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# Regulatory justifications: regulating European medicines to maximise market potential

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The justification for regulating is generally considered to rely on benefitting interested groups. Whereas, the traditional view is that regulators act as impartial arbiters balancing competing public and private interests, modern accounts consider regulation to be dominated by single interests, such as those of industry. This article challenges these theories by arguing that regulators are substantively (not just procedurally) motivated to justify their actions according to the goals set for them by the bodies that empower them. In consequence, regulators understand their goals as market-based objectives, prompting them to focus on maximising market potential. This is demonstrated in the context of regulating medicines in Europe, through the European Patent Organisation, the CJEU, and the European Medicines Agency. The analysis identifies that regulating to achieve market benefits is a better predictor of regulatory behaviour, but this behaviour frustrates goal-achievement (relating to effective and affordable medicines) and only incidentally enables benefits to accrue to specific groups.

**Keywords:** regulatory theory; public and private interests; administrative decision-making; medicines regulation; patents; market authorisation

## 1. Introduction

In the context of regulation<sup>1</sup>, the traditional legal approach is to regard regulators as impartial arbiters, fairly balancing competing public interests and the special interests of particular groups (eg industry, trade organisations, patients, and professionals). This approach has been challenged within economic analyses and continues to be expanded upon through other disciplinary approaches within the political and social sciences, as well as within public administration.<sup>2</sup> More recently, academic commentary has linked consideration of outcomes (to determine why regulators prioritise specific interests) with how regulators are motivated to

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<sup>1</sup> 'Regulation' relates to a specific legislative instrument, otherwise 'regulation' relates to governance thereby extending beyond legislative instruments to include a wider raft of measures and decisions that moderate behaviour: C Scott, 'Regulation in the Age of Governance: the rise of the post-regulatory state' in J Jordana and D Levi-Faur (eds) *The Politics of Regulation: Institutions and Regulatory Reforms for the Age of Governance* (Edward Elgar Publishing, 2004).

<sup>2</sup> See, e.g., DA Farber and PP Frickey, 'The Jurisprudence of Public Choice' (1987) 65(5) *Texas Law Review* 873; W Streeck and PC Schmitter, 'Community, market, state – and associations? The prospective contribution of interest governance to social order' (1985) 1(2) *European Sociological Review* 119; SM King, BS Chilton and GE Roberts, 'Reflections on Defining the Public Interest' (2010) 41(8). *Administration and Society* 954; and P Coley, 'Public Interested Regulation' (2000-2001) 28 *Florida State University Law Review* 7.

act in particular ways.<sup>3</sup> The result is that understanding the interests that are served by regulation is split between: (1) those believing that the dominant interest is, and should be, that of the public, in which the regulator works for a ‘greater good’;<sup>4</sup> (2) those working on the presumption that actors behave from selfish motives, which causes regulators to follow private interests (eg maximising utility or wealth),<sup>5</sup> or being politically/institutionally motivated by self-interest (eg democratic benefits from votes, corporate bias or the prospect of administrative benefits);<sup>6</sup> and (3) those who believe that regulators have been captured by self-interested special interests (‘interest groups’).<sup>7</sup> Although regulatory capture is considered to occur when any sufficiently-positioned group is able to dictate policy, or to affect regulatory instruments or specific regulatory decisions, the majority of assessments in the field identify industry as the most likely group, even though the effects of its dominance could be ameliorated by incorporating public interest groups.<sup>8</sup>

The intention in this article is not to comprehensively review this field, but to highlight adherence of existing academic commentary to two possible motives for regulators’ actions: (1) being motivated towards good outcomes; or (2) being motivated towards selfish benefits of either the regulator or interest groups. While institutional theories have

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<sup>3</sup> A Ginosar, ‘Public-Interest Institutionalism: A Positive Perspective on Regulation’ (2014) 46(3) *Administration and Society* 301.

<sup>4</sup> This representing a context-based enumeration of community values supported by good reasons (M Feintuck, “The Public Interest” in *Regulation* (Oxford University Press, 2004)); being rights based (T Prosser, ‘Regulation and Social Solidarity’, (2006) 33(3) *Journal of Law and Society* 364); ethically based and embedded in legitimacy issues (R Brownsword and M Goodwin, *Law and the Technologies of the Twenty-First Century* (Cambridge University Press, 2012)) and as prudential decision-making running alongside moral legitimacy (R Brownsword, ‘Responsible Regulation: Prudence, Precaution and Stewardship’ (2011) 62(5) *Northern Ireland Legal Quarterly* 573); based on welfare economics (M Hantke-Domas, ‘The Public Interest Theory of Regulation: Non-Existence or Misinterpretation?’ (2003) 15 *European Journal of Law and Economics* 165); or deliberative (A Gutmann and D Thompson, *Why Deliberative Democracy?* (Princeton University Press, 2004)).

<sup>5</sup> Eg GJ Stigler, ‘The Theory of Economic Regulation’, (1971) 2 *Bell Journal of Economics & Management Science* 3; RA Posner, ‘Theories of economic regulation’ (1974) 5 *Bell Journal of Economics and Management Science* 335.

<sup>6</sup> Eg S Peltzman, ‘Toward a more general theory of regulation’ (1976) 19 *The Journal of Law and Economics* 211; S Peltzman, ‘Constituent Interest and Congressional Voting’ (1984) 27 *The Journal of Law and Economics* 181; G Becker, ‘The public interest hypothesis revisited: A new test of Peltzman’s theory of regulation’ (1986) 49 *Public Choice* 223; J Abraham, ‘On the prohibition of conflicts of interest in pharmaceutical regulation: precautionary limits and permissive challenges’, (2010) 70 *Social Science & Medicine* 648; AI Ogus, *Regulation: Legal Form and Economic Theory* (Hart Publishing, 2004) Ch 4.

<sup>7</sup> Eg M Bernstein, *Regulating Business by Independent Commission* (Princeton University Press, 1955); E Jackson, *Law and the Regulation of Medicines* (Hart, 2012); P Drahos, ‘Intellectual Property and Pharmaceutical Markets: a nodal governance approach’ (2004) 77(2) *Temple Law Review* 401.

<sup>8</sup> D Carpenter and DA Moss (eds), *Preventing Regulatory Capture: Special Interest Influence and How to Limit it* (Cambridge University Press, 2014), particularly Chapters 7 and 14; I Ayres and J Braithwaite, ‘Tripartism: Regulatory Capture and Empowerment’, (1991) 16(3) *Law & Social Inquiry* 435.

supplemented these motives of the regulator to incorporate values embedded within the decision-making process,<sup>9</sup> they leave unchallenged these core motivations.

This article supports an alternative explanation for behavioural norms: that actors are motivated to rationalise their behaviour to others<sup>10</sup> and this results in seemingly inconsistent outcomes that can appear to be in the interests of the public, or of particular groups, or of the regulators themselves. It follows that those involved in the regulatory system are motivated to act in ways which enable them to justify themselves to those that empower them (eg supranational institutions, Government, legal institutions, or the public). Requirements of accountability and transparency certainly underpin this perspective procedurally,<sup>11</sup> but this article argues that substantively the need to explain actions forces regulators to focus on tracing a clear and justifiable link between policy and practice. This can be distinguished from regulation within existing discourses, which is seen as interests-based on the evidence of benefits accruing to specific actors (eg acting in the interests of industry in preference to the public interest). The assertion made here is that regulators are predominantly concerned to explain their efforts relative to the goals they have been given: irrespective of whether the goals derive from political mandates, or legislative remits which are encapsulated within institutional aims (long-term goals) and developed through policies (mid-term goals). Collaterally this means that benefits accrue incidentally and that attempts to subvert regulation (eg through short-term party politics, lobbying or bias, etc) can have only a limited effect.

The regulation of medicines, existing and innovative, offers an ideal context in which to demonstrate the central claim of this article. The analysis focuses on just three key examples to evidence that regulators consistently justify their behaviour relative to the goals provided by those that empower them: the European Patent Organisation (EPOrg) which, together with the European Boards of Appeal, regulates the patent protection that facilitates the development of most innovative medicines; the judiciary, exemplified by the Court of Justice of the European Union (CJEU) in dealing with trade in medicines and rights granted over them; and the European Medicines Agency (EMA), which regulates market entry of innovative medicines, to confirm consistency even across independent agencies operating at different stages of the innovatory process. These examples are chosen to demonstrate that

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<sup>9</sup> For an overview of these theories see: R Baldwin, M Cave and M Lodge, *Understanding Regulation: Theory, Strategy, and Practice* (Oxford University Press, 2<sup>nd</sup> ed, 2012), at 53-65 and for the public policy discourse overview see (n 2) at 305-306.

<sup>10</sup> J Rawls, *A Theory of Justice* (Belknap Press, 1971).

<sup>11</sup> R Baldwin, *Rules and Government*, (Oxford University Press, 1995), at 47. This links the concept of good regulation with why and how regulation accrues to the benefits of particular actors/institutions.

regulators take a market-based view of their goals and become motivated to prioritise market considerations, making it the enduring reason guiding regulatory behaviour even where policies and practices change.

The article has three principal parts. First, the article provides a brief understanding of regulatory empowerment, identifies existing regulatory goals and makes the case that traditional accounts are insufficient to fully explain regulatory behaviour. Secondly, it is suggested that the justificatory basis for regulatory behaviour specific to medicines comes from regulators interpreting their goals as a requirement to maximise market potential. This means that regulators behave in response to changing market conditions and this can be understood by assessing current market potential for European medicines competing in global markets. Thirdly, the ways in which current market potential prompts specific regulatory practices are identified. This pattern is exemplified by: the implementation of core aspects of European patent law; decisions of the CJEU; and by the progressive regulatory initiatives adopted by the EMA. This suggests that, irrespective of which regulatory institution is assessed in a broader interpretation of medicines regulation, justifications are a good measure of actions. If regulators are truly focused on explaining their behaviour, market-based motives provide an accurate means of predicting how they will act. This enables a critique focused on any failure to achieve the goals set, in preference to one based on an idealised balancing of interests; and relates more directly to regulatory behaviour than assessing how interests accrue.

## **2. Empowerment and goals**

Before considering the institutional and policy goals of regulatory bodies and the degree to which these goals relate to specific regulatory practices, it is necessary to briefly consider how decision-making bodies are empowered.

### **2.1 Empowerment**

Regulatory institutions are empowered by the State, just as supranational organisations (such as the EU) are empowered by Member States, but this empowerment is not a static event. So one consequence of the assertion that regulators are motivated to explain their behaviour relative to the goals set by their empowering body is that it runs counter to existing evidence

about regulatory ‘drift’ and ‘shirking’.<sup>12</sup> Drifting and shirking recognise how far regulators’ actions depart from their original (empowering) legislative remit, or from their institutional aims or specific policy goals. Adopting an analysis focused on the motivations which link goals with actions argues instead that it is the rationalising basis for behaviour which prompts a change in regulators’ actions. In the context of medicines, what factually maximises market potential changes over time and it is this change which causes the original goals to be re-interpreted or re-prioritised. The result is that regulatory behaviour only appears to be mismatched to goals. This leaves open the question of how susceptible to change regulators’ goals are and this requires an example to expand on the nature of empowerment in a little more detail.

The EMA’s decision-making body, the Committee for Medicinal Products for Human Use (CHMP), has to account to: the EMA and through them to others within individual national regulatory agencies (eg through Management Boards,<sup>13</sup> which are constrained by the national regulatory decision-making bodies that empower them);<sup>14</sup> their decisions are also subject to supranational bodies within the EU (eg the Commission,<sup>15</sup> which in turn is accountable to the European Parliament and has its policy agenda set by the European Council);<sup>16</sup> CHMP decisions must comply with the legislative requirements determined by

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<sup>12</sup> DB Spence, ‘Administrative Law and Agency Policy-Making: Rethinking the positive theory of political control’ (1997) 14 *Yale Journal on Regulation* 407.

<sup>13</sup> Assessing the vertical accountability of the EMA to Member States via Management Boards, Buess identified that accountability does not reflect the level of autonomy (power) of the agency (M Buess, ‘European Union Agencies’ Vertical Relationships with the Member States: Domestic Sources of Accountability?’ (2014) 36(5) *Journal of European Integration* 509) and that, while the EMA displays both de jure and de facto political independence, there is far greater scope for horizontal (‘peer’) accountability coming from national regulatory and ministerial sources (M Buess, ‘European Union Agencies and their Management Boards: An assessment of accountability and democratic legitimacy’ (2015) 22(1) *Journal of European Public Policy* 94). Looking specifically at the Management Boards’ perspective at the EMA, Makhshvili and Stephenson identified that, while the Board considered that financial independence is crucial to maintaining autonomy, decision-making independence is far more influenced by the CHMP comprising members of the Member States’ National Competent Authorities and the Management Board influencing planning than by the Commission (L Makhshvili and P Stephenson, ‘Differentiating Agency Independence: Perceptions from Inside the European Medicines Agency’ (2013) 9(1) *Journal of Contemporary European Research* 4).

<sup>14</sup> Arguing that the EMA has greater autonomy compared to other agencies see: MLP Groenleer, ‘The Actual Practice of Agency Autonomy: Trading the developmental trajectories of the European Medicines Agency and the European Food Safety Authority’ in G Ekiert and A Martin (eds), *Open Forum CES Paper Series, The Minda de Gunzberg Centre for European Studies, Harvard University* (2011). <http://ssrn.com/abstract=1904462>, but that they are still constrained by design and accountability requirements, curtailing their complete autonomy, see: JG Christensen and V Lehmann, ‘Administrative Capacity, Structural Choice and the Creation of EU Agencies’ (2010) 17(2) *Journal of European Public Policy* 176.

<sup>15</sup> M Egeberg and J Trondal, ‘EU-level agencies: new executive centre formation or vehicles for national control?’ (2011) 18(6) *Journal of European Public Policy* 868.

<sup>16</sup> Eg B Hauray and P Urfalino, ‘Mutual Transformation and the Development of European Policy Spaces. The case of medicines licensing’ (2015) 16(3) *Journal of European Public Policy* 431.

the European Parliament, the Council of the EU and the Commission;<sup>17</sup> and these in turn will also be distinguished and enforced through the CJEU. Each of these related institutions is in turn accountable to broader political and administrative oversight within Member States, motivating them to be seen to promote public interests (satisfying political mandates) and interest groups (serving economic interests).

The implication is that embedded institutional aims and policy goals wax and wane in reflecting the public policy, political, legislative or administrative priorities of the empowering body.<sup>18</sup> These are framed to broader and more enduring goals, to ensure that the empowering body retains its credibility commitment.<sup>19</sup> This refers to the need to regulate consistently, because industry will not commit resources where the regulatory environment is open to reversal and investments can be lost. The effects of this commitment can be easily identified where the bulk of investment in stem cell technology in the USA went to multipotent stem cells, because both Democratic and Republican Governments permissively regulate them.<sup>20</sup> The flow of research investment did not change even when Democratic Governments signalled their approval of pluripotent stem cell developments, because Republican Governments regulate pluripotent stem cells prohibitively and this would necessarily result in lost investment over the long-term.<sup>21</sup>

As each empowering body (principal) relays its goal-setting to the body (agent) that it influences, changes in interpretation occur. This can be caused by the purposiveness of the communication,<sup>22</sup> which means that the understanding of the conveyor-principal and the recipient-agent may not match. So the principal and agent must agree a mutual purpose-based

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<sup>17</sup> Substantively through measures relating to practice (eg Regulation 1235/2010/EC amending, as regards pharmacovigilance of medicinal products for human use, (31.12.2010) OJ EU L348/1-16), as well as in terms of the embedded competency that was accorded to the EMA at its inception (Regulation 726/2004/EC laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, Title IV (30.4.2004) OJ EU L136/1-33).

<sup>18</sup> In assessing the impact of political motivations see: C Davis and J Abraham, *Unhealthy Pharmaceutical Regulation: Innovation, Politics and Promissory Science* (Palgrave Macmillan, 2013); and in assessing the broader relationship of political motives to the type of regulatory infrastructure (eg agency or network) see RD Kelemen and AD Tarrant, 'The Political Foundations of the Eurocracy' (2011) 34(5) *West European Politics* 922.

<sup>19</sup> B Levy and P Spiller, 'The Institutional Foundations of Regulatory Commitment' (1994) 10 *Journal of Law, Economics and Organization* 201; RD Tollison, 'Public Choice and Legislation' (1988) 74 *Virginia Law Review* 339, at 345 and notably as elevated to an independent, competing theory: J G Christensen, 'Public Interest Regulation Reconsidered: From Capture to Credible Commitment' (2010) *Jerusalem Papers in Regulation and Governance*, Working Paper No 19.

<sup>20</sup> Eg Centre for American Progress, 'Embryonic Stem Cell Research by the Numbers', 17 April 2007, [www.americanprogress.org/issues/technology/news/2007/04/17/2887/embryonic-stem-cell-research-by-the-numbers/](http://www.americanprogress.org/issues/technology/news/2007/04/17/2887/embryonic-stem-cell-research-by-the-numbers/).

<sup>21</sup> A Warren-Jones, 'Realising New Health Technologies: the problems of regulating human stem cells in the USA' (2012) *Medical Law Review* 1.

<sup>22</sup> P Nonet, 'The Legitimation of Purposive Decisions' (1980) 68 *California Law Review* 263.

meaning, or the agent must limit the scope of their interpretation to only the divergences it can justify. As the communication is repeated through different regulatory levels,<sup>23</sup> the distorting effect of the communication becomes magnified. In addition, the specific focus of the principal relative to that of the agent modifies the primacy of specific aspects of policy. For example, a politically focused goal-setter may intend something quite different to a public policy focused agent.

How stringently the agent will be motivated to adhere to the regulatory goals set for it by its principal will be influenced by factors such as the balance of power between them.<sup>24</sup> The more power the principal exerts, the more the agent is impelled to account closely to the goals the principal sets; the less the power exerted, the more the agent can be diverted to focus upon different goals as it wishes. Similarly, the nature of the deregulation that occurred in setting up the agency defines the agent's competence to act<sup>25</sup> and this may be treated more or less prescriptively. These are issues that have already been explored within actor-centred and institutional theories, and supplement this analysis in exploring how the dislocation between goals and actions takes effect to varying extents, depending upon the agency being considered. This article focuses instead upon the central communication and how it prompts regulatory behaviour.

Even this brief consideration demonstrates that in order to dominate regulation, interest groups such as industry, patient groups or medical professional associations would have to control the legislative process, judicial interpretations, all of the empowering policy-making bodies and the agency decision-makers in every regulatory agency. So, while there is no denial that corporate bias or other self-interests undoubtedly influence regulation, they are arguably only a minor part of a conglomeration of influences brought to bear at different stages and on different levels of regulation. Regulation is hierarchical, with requirements to account for behaviour irrespective of whether the regulator is a policy- or decision-maker. As such a more significant influence is the need to explain behaviour to those that empower in

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<sup>23</sup> Presuming a model of multi-level regulatory governance in which regulation occurs vertically (hierarchically), and respecting that it also operates horizontally (between peers).

<sup>24</sup> For example, the lack of scientific knowledge by those that empower the CHMP gives it primacy over the Commission, Select Committee and the Council, see T Gehring and S Krapohl, 'Supranational regulatory agencies between independence and control: the EMEA and the authorization of pharmaceuticals in the European Single Market' (2007) 14(2) *Journal of European Public Policy* 208.

<sup>25</sup> J Donahue and R Zeckhauser, *Collaborative Governance: private roles for turbulent times* (Princeton University Press, 2011). For more on methods of incorporating public interests in policy formation see: C Sirianni, *Investing in Democracy: Engaging citizens in collaborative governance* (Brookings Institute, 2009), Chapter 2.

terms of the goals they have set. This requires some exploration of how goals relate to practices in the specific context of medicines regulation.

## 2.2 Goals

Once a new medicine is invented and this becomes known, social pressure immediately focuses on gaining access to it<sup>26</sup> and early access is in both the regulator's and industry's interests. The result of withholding access is often that patients die or receive less beneficial treatments, making it imperative that unnecessary constraints on access to originator medicines (new small molecule chemicals (SMCs), biologics and combinations)<sup>27</sup> are not imposed. As a result, it is easy to see why one of the most debated issues affecting modern medicine is how regulation can secure timely access to originators where the existence and proliferation of medicines relies upon market exclusivity.

Existing discourses around this nexus of public/industry interests in the context of regulating medicines cast the pharmaceutical industry as fixated on exclusivity<sup>28</sup> and the public as served by increased access<sup>29</sup> to medicines.<sup>30</sup> The inherent presumption is based on an understanding of regulatory bodies, such as the EPOrg (and its decision-making body, the European Patent Office (EPO)) and the EMA, as being neutral arbiters balancing the competing interests of industry and the public. This construction enables regulation to be critiqued on the degree of deviance from a maximal equilibrium.<sup>31</sup> Yet analysis of the policy and practice governing the EPOrg and the EMA identifies a very different motivational perspective, which challenges both this traditional construction of neutrality, as well as dominant interest perspectives.

Evidencing links between European regulators' aims and their priorities, which are given practical application through agency practice (changing/overlaying existing

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<sup>26</sup> Eg J Siegel-Itzkovich, 'Patients demanding access to cancer drugs call off hunger strike', (2006) 332 *British Medical Journal* 1352; European Patients' Academy on Therapeutic Innovation, 'Patient-led European Patients' Academy on Therapeutic Innovation' launched, educating patients about medicines R&D', 27 March 2012, [www.patientsacademy.eu/index.php/en/news/press-releases/45-eupati-launch-pr](http://www.patientsacademy.eu/index.php/en/news/press-releases/45-eupati-launch-pr).

<sup>27</sup> Combinations refer to SMCs with more than one active ingredient, as opposed to 'combination products' which refer to medical devices/treatments which amalgamate biological and man-made materials.

<sup>28</sup> Through patent protection or trade secrecy and (for medicines) additionally through supplementary protection certificates (SPCs) and market exclusivity of clinical trials data.

<sup>29</sup> Accessibility is about physically obtaining innovations (either to continue development or proliferated to end-markets) conveniently, which are safe and reliable, in sufficient quantity, affordably and timely.

<sup>30</sup> In a global context, 'access to medicines' and 'equality of access' debates (eg CM Ho, *Access to Medicine in the Global Economy* (Oxford University Press, 2011)); in a European/domestic context, concerning 'access to novel medicines': eg RE Epstein, *Overdose: How excessive government regulation stifles pharmaceutical innovation* (Yale University Press, 2006).

<sup>31</sup> Eg N Tuominen, 'An IP perspective on defensive patenting strategies in the EU pharmaceutical industry', (2012) 34(8) *European Intellectual Property Review* 541.

institutional norms) and are supported by legislative instruments and court decisions, is easily proven. In the context of medicines regulation, economic interests within institutional aims and policy documents that are put into effect through specific legislative instruments can easily be identified within the broader policy landscape in the EU.<sup>32</sup> While these goals constrain the standards of decision-making bodies within the EMA, for example, it is argued that this does not identify what prompts the agency to implement its aims and policies as specific decisions/operating practices to explicitly govern its behaviour. It is a fully explanatory link between goals and behaviour which is missing, but which is necessary to open up regulatory behaviour to public scrutiny.

In terms of patenting innovative medicines, the facilitative nature of the EPOrg is evident in its inception,<sup>33</sup> as well as being embedded within the EPO's institutional framework through its mission statement, which is to 'support innovation, competitiveness and economic growth across Europe'.<sup>34</sup> Clearly this is a remit which already marks the interests of the regulator as partisan, undermining any presumptions of neutrality. These aims can be linked to the broad practices of the EPO supporting: innovation through the provision of patent rights and the Appeal Board decisions which generally interpret the law in favour of patentability;<sup>35</sup> competitiveness through ensuring favourable regulatory comparability with competitor patent-granting bodies to ensure against a 'brain-' or 'tech-drain' to countries outside of Europe;<sup>36</sup> and economic growth which is monitored by a Chief Economist,<sup>37</sup> and encouraged by working with other countries to ensure that their regulatory environment and enforcement is advantageous to European innovators.<sup>38</sup> While this describes why broad

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<sup>32</sup> Eg The European Commission states that it 'plans its work, including the drafting of new legislation, based on the political priorities set by the President' (European Commission webpages, [http://ec.europa.eu/atwork/planning-and-preparing/index\\_en.htm](http://ec.europa.eu/atwork/planning-and-preparing/index_en.htm)), which results in policy documents (eg the 2008 European Commission report, Safe, Innovative and Accessible Medicines: a Renewed Vision of the Pharmaceutical Sector, (2008) COM(2008) 666 final, especially at 4, 14-15, [http://ec.europa.eu/health/human-use/package\\_en.htm](http://ec.europa.eu/health/human-use/package_en.htm)) and the Communication from the Commission, Pharmaceutical Sector Inquiry Report, SEC(2009) 952 (2009)); and incorporated within legislative instruments (eg Regulation 536/2014/EC on clinical trials on medicinal products for human use (2014) OJ EU L158/1).

<sup>33</sup> Under the European Patent Convention 1973, in which the Preamble states its purpose to be: '...to strengthen co-operation between the States of Europe in respect of the protection of inventions'.

<sup>34</sup> EPO website: [www.epo.org/about-us/office/mission.html](http://www.epo.org/about-us/office/mission.html) and this is replicated in the intention of the unitary patent to be an instrument to facilitate the proliferation of technology throughout Europe (Regulation 1257/2012 implementing enhanced cooperation in the area of the creation of unitary patent protection, Recital (1) (31.12.2-12) OJ EU L361/1-8).

<sup>35</sup> Eg T144/83 DU PONT/Appetite Suppressant [1987] EPOR 6.

<sup>36</sup> Eg Trilateral Project B3b, Report on Comparative study on biotechnology patent practices: Comparative study on "reach-through claims" (2001) Trilateral Projects, EPO.

<sup>37</sup> The present being Theon van Dijk, [www.epo.org/news-issues/news/2013/20130904.html](http://www.epo.org/news-issues/news/2013/20130904.html).

<sup>38</sup> The ECAP project was the initiative of the EPO to work with the ASEAN (Association of South East Asian Nations) in developing and enforcing IP rights (<http://www.ecap-project.org/>), the effect of which is to make it easier for those with a European patent to obtain rights within South East Asian countries.

practices can be accounted for by being linked to the institutional/policy aims that prompt them, it does not account for specific regulatory decisions, changing practices,<sup>39</sup> or why other implementing options were not adopted. So what is missing is a motivation which accounts for this broader tranche of practices.

Similarly, in terms of the EMA it is possible to identify the institutional aims, which are split between the need to provide scientific evaluation to promote public health and to ‘support research and innovation to stimulate the development of better medicines’.<sup>40</sup> This identifies that there is more than a facilitative role expected of the EMA, but how much its duty to secure public safety is/should take priority over its facilitative role is debatable. The pertinent point here is that these institutional aims can be traced directly to policy documents as they have changed over time and to the practices that have given effect to them. For example, the aim of facilitating the development of better medicines resulted in a policy to promote rapid access to safe and effective medicines in both the 2005<sup>41</sup> and 2011<sup>42</sup> policy instruments, but the 2005 policy gave rise to the Fast Track system of market authorisation for therapeutic equivalence and where there are no new active pharmaceutical ingredients (APIs); and the 2011 policy gave rise to the Early Access to Medicines Scheme (EAMS) and a pilot for adaptive licensing (an adaptive pathway). The policy goal had not changed, but the practical application took an entirely different form. This indicates that what is missing is an understanding of how the motivation to act prompted a change in the implementation of an enduring policy goal.

This brief assessment goes some way towards linking aims/policies with practices, supporting the point that the goals alone are insufficient to account for all regulatory behaviours or even for the choice of goals prioritised. Within this analysis, there is a clear commonality in regulators prioritising market considerations (‘economic growth’, developing ‘better medicines’ interpreted as encouraging early access) over collateral aims and policies (such as safety, reliability or training). Similarly the regulatory goals are not formulated by reference to the pursuit of equally worthy ambitions which are excluded, such as achieving

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<sup>39</sup> For example, why the general principle to construe exclusionary provisions narrowly may suddenly be departed from: see G2/06 and T1372/04 WARF/Use of Embryos [2009] EPOR 15.

<sup>40</sup> EMA Mission Statement, [www.ema.europa.eu/ema/index.jsp?curl=pages/about\\_us/general/general\\_content\\_000106.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000106.jsp) [italics added] and derived from Regulation 726/2004/EC laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (2004) OJ EU L136/1.

<sup>41</sup> EMA, The European Medicines Agency Road Map to 2010: preparing the ground for the future EMA/H/34163/03/Final.

<sup>42</sup> EMA, *Road Map to 2015: the EMA's contribution to science, medicines and health* (2011), [www.ema.europa.eu/docs/en\\_GB/document\\_library/Report/2011/01/WC500101373.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101373.pdf).

social progress. For example, in the context of the EMA it could be expected that an emphasis be placed on promoting the development of cures in place of existing treatments, rather than the current emphasis on developing personalised medicines in place of traditional chemical-based medicines where the main benefits are to reduce side-effects. This analysis cannot fully account for why market concerns take priority over other considerations in either policy or decision-making processes, other than suggesting that collateral aims/policies may not be as successfully justifiable across so many diverse contexts (eg not as desirable to those that empower the regulator).

Identifying that market considerations are what link regulatory goals with practices would explain how goals and practices may change, but the justification remains the same. Goals change with different market strategies and practices change in response to changing market trends. So being able to predict regulatory behaviour relies upon understanding precisely what those market trends are.

### **3. Market potential as justification for policy implementation**

In order to confirm that regulators are motivated to consider market trends, there must be a demonstrable link between the institutional aims and policy goals identified in the previous section and existing market profiles. The link suggested in this article is that regulators interpret their goals as market-based objectives, motivated by markets being more favourable to their empowering body, but also because markets are a more achievable ambition than aiming at economic benefits. Regulators can demonstrate they have achieved economic progress if they can show their actions are designed to maximise market potential, because it is a moot point that taking advantage of market trends results in economic benefit. This gets around having to prove that regulatory behaviour directly result in economic growth, such as being linked to improvements in the balance of trade, or to gains in specific companies' market share or sales.

Market trends within Europe relate to appreciating its competitive strengths, its scope to exploit emerging markets and ways of minimising competitors' advantages and this makes it necessary to consider Europe's market potential in the broader context of competitive global markets in medicines.

As one of the leading producers of originator medicines,<sup>43</sup> it is crucial that Europe secures foreign and domestic markets by developing novel, effective and affordable medicines,<sup>44</sup> as timely as possible. At present, this focuses on ensuring that pharmaceutical innovation is sustainable and can withstand up-coming challenges. Crucially this means that market growth can be maximised if: regulation supports Europe's strengths in developing originator medicines; Europe is well-placed to deal with market growth in Brazil, China, India, North America; and parallel importers within Europe can be controlled.<sup>45</sup> This requires a brief understanding of how global markets interface with key legal rights governing medicines development and proliferation.

The implementation of the Agreement on Trade-Related Aspects of Intellectual Property Rights 1994 (TRIPs) was designed as a mechanism for enabling developed country pharmaceutical industries to exploit foreign markets by globally disseminating patent rights. In the context of medicines regulation, these markets had been inaccessible due to the risk of copying, which enables medicines to be marketed at much lower prices compared to the development costs (R&D) which must be offset by originator producers. Reluctance to implement TRIPs in developing and Least Developed Countries (LDCs) resulted in TRIPs being used by developed countries as a platform for Free Trade Agreements (FTAs) (known as TRIPs-Plus), demanding further exclusivity protection beyond patents.<sup>46</sup>

This revolves around three product-market identities: originators (confined to countries with strong patent protection); generics (which legitimately copy originators because the patent is no longer active); and 'illegal generics' (which replicate originators protected by patent rights in another country, but which are either not prohibited/not enforced in the country of production). In the short-term, TRIPs-Plus provisions benefit European originator producers because FTAs secure foreign markets ahead of national generic and illegal generic companies by providing similar or even greater exclusivity than in Europe. For example, European pharmaceutical companies increased market presence in Colombia with

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<sup>43</sup> The European Federation of Pharmaceutical Industries and Association, *The Pharmaceutical Industry in Figures report* (2013), p7, identifies that the UK and Germany are market leaders, [www.efpia.eu/uploads/Figures\\_Key\\_Data\\_2013.pdf](http://www.efpia.eu/uploads/Figures_Key_Data_2013.pdf).

<sup>44</sup> (n 42).

<sup>45</sup> (n 43) at 4. Parallel importers will be discussed in 4.2.1.

<sup>46</sup> Requiring that equivalent supplementary protection and data exclusivity measures are adopted, and that data linkage (preventing market authorisation ahead of proven patent expiry) is introduced. For more see: D Acquah, 'Extending the Limits of Protection of Pharmaceutical Patents and Data Outside the EU-Is there a Need to Rebalance?' (2014) 45(3) *International Review of Intellectual Property & Competition Law* 256; R Bhardwaj et al., 'The Impact of Patent Linkage on Marketing of Generics Drugs', (2013) 18 *Journal of Intellectual Property Rights* 18 (2013) 316.

the aim of manufacturing medicines locally and distributing in the Andean region and Central America.<sup>47</sup>

These access-to-market mechanisms have been tethered to restrictions on access-to-resources needed as starting materials for developed country originators, protected through the Convention on Biological Diversity 1992 (CBD), the Bonn Guidelines,<sup>48</sup> and more recently the Nagoya Protocol 2010.<sup>49</sup> Arguably Nagoya Protocol provisions on capacity building<sup>50</sup>—in concert with technology transfer and benefit sharing provisions—provide the basis for developed countries within Europe growing ‘endogenous research’ in developing and LDCs to gain access to starting materials in the short-term and creating future competitors in the long-term. Attempts to balance the risk of stifling national growth in LDCs before national industry building can take hold is a key reason that TRIPs implementation has again been delayed<sup>51</sup> and is likely to continue being put off as long as developed countries’ interests dominate global regulation.

Friction between competing interests results in seemingly immutable divisions,<sup>52</sup> but inexorably TRIPs is shifting global pharmaceutical capabilities and, with them, changing global markets. As countries are required to comply with TRIPs, shifts occur because national medicine production must either accommodate new laws or adapt to fill emerging market gaps. For example, countries which traditionally produced illegal generics (eg India), but now newly TRIPs-compliant, are constrained to produce generics which must wait for originator medicines to come off patent. The alternative is that medicine production is enjoined or seized as counterfeits as soon as they enter a jurisdiction in which patent rights

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<sup>47</sup> Eg in 2014, Abbott bought Lafrancol (which was previously bought by Synthesis) which made it the second largest pharmaceutical company in Colombia, just behind the Colombian pharmaceutical company Tecnoquimicas SA, see: El Tiempo, ‘Abbott Colombia Pega Salto en Escalafon Farmaceutico’, 12 June 2014, [www.eltiempo.com/archivo/documento/CMS-14108896](http://www.eltiempo.com/archivo/documento/CMS-14108896).

<sup>48</sup> Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilisation adopted by the Conference of the Parties of the CBD at its sixth meeting, The Hague, April 2002.

<sup>49</sup> For more see: C Herrlinger and M Kock, ‘Biodiversity Laws: An Emerging Regulation on Genetic Resources or ‘IP on Life’ through the Backdoor?’ (2014) 13(4) Bio-Science Law Review 119.

<sup>50</sup> Eg on capacity building notably Articles 18, 22 and 23 of the Nagoya Protocol, adopted through Regulation 511/2014/EC on Compliance Measures for Users from the Nagoya Protocol on Access to Genetic Resources and Fair and Equitable Sharing Benefits Arising from their Utilisation (2014) OJ EU L150/59.

<sup>51</sup> Council for TRIPs, Extension of the Transition Period Under Article 66.1 (WTO Document IP/C/24, 2013).

<sup>52</sup> Eg O Fasan, ‘Commitment and compliance in international law: a study of the implementation of the WTO TRIPs Agreement in Nigeria and South Africa’, (2012) 20(2) African Journal of International & Comparative Law 191; L Laxman and AH Ansari, ‘The interface between TRIPs and CBD: efforts towards harmonisation’, (2012) 11(2) Journal of International Trade Law & Policy 108; P Xiong, ‘Patents in TRIPs-Plus provisions and the interpretation of free trade agreements and TRIPs: do they affect public health?’ (2012) 46(1) Journal of World Trade 155.

exist.<sup>53</sup> This shift has the effect of spreading the generics market out from developed countries with robust pre-TRIPs patent protection, because generic producers in developing and LDCs have far lower overhead costs and can undercut production costs in comparison with developed country producers.<sup>54</sup> For example, India already offers pharmaceutical companies skilled scientist and research facilities for a fraction of Europe's cost.<sup>55</sup> Neither is technological complexity proving a barrier to competition. India is preparing to position itself as a global leader of biosimilars,<sup>56</sup> irrespective of it being more difficult to replicate them from biologics (compared with generics from SMCs). Similarly China is capacity building its supply of starting materials essential for the development and production of biologics.<sup>57</sup>

At the same time global demand for cheap illegal generics, unmet by newly legitimate generic-producing countries, is likely to be filled by LDCs with little pre-existing manufacturing capacity. This creates potential for new global centres of illegal generic production, and increases national manufacturing capabilities. Developing countries with manufacturing capacity are outsourcing supply to LDCs looking to grow their manufacturing or distribution networks. For instance, Cipla, (an Indian generic company) established business links with Uganda's pharmaceutical company Quality Chemical Industry to supply not only national demand, but demand in neighbouring LDCs.<sup>58</sup> Another example relates to transferring technology from developing countries to LDCs inherent in the agreement enabling Brazil to construct a manufacturing facility for the production of first-line anti-retroviral medicines in Mozambique.<sup>59</sup>

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<sup>53</sup> Eg Delhi High Court decision in *Glenmark v Merck Sharp* [2015] PT Jyothi Datta, 'Delhi HC: Glenmark can't sell diabetes drug Zita, Zita-Met' 20 March 2015, *The Hindu Business Line*, [www.thehindubusinessline.com/companies/glenmark-loses-diabetes-drug-case-to-merck/article7015446.ece](http://www.thehindubusinessline.com/companies/glenmark-loses-diabetes-drug-case-to-merck/article7015446.ece); Request for Consultations by India, European Union – Seizure of Generic Drugs in Transit, WT/DS408 (May 11, 2011) [www.wto.org/english/tratop\\_e/dispu\\_e/cases\\_e/ds408\\_e.htm](http://www.wto.org/english/tratop_e/dispu_e/cases_e/ds408_e.htm); Request for Consultations by Brazil, European Union – Seizure of Generic Drugs in Transit, WT/DS409; Regulation 608/2013/EU concerning customs enforcement of intellectual property rights ((2013) OJ EU L181/15), which states that in-transit goods which do not clearly identify where they are continuing onto must either be proven to be in transit or risk being destroyed for breaching patents (Art 2(1)(e)) or medicinal SPCs (Art 2(1)(f)).

<sup>54</sup> In 2013 India accounted for 40% (by volume) of USA generics import and this is expected to increase with emphasis in developed countries on cost-effective care (eg Obamacare): India Ratings & Research, *Impact of 2013 US FDA Actions on India Pharma* (Special Report) (India Rating & Research, 2014).

<sup>55</sup> S Chaudhuri, *The WTO and India's Pharmaceutical Industry: Patent Protection, TRIPs and Developing Countries* (Oxford University Press, 2009).

<sup>56</sup> H Malhotra, 'Biosimilar and non-Innovator Biotherapeutics in India: An Overview of the Current Situation', (2011) 39 *Biologicals* 321.

<sup>57</sup> W Hoffman, 'The Shifting Currents of Bioscience Innovation', (2014) 5(1) *Global Policy* 76.

<sup>58</sup> In-Pharma, 'Uganda's QCI to Invest \$80m in AIDS and Anti-malarial Drug Capacity' (In-Pharma, *Technologist.com*, 2011).

<sup>59</sup> WHO, WIPO and WTO (2013) *Promoting Access to Medical Technologies and Innovation: Interaction Between Public Health, Intellectual Property and Trade* (London, 2013).

The impact of international regulation fails to address general domestic demands for medicines specific to LDCs,<sup>60</sup> or to encourage local investment in R&D.<sup>61</sup> The Doha Declaration 2001, Paragraph 6<sup>62</sup> enables LDCs with no manufacturing capacity to compulsorily license medicines from another country,<sup>63</sup> but is arguably limited to public health problems such as widespread epidemics and only in limited quantities even though not currently confined to emergencies.<sup>64</sup> In the long-term these global industry shifts could help to grow domestic capabilities in these LDCs, but in the meantime Doha is debatably little more than a limited exception to protect public health and research use.

This analysis demonstrates that European regulators are engaged in facilitating access to medicines globally (beyond humanitarian contexts), even in the face of inevitably helping to grow the competitors who are already pricing pharmaceutical manufacturers within Europe out of the market. The production of generics is already a migrating market. Accessing new markets (open with TRIPs-compliance) is a collaborative effort, engaging with national industry in manufacturing and distributing patented medicines on a sliding scale of diminishing returns over time. This is because acceptance of restrictive terms under TRIPs-Plus provisions will only prevail during periods of growth in domestic capabilities. As soon as developing and LDCs have established their own industries, trade negotiations will become a more balanced affair. In the meantime, European regulators have a clear incentive to grow specific markets: (1) encouraging originators enables Europe to expand markets it

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<sup>60</sup> C Correa, *Pharmaceutical Innovation, Incremental Patenting and Compulsory Licensing* (Research Paper 41, South Center, 2011); see also C Correa, *Integrating Public Health Concerns into Patent Legislation in Developing Countries* (South Centre, 2010).

<sup>61</sup> J Arkinstall et al, 'The Reality Behind the Rhetoric: How European Policies Risk Harming Access to Generic Medicines in Developing Countries', (2011) 8(14) *Journal of Generic Medicines* 14.

<sup>62</sup> Doha Declaration, Paragraph 6, WT/MIN(01)/DEC/2 (2001), [www.wto.org/english/thewto\\_e/minist\\_e/min01\\_e/mindecl\\_trips\\_e.htm](http://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm) and WT/L/540 and Corr.1(2003), [www.wto.org/english/tratop\\_e/trips\\_e/implem\\_para6\\_e.htm](http://www.wto.org/english/tratop_e/trips_e/implem_para6_e.htm); implemented within Europe through Regulation 816/2006/EC on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export to countries with public health problems ((2006) OJ L157/1), and implemented within the UK as s128A, UK Patents Act 1977.

<sup>63</sup> Eg *Natco Pharma Ltd v Bayer Corporation* [2013] The Intellectual Property Appellate Board, (Order No 45 of 2013), [www.ipab.tn.nic.in/045-2013.htm](http://www.ipab.tn.nic.in/045-2013.htm).

<sup>64</sup> Originally defined as a 'national emergency or other circumstances of extreme urgency' (Article 31(b), TRIPs) and designed to enact the UN Millennium Development Goals (UN Millennium Development Goals 2000, Development Goal III, Resolution 19; currently MDG set to expire in 2015, [www.un.org/millenniumgoals/](http://www.un.org/millenniumgoals/)). This interpretation was supported by the World Trade Organisation (WTO), 'Declaration on the TRIPs Agreement and Public Health' (9-14<sup>th</sup> November 2001), Ministerial Conference Fourth Session (WT/MIN(01)/DEC/W/2) ('Doha Declaration'), para 5(c); although disputed by some commentators P Vandoren and J C van Eckhaute, 'The WTO Decision on Paragraph 6 of the Doha Declaration on the TRIPs Agreement and Public Health: Making it work' (2003) 6(6) *Journal of World Intellectual Property* 779 and carried into the wider 2005 Decision wording which exemplifies use as 'only in the case of a national emergency or other circumstances of extreme urgency or in cases of public non-commercial use': WTO General Council, Annex to the Amendment of the TRIPs Agreement (6 December 2005) WT/L/641 which had until 31<sup>st</sup> December 2015 to be accepted.

already leads; (2) promoting newly-valued medicines responds to market gaps, arguably increasing the potential for down-stream development and quickening the pace of the proliferation of up-stream technology; and (3) in expanding earlier access to generic production Europe may maintain its existing market lead over an expanding field of global competitors.

If these three market potentials correlate to existing and recent changes in regulatory behaviour, it confirms that regulators are motivated to interpret their goals relative to market trends and justify their behaviour as supporting maximising current market potential. Inherent within this is a need to assess the degree to which regulators can/cannot effectively support these market potentials and the degree to which this equates to achieving the goals set in either promoting economic growth or securing better medicines. This enables a distinction to be made between regulators being incapable of achieving their goals within the limits of their existing powers and goals being capable of being affected but not being met, both of which identify that regulators are more focused on explaining their behaviour than on actually achieving their goals.

#### **4. Practical implementation of market potential**

##### **4.1 Patents: regulating the development of medicines innovation**

Patents are often described as monopolistic, but this presumes an innovation flow which ignores how many patented medicines never reach the market and that, even when successfully marketed, individual patents represent very different levels of ‘market grab’.<sup>65</sup> Focusing on exclusivity also overlooks that patents fundamentally require disclosure of the innovation so it can be recreated (eg having the knowledge from a published patent<sup>66</sup> for full proliferation once exclusivity expires),<sup>67</sup> and facilitate access in the life of the patent for limited purposes (eg being licensed, for resale as a parallel trader or falling within an exempted category).<sup>68</sup> Hence, patents both deter access (by imposing a period of exclusivity) and encourage access (by protecting investment, incentivising creation and requiring disclosure). Without patents innovators would not put their medicines into the public domain

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<sup>65</sup> Market grab means the value of the patent in terms of market share, which is predominantly reliant upon the relationship of the patented product/process to the existing market, but is similarly reliant on other factors which contribute to market share such as the branding strategy, status of the company in the field, number and nature of competitors, etc.

<sup>66</sup> European Patent Convention 2000 (EPC), Art 83; G2/98 Requirement for claiming priority of the same invention [2001] OJ EPO 413.

<sup>67</sup> EPC, Art 63(1) granting 20 years of patent protection from the date of first filing.

<sup>68</sup> See Unified Patent Court Agreement (2013) OJ EPO C175/1, Art 27 and this includes defensible use.

(by marketing if protected by trade secrecy,<sup>69</sup> or data/market exclusivity) until they were sure they had exhausted all commercial value.

If there must be patents, the question is not whether they are restrictive, but how they relate to market growth? The answer relies on three factors which are central in determining how effectively a patent results in market grab: (1) the strength of the patent; (2) how the innovation relates to the existing technological field; and (3) how inaccessible licenses are. Whether or not this market grab has the effect of encouraging innovation proliferation, and by association increases economic growth, or slows down the pace of innovation is also related to the breadth of research exemptions. While broader exemptions reduce the restrictive effect of patents to facilitate the growth of competitors and increase the pace of innovation, narrow exemptions facilitate strong lead/originator rights by keeping competitors to a minimum and slowing the pace of innovation. In combination, these are the most crucial mechanisms by which to identify the extent to which patent regulators can affect markets/economic growth.

#### 4.1.1 Strength of patents

Patent provisions<sup>70</sup> give the patent holder exclusionary rights over the patented product/process,<sup>71</sup> and there are three relevant forms of patent in this context: product per se; ‘use claims’; and processes.

##### Product per se patents

Product per se patents are the strongest form of protection, extending to the product no matter how it is produced or what its use. Traditionally the most criticised for excluding access, product per se rights convey the potential for market control and historically resulted in rights over medicines being excluded.<sup>72</sup> For public interest reasons, the patient’s best interests should guide treatment decisions (rather than the avoidance of licence fees) and public interest is

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<sup>69</sup> Protected by common law within individual Member States (eg in the UK see: *Coco v AN Clark (Engineers) Ltd* [1969] RPC 41; *Faccenda Chicken Ltd v Fowler* [1987] Ch 117; *Mason v The Provident Supply and Clothing Co* [1913] AC 724, *Lindner v Murdock’s Garage* [1950] 83 CLR 629; *Terrapin Ltd v Builders’ Supply Co* [1967] RPC 375, but see *VestergaardFrandsen v Bestnet Europe Ltd* [2010] FSR 2 and currently the subject of a new European Directive on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure (provisionally agreed 18 December 2015: <http://data.consilium.europa.eu/doc/document/ST-15382-2015-REV-1/en/pdf>).

<sup>70</sup> Unitary patents are granted through the EPO and sit alongside the existing bundle of national rights (eg UK Patents Act 1977 (as amended) (UKPA), s139(7)), adopting Member States’ legal provisions in as much as they comply across Europe, (Regulation 1257/2012/EC (n 34), Arts 3, 5 and 7); Unified Patent Court Agreement (n 68), Art 25.

<sup>71</sup> See Unified Patent Court Agreement (n 68), Art 25; eg UKPA, s60 (‘others’ meaning third parties without license or exemption/defence).

<sup>72</sup> Former (pre-TRIPs compliance) India Patent Act 1970; see also Section 3(1) (x) the Zanzibar Industrial Property Act (Tanzania) 2008.

similarly the underlying rationale for requirements for moral innovation.<sup>73</sup> Within Europe such limitations have gradually been eroded—exclusions affecting only some surgical, therapeutic or diagnostic techniques which directly affect treatment,<sup>74</sup> and only some immoral innovations being prevented.<sup>75</sup> Such erosions represent market expansion opportunities. At root, product per se patents restrict only to the extent that they exclude third parties so the innovator can develop and market; or by requiring royalties for third parties to develop related competitor products or next generation innovations. Innovations which do not rely on the originator are unrestricted by it. This means that on a general basis, patent law has developed to provide scope to ‘invent around’ existing rights and this is essential for keeping up the pace of innovation with healthy competition.

*‘Use-claims’*: newly-valued medicines

More recently patent law has allowed that new purposes for existing products/originators is protectable through expanding contexts of use claims (specific to medicines these are known as ‘indications’)<sup>76</sup> Patent law practice has diverged on the issue of whether a new technical effect on its own can warrant protection, but the pertinent point here is that there has been a definitive lowering of qualification thresholds in accepting the patentability of innovations which are only marginally new and inventive.<sup>77</sup> Protection to these use-bound indications is only good against infringers using the same medicine to treat the same condition or to achieve the same effect.<sup>78</sup> The originator must be licensed (protecting his initial investment), but offering protection to dependent technologies (new uses or new therapeutic effects) facilitates increased fields of competitors, maximising the potential for next generation

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<sup>73</sup> EPC, Art 53(a); T315/03 HARVARD/Oncomouse [2006] OJ EPO 15; G2/06 and T1372/04 WARF/Use of Embryos [2009] EPOR 15; Case C-34/10 Brüstle v Greenpeace [2011] ECR I-9821; Case C-364/13 International Stem Cell Corp v Comptroller General of Patents [2014] Opinion of Advocate General July 2014, <http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1414505526856&uri=CELEX:62013CC0364> [2013] EWHC 807 ; T2221/10 TECHNION Culturing Stem Cells [2014] EPOR 23.

<sup>74</sup> EPC, Art 53(c); G1/07 MEDI-PHYSICS/Treatment by Surgery [2010] EPOR 25; G2/08 ABBOTT RESPIRATORY/Dosage Regime [2010] EPOR 26; G1/07 and T245/87 SIEMENS/Flow Measurement [1989] 5 OJ EPO 171; G1/04 CYGNUS/Diagnostic Methods [2006] 5 OJ EPO 334 (respectively).

<sup>75</sup> See Brüstle (n 73), distinctions based on potential for life and not objectifying embryos are very open to interpretation, undermining their moral legitimacy.

<sup>76</sup> EPC, Art 54(4); T1020/03 Method of Administration of IGF-I/GENENTECH [2007] OJ EPO 204; G2/08 (n 74).

<sup>77</sup> EPC, Art 54(5) permitting 2<sup>nd</sup>/subsequent indications; G2/88 MOBIL/Friction Reducing Additive [1990] EPOR 73; T509/04 ALLERGAN (unreported), cited in UK-IPO Examination Guidelines, Examination Guidelines for Patent Applications relating to Medical Inventions in the Intellectual Property Office (May 2013), para 145 see T1020/03 (ibid) and in the UK: contra Merrell Dow v Norton [1996] RPC 73; Actavis v Janssen [2008] EWHC 1422; and EPO approach to selection inventions approved in *Dr Reddy’s v Eli Lilly* [2010] RPC 9.

<sup>78</sup> Depending on the interpretation of the Bolar/Research exemption, indications may infringe the originator if they do not obtain a licence (discussed at 4.1.4 below).

market exploitation to happen quicker. In effect, by rewarding innovatory effort on existing products (patented or not), the patent regulator can create new market potential from existing technology; proliferate that technology more widely in up-stream markets; which then quickens the pace of innovation.

Problems arise with ‘follow-on’ medicines, sub-categorised for clarity as ‘me-better toos’ and ‘me toos’, both of which are distinguished from generics as not being copies. ‘Me-better too’ medicines offering no additional therapeutic value are generally the result of the ‘race to invent’ the originator,<sup>79</sup> or attempts to invent around it once it has been patented. Any innovation only becomes protectable if it is sufficiently different from existing technology and, for me-better toos falling within the same class<sup>80</sup> as the originator, this rests on achieving the same therapeutic benefit for the same use by a different means (eg targeted to a different active ingredient, DNA-sequence or protein product not disclosed by the originator).<sup>81</sup> The social value of me-better toos is that they may offer a clinical benefit: this can be crucial in developing pharmaceuticals where side-effects, contra-indications, building up resistance after frequent use, or adverse reactions to specific phenotypes may require different treatment options.

Me toos on the other hand should be unpatentable because they offer nothing new: they merely re-claim the existing innovation. The difficulty of factually distinguishing a me-better too from a me too is part of the reason why commentary is split on the value of follow-ons.<sup>82</sup> In a competitor, it is likely the patent holder will instigate infringement proceedings or challenge attempted patenting, but difficulties arise where it is the patent holder claiming a me too. This is because it can be extremely difficult to detect a me too on examination (particularly in the context of a biologic), there may be no competitors capable of bringing

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<sup>79</sup> See: JA DiMasi and LB Faden, ‘Competitiveness in follow-on drug R&D: a race or imitation’, January 2011, 10(1) *National Review of Drug Discovery* 23.

<sup>80</sup> Classification of medicines relies upon the Anatomical Therapeutic Chemical Classification System, which groups medicines in terms of their discrete biological systems within the body, therapeutic effect, pharmacological group, chemical family, specific chemical name and cross-referenced to its defined daily dosage: WHO Guidelines for ATC classification and DDD assignment (2013, as amended), [www.whocc.no/filearchive/publications/1\\_2013guidelines.pdf](http://www.whocc.no/filearchive/publications/1_2013guidelines.pdf).

<sup>81</sup> They have either varied the product claimed or provided an equivalent technology beyond the scope of the originator patent. In the UK: *Kirin-Amgen v Transkaryotic Therapies (No 2)* [2005] RPC 9; *PLG Research Ltd v Ardon International Ltd* [1995] FSR 116; *Kastner v Rizla Ltd* [1995] RPC 585; *Improver v Remington* [1990] FSR 181; *Catnic Components Ltd v Hill & Smith Ltd* [1982] RPC 183.

<sup>82</sup> J Cohen, L Cabanilla and J Sosnov, ‘Role of follow-on drugs and indications on the WHO essential drug list’ (2006) 31(6) *Journal of Clinical Pharmacy and Therapeutics* 585; see also RA Bouchard et al, ‘The Pas de Deux of Pharmaceutical Regulation and Innovation: Who’s Leading Whom?’ (2009) 24 *Berkeley Technology Law Journal* 1461.

proceedings, and legal practitioners' reputations often hinge on the length of time they are able to 'evergreen' their clients' proprietary rights.<sup>83</sup>

While patents allow innovation which is an alternative to originators with no requirement to be better, innovation development is primarily motivated by the potential for remuneration by healthcare payers. Within this selection process, the role of health technology assessments<sup>84</sup> (HTAs) is central and these are focused on identifying value to justify cost.<sup>85</sup> Even without remuneration decisions being directly 'value-based',<sup>86</sup> clinical trials have become more frequently designed to demonstrate efficacy relative to a reference product (the currently funded in class),<sup>87</sup> to maximise potential adoption. The limitations of patents to incentivise innovation is exemplified by antibiotic development, which until recently remained undeveloped largely because of the inability to demonstrate added value.<sup>88</sup>

This suggests that regulatory bodies charged with goals directed to innovation/economic growth are hampered in achieving this aim, because they are only one of a number of regulatory bodies that affect growth. In this instance, it makes no difference that the patent system requires only difference, rather than advantage, because trials management is geared towards remuneration restrictions. Conversely, if the patent regulator is to be capable of achieving its economic goals, better mechanisms for identifying and preventing me too's are required and yet this is not being sought at present.

## Process patents

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<sup>83</sup> For an example of attempted evergreening: *Merrell Dow v Norton* (n 77).

<sup>84</sup> These assessments examine the social, economic and value of new medicines to advise healthcare commissioners and providers.

<sup>85</sup> Eg in England, the National Institute for Health and Care Excellence (NICE) permit for a range of approaches to HTAs, but all are focused on benefits: <http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9/the-reference-case> and the introduction of the NHS Scorecard, ensures uniform adoption/proliferation of the innovations selected: [www.england.nhs.uk/ourwork/innovation/innovation-scorecard/](http://www.england.nhs.uk/ourwork/innovation/innovation-scorecard/).

<sup>86</sup> Intentions to introduce Value-Based Pricing in England in January 2014 on the back of the Health and Social Care Act 2012, were abandoned after receiving much criticism (eg B Arzymanow and J Manning, Value-based pricing: the wrong medicine for the nation? (Health 2020.org, 2013), [www.2020health.org/dms/2020health/.../reports/VBPRReport\\_6-5-13.pdf](http://www.2020health.org/dms/2020health/.../reports/VBPRReport_6-5-13.pdf)).

<sup>87</sup> Eg SJ Pocock, 'The pros and cons of non-inferiority trials', (2003) 1717 *Clinical Pharmacology Fundamental & Clinical Pharmacology* 483; the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q10 Guidelines adopted by the EMA, 'ICH guideline Q10 on pharmaceutical quality system', 14 May 2014 (EMA/CHMP/ICH/214732/2007), at 8 referenced to Q8, [www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/09/WC50002871.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC50002871.pdf).

<sup>88</sup> Westminster Health Policy Forum, 'Healthcare innovation: medicines, technology, service delivery and regulation', 29th October 2013; M Tran, 'Call for new generation of antibiotics to fight off superbugs' (2 July 2014) *The Guardian*, [www.theguardian.com/society/2014/jul/02/call-new-generation-antibiotics-fight-superbugs](http://www.theguardian.com/society/2014/jul/02/call-new-generation-antibiotics-fight-superbugs).

Process patents are a far narrower form of protection in comparison with product per se protection, because (although they collaterally protect the product directly resulting from the process)<sup>89</sup> infringement relies on use of the process. Generally more than one procedure results in any given medicine, so potential dangers are limited to ring-fencing where every discernible method of obtaining a ‘platform’<sup>90</sup> medicine excludes competitors. Frequency is undocumented, but is likely to be rare. Product per se and process patents are generally claimed together and combined rights can cause a greater restrictive effect.

### Combining forms of protection

Product per se and process patents on originators restrict unlicensed use of medicines fitting the patent claim and a small amount of improvement/diversification which falls within the original patent (eg APIs in the same chemical family originally claimed, products in capsule, liquid or double strength forms). Developing the originator to treat different conditions, where there is a clinical benefit or offering therapeutic value (even if it is only a better dosage regime),<sup>91</sup> can attract separate patent protection (subsequent indications), as can the development of novel manufacture or supply processes.<sup>92</sup> This enables innovation development to take as many routes as possible, resulting in different medicines or treatment options. Innovation spreads quickly, enhancing trade potential, but this benefit is diminished by: the confusion of purchasing decisions resulting from patents and licences; and the increase in competition (eg reducing the possibility for an originator patent owner to ‘reserve markets’ in subsequent indications).

In an attempt to secure its goal (economic growth) by maximising market potential, the EPO gives the strongest protection to originators and changed its regulatory practices to promote protection of newly-valued medicines. In some respects the EPO is hampered in actually achieving growth, because it is only one of a number of regulatory bodies that affect innovation. This was exemplified by it making no difference that the patent system requires only difference, rather than advantage, because trials management is already geared towards remuneration restrictions. Understanding the justificatory role of market potential identifies that the patent regulator is not achieving its goals and to do so there must be: greater co-

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<sup>89</sup> See Unified Patent Court Agreement (n 68), Art 25(b) and (c); and eg UKPA, s60(1)(b) & (c); *Pioneer Electronics v Warner Music* [1997] RPC 757.

<sup>90</sup> A technological leader in its field, discussed in 4.1.2 below.

<sup>91</sup> G2/08 (n 74).

<sup>92</sup> T958/94 *Anti-tumoral Agent* [1997] OJ EPO 241.

ordination between regulators; better mechanisms for identifying and preventing me toos; and more consideration of the collateral impacts of adopting specific regulatory practices.

So while it is clear that the EPO regulates to maximise market potential in the hope that it will result in economic growth, the scope for actually securing economic growth must be considered relative to how much of the market can be secured by even the strongest patents. This requires an examination of other factors which affect market grab, specifically how the patent right sits in the technological field to which it relates and licensing rights, both of which are predominantly outside of the regulator's control.

#### 4.1.2 Innovation relative to the technological field

Irrespective of how strong the patent, its effect is reliant upon how much the innovation dominates a specific field of technology. Any patent on a technological breakthrough has a restrictive effect, but it becomes 'foundational' when it relates to a platform technology. This technology may be the first in a new field of innovation (eg monoclonal antibody technology or recombination), or the beginning of a broad/long chain of innovation.<sup>93</sup> The fear is that foundational patents on platform technology create a bottleneck because access relies on licences. Monoclonal antibody technology and recombination both began with a single breakthrough giving rise to entirely new scientific specialties, but only the initial innovation in recombination was patented.<sup>94</sup> So this goes some way towards dispelling myths that patents restrict technological development: patents may temporarily slow the pace of innovation by restricting initial access by requiring licenses, but in the long-term represent no numerical loss of development. Irrespective of how the chain of innovation diverges as it nears the point of end-use by consumers, without access to platform technology the best prospect for developing effective and non-toxic medical treatments may never exist. So this is a very high-stakes issue.

This analysis demonstrates that regulators cannot totally control economic growth by regulating patents, because any restrictions on continuing technological development or market proliferation are commensurate with how difficult/how long rival and replacement innovations take to create. Even where rights cannot be circumvented, competitors (who were racing to the patent office, but were unable to achieve sufficient novelty) can become

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<sup>93</sup> 'Broad' referring to parallel technologies which derive from a single originator and have many immediate markets; 'long' referring to innovations which rely upon the previous step for development and progress towards a single end-market.

<sup>94</sup> Eg M Clark, 'Empowering the inventor – the case of monoclonal antibodies', (2005) 23 Nature Biotechnology 1047.

potential licensees in the ensuing race to develop the next generation of innovation. So the economic value of the patent rests on its market grab and this is far more affected by how the innovation relates to other products in the market and dependence on licences, than on the strength of the patent.

#### 4.1.3 Restrictive effects on licences

Licences can apply to innovations within the same generation (newly-valued medicines), or in the development of new generations where the licence follows the same chain of innovation (eg producing a diagnostic test kit following the development of a biologic). Innovation development in the same generation can result in ‘patent thickets’ (where closely related narrow patent rights are held by different owners), or ‘patent clusters’ (where they are claimed by the same patent holder) and this can preclude marketing. Where narrow rights are owned by the same innovator, it has the equivalent effect of claiming too broadly. ‘Licence stacking’ over successive generations can jeopardise development by pricing innovation out of the market (the licensing fees being larger than returns on development), or by the sheer volume of rights (tracking down so many parties).<sup>95</sup> This connection between legal patents and licensing is undeniably restrictive but, despite the terminological focus on patents, the absence of patents would not lessen licences. Instead restrictions would be based on commercial licences over trade secrecy, data/market exclusivity rights or centre on know-how.<sup>96</sup>

Short of being an industry standard, the cumulative effect of a plethora of patents/licences is the potential to dominate a particular medical research area or a market for a specific medical condition. It can also lead to self-competing, where a single pharmaceutical company markets: originator medicines that have fallen out of patent protection but retain brand-loyalty; self-generic versions to compete with generics from competitors; subsequent indications for treatment in closely related medical conditions; me-better too medicines; and product delivery variations on the originator, indications and the me-better toos. While not all of these categories may be exploited conjointly, staggering market entry can extend the duration of exclusivity. From the consumer’s perspective there is no expectation that four apparently competing medicines come from the same producer and

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<sup>95</sup> (n 36).

<sup>96</sup> Know-how relates to proprietorial information which relates to practical knowledge, such as what temperature tolerances new vaccines must be kept at to avoid becoming attenuated.

this creates scope for price fixing, which relies on regulation through competition law.<sup>97</sup> Even where pricing does not amount to anti-competitive practices, the use of discount pricing, bulk offers and other normal retail tools confuse medicine purchasing decisions.

The vast bulk of licensing patented technology is left to the industry to govern (compulsory licensing and licenses as of right being nominal regulatory interventions) and this shifts the restrictive effects of licenses away from patent regulation and onto the failure of competition law to prevent ‘sharp practices’ which do not breach formal competition rules. The European Commission is already committed to increasing competition law scrutiny,<sup>98</sup> and practices falling short of the rules,<sup>99</sup> but monitoring and enforcement is intended to be a co-operative endeavour between the industry, ‘market participants’ and regulators.<sup>100</sup> There is no evidence that ‘market participants’ was ever intended to mean the patient groups, commissioners and doctors included in the consultation prior to the 2009 Pharmaceutical Sector Inquiry.<sup>101</sup> This indicates that regulation is firmly prioritising competitive market considerations over collateral economic or social concerns that may relate to the selection of health targets, cost-efficiencies or marketing strategies that may be of interest to the groups excluded from the regulatory process.

Enabling a patent holder to control subsequent innovation in the same field can be justified by the fact that ensuing developments inherently rely upon the original contribution for their existence. The patent holder is usually in the best position (as the leader in the field) to exploit the development most effectively and speedily (eg having the manpower and know-how, or in identifying licensees). Conversely, developing the originator medicine for unrelated medical contexts is far less likely to be carried out by the patent holder (their field of expertise being determined by existing manpower, the potential to buy-in expertise as needed and existing marketing networks). This is not a result of the size of the R&D

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<sup>97</sup> Unfair competitive practices: TFEU, Article 101; eg T77/08 Dow Chemical Co v EC [2012] 4 CMLR 19; or dominant market position under TFEU, Article 102; Case C-457/10 AstraZeneca v EC [2013] 4 C.M.L.R. 7, or other dubious trading practices such as paying generic competitors to stay out of the market: Case T-472/13 Lundbeck v Commission [2013] EU Focus 310, 8-9; on appeal C-325/76 [2013].

<sup>98</sup> See Pharmaceutical Sector Inquiry Report (n 32), p522; European Commission, The 4<sup>th</sup> Report on the monitoring of patent settlements (January-December 2012), <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>.

<sup>99</sup> See Pharmaceutical Sector Inquiry Report (n 32) p524.

<sup>100</sup> See Pharmaceutical Sector Inquiry Report (n 32) p524-525.

<sup>101</sup> The Patent Settlement and Antitrust monitoring reports that have been issued since the Sector Inquiry certainly support this reading, <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>.

enterprise, as even large pharmaceutical companies need to out-source or license further development as medical innovation becomes increasingly specialised and costly.<sup>102</sup>

Permitting indications with therapeutic benefits, encouraging off label uses<sup>103</sup> to be brought within the scope of formal protection, and facilitating me-better too medicines as clinical alternatives demonstrates that patent regulation nurtures dependent innovation. This secures the widest saturation of innovation. Promoting development of clinical alternatives can be inhibited post-patent and creation rests on introducing specific incentive schemes, or changing the selection criteria for healthcare remuneration. Undetectable me toos, which are against everyone but the rightholders' interests, are the cost of maximising the potential of newly-valued medicines. Far more of the restrictive effect of innovation ownership is incidental to the patent right, because it emanates from the right relative to the existing technology in the market and this is an aspect which is beyond the control of regulators and industry; or it emanates from licensing, and regulators are only beginning to respond to the reality of market practices. This requires a focus on activities that fall outside traditional concepts of unfair competitive practice and market dominance definitions (eg paying competitors not to produce generics). Regulating market growth transcends a single regulator and necessitates oversight of: all forms of marketing; product liability beyond manufacturing failure; as well as regulating anti-competitive practices. This demonstrates that patent regulators on their own have a very limited potential to actually achieve the policy goals they are intended to work towards.

If goal-achievement is the focus of regulatory efforts, recent initiatives would be on facilitating economic growth by: properly policing me toos, preventing their unwarranted exclusivity; bringing licensing within the regulatory sphere; and co-ordinating the efforts of different regulators. Instead, what is achieved is entirely in line with maximising market potential by: providing strong product rights (supporting R&D); introducing lowered novelty thresholds (expanding R&D proliferation, but diluting rights in the market); and facilitating a broader range of follow-on patents (warranted or not, supporting newly-value medicines) in order to encourage market proliferation. These changes can only hope to yield greater economic growth, but they fall short of being able to ensure it.

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<sup>102</sup> See Pharmaceutical Sector Inquiry Report (n 32); WHO Commission Report, Public Health: innovation and intellectual property rights (WHO, 2006).

<sup>103</sup> Meaning use of an originator for a medical purpose not identified in clinical trials, or authorised for market use (protectable as indications: having the same therapeutic benefit, used in a new treatment context).

Beyond the effect of the patent itself, patent regulators utilise other mechanisms to encourage the proliferation of technology. A fundamental mechanism<sup>104</sup> is the research exemption, which enables regulators to balance existing rights/market shares with supporting the development of competitors who may be developing competing products, generics or the next generation of innovations.

#### 4.1.4 Falling within the research exemption

Concerns regarding the restrictive effects of patent rights often relate to the potential to prevent further medical research. To ameliorate the possibility of inhibiting the proliferation of medicines and in an effort to harmonize existing domestic research exemptions, the EU introduced the Bolar exemption.<sup>105</sup> This laid down a minimum requirement that Member States exempt from infringement the use of proprietary medicines in obtaining market authorisation for generics.<sup>106</sup> This clearly includes biosimilars with bioequivalence which do not require additional testing.<sup>107</sup> What is less clear is what else may fall within this exemption. Does it include testing: combination medicines; combination advanced therapies;<sup>108</sup> new therapeutic value for existing medicines, or obtaining information for public health reasons?<sup>109</sup> Are activities other than testing (such as manufacture, supply and importation) also within the scope of the exemption? Does it make a difference if the tests are conducted by a third party to the market authorisation, such as a clinical research organisation (CROs)? Could it include the HTAs which run in tandem with the market authorisation procedure within Member States?

In consequence of the lack of detail and the scope to provide more protection, Member States' Bolar/research exemptions are individualised, but categorise into broad or narrow.<sup>110</sup> Germany exemplifies a broad interpretation, capturing any experimental activities with a

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<sup>104</sup> For more see (n 21).

<sup>105</sup> Directive 2004/27/EC amending Directive 2001/83/EC (2004) OJ L136/34, importing a new Article 10(6) into Directive 2001/83/EC.

<sup>106</sup> See Unified Patent Court Agreement (n 68), Art 27(b), UKPA, s60(5)(i)(i).

<sup>107</sup> Therapeutic or Bioequivalence mean the generic/biosimilar medicines (respectively) perform in the same way as the originator. For generics this relies on having the same active ingredient, but combinations may require additional testing as will some biosimilars (eg resulting from unreliable targeting, lack of interface with regulatory regions, normal errors in transcription). This latter point is the reason the EMA introduced specific guidelines: Directive 2004/27/EC (n 105), introducing a new Article 10(2)(b) into Directive 2001/83/EC, listing general and specific scientific guidelines for biosimilars.

<sup>108</sup> Combination medicines are those with more than one active ingredient. Analogously this translates to biologics with more than one sequence target/cellular product, and in the context of advanced therapies (such as stem cells and human tissue) refers to the combination of biological and manufactured materials.

<sup>109</sup> UK Intellectual Property Office (UKIPO), *The Research and Bolar Exemptions: An informal consultation on patent infringement in pharmaceutical clinical and field trials* (HMSO, 2011).

<sup>110</sup> For more detail, see: L Cohen and L Peirson, 'The UK research and 'Bolar' exemptions: broadening the scope for innovation?', (2013) 8(11) *Journal of Intellectual Property Law & Practice* 837.

patented medicine, irrespective of whether it is commercial, and including clinical trials to obtain market authorisation for indications or a generic.<sup>111</sup>

Traditionally, the UK exemplified the narrow interpretation. The research exemption which pre-dated the Bolar exemption in Europe distinguished between testing and discovery (within the exemption) and merely confirming or seeking market authorisation (as falling outside).<sup>112</sup> This latter aspect was amended in the context of originator medicines to accommodate the EU Bolar exemption, which was construed narrowly to exclude activities relating to market authorisation of indications, but allowing any activities necessary to obtaining market authorisation of generics (including manufacture, import and supply of samples).<sup>113</sup> Arguably research tools (defined as the use of protected products ‘on another invention’) were excluded from the exemption.<sup>114</sup> In the context of stem cells, the limitations on patenting stem cells per se means that future patents are likely to be claimed by reference to the cells into which stem cells can be specialised or their specialisation as ‘factory’ cells for clinical trials. This brings stem cells within the definition of research tools where they are not being used for direct therapeutic benefit on patients: so research tool stem cells fall outside of the research exemption. This interpretation is supported by the enduring construction of exemptions as allowing activities which do not impinge upon marketability. For research tools the interim research market is their end market, so an exemption which includes such tools would have the effect of stopping them from being developed or traded. Suggestions that the Bolar exemption should include research tools (because it is intended to expedite generic entry and rights over tools can delay this)<sup>115</sup> are undermined by the range of tools generally available which has the effect of reducing fees (eg the licensing fees are considerably cheaper than those for originator medicines), and tools without rights which can easily be copied will cease to be developed.

The UK Legislative Reform (Patents) Order 2014<sup>116</sup> changed the pre-existing protection of market value and introduced supplementary provisions which broaden the exemption considerably. As such it represents an example of legislative measures being introduced to maximise market potential, because it facilitates generics reaching the market more quickly. The

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<sup>111</sup> Clinical Trials I [1997] RPC 623; Clinical Trials II [1998] RPC 423 (respectively).

<sup>112</sup> See Unified Patent Court Agreement (n 68), Art 27(d); UKPA, s60(5)(b); *Monsanto v Stauffer Chemical Co* [1985] RPC 515, para 3.

<sup>113</sup> UKIPO Guidance on the Bolar exemption, [www.ipo.gov.uk/p-policy-pharmaceutical.htm](http://www.ipo.gov.uk/p-policy-pharmaceutical.htm); Medicines and Healthcare products Regulatory Agency (MHRA) Guidance, [www.mhra.gov.uk/home/groups/comms-ic/documents/website\\_resources/con007679.pdf](http://www.mhra.gov.uk/home/groups/comms-ic/documents/website_resources/con007679.pdf).

<sup>114</sup> *Smith, Kline and French v Evans Medical* [1989] FSR 513; MHRA Guidance (ibid); UKIPO, *The Patent Research Exemption: A consultation* (HMSO, 2008) 5; UKIPO Guidance (ibid).

<sup>115</sup> (n 110) p842.

<sup>116</sup> HMSO, implemented on 1 October 2014, [www.legislation.gov.uk/ukdsi/2014/978011114537](http://www.legislation.gov.uk/ukdsi/2014/978011114537).

stated intention of the measure is to remove barriers to conducting clinical trials in the UK (making innovation more likely to be patented and marketed here first) and lessening the burden of litigation on industry (speeding up market entry for generics and dependent technology).<sup>117</sup> The main provision, in addition to the existing research exemption, stipulates that ‘anything done in or for the purposes of a medicinal product assessment...is to be regarded as done for experimental purposes’.<sup>118</sup> This is an extremely broad approach to activities and, in tandem with the following provision extends the exemption to trials for indications.<sup>119</sup> The context of testing is extended from the market authorisation already permitted by the Bolar exemption to include HTAs and regulatory requirements necessary for market entry that may additionally apply and this is irrespective of whether it occurs in the UK or abroad.<sup>120</sup> The changes adopt a broad interpretation of medicinal products, including originator medicines, combination medicines, advanced therapies, and combination advanced therapies.<sup>121</sup> The absence of stipulations on whose activities are exempt suggests that it extends to CROs, but this is open to debate. Whether third party supply of active ingredients is covered by the Bolar exemption is a question that was referred to the CJEU by the German Court of Appeal,<sup>122</sup> but has since been withdrawn and so a prime opportunity for clarification has been missed.

These UK provisions undoubtedly benefit the development and access to the market of competitors developing their own originators (eg facilitating inclusion of existing originators in trials as comparators) and newly-valued medicines. These changes mean that generics/biosimilars (irrespective of whether they additionally require trials to demonstrate equivalence) and copies of advanced therapies will be able to put authorisation in place, ready for market entry as soon as the patent/SPC or data/market exclusivity period expires. This clearly serves the need for faster access to markets of generics that market potential identifies. Mediating between researchers (wanting access to products/processes) and patent holders (preserving the value of patent rights where researchers are the end-market) is incredibly difficult. In the UK, clearly the balance has changed radically in widening the research exemption in line with maximising market potential.

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<sup>117</sup> Impact Assessment No 142 (2014), [www.legislation.gov.uk/ukdsi/2014/978011114537/impacts](http://www.legislation.gov.uk/ukdsi/2014/978011114537/impacts).

<sup>118</sup> (n 116) including a new sub-section 6D into UKPA s60.

<sup>119</sup> (n 116) sub-section 6E.

<sup>120</sup> Ibid.

<sup>121</sup> (n 116) sub-section 6F.

<sup>122</sup> *Polypharma Pharmaceutical Works v Astellas Pharma* [2014], <https://docs.google.com/viewer?a=v&pid=sites&srcid=ZGVmYXVsdGRvbWFpbXwYWxpdiGNhc2VzfGd4OjEwM2Q1ZDUxOGVhOWM2N2I>.

It is unfortunate that the new provisions do not clarify that research tools fall outside of the exemption. The reality at present is that many pharmaceutical companies waste money obtaining legal advice to ensure they are within the research exemption, and smaller companies simply ignore the potential for liability and hope not to get caught infringing. The new provisions in the UK will at least allay some of these fears, but mediating these concerns could be served by far better educational and advice mechanisms in preference to just widening the exemption and creating new boundaries of uncertainty.

Pan-European and individual nations' patent regulators are focused on justifying their behaviour relative to the goals set for them, evidenced by practices which closely match market potential. Within this analysis it is clear that regulating activities beyond market potential is not being carried out and neither is there any perceived effort to expand competencies to regulate behaviours (eg licensing) which have a far more direct impact on the market proliferation of technology, giving regulators greater potential to achieve economic growth. This supports the assertion that the EPO and its network of Member States' patent offices, the European Appeal Boards and Member States' legislative measures all regulate towards the same justificatory approach. While these are contextually linked bodies, the question becomes whether the same justificatory behaviour is evident amongst less closely related and unrelated institutions regulating modern medicines.

## **4.2 The CJEU**

This part of the analysis assesses two aspects of the CJEU – regulating trade in medicines and regulating rights over the development of medicines - to identify that the same justificatory basis as that adopted by the EPO is being replicated by judicial regulators.

### **4.2.1 The CJEU moving away from entrenched EU policies**

While the overarching policy of the EU relates to promoting the 'economic and social progress'<sup>123</sup> of its Member States, an inherent part of this has been devoted to ensuring the free movement of goods,<sup>124</sup> that can only be departed from on justified grounds<sup>125</sup> which do not discriminate against traders simply because there are existing commercial rights.<sup>126</sup>

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<sup>123</sup> Preamble, Treaty on the Functioning of the EU (TFEU) (Consolidated Version), (26.10.2012) OJ EU C326/47-390.

<sup>124</sup> TFEU Arts 34 and 35.

<sup>125</sup> TFEU, Art 36.

<sup>126</sup> TFEU, Art 37.

In practice, this has led to the creation of a new type of competitor for the pharmaceutical industry, a ‘parallel importer’ who legitimately purchases patented medicines from markets in one EU country and imports them into another country to sell in competition with the patent holder (the originator producer or his licensee). This presents a problem for the patent holder, because the parallel importer is able to undermine his market share by either under-cutting the retail price, or offering the medicine in a more marketable form (eg packaged more conveniently for consumers). Importing for resale outside of the EU, the parallel importer’s ‘shadow’ medicines infringe the patent right and the importer is legally liable. Within the EU, commitment to the free movement of goods between Member States<sup>127</sup> means that the patents over the tangible resale products have been ‘exhausted’/must be ‘adjusted’ by the first sale to the parallel importer.<sup>128</sup> This acts as a defence against activities which would otherwise infringe. In recognising that the patent holder retains an interest in protecting the goodwill he has built up in selling his medicines to consumers, the parallel importer only becomes liable: if his trade results in diminishing the reputation of the patent holder;<sup>129</sup> or for repackaging,<sup>130</sup> rebranding,<sup>131</sup> or relabelling<sup>132</sup> medicines detrimentally to the interests of the patent holder or adversely affecting the free movement of goods.<sup>133</sup>

Enabling a parallel importer to legitimately trade patented medicines should discourage the patent holder from charging widely disparate prices for the same medicine based on what different EU markets can bear. The problem is that the lower prices are often the result of governments artificially depressing reimbursement prices.<sup>134</sup> The consequence is that pharmaceutical companies look to countries where they are able to dictate prices (such as

<sup>127</sup> Notably the exception in Art 36 to ‘the health and life of humans rank first among the property or interests protected’, Case C-104/75 *De Peijper* [1976] ECR 613, but must not be limited to protecting domestic interests and must be proven: Case C-319/05 *Commission v Germany* [2007] ECR I-9811; Case C-270/02 *Commission v Italy* [2004] ECR 1559; and imported into the Unitary Patent on the proviso that it is subject to valid reasons for opposing market proliferation (eg market recall on safety grounds): Regulation 1257/2012/EC (n 34), Art 6; Unified Patent Court Agreement (n 68), Art 29 (the Unitary Patent taking effect when the UPC Agreement is ratified by 13 Member States including the UK, Germany and France).

<sup>128</sup> *ibid*, TFEU, Art 37; *Deutsche Grammophon Gesellschaft v Metro-SB-Grossmärkte* [1971] ECR 487; *Terrapin v Terranova* [1976] 2 CMLR 482.

<sup>129</sup> Case C-276/05 *Wellcome Foundation v Paranova Pharmazeutika Handels* [2008] ECR I-10479; *Dansk Supermarked v Imerco* [1981] ECR 181; *Parfums Christian Dior v Evora* [1998] 5 RPC 166.

<sup>130</sup> *Boehringer Ingelheim v Dowelhurst Ltd* [2002] FSR 61, [2004] EuLR 757; *Loendersloot v Ballantine & Son* [1998] FSR 544; *Bristol-Myers Squibb v Paranova* [1997] FSR 102.

<sup>131</sup> *American Home Products v Centrafarm* [1978] ECR 1823.

<sup>132</sup> Case C-348/04 *Boehringer Ingelheim v Swingward* [2008] All ER (EC) 411; *Glaxo Group v Dowelhurst Ltd (No 2)* [2000] FSR 529; *Loendersloot v Ballantine & Son* [1998] FSR 544.

<sup>133</sup> Technically this included importing a product in order to develop a generic for market authorisation using a patented medicine (even if legitimately purchased) (*Generics BV v Smith Kline & French Labs* [1997] 22 RPC 801), but the Bolar exemption arguably removed this.

<sup>134</sup> For an analysis of how healthcare pricing can maximise public interest see: L Ho, *Health Policy and the Public Interest* (Routledge, 2012).

the UK where prices are capped relative to a percentage profit calculation, incentivising the industry to inflate costs)<sup>135</sup> to recoup investment in R&D. Parallel imports should also discourage patent holders varying the quantities of specific medicines which can be purchased, but again this is often required by individual Member States' regulations.<sup>136</sup> This leaves patent holders with no means of reducing the potential for parallel traders to erode their profits.

The rationale of the EU is that legitimising parallel trade enhances access to medicines by creating secondary markets promoting price competition and ensuring sufficient supplies to meet demand in the country the medicines are imported into. Although the patent's value is retained by the first sale to the parallel importer, parallel importation demonstrably creates shortages as supplies gravitate to countries offering the highest sales profit.<sup>137</sup> Recognising this detrimental effect and the up-scaling of parallel trade from independent traders to wholesalers 'competing' with the very producers who supply them prompted the CJEU to go against accepted policy which supports parallel trade. The CJEU instead supported the patent holders even in the context of anticompetitive practices and being in dominant market positions.<sup>138</sup>

Pharmaceutical companies such as GSK are advocating a dual pricing regime that would discriminate against parallel traders without success as yet,<sup>139</sup> but this may simply be a matter of time in light of the All-Party Pharmacy Group (APPG) report calling for

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<sup>135</sup> Intentions to introduce Value-Based Pricing with the implementation of the Health and Social Care Act 2012 have been replaced by another five year agreement between the Department of Health (DoH) and the Association of the British Pharmaceutical Industry (ABPI) which enables the industry to set its own prices subject to a percentage profit cap and spend-to-cost restrictions (see: DoH, ABPI, The Pharmaceutical Price Regulation Scheme 2014 (December 2013), [www.gov.uk/government/publications/pharmaceutical-price-regulation-scheme-2014](http://www.gov.uk/government/publications/pharmaceutical-price-regulation-scheme-2014), point 6.1 in particular and n 86). For evidence of the inflation see: DW Light and R Warburton, 'Demythologizing the High Costs of Pharmaceutical Research' (2011) 6 *BioSocieties* 34-50.

<sup>136</sup> Eg in the UK the Medicines (Sale or Supply) (Miscellaneous Provisions) Amendment (No. 2) Regulations 1997, SI 1997/2045 prevents the general sale of paracetamol in packages of more than 16 tablets.

<sup>137</sup> All-Party Pharmacy Group (APPG), Report of the APPG Inquiry into Medicines Shortages (2012) APPG, [www.appg.org.uk](http://www.appg.org.uk); F Liberatore, 'UK calls for ban for parallel trade of prescription medicines – what are the EU competition law implications?' (2013) 34(4) *European Competition Law Review* 189.

<sup>138</sup> (Joining C-2/01 and C-3/01) *Bayer Adalat* case [2004] ECR I-23 the CJEU ruled that a non-dominant pharmaceutical company is not caught by unfair competitive practices (TFEU, Article 101) measures by unilaterally imposing trade conditions on a wholesaler which indirectly amounted to preventing export of medicines in parallel to their subsidiaries; and Case C-53/03 *Syfait v GlaxoSmithKline* [2005] ECR I-4609 extending this ruling to cover dominant pharmaceutical companies (TFEU, Article 102), in this case refusing to supply to a wholesaler in order to prevent parallel trade because it would reduce domestic supply.

<sup>139</sup> Case T-168/01 *GSK v Commission* [2006] (unreported); Case C-501/06 [2010] 2 CMLR 10, remitted back to the Commission to consider if imposing price differentials to inhibit parallel trade comes within TFEU, Art 101(3) exempting restrictive practices which contribute 'to improving the production or distribution of goods or to promoting technical or economic progress, while allowing consumers a fair share of the resulting benefit'.

prescription medicines to be protected from parallel trade.<sup>140</sup> Any type of medicine is too important to be arbitrarily subject to free movement which is recklessly untied to market demand. This argues that patents, which are traditionally considered exclusionary, may become the mechanism ensuring domestic supply of medicines.

Yet it is undeniable that the absence of a secondary sales market removes incentives for producers to lower their prices. Collaterally this can increase health tourism, particularly in neighbouring countries with wide price disparities. Neither can this be entirely off-set by self-regulation through the public choosing not to purchase. Even general sale medicines are not strictly ‘choice purchases’: a plaster is not an essential purchase but risk of infection (however minimal) urges it.

This analysis exemplifies that the CJEU has breached existing EU policies in order to maximise market potential by helping to ensure that secondary sales markets do not undermine supply, creating surpluses and shortages in different Member States. This supports a regulatory focus on market maximisation rather than economic growth, because it prioritises availability of products at the expense of affordability. Arguably this is another instance of regulators not being sufficiently empowered, as regulating prices effectively in this context should more obviously be a matter of trade tariff agreements imposing import duties than judicial decisions imposing arbitrary penalties on individuals. Does the CJEU similarly adopt a market potential approach in enforcing proprietary rights collateral to patents?

#### 4.2.2 The CJEU expanding exclusionary rights

Extending the duration of patent rights to medicines, which have not already been the subject of a Supplementary Protection Certificate (SPC),<sup>141</sup> with an additional period of exclusivity is generally considered to limit access to generics by delaying their market entry. The justification is that the time given is directly proportionate to the time lost between patent grant and marketing authorisation.<sup>142</sup> This is enforced strictly, as evidenced by *AstraZeneca v. Comptroller of Patents*,<sup>143</sup> in which the duration of protection was calculated relative to the first grant of market authorisation, irrespective of central EMA authorisation having been

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<sup>140</sup> See APPG Report, 2012 (n 137).

<sup>141</sup> Administered territorially through Member States: Regulation 469/2009/EC concerning the supplementary certificate for medicinal products (2009) L152 OJ EC 1-10, Art 3(c).

<sup>142</sup> Minus five years and up to a maximum of 5 years: *ibid*, Art 13.

<sup>143</sup> *AstraZeneca v Comptroller of Patents* [2012] EWHC 2840 confirmed by the CJEU: Case C-617/12 [2014] C102 OJ 8.

withheld and the first authorisation subsequently being withdrawn (both of which delayed its eventual market entry).

While this appears to run counter to regulating to maximise markets, the introduction of the European Regulation on SPCs has been followed by a plethora of decisions from the CJEU on referrals from Member States,<sup>144</sup> expanding SPC protection beyond originators. Protection includes new uses of known active ingredients (indications and combinations), provided they fall within the original claim (implicitly if not explicitly) which was subject to patent rights when the first market authorisation was applied for and seemingly irrespective of who owns the originator product or the market authorisation.<sup>145</sup> The rationale is that ‘the fundamental objective of the SPC Regulation is to ensure sufficient protection to encourage pharmaceutical research, which plays a decisive role in the continuing improvement in public health’,<sup>146</sup> and this is interpreted as protecting the investment expended in identifying new value in existing active ingredients. So market potential is clearly a motive in the changing judicial regulation of SPCs, even though an important limitation to the extension of SPCs is that combinations will not be accorded separate certificates where they do not represent distinct technical advances<sup>147</sup> under the patent.<sup>148</sup> These changes replicate the increased scope for patenting new indications and combinations into an ability to extend the rights to them (patents, SPCs, data and market exclusivity) so that they expire long after marketing. Hinging SPC protection around whether the ‘sole subject-matter’<sup>149</sup> of the original invention has already been given protection at least prevents the risk of ‘stacking’ SPCs on me toos. In the long-term there is a risk that the industry will be motivated to fragment the innovation claims, submitting multiple patent applications rather than multiple claims in a single application.<sup>150</sup>

The reliance upon the pharmaceutical industry to submit to formal regulatory requirements which are not independently policed is a key facet of SPCs. Regulators work in

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<sup>144</sup> (n 141) in the courts eg Case C-631/13 Arne Forsgren v Österreichisches Patentamt [2015] ECR 0; Case C-484/12 Georgetown University v Octrooicentrum Nederland [2013] WLR(D) 487; C-130/11 Neurim Pharma v Comptroller of Patents [2013] RPC 23; Case C-574/11 Novartis AG v Actavis Deutschland [2012] C133 OJ 13; Case C-442/11 Novartis AG v Actavis UK Ltd [2012] C133 OJ 12; Case C-6/11 Daiichi Sankyo Company v Comptroller-General of Patents, Designs and Trade Marks [2012] C73 OJ 10.

<sup>145</sup> See C-130/11 (ibid), and Case C-493/12 Eli Lilly v HGS [2013]; [2014] EWHC 2404 (Pat).

<sup>146</sup> See C-130/11 (n 144) point 22, reaffirming the SPC Regulation (n 141, Recital 2).

<sup>147</sup> Unity of invention resolves this issue (EPC, Art 82; G2/92 Non-payment of further search fees [1993] OJ EPO 591), but this relies upon a new technical effect which would not be an obvious variation of the central innovation in the patent.

<sup>148</sup> Case C-443/12 Actavis v Sanofi [2014] C 52 OJ 30.

<sup>149</sup> Case C-577/13 Actavis v Boehringer [2015] <http://curia.europa.eu/juris/document/document.jsf?text=&docid=162830&pageIndex=0&doclang=en&mode=lst&dir=&occ=first&part=1&cid=311680>, confirming Case-C443/12, ibid.

<sup>150</sup> This could result in provisions governing the unity of invention (EPC, Art 82 and Rule 44) being used by examiners to counter this, rather than its current value as a tool for applicants.

isolation without co-ordination with other bodies<sup>151</sup> granting SPCs, licensing market entry and enforcing against anti-competitive practices, and the lack of co-ordination between different regulators is clearly being taken advantage of by the industry. Examples of regulatory abuse are rife. Astra Zeneca lost its challenge against the €52.2m fine imposed by the European Commission<sup>152</sup> for abusing the SPC system in order to prevent generic competitors entering the market. Neither is this just a trail of litigation at the European level, as demonstrated by the Italian Council of State's recent decision to reinstate the decision holding Pfizer liable for abusing a legally obtained SPC to keep out generics.<sup>153</sup> Utilising SPCs aggressively to limit competitors are not the only forms of abuse: supplying misleading information about dates to obtain the SPC in the first place is only one example of competitive tactics.<sup>154</sup> In the USA, GSK's record \$3b fine demonstrates that abuse of regulatory mechanisms also extends to providing misleading information about safety and pricing in order to obtain a market advantage.<sup>155</sup> The same company also faced \$490m fines and suspended prison sentences for executives over an alleged £320m of bribes to Chinese officials and healthcare providers to secure market share and charge higher unit costs.<sup>156</sup> It is demonstrative of regulatory intent that, while European and Member States' competition regulators are increasingly enforcing against such conduct where it limits the potential for generics (maximising a market potential), greater emphasis upon regulating between competences has not been targeted.

SPCs are not intrinsically restrictive other than being designed to extend patent rights which have been expended during clinical trials: so there is no loss of public access. It is also notable that, while SPCs are regulated through the patent system, they are regarded as part of an administrative process in contrast to the legal nature of patent regulation, but these SPC

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<sup>151</sup> Even where there are co-operative analyses between regulatory bodies, which recognise the synergies in forms of regulating, there is no real drive to co-ordinate activities more effectively: WTO, WIPO, WHO Trilateral Report, Promoting Access to Medical Technologies and Innovation: intersections between public health, intellectual property and trade (2012), [www.wipo.int/export/sites/www/freepublications/en/global\\_challenges/628/wipo\\_pub\\_628.pdf](http://www.wipo.int/export/sites/www/freepublications/en/global_challenges/628/wipo_pub_628.pdf); for an analysis of network theory relative to European patents see: S Borrás, 'The governance of the European Patent System: effective and legitimate?' (2006) 35(4) *Economy and Society* 594-610.

<sup>152</sup> Case C-457/10 *AstraZeneca v Commission* [2013] C26 OJ 2.

<sup>153</sup> Case 7467/2012 *Pfizer v Italian Competition Authority* [2014] N 00116/2014 Reg.Prov.Coll; for more see A Spillman, 'Transparency Obligation for Holders of EU IP Assets in the Pharmaceutical Industry' (2014) 9(2) *Journal of Intellectual Property Law & Practice* 125.

<sup>154</sup> L Howard (Genericsweb), 'Strategic Use of Supplementary Protection Certificates (Part 2)', (2010) 7 *Journal of Generic Medicines* 294.

<sup>155</sup> Department of Justice, 'GlaxoSmithKline to Plead Guilty and Pay \$3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data', 2 July 2012, [www.justice.gov/opa/pr/2012/July/12-civ-842.html](http://www.justice.gov/opa/pr/2012/July/12-civ-842.html).

<sup>156</sup> BBC News, 'GlaxoSmithKline fined \$490m by China for bribery' 19 September 2014, <http://www.bbc.co.uk/news/business-29274822>; D Roland, 'GSK bribery scandal could cause 'irreparable damage', says China', 16 July 2014 *The Telegraph*.

extensions have emanated from the CJEU. Both patents and SPCs have clearly expanded to accommodate a need to create more originators (including dependent technologies) and, excessive rights extending to me toos at patent grant are curbed within the SPC process, limiting the time that generics will be held out of the market. This is precisely the same profile that existing market potential identifies, enabling the patent, SPC and CJEU to justify their actions on the basis of facilitating economic growth.

The failure is that regulation is not effectively co-ordinated to prevent individual innovators obtaining more exclusivity than is warranted, or for a holistic approach to regulating industry. In focusing upon the market potential of an SPC in shepherding new combinations and newly-valued medicines to market, European regulators enable the industry to fragment medical products that will eventually saturate the market with nearly indistinguishable alternatives. In normal competitive markets this would result in a price war, but the reimbursement policies which attend medicines marketing frustrate this potential benefit.

All of the regulators so far assessed are arguably all attendant to the patent right, providing a possible reason for their behaviour conforming to the same rationality. So is the EMA, governing market entry, similarly focused on the same market potential as the patent system?

## 4.3 The EMA

### 4.3.1 Facilitating generic entry

There is no doubt that the EU Commission<sup>157</sup> and the EMA<sup>158</sup> are committed to promoting a robust generics market with early entry promoting access. This is demonstrated by generic medicines being able to fast-track market authorisation<sup>159</sup> once the patent term has expired, to speed up market entry.<sup>160</sup> Yet data/market exclusivity restrict market entry,<sup>161</sup> commonly outlasting all other rights and making it a source of criticism.<sup>162</sup> After 8 years, generics/biosimilars can be applied for, but it is another 2 years before they gain market entry. This is not based on timelines for submitting applications, because 2 years is too long in the case of most SMCs/some biosimilars and too short for many biosimilars.<sup>163</sup> Mechanisms designed to protect the R&D investment of originator medicines should correlate to a profit margin:<sup>164</sup> a blanket duration (irrespective of type of innovation) creates a system which rewards scrimping on R&D or encourages extra R&D costs to unnecessarily inflate the prices charged to the consumer.

Once market authorisation has been granted to the originator, data exclusivity requires a balance between: (1) disclosure in the public interest for safety and the validity of public decision-making;<sup>165</sup> and (2) non-disclosure of proprietorial information that is commercially valuable.<sup>166</sup> The EMA's commitment to the EU's focus on transparency<sup>167</sup> resulted in policy

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<sup>157</sup> Pharmaceutical Sector Inquiry (n 32) and since on the European Commission's follow up, <http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/>.

<sup>158</sup> (ns 40 and 41), points 3.3 and 5.2.1.

<sup>159</sup> Directive 2001/83/EC (as amended) on the community code relating to medicinal products for human use [2001] OJ L311/67 ; Regulation 726/2004/EC (n 17); Regulation 658/2007/EC (as amended) concerning financial penalties for infringement of certain obligations in connection with marketing authorisations [2007] OJ L155/10; Regulation 507/2006/EC on the conditional marketing authorisation for medicinal products for human use [2006] OJ L92/6; and Regulation 2049/2005/EC rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises [2005] OJ L329/4.

<sup>160</sup> Fast-tracking rests on 'piggybacking' the generic medicine's market authorisation procedure on the safety, quality and efficacy data originally submitted to the EMA for the originator medicine.

<sup>161</sup> 8 years data exclusivity; 2 years market exclusivity (10 years consecutively); and an additional year if a new indication has been identified in the first 8 years: Directive 2004/27/EC (n 105); Regulation 726/2004/EC (n 17) Art 14(11).

<sup>162</sup> Eg P Andanda, 'Managing intellectual property rights over clinical trial data to promote access and benefit sharing in public health', (2013) 44(2) International Review of Intellectual Property & Competition Law 140; S Matilal, 'Do developing countries need a pharmaceutical data-exclusivity regime?', (2010) 32(6) European Intellectual Property Review 268.

<sup>163</sup> Timelines relate to harmonisation. Individual Member States variously provided 6 and 10 years data exclusivity: European Generics Medicines Association, Data Exclusivity (2004), [www.egagenerics.com/gen-dataex.htm](http://www.egagenerics.com/gen-dataex.htm).

<sup>164</sup> Break-even is the point at which outlays and revenue balance each other, enabling all other revenue to be profit: for a SMC break-even will occur much earlier during marketing than for a biologic, because its R&D costs will be much lower.

<sup>165</sup> Eg results of clinical and non-clinical trials.

<sup>166</sup> Eg know-how on the creation of the product, quality issues, the manufacture procedure, details of suppliers.

preferences for non-disclosure becoming more permissive and enabling disclosure of anonymised trial data.<sup>168</sup> The change resulted in InterMune and AbbVie instigating proceedings against the EMA's intended disclosure of trial data.<sup>169</sup> In the AbbVie case, the CJEU sent the decision to grant an injunction back to the General Court, because it had not required proof that disclosure constituted a 'risk of serious and irreparable harm' to fundamental rights to confidentiality.<sup>170</sup> Both InterMune and AbbVie withdrew their cases after the EMA redacted the documents,<sup>171</sup> leaving the issue unresolved. The medical community remain concerned that the EMA's revised plans to limit access, provide data in a less usable form and allow 'even details of study designs, statistical analyses and study results' to be redacted demonstrate they are renegeing on disclosure in the public interest.<sup>172</sup> The implementation of the EU Clinical Trials Regulation scheduled for 2016 should resolve this issue with the introduction of the EU database.<sup>173</sup> This makes it a statutory requirement for all clinical trials to be on the database while trials are ongoing, to be publicly accessible, with easily searchable information,<sup>174</sup> and data is presumptively public (with confidentiality an exception in limited, specified contexts), which in the case of commercial confidentiality is still subject to 'overriding public interest in disclosure'.<sup>175</sup>

Access to trial data makes it easier for generics/biosimilars to target medicines as they are developed and the industry fear is that this facilitates market entry on the day that market exclusivity expires even where additional trials are required. In tandem with the Bolar/research exemptions (particularl in the UK), there is certainly likely to be an erosion of

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<sup>167</sup> Generally see: Directorate-General for Internal Policies, Policy Department (Citizens' Rights and Constitutional Affairs: Civil Liberties, Justice and Home Affairs), Openness, transparency and access to documents and information in the EU (2013), [www.europarl.europa.eu/RegData/etudes/note/join/2013/493035/IPOL-LIBE\\_NT\(2013\)493035\\_EN.pdf](http://www.europarl.europa.eu/RegData/etudes/note/join/2013/493035/IPOL-LIBE_NT(2013)493035_EN.pdf); specifically in post-market contexts: Directive 2010/84/EU amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use [2010] OJ L348/74, Art 107(2) facilitating public access to adverse drug reaction reportage; Regulation 1235/2010 amending pharmacovigilance measures on advanced therapy medicinal products [2010] OJ L348/1.

<sup>168</sup> Gathering momentum notably because of: the Cochrane Collaboration, [www.cochrane.org/about-us](http://www.cochrane.org/about-us); B Goldacre, *Bad Pharma* (Fourth Estate, 2012); the AllTrials.net collaborative initiative (2014), [www.alltrials.net/find-out-more/](http://www.alltrials.net/find-out-more/).

<sup>169</sup> Case C-390/13, T-73/13 EMA v InterMune [2014] 2 CMLR 21; Case C-389/13, T-44/13 EMA v AbbVie [2014] 2 CMLR 21.

<sup>170</sup> Case C-389/13 (ibid), para. 43.

<sup>171</sup> S Bodoni, 'AbbVie Drops EU Court Bid to Block Clinical-Trial Data Release', 3 April 2014 Bloomberg News; InterMune similarly dropped their action in June 2014: J Murray, 'A surprising development in the case of InterMune vs the EMA', 10 June 2014 The BMJ Blogs.

<sup>172</sup> T Groves, 'The European Medicines Agency gets cold feet at the last minute', (2014) 348 British Medical Journal g3561.

<sup>173</sup> See Clinical Trials Regulation 536/2014/EC (n 32).

<sup>174</sup> See Clinical Trials Regulation 536/2014/EC (n 32), Art 81, Recitals 67 and 68.

<sup>175</sup> See Clinical Trials Regulation 536/2014/EC (n 32), Art 81(4), Recital 68 further distinguishing disclosure for validity outside of commerciality.

market lead for originators relying on more complex modern medicines struggling to fit within the existing two years between disclosure and marketability. This reflects the market-based focus in supporting quicker market entry of generics/biosimilars. In addition, clinical trial transparency facilitates rationalisation of newly-valued medicines, maximising funding/resource allocation by reducing the scope to duplicate innovation. As such, the EMA's focus falls completely in line with the justifications inherent in changes within the patent system. In the context of market authorisation, how much quicker generic entry will be may rest on how much privacy the industry will be able to claw back under cover of know-how (eg. product tolerances, supplier information, business practices, etc.) after the Trials Regulation database is operational.

This market-based focus is also evident in recent initiatives undertaken by the EMA following the introduction of its 2011 policy.<sup>176</sup>

#### 4.3.2 Increasing the pace of innovation to market

European Regulations permit the compassionate use of originator, combination and newly-valued medicines either in clinical trials or at pre-market authorisation where a life-threatening condition has no 'satisfactory' treatment.<sup>177</sup> Member States such as the UK have taken up this opportunity through their EAMS initiative to grant access to medicines identified as Promising Innovation Medicines (PIM, discerned after assessing the clinical trial data); or based on a scientific opinion.<sup>178</sup> Although the UK's Medicines and Healthcare products Regulatory Agency restrict access to medicines in Phase III trials (quality and comparative efficacy), in exceptional circumstances a Phase II trial (efficacy: usually first trial in sufferers) suffices.<sup>179</sup>

In addition, the EMA launched a pilot on adaptive licensing,<sup>180</sup> based on an understanding of evidence-based medicines as being a continuum, in which market entry can be shifted from post-Phase III trials to grant after earlier phases if trials are redesigned. For example, Phase I ('first in man' toxicity trials usually on healthy participants) and Phase II (efficacy) could be sufficient if combined (toxicity and efficacy on sufferers). This has the advantage of reducing risks to the healthy and can be accessible to patients with a range of conditions, but could yield confusing results on dosage and effectiveness.

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<sup>176</sup> n 42.

<sup>177</sup> See Regulation 726/2004/EC (n 17), Arts 83(2), 3(1) and (2).

<sup>178</sup> Eg from the EMA's Committee for Medicinal Products for Human Use.

<sup>179</sup> Introduced by the MHRA in April 2014, see: MHRA, Guidance for Applicants for the EAMS (2014)

<sup>180</sup> EMA documents on adaptive licensing pilot project, [www.ema.europa.eu/ema/index.jsp?curl=pages/news\\_and\\_events/news/2014/03/news\\_detail\\_002046.jsp&mid=WC0b01ac058004d5c1](http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/03/news_detail_002046.jsp&mid=WC0b01ac058004d5c1).

These initiatives appear to be regulating in the public interest by promoting public health and supporting better medicines, but they blur distinctions between ‘trial participants’ and treating ‘patients’. Both EAMS and adaptive licensing are subject to entirely different legal protection, so liability regimes will need to be revised allocating responsibility between products and doctors for medicines with risk profiles which are much less apparent. In addition, there is general agreement that prescribing off-label must be strictly prohibited, but little evidence of strategies to ensure compliance. Making participants pay to receive medicines just by redefining them as patients is hardly in their interests or society’s. Instead both of the early access initiatives can be argued to be in industry’s interests, gaining new trial participants and earlier market entry. This has two counter-arguments: (1) EAMS participants are likely to skew trial data because trials customarily become available to the least sick in Phase II and Phase III to optimise the potential to prove efficacy (although it could be supposed there is always the potential for not including them or for lost data);<sup>181</sup> and (2) adaptive licensing raises concerns over calculating SPC protection (up to first marketing or first adaptive license).

Clearly the EMA is not acting as a neutral arbiter or benefitting special interests. Instead the EMA is paving the way for personalised medicines, maximising the potential to market drugs that would be in trials under the current procedure. This ensures that the new generation of originators (niche-busters),<sup>182</sup> can have their reduced market returns (resulting from being effective for fewer patient groups) offset by drastically reduced R&D costs so they can maintain profit margins. This may align with industry producers invested in personalised medicines, but it more importantly ensures that Europe is positioned as a leading producer of personalised medicines. As such, this confirms that different agencies regulating very different aspects of medicines markets are linked by a common commitment to maximise market potential.

## 5. Conclusion

Existing discourses on regulatory prioritisation of competing interests presume a motivation which is fixed either on good outcomes or selfish interests. This analysis challenges those

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<sup>181</sup> Eg Roche failed to report 80,000 illnesses/deaths in post-authorisation Phase IV trials: H. Marshall, ‘European Medicines Agency assesses safety reporting at Roche’, (August 2012) 13 *The Lancet* e331.

<sup>182</sup> Personalised medicines, see: SG Gibson and T Lemmens, ‘Niche Markets and Evidence Assessment in Transition: a critical review of proposed drug reforms’, (2014) 22(2) *Medical Law Review Special Edition* 200.

presumptions, arguing instead that regulators are motivated to focus on the need to explain their behaviour relative to the goals that have been set for them by the various bodies that empower them. While changes between principals and agents may vary with the political, public policy, legislative or administrative prioritisations of the principal, this analysis exemplifies the importance of understanding regulation occurring between independent regulators. Assessing regulators through an understanding of how policy is translated into practice, reveals a single rationalising basis: goals are to be interpreted as market-oriented, prompting regulators to maximise market potential. This aligns with a procedural need for administrative accountability, but being substantive, it is systemically independent.

European medicines regulators are charged by those who empower them to act in the interests of securing economic/innovation growth and this has been tested across two independent agencies (EPOrg and the EMA). There is a clear link between how these goals are translated into practical regulatory activities, whether that is: interpreting existing legislation during decision-making processes (evidenced by patent regulators); legislatively in the introduction of new instruments (exemplified by the UK Legislative Reform (Patents) Order 2014); being supported judicially in expanded understandings (evidenced by the CJEU and the European Boards of Appeal); or implementing and operating regulatory initiatives (evidenced by the EMA). The unifying concept that rationalises all of the activities in order to appear to aim at growth is the need to act for the benefit of existing market potential. There is no suggestion that the compilation of sources that underpin the market potential identified here is relied upon by the regulators analysed, but they are clearly working to an uncannily similar market view which is evidenced in how changes in regulatory behaviour match market potential. Maximising market potential is the enduring factor, even though its implementation may change over the medium-term to reflect emerging market trends. It is this which registers as changing regulatory practices. In the political and policy domains, it is suggested that the credible commitment of the regulator ensures that market considerations endure within long-term goals, minimising the influences from extreme short-term political positioning and special interests, ensuring that strategic change happens slowly.

The side-effect of the focus on market-based justifications is that regulators dissipate their efforts, which should be focused on actually achieving or moving towards the goal set. In the context of the patent system, global and European shifts in industry capabilities and market demands incentivise regulators to promote the proliferation of originator medicines and create newly-valued medicine. Granting patents to the best able to develop first inevitably results in originator rights developing quicker and across more right-owners. This

comes at the cost of creating narrower rights to make room for more competitors, new combinations and newly-valued medicines. This has two main consequences: (1) it means that the ‘evergreening’ of rights by reclaiming innovation (me toos) is not being censured; and (2) it reduces the scope for originator patent holders to expand their existing research. While there are some justifications for curbing overly broad originator rights already granted in order to more fully exploit existing technology, this runs the risk of resulting in fragmentation. Fragmentation of patent rights dis-incentivises follow on research which cannot navigate patent thickets and, if it is close enough to down-stream markets, fragmentation can lead to product gluts which cannot be resolved by normal competitive mechanisms.

Comprehensively regulating licensing would have a far more constructive impact on mediating originator and follow on rights, but this is left largely unchecked by the patent regulator and this demonstrates an indifference to goal-achievement. At a pan-European level there is no need to consider all of the adverse impacts of these patent nuances, but individual nations such as the UK have been prompted to expand their research exemptions in order to encourage earlier generic entry to markets in the hope of securing domestic and global advantages against an increasing field of global competitors, resulting in a further erosion of originator rights.

The reliance on market potential as an explanatory link to the goals set in patent regulation is replicated by other regulators. The commitment of the CJEU to ensuring the flow of medicines is so strong it resulted in a departure from entrenched EU policy protecting the free movement of goods and the trade presence of parallel importers, but at the cost of increased costs of medicines. Clearly this is also not intended to be goal-achieving where it ignores the more appropriate tools of duties placed on the import/export of goods. Similarly, although the CJEU replicated the intention to benefit an expansion of originators and newly-valued medicines, generously granting SPC protection, they have at least stopped short of SPC ‘stacking’ which could extend patent protection far longer than the upper five year limit. The EMA is dismantling data exclusivity in its haste to herald quicker market entry for generics/biosimilars, but even within the new Clinical Trials Regulation there is plenty of scope for secrecy so only time will tell how much lead time will be eroded in the process. Early access and adaptive licensing initiatives bring quicker market entry of less safe medicines, paving the way for niche-busters and taking advantage of the desperation of the ill. Such initiatives will undoubtedly reduce the costs of trials and erode safety standards even as they evidence innovation growth and it is difficult to see how this can benefit any long-

term interests. Instead this promises to leave it to post-market regulators (high profile product withdrawals under the adverse drug reportage system; product liability cases and medical negligence claims) to resolve the problems that arise from pushing improperly tested medicines onto the market.

The goal of regulating to secure timely access to safe, effective and affordable medicines has never been more important, or so far from what regulators are actually motivated to achieve.