

SPC News 23 – July 2009

LATEST NEWS ON MEDICINAL PRODUCTS SPCs in EUROPE

What is the situation in July 2009?

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 No. 1901/2006 on medicinal products for paediatric use entered into force, with direct effect in member states, on 26 January 2007.

As far as intellectual property is concerned, the main paediatric reward is a six-month extension of the SPC.

▶ Situation on 15 July 2009

We noticed applications for paediatric extension for 2 active substances.

▪ Caspofungin

The corresponding applications were filed in August 2008.

For the time being the status of these applications is as follows

- Paediatric extension granted in The Netherlands
- Paediatric extension application published in Belgium, Finland, France, The United Kingdom and Ireland. It is important to note that the UK Patent Office refused the paediatric extension because the application does not include an authorisation containing a statement of compliance with an agreed completed paediatric investigation plan as referred to in Article 36(1) of EC Regulation 1901/2006.

▪ Losartan

The corresponding applications were filed in February 2009.

For the time being the status of these applications is as follows

- Paediatric extension granted in France and The Netherlands
- Paediatric extension application published in Austria, Belgium, Germany, Denmark, Finland, The United Kingdom and Ireland. It is important to note that the UK Patent Office refused the paediatric extension because a statement on compliance with agreed PIP was not included in the marketing authorisation and authorisation in all the EU member states must be confirmed before the six-month extension to the SPC can be granted.

▶ Potential paediatric extensions for the next years

We reviewed EMEA decisions agreeing on PIP or granting waivers and noted data for medicinal active substances that are protected by a supplementary protection certificate due to expire in the next three years.

In addition to losartan (see above), we identified 10 products which could benefit from paediatric SPC extensions:

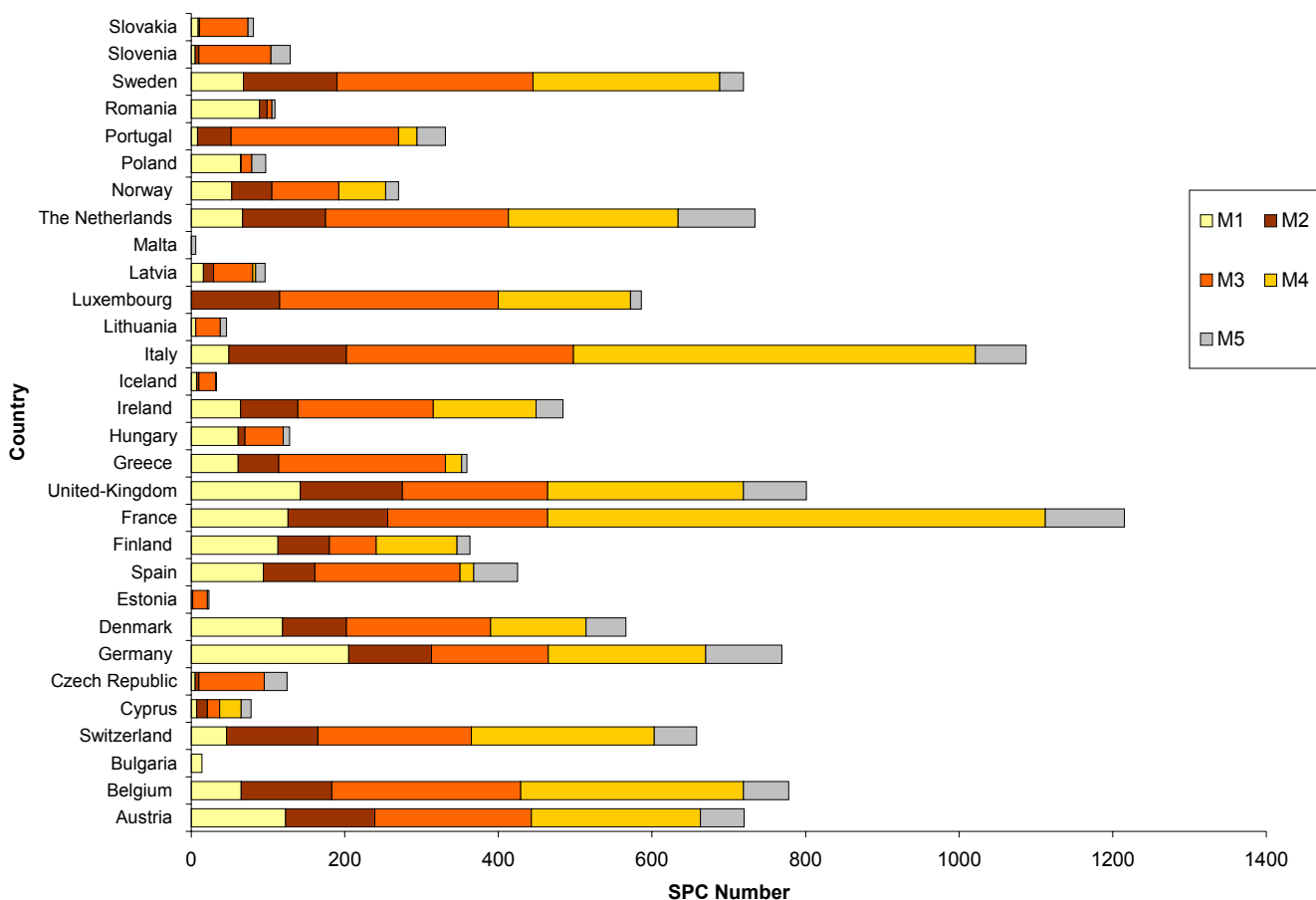
- anastrozole, docetaxel and pramipexole, protected by SPCs expiring in 2010,
- atorvastatin, latanoprost and valsartan, protected by SPCs expiring in 2011,
- zoledronic acid, rabeprazole, montelukast and candesartan, protected by SPCs expiring in 2012.

❖ Medicinal Product SPCs in Europe from 1991 to 2008

About 11900 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 2008, and published until the end of June 2009.

In the graph below, is shown, for each country the number of SPCs filed from 1991 to 2008, dispatched according to their status.

1991-2008 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.

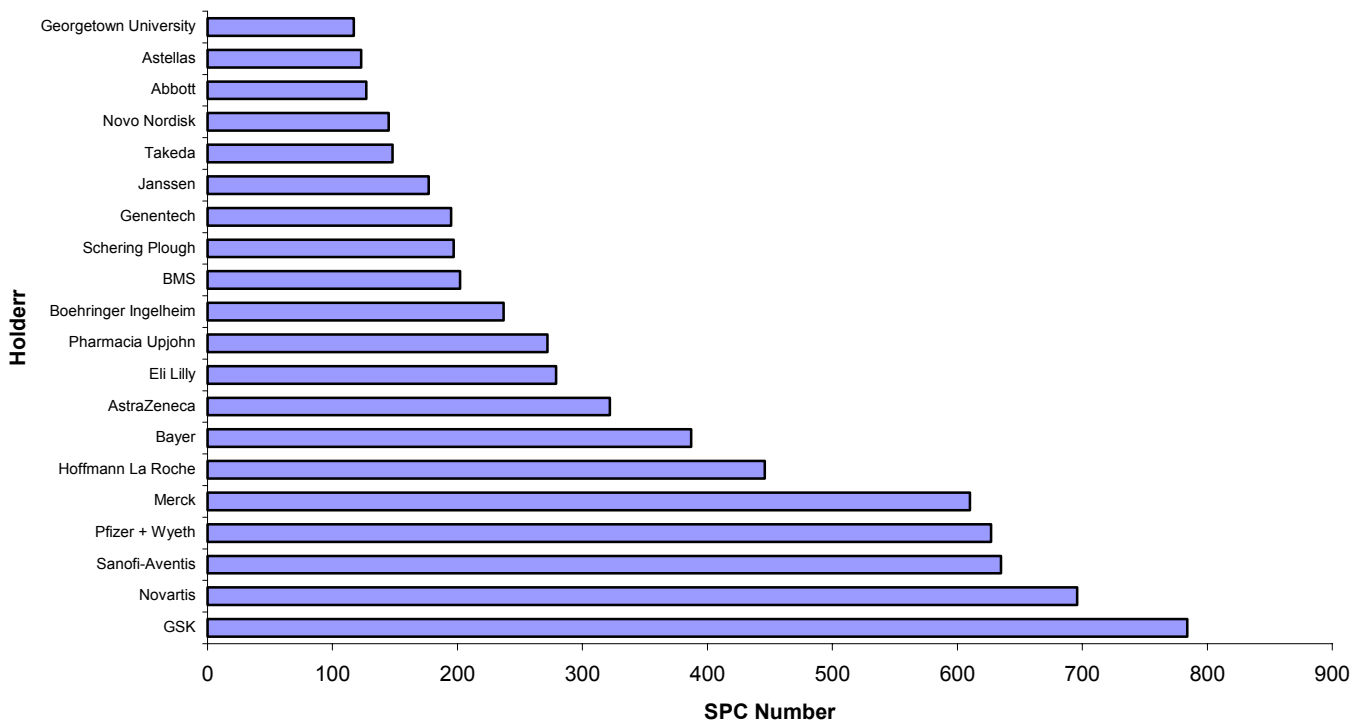
So for SPCs in force in June 2009 we noted:

- in the twelve new EU countries (SPC EU Regulation since 2004 or later) there are few SPCs in force : 0 to 14 SPCs per country
- in Spain, Greece, Portugal and Iceland (SPC EU Regulation since 1998) there are 67, 53, 44, 3 SPCs in force, respectively
- in Denmark, Finland, Ireland and Norway (SPC EU Regulation since 1993 or 1994) there are 83, 67, 75, 52 SPCs in force, respectively
- in Austria, Belgium, Switzerland, Germany, France, United-Kingdom, Italy Luxembourg, The Netherlands, Sweden (SPC EU Regulation since 1993 or 1994 or Swiss Law) there are 108 to 134 EU or CH SPCs in force.

There are no more national SPCs in force in France and Sweden and only 19 in Italy.

In the graph below, is shown, the number of SPCs filed from 1991 to 2008 by the first 20 holders.

1991-2008 SPCs – Main Holders



For 2 of the first main European holders, we mentioned below medicinal products with valid SPCs.

SANOFI-AVENTIS

- *Oral antiplatelet agent*
 - Clopidogrel: 17 SPCs in force in AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, NL, NO, PT, SE with expiry date January or February 2013.
- *Drugs for cardiovascular system*
 - Icatibant: 19 SPCs or SPC applications in BE, DE, DK, ES, FI, GR, HU, IE, IT, LV, LU, LT, NL, NO, PT, SE and CZ, FR, GB (filed in 2009) with expiry date November 2014 (August 2014 in DK and FI, December 2017 in LT and June 2018 in LV); no SPC in Austria and Switzerland.
 - Irbesartan: 17 SPCs in AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, NL, NO, PT, SE with expiry date August 2012.
 - Irbesartan + hydrochlorothiazide: 16 SPCs in AT, BE, CH, DE, ES, FI, FR, GB, GR, IE, IT, LU, NL, PT, SE, SK and Danish SPC application pending with expiry date October 2013 (February 2014 in Switzerland, February 2016 in Slovakia); SPC application rejected in Norway and Czech Republic.
- *Antiobesity drug*
 - Rimonabant: 26 SPCs or SPC applications AT, BE, CH, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LV, LU, LT, NL, NO, PL, PT, SE, SI, SK with expiry date November or December 2019 (June 2021 for Estonian and Latvian SPCs referring to 1998 patents); no corresponding patent in Bulgaria and Romania
- *Antineoplastic treatment*
 - Detoxifying agent
 - ▶ Rasburicase: 19 SPCs in AT, BE, CH, CZ, DE, DK, ES, FI, FR, GB, GR, HU, IE, IT, LU, NL, NO, PT, SE and SPC application in Latvia with expiry date July 2015 (January 2017 in Portugal and February 2016 for Czech SPC referring to 1995 patent); SPC application referring to 1996 patent rejected in Lithuania, Poland and Slovenia.
 - Monoclonal antibodies
 - ▶ Panitumumab alone or combined with other antineoplastic agents: 42 SPCs or SPC applications co-owned with Yeda Research and Development in AT, BE, CH, DE, ES, FR, GB, GR, IT, LU, NL, SE with expiry date September 2014.

- *Insulins*

- Insulin glargine: 18 SPCs filed in AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, HU, IE, IT, LU, NL, NO, PT, SE with expiry date November 2014 (February 2015 in Portugal).

- Insulin glulisine: 18 SPCs in AT, BE, CH, CZ, DE, DK, ES, FR, GB, GR, HU, IE, IT, LU, NL, PT, SE, SK and 3 SPC applications in FI, NO, PL with expiry date September or October 2019 (May 2020 in Portugal).

- *Macrolide Antibacterials*

- Telithromycin: 21 SPCs in AT, BE, CZ, DE, DK, ES, FI, FR, GB, GR, HU, IE, IT, LU, LV, NL, NO, PT, SE, SI, SK and 2 SPC applications in Poland and Romania with expiry date July 2016; Estonian SPC application refused; no SPC in Switzerland.

ASTRAZENECA

- *Nervous system*

- Anesthetics

- ▶ Ropivacaine: 16 SPCs in AT, BE, CH, CY, DE, DK, FI, FR, GB, IE, IS, IT, LU, NL, NO, SE with expiry date September 2010 (December 2011 in Switzerland and Cyprus).

- Analgesics

- ▶ Zolmitriptan: 20 SPCs in AT, BE, CH, CZ, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, NL, NO, PT, SE, SI, SK with expiry date March 2012; SPC application refused in Latvia.

- Thiazepines

- ▶ Quetiapine: 17 SPCs in AT, BE, CH, DE, DK, ES, FI, GB, GR, IE, IT, LU, NL, NO, PT, RO, SE with expiry date March 2012; Bulgarian SPC application withdrawn and 1 German SPC application withdrawn, no SPC in France.

- *Antineoplastic treatment*

- Antimetabolites

- ▶ Raltitrexed: 12 SPCs in AT, BE, CH, FI, FR, GB, IE, IT, LU, NL, NO, PT with expiry date August 2010 (March 2012 in Switzerland); no SPC in Germany, Denmark, Sweden.

- Hormone antagonists

- ▶ Anastrozole: 14 SPCs in AT, BE, CH, DE, DK, FI, FR, GB, IE, IT, LU, NL, NO, SE with expiry date August 2010 (May 2011 in Switzerland); Romanian SPC application pending and Spanish SPC application refused.

- *Beta-Lactams Antibacterials*

- Ertapenem: 22 SPCs in AT, BE, CH, CZ, DE, DK, ES, FI, FR, GB, GR, HU, IE, IT, LU, NL, NO, PL, PT, SE, SI, SK with expiry date April 2017 (February 2018 in Switzerland, October 2017 in Czech Republic).

- *Antithrombotic agents*

- Melagatran: 11 SPCs in AT, BE, CH, ES, FR, GR, IS, LU, NL, PT, SE, and SPC applications in DE, NO with expiry date December 2018 (June 2019 in Switzerland); Danish SPC refused, no SPC in FI, GB.

- Ximelagatran: 11 SPCs AT, BE, CH, ES, FR, GR, IS, LU, NL, PT, SE, and SPC application in DE with expiry date December 2018 (November 2019 in Switzerland); Danish SPC refused, no SPC in FI, GB.

- *Leucotrien receptor antagonists*

- Zafirlukast: 10 SPCs in BE, CH, ES (2), FI, GB, IE, IT, LU, PT with expiry date January 2011 (April 2011 in Switzerland); no SPC in other EU countries.

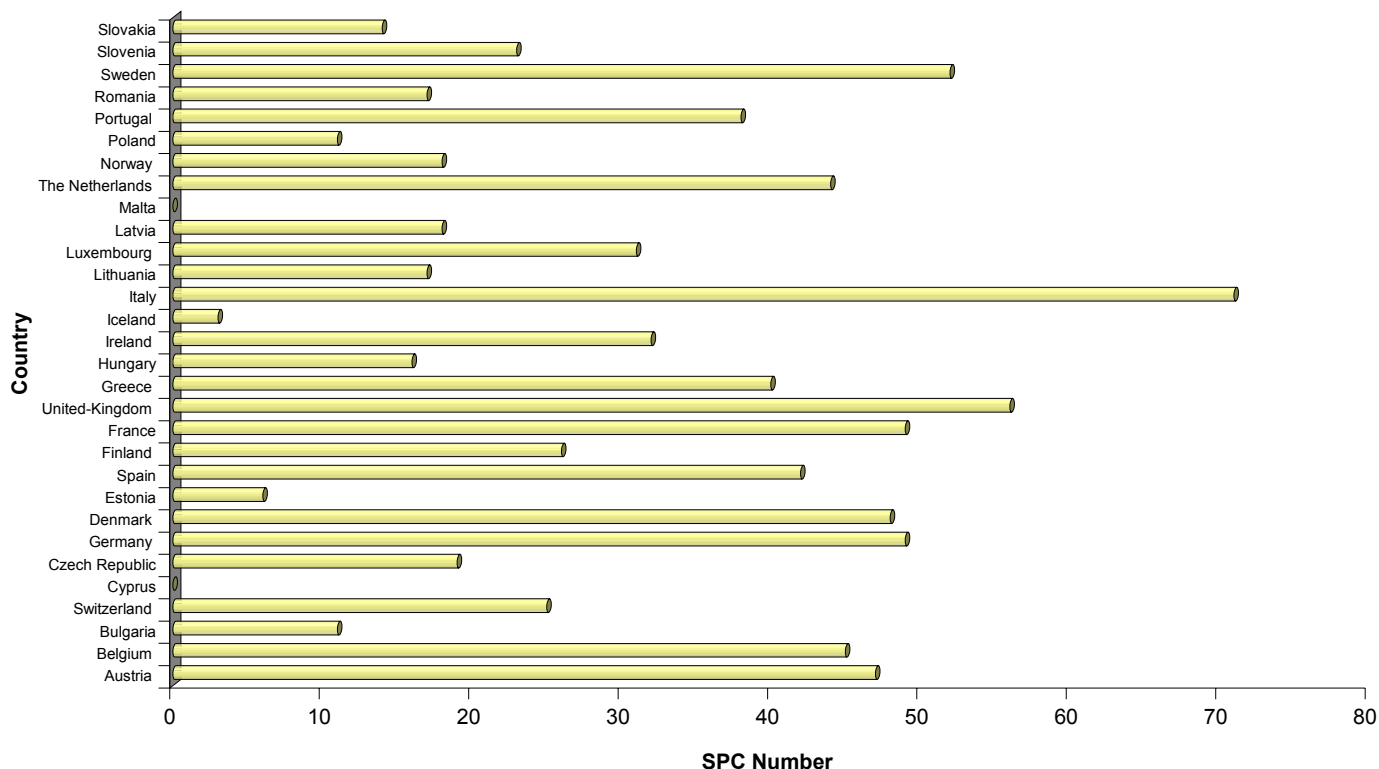
❖ Medicinal Product SPCs in Europe in 2008

How many SPCs?

868 SPCs filed in 2008 were published at the end of June 2009.

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

Medicinal Product SPCs filed in 2008



Which medicinal products?

The 868 SPCs filed in 2008 and published at the end of June 2009 cover about 100 different products (active ingredients, combinations of active ingredients, or formulations).

► Among these 868 SPCs, about 18,3% relate to antineoplastic agents, 15,7% to influenza or papillomavirus vaccines, 14,6% to antiviral agents, and 10% to glucose lowering agents.

► We noted products, for which were lodged at least 20 SPCs. These products can be roughly sorted according to their therapeutic category:

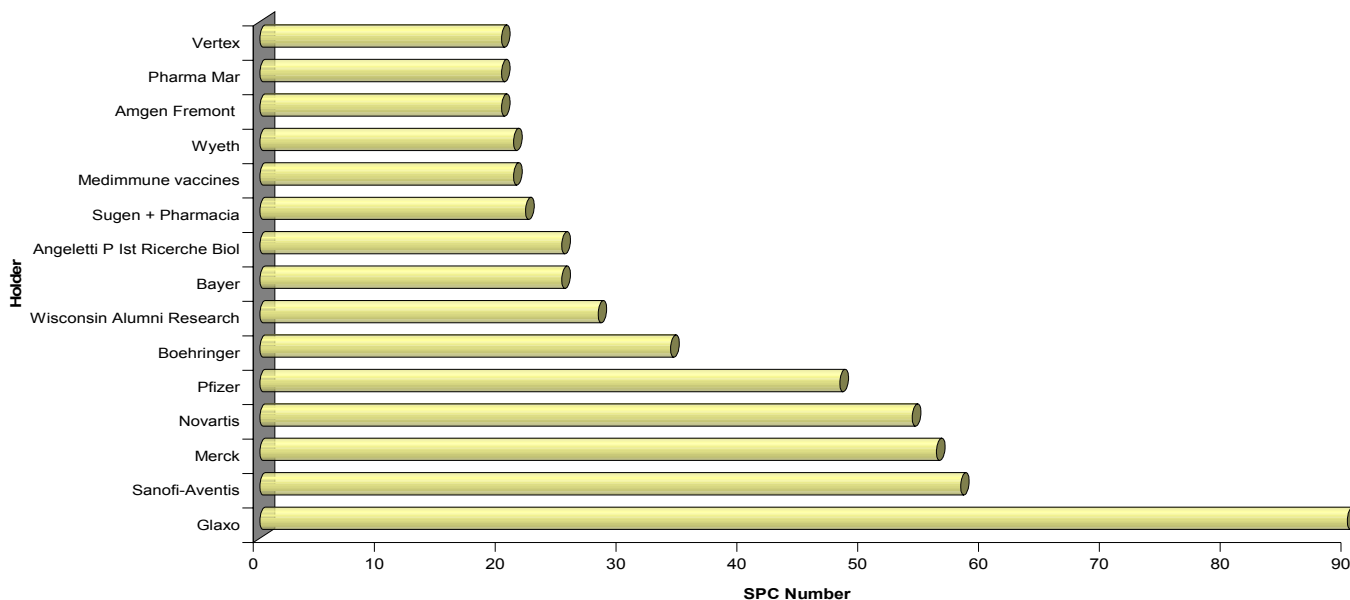
- **Glucose lowering agents:** metformin and vildagliptin combination (30), metformin and sitagliptin combination (27)
- **Direct thrombin inhibitors:** dabigatran etexilate (26)
- **Antivirals:** efavirenz+emtricitabine+tenofovir disoproxil fumarate combination (45; 23 referring to Merck, 16 to Gilead Sciences, 3 to Emory University and 3 to Shire patents), raltegravir (25), fosamprenavir (20), maraviroc (23)
- **Vaccines:** H5N1 influenza vaccine (96; 29 referring to GlaxoSmithkline Biologicals, 21 to Medimmune Vaccines, 18 to Mount Sinai School of Medicine and 28 to Wisconsin Alumni Research Foundation patents), Papillomavirus vaccine (27; Cervarix® 17, Gardasil® 10)
- **Antineoplastic agents:** panitumumab (62; 20 referring to Amgen Fremont, 42 to Aventis Holdings and Yeda Research and Development patents), lapatinib (25), sunitinib (22), temsirolimus (21), trabectedin (20)
- **Drugs used in nicotine dependence:** varenicline (20).

Who filed Medicinal product SPCs and for which products?

Out of the 868 SPCs filed in 2008 and published at the end of June 2009, we noted 15 holders which lodged at least 20 SPCs (542 SPCs).

For these 542 SPCs, the figure below represents the number of SPCs sorted by holder.

Medicinal Product SPCs – Main Holders



We identified the medicinal products for which SPCs were filed by the first 9 SPC holders in 2008.

GlaxoSmithkline Biologicals: SPCs for H5N1 influenza vaccines or to measles-mumps-rubella vaccine and *Glaxo*: SPCs filed for lapatinib, fluticasone furoate or nelarabine.

Aventis Holdings and Yeda Research: SPCs for panitumumab and *Sanofi-Aventis*: SPCs for icatibant.

Merck: SPCs for efavirenz+emtricitabine+tenofovir disoproxil fumarate combination, metformin and sitagliptin combination or fosaprepitant.

Novartis: SPCs for vildagliptin or metformin and vildagliptin combination.

Pfizer: SPCs for maraviroc or varenicline.

Boehringer: SPCs for dabigatran etexilate or Lawsonia vaccine.

Wisconsin Alumni Research: SPCs for H5N1 influenza vaccines.

Bayer: SPCs for rivaroxaban or drospirenone and ethinylestradiol combination.

IRBM P. Angeletti: SPCs for raltegravir.

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❖ *French decisions affecting SPCs*

As usual, there are very few French decisions relating to patents. We mention however a few decisions relating to SPCs.

✓ *Decisions affecting Zinnat® drugs*

Two decisions of TGI Paris relate to French SPC 92C0212 referring to French patent FR2531087:

TGI Paris (20/02/2009) Glaxo Group Ltd and Laboratoire GlaxoSmithKline / Qualimed and Merck Génériques,

TGI Paris (20/02/2009) Glaxo Group Ltd and Laboratoire GlaxoSmithKline / Sandoz

French SPC 92C0212 expired on 8 August 2008. This SPC was referring to FR2531087 patent relating to amorphous cefuroxime axetil.

According to these decisions the Court revoked French SPC 92C0212, for lack of novelty of claims 1 2 and 3 and for lack of inventive step of claims 4, 5, 7, 8, 11 and 13 of French patent FR2531087 over GB1571683 patent relating to cefuroxime axetil.

✓ *Other decisions*

We noted 3 decisions relating to French SPCs

➤ Cour d'appel de Paris rejected on 14/01/2009 Medimmune Vaccines appeal against the decision of the French Patent Office granting a SPC for A/Vietnam/1194/2004 (H5N1) whole virus inactivated antigen and not for Daronrix® drug: new plea in law, no substantive decision.

➤ The French Patent Office rejected on 26/09/2008 a SPC application for lipid complex of amphotericin B, a phosphatidyl choline and a phosphatidyl glycerol on the grounds that the 2 phospholipids were mere excipients and the SPC application did not refer to the first marketing authorisation for amphotericin B.

➤ Cour d'appel de Paris rejected on 11/04/2008 Novo Nordisk appeal against the refusal by French Patent Office of a SPC application for somatropin because the MA referred to was not the first MA for somatropin.