

Current Patents Gazette

Patenting in Context

News & Highlights from week 0813

In what should be the final issue of the UK Patents and Designs Journal (PDJ No. 6201), if all goes to plan, there are two events recorded concerning EC Regulations 1768/92 and 1610/96, i.e. Supplementary Protection Certificates (SPCs).

On March 1, 2008 **Novartis Ag's** SPC for **rivastigmine** came into force on **GB2203040** and will expire in just over four years time on July 30, 2012. SPCs have been granted on several European equivalents, which entered into force at about the same time and will also expire around July 31, 2012. SPCs have also been granted on **EP0193926** which covers the racemic form and is owned by **Proterra** and licensed to **Novartis**. These, however, expire in March 2011. GB2203040 and equivalents claim the S-enantiomer which is the commercial form of rivastigmine, marketed as **Exelon**. Paragraph IV challenges have been submitted by **Watson Pharmaceuticals** and **Dr Reddy's Labs** against both US equivalents in support of their ANDAs for generic rivastigmine tartrate capsules in all four marketed strengths, whilst **Sun Pharmaceuticals** only filed a challenge against Novartis' US5602176. In December 2007, Watson agreed not to market its generic version of rivastigmine prior to an undisclosed date in return for a license to relevant US patents. Indian generics companies Sun and Dr Reddy's also entered similar settlement agreements

in December 2007 and January 2008 respectively, which involved dismissal of the lawsuits in the US. Under the terms of the agreement, the companies will launch their generic versions "sometime" before the expiry of the Orange Book patents claiming rivastigmine; however, the exact date of launch was not disclosed. Exelon is indicated for the treatment of mild-to-moderate Alzheimer's disease, and mild-to-moderate dementia associated with Parkinson's disease (PD). Worldwide sales of Exelon reported by Novartis for 2007 were \$632 million, representing a 14% year-on-year growth in local currency terms.

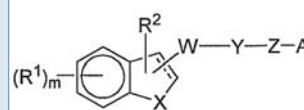
Also reported in this week's PDJ is the entry into force on March 4, 2008 of the SPC granted to **BTG International** on **GB2202851** protecting the veterinary vaccine **Heptavac P Plus** until July 18, 2011. SPCs were also granted on equivalents in Italy and Portugal, which expire November 2011.

Not yet reported in the PDJ is the SPC application filed in the UK by Spanish company, **J. Uriach & CIA** for **rupatadine** on **EP0577957**. Rumatadine (**Rupafin** or **Tamalis**) is a dual antagonist of platelet-activating factor (PAF) and histamine H1 receptors and has been developed and launched by Uriach for the treatment of allergic rhinitis; the drug is also in development for the potential treatment of

urticaria. If granted, the SPC will enter into force in May 2013 and expire July 3, 2016, fifteen years after the first European approval in Spain. SPCs have already been granted for EP0577957 in Belgium, Luxembourg, Portugal, Greece, Ireland and Spain, expiring July 2016. Uriach claimed the use of the compound in **EP0577957**, which refers to an earlier patent by **Schering-Plough**, **WO9200293**, which claims methylpyridine-substituted benzo(5,6)cyclohepta (1,2-b) pyridine derivatives as histamine and PAF antagonists and also includes rumatadine in its generic claims. Uriach stated however, that in WO9200293 only two compounds, both of them 4-pyridyl derivatives, were prepared and that 3-pyridyl derivatives, such as rumatadine, belong to a new class of dual PAF and histamine antagonists which was principally undisclosed prior to EP0577957. **Recordati** obtained a license in 2003 from Uriach for the sale of rumatadine in Spain, and has since signed license agreements with Uriach for the marketing

and sale of rumatadine in Italy and France. The agreements also include options for Germany, Poland and the UK. In 2007, the product was licensed to **Mistral Pharma** for the treatment of allergic rhinitis in Canada.

As mentioned earlier, this week sees the last issue of the **UK PDJ** as the **UKIPO** will be implementing a new service on 2nd April 2008, to replace the current Journal. UKIPO states that the current publishing process will cease at the end of March and will be replaced with a web based, searchable database for published patents data, with supplementary web pages to manage official patents notices and designs data. The searchable database will be updated on a weekly basis every Wednesday and will include data on UK applications filed, published or granted, EP/UK patents, UK ceased and expired patents and UK terminated applications, along with other proceedings under the Patents Act and Supplementary Protection Certificates.



First lipoic acid synthase (LASY) activators from Dr Reddy's metabolic disorders program

UK Initial Applications

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A0 applications filed February 8th – February 24th 2008 – expected to see publication in late August 2009

• **AquaPharm BioDiscovery** has filed a new UK initial application claiming novel **antimicrobial compounds** (GB0803060). The company, located at the **European Centre for Marine Biotechnology** at Oban, specializes in bioproduction based on marine organisms. Its work to date has focused on carotenoids, such as zeaxanthin and astaxanthin, with claims to their production in **WO2004048589** and **WO2006120400**.

AquaPharm Biodiscovery is also developing a strong pipeline of anti-infective candidates identified from its library of novel marine bacteria. It has a particular interest in antibiotic and antifungal agents which target drug resistant micro-organisms such as MRSA and *Candida albicans*. The company's website lists several potential candidates including novel peptides and small molecule antibiotics.

• **Atazoa** has filed an application claiming **biological materials and uses thereof** (GB0802980). This appears to be the first filing from this **Imperial College** spin off, which was incorporated in June 2003. The company was established by Professor Robert Winston, a notable fertility expert and Labour peer based at Imperial College, and Professor Carol Readhead of the **California Institute of Technology**. Atazoa's primary focus is genetic engineering of animals' immune systems, particularly pigs, to reduce the chances of organ rejection after transplantation into human patients. In September 2007, Atazoa was reported to have relocated its organ transplant research to Missouri, US, after UK restrictions on animal research prevented it from conducting key

experiments. The company's approach involves altering pigs' testes to produce sperm containing new genes, thus allowing GM animals with transplant compatible immune systems to be conceived naturally. The **Department for Environment, Food and Rural Affairs (DEFRA)** banned Atazoa from using modified male pigs for breeding, citing EC directives on transgenic farm animals.

• **Gene Bridges** has filed a new UK initial application covering a **method of nucleic acid recombination** (GB0803109). This **EMBL** spin-off develops and commercializes innovative DNA engineering technologies, based primarily around its proprietary Red/ET Recombination system. In April 2007, the company entered into a major collaboration with **BASF** to exploit this technology, utilizing BASFs expertise in biotechnology, process development and product application. The Red/ET system is based upon work originally disclosed in EMBL's **WO9929837** and **WO0104288**, with further recombination methods claimed in Gene Bridges' **WO02062988**.

• **Phoqus Pharmaceuticals (UK)** has filed GB0802873 to protect **pharmaceutical dosage forms for delayed and extended release**. This probably refines the concept that underlies **Chronocort**, the modified-release circadian hydrocortisone being developed in collaboration with **Sheffield University** spin-off **Diurnal** – see for example the university's **WO03015793**. The electrostatic tablet coating process used for Chronocort is known as **Qtrol**, and supporting technologies include the **Qdis**

fast-dissolving formulation and **LeQtradose** for low-dose combinations. By mid-2007 the company was expecting phase III adrenal insufficiency and congenital adrenal hyperplasia trials to commence early in 2008, with a late 2009 launch predicted for Chronocort.

• **Queen Mary & Westfield College** is claiming a **synthetic scFv analog to the 6313/G2 monoclonal antibody variable regions** (GB0802931). These correspond to the angiotensin II type 1 receptor, and the invention represents a continuation of work at **Queen Mary, University of London (QMUL)** started in 1994 by Professor Gavin Vinson – see **WO9532725**. This wide-ranging interest in the role of angiotensin in steroidogenesis extends to hypertension and cancer, but also more recently to fertility and sperm function, as demonstrated by **WO2005051412**. It seems however that the February 18 filing of the present application was timed to anticipate the March 2008 issue of *Endocrine Related Cancer*, in which Prof Vinson and colleagues explain how R6313/G2 is superior to AT1 antagonists such as losartan in suppressing cell proliferation in certain types of cancer, including breast tumors.

• **Queen Mary & Westfield College** is claiming **genetic variations associated with celiac disease** (GB0803004). A few days after this application was filed, the college, now known as **Queen Mary, University of London**, issued a press release describing the work of Professor David van Heel in this field, itself reporting a paper published online in the March 2008 issue of

Nature Genetics. The research is sponsored by The **Wellcome Trust** and by **Coeliac UK**. However, Prof van Heel's earlier work on the genetic basis for gastrointestinal disease seems to have been supported by **Oxagen**, whose **WO03052412** describes IBDP1, a novel gene associated with inflammatory bowel disease.

• **The University of Nottingham** is claiming **synthetic operon construction in clostridia** (GB0802842). This seems to follow on from the work described by **Morvus Technology** in **WO2007148091**, published a few weeks before the present filing, which names inventors associated with the university. Morvus is claiming a modified Group II intron useful for introducing mutations into bacterial cells, especially those of *Clostridium*. Further background to this **MRC**-sponsored work is given in an August 2007 press release from the university reporting the work of Professor Nigel Minton of its Centre for Healthcare Associated Infections, where the much-publicized phenomenon of nosocomial *Clostridium difficile* infections is a particular target. Prof Minton's team have developed the ClosTron knockout system to target specific genes in clostridial species. Apparently Dr Peter Mullany at **UCL** is participating and sharing the BBSRC funding. Carmarthen-based Morvus, located at Porton Down until mid-2007, includes in its research portfolio MorClos. This is an adaptation of Minton's technology to the discovery of a drug expressing a prodrug-activating enzyme at tumor sites.