

might fall under scrutiny of competition law and incur a fine. The use of certain ways of action permitted by other branches of law²³⁵ does not preclude the application of competition law.^{236, 237}

Finally, a comment needs to be made regarding the objection on Xalatan paediatric studies.²³⁸ Although the percentage of children who need such drug is low (around 1%) it is duty of the health system to guarantee that a safe drug is available to them. The scope of paediatric extension is to give an incentive to companies to provide such drugs, therefore the ICA point of view cannot be shared and Pfizer's use of paediatric extension should have not been penalized.

C. Patent Strategy and Innovation

The main criticisms on pharmaceutical R&D are directed to the reduced number of NCEs approved by the FDA and the EMA and to the reduced number of new breakthrough drugs compared to “me-too drugs” (follow-on drugs). Nonetheless, drugs based on new biological mechanisms continue to be discovered (e.g. Isentress the first HIV-integrase inhibitor introduced by Merck in 2007).²³⁹ The reasons for the apparent reduction of NCEs are various.²⁴⁰ However, these are not within the scope of the present study.

235 E.g. AstraZeneca deregistered a Marketing Authorisation, which *per se* is not forbidden by the regulations guiding the pharmaceutical market.

236 See AstraZeneca *supra* note 223 at ¶677.

237 Josef Drexl, *Astra Zeneca and the EU Sector Inquiry: when do patent filings violate competition law?*, Max Planck Institute for Intellectual Property and Competition Law Research Paper No. 12-02, 21 (2012).

238 Vanessa Peden, Imti Choonara, Brian Gennery, Hilary Done, Recruiting Children to a Clinical Trial, 4 Paed. Perinat. Drug Ther. 75, (2000): “In children, one can only study those children who are to undergo a clinical procedure and may benefit from a medicine.”.

239 John E. Calfee, White Paper on Pharmaceutical Market Competition Issues, June 2, 2008, available at <http://62.102.106.100/content/default.asp?PageID=559&DocID=4894> (last visited Aug. 3, 2012).

240 See Chapter I of this thesis.

Innovation may be regarded as the creation of an improved product. Based on this understanding, the question arises whether improvements made on existing drugs can be disqualified. The TRIPS agreement states “[...] patents shall be available for any inventions,[...], in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. [...] without discrimination as to [...] the field of technology [...]”.²⁴¹ Technical advance in most cases proceeds incrementally and innovators are able to obtain patents on improvements. Such improvements in the pharmaceutical field may be of considerable practical significance to patients and other customers. It has been stated that “[s]ignificant incremental innovation to existing pharmaceutical products has been occurring in the form of supplementary approvals for new dosages, formulations, and indications. These innovations account for a substantial share of drug utilisation and associated economic and medical benefits. Productivity trends for research and development based on counts of new molecular entities alone have therefore overlooked an important source of innovation in pharmaceuticals.”²⁴² As already mentioned, also the EU Commission in its recent sector inquiry recognized the importance of subsequent improvements made to the initial invention.²⁴³

For example, patents on drugs combinations are very often criticized with respect to their inventive step. They are often seen by various interest groups as deviating resources from original research dedicated to identifying treatments for unmet medical conditions. However, advances made in the field of the so-called combination therapies are in many therapeutic areas indispensable (e.g. viral diseases or cancer) as already mentioned earlier.²⁴⁴ Combination therapies can have superior effect compared to the single components. In

241 Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), Art. 27, Apr. 15, 1994.

242 Ernst R. Berndt, Iain M. Cockburn, Karen A. Grepin, *The impact of Incremental Innovation in Biopharmaceutical*, 24 *Pharmacoeconomics* 69, (2006).

243 See sector inquiry *supra* note 120.

244 See section IV A 4 of this thesis.

the case of Latanoprost, research into drug combinations has been carried out, as no drug modulating the intraocular pressure was able alone to address the needs of the complete (and growing) patient population. While achieving an average reduction in eye internal pressure of about 30% by treatment with Latanoprost results to be sufficient in the majority of the patients, there is however a significant patient subpopulation, where this reduction of ocular hypertension still does not lead to a curative effect. Xalacom (Latanoprost plus Timolol) allows reducing further the intraocular pressure in patients where Xalatan alone has an insufficient effect.²⁴⁵ This demonstrates that research carried out in this area is of interest to the public and thus patents are important to incentivise investment in such research. On the other hand, patent law should guarantee that only for demonstrated new increments companies will receive exclusivity. Patent protection on Xalacom could not be obtained because the originator company had been publishing more than 2 years before the priority date the results of a clinical study demonstrating exactly the unexpected over-additive (synergistic) effect.^{246, 247}

Research in formulation attracts similar criticisms. The new and improved composition aimed for in the case of docetaxel tried to overcome a safety issue. As the drug in its original formulation is dosed intravenously in a solution with a fairly high content of ethanol, in some cases the occurrence of alcohol intoxication during infusion was observed.²⁴⁸ These events were particularly pronounced in patients with a history of alcohol dependence.²⁴⁹ The identification of a low-alcohol formulation could provide the patient benefit needed and remediate the problem noticed and therefore, cannot be seen as a de-

245 William C. Stewart, *Combination Therapy: Is the Whole Greater?*, Rev. Ophthalmol., Jun. 15 2005.

246 See Diestelhorst *supra* note 82.

247 This demonstrates the importance of an effective internal review process prior to external publication to hold back important research results until a patent application has been filed.

248 *Supra* note 41.

249 Anonymous, *Docetaxel: Alcoholic intoxication due to alcohol excipient: case report*, Reactions Weekly 13, Issue 1375 (Oct. 9, 2011).

viation of resources. This improved composition was subsequently patented, investigated in clinical trials and market authorisation was obtained. However, the patent family protecting this improvement got under fire by generic drug providers and in the end got revoked or was held unenforceable. In this context, it is important to note, that the revocation due to obviousness was mainly caused by the drafting of the patent application and especially its claims which on one hand did not take sufficient account of pre-existing own patents and on the other hand left room for interpretation.²⁵⁰ In summary, the originator had basically failed to protect his new invention by not delimiting it sufficiently clear from the prior art.

In addition, competition is fostered because further innovation is open to anyone. For example with respect to Xalatan first, several follow-on drugs based on prostaglandine derivatives have been developed by various companies (e.g Saflutan, Travatan, Lumigan); and second, further studies on improved formulations attempting to address side effects were sponsored mainly by competitors, as already mentioned.²⁵¹

D. Summary: Taxotere v Xalatan

A comparison of the originator filing activity concerning the two drugs Taxotere and Xalatan can be made. Successive to the filing of their respective basic patent, activity in the different areas of research was correlated to the studies necessary for their commercialization: in particular formulations, process and drug combinations in the case of Taxotere and formulations, process and delivery devices in the case of Xalatan.

In the case of Taxotere, the originator company's filing activity continued up to the expiry date of the basic patent (2011). In its later phase it was mainly directed to the finding of more practicable for-

²⁵⁰ See Aventis *supra* note 145.

²⁵¹ See section IV B 1 a) of this thesis.