



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Office of the Executive Director

# Annual report highlights

## 2010



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An agency of the European Union



# Introduction by the Acting Executive Director

**Andreas Pott**

The year 2010 saw many changes at the European Medicines Agency, the most poignant of which was the departure of the Agency's Executive Director, Thomas Lönngren. Thomas left the Agency in December after ten successful years at its helm, overseeing the phenomenal growth of the Agency, not only in terms of sheer size, but also in the range of its activities.

In the lead-up to his departure, much effort was put into evaluating where the Agency currently stands and making preparations for the future. A report on the evaluation of the Agency, carried out by Ernst & Young, was published at the beginning of the year. The report praised the Agency for its efficiency and effectiveness in delivering high-quality scientific opinions on medicines for human and veterinary use, but also highlighted the need for the Agency, together with the European Commission and regulatory authorities in the Member States, to continue to adapt to future challenges and address new developments and responsibilities. Throughout the year, we worked to develop a new five-year strategy for the Agency – the 'Road map to 2015', adopted by the Management Board and published in December – which should help to ensure the Agency is fit to tackle the challenges ahead.

With increases in workload in almost all areas, this was another busy year for the Agency. On the human side, the number of post-authorisation activities, orphan-medicine designations, scientific-advice procedures and referrals continued to grow. The year also saw a number of high-profile opinions being established, such as the recommendation to suspend the marketing authorisation for Avandia and other medicines containing rosiglitazone, the suspension of the anti-obesity medicine sibutramine, and investigations into the childhood vaccines Rotarix and Rotateq, following the detection of unexpected viral material. Workload also increased on the veterinary side, with the number of applications for marketing authorisation and referrals exceeding expectations, and requests for scientific advice almost doubling in comparison with the previous year.

On top of the increasing volume of core business activities, the Agency reached a number of important milestones during the course of the year. In July, we launched a new website for the Agency, giving our online audiences easier access to information on medicines, to guidelines, to regulatory and scientific advice, and to information on other Agency activities. In October, we published new rules on conflicts of interests, addressing our need to access Europe's best scientific experts while ensuring they have no financial or other interests that could affect their impartiality. And in November, we took a major step forward in transparency, publishing a policy on access to documents that gives wider public access than ever before to the documents we hold concerning both human and veterinary medicines.

We implemented a series of measures to strengthen the Agency's procurement procedures in 2010, following some technical errors that had occurred over the previous few years. These errors, which occurred primarily due to the rapid diversification of the Agency's activities, contributed to the European Parliament's vote to postpone the discharge for the 2009 budget – the first time this has happened since the Agency was established, in 1995. I am pleased to report that the Agency has now addressed all of the errors, and we expect a successful discharge of the budget in the near future.

I am grateful for the hard work, dedication and support of all of the Agency's staff, the members of its committees, working parties and working groups, and the Management Board, who enabled the Agency to meet its commitments successfully, despite increases in workload throughout the year. As we look forward to 2011, I am sure that the Agency will take new challenges in its stride, including the appointment of a new Executive Director and the implementation of new legislative requirements, while continuing to fulfil its core business of protecting public and animal health in the European Union.

# Highlights in 2010

## First quarter: January-March 2010

- European Medicines Agency (EMA) launches consultation on its 'Road map to 2015'.
- EMA adopts first opinion on compassionate use, for oseltamivir, to treat patients with a life-threatening condition due to pandemic or seasonal flu.
- EMA and EUnetHTA Joint Action start collaboration on improving European public assessment reports (EPARs) for better contribution to relative effectiveness assessments.
- EMA and US FDA agree to accept a single orphan-drug-designation annual report.
- EMA and Swissmedic agree sharing of information on H1N1 pandemic medicines.
- EMA Management Board emphasises the importance of the European medicines network during the H1N1 pandemic.

## Second quarter: April-June 2010

- EMA's Committee for Advanced Therapies issues public statement on concerns over unregulated medicinal products containing stem cells.
- EMA launches public consultation on ethical and good-clinical-practice (GCP) aspects of clinical trials conducted in third countries.
- Committee for Advanced Therapies gives first certification opinion for an advanced therapy medicinal product.
- EMA holds workshop to review success of ten years of orphan-medicines legislation in Europe.
- EMA launches European paediatric research network (Enpr-EMA).
- EMA holds workshop with European and international experts to discuss the way forward in stem-cell research and development.
- EMA's SME Office wins award for 'Most significant contribution to mediscience sector'.
- EMA and European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) sign cooperation agreement.
- EMA and European Network of Centres for Pharmacoepidemiology & Pharmacovigilance (ENCePP) launch 'ENCePP studies' - a seal for transparent, state-of-the-art safety studies.

## Third quarter: July-September 2010

- EMA launches its new website.
- Joint EMA and European Commission workshop starts reflection process on the way forward for the Agency and the European regulatory network.
- EMA publishes policy on communicating safety issues relating to human medicines.
- EMA starts review of Pandemrix over narcolepsy concerns.
- EMA recommends suspension of Avandia, Avandamet and Avaglim over cardiovascular concerns.
- EMA and US FDA extend their confidentiality arrangement indefinitely.

- EMA holds international workshop on clinical trials in the context of global medicines development.
- EMA holds the first scientific workshop on nanomedicines.
- New pharmacovigilance legislation is adopted by European Parliament.

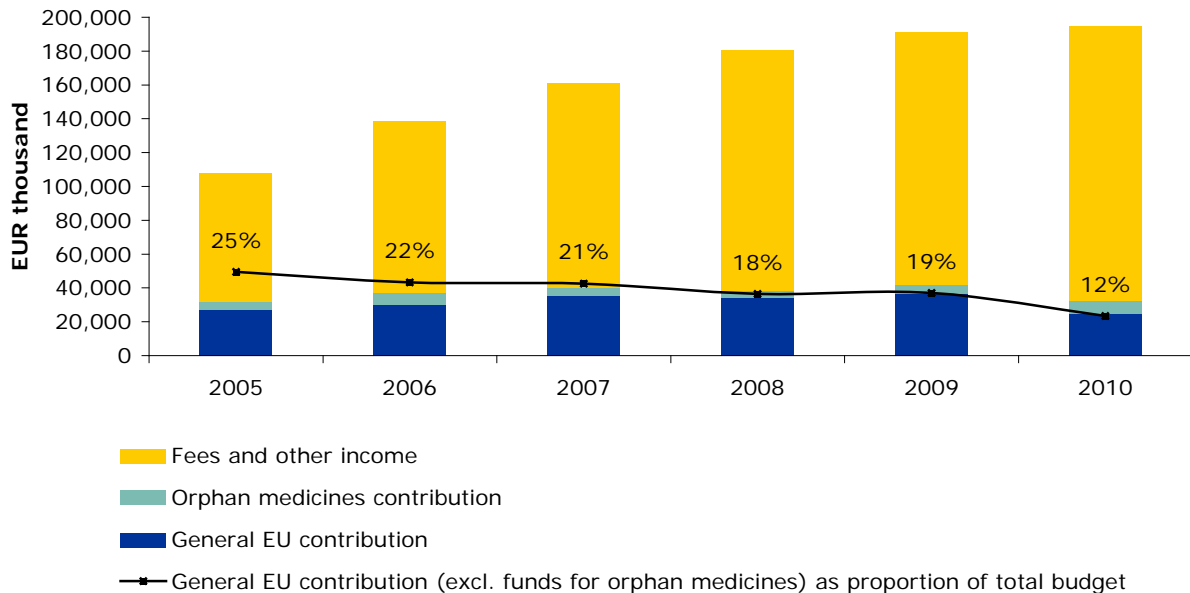
#### **Fourth quarter: October-December 2010**

- EMA strengthens rules on conflicts of interests for its scientific experts.
- EMA and other stakeholders launch pilot for multi-stakeholder consultations in early-stage drug development.
- EMA adopts new fees for marketing-authorisation applications.
- EMA receives the 1,000th application for a paediatric investigation plan (PIP) or waiver.
- EMA publishes a new access-to-documents policy.
- EMA and Massachusetts Institute of Technology launch a joint project on regulatory science.
- European Commission starts recruitment procedure for the EMA's new Executive Director.
- EMA Management Board launches new 'Road map to 2015'.
- EMA completes its safety review of Avastin, used in breast cancer.
- EMA and European Centre for Disease Prevention and Control (ECDC) sign a cooperation agreement.
- EMA launches SME database to facilitate interaction between small and medium-sized enterprises.

## Key figures in 2010

In addition to the progress made in many priority areas, 2010 saw an increase in almost all areas of activity of the Agency's core business.

**Figure 1.** EMA budget evolution

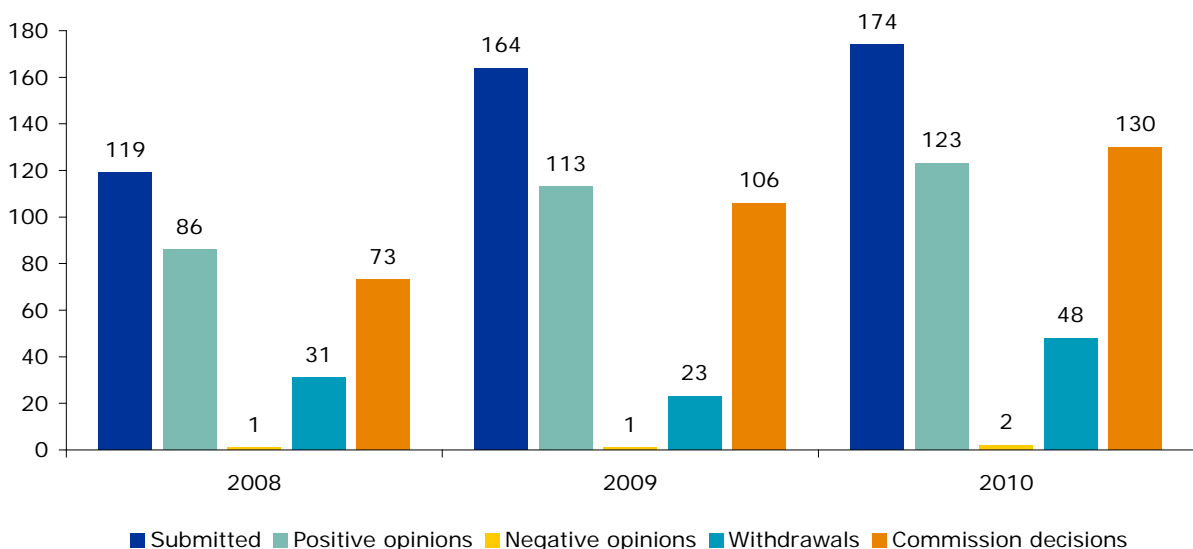


## Human medicines

### Orphan medicines designation

*Orphan medicines are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union, or where for economic reasons such medicines would not be developed without incentives.*

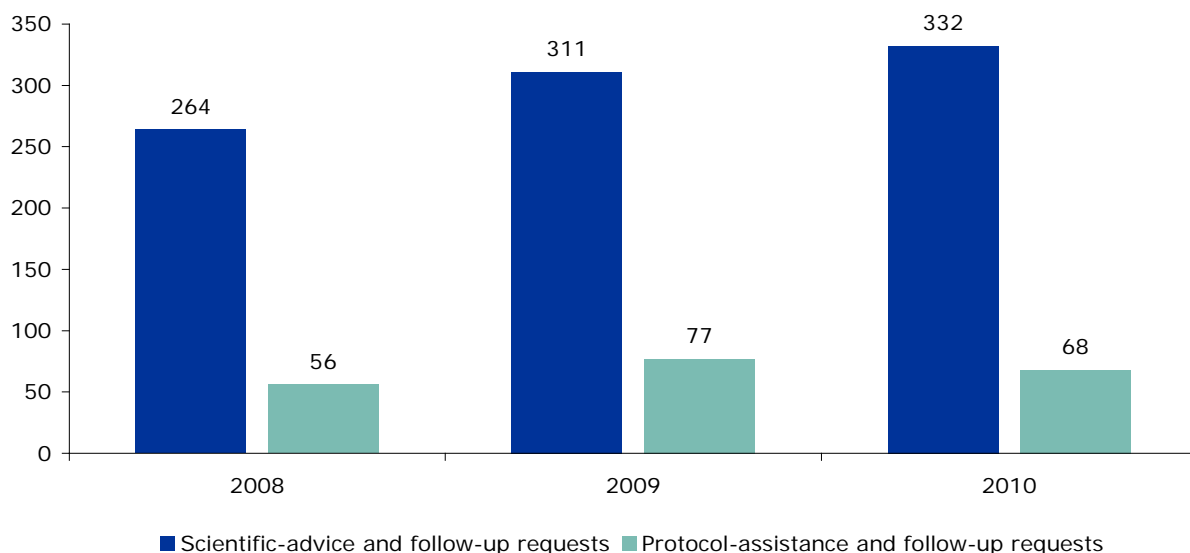
**Figure 2.** Orphan medicines designation



### Scientific Advice

The Agency provides scientific advice and protocol assistance to sponsors during the phase of research and development of medicinal products. Scientific advice is considered as a means to facilitate and improve earlier availability of medicinal products to patients and healthcare professionals, and as a means to promote innovation and research.

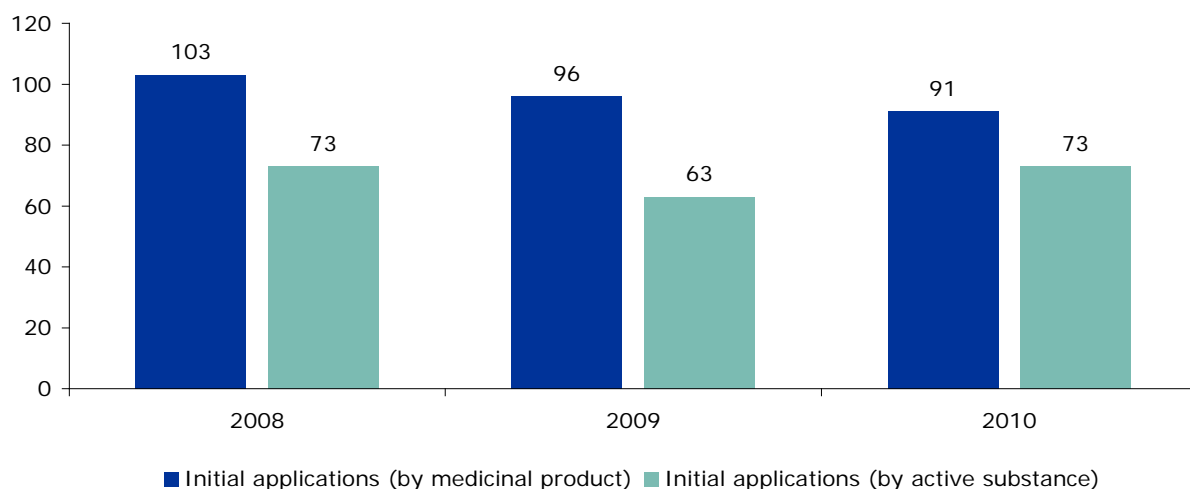
**Figure 3.** Scientific-advice and protocol-assistance requests received



### Initial evaluation

Initial evaluation covers activities relating to the processing of marketing authorisation applications for medicines, from pre-submission discussion with future applicants, through evaluation by the CHMP, to the granting of a marketing authorisation by the European Commission.

**Figure 4.** Initial-evaluation applications received

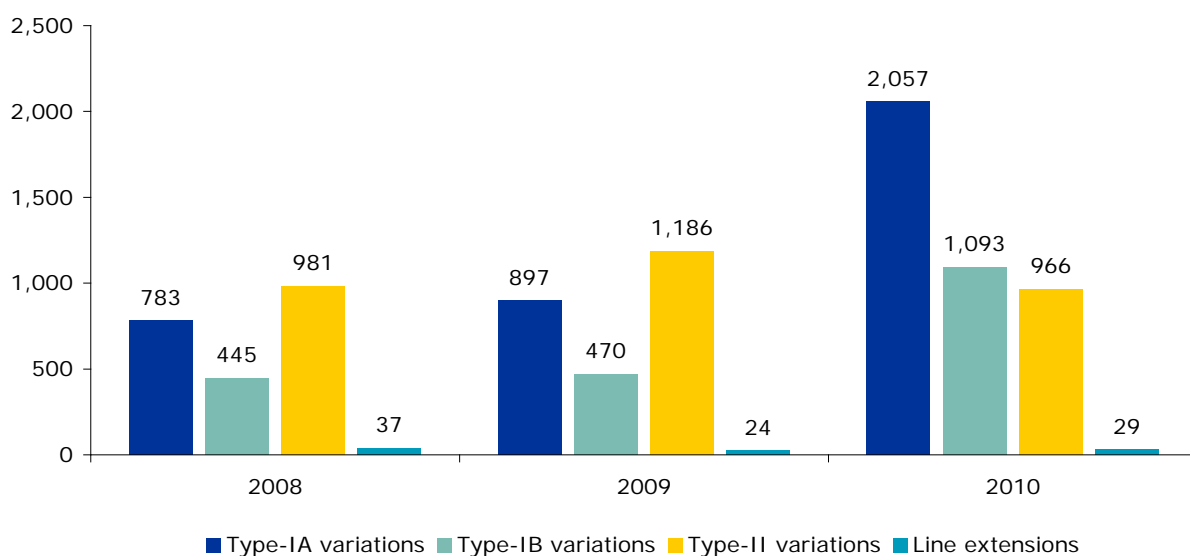


There was a 5% decrease to 91 applications for initial evaluation of medicines. These relate to 73 applications by active substance, representing an increase of 16% compared to 2009. Of the applications received, 46 related to new medicines, 12 of which were designated orphan medicines. Almost half (44) of all applications were for biosimilar or generic medicines and hybrid or informed-consent applications.

### Post-authorisation activities

Post-authorisation activities relate to variations, extensions of marketing authorisations and transfers of marketing authorisations.

**Figure 5.** Post-authorisation applications received

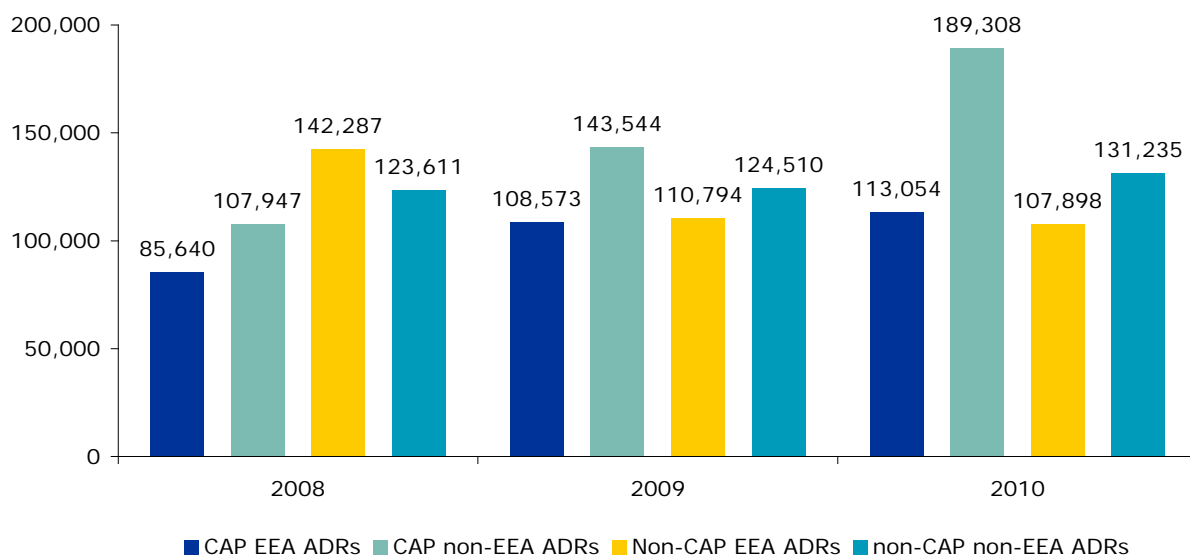


The distribution of types of variations changed significantly throughout the year as a consequence of the new legislation on variations.

### Pharmacovigilance and maintenance activities

Pharmacovigilance covers the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADRs) or any other drug-related problem. This includes the management of suspected ADRs in the pre- and post-authorisation phase, periodic safety-update reports (PSURs), risk-management plans (RMPs) and post-authorisation safety and efficacy/effectiveness studies.

**Figure 6.** EEA and non-EEA adverse-drug-reaction reports received

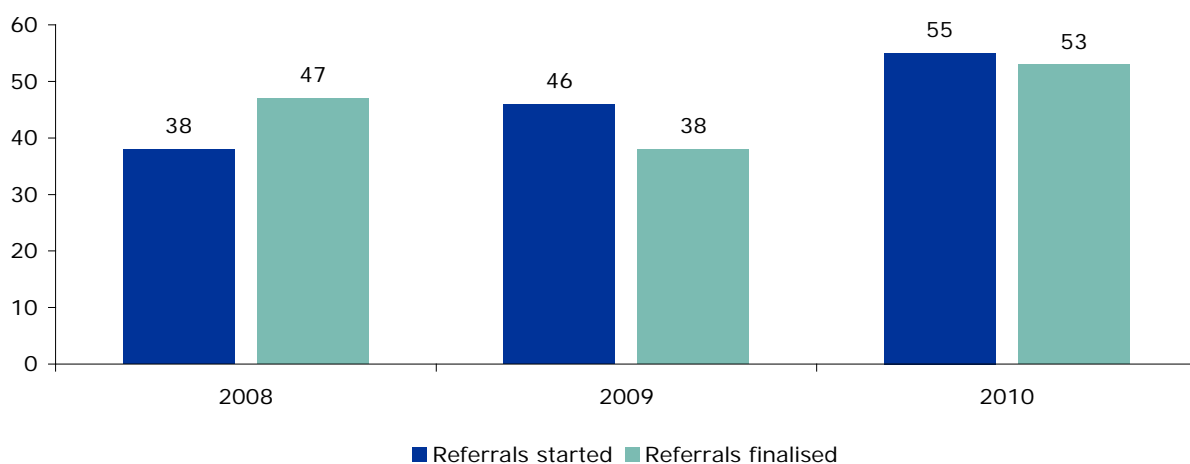


EEA = European Economic Area. CAP = centrally authorised product. ADR = adverse drug reaction.

### Referral procedures

Referral procedures are used to resolve disagreements and address concerns among Member States. In a referral, the European Medicines Agency is requested to conduct, on behalf of the European Community, a scientific assessment of a particular medicine or class of medicines to agree on a recommendation for a harmonised position across the European Union.

**Figure 7.** Referral procedures started and finalised

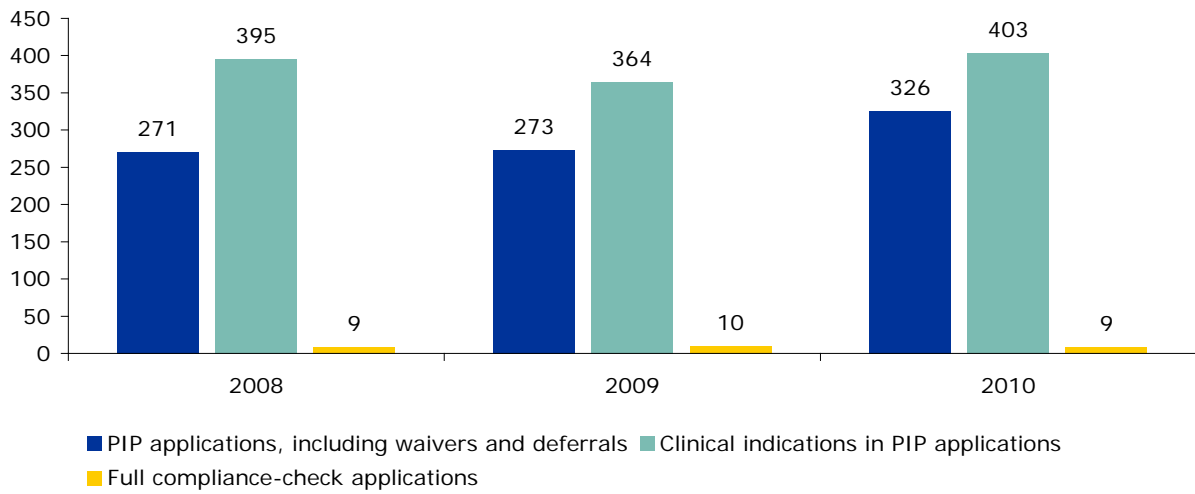


### Medicines for children

This area covers the Agency's activities relating to the assessment and agreement of, and verification of compliance with, paediatric investigation plans (PIPs) and waivers by the Paediatric Committee (PDCO).



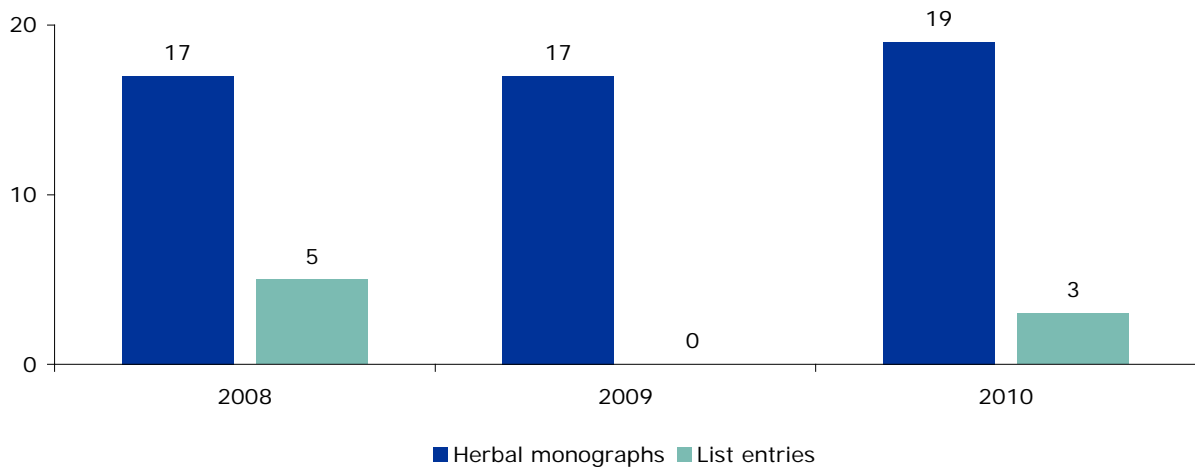
**Figure 8.** Paediatric-investigation-plan (PIP) applications



### **Herbal medicines**

*The Agency's Committee on Herbal Medicinal Products (HMPC), with a view to promote an increasingly harmonised process for licensing and information on herbal substances across the EU, establishes Community herbal monographs for traditional and well-established herbal medicines as well as a draft list of herbal substances, preparations and combinations thereof for use in traditional herbal medicines.*

**Figure 9.** Herbal medicines

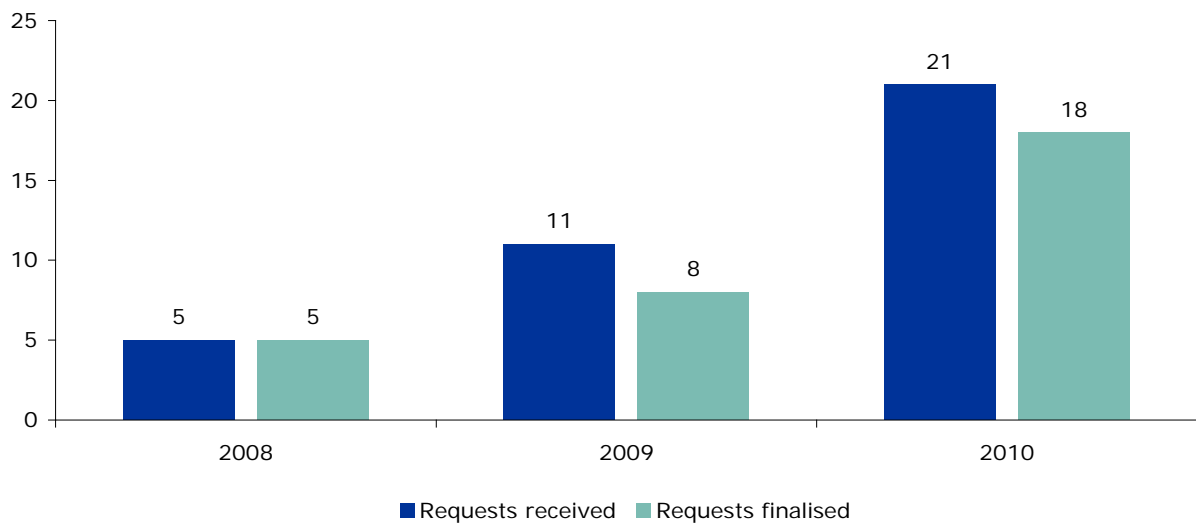


## Veterinary medicines

### Scientific advice

Scientific advice is provided on any aspect of research and development relating to quality, safety or efficacy of medicines for veterinary use, and to the establishment of maximum residue limits. Scientific advice is considered as a means to facilitate and improve earlier availability of veterinary medicines and as a means to promote innovation and research.

**Figure 10.** Scientific-advice requests received and finalised

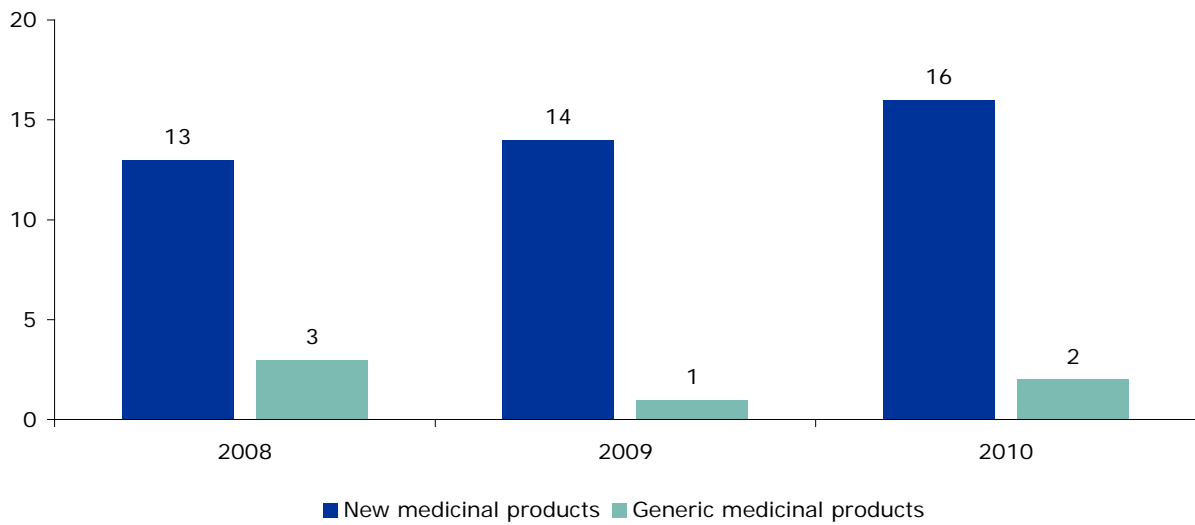


Uptake of scientific advice by companies developing medicines for veterinary use was strong in 2010, especially among small and medium-sized enterprises. Eight requests were for minor use/minor species (MUMS)/limited markets.

### Initial evaluation

The initial evaluation phase covers activities relating to the processing of marketing authorisation applications for veterinary medicines, ranging from pre-submission meetings with future applicants, through evaluation by the Committee for Medicinal Products for Veterinary Use (CVMP), to the granting by the European Commission of the marketing authorisation.

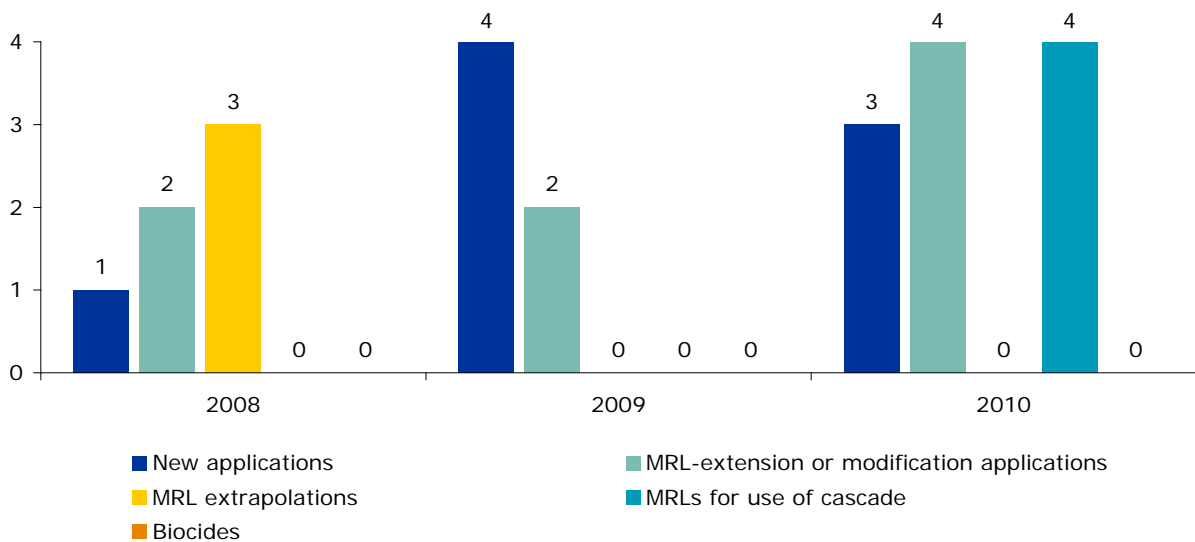
**Figure 11.** Initial-evaluation applications



**Maximum Residue Limits**

The use of veterinary medicines in food-producing animals may result in the presence of residues in foodstuffs obtained from treated animals. The Agency establishes maximum residue limits (MRLs) for pharmacologically active substances used to treat animals, to provide for the safe use of foodstuffs of animal origin, including meat, fish, milk, eggs and honey.

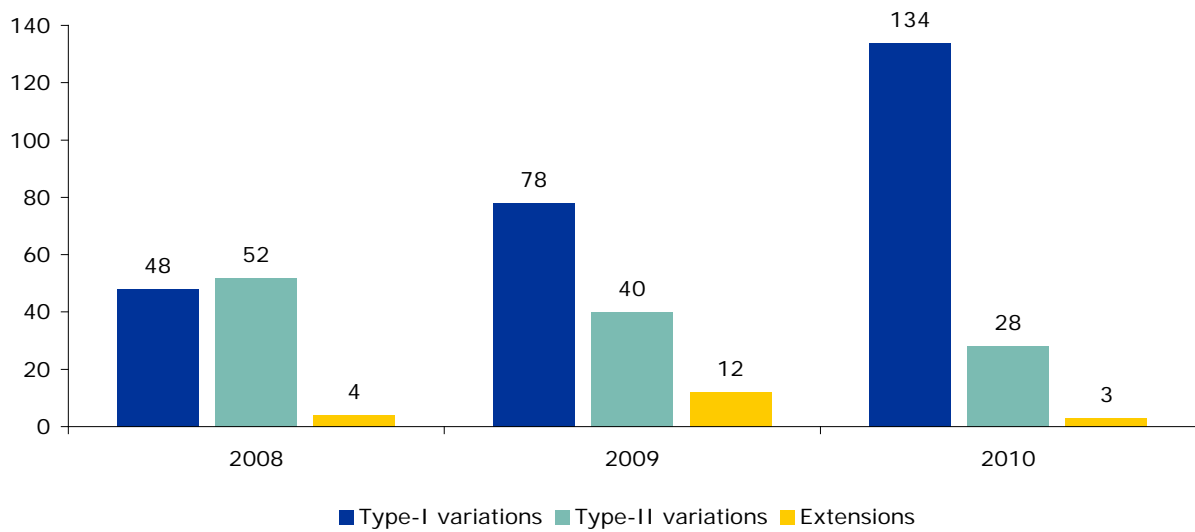
**Figure 12.** Applications for maximum residue limits (MRLs)



**Post-authorisation activities**

Post-authorisation activities relate to variations of marketing authorisations, including extensions of marketing authorisations and transfers of marketing authorisations.

**Figure 13.** Post-authorisation applications received

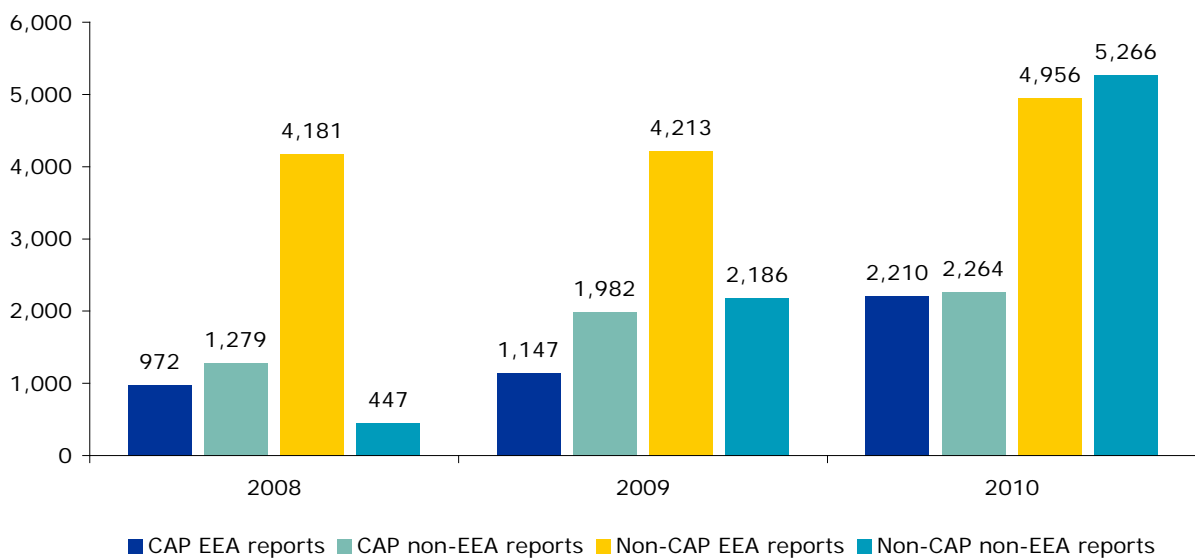


As was the case with human medicines, a redistribution of post-authorisation applications was observed, due to the new legislation on variations.

**Pharmacovigilance and maintenance activities**

Pharmacovigilance covers the activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADRs) or other drug-related problems. It aims at ensuring that post-authorisation monitoring and effective risk-management are continuously applied to veterinary medicines throughout the EU.

**Figure 14.** Reports on serious suspected adverse drug reactions (ADRs) in animals and humans

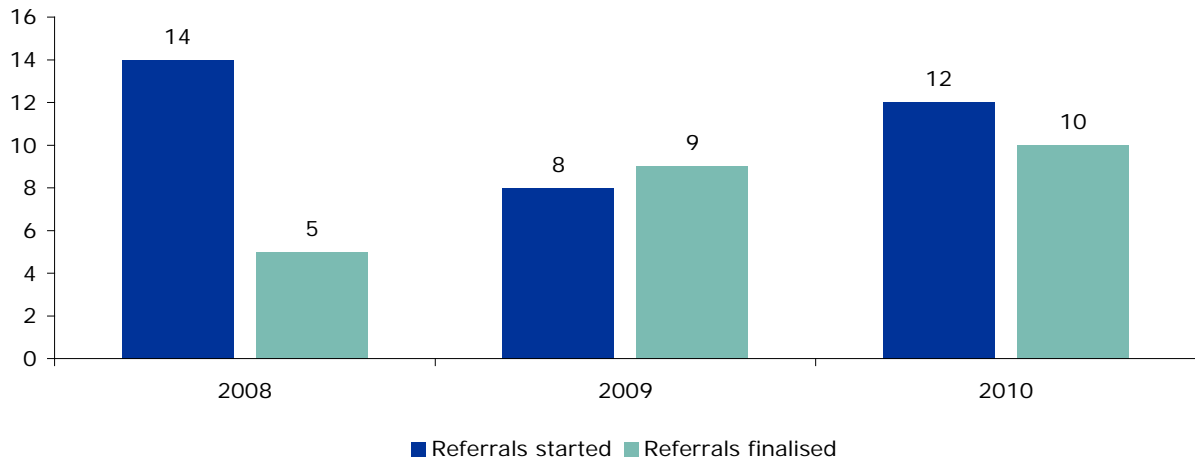


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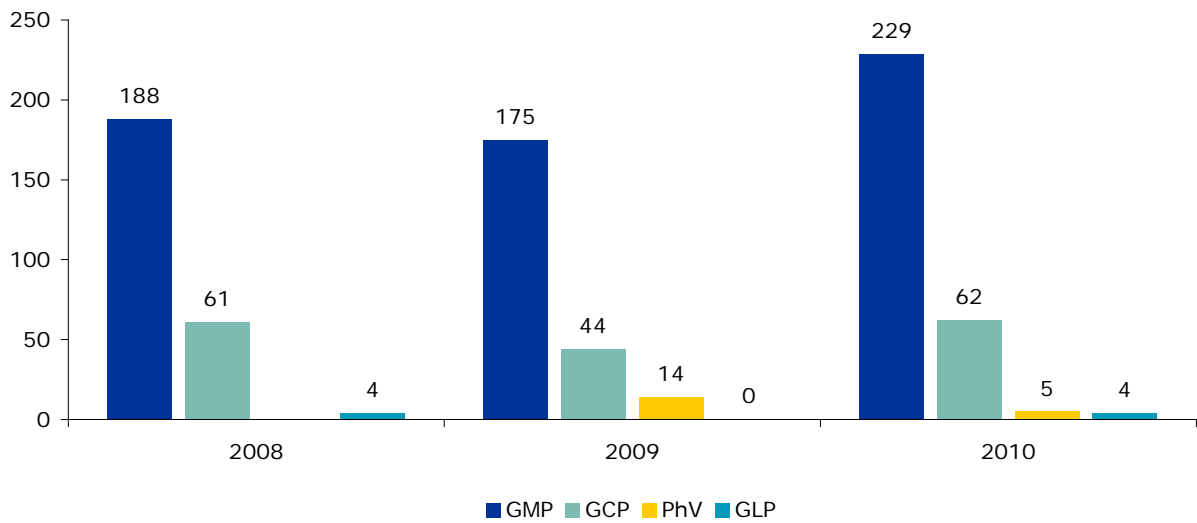
**Figure 15.** Referral procedures started and finalised



## Inspections

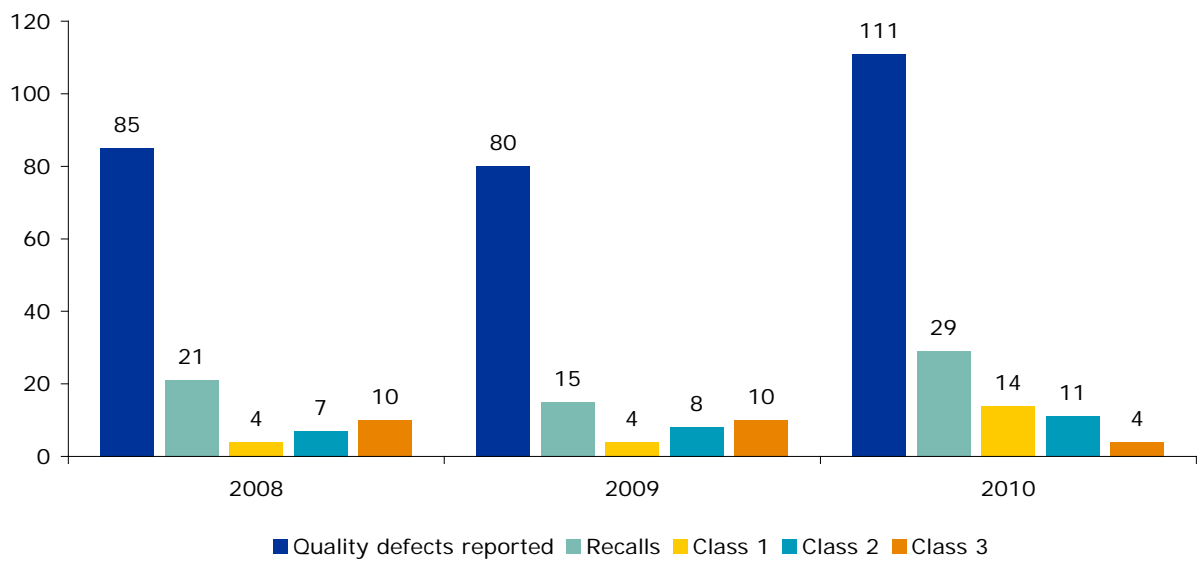
The Agency coordinates the verification of compliance with the principles of good manufacturing practice (GMP), good clinical practice (GCP), good laboratory practice (GLP), and with pharmacovigilance obligations and certain aspects of the supervision of authorised medicinal products in use in the European Union. It does this through inspections requested by the CHMP or CVMP in connection with the assessment of marketing-authorisation applications and/or the assessment of matters referred to these committees in accordance with EU legislation.

**Figure 16.** Number of inspections



The total number of inspections was 20% above the forecast, mainly due to an unexpected increase in the number of good-clinical-practice (GCP) inspections requested.

**Figure 17.** Number of quality defects reported



## ***Significant recommendations for approval in 2010***

### **Public-health benefits of medicines for human use recommended for approval in 2010**

The most notable new medicines for human use recommended for marketing authorisation by the Agency's Committee for Medicinal Products for Human Use (CHMP) in 2010 include the following:

- Two H1N1 pandemic vaccines intended for the prophylaxis of influenza in an officially declared pandemic situation.
- A new H5N1 mock-up pandemic-influenza vaccine intended for the prevention of influenza during an officially declared pandemic situation (a mock-up pandemic vaccine is not intended for stockpiling, but can be used to speed up the availability of a final vaccine in the event of a pandemic, once the pandemic strain has been identified).
- Prepandemic-influenza vaccines intended for immunisation against the H5N1 subtype of the influenza-A virus.
- A nasally administered influenza vaccine intended for the prophylaxis of influenza in children.
- A diagnostic agent intended as a pharmacological stress agent for radionuclide myocardial perfusion imaging.
- A designated orphan medicine produced using recombinant DNA technology, intended for the treatment of angioedema attacks. It is extracted from the milk of rabbits that have had a gene (DNA) inserted, which makes them able to produce the human protein in their milk.
- A designated orphan medicine intended for the treatment of Gaucher disease. The product is of major public-health interest in light of the shortage of the authorised medicine for the treatment of this disease.
- Two designated orphan medicines intended for the treatment of pulmonary conditions; one for suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in cystic fibrosis, and another for idiopathic pulmonary fibrosis.
- A designated orphan medicine intended for the treatment of inborn errors in primary bile acid synthesis due to enzyme deficiencies.
- A designated orphan medicine intended for the treatment of patients with chronic lymphocytic leukaemia.
- A medicinal product intended for maintenance treatment of severe chronic obstructive pulmonary disease associated with chronic bronchitis in adult patients as add-on to bronchodilator treatment, presenting an oral treatment with a new mode of action.
- Two medicinal products intended for the treatment of psychiatric conditions; one for moderate to severe manic episodes associated with bipolar I disorder, and another for the treatment of schizophrenia.
- A medicinal product intended for the treatment of a musculoskeletal condition known as Dupuytren's contracture, presenting a non-surgical alternative.

## **Animal-health benefits of medicines for veterinary use recommended for approval in 2010**

The most notable new medicines for veterinary use recommended for marketing authorisation by the Agency's Committee for Medicinal Products for Veterinary Use (CVMP) in 2010 include the following:

- Four vaccines against bluetongue disease. These vaccines were authorised under exceptional circumstances to protect cattle and sheep against clinical signs, and to reduce or prevent transmission of serotypes 1, 2, 4 and 8 of the highly variable bluetongue virus. Authorisation at EU level makes vaccines immediately available for use as part of national and transnational disease-control campaigns against this highly virulent and contagious disease of domestic livestock.
- A vaccine to reduce the shedding of *Coxiella burnetii* by infected cattle and goats. An extensive outbreak of this bacterial disease, which is the causative agent of Q fever in man, occurred in the Netherlands in 2009. The CVMP therefore considered it appropriate to recommend that the product be authorised under exceptional circumstances on the basis of a positive benefit-risk balance while further studies are carried out to determine more precisely the efficacy in goats.
- Two novel medicines for the treatment of ectoparasites, mainly fleas, in domestic pets. These types of treatment remain a priority area for the companion-animal health sector.

*Characters: 16.587*