prosecution history of EP '508.

Recourse to the prosecution file

In support of its case of non-infringement, Actavis relied upon the prosecution history of the patent. This gave rise to a question of general application: whether, and if so when, is it permissible to have recourse to the prosecution of a patent when considering whether a variant infringes that patent?

Lord Neuberger concluded that the UK courts should adopt a "sceptical, but not absolutist, attitude" to a suggestion that the contents of the prosecution file of a patent should be referred to when considering a question of interpretation or infringement, along substantially the same lines as the German and Dutch courts. He explained that his "current view" was that reference to the file would only be appropriate where:

"(i) the point at issue is truly unclear if one confines oneself to the specification and claims of the patent, and the contents of the file unambiguously resolve the point, or

(ii) it would be contrary to the public interest for the contents of the file to be ignored."

Lord Neuberger said that the second type of circumstance "would be exemplified by a case where the patentee had made it clear to the EPO that he was not seeking to contend that his patent, if granted, would extend its scope to the sort of variant which he now claims infringes". Turning to the prosecution file of EP '508, the examiner had rejected claims using "antifolate" terminology for reasons of disclosure and clarity (Articles 83 & 84 EPC). In response, Lilly proposed amended claims using the word "pemetrexed". The examiner objected to these claims on the basis of added matter (Article 123(2) EPC), saying there was no basis for such terminology because pemetrexed was a distinct compound from pemetrexed disodium. Reserving its position, Lilly filed new claims using "pemetrexed disodium" wording and the application proceeded to grant.

Lord Neuberger said that, although it was unnecessary to decide the issue, in his view the examiner had been wrong to take the view that the patent should be limited to pemetrexed disodium because the teaching of the patent did not expressly extend to any other antifolates. However, even if the examiner was right or at least justified in taking the stance that he did, this did

not have any bearing on the question of whether any pemetrexed salts other than pemetrexed disodium should be within the scope of the patent pursuant to the doctrine of equivalents. Lord Neuberger said ([89]):

> *"The whole point of the doctrine is that it entitles a patentee to contend that the scope of protection afforded by the patent extends beyond the ambit of its claims as construed according to normal principles of interpretation."*

So the contents of the prosecution file did not justify departing from the preliminary conclusion that the Actavis products directly infringed claim 1.

Conclusion on direct infringement

Accordingly, Lord Neuberger concluded that the Actavis products would directly infringe the UK designation of EP '508.

Indirect infringement

Finally, Lord Neuberger confirmed the conclusion of the Court of Appeal (over turning Arnold J) that the Actavis products also indirectly infringed the UK designation of EP '508.

The expression "pemetrexed disodium" was not limited to the solid, or crystalline, chemical. Accordingly, even if pemetrexed dipotassium would not of itself infringe if it was administered with vitamin B12, at least provided that the ratio of sodium ions to pemetrexed ions was at least 2:1, there would be infringement when it was administered in saline solution, because the solution would contain pemetrexed disodium.

Comment

The UK Supreme Court's judgment in Actavis v Eli Lilly marks the most significant development in UK patent law for decades.

Apparently aligning the UK law of infringement more closely with that of Germany, the (re-) introduction of a doctrine of equivalents can be expected to assist patent proprietors in defending their monopoly against immaterial variants, to reduce the incidence of inconsistent conclusions on infringement as between the courts of the UK and those of other major EPC jurisdictions, and to smooth the way for the harmonisation of the law regarding infringement expected with the coming into force of the Unified Patent Court.

Also importantly for patentees, the existence of a doctrine of equivalents potentially provides greater wriggle room, when seeking an effective and meaningful scope of protection which is also justified by the level and scope of the invention disclosed.

The UK Supreme Court's decision is one, therefore, that should be considered without delay by inventors, patent attorneys, litigators and potential infringers alike.

If you enjoyed this article, please explore Gordon Harris' article titled *Actavis v Eli Lilly* – Should We Have Seen it Coming?, available at https://gowlingwlg.com/en/united-kingdom/insights-resources/actavis-v-eli-lilly-should-we-have-seen-it-coming-

Introducing the revised Lambert Toolkit

Can model agreements help accelerate business development and licensing?

By S.S. Vasan - PHE & University of York, Christine Reid - Partner, Northwood Reid, Rupert Osborn - CEO, IP Pragmatics

The Lambert Toolkit was created to help improve the process of negotiating collaborative research agreements between universities and business through a series of model agreements and guidance. A review by IP Pragmatics in 2013 showed that it would be useful to keep the Toolkit alive by updating the model agreements and guidance. The revised Lambert Toolkit which was launched in October 2016 was meant to address that. Has it?

About the Authors

S.S. Vasan is Public Health England's Senior Business Development Manager and Honorary Visiting Professor at the University of York. A former McKinsey consultant and Rhodes Scholar, he previously worked for Oxford University and as Head of Public Health for its spin-out company Oxitec. He co-authored the fast track model agreement (www.bit.do/fast-track) and received the Impact Award for Contribution to Society on behalf of his team for knowledge exchange and commercialisation during the Ebola crisis.

Christine Reid is founding Partner of the firm Northwood Reid and Legal Adviser to the Lambert Working Group. Her clients include national and multi-national companies, academic institutions, public sector research establishments, Research Councils and a regional development agency.

Rupert Osborn is the CEO & Principal Consultant of IP Pragmatics Limited. He has worked in the field of technology commercialisation since 1996. His specific areas of expertise are licensing strategy, negotiation and innovation management. His experience covers the commercialisation of different forms of intellectual property including trademark, copyright and patent licensing.

The Lambert Toolkit

The Lambert Toolkit was first developed in 2004 to help improve the process of negotiating collaborative research agreements between universities and business through a series of model agreements prepared by a Working Group representing industry and academia. The aim was to produce model agreements which represented a compromise that was fair and balanced, without favouring either party's interests, as well as guidance on their use and the issues commonly encountered in collaborative projects (not least the ownership and licensing of intellectual property rights).

The original Toolkit[i] followed an independent Review of Business-University Collaboration carried out in 2003 by Sir Richard Lambert, later Director-General of the Confederation of British Industry (CBI). He was tasked by HM Treasury to explore the opportunities arising from changes in business R&D and university attitudes to collaboration, and to highlight successful methods of collaboration between universities and industry, including small- and medium-sized enterprises (SMEs). His review made a number of recommendations to help shape policy in this area, and two of these led directly to the development of the eponymous Lambert Toolkit.

Usage Review

The Intellectual Property Office (IPO) commissioned a review in collaboration with PraxisAuril[ii], as well as with the CBI and Innovate UK[iii]. This review, conducted by IP Pragmatics Limited in 2013[iv], relied on evidence from a wide spectrum of public and private organisations collected through an online survey (256 responses), and supplemented by in-depth interviews (48 organisations).

The key findings were as follows:

- Knowledge of the Lambert Toolkit was well established in the research and innovation community, albeit with some differences between SMEs, multi-nationals, and across industry sectors.
- Where the model agreements were used, they were often used in practice not as a first choice, but rather as a compromise position.
- The Toolkit was valued as a good solid foundation for negotiation, a source of clauses that can help resolve negotiation points, and an independent example of a fair and reasonable approach, and its influence therefore extended much more widely than simply to those who used the model agreements.
- The Toolkit can help identify and reach workable solutions to the key issues which arise from different university and industry missions and priorities, and which underlie some of the reasons that the model agreements are not always chosen as a starting point.
- Improvements were suggested to the Toolkit; the most common recommendations being to bring the model agreements up-to-date, to provide additional guidance and to improve awareness and uptake.

The Updated Lambert Toolkit

It was clear that the Lambert Toolkit had a positive influence on some innovative research partnerships between UK universities and businesses, but the IP Pragmatics' review identified ample scope to develop these foundations through better communication of the best use of the existing tools, targeting them at the organisations that need them the most with endorsement of their benefit in different situations.

Accordingly, the Lambert Working Group was refreshed and worked on updating the Toolkit and extending the guidance in areas such as state aid and the charitable status of universities, data protection and anti-bribery. The revised Lambert Toolkit[v] was launched on 6 October 2016 at the AURIL annual conference in Edinburgh by the then Minister of State for Energy and Intellectual Property, Baroness Neville-Rolfe.

Since then, a number of professional bodies have conducted special events across the UK to promote awareness about the Toolkit, with the authors of this article and our colleagues as invited speakers[vi]. Our reflections in this article have been shaped by our interactions with current and potential users of the Toolkit in these fora.

A key and recurring topic of discussion was whether the updated Toolkit is better placed to address the key recommendation of the review, viz. to improve uptake by industry.

The objectives of the Toolkit are to:

- facilitate negotiations between potential collaborators;
- encourage potential collaborators to agree the principal terms before discussing the wording of the collaboration agreement;
- reduce the time, money and effort required to secure agreement;
- inform less experienced collaborators; and
- provide examples of best practice.

The revised Lambert Toolkit consists of:

- heads of terms to help potential collaborators identify and agree the key issues before looking at the wording of any agreements;
- seven 1-to-1 model research collaboration agreements (numbered 1 to 6, plus 4A), details of which have been summarised in this article (**Table 1**);

- a decision guide to help potential collaborators to decide which of the seven collaboration agreements might be most useful to them;
- four multi-party consortium agreements (called A to D), details of which have also been summarised in **Table 1**;
- guidance notes on all the model agreements and on issues such as state aid, charitable status, warranties, liability and data protection;
- model variation agreements for both the collaboration and the consortium agreements; and
- a fast track model agreement (described in detail separately).

The model agreements are starting points and their use is not compulsory. Each model agreement envisages a different set of circumstances, and therefore provides a different approach as to who is to own and have rights to use the intellectual property in the results of the project. None of the Lambert agreements is sector-specific, allowing for flexible use. The Toolkit is provided free of charge for anyone to use.

Table 1: Summary of the Lambert Model Agreements

Research Collaboration Agreement	Terms (see http://bit.do/lambert2)	Owner of the Intellectual Property Rights in the Results
1	The Industrial Collaborator has non-exclusive rights to use the Results, possibly in a specified field/territory for any purpose	Academic/ Research Institution
2	The Industrial Collaborator has non-exclusive rights to use the Results, possibly in a specified field/territory for any purpose and an opportunity to negotiate an exclusive licence of some or all of the Institution IPR	Academic/ Research Institution
3	The Industrial Collaborator has non-exclusive rights to use the Results, possibly in a specified field/territory for any purpose and an opportunity to negotiate an assignment of some or all of the Institution's IPR	Academic/ Research Institution
4	The Academic/Research Institution has right to use the Results for academic and research purposes and there are academic publication rights	Industrial Collaborator
4A	Each party has right to exploit certain Results created during the project and takes assignment of those Results. The Academic/Research Institution has the right to use the Industrial Collaborator's Results for academic and research purposes, there are academic publication rights and the Industrial Collaborator has the right to use the Academic/Research Institution's Results for research purposes	Academic/Research Institution and the Industrial Collaborator
5	Contract research: the Academic/Research Institution has no right to use the Results for academic and research purposes and there is no academic publication without the Industrial Collaborator's permission	Industrial Collaborator
6	Knowledge Transfer Partnership: the Academic/Research Institution has the right to use the Results for academic and research purposes and there are academic publication rights	Industrial Collaborator
Fast track model agreement	Contract research: no publication by the Institution without the Collaborator's permission which cannot be unreasonably withheld The Institution has the right to use Results for academic and research purposes Confidential Information excludes Results The Institution can notify Global Stakeholders that they are carrying out the Work, timeline, details of the Developer, Materials, etc. The Institution has the right to publish the Results (including 'poor' or 'negative' results) and make them available in databases set up by Global Stakeholders Discount if a Product is sold back to the Institution or Commissioning Bodies	Collaborator (or Developer)

Consortium Agreement	Terms
A	Each member of the consortium owns the IPR in the Results that it creates. They grant each of the other parties a non-exclusive licence to use their Results for any purpose.
B	There is a lead exploitation party. The other parties assign their IPR in the Results or grant an exclusive licence to the lead exploitation party. The Lead Exploitation Party undertakes to exploit the Results and share the proceeds with the other parties.
C	Two of the four parties are best placed to exploit different Results. Each of the two takes an assignment of the IPR in specific Results, undertakes to exploit those Results and share the proceeds with the other parties.
D	Each member of the consortium owns the IPR in the Results that it creates. They grant each of the other parties a non-exclusive licence to use those Results for the purposes of the project only. If any member of the consortium wishes to exploit another's Results, it must negotiate a licence or assignment with the owner of those Results.

Fast Track Model

The revised Toolkit also contains the fast track model agreement developed by Public Health England (PHE)[vii]. According to its CEO Duncan Selbie[viii]: "The PHE fast track evaluation agreement was developed during the Ebola crisis to make it easier for public bodies that need to respond to rapidly-evolving situations to work in an agile way, and at short notice, with industry and academia. It provides a framework that protects the interests of the taxpayer but involves a minimum of negotiation and legal drafting, which could otherwise be a barrier during a period of emergency response."

During an emergency like Ebola or Zika, failure to achieve quick consensus is not an option. Public bodies and global stakeholders must avoid duplication of efforts and promptly share information on which countermeasures are promising and which are dead-ends in order to ensure a coordinated global response.

The ability to use the results for non-commercial purposes will be critical to allow further research and evaluation. If public sector resources are diverted towards fast track evaluation and development of a countermeasure, then it is also reasonable to expect a fair value for the taxpayer if it is sold back to the public in the future.

This way of working yields significant public health benefits, therefore the fast track agreement has gained wider acceptance in US, Canada, Australia, etc[ix]. It has also contributed to PHE winning the PraxisUnico and UK Research Councils Impact Award for Contribution to Society[x]. Efforts are underway to adapt the Toolkit (including the fast track model agreement) in emerging economies like Brazil, China, India and Korea to support knowledge exchange internationally.

> "The fast track model agreement is useful in public health emergencies because failure to achieve quick consensus is not an option, for example during the Ebola crisis"

Perceptions so far

In the PraxisUnico-Auril Annual Conference at Sheffield (15 June 2017 – see photo), we conducted a straw-poll of the 70 delegates who came to our talk. It gave a useful insight on perceptions, even if it is not statistically accurate (**Table 2**). It is too early to assess the true impact of the updated Lambert Toolkit, but most of the professionals we met were aware of the Toolkit and a majority of them are using them. This is our target audience and therefore unsurprising; however, the number of people aware of and using the Toolkit was lower at the Chartered Institute of Patent Attorneys Congress (28 September 2017).

Early data such as click statistics seem to suggest that the 1-to-1 model agreements are more popular than the multi-party consortium agreements[xi]. The guidance and the decision tree are widely praised as useful tools. The Toolkit does not yet cater for business-to-business collaborations which might especially benefit SMEs. We also heard an interesting application of these model agreements, whereby two parties decided the type collaboration they should enter into by looking at the type of model agreement they were prepared to sign!

The reconstitution of the Lambert Working Group, and the fact that the revised Toolkit is hosted on a neutral website (of the Intellectual Property Office) have enabled wider acceptance of the model agreements. However, the model agreements cannot cover every situation so the closest one should be used as a starting point for negotiation in order to achieve a reasonable compromise. Academic partners should also remember that the minimum for industry is almost always a non-exclusive licence. We feel that these key points are now better understood, at least by everyone who attended the UK professional events at which we spoke.

> “Lambert Agreements cannot fit every situation so the closest model agreement should be used as a starting point for negotiation to achieve a reasonable compromise”

Table 2: Straw poll at the Sheffield conference session

Q1 - Were you NOT aware of Lambert 2 Toolkit before today?

Only 9% (6 out of 70) not aware

Q2 - Have you reviewed collaboration agreement processes since the revised Lambert Toolkit launch in October 2016?

6% (4 out of 70) did

Q3 - Has the Toolkit informed collaboration / consortium agreements or how you develop them?

10% (7 out of 70) said "yes, but marginally"

Q4 - Are you still using the model agreements?

Majority (about 67%) said yes

Q5 - Any observations on usage?

There were observations on the decision tree, state aid and knowledge transfer partnerships (Lambert 4A Agreement). More details are presented under the section 'Perceptions so far' and in our blog.[xi]

We believe that the Lambert Principles (**Table 3**) underlying the original Toolkit and its revision(s) have not changed and will not change. We continue to stress the importance of saving time through the use of "Heads of Terms" and by anticipating the collaboration agreement terms when applying for Knowledge Transfer Partnerships (Lambert model agreement 4A). The guidance document has a wealth of resources clarifying issues such as state aid, the charitable status of universities, anti-bribery and data protection.

Table 3: Enduring Lambert Principles

Rights to use IPR are key – the minimum for industry is a non-exclusive licence

One size does not fit all

Model agreements cannot fit everyone's way of working

Different approaches/spectrum of solutions are needed

Only a starting point/negotiation – cannot run on automatic pilot

Ease/speed the process – cannot solve every issue

Cannot cover every scenario – but can cover common scenarios

Aim for a workable and reasonable compromise

It is important to remember that the Toolkit is a means to an end (viz. successful contracts, outcomes and wealth creation). It will need to be updated regularly, for instance, the introduction of the European Data Protection Regulation on 25 May 2018 will necessitate appropriate updates to the data protection provisions of the model agreements and the guidance on data protection. The IPO is also working with key stakeholders to conduct a survey to understand how the Toolkit is being used, by whom (both universities and industry) and what future revisions may be needed.

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i. Lambert Review of Business-University Collaboration, Final Report (ISBN: 0-947819-76-2), HM Treasury: December 2003. Available at http://bit.do/lambert1
ii. AURIL (Association for University Research and Industry Links) and PraxisUnico have merged effective 1 April 2017 to form a single organisation representing the Knowledge Exchange and Commercialisation (KEC) profession in the UK. Their new identity "PraxisAuril" was formally revealed at the AURIL annual conference in Bristol on 5-6 October 2017.
iii. Innovate UK was then known as the Technology Strategy Board (TSB).
iv. Collaborative Research between Business and Universities: The Lambert Toolkit 8 Years On (ISBN: 978-1-908908-72-8), Intellectual Property Office: 8 May 2013. Available at http://bit.do/lambert-usage
v. Available at http://bit.do/lambert2
vi. For example, the Licensing Executives Society of Britain & Ireland conducted seminars in London (10 November 2016) and Manchester (20 June 2017). This topic was prominently covered at the Institution of Engineering and Technology's Horizontal Innovation Conference (30 January 2017) and at the Chartered Institute of Patent Attorneys Congress (28 September 2017), both of these in London. The PraxisUnico-Auril Annual Conference in Sheffield (15 June 2017) had an informative session titled "H2GL2: The Hitchhikers Guide to the Lambert 2 Toolkit" attended by 70 delegates.
vii. Available at http://bit.do/fast-track
viii. Duncan Selbie's Friday Message, Public Health England: 7 October 2016. Available at http://bit.do/fast-track-duncan
ix. See US National Library of Medicine's Disaster Lit, for instance, at https://disasterlit.nlm.nih.gov/record/13585. The Toolkit has also been adopted as best practice in government-to-government interactions through the Australia-Canada-UK-US Medical Countermeasures Consortium and the five eyes BSL4Znet between these four countries plus Germany.
x. Winners of Impact Awards 2015 announced. PraxisUnico & RCUK: 15 September 2015. Available at http://bit.do/impact-awards-2015
xi. See our blog http://bit.do/praxis-lambert-blog for caveats on this

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Medius Deal Watch

December 2017's review of the top deals by value in the healthcare sector

By Roger Davies, Medius Associates Ltd

"The avoidance of taxes is the only intellectual pursuit that carries any reward"

John Maynard Keynes

Pharmaceutical companies are renowned for scientific expertise and development of innovative medicines. Less well known are the boffins in the tax departments of US companies who have devised tax inversions and complex tax avoidance schemes such as the 'Double Irish with a Dutch Sandwich'. These schemes have been difficult to swallow for the US Government. The new tax legislation may relieve its indigestion. It changes taxation from worldwide to territorial, reduces headline corporation tax from 35% to 21% and allows companies to repatriate overseas cash at a tax rate of 15.5%. However it is not all good news for companies. There are proposed reductions in R&D tax breaks that could increase the cost of developing orphan drugs, limits on shifting income via transfers of intangible assets and a tax on cross border transactions that will affect supply chains.

About the Author

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Without doubt, the complexities of the new US tax regulations will continue to make tax avoidance a rewarding intellectual pursuit.

One of the key questions for those involved in M&A is whether the repatriation of over $100bn by the US pharma companies will lead to an increase in M&A transactions following the decline in 2017. According to a report by Reuters, an analyst at SunTrust reviewed the last repatriation tax holiday in 2004 when pharma companies repatriated more than $90bn "but there was no massive wave of M&A. Only three U.S. companies consummated deals in excess of $1 billion the following year".

If history repeats itself it is unlikely that there will be a surge in pharma M&A transactions not least of all because shareholders will be seeking a share of any repatriated cash in the form of share buy backs or increased dividends. For example, Pfizer announced on 17th December that it will be increasing its quarterly dividend by 6% and the Board has authorised $10bn for share buy backs.

"Markets can remain irrational longer than you can remain solvent"

John Maynard Keynes

Another factor working against a significant increase in M&A in 2018 is the perception that the valuations of companies are too high. The US stock market is at record levels. A survey of fund managers by Bank of America Merrill Lynch found that a net 48% of them thought equities were overvalued. High valuations have been mentioned by a number of big pharma companies including Pfizer and GSK. Companies are well aware of the evidence that most acquisitions provide more value for the seller than the buyer. Unless there is a stock market collapse next year Deal Watch (DW) expects that M&A will be driven mainly by strategic fundamentals rather than financial opportunism.

"Successful investing is anticipating the anticipations of others"

John Maynard Keynes

The point about strategic fundamentals e.g. vertical integration, is demonstrated by the biggest acquisition of 2017, CVS Health's purchase of Aetna for $77bn including debt. In the US Aetna is the third largest health insurer and CVS Health consists of a large retail pharmacy chain, walk-in clinics, home care and also acts a pharmacy benefit manager. The merger, if approved by the Competition Authorities, will provide a vertically integrated operation that will link Aetna's patient records to dispensing and purchasing of medicines. As well as synergy benefits of $750m the merger is seen as a defensive strategy, namely, "anticipating the anticipation of" Amazon's entry to the prescription medicine market.

According to a report from CNBC, Amazon has had discussions with generic companies in the US, Mylan and Sandoz. Maybe it is these discussions plus the expectation that companies like CVS and perhaps Amazon will continue to drive down medicine prices in the US that have prompted the CEO of Novartis to mention that the company may exit the oral solid dose generic market in the US. In October Novartis announced the closure of a factory in Colorado. This month Teva announced that it will reduce its workforce by 25% and close or sell a number of sites.

The generics market has seen consolidation over the past few years and this seems likely to continue in 2018. Amazon has decimated book shops and record stores. If Amazon enters the pharmaceutical market it will be interesting to see how it deals with the highly regulated pharmaceutical market particularly in Europe.

Consumer Health M&A – The industry is consolidating again

Another M&A deal driven by strategic fundamentals, in this case geographic expansion, is the acquisition of Atrium Innovations by Nestlé Health Science for $2.3bn. Nestlé Health Science is focussed on the "therapeutic role of nutrition to change the course of health management for consumers, patients, doctors and nurses". Atrium Innovations based in Canada has a range of probiotics, plant-based protein nutrition, meal replacements and multivitamin products. Some 80% of Atrium's $700m sales (10% of Nestlé Health Science – see OTC Toolbox article 6th December 2017) are in the US. The company is owned by a consortium of funds led by Permira who acquired the company in early 2014 for $1bn. The sale price of $2.3bn, assuming no further funding was provided during the four years, represents an internal rate of return of around 23% for the investors which, in this day and age, is not to be sniffed at.

Nestlé's acquisition of Atrium is the latest example of concentration in the OTC pharmaceutical market. Over the past few years Novartis has joined forces with GSK, Merck & Co has divested its OTC unit to Bayer and Boehringer Ingelheim has swapped its consumer business for Sanofi's animal health. Further major changes in the OTC pharmaceutical market are in the pipeline. Merck KGaA's consumer health business with $1bn sales is on the market and there have been comments from Pfizer recently that suggest it may sell its consumer business with sales of $3.5bn. Perrigo and Stada are said to be bidding for the Merck KGaA unit. In the meanwhile smaller companies are just as busy.

For example this month, Alliance Pharma in the UK is set to acquire Vamousse, a head lice treatment, for up to $18m and Ametop, a topical anaesthetic gel, for $8m. Similarly, Recordati purchased from Bayer Consumer Health the laxative Transipeg for France with $12m sales for an undisclosed amount.

Prescription Drugs M&A – Why license technology, why not acquire the company or take an option to do so?

Some big pharma companies continue to acquire, rather than license, technology companies where there is a complementary technology. An example of this is Gilead's acquisition of Cell Design which has two technologies for engineering CAR-T cells. This fits perfectly with Gilead's acquisition of Kite for $11.9bn in August especially as Kite already had a 12.2% share in Cell Design. This helps deal with the long term development of new cell therapies but is the market ready for these types of treatments? Apparently in the US only five patients have been treated with Yescarta, Gilead's CAR-T treatment for lymphoma, and there is a waiting list of 200 patients. This is in spite of a report at the ASH annual meeting this month

Deal Watch Table December 2017

Licensor / Acquisition target	Licensee / Acquirer	Deal type*	Product /technology	Headline (upfront) $m
Aetna (US)	CVS Health (US)	Company acquisition	Health insurer acquired by PBM and retail pharmacy company	77,000
Atrium Innovations (CA)	Nestlé Health (CH)	Company acquisition	Range of nutrition and multivitamin products	2,300
Ignyta (US)	Roche (CH)	Company acquisition	Oncology product range in development incl. entrectinib, a tyrosine kinase inhibitor for NSCLC	1,700
AskAt (JP)	Arrys (US)	Licence[1]	Two pre-clinical prostaglandin E2 receptor 4 antagonists	1,200+ (ND)
Sucampo (US)	Mallinckrodt (US)	Company acquisition	Lubiprostone + orphan drug pipeline	1,200
Autifony (UK)	Boehringer Ingelheim (DE)	Option for asset purchase	Kv3.1/3.2 positive voltage gated potassium channel modulator platform incl. Phase 1b compound	737 (29)
Halozyme (US)	Alexion (US)	Licence	Subcutaneous drug delivery technology for 4 targets	680 (40)
Cell Design Labs (US)	Gilead (Kite) US	Company acquisition	Two technology platforms for engineering CAR-T cells	567 (175)
Depomed (US)	Collegium (US)	Commercialisation[2]	Nucynta (tapentadol) product range marketed in US	550+ (10)
Idorsia (CH)	Roche (CH)	Option to licence	Discovery of cancer immunotherapy compounds	460 (15)
Mitobridge (US)	Astellas (JP)	Exercise of option. Company acquisition	Technology to discover and develop novel drugs that improve mitochondrial functions	450 (225)
ReMynd (BE)	Novo Nordisk (DK)	Licence	Pre-clinical ReS39 programme to develop compounds for treatment of diabetes	411 (ND)
Genescript (Legend) (CN)	J&J (Janssen) (US)	Licence and collaboration	Phase 1 CAR-T immunotherapy for multiple myeloma	350+ (350)
Athenex (US)	Almirall (ES)	Licence to research, develop and commercialise[3]	KX2-391 (Phase 3) topical dual Src kinase and tubulin polymerisation inhibitor for actinic keratosis	275 (55)
Carmot Therapeutics (US)	Amgen (US)	Licence and collaboration	Discovery platform for small molecule drugs to treat Parkinsons and other diseases	240+ (ND)
XOMA (US)	Rezolute (US)	Licence to develop and commercialise	XOMA358 Phase 2a Mab that inhibits effects of elevated insulin	240 (18)
Idorsia (CH)	J&J (Janssen) (US)	Exercise of option. Collaboration to develop and commercialise	Aprocitentan (Phase 2) an orally active dual endothelin receptor antagonist for treatment of resistant hypertension	230
Basilea (CH)	Pfizer (US)	Extension of licence[4]	Cresemba (isavuconazole) pre-registration anti-fungal	226 (3)
Arena (US)	Everest (CN)	Licence to develop and commercialise[5]	Ralinepag and etrasimod Phase 2 for pulmonary arterial hypertension and ulcerative colitis respectively	224 (12)
Tracon (US)	Ambrx (CN)	Licence to develop and commercialise[6]	TRC 105 (carotuximab) in Phase 3 for treatment of angiosarcoma	144 (3)
Ardelyx (US)	Shanghai Fosun (CN)	Licence to develop and commercialise[7]	Tenapanor (Phase 3) for treatment of irritable bowel syndrome with constipation	125 (12)
Morphosys (DE)	I-Mab (CN)	Licence to develop and commercialise[8]	MOR202 (Phase 1/2a) Mab targeting CD38 for treatment of multiple myeloma	120 (20)
Confu (BE)	Roche (CH)	Licence to develop, manufacture and commercialise	Research collaboration G-protein coupled receptor agonists	103 (7)
vTv Therapeutics (US)	Huadong Medicine (CN)	Licence to develop, manufacture and commercialise[4]	GLP-1r agonist in Phase 2 for Type 2 diabetes	103

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3. US and Europe including Russia
4. China and Asia Pacific
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that after a median 15.4 months, 42% of previously treated non-Hodgkin's lymphoma patients were still responding to the therapy and 40% continued to show complete responses.

Clearly the product is very effective so the question is whether the product is not being used because of the high price of $373,000 per one-time treatment or because health insurers and hospitals have not yet put in place the procedures to deal with CAR-T. Probably it is a bit of both. However until this situation becomes clearer the uptake of Yescarta, at least in the short term, is a major risk for Gilead and equally so for Novartis' CAR-T therapy Kyrmiah priced at $475,000.

Another example of M&A in the oncology sector is Roche's acquisition of Ignyta for $1.7bn. Ignyta has a strong pipeline with one product, entrectinib a tyrosine kinase inhibitor for NSCLC, in Phase 2 and two other products in Phase 1. The price paid by Roche was not cheap. The share price premium was over 70% for a company with annual losses of over $100m. The premium paid by Mallinckrodt for Sucampo was over 50% but it still looks like an expensive acquisition with the price of $1.2bn representing 14x 2016 EBITDA.

An alternative to acquiring a technology company is to take a licence and include an option to buy the company at a later date. Over the last several years there has been a significant increase in the number of M&A options being included in licensing deals. Some of these deals are reaching the end of the option period and are being either exercised or terminated. This month Astellas has exercised its option to acquire the US company Mitobridge for $450m. Four years' ago Astellas and Mitobridge (then Mitokyne) set up a R&D collaboration to discover and develop novel drugs that improve mitochondrial functions. At the time Astellas joined a consortium of investors who provided $45m Series A equity funding. As part of the collaboration agreement, Astellas had an option at certain points in time to acquire the company during the five year agreement. Mitobridge now has a drug for treatment of Duchenne Muscular Dystrophy in Phase 1. The 2013 collaboration deal had a headline value of $730m and stated that the buy -out price could be over $500m. In the event Astellas paid $225m upfront ($165m after adjusting for its existing stake) with a further $225m contingent on "advances in clinical programs". Looks like Astellas got a good deal.

Astellas had an option to buy the company. Another approach is to have an option to buy an asset. This is what Boehringer Ingelheim has done in the deal with Autifony. It has paid $29m upfront with a further $21m possible during the option period to acquire

Autifony's Kv3.1/3.2 positive voltage gated potassium channel modulator platform including a lead compound in Phase 1b for treatment of schizophrenia. If the option is exercised a further $687m in development and pre-commercialisation milestones is payable. DW wonders if there was any connection between this deal and the resignation two days before of Boehringer's Finance Director because, according to the announcement, "it has not always been possible to reconcile divergent views and perspectives". The Finance Director leaves at the end of this month.

Licensing without options and…

This month sees a raft of new licensing agreements ranging from discovery technologies to Phase 3 products. The discovery projects are invariably licensed in by big pharma companies e.g. Novo Nordisk and Amgen. In these examples the headline values are over $200m but in neither case is the upfront disclosed probably because it is a small amount.

Building on a long standing successful relationship is always a good business development strategy for big pharma. This is what BMS has done with Ono. The development and commercialisation of Opdivo (nivolumab) for treatment of melanoma has been a great success with annual sales of around $5bn. BMS has now established a new project with Ono to develop and commercialise (except for Japan, China and SE Asia) Ono's prostaglandin E2 receptor 4 antagonist to increase the effectiveness of immuno-oncology drugs. BMS is paying $40m upfront plus undisclosed milestones. Pfizer has also built on its relationship with Basilea by extending its licence for isavuconazole to include China and Asia Pacific for $226m.

Drug delivery companies often struggle to find licensees for their technologies but Halozyme has bucked the trend. Its subcutaneous drug (sc) delivery technology has previously been licensed to seven big pharma companies including Roche who has launched sc versions of Herceptin and MabThera. This month Alexion has become the latest licensee with a deal valued at $680m (four targets at $160m each plus $40m upfront).

…licensing with options

In the same way that M&A is being driven partly by exercise of options, so too is licensing. Idorsia has been involved in two option deals this month. The first is a $460m cancer immunotherapy discovery project with Roche. Roche pays $15m upfront and $35m if the option is exercised. The second is the exercise of an option arising from the acquisition earlier this year of Actelion by J&J (Janssen).

Prior to the acquisition, Actelion's R&D unit was set up as a spin-out company called Idorsia managed by Actelion's founder. As part of the acquisition deal, Janssen was given an option to license from Idorsia aprocitentan, a treatment for resistant hypertension in Phase 2. The study completed in May and Janssen has now exercised the option for $230m. Idorsia and Janssen will jointly share development costs but Janssen has worldwide commercialisation rights paying royalties of 20% (up to $0.5bn sales), 30% (on sales between $0.5bn and 2bn) and 35% (on sales over $2bn). Wow!

Perhaps royalties of 20% to 35% are not so uncommon, at least where the licensor has co-funded development. For example in the early 2016 deal with Gilead for filgotinib for the treatment of inflammatory indications such as RA and Crohn's disease, Galapagos agreed to pay 20% of the development costs and had an option to co-promote the product.

This month Galapagos has decided to opt-in to co-promote the product in the big 5 European countries plus Benelux. In the co-promotion countries there will be a profit share but in other countries Gilead will pay Galapagos tiered royalties of 20% to 30%, not much different to the rates being paid by Janssen to Idorsia.

"The difficulty lies not so much in developing new ideas as escaping from old ones" *John Maynard Keynes*

Licensing out by small and mid-sized companies is a bit of a lottery especially to big pharma companies who are prone to change strategy or priorities on development and commercialisation of in-licensed products. Of course the lottery also applies to medium or small companies who may have insufficient expertise or resources or financial problems.

A case study of the licensing out lottery is Grünenthal's tapentadol sold as Nucynta in the US. This was originally licensed to J&J, a big pharma partner with expertise in pain for the US, Canada and Japan where Grünenthal did not have a marketing presence. J&J was a good choice of partner for Grünenthal. The product was launched in the US in 2008. In 2015 J&J decided to divest its US licence rights to Depomed for $1.05bn. Depomed was a smaller company with a portfolio of pain products so it appeared to be a reasonable replacement commercialisation partner for Nucynta. However Depomed had to borrow over

$0.5bn to pay J&J which increased its finance costs by over $60m per annum. This pushed Depomed into a loss and by the end of 2016 Depomed had a net loss of $89m on sales of $456m. With continued losses in 2017, the management was changed and the new CEO adopted a new strategy.

This month Depomed announced a reduction in staff and a transfer of Nucynta commercialisation rights to Collegium, a small company with sales of around $30m. In 2016 Nucynta had annual sales of $281m representing 60% (!) of Depomed's total sales. Collegium will pay a small ($10m) upfront plus a royalty of 58% on annual sales up to $233m, 25% between $233m and $258m and 17.5% over $250m subject to a minimum of $135m per year for the first four years. Nucynta sales are slowly declining so Depomed is unlikely to earn more than the minimum royalty in the next four years. However the Collegium deal is part of a company restructuring so the reduction in costs may help Depomed reduce its debt and interest payments.

More importantly, given the changes of commercialisation partner Grünenthal has endured over the past 10 years, is this latest change a good deal for Grünenthal? Well according to Grünenthal's press release "Grünenthal concluded and agreed that transferring Nucynta to Collegium would be the best option. This agreement should give Grünenthal a more committed partner and provides a pre-agreed fixed minimum royalty income stream over the next few years, if the partner performs within a given range of revenue achievements". Presumably Grünenthal had little choice but to accept the Depomed / Collegium deal but in doing so it has agreed to reduce royalties by $3.2m if sales drop to $220m per annum and gets an incremental $1.2m if sales reach $240m. Another issue is whether Depomed will continue to develop another Grünenthal product, cebranopadol, acquired in late 2015.

This case study demonstrates some of the difficulties mid-sized companies face licensing out products in major markets. The difficulty is not so much in finding new partners as escaping from old ones.

Conclusion

In looking at deals each month certain patterns start to emerge. This month there are three:

- Out of the 24 deals in December's DW Table, excluding the top 2, 13 or 59% of the product innovators, licensors or acquisition targets, are US based companies.
- Five of the six European licensor companies are spin-outs.
- Out-licensing to China is becoming increasingly important. Five out of the 22 deals are out-licenses to Chinese companies for territories including China.

The message, at least from this month, is that if you are in-licensing new products go to the US or to European spin-out companies and if you are out-licensing go to China.

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