

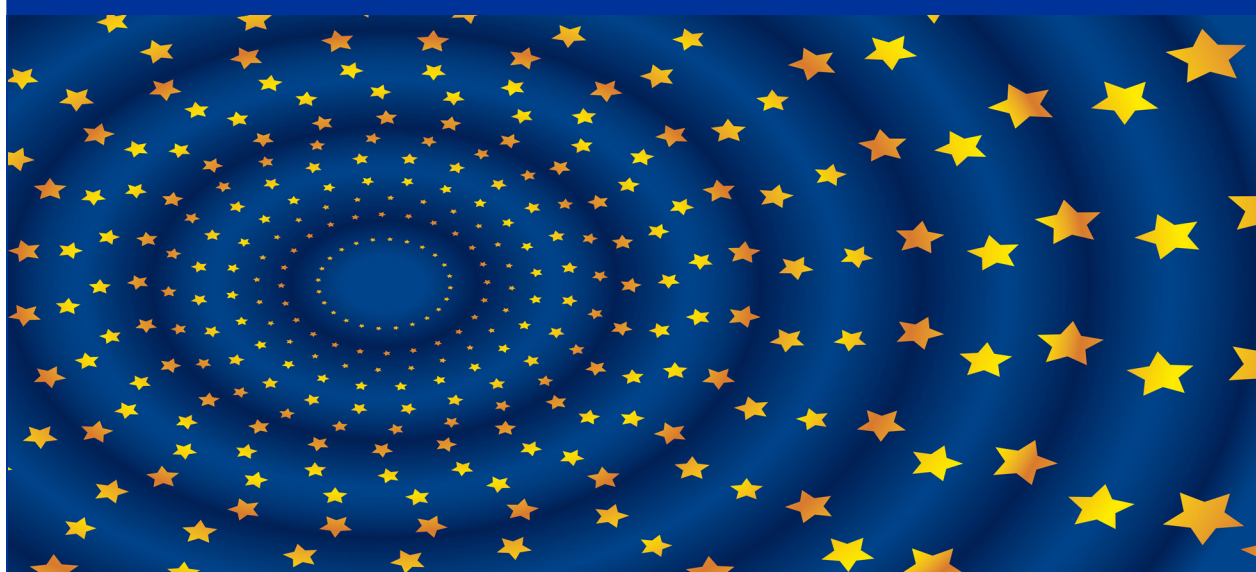


EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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# Annual report 2009

Adopted by the Management Board in March 2010



7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom

**Telephone** +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416

**E-mail** [info@ema.europa.eu](mailto:info@ema.europa.eu) **Website** [www.ema.europa.eu](http://www.ema.europa.eu)

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## **Note on annexes**

Please note that the annexes of this report are published as a separate document, available on the website of the European Medicines Agency at: <http://www.ema.europa.eu/htms/general/direct/ar.htm>

## **Mission statement**

The mission of the European Medicines Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.

### ***Legal role***

The European Medicines Agency is the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

The Agency provides the Member States and the institutions of the EU the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

### ***Principal activities***

Working with the Member States and the European Commission as partners in a European medicines network, the European Medicines Agency:

- provides independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to public and animal health that involve medicines;
- applies efficient and transparent evaluation procedures to help bring new medicines to the market by means of a single, EU-wide marketing authorisation granted by the European Commission;
- implements measures for continuously supervising the quality, safety and efficacy of authorised medicines to ensure that their benefits outweigh their risks;
- provides scientific advice and incentives to stimulate the development and improve the availability of innovative new medicines;
- recommends safe limits for residues of veterinary medicines used in food-producing animals, for the establishment of maximum residue limits by the European Commission;
- involves representatives of patients, healthcare professionals and other stakeholders in its work, to facilitate dialogue on issues of common interest;
- publishes impartial and comprehensible information about medicines and their use;
- develops best practice for medicines evaluation and supervision in Europe, and contributes alongside the Member States and the European Commission to the harmonisation of regulatory standards at the international level.

### ***Guiding principles***

- We are strongly committed to public and animal health.
- We make independent recommendations based on scientific evidence, using state-of-the-art knowledge and expertise in our field.
- We support research and innovation to stimulate the development of better medicines.
- We value the contribution of our partners and stakeholders to our work.

- We assure continual improvement of our processes and procedures, in accordance with recognised quality standards.
- We adhere to high standards of professional and personal integrity.
- We communicate in an open, transparent manner with all of our partners, stakeholders and colleagues.
- We promote the well-being, motivation and ongoing professional development of every member of the Agency.

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## **Foreword by the Chair of the Management Board**

***Pat O'Mahony***

I am pleased to write this short message as a foreword to the annual report of the European Medicines Agency for 2009. The report provides a detailed overview of the activities of the Agency during the year. Probably the most striking illustration of the effectiveness of the Agency was demonstrated by the coordinated response to the H1N1 influenza pandemic. The preplanning conducted by the Agency allowed for a rapid response once the pandemic was declared and an intensive concentrated scrutiny of product applications leading to the approval of pandemic vaccines. This episode also demonstrated the importance of the extensive inter-agency and international collaboration which the Agency has nurtured and developed, apparent in this case, but also in other areas such as joint inspections with international partners and activity in the area of tackling the development of anti-microbial resistance.

Substantial increases were seen across many of the core activity areas, including scientific-advice requests, orphan designations, variations and safety-related activities. While a reasonably steady state for submission of applications was seen for veterinary medicines, there was a considerable increase in the number of requests for scientific advice and in pharmacovigilance activities. In the important area of inspections, while the ambitious targets were not met, overall activity was still substantial. In all corporate and administrative areas, activities increased in line with the overall increased activity across the organisation. Telematics projects were also significantly advanced. A process of internal reorganisation was completed by year end, as were the development and launch of a new visual identity for the Agency. Interaction with patients and healthcare professionals further progressed in 2009, and the issue of transparency continued to receive added focus. Finally, as we come to the end of the effective lifetime of the current strategic roadmap for the Agency, considerable work took place on the development of a strategic plan for 2011 to 2015, and this document was published for public consultation by year end.

I would like to record my thanks to all staff of the Agency, all those contributing to the various committees and working parties, and my colleagues on the Management Board for their ongoing efforts during 2009 in the service of patients and consumers. I would also like to express my thanks to the Executive Director for his exceptional commitment and leadership of the organisation throughout the year. I thank colleagues at the European Commission and the Parliament for their ongoing support and guidance to my work as Chair of the Management Board and to the work of the Agency. I also thank all colleagues from within the network of national medicines regulatory authorities throughout the Member States for their ongoing support.

## **Introduction by the Executive Director**

***Thomas Lönngren***

In 2009, the European Medicines Agency delivered very good results across the range of its activities. Core activities relating to medicines for human and veterinary use were conducted to a high level of quality, and regulatory timelines were consistently met. In many areas, the Agency was able to make a significant further contribution to public and animal health in the European Union (EU).

The public-health issue to which the Agency devoted most attention in 2009 was the outbreak and rapid global spread of the H1N1 influenza ('swine flu') virus. The fast-track review of pandemic vaccines – and the close monitoring of these vaccines once they were being used to vaccinate millions of European citizens – demonstrated to Europe and to the world that the European medicines network can deliver high-quality scientific assessments even under enormous pressure.

When the first reported cases of infection emerged from Mexico, in April, the Agency reacted quickly, working closely with its European and international partners to monitor the situation and develop appropriate measures to deal with the emerging crisis, including meeting with vaccine manufacturers and influenza experts from across the EU to prepare for the development and authorisation of vaccines that could be used to protect people and minimise the spread of the virus.

While awaiting the availability of vaccines, the Agency worked to facilitate the use of existing antiviral medicines that had shown effectiveness in treating people infected with the virus. In early May, the Agency's Committee for Medicinal Products for Human Use (CHMP) recommended that the shelf-life of one of these medicines (Tamiflu) be extended, so that stocks of the medicine that would otherwise need to have been disposed of could continue to be used in the event of a pandemic being declared.

Once a pandemic had been officially declared by the World Health Organization and the strain of the virus had been identified, in June, pharmaceutical companies were in a position to begin submitting data on H1N1 vaccines to the Agency. The CHMP took the unprecedented measure of reviewing these data on a rolling-review basis as and when they were received, rather than waiting for exhaustive data to become available. This was done to fast-track the assessment process so that the urgent public-health need for vaccines could be met before the autumn, when an intensification of the spread of the virus was expected in Europe.

Thus, the CHMP was able to give positive recommendations for two pandemic-influenza vaccines (Focetria and Pandemrix) by late September, and for a third one (Celvapan) in early October. On the basis of these scientific recommendations, the European Commission granted EU-wide marketing authorisations for all three vaccines, making them available for use by health authorities in the EU Member States as part of their national vaccination programmes. By the end of the year, 29.4 million people in Europe had been vaccinated with one of these products.

During the year, the Agency continuously monitored the safety data for influenza vaccines and antivirals, to establish and revise, where necessary, their benefit-risk profile. Updated product information in all EU languages, weekly pharmacovigilance reports and much other scientific and regulatory information was published in a dedicated section of the Agency's website.

That the EU medicines system was able to deliver an appropriate response to this public-health crisis was further evidence of its robustness and good functioning. The results achieved under intense pressure were due to the sustained commitment and cooperation of the national authorities of the Member States, the European Commission, the European Directorate for the Quality of Medicines and HealthCare, the European Centre for Disease Prevention and Control, the European Food Safety Agency and the European Medicines Agency, as well, of course, of the pharmaceutical industry.

The influenza pandemic was by definition a global challenge, so much credit for the achievements in Europe is also owed to the international partners with which the EU enjoys a mutually beneficial working relationship, notably the World Health Organization and the medicines authorities of the United States, Japan, Canada and Australia, among others.

Although the Agency devoted significant time and resources in 2009 to its involvement in managing the unanticipated influenza pandemic, it was still able to achieve very good results in delivering on its ambitious work programme for the year, as detailed in the body of this annual report.

For their outstanding dedication and hard work throughout what was one of the most active and challenging years in the history of the Agency, I am very grateful to all members of the Agency's scientific committees, working parties, staff and Management Board, whose efforts contributed greatly once again not only to the success of our organisation, but to the protection of public and animal health in Europe.

# 1. The European Medicines Agency in the European System

## 1.1. European medicines network

*The European medicines network – a partnership between the European Medicines Agency, the European Commission and more than 40 medicines regulatory authorities in the European Union (EU) and the European Economic Area (EEA) – is the basis of the Agency's success. The network gives the Agency access to a pool of experts, allowing it to source the best-available scientific expertise for the regulation of medicines in the EU. Experts participate in the work of the Agency as members of the scientific committees, working parties, scientific advisory groups and related groups.*

### H1N1 influenza pandemic

The network demonstrated its strength during the 2009 H1N1 influenza pandemic. The Agency activated its influenza pandemic crisis management plan in April 2009, following the initial outbreak, and subsequently stepped up activities as the World Health Organization (WHO) raised the pandemic level. The mobilisation of scientific experts from all over the EU made it possible to fast-track the rolling review of three authorised pandemic mock-up vaccines, so that the change to the pandemic viral strain could be authorised by the autumn of 2009.

The European Medicines Agency Task Force (ETF) played a pivotal role in the Agency's pandemic activities. This multi-disciplinary group, made up of members of the Agency's Committee for Medicinal Products for Human Use (CHMP), the Paediatric Committee (PDCO), the Biologics Working Party (BWP), the Vaccines Working Party (VWP) and the Pharmacovigilance Working Party (PhVWP), representatives from the European Commission and the European Directorate for the Quality of Medicines & HealthCare (EDQM) and Agency staff, met every week to discuss all available data on pandemic vaccines and to provide advice to the Agency.

Another important group established to deal with the influenza pandemic was the Pharmacovigilance Rapid Response Expert Group (PREG). This group of EU pharmacovigilance experts met weekly to look at the safety of all vaccines and antivirals used during the pandemic.

### Other initiatives

While many resources were dedicated to deal with the influenza pandemic, the European medicines network also made progress on a number of other initiatives.

- Work on the European Risk Management Strategy (ERMS) continued in 2009 in accordance with the rolling two-year work programme. The Early Notification System for planned CHMP recommendations for regulatory action (based on identified safety concerns), introduced in 2008 to improve the coordination of communication to the general public in relation to safety concerns addressed by the Committee, was further developed in 2009.
- The Agency worked jointly with the Heads of Medicines Agencies (HMA) as part of a joint Training Project Team to develop a training strategy for the regulatory network.
- Work further progressed to simplify the contractual arrangements with the Member States for their services to the Agency through the development of a cooperation agreement. Following extensive discussions at the level of the HMA and the Agency's Management Board, the HMA agreed to the cooperation agreement in October 2009. A written procedure for adoption by the Management Board was initiated at the end of December.

- Drawing from the scientific expertise available within the EU medicines system, several expert groups were established in 2009: biomarker task groups, an ad hoc expert group on nanopharmaceuticals, and an expert group on statistics and methodology.

## **Preparation for enlargement**

- Enlargement activities were performed under the Transition Instrument for Pre-accession Assistance (IPA) programme for supporting the participation of EU candidate countries (Croatia, the Former Yugoslav Republic of Macedonia and Turkey) in the Agency's activities. The programme, which sought to familiarise the national competent authorities of these countries with the work performed by the European Medicines Agency, ended in September 2009.
- A new two-year IPA programme for supporting enlargement activities of the candidate countries and potential candidate countries of the Western Balkans, including Albania, Bosnia-Herzegovina, Kosovo, Montenegro and Serbia, was launched on 16 September 2009. Nominated representatives of beneficiary countries were invited to participate in meetings and training sessions held at the Agency. A workshop on good manufacturing practice was organised in October, in Istanbul, Turkey.

### **1.2. European cooperation**

*This area covers: contribution to new legislation initiated by Directorates-General of the European Commission; partnership with European Commission Directorates-General, namely DG Enterprise and Industry, DG Health and Consumers, DG Research and DG Development; cooperation with EU agencies, namely the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA); cooperation with the European Directorate for the Quality of Medicines and HealthCare (EDQM).*

### **Contribution to the EU's response to the H1N1 influenza pandemic**

The EU-wide response to the outbreak of the H1N1 influenza pandemic required a high level of cooperation and interaction between the European Commission and the EU agencies involved in the protection of public health.

The European Medicines Agency regularly briefed the Health Security Committee, a network of public health officials from the Member States coordinated by the European Commission. In addition, the Agency cooperated very closely with the European Commission (DG SANCO and DG Enterprise) and ECDC in a task force. Work on vaccine surveillance resulted in a European strategy for influenza H1N1 vaccine benefit-risk monitoring, published jointly with ECDC.

### **Other initiatives in 2009**

- The Agency continued its collaboration with DG Research in the field of research to be funded by the 7th Framework Programme.

The Agency, ECDC, EFSA and the Scientific Committee on Emerging and Newly Identified Health Risks published a joint scientific opinion on minimising the risks of transmission of antimicrobial-resistant organisms from animal to man in food (zoonoses).

The Agency and ECDC published a joint report on multidrug-resistant bacteria in the EU and development of new antibacterial agents.

The Agency continued to contribute actively to the action plan to deliver the Community Animal Health Strategy, realising objectives in the areas of promoting the availability of veterinary medicines and facilitating the authorisation of vaccines against antigenically variable viruses.

### **1.3. International cooperation**

*These activities cover cooperation at international level, including: the Agency's participation in the International Conference on Harmonisation (ICH), the International Cooperation on Harmonisation for Veterinary products (VICH) and the Codex Alimentarius, and its work with the World Health Organization (WHO), the World Organisation for Animal Health (OIE), the US Food and Drug Administration (FDA), the US Department of Agriculture (USDA), the Japanese, Canadian and Australian authorities, and with other non-ICH regulatory authorities. Collaboration with the European-based Organisation for Economic Co-operation and Development (OECD) and the European Directorate for the Quality of Medicines and HealthCare (EDQM) are also covered, as these organisations include international partners in addition to European partners.*

### **Unprecedented levels of international exchange activities due to H1N1 pandemic**

The H1N1 influenza pandemic resulted in an unprecedented level of international cooperation activity at bilateral and multilateral level. The Agency had regular exchanges with regulators from Australia, Canada, Japan, the United States and experts from the World Health Organization. These activities, and the fact that everybody was faced with very similar challenges, brought regulators worldwide closer together.

### **Other activities**

- The development of the Agency's international strategy started with the appointment of an International Liaison Officer in the beginning of 2009. By the end of the year, the international strategy was included as an important part of the Agency's Road Map to 2015 and integrated in the consultation document, which was adopted by the Management Board for public consultation during its December 2009 meeting.
- Bilateral relations with the US FDA and the Japanese authorities were greatly increased when the notion of liaison placements was agreed. In June 2009, an FDA official took up a posting at the Agency, followed by an official from the Japanese authorities, who took up a liaison post in November 2009. The European Medicines Agency appointed a staff member as a liaison officer to the FDA in July 2009.
- The confidentiality arrangements with the US FDA are now firmly established. Interactions with the FDA doubled relative to the previous year. In October 2009, the two agencies reviewed their existing interaction, noted the increasing maturity and frequency of collaborative activities and agreed to add a new cluster on blood products for further cooperation. A revised procedure for parallel scientific advice was also published and the number of such requests increased relative to previous years.
- A joint good clinical practice (GCP) initiative with the FDA was launched on 1 September 2009, marking the start of an 18-month pilot.
- Increased activity took place within the veterinary medicines cluster of the cooperation agreement with the FDA, particularly in areas of technical requirements for authorisation and for the safety of veterinary products and their residues.

- In April 2009, the Agency and Health Canada had a bilateral meeting during which they agreed an implementation plan for their confidentiality arrangement. This provided the opportunity to extend some cluster activities with the FDA to include Health Canada. A first trilateral teleconference on veterinary matters took place during 2009 and Health Canada started to participate as an observer to the oncology discussions.
- In August 2009, the Agency signed its latest confidentiality arrangement with the Australian Therapeutic Goods Administration (TGA), bringing the number of confidentiality arrangements in place up to four.
- Outside the established confidentiality arrangements, the Agency participated at two meetings with the Chinese State Food and Drug Administration, with particular focus on good manufacturing practice (GMP) and issues relating to clinical trials. A specific action plan on inspections is under development.
- The Agency also supported the European Commission in discussions with India, within the framework of the working group on pharmaceuticals, and with Russia in the EU-Russian dialogue sub-group on pharmaceuticals.
- The Committee on Herbal Medicinal Products (HMPC) provided input to the European Commission on the establishment of draft herbal monographs for several Indian medicinal plants, having considered the extent of their traditional use in the EU Member States.
- Although interactions with the WHO were mainly focused on the H1N1 pandemic, discussions on streamlining Article 58, which allows the Agency to give scientific opinions on medicines that are intended for use outside the EU, and on the WHO prequalification procedure commenced.
- Substantial progress was made on a number of ongoing pilot projects for joint inspections: two GMP inspections on finished products were conducted jointly with the FDA; the pilot project with the FDA and TGA on joint active pharmaceutical ingredients GMP inspections also matured considerably, with 60 inspection results shared, and seven joint inspections performed.

## **Mutual-recognition agreements**

*Mutual-recognition agreements (MRAs) between the European Community and partner (third) countries include specific annexes relating to medicinal products and GMP. These allow EU Member States and the MRA partner to mutually recognise conclusions of inspections of manufacturers carried out by the respective inspection services of the other party, and to mutually recognise the manufacturer's certification of conformity to specifications for each batch without re-control at import. The Agency is responsible for implementation and operational aspects of these MRAs. MRAs with Australia, New Zealand, Switzerland, Canada and Japan are currently operational, but with slightly different provisions as to scope and applicability.*

- The remaining evaluation work and follow-up with new Member States (Bulgaria and Romania) was completed, in preparation for inclusion in the European Union-Canada MRA.
- The Agency reviewed the impact of implementation of ICH quality guidelines (quality risk-management, pharmaceutical quality systems) in EU GMP on the equivalency with MRA partners.
- Practical implementation of EudraGMP on operation of exchange of information with MRA partners was further explored, and the first partners began to use the system.

## **1.4. Transparency and communication**

### **Public consultation on transparency policy launched**

Responding to increasing stakeholder expectations, the Agency launched a public consultation process on a new transparency policy, bringing together in one comprehensive document the Agency's vision on its level of openness towards its stakeholders.

The policy proposes to focus on three main objectives for achieving a robust and consistent approach towards transparency in all areas of its activity. These include: to make the daily operations of the Agency more transparent; to strengthen the Agency's interaction with its stakeholders, in particular patients and healthcare professionals; to promote a harmonised approach to transparency across the European medicines network.

As part of the public consultation process, the Agency held a second workshop on transparency, in October 2009, to analyse and review all comments and feedback received. The draft transparency policy is currently being updated accordingly before its final adoption and publication.

### **Draft access to documents policy considered**

Following public consultation on the Agency's draft access to documents policy, comments received have been reviewed by the Access to Documents Advisory Group (ADAG) and a revised policy is being prepared. The need for continuous reflection on the Agency's activities in the area of transparency was underlined by the continuing increase in the number of requests received for access to both documents and information.

### **EudraVigilance access policies**

Public consultations on the Agency's draft EudraVigilance access policies in relation to human and veterinary medicines were completed in spring 2009. The outcomes of the consultations were presented to the Heads of Medicines Agencies, the respective Pharmacovigilance Working Parties and the EudraVigilance Expert Working Group. Work is now under way to revise the draft policies. The consultation revealed a wish from stakeholders for some divergence between the policies for human and veterinary medicines. The extent to which this is feasible or desirable is being considered together with the HMA.

### **Report published on stakeholders' expectations on information on benefit-risk evaluation of medicines**

The Agency published on 23 June 2009 a report on patients', consumers' and healthcare professionals' expectations on information on the benefit-risk evaluation of medicines. This was the result of an extensive survey among patients' and consumers' organisations and healthcare professionals' organisations.

### **Study on benefit-risk communication**

In cooperation with King's College London, the Agency initiated a study on its benefit-risk communication activities. Looking at a number of recent high-profile examples, the study aims to describe the Agency's approach to benefit-risk communication and will make proposals for future implementation.

## **New visual identity unveiled**

The Agency unveiled its new visual identity on 8 December 2009. The new identity was developed primarily to ensure that the communications materials of the Agency are created with a consistent look and feel, to communicate to the public a clearer message about its role and activities.

The new logo – a stylised representation of a mortar and a pestle – was tested with over 500 people from a broad spectrum of the Agency's key audiences, including patients, healthcare professionals, pharmaceutical companies and the public.

Accompanying the logo is a three-word strapline that represents the 'three pillars' on which all of the Agency's work is based:

- *science*, representing the scientific expertise that guides the Agency in all of its regulatory decision-making;
- *medicines*, representing the Agency's focus on assessing and monitoring medicines to ensure their quality, safety and efficacy;
- *health*, representing the purpose for which the Agency was created, namely to protect and improve public and animal health.

With the launch of the new visual identity, the Agency also discontinued use of its former acronym 'EMEA'.

## **Work on relaunch of the Agency's website continued**

The development of a new public website for the Agency was nearing completion by the end of 2009. With the current website being visited more than 700,000 times each month, the new site is being designed with the needs of the public in mind, offering improved navigation and search functionality, and providing better access to information on public-health issues.

## **Publications by the Agency**

Agency staff and members of the scientific committees published 23 articles in scientific journals ranging from the Regulatory Affairs Journal to the New England Journal of Medicine. Topics covered included advanced therapies, paediatric medicines and pandemic preparations. A full listing of publications is available in Annex 17.

### ***1.5. Support for innovation and availability of medicines***

The Agency operates a number of processes and procedures that contribute to the innovation and availability of medicines for human and animal use. These include the provision of scientific advice, provision of support to small and medium-sized enterprises, operation of procedures with shorter regulatory timeframes, and stimulation of applications for products intended for non-EU markets in the context of cooperation with the WHO.

The Agency also invites discussions on innovative therapeutic approaches and new development methods for human medicines, in line with the recommendations of the Agency's think-tank report<sup>1</sup>.

Promoting the availability of veterinary medicines, the Agency continued its contribution to the implementation of the action plan arising from the HMA Taskforce on Availability. A particular highlight

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<sup>1</sup> Innovative drug development approaches - Final report from the EMEA/CHMP-Think-Tank group on innovative drug development ([EMEA/127318/2007](#)).

was the introduction in September 2009 of a range of measures to promote the authorisation of products for minor uses/minor species or limited markets.

The Agency also closely cooperates with the European Commission on fostering innovation in the context of the Innovative Medicines Initiative (IMI), 7th Framework Programme and the European Technology Platform for Global Animal Health.

## **Small and medium-sized enterprises**

*The Agency's SME Office has the sole remit of offering assistance to small and medium-sized enterprises (SMEs). The office aims to facilitate communication with SMEs through dedicated personnel within the Agency who respond to practical or procedural enquiries, monitor applications, and organise workshops and training sessions for SMEs.*

In 2009:

- the Agency received 217 requests for qualification as an SME and 221 requests for renewal of SME status;
- the majority of the 361 companies that had a decision on assignment or renewal of SME status were companies developing medicinal products for human use, 24 were veterinary companies, 16 were companies developing products for both human and veterinary use, and 21 were regulatory consultants;
- 93 requests for administrative assistance were received from recognised SMEs;
- 80 fee reductions or deferrals were granted.

In May 2009, an SME initiative review meeting was held with stakeholders. It was agreed that the high uptake of SME companies into the scheme underlines the importance of existing measures and the significant role the SME Office now plays as a service provider. Proposals put forward for strengthening the initiative were published in a report of the meeting.

The Agency strengthened the support it provides to SMEs during the critical period between obtaining scientific advice and submitting a marketing-authorisation application, by providing more regulatory and administrative assistance to improve the success rate at the time of initial evaluation. The SME Office routinely participated in centralised marketing authorisation application (MAA) pre-submission meetings with SME companies. In addition, in-depth briefing meetings were initiated with four companies preparing for a submission of an MAA. These meetings were deemed useful and will be rolled out further in 2010.

### **1.6. Methodology and outcomes-assessment projects**

As the European Medicines Agency takes a stronger public health role, it is becoming increasingly important to be able to measure whether the Agency is able to achieve its ultimate public health purpose. At the same time, it is also increasingly important for the Agency to explain to its stakeholders how it has reached its scientific conclusions.

In 2009, following internal and external consultation, the Agency started a number of pilot projects.

## **Benefit-risk assessment methodologies**

A collaboration with the London School of Economics and the University of Groningen was begun, aimed at developing and testing tools and processes for balancing multiple benefits and risks as an aid to informed regulatory decisions about medicinal products. The project started with a scoping exercise,

which has the objective of reporting on current methods, tools and strategies for benefit-risk assessment, and on opportunities for improvement. A draft report on the current practice of benefit-risk assessment in the EU regulatory network is in the process of being finalised.

## **Assessing the impact of scientific advice**

An assessment of the impact of scientific advice on the outcome of marketing-authorisation applications was completed and the findings were published in an article in the November 2009 issue of the European Journal of Clinical Pharmacology.

## **Scientific memory database**

The migration of all pre-authorisation data into the scientific memory database was completed. New elements for post-authorisation extension of indications were identified and new fields relating to clinical-trial data were introduced.

## **Evidence base for decisions on orphan drugs**

In collaboration with the Belgian Healthcare Knowledge Centre (KCE), the Agency looked at the evidence base for decisions on orphan drugs. A report on the project was published.

### **1.7. Integrated management at the Agency**

*The Agency operates an integrated management system to assure its processes and output. The main components of the system include: a quality-management system; a risk-management system; an Audit Advisory Committee; self-assessments, audits, internal controls and management reviews; benchmarking with partners in the European network of medicines agencies; human resource management; business and financial management; health and safety and environmental policies; and business continuity planning.*

## **Internal reorganisation**

The Agency implemented a series of changes to its internal organisation, aimed at improving the functioning of the Agency and the way in which it delivers its core tasks.

Taking into account the increasing complexity of the Agency's operations, the resulting reorganisation includes the following key changes:

- The lifecycle management of medicines for human use is brought together into a single unit, the Human Medicines Development and Evaluation Unit, responsible for the provision of advice during R&D, through to management of the review process and changes to products after they have been approved.
- The creation of a Patient Health Protection Unit, which contributes to patient health protection from the multiple perspectives of pharmacovigilance, risk and crisis management, patient and healthcare professional information, inspections (for both human and veterinary products) and appropriate regulatory compliance. The Unit is also in charge of EU procedures for both centrally and non-centrally authorised products.
- Within the Veterinary Medicines and Product Data Management Unit, a single sector was created with responsibility for all areas of veterinary medicines (development, evaluation and maintenance of veterinary medicines, public and animal health, and veterinary regulatory affairs) and a single

sector was created for the management of product data and documentation related to applications and for the development of IT systems to support scientific business processes.

## **New Road Map under way**

Preparations began for a new Agency Road Map to 2015. Adopted by the Agency's Management Board for public consultation in December 2010, the new strategic vision continues the previous Road Map initiative, setting out the Agency's priorities for the next five years.

## **External evaluation of the Agency**

The Agency assisted the European Commission in its evaluation of the Agency and the impact of its activities, which will be one element in the preparation of the review of the pharmaceutical legislation.

## **Quality management**

Findings from audits carried out by the European Court of Auditors, the European Commission's Internal Audit Service and the Agency's Internal Audit sector underlined that the Agency's integrated quality management system is well implemented, established procedures are adhered to and the controls are in place provide a reasonable level of assurance.

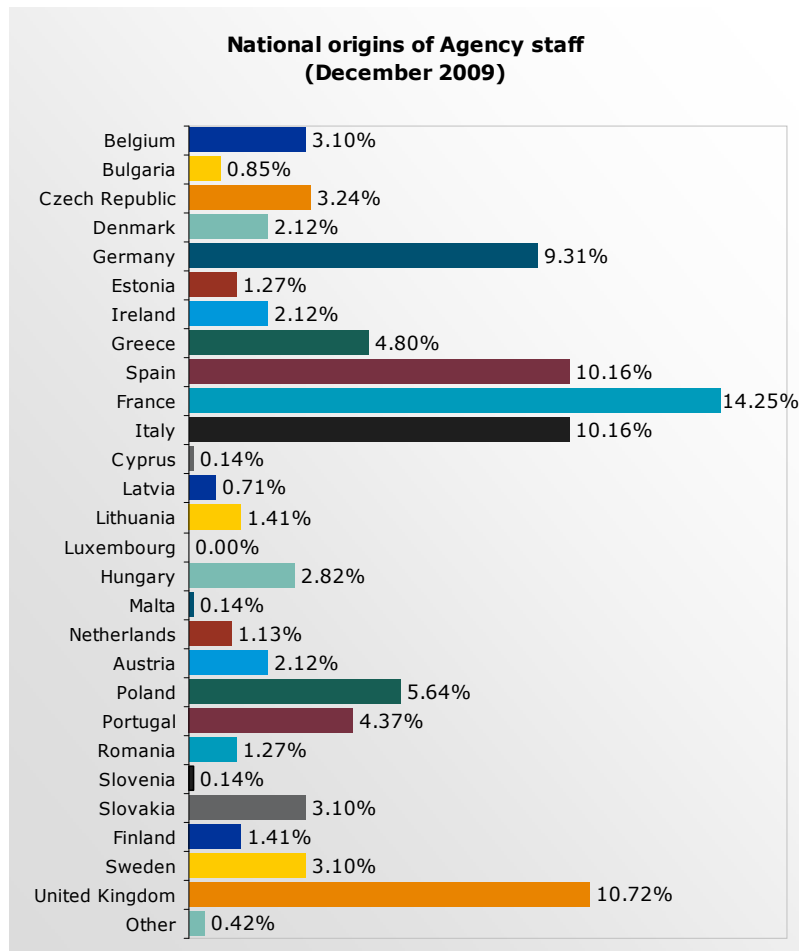
The Internal Audit sector carried out eight audits in 2009. An additional two audits that addressed a number of IT issues were carried out by external providers.

The Agency also carried out a review of the effectiveness and efficiency of its integrated quality management system, including its internal control standards.

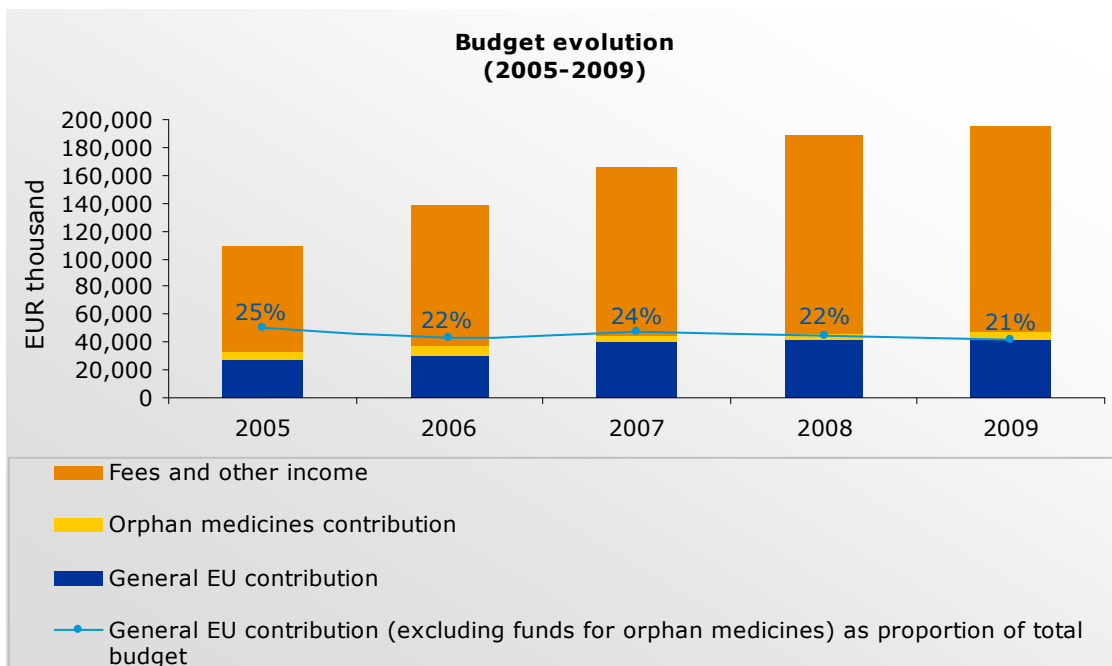
## **Budget and staff**

- For 2009, the Agency's Management Board approved a total of 530 temporary agent posts.
- By the end of 2009, the Agency had a total of 511 temporary agents, as well as an additional 200 seconded experts, contract agents, trainees and interim staff.
- The Agency's total budget in 2009 was €194,389,000 – a 6% increase compared to 2008.
- 75.1% of the Agency's revenue came from fees paid by the pharmaceutical industry, 23.9% from the EU budget and 1.0% from miscellaneous other income.

**Figure 1.**



**Figure 2.**



## 2. Medicines for human use

### 2.1. Orphan medicinal product designation

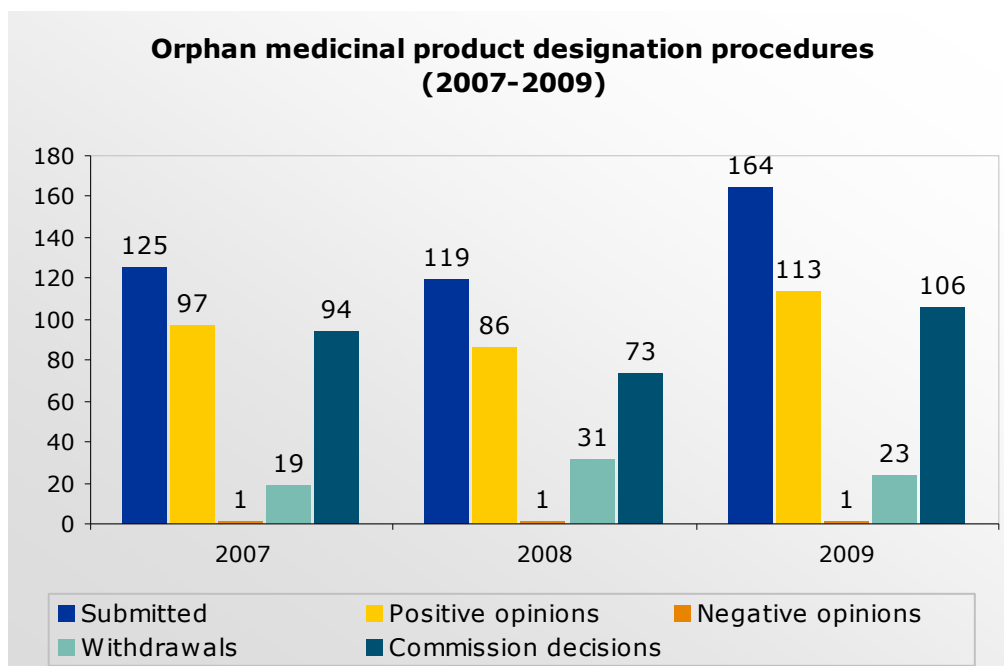
Orphan medicinal products are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than five in 10,000 persons in the European Union, or where for economic reasons such medicines would not be developed without incentives.

Applications for orphan designation are assessed by the Committee for Orphan Medicinal Products (COMP).

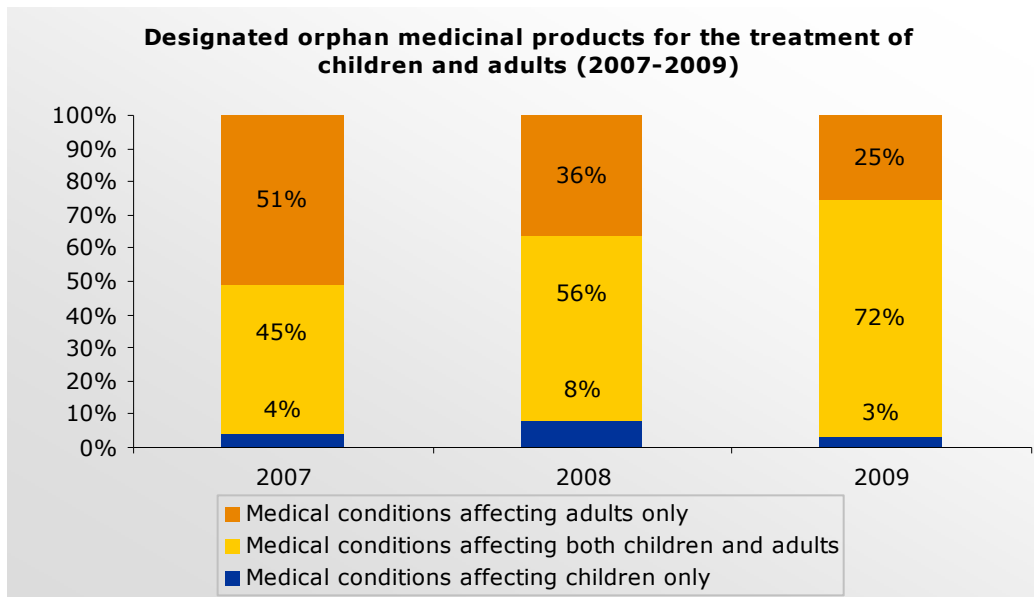
#### Core activities

- A total of 164 applications for orphan designation were submitted in 2009 – an increase of 38% over the previous year.
- The COMP adopted 113 positive opinions – the highest number ever. One application received a negative opinion and 23 applications were withdrawn prior to the adoption of an opinion.
- An increasing number of orphan-designated medicines appear to be intended for the treatment of children with rare diseases. In 2009, 75% of designated orphan medicines were for conditions affecting children, compared to 64% in 2008 and 49% in 2007.
- As in previous years, most COMP opinions were on products intended for use in cancer treatment.
- The average time taken to evaluate applications was 60 days.
- In line with its responsibility to review whether or not a designated orphan medicinal product still fulfils the designation criteria prior to the granting of a marketing authorisation, the COMP adopted 12 opinions, 11 of which recommended to the European Commission that the medicines concerned be kept in the Community registry of orphan medicinal products. One negative opinion was adopted.

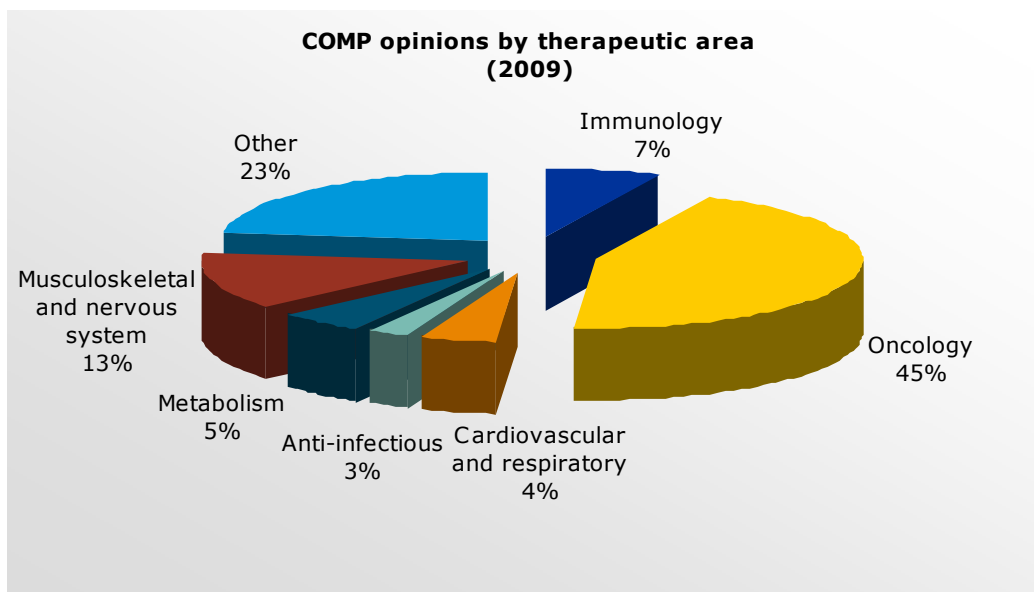
Figure 3.



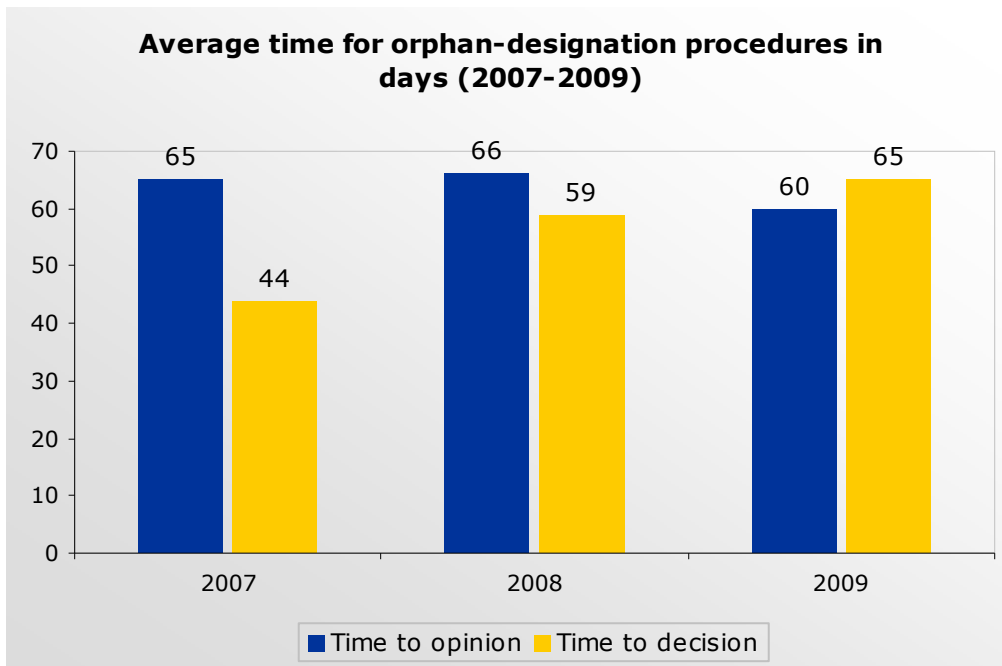
**Figure 4.**



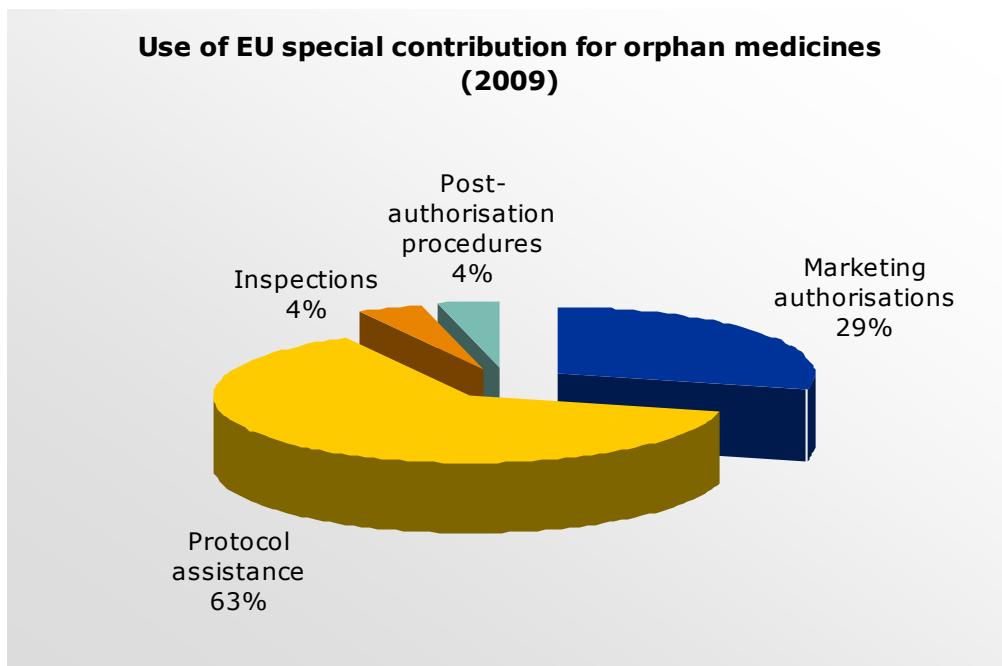
**Figure 5.**



**Figure 6.**



**Figure 7.**



## Specific objectives

### ***Review of the period of market exclusivity***

- The Agency began implementing the Commission guideline on Article 8(2) of Regulation (EC) No 141/2000 with a draft procedure giving guidance on the process to be followed. The guideline pertains to the review of the period of market exclusivity of orphan medicinal products. If available evidence shows that an orphan-designated medicine is sufficiently profitable, the period of market exclusivity may be reduced from ten to six years.

## Cooperation with the US FDA

- Cooperation with the US FDA progressed. The two agencies agreed to recommend the use of a common application form for orphan designation.
- Initial agreement was reached on a new initiative, namely the submission of a common annual report on the progress of development for orphan-designated medicines to both agencies.
- The two agencies held discussions to explore the reasons for divergent opinions on orphan designation. The two agencies are currently sharing information at the time of submission of applications.

Key performance indicator	Target	Outcome
Percentage of applications reviewed within 90-day timeline	100%	100%
Percentage of summaries of COMP opinions published within one month of the European Commission's decision on designation	70%	84%

## 2.2. Scientific advice and protocol assistance

*The Agency provides scientific advice and protocol assistance to sponsors during the phase of research and development of medicinal products. Scientific advice is provided on any aspect of research and development relating to quality, safety or efficacy of medicinal products. In addition, the Agency provides advice to sponsors of designated orphan medicines in the form of protocol assistance, which can include advice on the significant benefit of a product.*

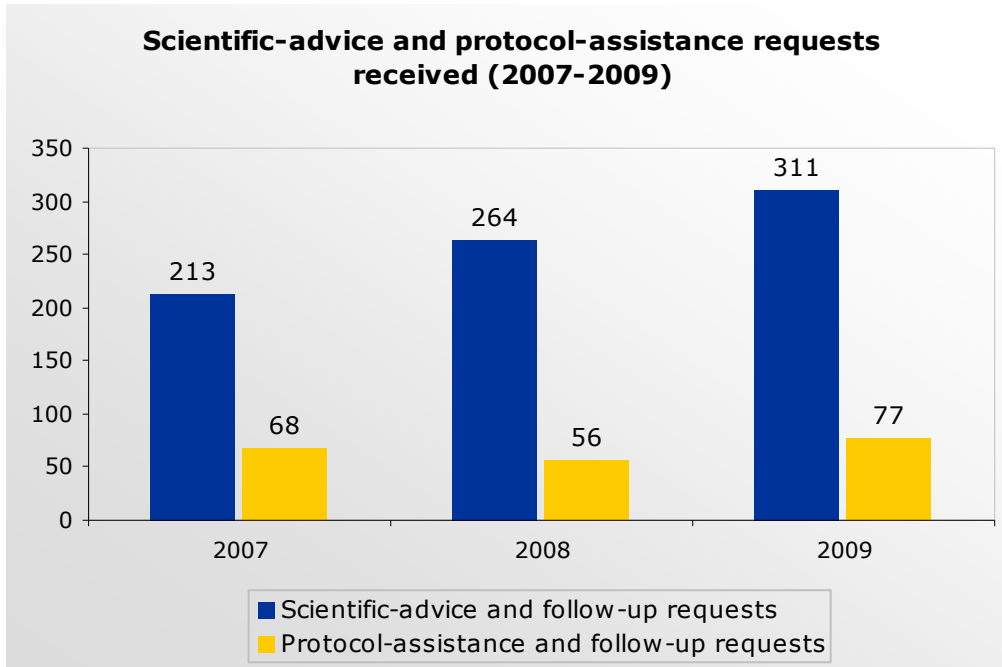
*Scientific advice and protocol assistance are key areas of activity for the Agency, in particular with respect to fostering new innovative technologies and therapies. The Agency considers scientific advice as a means to facilitate and improve earlier availability of medicinal products to patients and healthcare professionals, and as a means to promote innovation and research.*

### Core activities

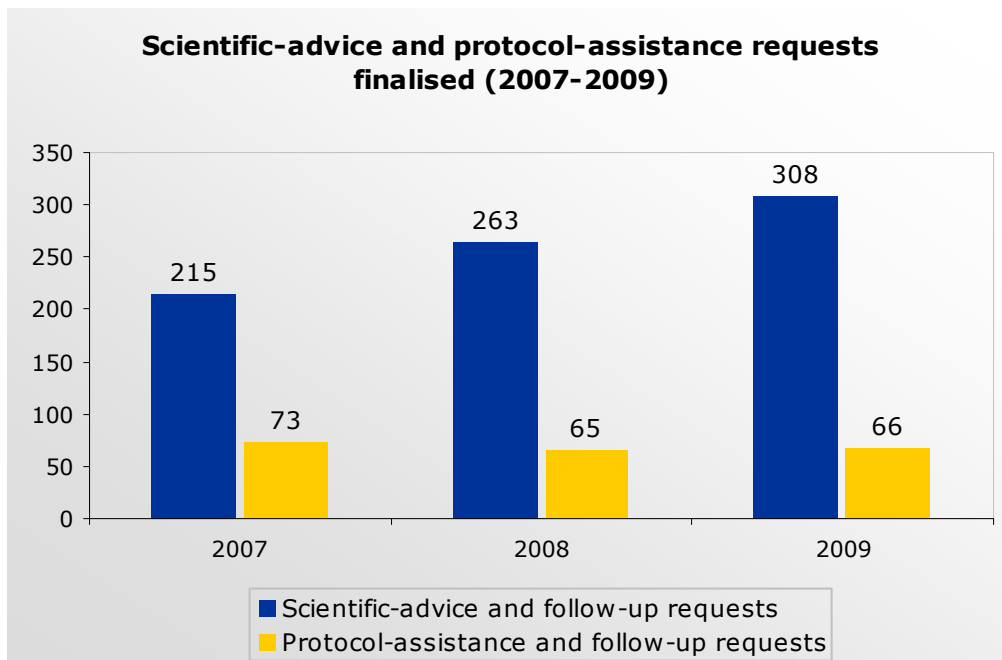
- The Agency received 311 requests for scientific advice – 18% more than in 2008.
- Following a decrease in 2008, the number of requests for protocol assistance for orphan-designated medicines was up again – 77 requests were received in 2009, compared to 56 in 2008.
- A total of 374 scientific-advice and protocol-assistance requests were finalised in 2009 – more than in any previous year.
- The timeline for the delivery of scientific advice and protocol assistance has remained stable over a number of years. In 2009, the mean duration was 71.7 days.
- As in previous years, the therapeutic area with the highest number of requests received was oncology, followed by metabolic and alimentary tract conditions, central nervous system conditions and general anti-infectives.
- Half of all requests related to questions on the clinical development of medicines.

- The majority of requests (61%) submitted to the Agency concerned questions related to phase-III clinical trials, followed by questions related to phase-II and phase-I clinical trials. Only 4% of requests received were on questions relating to phase-IV post-marketing surveillance studies.

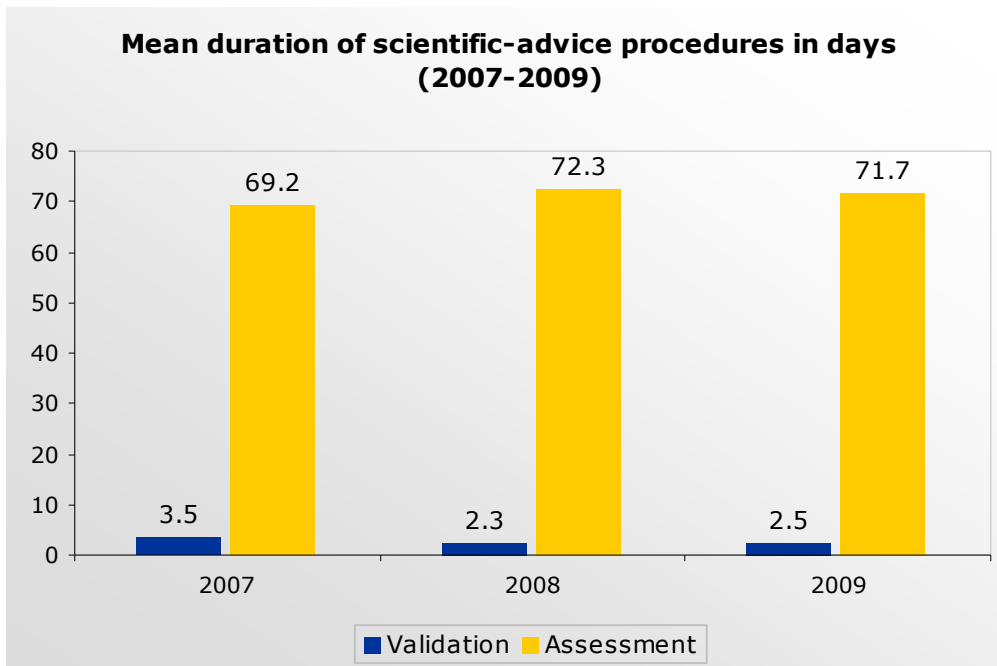
**Figure 8.**



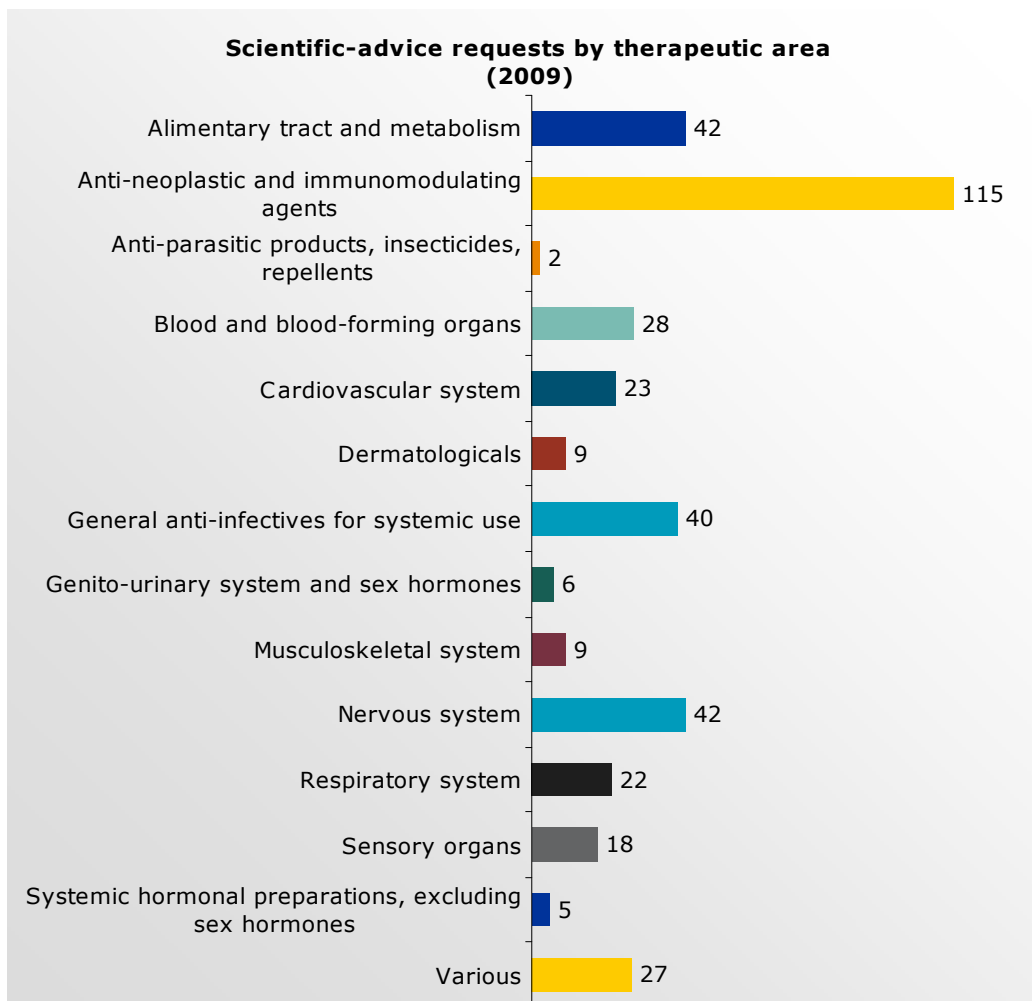
**Figure 9.**



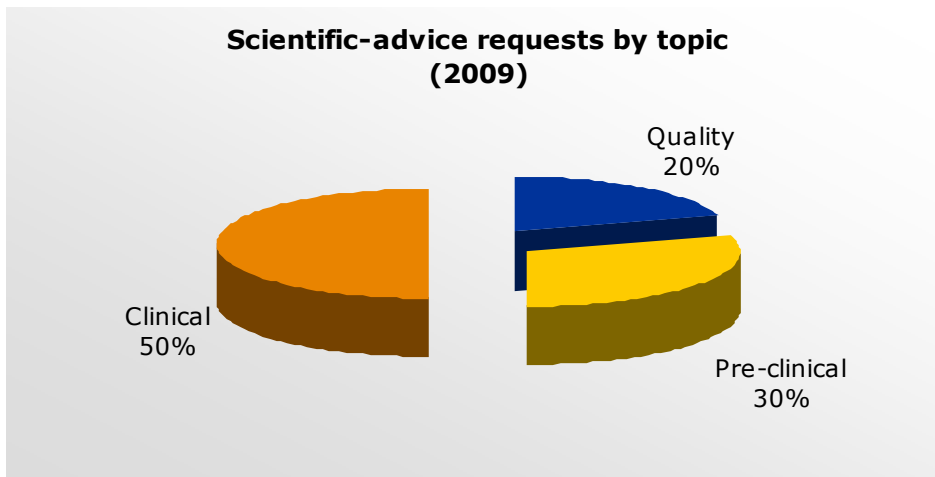
**Figure 10.**



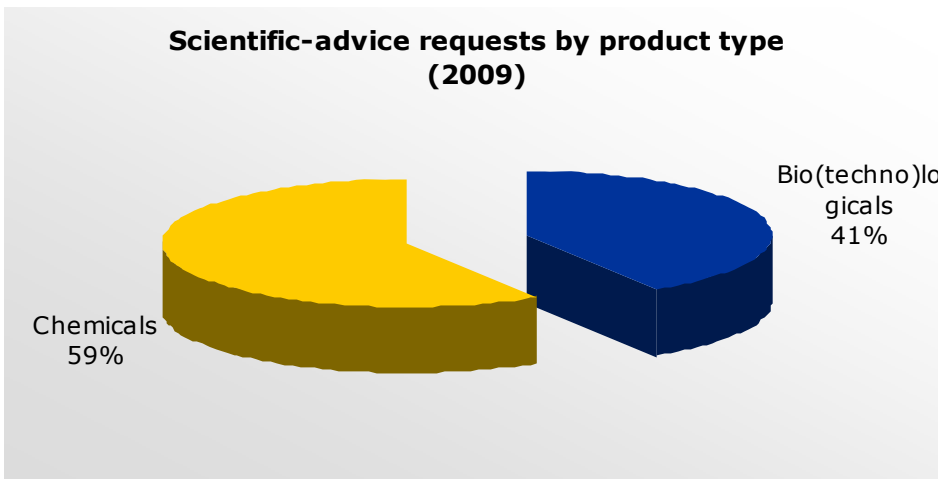
**Figure 11.**



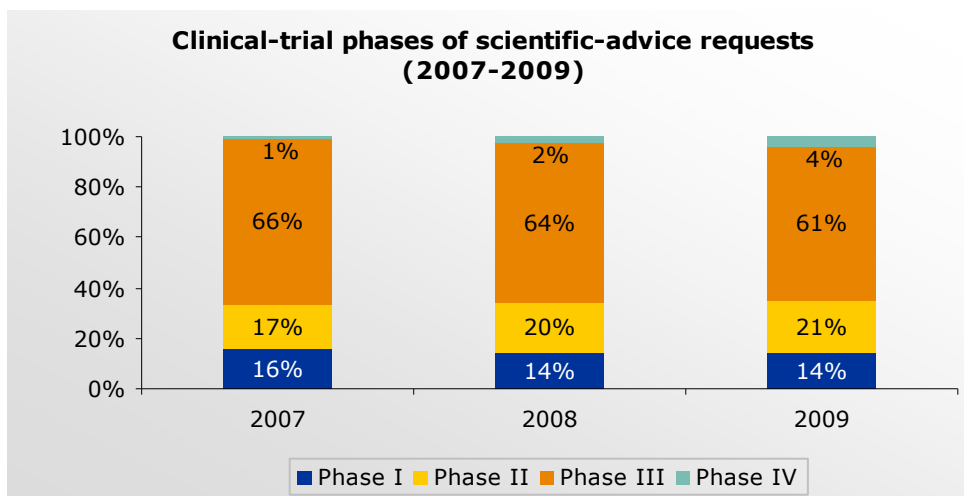
**Figure 12.**



**Figure 13.**



**Figure 14.**



## Specific objectives

### **Scientific-advice procedure for biomarkers**

- The Agency completed the implementation of a scientific-advice procedure on biomarkers to support the qualification process in drug development by streamlining and formalising the process for scientific advice on novel methodologies.

### **Adaptive clinical-trial design**

- This year was the third year of implementation of the final report from the EMEA/CHMP think-tank group on innovative drug development: Innovative drug development approaches (EMEA/127318/2007). As part of this project, the Agency held a joint workshop with the European Federation of Pharmaceutical Industry Associations (EFPIA) on adaptive design in confirmatory clinical trials. This workshop, held in April 2009, gave experts from regulatory authorities, the pharmaceutical industry and academia a platform to discuss current trends and issues in this field. A report has been finalised for publication.

### **New procedure for urgent and minor follow-up requests**

- In a bid to shorten timelines, the Agency implemented a new procedure for urgent and minor scientific-advice follow-up requests, making it easier for companies developing new medicines to receive clarification of previous advice.

Key performance indicator	Target	Outcome
Scientific-advice and protocol-assistance requests evaluated within the procedural timelines	100% of requests	100%
External experts involved in procedures	50% of SA and PA requests	48%

## 2.3. Initial evaluation

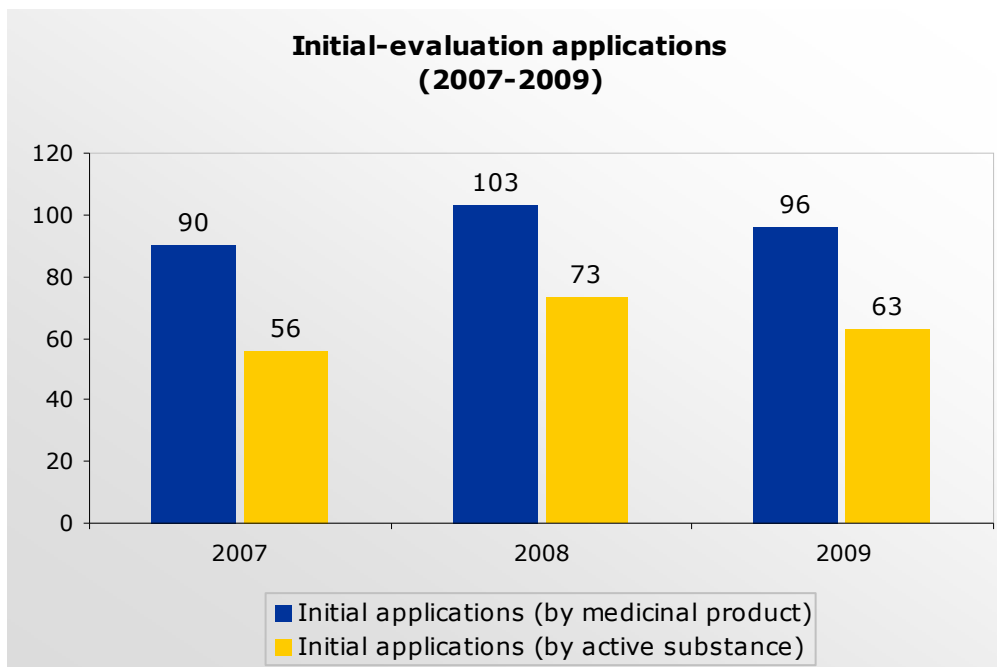
*Initial evaluation covers activities relating to the processing of applications for medicinal products (orphans, non-orphans, biosimilars, generics, etc.) from pre-submission discussion with future applicants, through evaluation by the CHMP, to the granting of a marketing authorisation by the European Commission. These activities culminate in the production of a European public assessment report (EPAR). Applications for certification of compliance with EU legislation of plasma master files are processed in a similar manner, but without the production of an EPAR. Opinions are also provided on ancillary medicinal substances and blood derivatives used in medical devices. The Agency provides regulatory advice to industry during pre-submission meetings.*

### **Applications received**

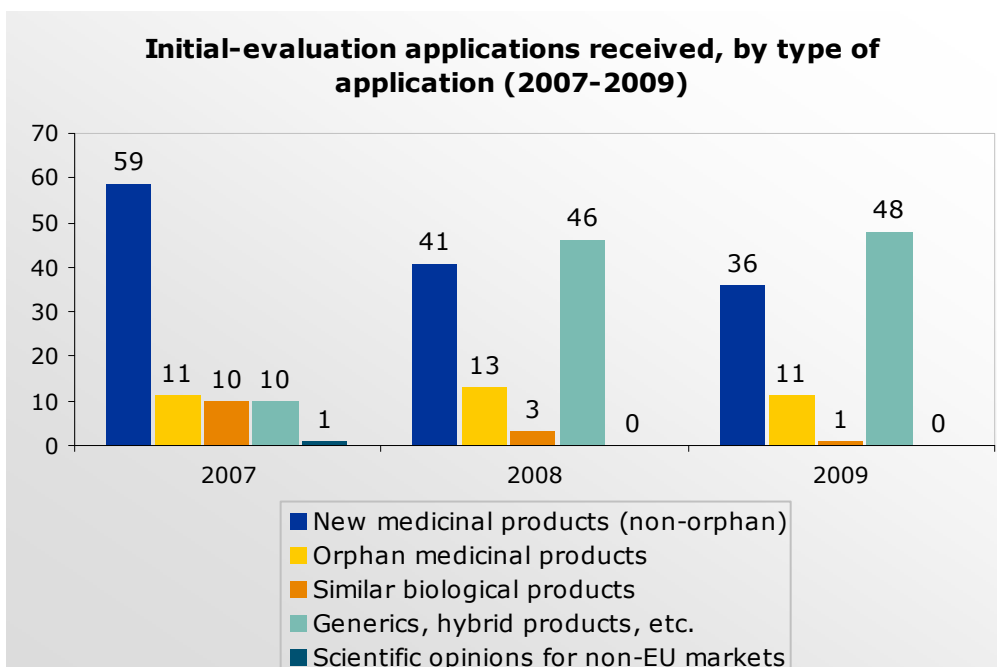
- In 2009, the Agency received a total of 96 applications for marketing authorisation for human medicines. Excluding multiple applications, this relates to 63 applications by active substance. Compared to 2008, this is a decrease of 7% in the total number of applications and by 16% in terms of applications by active substance.
- Fifty percent of applications received in 2009 were for generic and hybrid medicines and informed consent applications. The number of these applications actually received (48) is over 60% higher than the forecast (29).

- Eleven applications for orphan-designated medicines were received.
- Blood disorders and immunotherapy/oncology were the therapeutic areas in respect of which most applications were received, followed by medicines intended to treat cardiovascular diseases, anti-infectives and medicines to treat neurological disorders.

**Figure 15.**



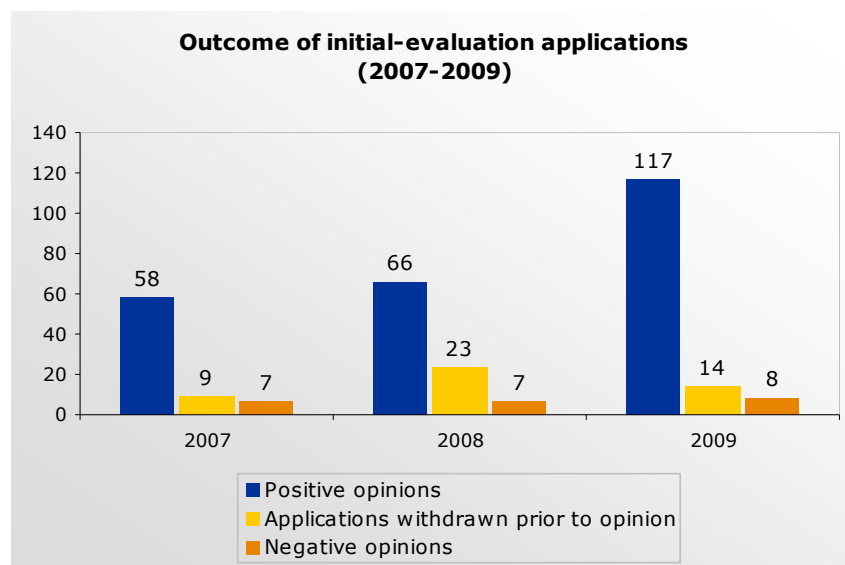
**Figure 16.**



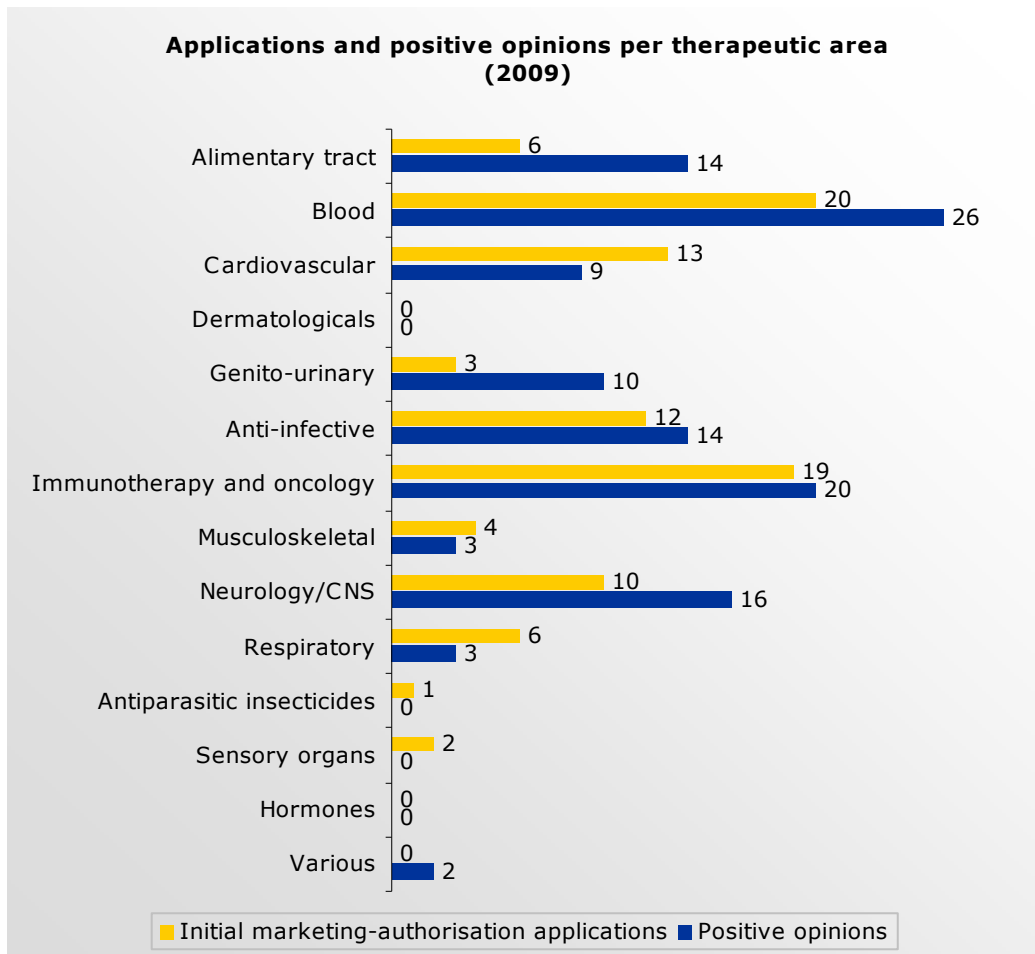
## Opinions adopted

- The Agency adopted a total of 125 opinions in 2009, the highest number of opinions ever adopted in one year.
- One hundred and seventeen applications received a positive opinion; eight applications received a negative opinion.
- Fourteen applications were withdrawn prior to the adoption of an opinion.
- Assessment times were down considerably in 2009. The CHMP took an average of 157 days for the assessment of an application. Clock-stop time, i.e. the time given to a company to respond to questions from the CHMP, averaged 118 days. The relatively short time is due to the high number of generic applications.

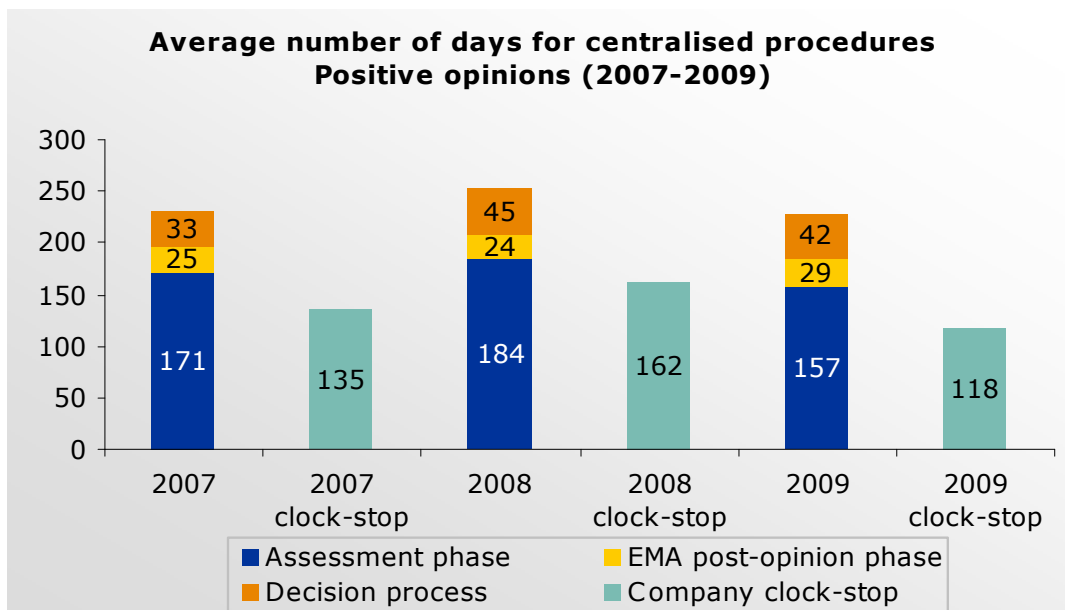
**Figure 17.**



**Figure 18.**



**Figure 19.**



## Public-health benefits of medicines recommended for approval in 2009

Medicinal products of notable public-health interest that received a positive opinion from the CHMP in 2009 included the following:

- The first tissue-engineered product approved as an advanced therapy medicinal product. It contains chondrocytes (characterised viable autologous cartilage cells) used for the repair of single symptomatic cartilage defects of the femoral condyle of the knee. The medicine is prepared specially for each individual patient using a biopsy (a small tissue sample) that is taken from the patient's cartilage in the knee. The cartilage cells are then grown and expanded in the laboratory and subsequently placed into the defect in the patient's cartilage by surgery.
- The first medicinal product eligible to be authorised "in the interests of patient or animal health at Community level" (under Article 3(2)(b) of Regulation (EC) No 726/2004) was approved for availability without prescription. The product is for short-term treatment of reflux symptoms (e.g. heartburn or acid regurgitation) in adults.
- The first biotechnological medicinal product for the treatment of osteoporosis in postmenopausal women at increased risk of fractures. This medicinal product reduces the risk of vertebral, non-vertebral and hip fractures. It is also indicated in men with prostate cancer receiving hormone ablative therapy, where it reduces the risk of vertebral fractures.
- The first antiarrhythmic medicinal product approved via the centralised procedure for use in adults who have had atrial fibrillation in the past or who currently have non-permanent fibrillation. It is used to prevent the atrial fibrillation coming back or to lower the heart rate. It works mainly by blocking channels through which charged particles of potassium move in and out of the muscle cells.
- Two orphan medicinal products approved for the treatment of cryopyrin-associated periodic syndromes (CAPS), a group of diseases where patients have a defect in the gene that produces a protein called cryopyrin. This leads to inflammation in many parts of the body and possibly to severe disabilities.
- An orphan medicine to treat primary apnoea in premature newborns, a condition in which newborns stop breathing for more than 20 seconds with no obvious cause. The product stimulates the nervous system to resume breathing.
- An orphan medicine to treat symptoms of Lambert-Eaton myasthenic syndrome (LEMS) in adults. LEMS is a disease in which patients have muscle weakness because of a failure of nerves to transmit electrical impulses to muscles.
- A new medicine for preventing organ rejection provided in a pharmaceutical form that allows for making fine adjustments in dosing, thereby representing an alternative for young children and others unable to swallow capsules. The medicine is used for the prophylaxis of transplant rejection in kidney, liver and heart recipients, and in the treatment of rejection resistant to treatment with other immunosuppressive medicinal products.
- Two immunosuppressant medicines used for the treatment of rheumatic diseases. Both medicines act by blocking tumour necrosis factor alpha, thereby reducing the inflammation and other symptoms of these diseases.

## Specific objectives

- Continuous improvement of the assessment work is one of the Agency's perennial objectives. As part of this, the Agency developed a checklist to control the quality of assessment reports and opinions across a range of centralised applications. A pilot project was initiated and is still ongoing.
- With the introduction of new pieces of legislation over the past years, marketing-authorisation applications nowadays have to demonstrate compliance with an increasing number of requirements, such as compliance with paediatric investigation plans or requirements from the Advanced Therapies Regulation. To facilitate the validation of complex applications, the Agency introduced quality-control elements to streamline the processes involved. Checks were implemented for paediatric compliance at validation.
- The Agency reinforced its pre-submission activities to further facilitate use of the centralised procedure for generic, non-prescription and Article 58 products. As part of this, the Agency increased the number of meetings held with companies in the phase prior to the submission of an application, in particular with applicants for generic medicines.
- Progress was made with the Product Information Management (PIM) project in 2009. PIM is designed to improve the efficiency, quality and control of the exchange, review and dissemination of product-information documents in the centralised procedure by the adoption of a structured XML-format document. The Agency started a migration analysis and a detailed planning exercise. A plan for the implementation of PIM in the centralised procedure was published in September 2009.
- The Agency successfully carried out the second and third steps of the implementation plan for electronic-only submissions. The use of electronic-only applications is strongly recommended to all applicants and, from 1 January 2010, the electronic Common Technical Document (eCTD) format is mandatory for all electronic submissions.

Key performance indicator	Target	Outcome
Percentage of applications evaluated within the regulatory timeline of 210 days	100% compliance	99%
Percentage of accelerated assessment applications evaluated within the regulatory timeline of 150 days	100% compliance	No opinions adopted
Percentage of opinions sent to the European Commission within the regulatory timeline of 15 days	95% compliance	99%
Percentage of plasma-master-file applications evaluated within the regulatory timeline	100% of applications	100%

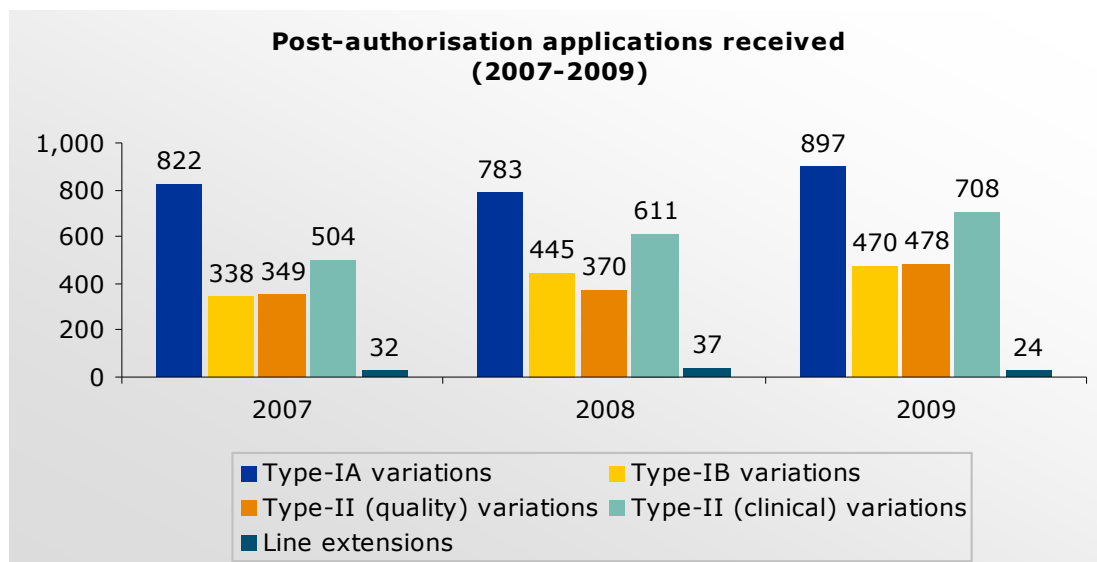
### 2.4. Post-authorisation activities

*Post-authorisation activities relate to variations, line extensions and transfers of marketing authorisations. Variations to marketing authorisations can be either minor (type-IA or IB) or major (type-II) changes. Variations concern quality, clinical or non-clinical-related aspects, including extensions of indications.*

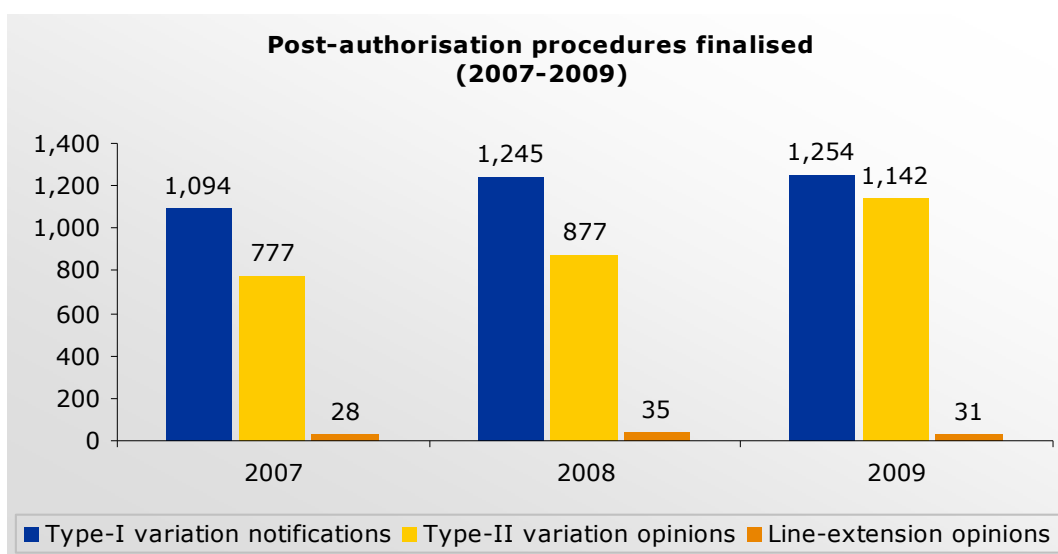
## Applications received

- The number of applications for variations and line extensions to existing marketing authorisations continued to rise. A total of 2,577 applications were received in 2009 – almost 15% more than in 2008.
- The increase was particularly noticeable for type-II variation applications, where the number rose by 21% compared to the previous year.
- Adopted post-authorisation opinions and notifications rose by almost 13% compared to the previous year. While the number of type-I variations remained fairly stable, the number of type-II variations increased by 30%.
- In September and October, the CHMP gave opinions on changes to the marketing authorisations for three pandemic influenza 'mock-up' vaccines, to include the H1N1 strain, so that they could be used in the management of the influenza pandemic that was declared by the World Health Organization in June 2009.
- A total of 55 positive opinions, including 16 duplicates, recommending new indications or the broadening of patient populations for authorised medicines were adopted by the CHMP, giving new treatment options to patients.
- Negative opinions recommending the refusal of an extension of existing indications were adopted for three medicines.
- New contraindications were recommended for seven centrally authorised medicinal products or classes of medicinal products (class labelling). In addition, the Committee finalised 251 type-II variations relating to updated recommendations on undesirable effects, special warnings and precautions for use for centrally authorised medicinal products or classes of medicinal products.

**Figure 20.**



**Figure 21.**



## **Public-health impact of positive opinions for new indications**

### ***Recommendation to authorise strain-change in pandemic mock-up vaccines***

In autumn 2009, the Agency recommended the variation of three previously authorised mock-up pandemic-influenza vaccines to include the H1N1 virus strain, making them effectively available for use during an influenza pandemic. 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. The recommendation to authorise Celvapan, Focetria and Pandemrix for use during the H1N1 influenza pandemic was endorsed by the European Commission within a few days. The assessment and final approval of the vaccines in line with the preparedness plan meant that authorised vaccines were available to public health authorities in the Member States from the end of September for use in their vaccination campaigns.

### ***Recommendations for antivirals during an influenza pandemic***

In May 2009, ahead of the WHO's declaration of an influenza pandemic, the Agency gave a number of recommendations on the use of the centrally authorised medicine Tamiflu (oseltamivir) during an influenza pandemic.

To increase available stock, the Agency recommended that the shelf-life of Tamiflu capsules be extended from five to seven years.

The Agency gave guidance on the use of Tamiflu in children under one year of age and on the use of the nationally authorised medicine Relenza (zanamivir) in pregnant and breastfeeding women in the case of a declared H1N1 influenza pandemic.

### ***New treatment options for patients***

The majority of new indications related to medicinal products approved for the treatment of various forms of cancer (e.g. lung, head and neck, gastrointestinal, ovarian, leukaemia and lymphoma), cardiovascular conditions (e.g. pulmonary arterial hypertension and atherothrombotic cardiovascular disease), metabolic conditions (e.g. diabetes mellitus) and skin conditions (e.g. atopic dermatitis).

A number of authorised medicinal products had their authorisations extended to include use in children and adolescents with schizophrenia, partial seizures, active polyarticular juvenile idiopathic arthritis or asthma.

Medicines that had their use extended included:

- Alimta (pemetrexed), for the maintenance treatment of lung cancer;
- Erbitux (cetuximab), for the treatment of recurrent and/or metastatic cancer of the head and neck;
- Glivec (imatinib), for the adjuvant treatment of adult patients following resection of Kit (CD117)-positive gastrointestinal stromal tumours;
- Mabthera (rituximab), for the treatment of chronic lymphocytic leukaemia;
- Torisel (temsirolimus), for the treatment of relapsed and/or refractory mantle cell lymphoma;
- Yondelis (trabectedin), for the treatment of patients with relapsed platinum-sensitive ovarian cancer;
- Adcirca (tadalafil), for the treatment of pulmonary arterial hypertension;
- Micardis, Pritor and Kinzalmono (telmisartan), for the reduction of cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke or peripheral arterial disease), or type-2 diabetes mellitus with documented target organ damage;
- Januvia, Tesavel, Xelevia (sitagliptin), to add monotherapy in patients for whom metformin is inappropriate, due to contraindications or intolerance;
- Protopic (tacrolimus), for the maintenance treatment of moderate to severe atopic dermatitis, following initial response to tacrolimus treatment;
- Abilify (aripiprazole), for the treatment of schizophrenia in adolescents aged 15 years and older;
- Keppra (levetiracetam), for the adjunctive treatment of children and infants from one month of age with partial seizures, with or without secondary generalisation;
- Orencia (abatacept), for the treatment of moderate to severe active polyarticular juvenile idiopathic arthritis in paediatric patients from six years of age;
- Xolair (omalizumab), for add-on therapy to improve asthma control in children aged six to 12 years with severe persistent allergic asthma.

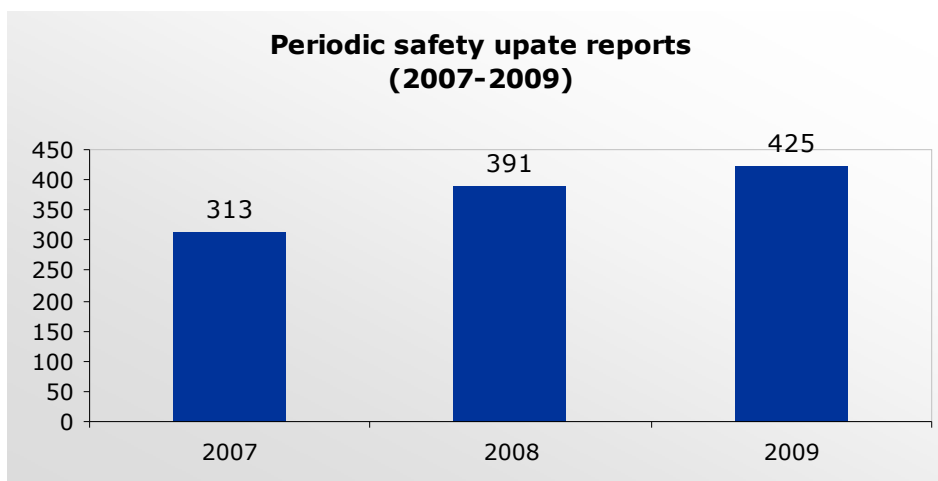
## **Specific objectives**

### ***Implementation of new variations procedure***

- The implementation of the new legislation on variations, which came into force on 1 January 2009, was a priority during the year. The Agency reviewed existing procedures to reflect all changes, relating, for example, to grouping, worksharing, classification of unforeseen variations and recommendations introduced by the new regulation. The guideline on classification of variations was adopted by the European Commission following a public consultation. The Agency supported the Commission in the development and drafting of the guideline.
- The Agency supported also the Commission with the development and drafting of the procedural guideline.

- Following an analysis of the financial impact, the Agency's Management Board adopted revised implementing rules, with the aim of maintaining the Agency's fee income from variations. This followed consultation with the Commission and the Heads of Medicines Agencies.
- The Agency provided training to staff and European experts on the updated post-authorisation guidance, to ensure that everybody involved in the management of variation procedures is aware of the new requirements.

**Figure 22.**



#### ***Handing of conditionally approved medicines in the post-authorisation phase***

- The Agency reviewed its limited experience with the handling of conditional marketing authorisations and their renewals. These types of marketing authorisations can be granted for medicines that address specific, unmet public-health needs, even though further evidence on the medicine is still awaited. The Agency reviews new information within one year and updates the product information as necessary.
- The outcome of the review will be reflected in a revised version of the guideline on conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 ([EMEA/509951/2006](#)).

Key performance indicator	Target	Outcome
Percentage of type-IA variations completed within the legal timeframe	100% compliance	95%
Percentage of type-IB variations completed within the legal timeframe	100% compliance	100%
Percentage of type-II (quality) variations completed within the legal timeframe	100% compliance	100%
Percentage of type-II (clinical) variations completed within the legal timeframe	100% of applications	100%
Percentage of applications meeting the legal timeline of 27 days for the linguistic post-opinion check	100% of applications	75% (92% within 30 days)
Submission of outcome reports for post-authorisation commitments to applicants/MAHs within two weeks of the CHMP meeting	100% of reports	90% (1,774 reports were handled)

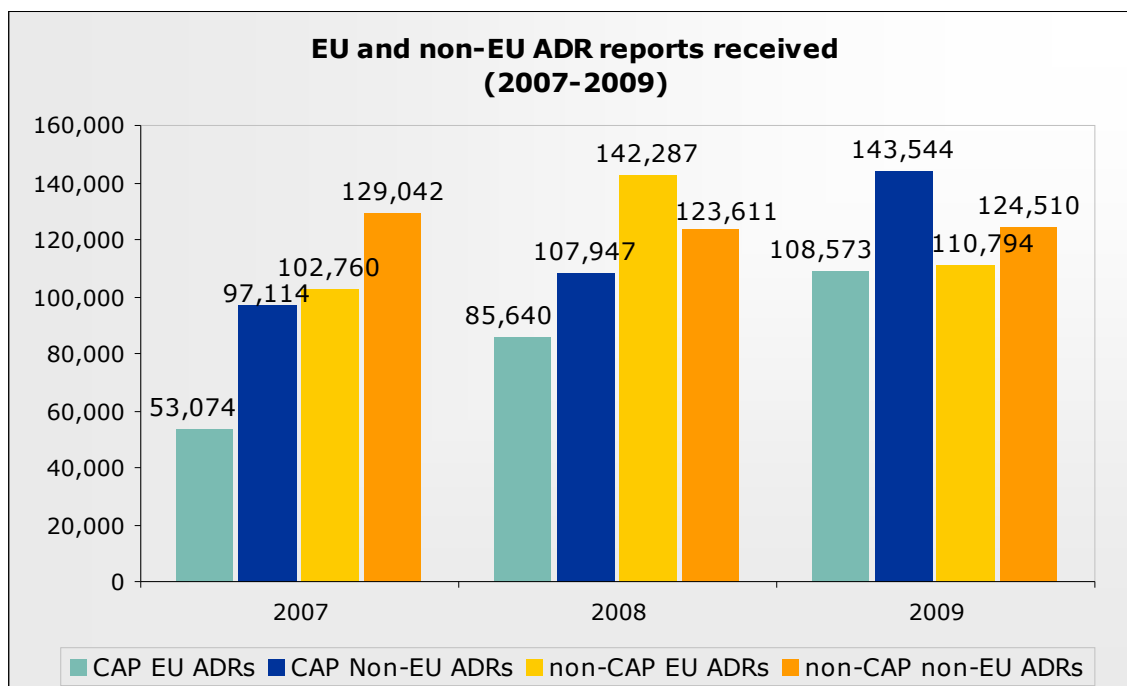
## 2.5. Pharmacovigilance and maintenance activities

Pharmacovigilance activities include the management of suspected adverse drug reactions (ADRs) in pre- and post-authorisation phases (individual case safety reports), periodic safety-update reports, risk-management plans and post-authorisation safety and efficacy/effectiveness studies. They further encompass support to detection and management of signals for centrally authorised medicinal products, support to the EU Risk Management Strategy and the coordination of monitoring of the safety of medicines in the EU.

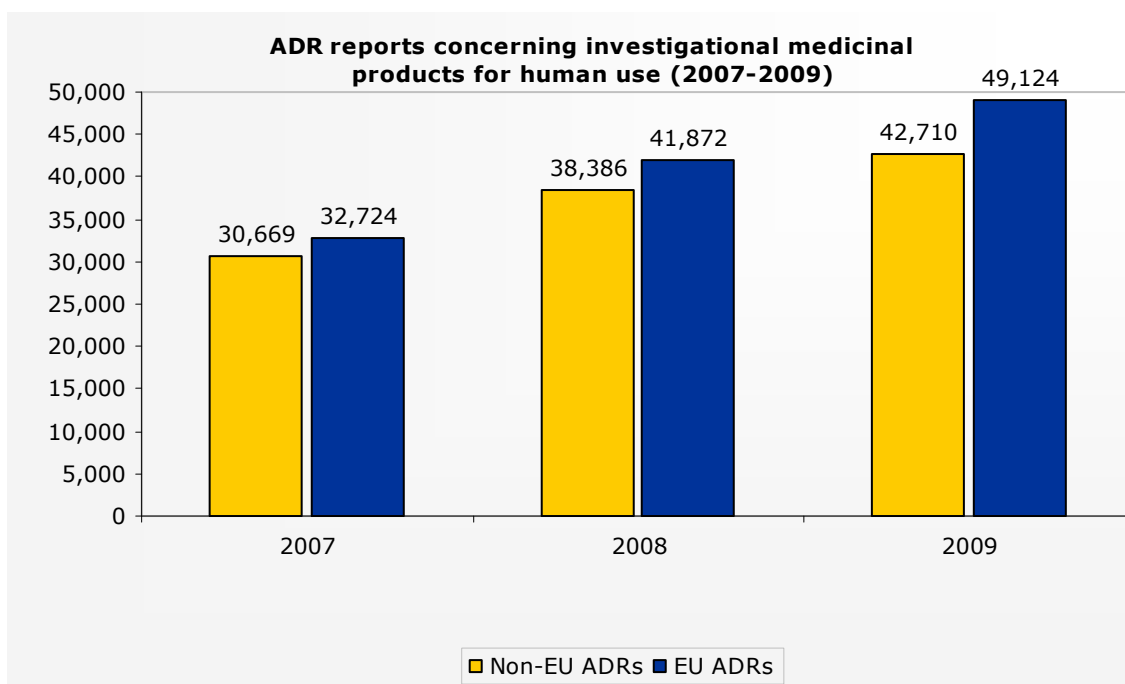
### Core activities

- In 2009, 487,421 individual case safety reports (ICSRs) relating to authorised medicines were received – a 6% increase over the previous year.
- The Agency received 91,834 reports of suspected unexpected serious adverse reactions (SUSARs) relating to medicines used in clinical trials – an increase of 14% over the previous year.
- The number of medicinal products processed in the EudraVigilance Medicinal Products Dictionary was 35,979.
- A six-month pilot with marketing authorisation holders and sponsors of clinical trials on the notification of adherence with the expedited reporting timelines of ICSRs was initiated in October 2009.

Figure 23.



**Figure 24.**



## Specific objectives

### ***Pandemic pharmacovigilance***

- Pharmacovigilance of antivirals and vaccines used during the influenza pandemic was a major activity in 2009. The Agency, in close collaboration with the European Centre for Disease Prevention and Control (ECDC) and the Heads of Medicines Agencies (HMA), developed a European strategy for benefit-risk monitoring of influenza A/H1N1 vaccines. The strategy was published in October 2009.
- To ensure continuous monitoring of the medicines used for the management of the influenza pandemic, the Agency set up the Pandemic Pharmacovigilance Rapid Response Expert Group (PREG). This group of pharmacovigilance experts from the Member States and the Agency looked at all side effects reported with the pandemic vaccines or antivirals. The group's assessment formed the basis of the weekly pandemic pharmacovigilance updates published on the Agency's website. The first weekly update was published on 3 December 2009.
- By the end of the year, at least 29.4 million people in Europe, including at least 218,000 pregnant women, had been vaccinated with one of the three centrally authorised vaccines (Celvapan, Focetria or Pandemrix). As of 27 December 2009, a total of 11,126 reports had been received by EudraVigilance since the authorisation of these three vaccines. The vast majority of the adverse drug reactions were considered non-serious.

### ***Implementation of the ERMS***

- A pilot phase for the EU Regulatory System Incident Management Plan for medicines for human use was launched on 1 June 2009. This plan is designed to improve the handling and coordination of any potential crisis with a medicine in the European medicines system. Since its launch, the management plan was triggered on several occasions.

- Transparency and communication within the EU regulatory system was further enhanced through the adoption by the HMA of a policy on the publication of monthly reports of the Pharmacovigilance Working Party (PhVWP). The policy was implemented in September 2009. Since then, these reports have been published monthly, providing information on the outcome of discussions at the PhVWP on safety aspects of non-centrally authorised products that are not subject to a formal referral procedure.

### ***Innovative Medicines Initiative (IMI)***

- In April 2008, the Agency-led PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium) project was accepted for funding by the Innovative Medicines Initiative Joint Undertaking (IMI JU). The official start date of the project was 1 September 2009. PROTECT is a collaborative European project aiming to develop innovative methods in pharmacoepidemiology and pharmacovigilance. The Agency coordinates the project and manages a multinational consortium of 29 public and private partners. The project will run over five years, with a total funding of EUR 20 million. Half of the funding will be in-kind contributions from the participating EFPIA companies.
- In addition to PROTECT, the Agency also contributes to the IMI-funded project Eu2P, which focuses on the development of a comprehensive and flexible pan-European training and education programme for specialists and non-specialists in the fields of pharmacoepidemiology and pharmacovigilance.

### ***Maintenance and strengthening of EudraVigilance***

- EudraVigilance, the EU database and data-processing network on adverse drug reactions was further developed in line with the project plan agreed by the EudraVigilance Steering Committee. Where possible, the ongoing standardisation work has been taken into account as part of the definition of requirements. A EudraVigilance data-management tender was published on 6 October 2009 and the evaluation of the responses is currently ongoing.

### ***Pilot on signal management***

- The Agency conducted a successful pilot on signal management with monthly reporting to the PhVWP. Key principles, including roles and responsibilities, were agreed for signal management for medicinal products for human use irrespective of the marketing authorisation procedure. The EudraVigilance Support Programme was initiated at the end of January 2009 to assist Member States in their signal detection and evaluation activities. Reaction-monitoring reports for the surveillance of some medicinal products, such as the pandemic-influenza vaccines, were prepared on a weekly basis for the rapporteurs and the Member States. The European Pharmacovigilance Issues Tracking Tool (EPITT) is now routinely used to support the signal-management process.

### ***Implementation of ENCePP***

- In accordance with the 2009 work plan of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCEPP), work focused on developing the database of ENCePP research centres (made publicly available in December 2009 and to be populated in 2010), the establishment of the ENCePP Steering Group, and the drafting of an ENCePP code of conduct and a checklist of methodological research standards (both documents were released for public consultation in November 2009). This preparatory work should allow an operational system to be achieved in 2010.

- Furthermore, a procurement procedure for funding by the Agency of safety studies was initiated and applications received are being evaluated.

### ***Risk-management plans***

- The review and learning project for risk-management plans (RMPs) further progressed, and the RMP guideline is now being updated to include accumulated experience.
- Work is also ongoing on research projects looking at the outcome of risk-minimisation activities for centrally authorised medicines.

### ***Paediatric pharmacovigilance***

- Initiatives were taken to facilitate the monitoring of adverse drug reactions to centrally authorised medicines in children. An action plan on paediatric pharmacovigilance, based on EudraVigilance data, was adopted in May 2009, in order to further strengthen the intensive monitoring of paediatric use of medicines.

### ***Pilot phase on patients' participation in PhVWP***

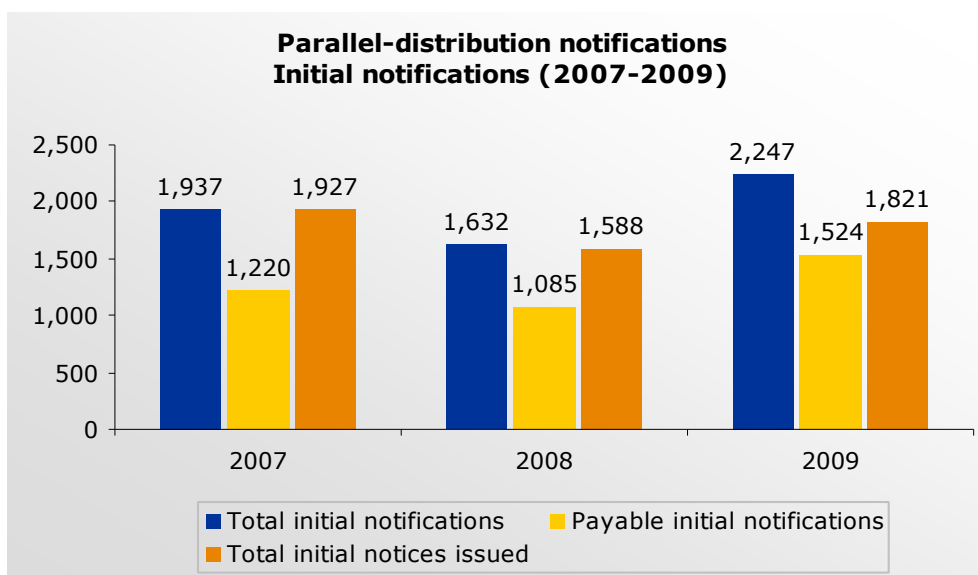
- A pilot phase on patients' representatives' participation in PhVWP meetings was successfully completed and work is underway to involve one patient representative as observer (and one alternate) in PhVWP meetings in 2010.

<b>Key performance indicator</b>	<b>Target</b>	<b>Outcome</b>
Percentage of RMPs peer-reviewed by the Agency as part of the assessment of variations and line extensions which result in a significant change to a marketing authorisation	80%	100%
Provide access to EudraVigilance data in line with new EU legislation	Marketing authorisation holders, healthcare professionals and patients	No access has been granted yet. The finalisation of the EudraVigilance Access Policy is progressing as outlined above
Percentage of ICSRs reported electronically for centrally authorised medicines	100%	100%
Percentage of serious adverse event and serious adverse reaction reports of combined advanced therapy medicinal products that were forwarded to the competent authorities for medical devices, tissue and cells according to the standard operating procedure	95%	No combined advanced therapy medicinal product was authorised in 2009

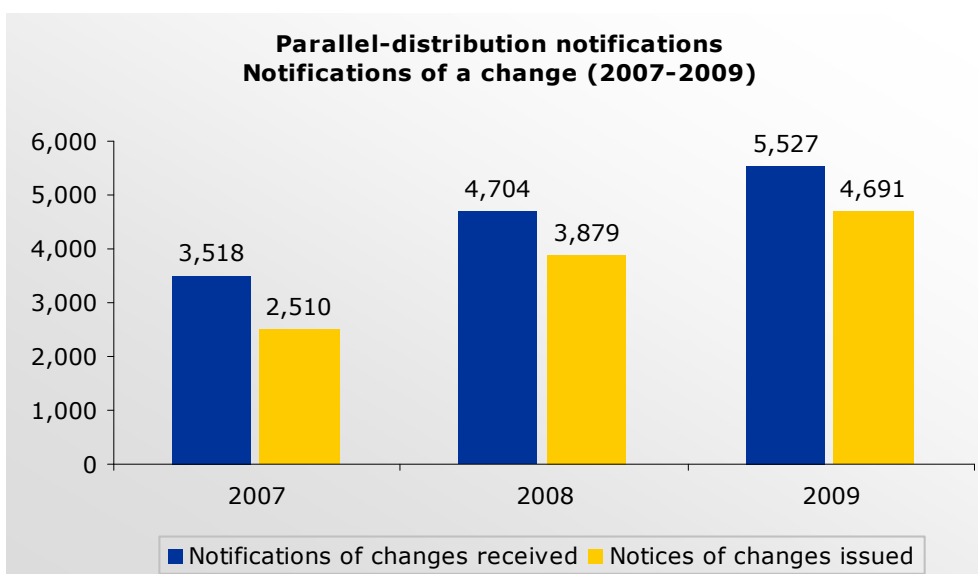
## 2.6. Parallel distribution and certificates

- The number of initial parallel-distribution notifications received in 2009 was 2,247 – 38% higher than in 2008.
- The number of notifications of a change rose by 18% to 5,527.
- The regulatory timelines for handling initial parallel-distribution notifications improved significantly (average handling time of 28 days compared to the regulatory timeline of 35 days, resulting in 78% of applications being handled within such regulatory timeline, the target being 70%).
- However, a backlog developed for the handling of notifications of a change. Remedial action was taken to address this.
- Six of the foreseen 20 medicines were sampled from the EU market and checked for compliance.

**Figure 25.**



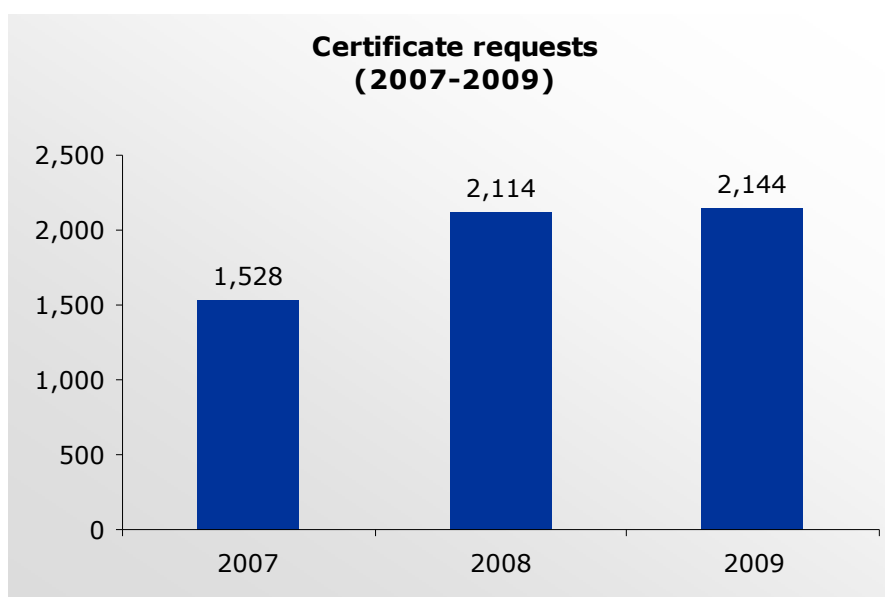
**Figure 26.**



Key performance indicator	Target	Outcome
Percentage of notifications checked for compliance within the regulatory timeline of 35 working days (5 days for validation and 30 days for regulatory check)	70%	78%

- The number of requests for certificates was forecast to increase by approximately 20%, due to the increased number of approved medicinal products. However, the actual figure was lower (2,144 versus the forecast of 2,590), which nonetheless represents an increase of 1% compared to 2008.

**Figure 27.**



Key performance indicator	Target	Outcome
Percentage of certificates issued to requesting parties within the timeline	90% compliance	98% compliance

## **2.7. Arbitration and Community referrals**

*Article 20 procedures (Regulation (EC) No 726/2004) require a CHMP opinion on the measures necessary to ensure the quality and safe, effective use of a centrally authorised product.*

*Arbitration procedures (either under Article 29(4) of Directive 2001/83/EC as amended or Articles 6(12) and 6(13) of Commission Regulation (EC) No 1084/2003) are initiated because of disagreement between Member States or because of disagreement of the marketing-authorisation holder with the Member States in the framework of mutual-recognition or decentralised procedures.*

*Article 30 referrals (Directive 2001/83/EC as amended) are mainly initiated in order to obtain harmonisation of authorisations for medicinal products authorised in the EU by the Member States.*

*Article 31 and 36 referral procedures (Directive 2001/83/EC as amended) are mainly initiated in case of EU interest and generally for safety-related issues.*

Article 16c(1)(c) and 16c(4) referrals (Directive 2001/83/EC as amended) are initiated by Member States regarding herbal medicinal products with a traditional use of at least 30 years, including at least 15 years in the EU, in order to obtain an opinion on the adequacy of evidence of the long-standing use (Article 16c(1)(c)) and regarding herbal medicinal products with a traditional use of less than 15 years in the EU, in order to obtain an opinion on eligibility for the simplified procedure (Article 16c(4)).

Article 107(2) procedures (Directive 2001/83/EC as amended) are initiated to obtain a rapid CHMP opinion further to an envisaged suspension or revocation of a marketing authorisation (or, optionally, a variation to the marketing authorisation) of a medicinal product in a Member State as a result of pharmacovigilance data.

Article 5(3) procedures (Regulation (EC) No 726/2004) require a CHMP opinion on any scientific matter raised by the Agency, the European Commission or a Member State.

Article 29 procedures (Regulation (EC) No 1901/2006) require a CHMP opinion on authorisation of a new indication, new pharmaceutical form or new route of administration relating to paediatric use.

## Core activities

- The number of procedures initiated was slightly higher than expected (46 instead of 43 procedures forecast), mainly due to an increasing number of procedures initiated under Article 107 of Directive 2001/83/EC, as amended, in the last half of 2009.
- Information on the outcome of the scientific review (e.g. press releases, question-and-answer documents, scientific conclusions and product information) was published as per the agreed proceedings.
- Some delays occurred with regard to the transmission to the European Commission of the annexes of opinions. While the annexes should be sent to the Commission on day 27 after the adoption of the opinion by the CHMP, this was only adhered to for one of the five procedures for which the translations had to be sent. The mean delay was 32 days. The reasons for these delays are various, including the very short timeframe for finalising the annexes, marketing-authorisation holders' unfamiliarity with the process and, in some cases, the very high number of individual marketing-authorisation holders involved.

Procedure type	Started in 2009	Finalised in 2009
Article 6(12) of Commission Regulation (EC) No 1084/2003	5	2
Article 6(13) of Commission Regulation (EC) No 1084/2003	1	0
Article 31 of Directive 2001/83/EC	4	4
Article 36 of Directive 2001/83/EC	0	2
Article 5(3) of Regulation (EC) No 726/2004	2	2
Article 16c(1)(c) of Directive 2001/83/EC	0	0
Article 16c(4) of Directive 2001/83/EC	0	0
Article 107(2) of Directive 2001/83/EC	5	2
Article 29 of Directive 2001/83/EC	13	16
Article 30 of Directive 2001/83/EC	10	7
Article 29 of Regulation (EC) No 1901/2006	6	3
Article 20 of Regulation (EC) No 726/2004	0	2
Totals	46	38

## Procedures of high public-health interest finalised in 2009

- The CHMP concluded a review of Ritalin and other methylphenidate-containing medicines. The review was initiated because of safety concerns, particularly over the possible risk of cardiovascular and cerebrovascular disorders. The CHMP concluded that methylphenidate-containing medicines remain suitable for the treatment of children aged six years or older and adolescents with attention deficit/hyperactivity disorder (ADHD). The Committee also recommended that the product information be made consistent across the EU so that all patients, carers and prescribers have the same information, for safer and more appropriate use of these medicines (Article 31 procedure).
- In a review of the safety and efficacy of dextropropoxyphene-containing medicines, the CHMP concluded on the basis of available data that the risks, particularly the risk of potentially fatal overdose, are greater than the benefits afforded by these medicines, and therefore recommended that their marketing authorisations be withdrawn across the EU (Article 31 procedure).
- A review of Atifor Chiesi 12 mcg/Forair/Atimos (Formoterol HFA 12mcg) and associated names was triggered by concerns that therapeutic equivalence of these medicines with the reference medicine is not established for children aged five years and above. The CHMP concluded that these medicines should not be used in children aged from five to 12 years because their efficacy could not be demonstrated in this age group (Article 36 procedure).
- A review of Raptiva (efalizumab) was started at the request of the European Commission, following concerns over the safety of the medicine, including the occurrence of progressive multifocal leukoencephalopathy. The CHMP concluded that the benefits of Raptiva no longer outweigh its risks, and that the marketing authorisation should be suspended (Article 20 procedure).
- In a review of safety and efficacy of valproic acid and valproate-containing medicines, the CHMP recommended the use of valproate for the treatment of manic episodes in bipolar disorder in patients who cannot take lithium, and concluded that the benefits of valproate-containing medicines in the management of manic episodes in bipolar disorder when lithium is contraindicated or not tolerated continue to outweigh their risks, and therefore recommended that all marketing authorisations for these medicines be varied either to include or to amend the indication for all solid formulations (e.g. tablets, capsules or granules) (Article 6(12) and Article 31 procedure).
- A review of benfluorex-containing medicines resulted in the recommendation to withdraw these medicines from the market because the CHMP concluded that their risks, particularly the risk of heart valve disease, are greater than their benefits in overweight patients with diabetes (Article 107 procedure).
- The CHMP recommended the revocation of the marketing authorisations for iodocasein/thiamine-containing medicines because of the risks of hyperthyroidism and thyrotoxicosis (Article 107 procedure).
- A review of Extraneal (icodextrin) 7.5% solution for peritoneal dialysis was started because of differences among Member States on whether to change the existing marketing authorisations in the Member States to include a test to measure the level of an impurity called peptidoglycan during the production process. The CHMP recommended approval of the type-II variation to update the finished product specification by including the peptidoglycan test (Article 6(12) procedure).

### **Paediatric referrals – Article 29 of Regulation (EC) No 1901/2006**

The CHMP finalised two procedures under Article 29 of Regulation (EC) No 1901/2006, the Paediatric Regulation. This allows companies to submit to the Agency an application for a new indication, a new pharmaceutical form or a new route of administration for medicines that are already authorised at the level of the Member States. Once the CHMP opinion has been transformed into a decision by the European Commission, the company will be able to obtain approval in all EU Member States where the medicine is authorised.

- The CHMP adopted an opinion for Arimidex (anastrozole) to reflect new clinical data on the use of anastrozole in the treatment of short stature in pubertal boys with growth hormone deficiency in association with exogenous growth hormone, and in the treatment of testotoxicosis. The Committee's opinion was that the data do not support the authorisation of the medicine for children. However, the information on the paediatric studies will be included in the product information.
- The CHMP recommended a line extension for Diovan (valsartan) to add an oral solution, a pharmaceutical formulation suitable for the paediatric population. The paediatric formulation has been developed for the treatment of children and adolescents between six and 18 years with hypertension. The CHMP also recommended that this indication be approved for the currently available presentations of Diovan (film-coated tablets).

### **Scientific opinions on any scientific matter – Article 5(3) of Regulation (EC) No 726/2004**

The CHMP can be asked to draw up an opinion on any scientific matter related to the evaluation of medicines for use in humans.

- At the request of the Executive Director, the CHMP conducted a review of the use of Tamiflu (oseltamivir) and Relenza (zanamivir) in the case of a declared influenza A/H1N1 pandemic. The CHMP concluded that the benefits of the use of Tamiflu outweigh its risks in the treatment of children under the age of one year. The Committee also concluded that the benefits of using Tamiflu and Relenza in pregnant or breastfeeding women outweigh the risks in case of a pandemic. Furthermore, the CHMP recommended an extension of the shelf-life of Tamiflu capsules from five to seven years.
- The Danish medicines authority asked for an opinion of the CHMP on bisphosphonates and the risk of osteonecrosis of the jaw. The CHMP concluded on the definition of osteonecrosis of the jaw related to bisphosphonates and noted that further studies regarding the mechanisms through which bisphosphonates may cause osteonecrosis of the jaw are required. Although the most important risk factors seem to be the potency of the bisphosphonate used, the dose and how it is given, the CHMP concluded that further research on risk factors is needed. Finally, the Committee concluded that further data are needed to determine the precise measures that could minimise the risk of osteonecrosis of the jaw, including looking at how intravenous bisphosphonates should be given, and looking into the risk of osteonecrosis of the jaw in patients taking bisphosphonates by mouth for long periods.

### **Procedures started in 2009 but not finalised**

- Review of the benefits and risks of Tysabri (natalizumab), in view of reports of cases of progressive multifocal leukoencephalopathy (Article 20 procedure).
- Review of overall benefits and risks of Regranex (becaplermin), in the light of concerns over the safety profile, especially with respect to the possible risk of cancer (Article 20 procedure).

- Review of modafinil-containing medicines, because of safety concerns relating to skin and hypersensitivity reactions and psychiatric disorders (Article 31 procedure).
- Review of modified-release oral opioids (containing morphine, fentanyl, oxycodone and hydromorphone) for the management of pain, due to concerns over the dissolution of the prolonged-release oral products and their sensitivity and interaction with alcohol, which may cause dose dumping and potential overdose (Article 31 procedure).
- Review of lipid-lowering fibrates (fenofibrate, bezafibrate, ciprofibrate and gemfibrozil), because of concerns over their long-term clinical benefit in the primary and secondary prevention of cardiovascular disease (Article 31 procedure).
- Review of sibutramine-containing medicines (Reductil, Zelim, and Reduxade), because preliminary data from a study on long-term cardiovascular effects of sibutramine treatment in a population with high cardiovascular risk suggest a possible increased risk of serious cardiovascular events (Article 107 procedure).
- Review of topical formulations of ketoprofen, because of concerns over serious photosensitivity reactions (Article 107 procedure).
- Review of Yaz 24+4 and Ethinylestradiol/drospirenon 24+4 (ethinylestradiol/drospirenone) and associated names, because of differences among Member States on whether to include the indication "Treatment of emotional and physical symptoms of PMDD (premenstrual dysphoric disorder) in women seeking oral contraception" (Article 6(12) procedure).
- Review of Genotropin and associated names, because of differences among Member States regarding the addition of "growth disturbance in children with severe forms of juvenile chronic idiopathic arthritis, requiring long-term systemic glucocorticoid treatment, for improvement of growth and body composition" as a new indication (Article 6(12) procedure).
- Review of Seroquel XR and associated names (quetiapine fumarate), because of differences among Member States on the extension of the indication of the prolonged release formulation of Seroquel to the treatment of major depressive disorders (Article 6(13) procedure).
- The CHMP had adopted a set of recommendations aimed at minimising the risk of nephrogenic systemic fibrosis (NSF) with gadolinium-containing contrast agents in patients at risk of developing the condition. Because the risk of developing NSF depends on the type of gadolinium-containing contrast agent used, the active substances have been classified into three categories of risk (high, medium, and low-risk groups), and the CHMP's recommendations for the different agents varied according to their risk classification (Article 31 procedure for medicines authorised by Member States and Article 20 procedure for centrally authorised medicines (Optimark, Vasovist)). A re-examination of the CHMP's opinion on gadolinium-containing contrast agents for products concerned by the Article 31 procedure is under way.

Key performance indicator	Target	Outcome
Percentage of arbitration and referral procedures evaluated within the legal timeline	100%	100%
Publication of question-and-answer documents for Community interest referral procedures (Art. 31, 36, 107(2)) at the time of the CHMP opinion	100%	100%
Publication of the CHMP opinion and assessment report for Art. 5(3) procedures at the time of the CHMP opinion	100%	100%

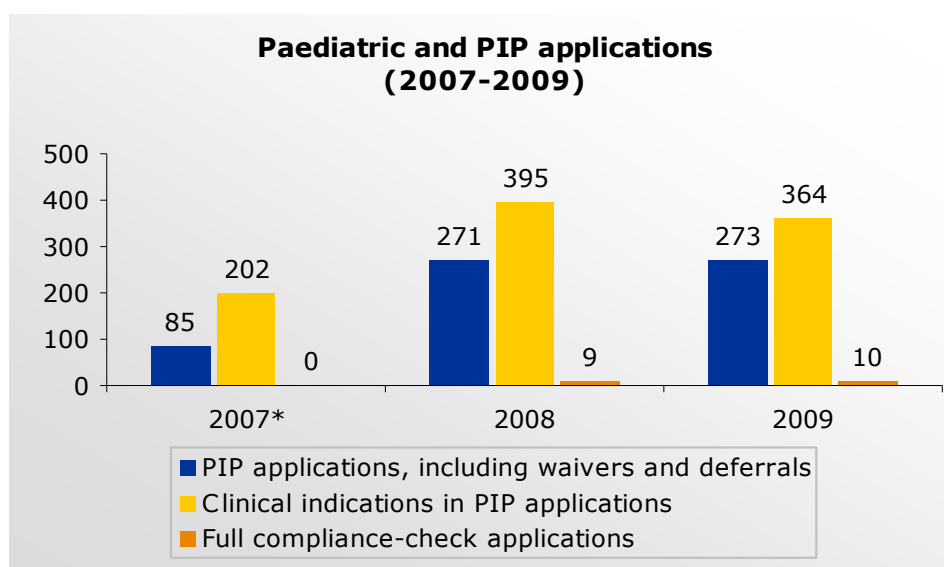
## 2.8. Medicines for children

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). An agreed PIP may lead to information on the paediatric use of medicines being included in a centralised or a national marketing authorisation, for new medicinal products, and in a paediatric-use marketing authorisation for off-patent products. It also includes agreement on the strategy for the establishment of the European network of paediatric research and the provision of information on clinical trials performed in children.

### Core activities

- In 2009, the Agency received applications for PIPs relating to 364 clinical indications. These correspond to 273 validated applications. This is about the same level of activity as in the previous year.
- The PDCO adopted a total of 253 opinions. Of these, 122 were positive opinions on PIPs, including potential deferrals; 67 were positive opinions on full waivers; 51 were positive opinions given for requests to modify already agreed PIPs. 13 opinions adopted by the PDCO were negative.
- Ten requests for full compliance checks were submitted to the Agency, and for these, the PDCO adopted eight positive opinions and one negative opinion. This is substantially below the forecast of 110 requests. The Agency did not foresee the higher number of requests for partial compliance checks not requiring a PDCO opinion (25 in 2009), and expected a significant number of requests for nationally authorised products. A compliance check is necessary before an application for a marketing authorisation can be considered valid. The Agency verifies that all required studies and measures have been carried out in accordance with the PIP.

Figure 28.



\* 2007 figures for the period July to December

## **Specific objectives**

### ***Streamlining PDCO assessment processes***

- The Agency continued to streamline the procedures for assessment of paediatric investigation plans, waivers and scientific advice, in light of the experience gained since the Paediatric Regulation was implemented. As part of this, a number of procedures were reviewed and updated procedural guidance was published.
- Work is ongoing on a procedure for strengthening the collaboration between the PDCO and the Scientific Advice Working Party.

### ***Liaison with paediatric learned societies***

- A number of paediatric learned societies were identified and invited to participate in the Agency's research network, the European Paediatric Network, and in expert meetings to discuss proposed PIP applications. As part of these efforts, the Agency organised several one-day expert meetings on topics such as diabetes, epilepsy, HIV and paediatric rheumatology. A further meeting was organised with the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), on paediatric hepatology.

### ***Inventory of paediatric needs***

- The Agency compiled the outcome of the survey of existing uses of medicinal products in the paediatric population in the Member States, in order to prepare the inventory of paediatric needs. Twenty out of 27 Member States submitted data, and the analysis is ongoing.

### ***Public access to paediatrics component of the EudraCT database***

- Development of a paediatric component in EudraCT, the EU database on clinical trials, was initiated. Public access to specified data, in line with guidance from the European Commission, will be delivered in 2010.

### ***Paediatric Research Network***

- The Paediatric Regulation provides for the Agency to develop a European network of existing national and European networks, investigators and centres with specific expertise in the performance of studies in the paediatric population. In a first step, the Agency started an initiative to identify all existing networks, centres and investigators with specific paediatric expertise. As part of this, the Agency held a workshop on the European Paediatric Network on 16 February 2009.
- Following the workshop, recognition criteria to be fulfilled by existing networks to become members of the European Paediatric Network were published for public consultation.

### ***Collaboration between European and US institutions on paediatric trials***

- The Agency, together with the Directorate-General Research of the European Commission, on the EU-side, and the National Institutes of Health (NIH) and the US FDA, on the side of the United States, started discussions on a new priority list for paediatric trials in the context of research into off-patent products. As part of these discussions, the Agency held a meeting with the NIH on criteria and methodology used for prioritisation.

Key performance indicator	Target	Outcome
Number of PIP or waiver opinions and decisions established within legal timelines	100%	100%
Number of paediatric trials entered into the EudraCT database	100%	Paediatric trial component of EudraCT still under development

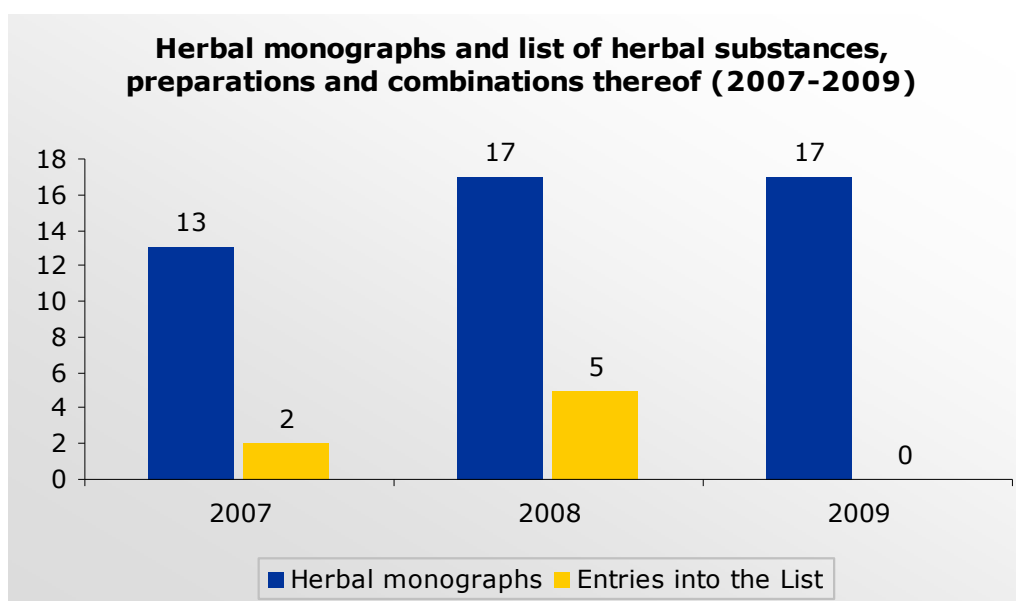
## 2.9. Herbal medicinal products

The Agency's activities in the area of herbal medicines include: establishment by the Committee on Herbal Medicinal Products (HMPC) of Community herbal monographs for traditional and well-established herbal medicinal products; establishment of a draft list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products; evaluation for referral and arbitration procedures concerning traditional herbal medicinal products; provision of opinions on herbal substances at the request of the CHMP; and provision of scientific opinions on questions relating to herbal medicines.

### Core activities

- The HMPC finalised 17 Community herbal monographs for traditional and well-established herbal medicinal products in 2009 – the same number as in 2008.
- Sixteen draft Community herbal monographs were published for public consultation.
- The Committee published five draft public statements on assessment work on herbal medicines for which a Community herbal monograph could not be established.
- No entry to the list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products was transmitted to the European Commission, and only one Community list entry was published for consultation.

Figure 29.



## Specific objectives

### **Cooperation with the European Food Safety Authority (EFSA)**

A joint meeting with EFSA took place in June 2009 to discuss the modalities of cooperation between both Agencies and their respective scientific groups on health claims and therapeutic indications for products containing herbal ingredients. A number of initiatives were identified to avoid the release of divergent positions in this field.

Key performance indicator	Target	Outcome
Number of Community herbal monographs (finalised/published for consultation)	20 Community herbal monographs	17 finalised 16 published for consultation 5 draft public statements released for consultation
Number of Community list entries (finalised/published for consultation)	5 Community list entries	0 transmitted to the European Commission 1 published for consultation

### **2.10. Advanced therapies and other emerging therapies and new technologies**

*This area relates to the activities undertaken by the Agency to support the scientifically sound development of advanced therapy medicinal products, including gene therapy, somatic cell therapy or human tissue engineered products, and other emerging therapies and new technologies that are not within the scope of the Advanced Therapies Regulation.*

#### **Establishment and activities of the Committee for Advanced Therapies**

The Agency's Committee for Advanced Therapies (CAT) was inaugurated in January 2009. The Committee deals with advanced therapy medicinal products (ATMPs) for human use that are based on gene therapy, somatic cell therapy or tissue engineering. These innovative medicines offer groundbreaking new treatment opportunities for diseases and injuries of the human body.

The CAT is a multidisciplinary committee made up of some of the best experts in the field. A large part of its work in 2009 was dedicated to implementing and further developing the regulatory framework for ATMPs, by drafting procedural and scientific guidelines for public consultation and helping applicants to prepare their applications for the procedures introduced by the new legislation.

The CAT also provided feedback to the Scientific Advice Working Party on scientific-advice requests for ATMPs, and to the Paediatric Committee on paediatric investigation plans for ATMPs.

A workshop for industry on the new procedures for ATMPs was held in April 2009, and a meeting with interested parties took place in September 2009. Training was also given to staff, CAT members and experts on procedural and scientific aspects of ATMPs.

### ***Marketing authorisation procedures for ATMPs***

- By the end of 2009, the Agency had received marketing-authorisation applications for three ATMPs.
- For one of these medicines, a tissue-engineered product containing chondrocytes, the CAT proposed a positive opinion to the CHMP.
- For another medicine, a gene therapy product containing sitimagene ceradenovec, the CAT adopted a draft negative opinion.
- The third medicine, a gene therapy product containing contusugene ladenovec, was withdrawn by the applicant prior to the adoption of a final opinion by the CHMP.

### ***Classification procedure***

The new classification procedure introduced by the Advanced Therapies Regulation received a great deal of interest from companies developing ATMPs. This procedure gives companies the opportunity to check whether the product they are developing can be considered an ATMP, in which case they can benefit from the new regulatory pathway for these types of medicines. The procedure is optional and takes place in advance of applying for a marketing authorisation.

- The CAT received 22 requests for classification in 2009, in respect of which 12 recommendations were adopted.

### ***Certification of quality and non-clinical data***

This is a new procedure introduced by the legislation on ATMPs, aimed at providing an incentive to small and medium-sized enterprises (SMEs) to conduct necessary studies to further develop their product.

- One request for certification of quality and non-clinical data from an SME developing ATMPs was received following the publication in July 2009 of Commission Regulation (EC) No 668/2009 implementing the ATMP Regulation.

## **Emerging therapies and innovative technologies**

### ***Biomarkers and other development methods***

- The Agency provided updates at international meetings on the experience it had gained with biomarkers and other development methods. Guidance to applicants on the qualification of novel methodologies for drug development was adopted by the CHMP and published in January 2009. Biomarkers play an increasingly important role at the global level for a more informed development of new medicines, and it is expected that they will contribute to an increased rate of success in making new medicines available to the public.
- The Agency discussed, with stakeholders, translational medicines development and new methods, such as modelling and simulation (M&S), in particular for medicinal products falling within the mandatory scope of the centralised procedure. Development of an M&S training plan was started in conjunction with the Scientific Advice Working Party and the new Biostatistics Expert Group (BSEG).
- In this context, the Agency also contributed to the IMI SAFE-T project, which relates to the qualification of translational safety biomarkers.

### ***Nanotechnologies in life sciences***

- The Agency established a working group of experts on nanotechnologies in life sciences. The first two meetings of this group were held in 2009.
- Other activities in this area included the completion of an overview of the Agency's experience on nanomedicines in the centralised procedure, and discussions at EU and international level on the definition of nanomedicines categories.

### ***Reinforced coordination between pharmaceuticals and devices authorities for the evaluation of targeted and combined medicinal products***

- A workshop with the pharmacogenomics expert group of the European Federation of Pharmaceutical Industry Associations (EFPIA) was held in the second quarter of 2009, which looked at how medicines and devices could be combined in the field of new therapeutic approaches.
- The Pharmacogenomics Working Party started a reflection paper on these issues.

### ***ITF activities***

- The Innovation Task Force (ITF), a multidisciplinary group that includes scientific, regulatory and legal competences, continued its activities in 2009.
- The group held 13 briefing meetings with companies developing medicines in the area of emerging therapies and new technologies.

<b>Key performance indicator</b>	<b>Target</b>	<b>Outcome</b>
Percentage of ITF briefing meetings organised within 60 days from receipt of a valid request	80% of meetings	85%
Percentage of regulatory advice requests and ITF regulatory advice on new, emerging and borderline medicinal products (excluding ATMPs) given within 60 days	80% of requests	100% (two advice requests from the Commission)
Percentage of applications handled by the Committee for Advanced Therapies within the procedural timelines (allowing adoption of the opinion by the CHMP within the legal timeline of 210 days)	100% of applications	100%
Scientific recommendations on advanced-therapy classification provided within the legal timeline	100% of requests	100%
Certification of quality and non-quality data issued within the procedural timelines	100% of requests	(no certification procedure finalised yet)

## **2.11. Provision of information to patients and healthcare professionals**

*The Agency has implemented processes and procedures aimed at the provision of targeted, understandable and accessible information for patients and healthcare professionals. In addition to summaries of opinions, European public assessment reports (EPARs) and information on arbitrations and referrals, the Agency provides a wide range of information. This includes EPAR summaries for the public, information on emerging safety issues, information on the withdrawal of applications prior to Commission decision and information on negative decisions, for new applications and for extensions to existing indications.*

### **Provision of information**

The Agency made further efforts in 2009 to provide high-quality, timely, targeted and understandable information.

- The Agency continued to systematically publish summaries of opinions at the time of the adoption of CHMP opinions for all medicines for which a recommendation for initial marketing authorisation or extension of an existing indication was adopted.
- In addition, specific press releases and question-and-answer documents were systematically published on safety-related issues, following the scientific assessment of centrally authorised medicines or, in the case of non-centrally authorised medicines, in the context of referral procedures initiated at the level of the CHMP.
- There was limited compliance with the objective to publish EPARs, for new medicines, and EPAR-updates, for existing medicines, within two weeks of the Commission decision. However, by the end of 2009, 87% of the EPARs on the Agency's website were up to date.

### **Transparency**

- In September 2009, the Agency began publishing monthly reports on the outcome of its Pharmacovigilance Working Party's scientific evaluation of non-centrally authorised medicines that are not subject to a formal referral procedure.

### **Interaction with patients and healthcare professionals**

- Interaction with patients' organisations further progressed in 2009, and all actions identified in the framework of interaction were implemented.
- The 2008 analysis of the degree of satisfaction of patients' organisations as regards their involvement in Agency activities was finalised and subsequently published.
- Discussions on the development of a formal framework for the Agency's interaction with healthcare professionals' organisations continued and should result in a final document by the end of 2010.

### **Product information quality, quality review of documents and translation**

- Activities in relation to the quality review of documents, including the translation of product-related information, progressed as scheduled.
- User-consultation was monitored through an analysis of all user-testing reports submitted between 2005 and 2009. The report was presented at the June 2009 Quality Review of Documents (QRD) plenary meeting, and follow-up on the outcome of the analysis is being undertaken.

Key performance indicator	Target	Outcome
Percentage of summaries of opinions published at the time of the CHMP press release	90%	100%
Percentage of initial EPARs published within two weeks of the Commission decision	80%	28%
Percentage of EPAR summaries published together with the EPAR	90%	100%
Percentage of assessment reports published within two months following withdrawal of a marketing-authorisation application	70%	50%
Percentage of refusal assessment reports published within two weeks of the Commission decision	70%	0%
Percentage of question-and-answer documents for Community interest referrals and Article 107(2) procedures published at the time of the CHMP opinion	100%	100%

## **2.12. Scientific committees, working parties and scientific advisory groups**

### **Committee for Medicinal Products for Human Use (CHMP)**

The CHMP is responsible for the scientific evaluation and provision to the European Commission of scientific opinions for the authorisation and maintenance of medicinal products. The CHMP provides scientific advice and protocol assistance to pharmaceutical enterprises during the process of medicines development. The CHMP also provides scientific opinions on medicinal products subjected to arbitration or referral procedures, on medicinal products intended for use outside the EU, and on any scientific matter at the request of the European Commission or the Executive Director of the Agency. Furthermore, the CHMP is involved in work undertaken in the fields of harmonisation of technical requirements for pharmaceutical regulation, pharmacovigilance and public-health threats.

The CHMP held 11 meetings in 2009, each of them lasting four days.

### **Committee for Orphan Medicinal Products (COMP)**

The COMP is responsible for making recommendations to the European Commission on the designation of orphan medicinal products for rare diseases. The COMP is also responsible for advising the European Commission on the development of policy on orphan medicinal products, and for assisting the liaison with international partners and patients' organisations on this issue.

The COMP met 11 times in 2009, with each meeting lasting up to two days.

### **Committee on Herbal Medicinal Products (HMPC)**

The HMPC establishes Community herbal monographs. Other core tasks include the establishment of a draft 'Community list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products', as well as the provision of scientific opinions to EU Member States and European institutions on questions relating to herbal medicinal products. With these activities, the HMPC helps to harmonise procedures and provisions concerning traditional herbal medicinal products laid down in the Member States, and helps to further integrate herbal medicinal products in the European regulatory framework.

The HMPC met 6 times in 2009, with each meeting lasting one-and-a-half days.

### ***Paediatric Committee (PDCO)***

The PDCO conducts assessment and agreement of paediatric investigation plans, and verifies their compliance. The PDCO also establishes lists of waivers of specific medicines or classes of medicines that are not suitable or necessary for the treatment of children. The PDCO advises the Agency on the development of a European network of paediatric research.

The PDCO met 11 times in 2009, with each meeting lasting up to three days. A twelfth meeting was held via written procedure in August 2009.

### ***Committee for Advanced Therapies (CAT)***

The CAT is a multidisciplinary committee, gathering together some of the best experts in Europe to assess the quality, safety and efficacy of advanced therapy medicinal products (ATMPs) and to follow scientific developments in the field. One of its main tasks is to prepare a draft opinion on each ATMP application before the CHMP adopts a final opinion on the granting, variation, suspension or revocation of a marketing authorisation for the medicine concerned.

Other responsibilities of the CAT include the evaluation and certification of quality and non-clinical data on ATMPs under development by small and medium-sized enterprises, and the provision of recommendations on the classification of ATMPs.

The CAT is the latest addition to the Agency's group of scientific committees, bringing the total number up to six.

The CAT met 11 times in 2009, including its inaugural meeting held on 15 and 16 January 2009.

### ***Standing and temporary working parties and scientific advisory groups***

The working parties of the Agency's scientific committees responsible for medicinal products for human use are involved in the development and revision of guidelines and the provision of recommendations and advice on medicinal products for which applications are made. In addition, they contribute to marketing-authorisation, traditional-use registration, post-authorisation and post-registration activities, according to the specific area of responsibility of each group. This includes providing advice and recommendations on general public-health issues relating to medicinal products.

Scientific advisory groups (SAGs) are established by the CHMP to evaluate and advise on specific types of medicinal products or treatments. They are composed of experts from academia and university hospitals, representing various schools of thought and medical practices in the EU. More than 21 SAG meetings took place in 2009.

## **Specific objectives**

### ***Involvement of stakeholders in work-planning of working parties***

The Agency is committed to increased involvement of stakeholders in the activities of the working parties. A number of stakeholder consultations were organised in 2009 to identify aspects of mutual interest and to define priority areas for inclusion in the working parties' work programmes.

### **Virtual meetings**

The Agency extended the use of virtual meetings in order to improve efficiency when involving experts and disseminating training in 2009. Teleconferencing, videoconferencing and web-based meetings were organised for several guideline-drafting groups and some plenary meetings.

### **Biostatistics Expert Group**

The Agency formally established the Biostatistics Expert Group (BSEG) of the Efficacy Working Party. Part of the mandate of this group will be to provide expert insight into methodological and statistical issues concerning the development of medicinal products and the design of tests and clinical trials. The group will also further develop the network of biostatisticians within the European medicines network.

## **2.13. Coordination Group for Mutual-Recognition and Decentralised Procedures – Human**

*The Agency provides secretarial support to the Coordination Group for Mutual-Recognition and Decentralised Procedures – Human (CMDh) and its sub-groups/working groups, in accordance with the approved rules of procedure. The work of the CMDh is essential for the effective authorisation and maintenance of more than 90% of medicines entering the EU market. The mutual-recognition procedure (MRP) and the decentralised procedure (DCP) are the primary authorisation routes for generic applications within the EU. Through its work on referral procedures and the identification of summary-of-product-characteristics (SPC) harmonisation lists, the CMDh supports the entry of such products into the EU market.*

### **Core activities**

The CMDh met 11 times in 2009, with each meeting lasting up to two-and-a-half days.

A full report on CMDh activities in 2009 is available at:

[http://www.hma.eu/fileadmin/dateien/Human\\_Medicines/CMD\\_h\\_/About\\_CMDh/Reports/CMDh\\_159\\_2010.pdf](http://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/About_CMDh/Reports/CMDh_159_2010.pdf)

The Agency's CMDh secretariat also coordinates the 60-day procedure, including communication with applicants, organisation of oral explanations, monitoring compliance with the respective timetable and communication of the outcome of 60-day procedures to interested parties in the CMDh press release.

- Twenty MRP applications and 19 DCP applications were referred to the CMDh in 2009.
- Agreement was reached for 14 MRP applications and 18 DCP applications. Two of the MRP applications and eight of the DCP applications had been referred to the CMDh in 2008.
- For three MRP and eight DCP applications, no agreement was reached, and they were subsequently referred to the CHMP in accordance with Article 29(4) of Directive 2001/83/EC as amended.
- The CMDh published on its website a table with all applications referred to the CMDh and, for the ones referred to the CHMP, a link to the respective Commission decision.

The CMDh finalised the 2009 list of medicinal products for SPC harmonisation and forwarded it to the European Commission.

## **Specific objectives**

### ***Implementation of paediatric legislation***

- The CMDh/EMA Sub-group on Paediatric Regulation met regularly in 2009 in order to prepare the worksharing for the assessment of paediatric studies submitted according to Articles 45 and 46 of the Regulation (EC) 1901/2006. The Sub-group agreed on the lists of active substances to be included in the consecutive waves of the worksharing procedure according to Article 45, and published this information on the CMDh website.
- The CMDh agreed on a document with recommendations for implementation of the Commission decisions following applications under Article 29 of the Paediatric Regulation.
- The CMDh published a Best Practice Guide to facilitate the assessment of information in a harmonised way according to Article 46 of the Paediatric Regulation.
- The CMDh also published a recommendation on Paediatric Use Marketing Authorisations (PUMA) and a recommendation for implementation of a compliance statement for the agreed completed PIP, including a related template.
- In July 2009, a workshop on the Paediatric regulation was held for assessors.

### ***Implementation of advanced therapies legislation***

- The CMDh worked together with the Agency to provide information on advanced therapy medicinal products legally available on the market, in order to plan the future workload of the CAT, CHMP, Agency and relevant national competent authorities.

### ***Implementation of the variations legislation***

- The Sub-group on Variation Regulation met regularly in 2009.
- The CMDh provided comments on the European Commission's draft guidelines regarding the Variations Regulation.
- A sub-group worked on the update of the CMDh best-practice guide for the submission and processing of variations in the MRP, and developed new chapters on grouping and worksharing, including the numbering system for grouping and worksharing. The best-practice guide was published in October 2009.
- The CMDh developed, in cooperation with the CMDv and the Agency, a best-practice guide for handling requests for recommendations on the classification of unforeseen variations, in accordance with Article 5 of Commission Regulation (EC) No 1234/2008.

### ***Improving the functioning of the CMDh***

- Work progressed on further improving the functioning of the CMDh in accordance with an agreed action plan.
- The CMDh published on its website a report on the outcome of the questionnaires to CMDh members and interested parties on the evaluation of the functioning of the CMDh and the main actions proposed to address the issues raised. Actions for improvement identified by this survey include the improvement of the CMDh website, the publication of presentations given in meetings with interested parties, the inclusion of a numbering system in CMDh documents, publication of the mandates of the sub-groups and the review of the rules of procedure of the CMDh.

### ***Influenza pandemic***

- The CMDh cooperated closely with the Agency on all aspects related to pandemic medicines authorised at the level of the EU Member States. For a coherent and systematic approach, the CMDh developed a pandemic plan, which was published in July 2009. The action plan was followed up regularly at the CMDh meetings.

## **2.14. Regulatory activities**

*The Agency provides regulatory and procedural advice to the pharmaceutical industry during the lifecycle of medicinal products, from scientific advice and pre-submission meetings with applicants through to post-authorisation and annual meetings with marketing-authorisation holders. It develops and updates guidance documents focusing on the key steps of the centralised procedure, as well as on issues of quality, safety and efficacy of medicinal products, to facilitate use of the centralised procedure and support the submission of applications of the required quality.*

*The Agency also works to continuously address regulatory and procedural issues affecting its committees, standing and temporary working parties, and associated groups.*

### **Specific objectives**

#### ***Support to scientific committees***

- In addition to the regulatory support provided throughout the lifecycle of medicinal products, the emphasis in 2009 was on regulatory support provided to the scientific committees and working parties, in particular to the CHMP, aspects handled at the level of the Paediatric Committee, and regulatory advice to the Committee on Advanced Therapies.

#### ***Influenza pandemic***

- Extensive regulatory support was provided in relation to the influenza pandemic. The Agency explored all possible regulatory pathways to bring pandemic vaccines to the market in a timely manner and provided advice to applicants, the European Commission and the national competent authorities.

#### ***Implementation of variations legislation***

- At the end of February 2009, the Agency provided to the European Commission draft guidelines on the detailed classification of variations and on the procedure for the handling of variations according to the new regulation. Extensive feedback was given to the European Commission on the comments received during the public consultation. The guidelines were published in November 2009 on the European Commission's website.
- Various regulatory guidance documents were updated, and regular training to the Agency's staff on various topics stemming from this new legislation was provided.

## 3. Medicines for veterinary use

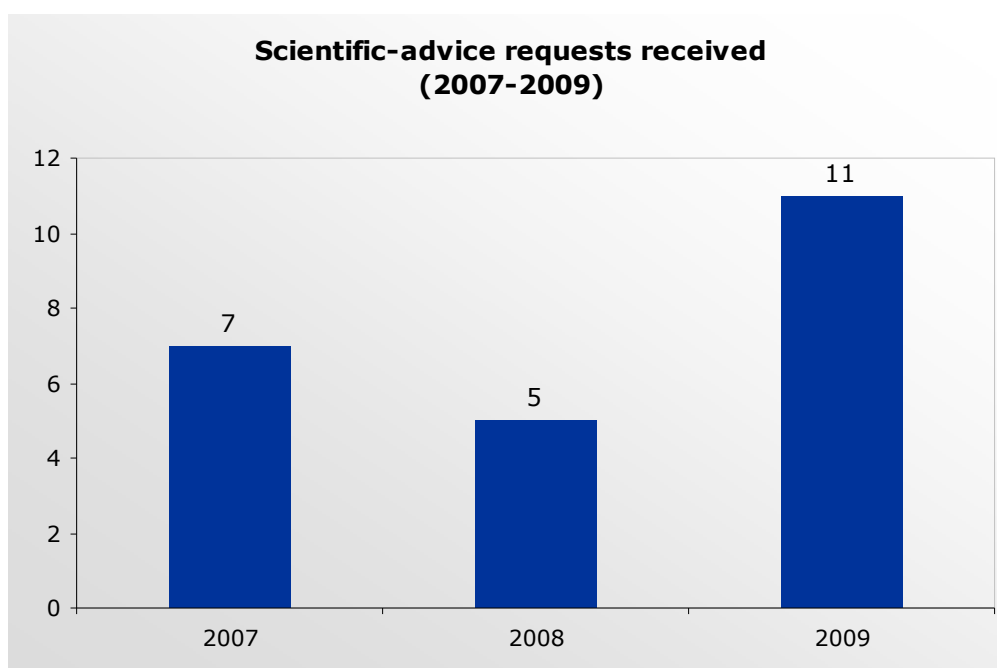
### 3.1. Scientific advice

*This priority area relates to the provision of scientific advice to applicants during the research and development of medicinal products. Scientific advice is provided on any aspect of research and development relating to quality, safety or efficacy of medicinal products, and to the establishment of maximum residue limits.*

#### Core activities

- A range of improvements were introduced in the scientific-advice procedure, and the procedure was more widely publicised among the veterinary pharmaceuticals industry. These measures resulted in a doubling of the number of applications received, and a continued increase of requests seems highly likely.
- Uptake of the procedure was strong among small and medium-sized enterprises (SMEs), indicating their keen interest in taking advantage of the incentives offered. Approximately 60% of requests in 2009 were from SMEs.
- An increase in applications for products to be authorised via the decentralised and mutual-recognition procedures was also seen, reflecting the efforts made to attract such applications.

**Figure 30.**



#### Specific objectives

- The criteria for providing free scientific advice in relation to the development of products indicated for minor uses/minor species (MUMS) or limited markets were amended in 2009, and a new policy offering the possibility of requesting classification of such products by the Committee for Medicinal Products for Veterinary Use (CVMP) came into force on 1 September. It is anticipated that this will provide an incentive for developing such products and increase the number of scientific-advice

applications for this type of product, thus contributing to the availability of products for MUMS and limited markets.

- A new category of scientific advice was introduced, allowing applicants to ask for a general review of the data requirements for a specific product intended for MUMS/limited markets in line with adopted guidelines on MUMS data requirements.

### **Promoting awareness of the scientific-advice procedure**

- The provision of scientific advice in parallel with the US Food and Drug Administration (FDA), as part of the European Commission/FDA confidentiality arrangements, was promoted among potential applicants. While no new applications for such joint advice have yet been received, potential applicants have shown interest.
- The veterinary scientific-advice procedure was also promoted at the SME stakeholders meeting in May 2009 and the MUMS workshop in October 2009.

Key performance indicator	Target	Outcome
Scientific-advice requests evaluated within the procedural timelines	90% of applications	100%

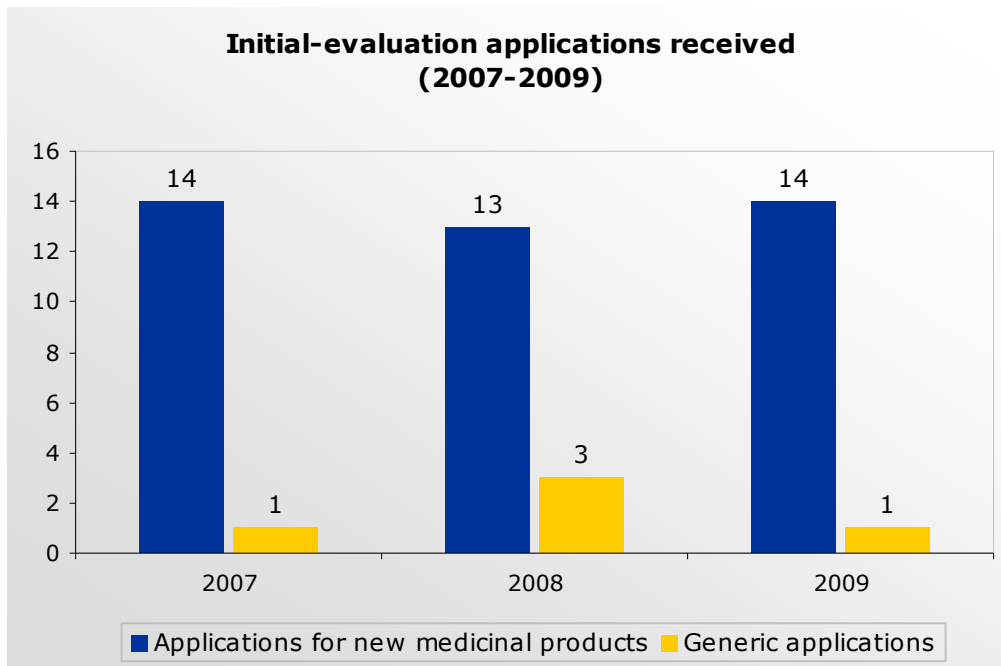
### **3.2. Initial evaluation**

*The initial evaluation phase covers a number of Agency activities ranging from pre-submissions with future applicants, through evaluation by the CVMP, to the granting by the European Commission of the marketing authorisation. The Agency publishes a European public assessment report (EPAR) once the Commission decision has been taken.*

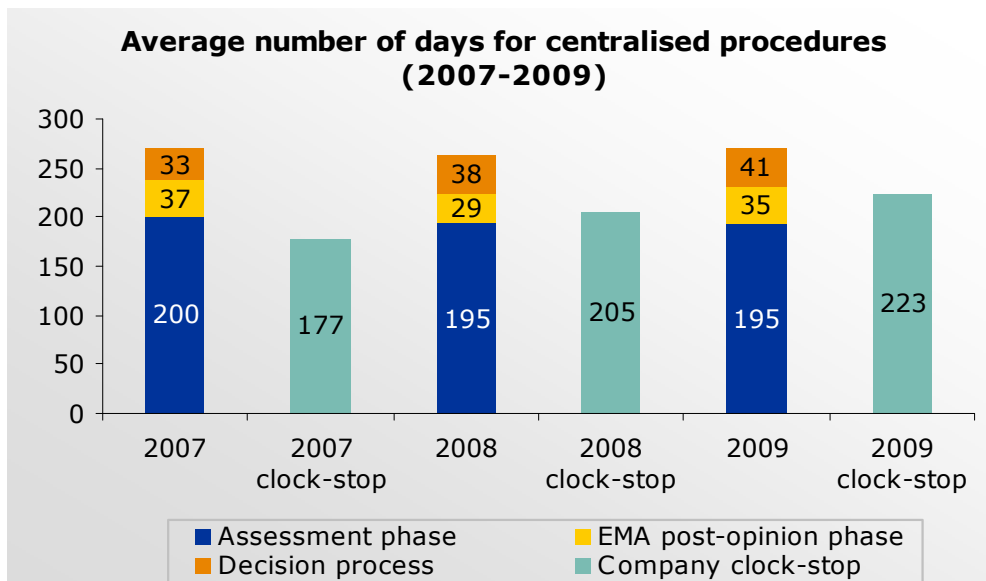
#### **Core activities**

- While for 2009 as a whole, a more steady state of submission of applications compared to 2008 was observed, the predicted increase of applications for new products was confirmed towards the end of 2009 with a surge in applications received in December. Judging by letters of intent received from applicants, this trend is expected to continue in 2010.
- The increase observed in recent years in terms of requests for authorisation under exceptional circumstances for vaccines against epizootic diseases of livestock (avian influenza and Bluetongue, in particular) continued. The interest in new vaccines for food-producing animals observed over the past years was confirmed with over 50% of new applications received concerning vaccines for these species.
- All new applications for pharmaceutical products were intended for companion animals.
- Only one application submitted for a new veterinary medicine concerned a generic product.
- Of particular interest in terms of animal health, the Agency issued a positive opinion for a vaccine that offers an alternative to surgical castration of piglets, thereby expanding the range of options for dealing with this challenging animal-health concern.
- The first centralised authorisation of a vaccine against Bluetongue disease provided a tool for control of this disease useable by all national control authorities within the EU.

**Figure 31.**



**Figure 32.**



### Specific objectives

- The peer-review initiative by the CVMP as part of the quality-assurance system was reviewed, following a pilot phase, and a modified version will be proposed as a permanent system for initial applications, extensions, major variations and MRL applications and referrals.
- The benefit-risk recommendations developed by the CVMP were implemented and a training programme for CVMP and working-party members was launched.
- The Agency provided input to the Heads of Medicines Agencies' task force on the review of the veterinary legislation, and a CVMP task force was set up to provide proposals for the future

veterinary legislation by March 2010. The objective is to develop proposals for consideration by the European Commission to improve the efficiency and effectiveness of authorisation procedures for veterinary medicinal products within the EU.

Key performance indicator	Target	Outcome
Percentage of products evaluated within the regulatory timeline of 210 days	100% of applications	100%

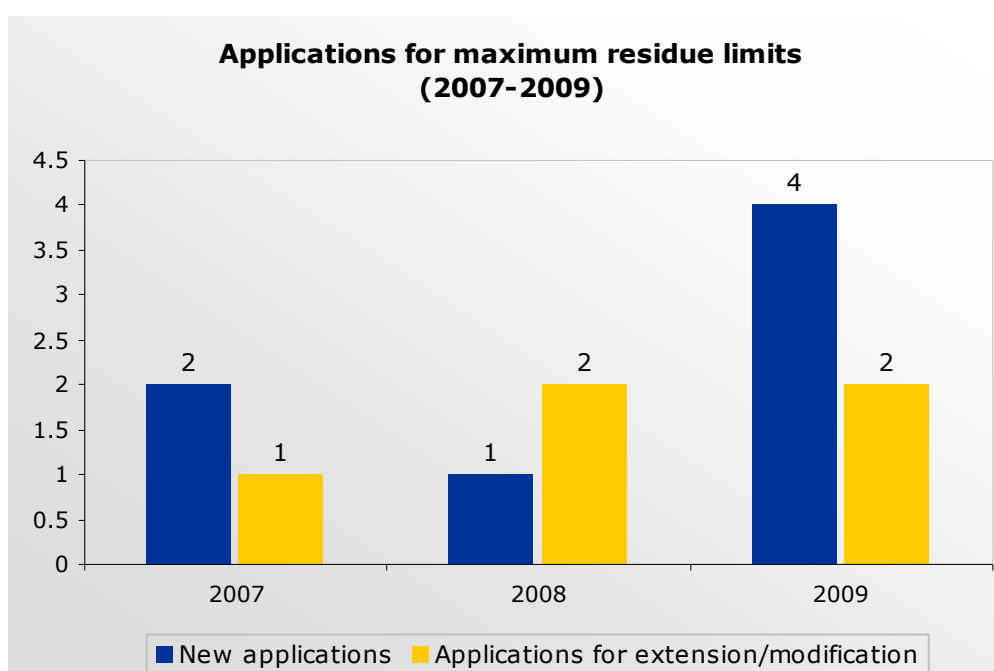
### 3.3. Establishment of maximum residue limits

The use of veterinary medicinal products in food-producing animals may result in the presence of residues in foodstuffs obtained from treated animals. Before a veterinary medicinal product can be authorised, an evaluation of the safety of residues must be carried out. The Agency establishes maximum residue limits (MRLs) for pharmacologically active substances used in veterinary medicinal products, to provide for the safe use of foodstuffs of animal origin, including meat, fish, milk, eggs and honey.

#### Core activities

- In 2009, the Agency received and validated four new applications for MRLs, of which one was a re-submission after a previous negative opinion.
- The number of applications submitted for extension or modification of MRLs remained low, with two applications, as predicted. No requests for extrapolations of MRLs were received.
- Concerns remain in this low interest in MRL extensions and extrapolations, as this indicates a continued lack of interest in extending existing marketing authorisations to minor species, despite the efforts of facilitating the marketing authorisations for MUMS products and establishing specific guidelines allowing reduced data requirements to cater for these products. The impact of the implementation of new incentives under Article 79 of Regulation (EC) No 726/2004 and the new MRL Regulation will be monitored in coming years.

Figure 33.



## Specific objectives

- Good progress was made on implementing the new MRL Regulation (Regulation 470/2009), adopted in June 2009. Proposals for extending the list of essential substances for horses, for withdrawal periods and MRLs for substances used under the cascade were prepared and are under review by the Commission.
- The CVMP has, since its inception, commented on draft Codex MRLs. This activity has now taken on a new significance in view of the potential for adoption of Codex MRLs within the EU that is foreseen within the new MRL Regulation. The CVMP reviewed and provided comments on 6 Codex MRLs in this context during 2009.

Key performance indicator	Target	Outcome
Percentage of applications evaluated within the 120-day timeline	100% of applications	100%

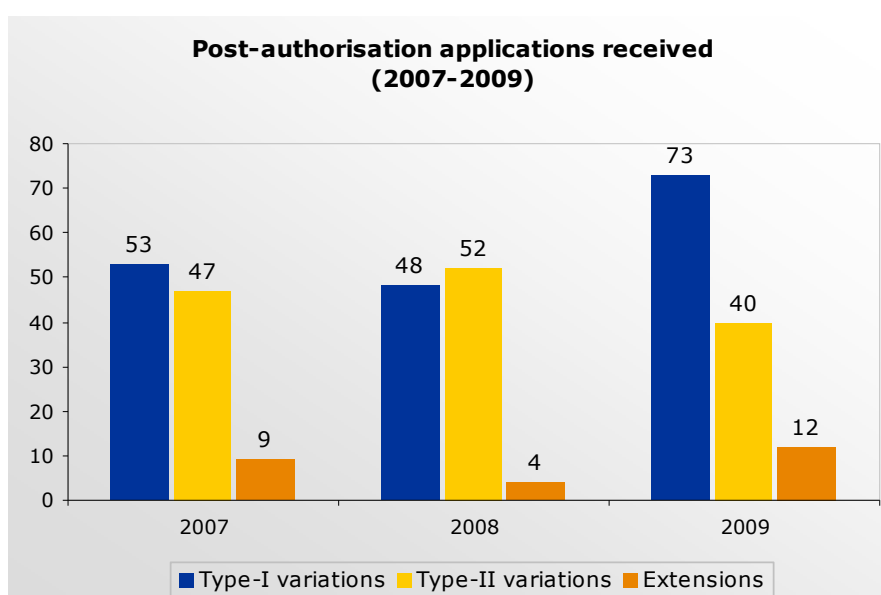
### 3.4. Post-authorisation activities

Post-authorisation activities relate to variations, line extensions and transfers of marketing authorisations. Variations to marketing authorisations can be either minor (type-I) or major (type-II) changes.

#### Core activities

- A higher number of type-I variations were received in 2009 than in the previous year. It is assumed that the increase was due to companies choosing to submit variations under the old and well-known Variations Regulation.
- The number of line-extension applications received in 2009 was slightly higher than in 2007, and considerably higher than the four received in 2008. The extensions concerned mainly antimicrobial, antiparasitic or anti-inflammatory products, and were mainly for new indications, pharmaceutical forms or new (food-producing) target species.

Figure 34.



## Specific objectives

The necessary guidance for implementing the new Variations Regulation was prepared and published, although partly in draft form. The updating of all guidance will be completed in 2010.

Key performance indicator	Target	Outcome
Percentage of applications for type-I and II variations and line extensions evaluated within the regulatory timelines	100% of applications	99% of applications  32 type-IAs were handled in 2009 with an average time of 10.1 days (well under the required timeline of 14 calendar days); one type-IA took 18 days  Type-IB and type-II variations were handled within the required timelines

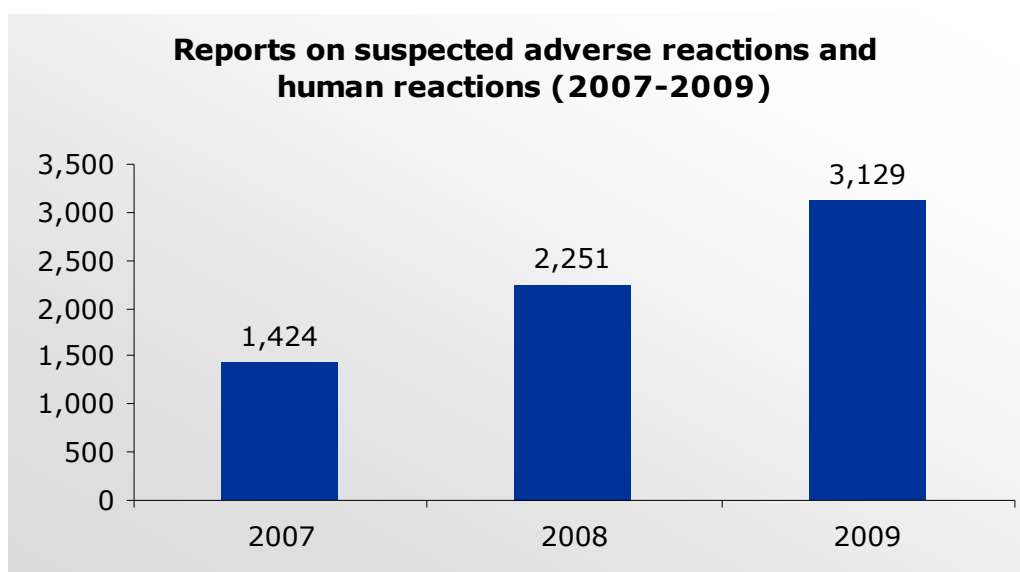
### 3.5. Pharmacovigilance and maintenance activities

*This activity relates to pharmacovigilance information, including adverse-reaction reports and periodic safety-update reports (PSURs). Pharmacovigilance remained a high priority for the Agency in 2009, to ensure that post-authorisation monitoring and effective risk-management are continuously applied to veterinary medicines throughout the EU.*

#### Core activities

- In total, 3,129 spontaneous serious suspected adverse reaction reports and human reaction reports regarding centrally authorised veterinary medicinal products were received and processed in 2009. This increase of approximately 40% over the number of such reports recorded in 2008 is likely to reflect greater awareness of the need to report suspected adverse reactions, rather than an absolute increase in the number of reactions occurring. Furthermore, the increased number of centrally authorised products reaching the market may also partly explain the increased reporting.
- Of these reports, 2,858 related to suspected adverse reactions in animals and 271 to reactions in humans following exposure to a veterinary medicinal product.
- Of the 2,858 reports of suspected adverse reactions in animals, 2,371 concerned companion animals (mainly dogs and cats) and 487 concerned food-producing animals (mainly cattle, pigs, and sheep).
- Reports relating to food-producing animals were double the number received in 2008. This was due to increased awareness of pharmacovigilance reporting requirements in the network of professionals who deal with food-producing animals, not to an increase in the number of adverse events occurring in domestic livestock.
- The number of safety-update reports received – 95 PSURs and 17 PSUR addendum reports – was largely as predicted. The streamlining of the procedure, with improved processes and more extensive implementation of the recommendation on PSUR assessment and management, led to an increase in the efficiency of the evaluation procedure.

**Figure 35.**



### **Specific objectives**

- A reflection paper on the concept of risk-management plans for veterinary medicines was published for consultation.
- At the end of 2009, Volume 9B of the revised 'Rules governing medicinal products in the European Union' was being finalised by a sub-group of the Pharmacovigilance Working Party (PhVWP-V), following receipt of comments from the European Commission on the earlier draft.

### **Progress with EudraVigilance Veterinary**

- The implementation and development of EudraVigilance Veterinary (EVVet) continued in 2009 in accordance with the EVVet Action Plan. Thirty-two competent authorities are registered, with a total of 150 different users. There are also 111 organisations registered (marketing-authorisation holders and third parties), with a total of 176 different users. All major companies are now registered and operating electronic reporting via EVVet.
- The database now contains about 27,000 adverse event reports from within the EEA and about 6,000 from outside the EEA (third-country reports), compared to 23,000 at the end of 2008. Of these, 2,100 concern reactions observed in humans related to the use of a veterinary medicinal product.
- With the further improvements of the Data Warehouse (DWH), training sessions for regulatory users and the ongoing development of guidance for use of EVVet data for signal detection, considerable progress was made in 2009 towards scientific analysis of EVVet data. In particular, for centrally authorised products, the CVMP is now using the DWH queries to directly access the EVVet data for continuous surveillance. The limiting factor before EVVet can be used efficiently for surveillance of all veterinary medicines in the EU remains the lack of product information for non-centrally authorised products.

Key performance indicator	Target	Outcome
Percentage of PSURs evaluated within the established timelines	80%	94%* of PSURs assessed
Percentage of suspected adverse reaction (SAR) reports evaluated within the established timelines	100%	100% of SARs

\* The assessment of PSURs submitted with renewals follows the evaluation procedure for the renewals; these PSURs were therefore not taken into account in this calculation.

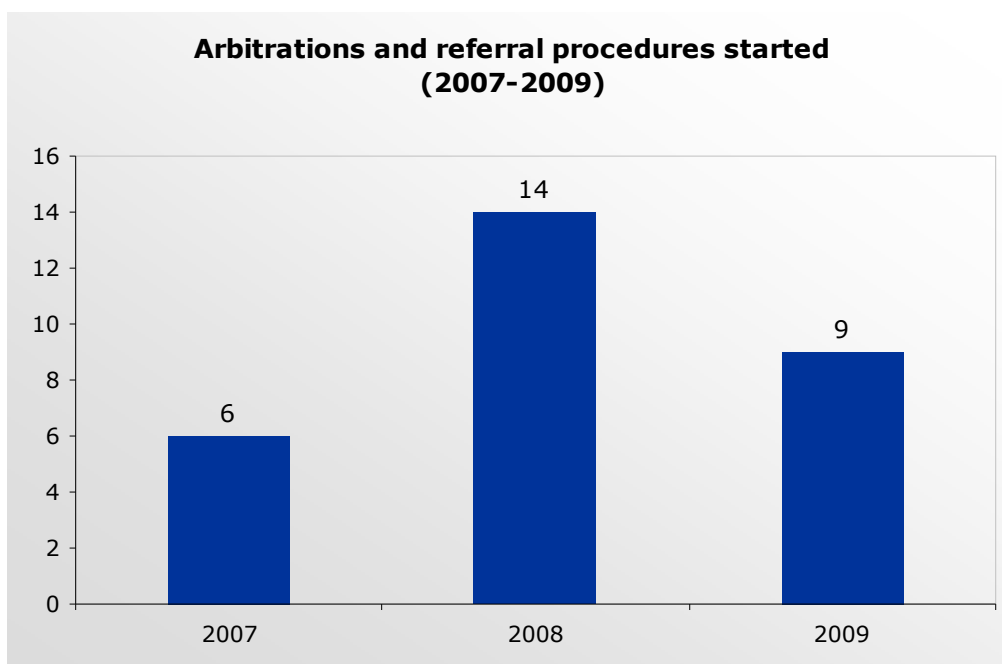
### 3.6. Arbitration and referrals

*Arbitration procedures are initiated because of disagreement between Member States within the framework of the mutual-recognition procedure (Article 33 of Directive 2001/82/EC, as amended). Referrals are initiated either in order to obtain harmonisation within the European Union of the conditions of authorisation for products already authorised by Member States (Article 34 of Directive 2001/82/EC) or in cases involving the interests of the Union or concerns relating to the protection of human or animal health or the environment (Articles 35 and 40 of Directive 2001/82/EC).*

#### Core activities

- The nine referrals submitted in 2009 was a considerably lower number than predicted. However, several of the referrals submitted under Article 35 concerned over 1,000 marketing authorisations, were very complex in nature or raised fundamental questions regarding the implementation of legislation, and therefore required high technical and regulatory input.
- The CVMP concluded a total of 15 referral procedures in 2009, of which five required re-examination following requests from applicants or marketing-authorisation holders.
- The lower number of Article 33 referrals indicates that several problems regarding interpretation of legislation or guidelines seem to have been solved, and that the recommendations given previously by the CVMP are being accepted by Member States.
- Eight of the referrals finalised in 2009 related to veterinary medicinal products containing antimicrobial substances, reflecting the ongoing high level of concern within the EU to ensure that such products are authorised with appropriate conditions of use.
- The Committee finalised a referral relating to the use of ivermectin-containing products, involving almost 300 products administered by injection to cattle, and was able, for the first time, to propose harmonised withdrawal periods for a class of products.

**Figure 36.**



### Specific objectives

- The CVMP made considerable progress on establishing internal guidance for the processing of referrals, as part of a range of activities aimed at maximising the efficiency of the process, ensuring consistency in approach and allowing for experience gained with previous referrals to be applied.
- A joint task force of CVMP members, CMDv members and the secretariat was set up to address, in particular, strategic considerations regarding referrals, aimed at developing tools for prioritisation, longer-term strategies and best use of resources of the network.

Key performance indicator	Target	Outcome
Percentage of arbitration and referral procedures managed within the legal timeline	100%	100%

### 3.7. Scientific committee

*The Committee for Medicinal Products for Veterinary Use (CVMP) is responsible for preparing the Agency's opinions on all questions concerning veterinary medicinal products, in accordance with Regulation (EC) No 726/2004.*

In addition to the routine work of the CVMP in terms of adopting decisions relating to the authorisation of veterinary medicinal products, the CVMP was active in the areas described below.

#### **Methodology for benefit-risk assessment**

- The CVMP developed a methodology for the systematic and scientifically robust assessment of the benefit-risk balance of medicines for veterinary use. Its recommendations were finalised in 2009,

following extensive public consultation. To ensure consistent understanding and application of the new guidance, training was provided to CVMP members and working parties.

### **Activities relating to antimicrobial resistance**

- The Agency and the CVMP, together with its Scientific Advisory Group on Antimicrobials (SAGAM), devoted much effort in 2009 to activities aimed at minimising the risks of the further development of antimicrobial resistance arising from the use of veterinary medicinal products.
- On the basis of recommendations from the SAGAM, the CVMP finalised its reflection paper on third- and fourth-generation cephalosporins, critically reviewing recent data on their use and their potential impact on resistance-development in relation to human and animal health, following public consultation in 2008. The document also includes recommendations aimed at minimising the development of resistance.
- In order to ensure full implementation by all Member States of the risk-management actions for (fluoro)quinolone-containing veterinary medicines, as previously proposed by the CVMP, the European Commission initiated an Article 35 referral concerning all veterinary medicinal products authorised in the EU containing these substances.
- On the basis of recommendations from the SAGAM, the CVMP adopted and published a reflection paper on meticillin-resistant staphylococcus aureus (MRSA) in food-producing and companion animals in the EU.
- A joint scientific report on MRSA in livestock, companion animals and food was prepared by the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency, with the CVMP contributing, titled 'MRSA in food-producing and companion animals in the European Union: Epidemiology and control options for human and animal health'.
- A joint scientific opinion on antimicrobial resistance, focusing on infections transmitted to humans from animals and food (zoonoses), was prepared and published by ECDC, EFSA, the European Medicines Agency, and the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). The joint opinion concluded that bacterial resistance to antimicrobials had increased in recent years worldwide, making it more difficult to treat some human and animal infections. The report recommended that surveillance activities be strengthened and the development of new antimicrobials and new strategies to combat the spread of resistance encouraged. Research is needed on other strategies to control infectious diseases in animals, such as vaccination programmes.
- The CVMP provided technical support to the European Commission on its involvement in the Codex Alimentarius Intergovernmental Task Force on Antimicrobial Resistance, which aims to develop methodology for risk assessment and risk management in relation to food-borne antimicrobial-resistant microorganisms.
- A joint meeting with the HMA and stakeholders was organised with the Czech Presidency to discuss how the HMA and the Agency could best cooperate with respect to implementing CVMP recommendations on antimicrobial resistance, promoting the prudent-use agenda and coordinating the collection of data on sales of antimicrobials used as veterinary medicines within the EU.
- The Agency initiated a project to coordinate at a European level the collection by Member States of harmonised data on use in the EU of antimicrobials in food-producing species and companion animals.

### **Environmental risk assessment**

- The CVMP, with the support of its Working Party on Environmental Risk Assessment, continued to provide advice on the implementation of the requirements of the amended veterinary directive regarding environmental risk assessment. This is a high-profile and difficult area in which the requirements for a thorough environmental risk assessment need to be weighed against the impact that excessive data requirements could have on the availability of veterinary medicines. Detailed practical guidance to applicants and competent authorities intended to facilitate carrying out the environmental risk assessments for veterinary medicinal products and to allow for a harmonised approach was finalised following public consultation of a reflection paper in 2008. An amended version of this guidance has since been published by the Commission as part of the Notice to Applicants.

### **Liaison with other scientific committees and EU institutions**

- The Committee maintained close working relationships with a number of other scientific committees of EU institutions to ensure consistency and relevant exchange of information. Notably, there were numerous exchanges with the scientific panels of the European Food Safety Authority.

### **Working parties and scientific advisory groups**

- The working parties of the CVMP continued to be very active during 2009, developing or updating a wide range of guidelines and guidance documents.
- Focus-group meetings and workshops involving external stakeholders were organised on the topics of bioequivalence of veterinary medicines, environmental risk assessment, fate of veterinary medicinal products in manure, and availability of veterinary medicines for bees.

## **3.8. Coordination Group for Mutual-Recognition and Decentralised Procedures – Veterinary**

*The Agency provides secretarial support to the Coordination Group for Mutual-Recognition and Decentralised Procedures – Veterinary (CMD(v)) and its subgroups/working groups.*

- The CMD(v) resolved a considerable number of disagreements between Member States regarding mutual-recognition and decentralised procedures, thus preventing referrals to the CVMP.
- A working group of the CMD(v) initiated a project for voluntary harmonisation of summaries of product characteristics for veterinary medicinal products. Clarification of the extent to which marketing authorisation holders are prepared to engage in this initiative on a voluntary basis is awaited, as their active involvement will be essential for the success of the scheme. The outcome of the pilot project will be considered within the Referral Task Force being established by CVMP.
- The secretariat provided support to the CMD(v) with development of guidance documents for applicants related to implementation of the revised Variations Regulation.
- The CMD(v) maintained close working relationships in 2009 with the European Commission and interested parties (IFAH-Europe, EGGVP and AVC) to ensure consistency and relevant exchange of information. The CMD(v) continued to respond to a range of questions submitted on subjects relating to mutual-recognition/decentralised procedures.

## 4. Compliance and inspections

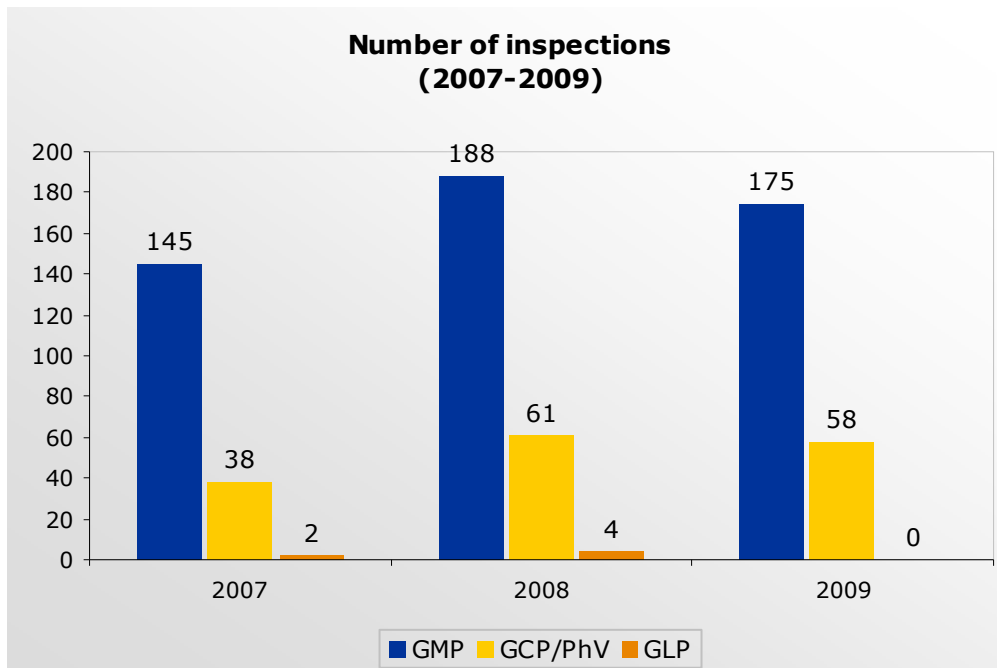
The Agency coordinates the verification of compliance with the principles of good manufacturing practice (GMP), good clinical practice (GCP) and good laboratory practice (GLP), and with certain aspects of the supervision of authorised medicinal products in use in the European Union. It does this through 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.

Similarly, the Agency coordinates pharmacovigilance inspections requested by the scientific committees and inspections of blood establishments within the plasma master file (PMF) certification framework. Communication and action by Member States in response to suspected quality defects and counterfeit medicines relating to centrally authorised medicines are also coordinated by the Agency.

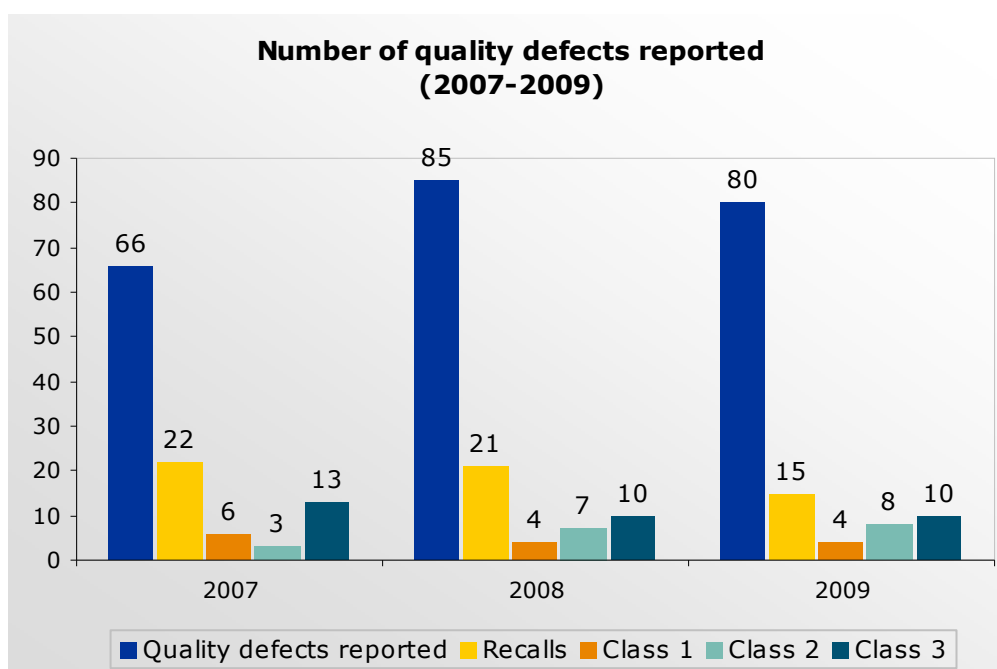
### 4.1. Inspections

- In 2009, 175 GMP inspections were conducted. This was below the forecast of 210.
- There were 44 GCP and 14 PhV inspections, which exceeds the target (50 were forecast).
- No GLP inspection was requested in 2009 (the target was two).
- Two joint GMP inspections with the US FDA were carried out. In addition, one inspection was performed in the API pilot.
- Eighty quality defects were handled in 2009, slightly fewer than in the previous year (85). However, 2009 was characterised by several high-profile manufacturing failures, with increasing international involvement demanding considerable resources from the Agency.

Figure 37.



**Figure 38.**



## Specific objectives

### *International cooperation*

- International inspection cooperation activities progressed significantly in 2009. In addition to the ongoing successful cooperation on joint inspections with the FDA on dosage-form manufacturers, the Agency took the lead in an initiative from the third summit of International Heads of Medicines Agencies to strengthen the approach to supervise active substances and supply chains in collaboration with international partners. A strategy paper was developed and discussed between interested authorities from the EU Member States, the United States, Canada, Australia and the WHO. The paper was finalised in October 2009 and presented to an international strategic meeting of GMP inspectors in Washington DC in November. Many areas of consensus were found and work is ongoing to progress these.
- The practical implementation of a pilot programme of inspections of API manufacturers commenced in 2009, involving the EU, USA, Australia and EDQM.
- The Agency and the FDA launched a joint initiative to collaborate on international GCP inspection activities in July 2009. Objectives of the initiative include the sharing of information on inspection planning, policy and outcomes and the conduct of collaborative inspections. By the end of 2009, one joint inspection was in preparation for early 2010.

### *Public access to EudraGMP*

- Following the launch of a new version of the EudraGMP database, the public was given access to information about manufacturing, importation authorisations and GMP certificates. EudraGMP can be accessed via: <http://eudragmp.ema.europa.eu>
- The EudraGMP database was initially launched in order to facilitate the exchange of information on compliance with GMP among the competent regulatory authorities within the European medicines network. EudraGMP now includes non-compliance statements. These statements are issued in

cases where the reporting inspection service is of the opinion that a manufacturer's non-compliance with GMP is so severe that regulatory action is required to remove a potential risk to public or animal health.

### **Pharmacovigilance inspections**

- The mandate of the Pharmacovigilance Inspectors Working Group was agreed by HMA and by the Agency's Management Board and subsequently published. Pharmacovigilance inspection policies for human and veterinary products were also published, as were inspection procedures in the area of veterinary pharmacovigilance inspections. The first pharmacovigilance inspection for a veterinary product was adopted by the CVMP in April 2009.

### **GCP inspections**

- The CMD/GCP subgroup made significant progress. The group finalised guidance for coordination of GCP inspections and cooperation between GCP inspectors, the reference and concerned Member States and CMDh in the context of the evaluation of the GCP compliance of marketing-authorisation applications for mutual-recognition and decentralised procedures.
- A revised GCP guideline specific to advanced therapies was prepared on behalf of the European Commission and published by the European Commission in December 2009.

<b>Key performance indicator</b>	<b>Target</b>	<b>Outcome</b>
Management of inspections within legislative timelines	100% of inspections	100% for GCP, GMP and PhV
Successful completion of collaborative inspections with the FDA	1 by end of 2009	1 GCP inspection request was being prepared for adoption by CHMP in Jan 2010, which will result in a joint inspection with FDA  GMP: 2 joint pre-authorisation, dosage-form manufacturer inspections were carried out in 2009

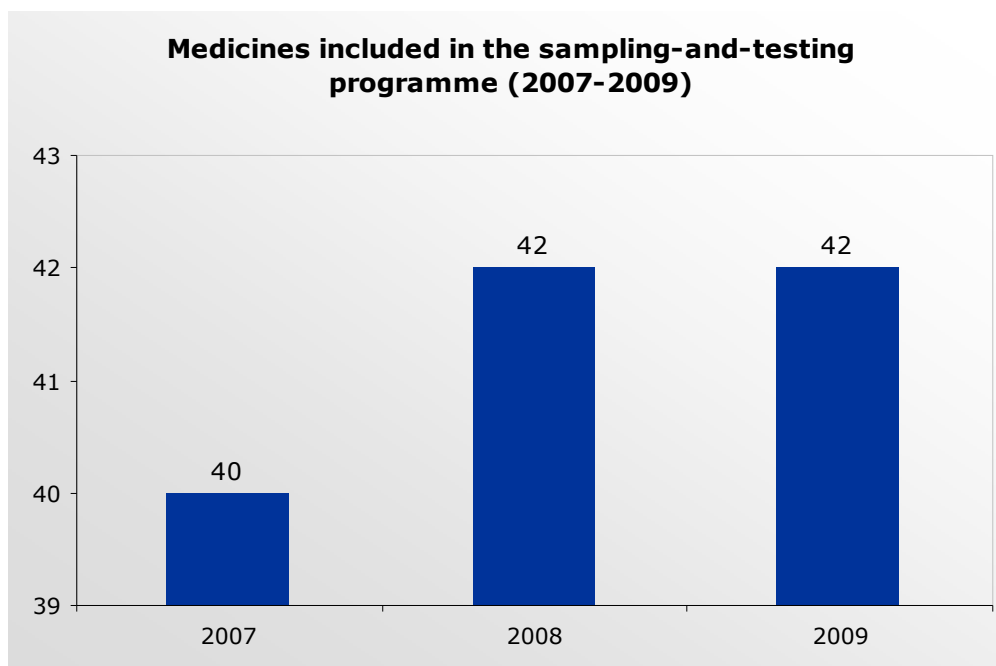
## **4.2. Sampling and testing**

*The objectives of the sampling and testing programme, derived from legal requirements, are to supervise the quality of centrally authorised medicinal products placed on the market and to check compliance of these with their authorised specifications. This ensures that the products actually on the market continue to meet public and animal health requirements. Sampling from the market in different countries is carried out by national inspectorates, and testing is performed by official medicines control laboratories, coordinated through the European Directorate for the Quality of Medicines and HealthCare (EDQM). A selection of centrally authorised products is included in each annual programme.*

- The sampling and testing programme for 2008 was successfully concluded and the 2009 programme was brought close to completion.

- Forty-two medicinal products were tested, as forecasted.
- The list of products for testing in 2010 was adopted and preparations made.

**Figure 39.**



### **4.3. Clinical trials**

The Agency is supporting capacity-building initiatives in the clinical-trial area involving regulators in developing countries.

An Agency working group on third-country clinical trials has been established to move forward the Agency's strategy in relation to the acceptance, as part of a marketing-authorisation application, of clinical trials conducted in third countries. The purpose is to reinforce the Agency's contribution to assuring that trials carried out in third countries have been conducted in accordance with the required good-clinical-practice and ethical standards. Four meetings took place in 2009 and a draft consolidated document, addressing the topics of the strategy paper, is under discussion.

The report 'Clinical trials submitted in marketing-authorisation applications to the EMEA: Overview of patient recruitment and the geographical location of investigator sites' was published in October 2009. The document, which is based on information collected since mid-2004, provides an overview of the distribution of the number of patients, investigator sites and pivotal clinical trials included in marketing-authorisation applications submitted to the Agency, of the number of sites subjected to inspection, and of the geographic location of these inspections.

## 5. EU telematics strategy and information technology

### 5.1. EU telematics strategy

The EU telematics strategy for pharmaceuticals is agreed between Member States, the European Medicines Agency and the European Commission. In order to implement European pharmaceutical policy and legislation, the various initiatives aim to increase efficiency, enhance transparency and support and facilitate the operation of procedures established by legislation.

In 2009, the European Medicines Agency marked its seventh year of implementation of the EU telematics strategy. The table below highlights developments in major systems during the year. It should be noted that there was no further development of EudraPharm in 2009.

System or process	2009 milestones
EudraCT	EudraCT is a database of all clinical trials commencing in the EU from 1 May 2004 onwards. It was established in accordance with Directive 2001/20/EC. During 2009, version 7.0 of EudraCT went live in production, with new features that enhance functionality and the user experience. During 2009, work also began on the development of a new public-facing website, which will enable EU citizens to query information currently held in the database.
EudraVigilance	EudraVigilance is a data-processing network and management system for reporting and evaluating suspected adverse reactions during the development of a medicine and following the medicine's authorisation in the European Economic Area. The first operating version was launched in December 2001. During 2009, work continued on improving functionality of the system's data-analysis capacities, in order to strengthen development of tools for data-quality management.
International standardisation	In 2009, the Agency took a key role in international standardisation efforts for the identification of medicinal products. The Agency continued to support and shape standards development with the International Organization for Standardization (ISO), European Committee for Standardization (CEN) and Health Level Seven (HL7). Outcomes are being integrated into ICT work programmes at the Agency.
EudraGMP	Following the launch of a new website in 2009, the EudraGMP database now provides public access to information about manufacturing, importation authorisations and GMP certificates. Version 2.0 of the password-protected EudraGMP database, also released in 2009, included non-compliance statements. These statements will be issued in cases where the reporting inspection service is of the opinion that a manufacturer's non-compliance with GMP is so severe that regulatory action is required to remove a potential risk to public or animal health.
EUTCT	The European Union Telematics Controlled Terms (EUTCT) system is a central repository and publication system for controlled-term lists used in the European medicines network. A new, non-password protected website was launched for general public use in 2009.

## 5.2. Information technology

In September 2009, the Information and Communications Technology (ICT) Unit was restructured to better meet the needs of the Agency. As a result, the Unit has the responsibility to:

- define the ICT strategy of the Agency in line with the Agency's roadmap;
- provide the Agency, other European institutions and bodies (whenever appropriate), partners in the European medicines network and other stakeholders with high-quality and advanced:
  - ICT infrastructure solutions and e-services,
  - support services,
  - unified telecommunications facilities, including solutions for physical and virtual meetings;
- deliver information systems required to support the Agency's corporate business processes;
- deliver information systems as defined in the EU telematics strategy for use by the European medicines network, pharmaceutical industry, healthcare professionals and the general public;
- promote and facilitate the European medicines network and public administrations, in collaboration with the European Commission;
- promote and facilitate the provision of information on medicinal products to citizens and enterprises.

### IT projects

#### Highlights of 2009

System or process	Milestone
Corporate records management system	New records management policies were endorsed by the Agency in 2009. Technical implementation planning was deferred due to the upgrade of the Agency's document management system in 2010.
Enterprise information architecture (EIA)	To enhance future Agency planning and resource allocation activities, an enterprise information architecture project began in 2009. Definition of the broad requirements of the EIA approach and the selection of external expertise to support the project was completed.
Agency resource planning	Business requirements gathering phase was completed and the system launch date revised to January 2011.
Web content management system (WCMS) for new Agency website	The project began in June 2009 with an assessment of business requirements for the development of the WCMS. The build and testing of the WCMS and migration of all content from the old website to the new WCMS began in 2009, and a revised launch date of April 2010 was set.
Product Information Management (PIM)	The Agency started a migration analysis and a detailed planning exercise, which included a proof of concept migration exercise involving a limited number of products, initiated before the end of 2009. The team worked on and subsequently published, in September 2009, a plan for the implementation of PIM in the centralised procedure.
eCTD/electronic submissions	The Agency successfully implemented the second and third steps of the implementation plan for electronic-only submissions. The use of electronic-only applications is strongly recommended to all applicants and, from 1 January 2010, the electronic Common Technical Document (eCTD) format is

System or process	Milestone
	<p>mandatory for all electronic submissions. A guidance document for non-eCTD electronic submissions was also published in January.</p> <p>Training and installation of the review tool continued during 2009 and will continue further into 2010 in the Member States. The review tool has been updated in accordance with the new Variation Regulation, as planned.</p> <p>Specific guidance on eCTD and active substance master files was developed in response to user requests.</p> <p>An electronic repository has been put in place for paediatric submissions, which are now electronic only.</p> <p>Implementation of electronic submissions of scientific advice and orphan product applications is ongoing.</p>
Siamed II	<p>Technical phase of project ongoing throughout 2009: framework DES 1.0 and DES for MAA phase 1A (update DTD in line with current forms), also known as DES 1.0, completed in June 2009. Prototype (authoring/validation tool), authoring tool (online/offline), validation tool, prototype (receiving tool) and receiving tool completed in November 2009. DES for MAA (human) + renewals (H&amp;V) phase 1B (RDM, EUTCT compliance), also known as DES 2.0, completed 90% during 2009, will be completed by the end of January 2010.</p>
Corporate GxP	<p>Ongoing, tightly controlled iterative development culminating in the delivery of the basic GMP version, which will be of production quality in April 2010.</p>
Business continuity planning (BCP) infrastructure	<p>Ongoing work in 2009 to ensure that all applications are virtualised, migrated and BCP-compliant.</p>

## IT implementation and maintenance

### Highlights of 2009

System or process	Milestone
Project management tracking system	<p>The Agency's new project management tracking system was deployed in 2009. This enables more efficient tracking of all IT development projects across the business.</p>
New IT service desk system	<p>A new IT service desk system to ensure better coordination and resolution of IT-related business requests was deployed in 2009.</p>
Managing Meeting Documents (MMD) system	<p>In 2009, the Agency's MMD system was further enhanced with the deployment of Wi-Fi capability.</p>
Eudranet infrastructure	<p>Major improvements to the Eudranet infrastructure were made in 2009.</p>
Business continuity planning	<p>The project to ensure that the systems component of the Agency's business continuity plan is compliant with requirements was completed in 2009. All systems were fully tested to ensure effectiveness in a disaster scenario. A key component of the project includes location-independent working.</p>
IP telephony system	<p>The specifications for a complete IP telephony system, encompassing the integration of telephony, telecommunications, virtual meetings, collaboration tools, computer systems and business logic, were completed in 2009 as per the business requirements. Procurement will begin in 2010.</p>

Key performance indicator	Target	Outcome
Percentage of systems downtime	2%	1%
Percentage of user satisfaction	80%	No tool currently in place to report on this KPI
Delivery of IT projects against plan and budget	90%	75%
Effective transition to production/operation	95%	85%
Corporate availability of services (excluding planned maintenance downtime)	98%	99%
Response time to 80% of corporate IT Service Desk requests	2 hours	On target: 91% of requests responded to within 2 hours
Response time to 15% of corporate IT Service Desk requests	1 day	On target: 99.4% of requests responded to within 1 day

## 6. Support activities

### 6.1. Administration

Administration tasks include: managing revenue, expenditure and accounts according to existing rules and regulations; recruiting, managing and administering staff and seconded personnel; supporting and servicing meetings organised by the Agency, providing support and assistance to delegates; providing and running the necessary infrastructure services for effective functioning of the Agency. To manage these tasks, close cooperation is required with the European Parliament, Council (Budgetary Authority), Commission and Court of Auditors, on matters relating to administration, budget, personnel, and to rules and regulations on finances, audit and accounting.

### Human resources

The principal objectives of the Human Resources sector are the development and timely and accurate management of the Agency's human resources, including personnel administration, recruitment procedures and professional training, as well as the provision of information to staff and other concerned persons.

- The number of staff employed at the European Medicines Agency was 511, with an additional 200 seconded experts, contract agents, trainees and interim staff.
- Thirty-three internal and external recruitment procedures were carried out. On top of this, 43 internal selection procedures took place in light of the restructuring (creating the new Section Head positions).
- Reinforced training and competence-development was put in place. The average number of training days taken by the Agency's staff was 9.4 days.
- The 360-degree performance-evaluation system for managers was introduced.
- The database for declarations of interests was implemented in November 2009.

	2007 (final)	2008 (final)	2009 (final)
Total staff	423 <sup>2</sup> + 124 <sup>3</sup>	469 <sup>2</sup> + 155 <sup>3</sup>	511 <sup>2</sup> + 200 <sup>3</sup>
Selection procedures	29	35	33 + 43
Mission claims	922	961	998
Salary payments	6,003	6,632	7,355

Key performance indicator	Target	Outcome
Personnel administration	Posts filled to 97% Agency-wide	96.42%
Training	10 days (includes on average 2.5 days informal/on-the-job training per head)	9.4 days of training per staff (includes 2.5 days informal/on-the-job training).

<sup>2</sup> Establishment plan minus vacancy rate.

<sup>3</sup> Number of national experts, contract agents, trainees and interims.

## Finance and budget

The objectives of the Finance and Budget sector are to manage the Agency's financial resources according to existing rules and regulations, and to ensure sound financial management and transparency of financial transactions for the Agency.

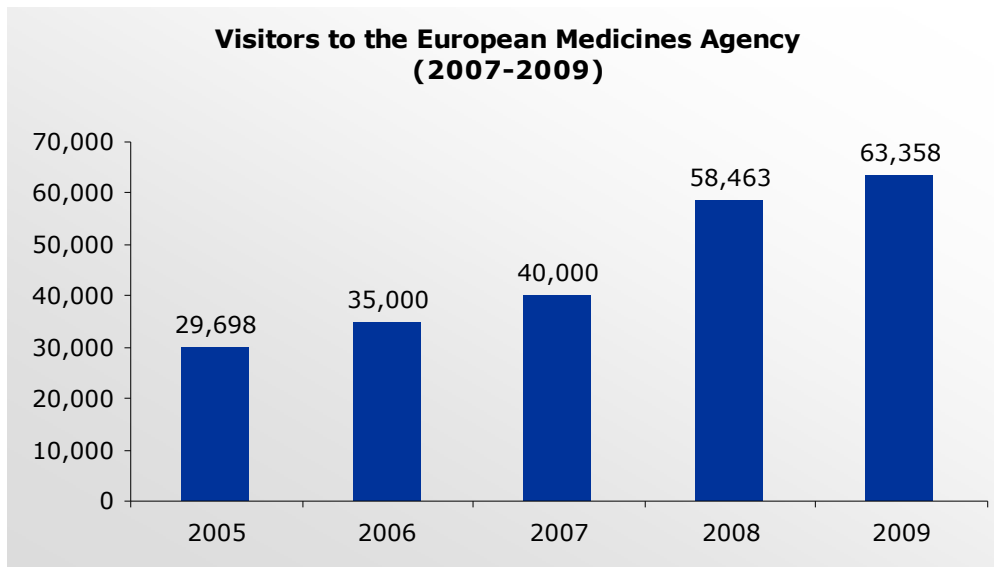
- The Agency's total budget in 2009 was EUR 194,389,000.
- The 'blueprint' phase for the integrated enterprise-resource-planning system (ERP) was completed in May 2009, with the 'realisation' phase due to be finalised in the second half of 2010.
- All bank accounts are reconciled to date. Financial accounts are up to date, and all financial reporting and legal dates were complied with.
- A steady rise in the number of transactions (approximately 10% p.a.) is noted year on year.

## Infrastructure services

The main aim of the Infrastructure Services sector is to ensure a safe and efficient work environment for staff, delegates and visitors. The sector covers a wide range of services, including office accommodation planning, acquisition of office space, environmental management system, contract management, security, telecommunications, reception, switchboard, archiving, mailroom, reprographics, technical assistance to meeting rooms, management of confidential waste, health and safety, fire and emergency plans, business continuity planning, asset management, office equipment and supplies, maintenance, refurbishment and fitting out, internal relocations, management of the catering facilities and, since 1 June 2009, commercial combined and buildings insurance. As of 1 May 2009, the Contracts and Procurement team was incorporated within Legal Affairs as part of the restructuring exercise.

- To match the requirements of the increases in staff numbers and delegates, as well as additional meetings, the first floor of the Agency was refurbished. It includes a new reception area, security offices and a number of small meeting rooms and delegate offices. The fourth floor was partly refurbished to create a larger meeting room and a break-out area for delegates. There were minor alterations to the fifth and eighth floors. The restaurant on the third floor was refurbished to create more dining space for the increased number of visitors and staff members.
- A feasibility study on future office premises for the Agency prior to the expiry of the current leases in 2014 is underway.
- An exercise to rehearse the business-continuity arrangements of the Agency's support services was successfully completed in October 2009, in cooperation with IT.
- The number of visitors to the Agency (made up largely of delegates for meetings and conferences) increased by 8%.

**Figure 40.**

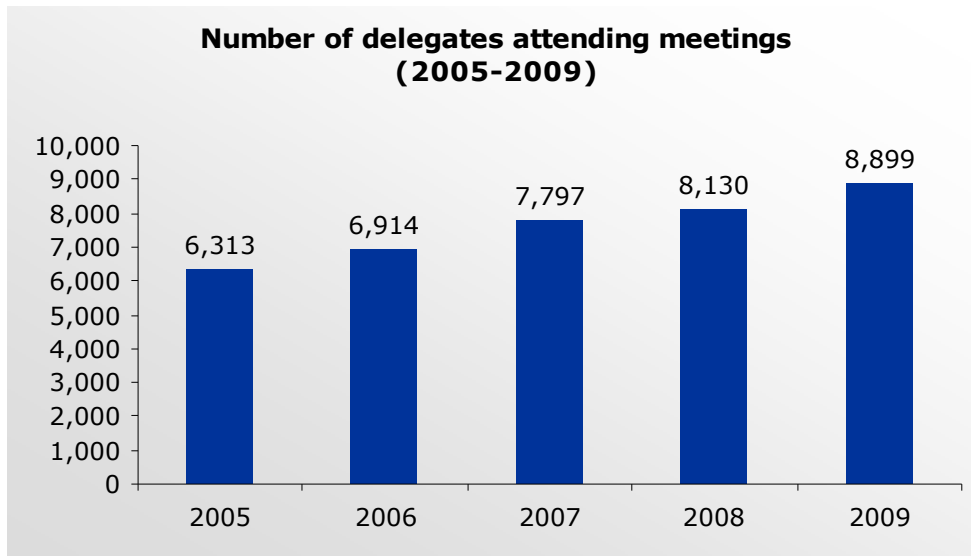


## **6.2. Meetings and conferences**

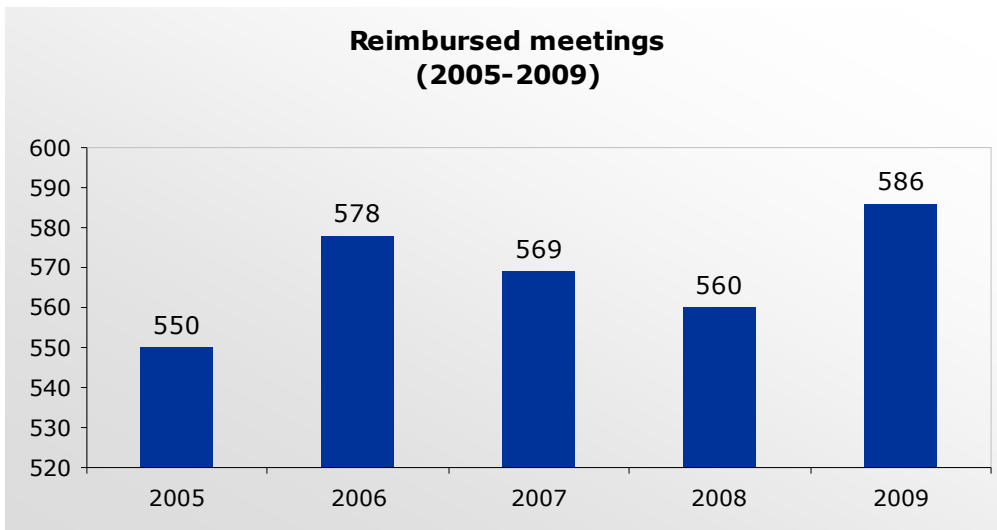
The Meetings and Conference Management sector provides support and services to meetings organised by the Agency, provides financial support to delegates attending meetings, and constantly monitors the meeting budget. The sector assists delegates with logistics and practical arrangements. This includes organisation of meetings, organisation of travel and hotel arrangements for delegates and hosts, reception of visitors, reimbursement of delegates' expenses and payment of suppliers' invoices, as well as preparation and follow-up of meeting-room facilities.

- The number of reimbursed meetings increased by 5% and the number of reimbursed delegates by 9.5%, compared to 2008. This was mainly due to the introduction of the new Committee for Advanced Therapies (CAT), to the influenza H1N1 pandemic, which required the organisation of emergency meetings, and to the participation of EU candidate countries' representatives as observers in the Agency's activities.
- New conference rooms were made available in 2009, thus avoiding the use of external facilities. The number of virtual meetings using the web-based Vitero system and Adobe connect increased from 125 virtual meetings in 2008 to 309 in 2009.

**Figure 41.**



**Figure 42.**



Key performance indicator	Target	Outcome
Delegates' satisfaction regarding travel and accommodation bookings	95%	100%
Assistance and satisfaction of interested parties (the European Medicines Agency, delegates, national authorities, suppliers)	95%	100%
Satisfaction with management of EU enlargement programmes	95%	100%

### 6.3. Document management and publishing

The Agency ensures full compliance with all regulatory and quality requirements in the areas of document and records management. For the sector involved, this means: ensuring best practice in document and records management; ensuring best practice in the areas of access to information and documents; providing staff with the most effective access to internal and external information needed to perform their professional duties; verifying the accuracy of translations (excluding medical product information); verifying the quality of documents (excluding content) and organising their publication; organising and supporting Agency exhibitions.

- Further progress on the development and implementation of an electronic records management system was made with the approval of the business classification scheme and retention plan in 2009. Product mailboxes for both human and veterinary products were officially launched in October 2009.
- The Agency received a total of 108 requests for access to documents (of which 38 were denied), compared to 124 (of which 31 were denied) in 2008. A total of 7,603 pages were released to the public, compared to 2,204 in 2008.
- The Agency received a total of 4,290 requests for information, compared to 4,069 in 2008.
- A total of 33,887 pages (624 jobs) were translated, compared to 36,345 pages (603 jobs) in 2008.

Performance indicator	Target	Outcome at end of 2009
Percentage of external requests for documents processed within established timelines	95%	100%
Percentage of external requests for information processed within established timelines	90%	76%
Percentage of translations processed within established timelines	100%	100%
Percentage of internal library requests for information processed and received within established timelines	95%	93%
Percentage of printed material processed and delivered within established timelines	100%	100%
Percentage of exhibition material processed and delivered within established timelines	100%	100%