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.

mulations improving patient comfort and moreover to the discovery of new combinations which could give better therapy results both in term of reduced side effects and patient response. Instead, in the case of Xalatan filing activity was observable during the first 15 years, ending however completely in 2003. The activity following the drug's launch from 1996 to 2003 was directed mainly to the discovery of new delivery devices to improve application of the drug and to new combinations. Another difference is the number of patent applications directed to the identification of alternative compounds resembling the structure of Taxotere (i.e. derivatives of the taxan core) while in the Xalatan case, such research does account for a more limited number of applications. This may be attributed to the different disease targeted. Since cancer cells may become resistant to a drug, there is a great need to identify alternative compounds.

In both cases there is strong indication that the filing of patents successive to the basic patent was not of any help in prolonging exclusivity after the end of the due protection. Most of the patent applications concerning new combinations of either Xalatan or Taxotere were not granted, leaving the commercialization of some important combinations open also to competitors and generic companies. Taxotere formulation patents were mostly attacked on grounds of invalidity due to obviousness and subsequently restricted and/or revoked. Patent applications regarding delivery devices for Xalatan were equally largely unsuccessful, as ocular delivery devices were known in the art, and no specific effects deriving from or influence on the use of Xalatan in such devices could be demonstrated.

Patents in the area of derivatives may be regarded as not having any influence on the marketed drug, neither during the monopoly time, nor at the later stage. Such patents may however be of significant value when the need arises to identify an improved version or a follow-on drug. In fact, this has happened in the Taxotere case, where upon expiry of the patent protection for docetaxel, the drug Jevtana[252] has been introduced into the market by Sanofi. In 2011, sales of Jevtana

252 See this thesis at § III A 2 f).

increased by 135.4% reaching 188 million.[253] However, as this drug is currently used as a second line treatment after Docetaxel it "is not expected to become a blockbuster with sales on par with [...] Taxotere".[254]

In both the presented case studies the used strategy did not help to avoid profit erosion after the generic market entrance. Concerning Taxotere it was announced: "As expected, sales of Taxotere® declined significantly (-67.5% to €150 million) in the fourth quarter, reflecting generic erosion in the U.S. (sales down 90.4% to €14 million) and Western Europe (sales decreased 84.2% to €23 million). Full year 2011 sales of Taxotere® were €922 million, down 57.0%."[255]

With respect to the second example analyzed in this thesis it appears that after commercialization of follow-on drugs although market shares declined[256] sales were maintained at high level[257] probably due to the growth of the patient base. However, with the generic entrance in 2011 sales decreased by two thirds.[258] The data for the two brand drugs relying on the latanoprost patent, Xalatan itself and Xalacom (latanoprost/timolol), indicates a decline of sales in the U.S. by two thirds to US $ 159 million in the first nine months of 2011. During the same period in Europe where SPC protection ended in January 2012 10% reduction of the sales was observed.[259] It has also been reported that in the near future the glaucoma therapeutics market will be dominated by generic drugs. New me-too drugs or product extension will likely not be able to capture a significant market share if they offer a safety and efficacy profile only slightly better than the mar-

253 Press release, Sanofi, 2011 Results Benefit from Genzyme Acquisition Net Sales and Business EPS1 up 9.2%2 in Q4 (Feb. 8, 2012), at 3.

254 Jessica Merrill, *2010 Drug Launches: A Year of Firsts Offers Hope for a Rebound*, 11 The Pink Sheet, Jan. 3, 2011, at 3.

255 *Supra* note 253.

256 Jeff Viksjo, *Pharmaceutical Treatments in Ophthalmology*, 1 Healthcare Observer 2, 3 (2009).

257 Anonymous, *News & highlights from week 40*, 12 Curr. Pat. Gaz. 1, (2009).

258 Anonymous, *Latanoprost SPC ends in top EU markets*, Generics bulletin, Jan. 13, 2012, at 24.

259 *Supra* note 258.

keted drugs. This situation could change only by the development of drugs with novel mechanism of action targeting the cause of the disease.[260]

E. Conclusion and Suggestions

A common theme in both case studies is that subsequent patent applications by the respective originator companies failed to adequately protect further advances (too early publication of own results and patent drafting). More care needs to be taken in regards of existing prior art. As already mentioned the invention must be more clearly delimited and the claims should me more specific to have a better chance to overcome obviousness requirements and to sustain an invalidity attack. Very important is also an effective document clearance inside the company to avoid novelty problems caused by prepublication as in the case of Xalatan.

In addition in the case of research on combination patents that aim to protect these results would be more useful and valuable if the combination could be administered in a single formulation. In this way the problem of off label use could be avoided.

Finally, because these secondary patents are often a weak strategy to cover investment in research a possible additional incentive could be a longer time of marketing exclusivity for a demonstrated clinical benefit as the additional year for a new use available in Europe.

260 Anonymous, *Patent expiries to hit glaucoma drug market growth until 2018*, The Pharma Letter, Sept. 18, 2011.