THOMSON

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Patenting in Context

DOLPHIN

The records appearing in this Gazette will be added to DOLPHIN, the database Of all pharmaceutical inventions in the next week. Based on the INPADOC database produced by the European Patent Office, it covers all national and international patents with relevance to pharmaceutical research and development published from 1968 onwards and selected patents from earlier years. DOLPHIN contains information on bibliographic data, contents, associated products, legal status, licensees and context of patents, which is presented in a format to convey all aspects of a patent at a glance.

News & Highlights from Week 0723

In a ruling released on Tuesday (June 5) this week, **Merck & Co**'s US patent **US5817340**, titled "Pharmaceutical compositions containing **famotidine** and **aluminum hydroxide** or **magnesium hydroxide**" was invalidated for obviousness. This is one of the patents cited in the FDA Orange Book for Pepcid Complete (famotidine + magnesium hydroxide + calcium carbonate), which is marketed as an OTC treatment for **heartburn** and **indigestion** by **Johnson & Johnson** in partnership with Merck. **Perrigo Co** had filed a Paragraph IV challenge against the patent as part of its ANDA for its generic **Famotidine Complete** tablets.

This ruling is particularly interesting as it is one of the first rulings since the US Supreme Court's April 30 ruling on obviousness in the KSR v Teleflex case and the judge in this case quoted extensively from that ruling. In the judge's opinion, two prior art references (Davis and Wolfe) had taught the use of famotidine with magnesium hydroxide. In addition, two prior art patents, **US5260072** and **US5075114**, taught the coating of famotidine granules to mask the bitter taste. Referring to the Supreme Court ruling, the judge stated "Under KSR, 'the combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.'" He felt that the '340 patent did no more than combine the predictable results of Davis and Wolfe with the predictable results of the '072 and '114 patents and was therefore invalid due to obviousness. Although he implied that he would also have found the '340 patent obvious using the "old" obviousness tests, the case shows how courts are applying the new ruling to pharmaceutical formulation patents.

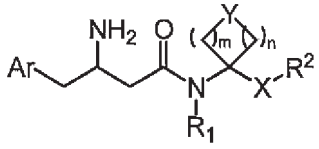
No UK SPCs were reported in this week's issue of the Patents and Designs Journal (PDJ No 6159); however, we can report the lodge of four SPC applications ahead of publication in the PDJ. This includes applications for **Du Pont De Nemours**' plant protective agent, **indoxacarb** and a veterinary drug known as **metaflumizone**, from **Nihon Nohyaku**.

Amylin Pharmaceuticals has made two SPC applications for **exenatide**, based on **EP1140145** disclosing exenatide formulations for **suppressing glucagon** and **EP996459** relating to the use of exenatide for treating **diabetes** and **gastric motility**. Should these be granted, both SPCs would provide protection until November 2021 based on the marketing approval date. However, as two SPCs can not be granted for the same product it seems likely that Amylin will have to choose which of the two patents they wish to further protect using the SPC.

In April 2005, exenatide was approved in the US as both a monotherapy and an adjunctive therapy to improve **glycemic** control in patients with type 2 diabetes; as an adjunct it is particularly for those who are taking **metformin**, a **sulfonylurea**, or a combination of both, but who have not achieved adequate glycemic control. Positive data for exenatide as a monotherapy were released in November 2005, and were to form the basis of a sNDA; an additional study to complete the monotherapy filing began during 2006. Exenatide was later approved in Europe in November 2006 as an adjunctive therapy.

Last week we reported that **sanofi-aventis** had been granted five year extensions on three patents for **Plavix** (clopidogrel sulphate) which expire between Feb 2013 and July 2016. In the Japanese Patent gazette published May 25, additional five year extensions were granted on the same patents for the use of Plavix in reduction of recurrence in patients suffering an **ischemic cerebrovascular disorder** (excluding cardiogenic cerebro-embolism). As the previous extensions were also for five years, the new grants do not change the expiry dates. A fourth extension was also granted to sanofi-aventis, but the use case was granted one extra day (one year and three days) compared to that granted for the product itself. Consequently, **JP3641584** expires June 13, 2020. In addition, former licensee, **Daiichi Pharmaceuticals** gained almost three years on **JP3397385**, which now expires September 6, 2016 (rights for Plavix were returned to sanofi-aventis when Daiichi merged with **Sankyo**).

Daiichi (now **Daiichi Sankyo**) also received extensions of just under 5 years on two related patents for **levofloxacin** (**Cravit**, **Levaquin**) used in treating **infections**. In the case of **JP1659502**, this did not affect the expiry as a five year extension had been granted in 2005. Divisional **JP2008845** had previously received lesser extensions and so the new grant extends protection until May 27, 2011.



New program from Toray: first small peptide based DPPIV modulators to emerge

UK initial ("A0") applications filed April 23rd - April 29th 2007

7TM Pharma is a biopharmaceutical company which focuses on new pharmaceutical drugs targeting **7TM receptors**, with a particular interest in metabolic disorders such as **obesity**. They have this week filed a UK initial application (GB0708226) for Y-receptor agonists. See **WO2007038942** disclosing Y4 and Y2 agonists useful for appetite control and treating obesity. 7TM Pharma is currently investigating **TM-30338** (Y2 & Y4 receptor agonist) and **TM-30339** (Y4 receptor agonist) used as appetite suppressants. Its website further discloses that they are also currently (preclinical development) targeting the Y2 receptor to develop a drug useful for treating peripheral arterial diseases (PAD) e.g. atherosclerosis.

Activotec is applying for patent protection (GB0708445) for compounds and their use. In a cluster of three international applications filed in March 2005 (**WO2006097693**, etc) the company first claimed technology for **solid phase peptide synthesis**, and the inventors' affiliations caused us to link that work with the **University of Southampton**. Subsequently, in **WO2007051987**, there were claims to **insulinotropic linear peptides**, and the timing of that publication makes it very likely that the new application, dated May 1st 2007, is also on the same theme. The 2002 university spin-out, now headquartered in Cambridge, markets its peptide technology under the **Activo P-11** brand. However, Activotec's scientific base remains in Southampton, where in March 2005 it merged with **Southampton Polypeptides**. In August 2006 the company announced significant progress in efforts to stabilise **GLP-1** against proteolysis, in its search for an effective **type 2 diabetes therapy**. The company, has access to the peptide technology described by its founder, **Dr Ram Sharma**, in **WO9005738**, an application filed jointly with the **Public Health Laboratory Service** but subsequently withdrawn.

Alligator Bioscience has filed an initial UK patent application (**GB0708376**) relating to **novel polypeptides** and their use. Although we have on record nine published applications associated with this Swedish company, only three were initially filed using the Alligator name. The earliest of these, WO2004046720, relates to methodology for identifying specific binding pairs. Other companies and institutions involved in the larger set of patents include **BioInvent Int**, the **University of Utrecht**, **JARI Pharma** and **AstraZeneca**. However, the company emerged in the early 1990s from the Department of Immunology at the **University of Lund**, and apparently filed its first patent application in 1997, probably in the context of the University's **FIND technology**. Two of the FIND inventors are now VPs of R&D and Business Development respectively, and their names serve to identify Bioinvent's **WO9858080** as the relevant case; along with two related later filings, this patent, granted in 2004 as **EP990044**, is concerned with in vitro molecular evolution of protein function.

Erasmus Universiteit Rotterdam has filed two UK initial applications for **germline manipulation 2** and **3** (**GB0708242**) and (**GB0708243**). This appears to be a new project. However in the past the applicant has published in British Journal of Cancer (2002) 86, 1586-1591, with the title, "A novel germ line mutation of PTEN associated with brain tumours of multiple lineages".

Inventanet is seeking patent protection (**GB0708395**) for a method of **accelerating bioinformatics algorithms**. This is achieved using graphics processing units. Operating from an address in Cowbridge near Cardiff, the company was incorporated in February 2004, quoting a general classification covering software consultancy and supply. However, it seems likely that **genetic sequence matching** is its sole focus, since a pair of applications were filed some three months previously covering a system for searching for similarities in strings of data (GB0701344, GB0702035). There is evidence that an internet domain name was originally registered for the company, but this seems to have expired by mid-2006.