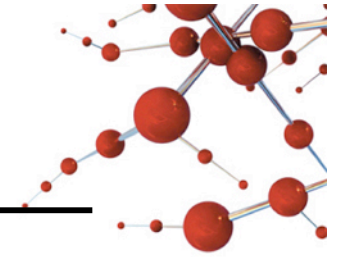


# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



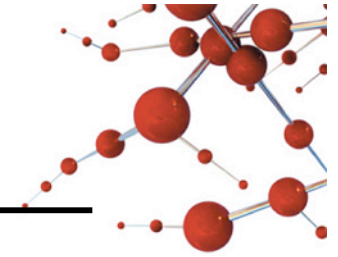
## *THE SIGNIFICANCE OF REGULATORY STRATEGY ON QUICK&SWIFT ENTRANCE TO THE PHARMACEUTICAL MARKET*

*Dr. D. M. Antoniadis  
Head of Global Regulatory Affairs and Drug Safety  
Pharmathen S.A.*



# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



## *Major factors involved in the product development/approval*

Development time planning – Consideration of API/FP patents

Development Committee – R&D / RA / QA / QC / IP

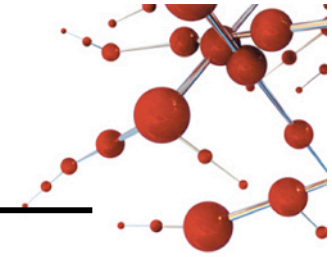
Agency meetings – Pre submission meetings / Scientific Advise

Submission strategy – Regulatory procedure selection based on basic patent expiry in the EU and rapid Global access to the market

GLP, GMP and GCP compliance audits-In parallel to the development (API manufacturer, FP Manufacturer, Clinical site)

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



## *PHARMATHEN S.A. REGULATORY ACHIEVEMENTS*

-1<sup>ST</sup>Generic Approval in the EU for the following products:

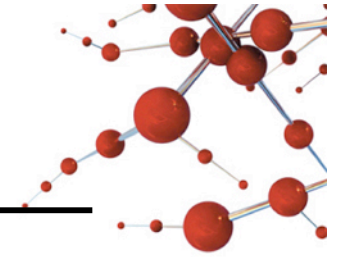
- a) Clopidogrel – Plavix-Sanofi
- b) Venlafaxine – Effexor - Wyeth
- c) Topiramate – Topamax – Janssen
- d) Ondansetron - Zofran - GSK
- e) Trandolapril – Gopten – Abbott
- f) Ibandronate – Bonviva/Bondronat – Roche
- g) Risedronate – Actonel – Procter&Gamble

-1<sup>st</sup> Greek Company to develop and approve new Pharmaceutical form of Innovator product, soon to be marketed by the innovator company

-1<sup>st</sup> Greek Company to submit and approve a product through the EMEA (simultaneous approval in all EU states)

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---

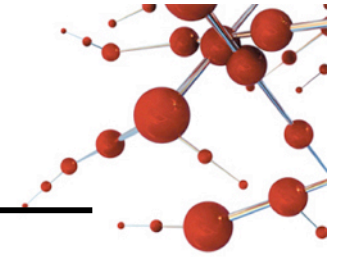


## *EUROPEAN APPROVAL PROCEDURES* *Centralised, Decentralised, Mutual Recognition & National submissions*

- POM, OTC, Generics, Repurposed Products
- Devices & drug-device combinations
- Small molecules & Biologics
- Advanced therapy products

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



## *APPROVAL PROCEDURES – CASE STUDY GREEK EOF (NATIONAL DRUG ORGANIZATION)*

Centralized (7-10 months, no major EOF involvement, immediate launch after approval, pending pricing timelines)

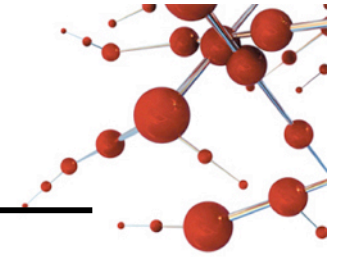
Decentralized (10-16 months + 8 months EOF phase)

Mutual Recognition (12-18 months national approval + 3 months MRP + 8 months EOF phase)

National submissions (18-30 months)

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---

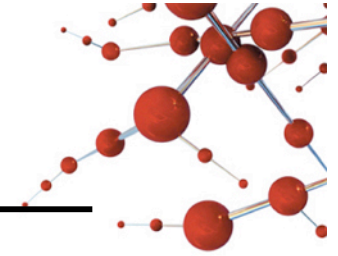


## *THE FIGURES*

- Number of Products developed yearly, 10-12, since 2005
- Number of products submitted through EU procedures per year 15-20
  - Number of Licenses received up to 12/2009 1680
  - Number of applications to conclude in 2010 1846

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



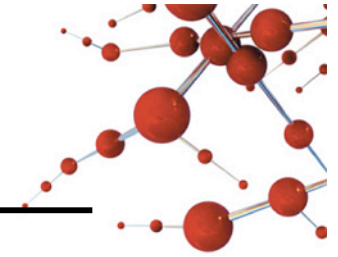
## *CASE STUDY – PLAVIX BY SANOFI AVENTIS CONTAINING CLOPIDOGREL (IN THE FORM OF BISULPHITE SALT)*

SANOFI Defence strategy, including:

- patents on the clopidogrel salt (bisulphite, expiry 2013)
- clinical indication patents (expiry 2017)
- finished product formulation patents
- Data exclusivity expiring 8/2008 (eroded for Germany 8 months before)
- and finally authority interference approach

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



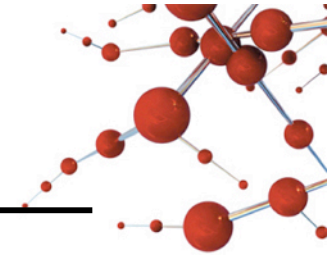
## *CASE STUDY – PLAVIX BY SANOFI AVENTIS CONTAINING CLOPIDOGREL (IN THE FORM OF BISULPHITE SALT)*

Pharmathen “assault” strategy:

- Selection of alternate salt eliminating Sanofi’s 2013 patents
- Removal from submitted PIL of patented indications
- Develop alternate formulation, submit and approve own formulation patent
- Submit following day after the data exclusivity, via the EMEA centralized procedure
- Address attempts to clinically degrade safety and efficacy of alternate salt, by numerous in-vitro studies in recognized laboratories, and submit Phase I clinical trial in humans performed in EMEA/FDA approved sites

# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



## *CASE STUDY – PLAVIX BY SANOFI AVENTIS CONTAINING CLOPIDOGREL (IN THE FORM OF BISULPHITE SALT)*

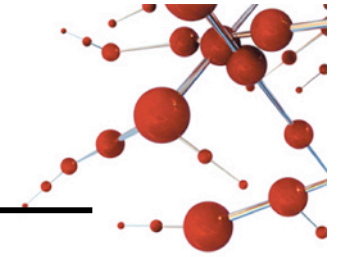
### Results of Previous Strategy

- Submission 1/8/2008
- Approval by mutual agreement of all 27 states on the 25/5/2009
- Marketing Authorization granted by the commission 25/7/2009
- UK launch 26/7/2009, over 5m euro gross profit
- 1<sup>st</sup> to launch in EL, 9/2009, 1<sup>st</sup> to launch in Scandinavia, Baltics, Italy, Spain, Hu, etc.
- Number of competitors concluded with similar timelines but never launched, since they forgot in the PIL the patented indications!!!
- Wise selection of salt, since competitor salt (HCL) did produce friability issues
- Wise selection of formulation since competitors with same salt could not scale up or achieve stable product
- Wise design of Clinical Trial, Sanofi failed to approve Clopidogrel+Aspirin tablet, since they used “easier” to Pharmathen’s design



# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



## ***CASE STUDY – PLAVIX BY SANOFI AVENTIS CONTAINING CLOPIDOGREL (IN THE FORM OF BISULPHITE SALT)***

### Results of Previous Strategy

- Clients of Pharmathen, who used alternate submission, achieved quicker approval
- The additional testing by Pharmathen, delayed approval of competitors with similar salt

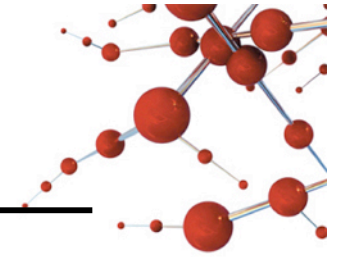
LONDON, May 29 (Reuters) - The European Medicines Agency has given a green light to six generic versions of Sanofi-Aventis and Bristol-Myers Squibb's blockbuster blood thinner Plavix, it said on Friday.

- The new generics are Clopidogrel 1A Pharma, Clopidogrel ratiopharm, Clopidogrel Acino and Clopidogrel Hexal, all from Acino ; Clopidogrel Teva, from Teva; and ***Grepid, from Pharmathen***



# PHARMATHEN – GLOBAL REGULATORY AFFAIRS

---



*WHY-WHEN-HOW:*

*THE MAJOR PARAMETERS UPON INITIATION OF A PROJECT,  
THAT EVERYONE INVOLVED NEEDS TO BE AWARE OF.*

*THANK YOU*