

SPC News 22 – May 2008

## *LATEST NEWS ON MEDICINAL PRODUCTS SPCs in EUROPE*

### What is the situation in May 2008?

Supplementary Protection Certificates in Europe are governed

- in the 27 EU countries, Norway and Iceland by EEC Regulation 1768/92, amended by Regulation (EC) No 1901/2006 of 12 December 2006 relating to medicinal products for paediatric use
- in Switzerland by National law of 3 February 1995.

### ❖ Paediatric SPC extensions in Europe

#### ► EC Regulation on medicinal products for paediatric use

Regulation (EC) No. 1901/2006 adopted on 12 December 2006 entered into force, with direct effect in member states, on 26 January 2007.

The Paediatric Regulation aims to

- facilitate the development and accessibility of medicinal products for use in the paediatric population,
- to ensure that medicinal products used to treat the paediatric population are subject to ethical research of high quality and are appropriately authorised for use in the paediatric population, and
- to improve the information available on the use of medicinal products in the paediatric population.

These objectives should be achieved

- without subjecting the paediatric population to unnecessary clinical trials and
- without delaying the authorisation of medicinal products for other age populations.

The Regulation introduces a series of obligations for pharmaceutical companies:

#### ◇ for unauthorised medicinal products

As of 26 July 2008, marketing-authorisation applications for new products not authorised in the EU prior to 26 January 2007 will have to include the results of studies conducted in compliance with an agreed Paediatric Investigation Plan (PIP), unless the EMEA has granted a deferral or waiver for their provision.

#### ◇ for authorised, patented medicinal products

As of 26 January 2009, the requirements described above also apply to applications to vary a marketing authorisation to add a new indication (including paediatric), a new pharmaceutical form, or a new route of administration. In these cases, the PIP and/or waiver must cover all existing and new indications, formulations and routes of administration.

The main paediatric reward is a six-month extension of the SPC, but it is linked to stringent requirements:

- product must be approved in all EU Member States;
- significant paediatric studies must be completed after January 2007;
- all relevant obligations under the PIP must be met;
- a relevant statement of compliance must be included in a marketing authorisation; and
- an application for SPC extension must be submitted with the national patent authorities at least six months (and, as from late January 2012, two years) before expiration of the SPC.

#### ► Situation on 15 May 2008

Until now EMEA did not issue any paediatric MA. We noticed 23 EMEA decisions

▪ 14 waivers in all age group for all conditions, indications (for Roflumilast, Flibanserin, Fosfluridine tidoxil, Naproxenod, Rosiglitazone maleate, Panobinostat lactate salt, Indacaterol maleate/Glycopyrronium bromide, Glycopyrronium bromide, Telmisartan/Ramipril, Indacaterol maleate, Lasofoxifene tartrate, Candesartan/Hydrochlorothiazide, Everolimus)

▪ 9 paediatric investigation plans (for Meningococcal meningitis vaccine, Ezetimibe, Paliperidone, Doripenem monohydrate, Montelukast sodium, Latanoprost, Caspofungin acetate, Losartan potassium, Recombinant L-Asparaginase).

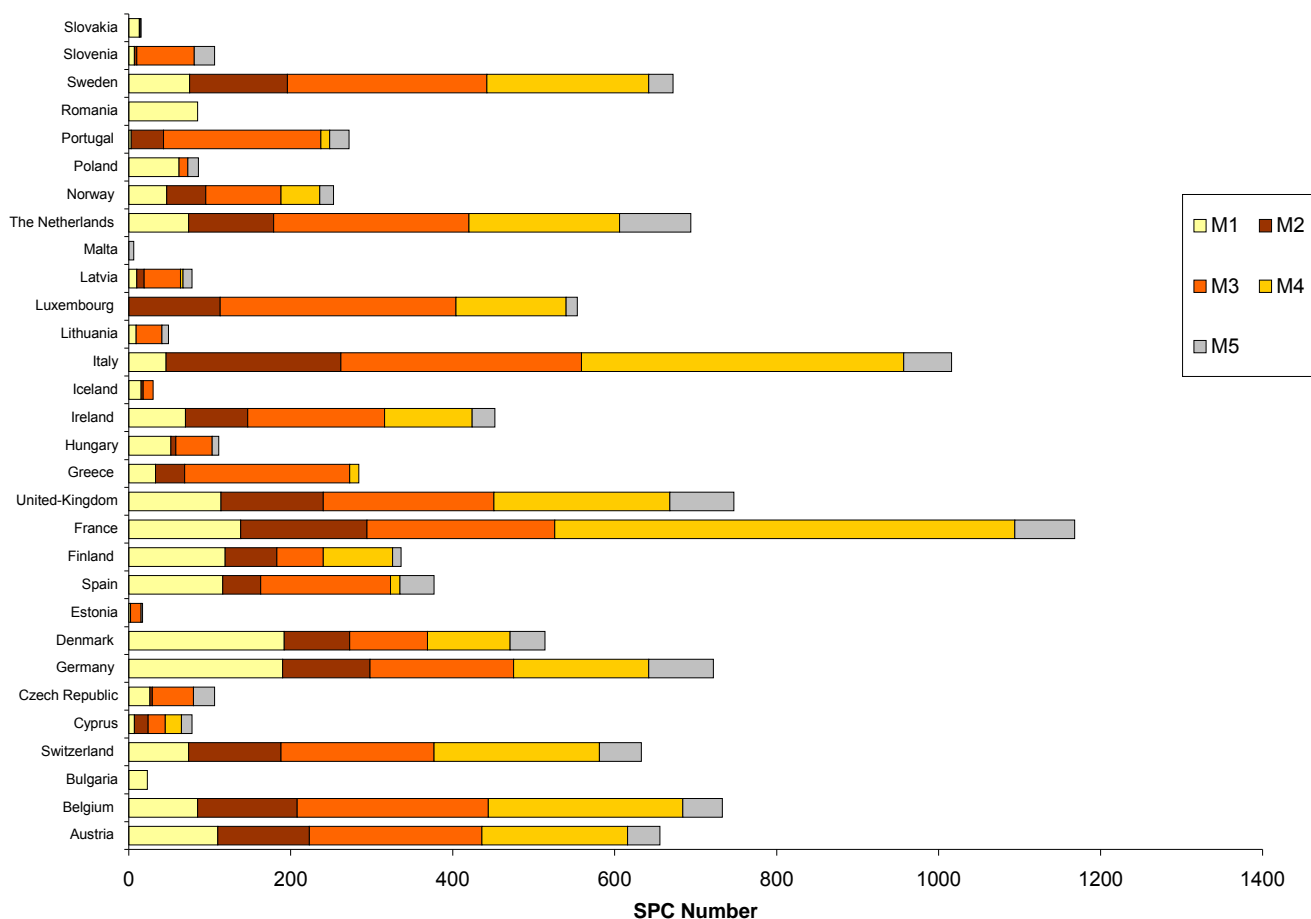
It seems that the first paediatric SPC extensions will be published in 2010 at the earliest.

❖ Medicinal Product SPCs in Europe from 1991 to 2007

About 10925 SPC applications for medicinal products regulated by EEC Regulation 1768/92 or National laws have been filed in European countries from January 1991 to December 2007, and published until the end of March 2008.

In the graph below, is shown, for each country the number of SPCs filed from 1991 to 2007, dispatched according to their status.

1991-2007 SPCs



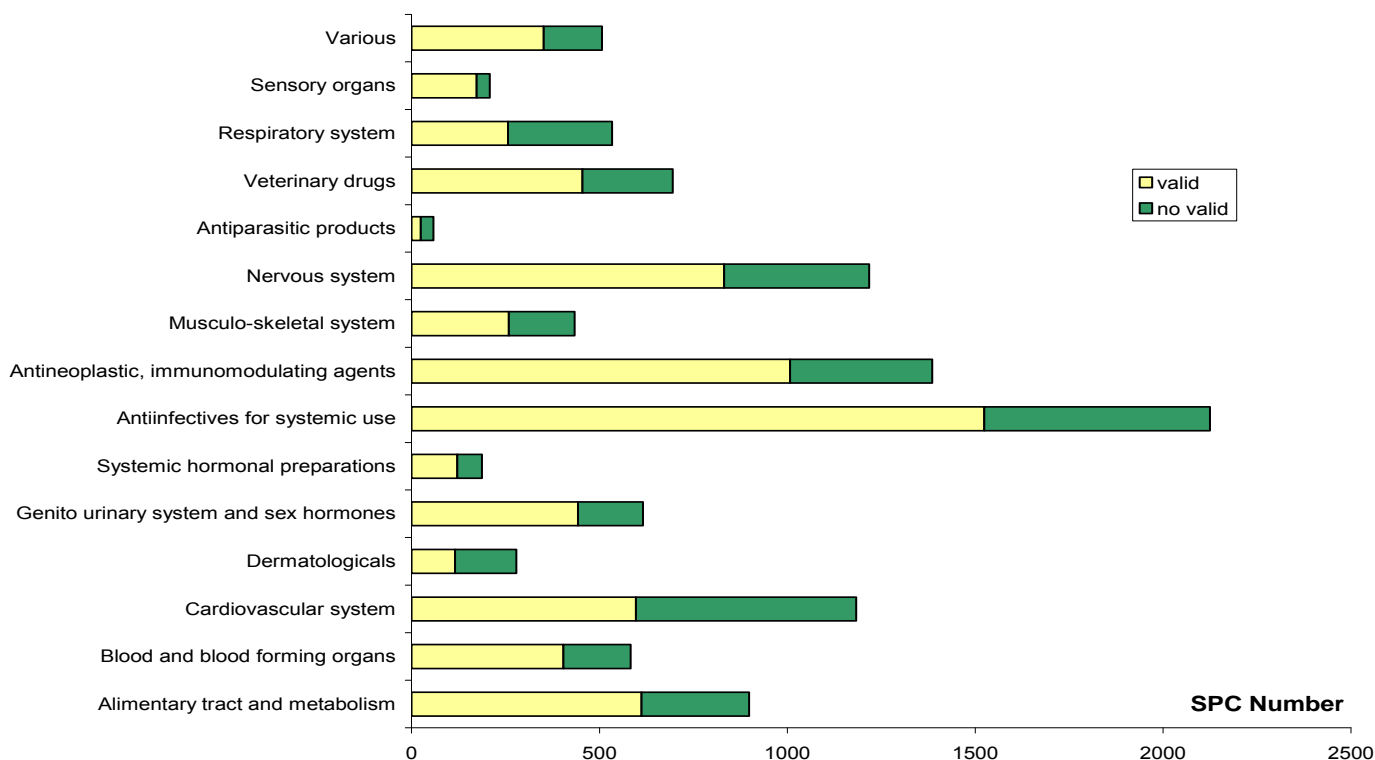
- M1 = SPC applications
- M2 = granted SPCs in force
- M3 = granted SPCs not yet in force
- M4 = expired, lapsed, invalid SPCs
- M5 = rejected or withdrawn SPC applications

The situation differs from one country to another due to the importance of the markets and/or to the applicable laws and/or to the date of entry in force of the EU Regulation:

- less than 20 SPCs in force in Bulgaria, Estonia, Lithuania, Malta, Poland, Romania, Slovakia, Czech Republic, Iceland, Slovenia, Hungary, Latvia, Cyprus
- less than 100 SPCs in force in Greece, Portugal, Spain, Norway, Finland, Ireland, Denmark
- less than 150 SPCs in force in The Netherlands, Germany, Austria, Luxembourg, Switzerland, Sweden, Belgium, United-Kingdom
- more than 150 SPCs in force in France and Italy.

In the graph below, is shown, the number of SPCs filed from 1991 to 2007 dispatched according to ATC code (first level) of the products and to the SPC status.

### 1991-2007 SPCs: Therapeutic activities

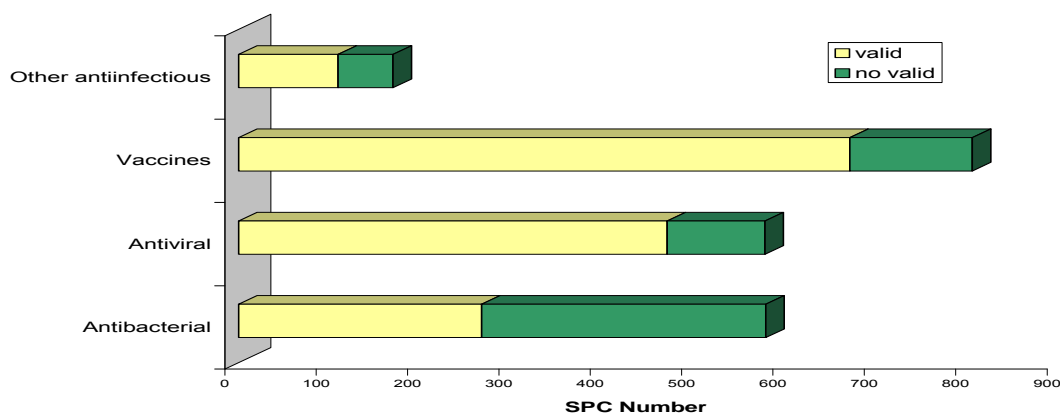


We noted SPCs for:

- antiinfectives for systemic use: 19.5% but only **16.1%** of SPCs still **valid**,
- antineoplastic and immunomodulating agents: 12.7% but only **10.15%** of SPCs still **valid**,
- drugs for nervous system use: 11.2% but only **10.3%** of SPCs still **valid**,
- drugs for cardiovascular system: 10.7% but **15.7%** of SPCs still **valid**.
- drugs for respiratory system: 4.9% but **7.4%** of SPCs still **valid**.

In the graph below, is shown the number of SPCs for antiinfectives filed from 1991 to 2007, dispatched according to the product specific activity and to the SPC status.

### 1991-2007 SPCs for Antiinfectives



We noted SPCs for:

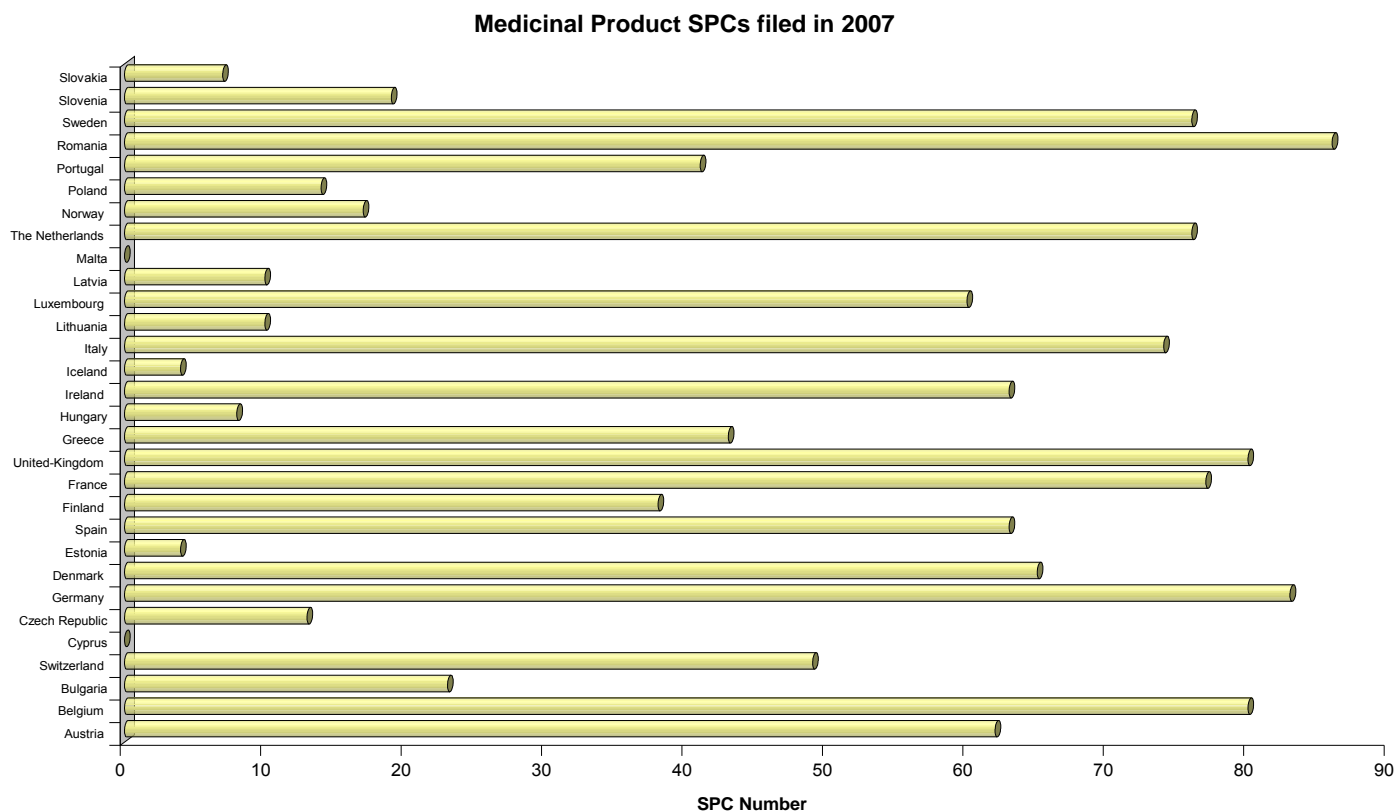
- antibacterial agents: 27.2% but only **17.6%** of SPCs still **valid**,
- antiviral agents: 27.1% but **31.0%** of SPCs still **valid**,
- vaccines: 37.8% but **44.2%** of SPCs still **valid**,
- other antiinfectious agents: 8.0% but only **7.2%** of SPCs still **valid**.

❖ Medicinal Product SPCs in Europe in 2007

**How many SPCs?**

1245 SPCs filed in 2007 were published at the end of March 2008.

In the graph below, is shown the number of SPCs for each country.



EU SPC Regulation entered in force in Bulgaria and Romania on 1<sup>st</sup> January 2007.

87 SPCs were filed in 2007 and published in Romania and 23 SPCs in Bulgaria.

**Which medicinal products?**

The 1245 SPCs filed in 2007 and published at the end of March 2008 cover about 170 different products (active ingredients, combinations of active ingredients, or formulations).

► Among these 1245 SPCs, about 38% relate to influenza or papillomavirus vaccines, 9% to glucose lowering agents, 6.6% to immunosuppressive agents and 6.3% to veterinary products.

► We noted 33 products, for which were lodged at least 10 SPCs. These products can be roughly sorted according to their therapeutic category:

- **Glucose lowering agents:** sitagliptin (39; 24 referring to Merck patents and 18 to Prosidion patents), exenatide (33), metformin and pioglitazone combination (15), metformin and rosiglitazone combination (17)
- **Agents acting on the renin-angiotensin system:** aliskiren (29), amlodipine and valsartan combination (22)
- **Antithrombic agents:** antithrombin alpha (24)
- **Antianemic agents:** erythropoietin beta methoxy-PEG (15), erythropoietin delta (11)
- **Antibiotics for topical use:** retapamulin (16)
- **Urology:** fesoterodine (38; 17 referring to Pfizer Health patents and 21 to Schwarz Pharma patents)
- **Sex hormones:** drospirenone and estrogen combination (11), testosterone (13)
- **Antivirals:** darunavir (14), telbivudine (16)
- **Vaccines:** H5N1 influenza vaccine (47; Focetria® 23, Daronrix® 21), Influenza trivalent vaccine (13), Papillomavirus vaccine (401; Gardasil® 268, Cervarix® 114)

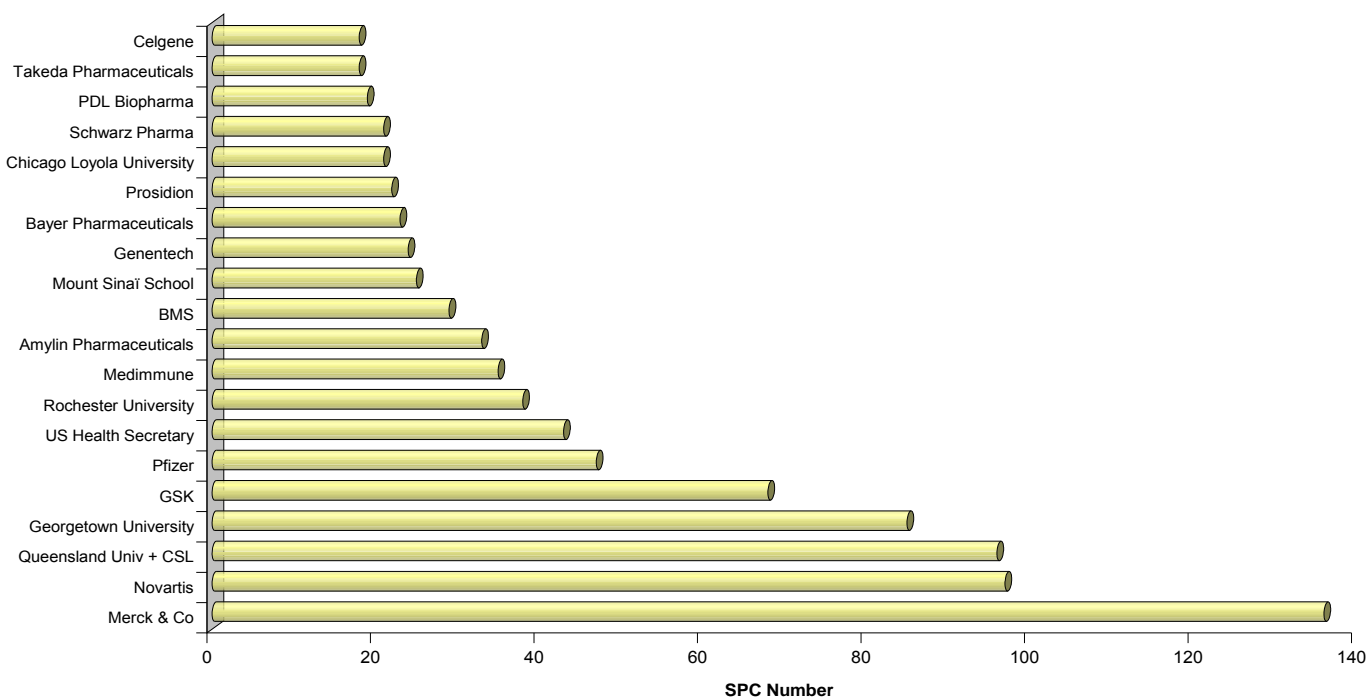
- **Immunosuppressive agents:** abatacept (15), lenalidomide (18)
- **Antimetabolite agents:** nelarabine (13)
- **Anti-inflammatory and antirheumatic agents:** lumiracoxib (13)
- **Bone diseases:** alendronate and colecalciferol combination (17)
- **Hypnotics:** melatonin (16)
- **Psychotics:** paliperidone (17)
- **Antiepileptics:** rufinamide (18)
- **Respiratory system agents:** nitric oxide (10)
- **Antineovascularisation agents:** ranibizumab (38; 21 referring to Genentech patents and 17 to PDL Biopharma patents)
- **Iron chelating agents:** deferasirox (12)
- **Paramagnetic contrast media:** gadofosveset (15)
- **Ultrasound contrast media:** perflutren (13)
- **Veterinary products:** antiemetics (maropitant: 18), antiobesity (mitratapide: 20)

**Who filed Medicinal product SPCs and for which products?**

898 SPCs out of these 1245 SPCs were lodged by 20 holders.

For these 898 SPCs, the figure below represents the number of SPCs sorted by holder.

**Medicinal Product SPCs – Main Holders**



All SPCs filed by Loyola University of Chicago, University of Rochester, US Secretary Department of Health and Human Services, University of Georgetown, University of Queensland + CSL limited relate to papillomavirus vaccines. Other SPCs for papillomavirus vaccines were filed by Medimmune (18), SmithKline Biologicals (12) and Merck & Co. (88).

All SPCs filed by Mount Sinai School of Medicine of New York University relate to H5N1 influenza vaccines. Other SPCs for H5N1 influenza vaccines were filed by Medimmune or Aviron (19) and Novartis Vaccines (3).

❖ Recent National or European decisions affecting SPCs

✓ Decisions relating to Chiron EPO181150 and EPO318216 patents

➤ **France**

Four decisions of Cour de cassation (3/04//2007)

These decisions confirmed Cour d'appel de Paris decisions rejecting Chiron appeal against the refusal by French Patent Office of 4 SPC applications (01C0023, 01C0024, 01C0025, 01C0026) because these applications related to products neither used for treating or preventing disease, nor administered with a view to making a medical diagnosis but to test reactants for in vitro diagnosis.

✓ Decision affecting Trifluçan® drugs

➤ **France**

Cour de cassation (3/04//2007)

According to this decision, Cour de cassation set aside Cour d'appel de Paris sentence of 12 October 2005 without ordering a new trial; Cour de cassation considered that National SPC 92C0372 was invalid because the product had already been the subject of the certificate 92C0371.

✓ Decisions affecting Fosamax® and/or Fosavance® drugs

➤ **France**

Two decisions of TGI Paris relate to French SPC 96C0032 referring to French patent FR2525223:

TGI Paris (15/02/2008) MSD Somerset Ltd / Teva Classics, Teva Santé

TGI Paris (15/02/2008) Arrow Generiques, EG Labo, Ratiopharm / MSD Somerset Ltd

According to these decisions the Court revoked, for lack of inventive step, the claims relating to pharmaceutical compositions suitable for the treatment of urolithiasis and inhibiting the bone reabsorption comprising a biphosphonic acid, and specifically 4-amino-1-hydroxybutan-1,1 biphosphonic acid. If these decisions are confirmed, SPC 960032 will no longer protect Fosamax® and/or Fosavance® drugs (Decisions open to appeal).

➤ **The Netherlands**

Rechtbank's-Gravenhage (13/02/2008)

According to this decision the Court revoked the Dutch part of Merck Sharp & Dohme's European Patent EP1175904, due to lack of inventive step.

➤ **Belgium**

Court of First Instance in Brussels (8/04/2008)

According to this decision the Court revoked the Belgium part of Merck Sharp & Dohme's European Patent EP1175904, due to lack of inventive step.

➤ **SPCs referring to EP1175904 (division of EP0998292 revoked by EPO)**

SPCs referring to EP1175904 patent (opposition procedure) were filed in all countries designated in European patent. SPCs were granted in Italy, Luxembourg, and Slovenia and refused in Portugal, SPCs applications are still pending in other countries (no SPC granted in Belgium and The Netherlands if 2008 court decisions are confirmed).

✓ Decision affecting aceclofenac

➤ **France**

TGI Paris (22/02/2008) S.A. Laboratorios Almirall, S.A.S. Almirall / Merck Generiques, S.A.S. Qualimed, S.A.S. Pharm'Depo, Merck Farma y Quimica

According to this decision, the Court revoked French SPC 98C0017, referring to EP0119332, due to the fact that the SPC was filed by a person other than the owner of the patent at the filing date. In fact Prodes filed SPC 98C0017 in 1998 whereas he was no more the owner since 25 January 1985, when the patent was transferred to Prodesfarma SA.

✓ Decision affecting memantine

➤ **Germany**

Bundespatentgericht (11/12/2007) Neuraxpharm Arzneimittel, Teva Pharmaceuticals, Synthon BV, Pliva Hrvatska, Chemo Ibéroca / Merz Pharma GmbH & Co.

According to this decision, the Court revoked the German part of EP0392059 and corresponding German SPC 10299048 for memantine (Decision open to appeal).

✓ Decision affecting combination of tenofovir disoproxil and emtricitabine

➤ **The United Kingdom**

Following a hearing, the Patent Office decided on 10/01/2008 to reject British SPC application GB05/041 because the basic patent protects tenofovir disoproxil and not the combination of tenofovir disoproxil and emtricitabine.

✓ Decision affecting sitagliptin phosphate monohydrate

➤ **The United Kingdom**

Following a hearing, the Patent Office decided on 14/04/08 to grant British SPC application GB07/046 which will take effect at the end of the lawful term of the basic patent, that is 5<sup>th</sup> July 2022, and its maximum period of duration will expire on 20<sup>th</sup> March 2022 (negative term). This implies that the SPC will never take effect. However if a successful application for a paediatric extension were eventually to be made, this term would be extended by six months, which would give a positive value and allow the SPC to take effect.

✓ SPCs for olanzapine

SPC applications referring to Eli Lilly EP0454436 or national corresponding patents were filed in most European countries for product "olanzapine" referring to 1996 EU MA and for product "olanzapine amorphous" referring to 2001 EU MA.

SPCs for olanzapine referring to 1996 MA were granted in Austria, Belgium, Germany, Denmark, Finland, France, United Kingdom, Ireland, Italy, Luxembourg, The Netherlands, Norway, and Sweden. SPCs for olanzapine referring to 2001 MA were granted in Austria, Greece, Italy, Luxembourg, and Portugal, but refused or withdrawn in all other countries.

Furthermore claims for revocation of the patents were lodged in several countries: Germany, Spain, Hungary, The Netherlands, The United Kingdom. In Spain, on 17 January 2008, Audiencia Provincial de Barcelona in the case Lilly versus Cinfa, Alter and Kern recognized the validity of the Spanish patent.