



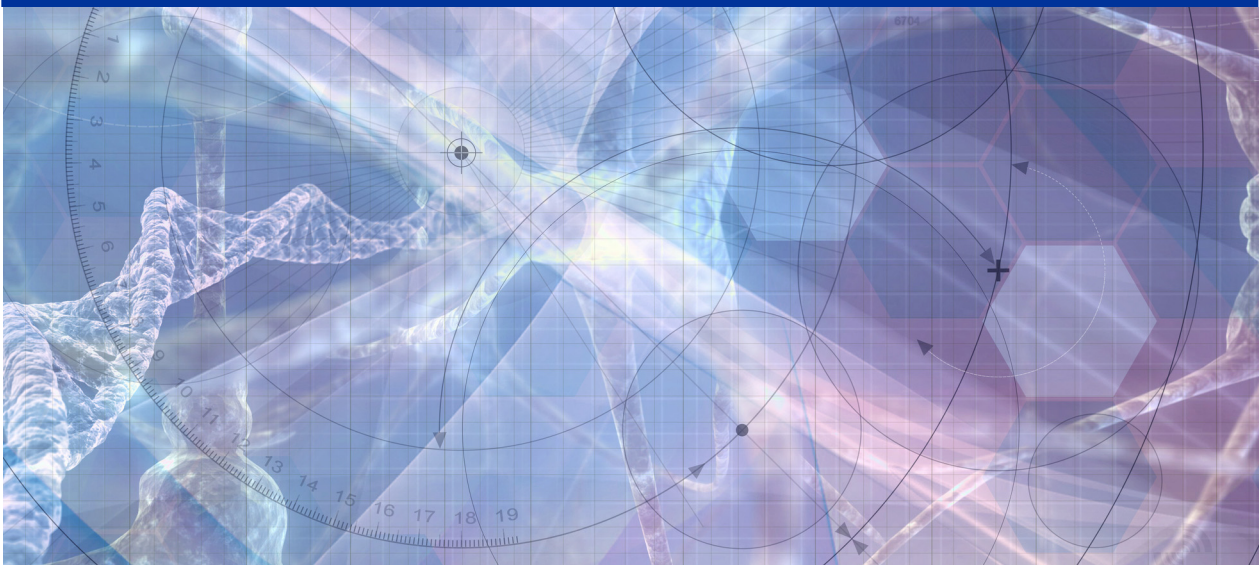
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Annual report

2010

Adopted by the Management Board in June 2011



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An agency of the European Union



Annual report

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Note on annexes

Please note that the annexes of this report are published separately on the website of the European Medicines Agency [here](#).

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 as Chair to write this short message as a foreword to the annual report of the European Medicines Agency for 2010. The report provides some detail of the extensive activities of the Agency during the year, and I commend the report to readers so you may appreciate the broad range of activities carried out.

In all areas of endeavour, including human medicines evaluation, orphan medicines, paediatric indications, traditional herbal medicines, veterinary medicines and compliance and inspections, it has been a busy and successful year. The work of the Agency has lived up to the slogan in its logo: Science, Medicines, Health, and the contribution to patient health and assessment and communication of benefit risk of products has been substantial.

I commend all the Agency staff involved in managing the various procedures conducted throughout the year. In tandem with this work, the Agency has continued to devote particular attention to the areas of transparency and communications, interaction with stakeholders, including patients and patients' organisations, and to support for innovation.

The year saw the publication of a comprehensive report on the evaluation of the European Medicines Agency and the European medicines network as a whole. The evaluation was carried out by Ernst & Young on behalf of the European Commission. The report authors found that the European medicines network, i.e. the Agency, the European Commission and the national competent authorities in the Member States, has been successful in delivering high-quality scientific opinions on medicines for human and veterinary use in an efficient and effective manner. Looking at the challenges that lie ahead, the report also highlighted that the system as a whole would have to adapt to be able to take on new responsibilities in the future. In preparing for that future, the Agency published its new road map, or strategic plan, for the five years to 2015, which sets out the Agency's vision for the future.

I would like to formally record my thanks to all the staff of the Agency, all those contributing to the work of the committees and working parties, and the Management Board for their contribution throughout the year. I would like to thank the Executive Director, Thomas Lönngren, in this last year of his 10-year tenure and wish him well after his retirement.

I thank colleagues from the European Commission and the Parliament for their ongoing support and guidance to the work of the Agency. Finally, my thanks to all colleagues from throughout the network for their ongoing support to me as Chair.

Introduction by the Acting Executive Director

Andreas Pott

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

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

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

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

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

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

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.

Adoption of the 'Road map to 2015'

The Management Board adopted the Agency's new 'Road map to 2015' at its December 2010 meeting. The new five-year strategy sets out the Agency's vision in further developing its role as a European public-health agency in the field of medicines. Building on the achievements made by the previous road map initiative, between 2005 and 2010, the new road map proposes three priority areas for future actions to strengthen the Agency's role in protecting and promoting human and animal health in the EU: addressing public-health needs, facilitating access to medicines, and optimising the safe and rational use of medicines.

The road map was developed so that its vision is consistent with, and complementary to, strategic directions provided by the European Commission, the Council of the European Union and the Heads of Medicines Agencies (HMA).

The road map is available on the Agency's website [here](#).

Outcome of the evaluation of the European Medicines Agency

The year started with the publication of a report on the evaluation of the European Medicines Agency and the European medicines network as a whole. The evaluation was carried out by Ernst & Young on behalf of the European Commission. The report shows that the European medicines network, i.e. the Agency, the European Commission and the national competent authorities in the Member States, has been successful in delivering high-quality scientific opinions on medicines for human and veterinary use in an efficient and effective manner. Looking at challenges that lay ahead, the report also highlighted that the system as a whole would have to adapt to be able to successfully address new developments and take on new responsibilities in the future.

Following publication of the report, a joint Commission and Agency conference held in June 2010 started a process of reflection, focusing on key questions such as: How can the Agency deal effectively with the increasing globalisation of the pharmaceutical industry? Is the Agency fit for new scientific developments, for instance advanced therapies or personalised medicines? How can regulators respond to requests from patients and healthcare professionals for more participation and transparency? How can the particular requirements of veterinary medicines best be accommodated?

Some of the proposals made during the conference were included in the Agency's new road map. For other proposals, deliberations are still ongoing, and the Agency and the European Commission will propose a process for their further consideration.

The 'Report on the outcome of the evaluation of the European Medicines Agency' is available [here](#).

The conference report is available [here](#).

Revised payment system

A proposal from the Executive Director for a revised system for remuneration for scientific work carried out by national competent authorities was not supported by the Management Board. It was concluded that no changes to the remuneration system will be implemented in 2010.

New conflicts of interests policy agreed

Following extensive discussion, the Management Board endorsed, at its October 2010 meeting, new rules on the handling of conflicts of interests of scientific committee members and experts. The new rules aim at balancing the need to secure Europe's best scientific experts for the evaluation and supervision of medicines, while ensuring that these experts have no financial or other interests in the pharmaceutical industry that could affect their impartiality.

The 'European Medicines Agency policy on the handling of conflicts of interests of scientific committee members and experts' is available [here](#).

Cooperation agreement and memorandum of understanding

The revision and simplification of the contractual arrangements ('Cooperation agreement') for services provided by the national competent authorities was concluded in 2010.

The annex to the 'Cooperation agreement', which sets out the responsibilities of the Member States regarding monitoring of the scientific level and independence of their experts (the 'Memorandum of understanding') was also discussed by the Heads of Medicines Agencies and adopted by the Management Board in 2010. The agreement and memorandum were signed by the Agency's Executive Director in December 2010 and sent to the national competent authorities for signature.

Meetings at the European Medicines Agency

The Agency provides facilities and service for meetings of the committees, working parties and other expert groups. The Agency assists delegates with logistics and practical arrangements.

In 2010, a total of 584 onsite meetings, with 8,447 reimbursed delegates, were held at the Agency. This is a slight decrease compared to 2009 because of an increase in the number of virtual meetings, which do not require the use of meeting rooms or reimbursement of participants.

Key performance indicator	Target	Outcome
Satisfaction of delegates and interested parties regarding support provided by the Agency	95% of respondents to be satisfied or very satisfied	90% satisfaction attained. Despite a number of unforeseen external events during 2010, flight and hotel arrangements were found for 100% of delegates. A new delegate satisfaction survey will be launched in May 2011.

Preparation for enlargement

The year 2010 was the second of the three-year Instrument for Pre-accession Assistance (IPA) programme, which supports the participation of Albania, Bosnia-Herzegovina, Croatia, the former Yugoslav Republic of Macedonia, Iceland, Kosovo under UNSC Resolution 1244/99, Montenegro, Serbia and Turkey in the work of selected EU agencies.

Under this programme, the Agency builds contacts and relationships with the beneficiaries to assist their future participation in the activities of the Agency and of the wider European medicines network.

- Representatives from IPA beneficiaries participated in selected Agency meetings and training courses.
- The IPA programme for supporting the Balkans involved assessing the level of harmonisation of each beneficiary and determining priority support areas as part of a follow-up programme, to help maximise the use of resources.
- Two conferences were organised in 2010: one at the Agency, on 1-2 February 2010, to formally introduce the enlargement programme to the IPA beneficiaries, and the second in Belgrade, Serbia, on 29-30 November 2010, which was attended by over 200 participants.

1.2. European cooperation

This area covers: contribution to new legislation initiated by the European Commission; partnership with European Commission Directorates-General, namely DG Health and Consumers, DG Enterprise and Industry, DG Research and Innovation, and DG EuropeAid Development & Cooperation; 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).

Preparation for implementation of new legislation

Preparation for the implementation of the new pharmacovigilance legislation started at the beginning of 2010. A cross-Agency task force was set up to review all the arrangements to be put in place. In parallel, work was undertaken to conduct an assessment of the impact of the legislation on the Agency's human and financial resources.

A similar approach was initiated in the second half of 2010 to prepare for the implementation of new falsified medicines legislation.

Pandemic-influenza activities

The first half of the year was dominated by activities relating to the H1N1 influenza pandemic. The Agency continued activities it had started in 2009 in relation to the scientific assessment of pandemic-influenza vaccines and antivirals. Until August 2010, when the World Health Organization declared the end of the pandemic, the Agency continued to publish regular pandemic-influenza pharmacovigilance reports¹, which provided information on adverse reactions reported after the use of centrally authorised pandemic-influenza vaccines and antiviral medicines in the EU.

In addition, the Agency participated in a number of EU-wide 'lessons learned' exercises, reviewing the performance of the complex system of healthcare actors during the pandemic.

¹ Published on the Agency's website [here](#).

The Agency evaluated its own activities during the 2009 and 2010 pandemic and prepared a report on its findings², following which it initiated its own pandemic programme, with the objective of revising the Agency's pandemic guidelines and preparedness plan to optimise its handling of future influenza pandemics.

EPAR improvements as a contribution to assessment of relative effectiveness by health technology assessment (HTA) bodies

The publication of the conclusions of the Pharmaceutical Forum gave the Agency a mandate to start interacting with HTA bodies. As part of this interaction, the Agency started a project in 2010 to work with the European Network for Health Technology Assessment (EUnetHTA), to look into how the information on the benefits and risks of medicines in European public assessment reports (EPARs) could make a better contribution to relative effectiveness assessments by HTA bodies. A first meeting was held in February 2010, and a follow-up meeting was held in June 2010. A plan to identify improvements in EPARs was established with EUnetHTA. Following this, new EPAR templates for the assessment reports were rolled out in October 2010.

Working with HTA bodies in early-stage drug development

A second project with HTA bodies was started in October 2010, when healthcare actors from Europe, including the Agency, clinicians, national HTA bodies, patient representatives, payers, regulators and drug developers, participated in a pilot process testing multi-stakeholder consultations in early-stage drug development. The purpose of the consultations is to improve clarity and alignment among the stakeholders with regard to what constitutes a medicine's value and the evidence required to demonstrate that value most effectively.

The first meeting, investigating how the Agency could cooperate in the area of scientific advice with national HTA bodies, was held on 25 October 2010. The meeting concerned an antidiabetes medicine early in the development stage. Further meetings were planned for 2011.

Review of veterinary legislation

- In response to the Commission consultation on better regulation for veterinary pharmaceuticals, the Committee for Medicinal Products for Veterinary Use (CVMP) prepared comments and a separate detailed reflection paper that were submitted to the European Commission and made publicly available in July 2010.

Minimising the risk of antimicrobial resistance arising from use of veterinary medicines

- The Agency intensified its activities in cooperation with the European Commission and other stakeholders to minimise the risk of antimicrobial resistance arising from the use of veterinary medicines. The CVMP provided technical support to the European Commission on its involvement in the Codex Alimentarius Intergovernmental Task Force on Antimicrobial Resistance, which finalised its recommendations for a methodology for risk assessment and risk management in relation to food-borne antimicrobial-resistant microorganisms.
- Major progress was achieved with the Agency's project³ to coordinate the collection by EU Member States of harmonised data on use in the EU of antimicrobials in food-producing species and companion animals. A pilot involving 10 Member States was launched in 2010. The project also adopted a template to be followed by Member States for collection of data on consumption of

² Published on the Agency's website [here](#).

³ European Surveillance of Veterinary Antimicrobial Consumption (ESVAC).

veterinary antimicrobials in a harmonised manner. Training on collection of data was provided for Member States.

Animal Health Strategy

- The Agency actively participated in two meetings of the Animal Health Advisory committee, which has been established to follow the Animal Health Strategy's progress. The Agency provided feedback to the Commission on the Agency's initiative in relation to veterinary medicines for bees and on several other areas in which the Agency contributes to the Commission's strategy.

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 of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) and the Codex Alimentarius, and the Agency's work with the World Health Organization (WHO), the World Organisation for Animal Health (OIE), the U.S. Food and Drug Administration (FDA), the U.S. Department of Agriculture (USDA), the Japanese, Canadian and Australian authorities, and 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.

Sharing of information on H1N1 pandemic medicines with Swissmedic

In February 2010, the Agency and Swissmedic, the Swiss Agency for Therapeutic Products, concluded an agreement allowing both agencies to exchange confidential information about the authorisation and safety of medicines used in the context of the H1N1 pandemic influenza. The agreement also created the opportunity to exchange information regarding lessons learned during the H1N1 pandemic.

Clinical trials outside the EU

On 6-7 September 2010, the Agency held an international workshop with a broad cross-section of stakeholders from around the world to discuss a way forward for a global framework for clinical trials that has at its heart the protection of the rights, safety and wellbeing of patients participating in clinical trials anywhere in the world.

The workshop was part of the consultation process on the Agency's 'Reflection paper on ethical and good clinical practice (GCP) aspects of clinical trials of medicinal products for human use conducted in third countries and submitted in marketing authorisation applications to the EMA'.

The reflection paper responds to the challenges arising from the increasing globalisation of clinical research. In marketing-authorisation applications submitted to the Agency between 2005 and 2009, only 38.8% of patients enrolled in pivotal clinical trials received their treatment at clinical-trial sites within the EU or EEA. These trials involved more than 44,000 clinical-trial sites in 89 countries. The data generated were used to support 347 marketing-authorisation applications, as well as some applications for a variation or a line extension of the existing marketing authorisation.

European Medicines Agency and U.S. Food and Drug Administration extend confidentiality arrangements indefinitely

In September 2010, the Agency and the FDA extended their confidentiality arrangements relating to medicinal products for human and veterinary use, following the positive experience gained since the

initial arrangements were signed in September 2003. This cooperation will now continue indefinitely without the need for further renewal.

International standardisation work

The Agency carried out a high number of activities in this area. Testing of the first and second draft international standard for individual case-safety reports (ICSRs) was conducted during 2010, and comments derived therefrom were submitted to the International Organization for Standardisation (ISO) and Health Level Seven International (HL7) – the global authority on standards for interoperability of health information technology, with members in over 55 countries. The completion of the international ICSR standard is expected during the second half of 2011.

Testing of the first draft international standards for identification of medicinal products (IDMP) was also conducted in 2010, and comments are being prepared for submission to the ISO in the beginning of 2011. Major contributions were also made in developing the corresponding HL7 models for substances, specified substances and message specifications.

Work in ICH focused on developing implementation guides and reviewing test results. To allow stakeholders to prepare for the implementation of the new ICSR and IDMP standards in a timely manner, two information days were organised by the Agency in collaboration with the US FDA and the EDQM.

Within VICH, several important guidelines harmonising the requirements for reporting of veterinary pharmacovigilance were finalised after many years of negotiation with international partners. These guidelines now pave the way for increased cooperation and improved efficiency in the future for both regulators and industry.

Mutual-recognition agreements

Mutual-recognition agreements (MRAs) between the European Union and partner countries include specific annexes relating to medicinal products and good manufacturing practice. 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.

Projects planned in this area relating to the re-examination of existing MRAs were postponed, pending the finalisation of the new anti-falsification legislation by the Council and Parliament.

Discussions with the Japanese authorities on developing an agreed work plan to fulfil the scope of the EU-Japan mutual-recognition agreement were started.

Certificates

The purpose of the Agency's scheme for certificates of medicinal products is to support the work of health authorities outside the EU, particularly those in developing countries. Certificates are issued by the Agency, on behalf of the European Commission, to confirm the marketing-authorisation status of products authorised by the European Commission through the centralised procedure or of products for which a centralised application has been submitted to the Agency. The certificates also confirm compliance with good manufacturing practice at the manufacturing site(s) where the medicinal product is produced in bulk pharmaceutical form. Health authorities can rely on centralised assessments to

support marketing in their own countries, thus facilitating access to these medicines and avoiding the need for costly and duplicative assessment work. The Agency also issues certificates for products it evaluates in the context of cooperation with the WHO (Article 58 of Regulation (EC) No 726/2004).

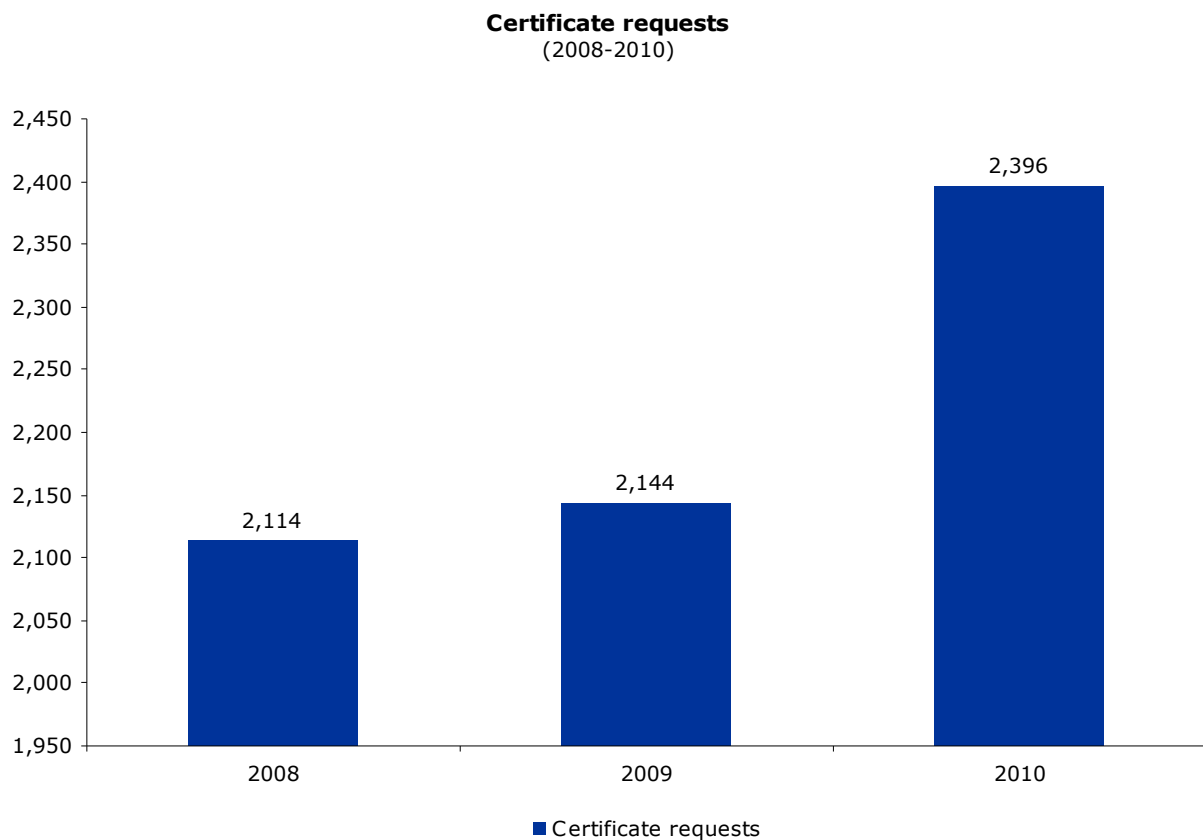
Discussion with the WHO

The Agency held discussions with the World Health Organization on a possible revision of the certification scheme, taking into account changing stakeholder needs and expectations. Some ideas for process improvements, including improvements to the design of the certificates to help authentication, were discussed at a meeting held in October 2010.

Certificate requests

Fewer initial requests for certificates were received than forecast. However, the total number of 2,396 is 13.5% more than were received 2009.

Figure 1.



Key performance indicator	Target	Outcome
Percentage of certificates issued to requesting parties within the timeline.	90% compliance.	90.5% compliance. Average processing time for issuing of certificates was 7 days.

1.4. Transparency and communication

The pharmaceutical legislation gives the Agency and the European network as a whole a mandate to increase the transparency of their activities and strengthen their communication with stakeholders. The areas of transparency and communication are a priority for the Agency.

The Agency provides targeted, understandable and accessible information for patients and healthcare professionals.

The Agency also coordinates the review of the quality of all product-related information submitted by sponsors and marketing authorisation holders.

Provision of information

Launch of the Agency's new website

The Agency launched its new website on 15 July 2010, following a complete redesign. The site was rebuilt to optimise usability for the Agency's key online audiences and to improve openness and transparency.

The Agency's website receives an average of half a million unique visits per month, and is a key resource for patients, healthcare professionals, regulators and those interested in the regulation and safety of medicines in the European Union.

Improving the product information for medicines

Following the finalisation of the guideline on summary of product characteristics (SmPC) and receipt of feedback from user-testing of package leaflets, the Quality Review of Documents (QRD) templates were reviewed, with particular emphasis on the benefit of taking the medicine and the patient-friendliness of the package-leaflet template. Public consultation highlighted an overall satisfaction regarding the new package-leaflet template. Following an in-depth analysis of the comments received, a joint workshop between the Agency and stakeholders was organised and the final annotated English product information QRD template was adopted, in November 2010.

Stemming from the 2009 work programme of the Committee for Medicinal Products for Human Use (CHMP), the EudraSmPC was launched early in 2010, with the aim of providing online training on the SmPC. A service to answer queries on the SmPC within the European regulatory network was also launched. The initiative is supported by the SmPC Advisory Group, which involves members of all scientific committees, the Pharmacovigilance Working Party, other working parties and Agency staff.

Interaction with patients' and consumers' organisations, and with healthcare professionals

Two patients' representatives were nominated as permanent observers to the Pharmacovigilance Working Party in 2010, following previous approval by the Agency's Management Board. This initiative built on the pilot phase carried out in 2009.

Different initiatives stemming from the 'Reflection paper on the further involvement of patients and consumers in the Agency's activities' were put into action, including the systematic involvement of patients and consumers in safety communications and in the benefit-risk discussions on medicines within the scientific advisory groups.

The revision of the framework for interaction with patients was delayed in order to integrate the outcome of a pilot on the involvement of patients in the benefit-risk evaluation of medicines.

The Agency's Management Board approved paying a special allowance to patient experts attending meetings at the Agency if it is demonstrated that they work on a voluntary basis for the organisation they represent and do not receive any other financial compensation for their work at the Agency. This is intended to facilitate participation of patients' representatives in the Agency's activities.

A framework for interaction with healthcare professionals is being prepared, in close cooperation with the EMA/CHMP Working Group with Healthcare professionals' Organisations, and will be presented to the Management Board in 2011.

Communication within the EU regulatory network

The Early Notification System was used extensively in 2010, allowing EU-wide coordination of communications on safety-related issues prior to their publication on the Agency's website.

A new policy on communicating safety-related issues relating to medicines for human use was published by the Agency in July 2010. The policy describes the various communication tools that are used, criteria for communicating on specific issues, the preparation and publication of communication material (including roles and responsibilities), the timing of the publication, coordination within the network and sharing of communications materials with other regulatory authorities, both in Europe and beyond. The policy is available on the website [here](#).

Publication of information about medicines

The number of European public assessment reports (EPARs) published within two weeks of the Commission Decision remains low, at 28% of the marketing authorisations granted.

Performance indicator	Target	Outcome
Percentage of summaries of opinions published at the time of the CHMP press release	90% of summaries of opinion	100%
Percentage of initial EPARs published within two weeks of the Commission decision	80% of marketing authorisations granted	28%
Percentage of EPAR summaries in a language understandable to the public, published together with the EPAR	90% of EPARs	100%
Percentage of withdrawal Q&A documents published at the time of the next appropriate CHMP monthly report	90% of Q&A documents	94% (one Q&A document was delayed by 24h)
Percentage of refusal Q&A documents published at the time of the CHMP opinion	90% of Q&A documents	100%
Percentage of Q&A documents for Articles 31, 36 and 107(2) procedures at the time of the CHMP opinion	90% of Q&A documents	100%

Transparency

There was much emphasis placed by stakeholders during 2010 on the openness of the Agency's operation, its proactive publication of documents and its approach towards requests for access to documents.

New access to documents policy adopted

The new policy on access to documents related to medicines for human and veterinary use was published in November 2010, following its endorsement by the Management Board. The new policy is part of the Agency's response to increasing public demand for more openness and transparency. It gives wider access than ever before to documents held by the Agency, while it ensures that personal data and commercially confidential information remain adequately protected. When finalising the access to documents policy, a draft recommendation from the European Ombudsman was taken into account.

Priority was given to the finalisation of this policy in 2010 before moving on to finalising the overall Agency transparency policy, following the outcome of the public consultation on the draft document.

Revised EudraVigilance access policy

Revised EudraVigilance access policies for human and veterinary medicines were adopted by the Management Board in December 2010. The revised policies reflect recommendations made by the European Data Protection Supervisor in his final opinion, published in September 2009, as well as recommendations of the European Ombudsman as submitted to the Agency in April 2010. As a result of the delay in the finalisation of the access policies, the first publication of aggregated data for centrally authorised products did not take place in 2010.

Increasing numbers of requests for access to documents and requests for information

In 2010, the Agency saw a further increase in activities relating to access to information. The number of requests for information grew by around 15% (from 4,290 in 2009 to 4,987 in 2010).

Access to documents activities remained at the level of the previous year.

Requests	2009	2010
Access to information	4,290	4,987
Access to documents, including appeals	116	114
Number of pages released	7,603	7,090

1.5. Support for innovation and availability of medicines

This relates to activities contributing to innovation and availability of medicines for human use via the European Medicines Agency Innovation Task Force and CHMP working parties' activities, continuing cooperation with the European Commission in the context of the Innovative Medicines Initiative (IMI) and the 7th Framework Programme, and continuing participation as an observer in US Critical Path Institute initiatives. For veterinary medicines, the Agency provides input to the European Technology Platform for Global Animal Health and the Action Plan for the Community Animal Health Strategy.

The following activities also contribute to innovation and availability of medicines: continued implementation of orphan, advanced therapy and paediatric medicines policies, reinforcement of activities on medicines for geriatric populations, provision of scientific advice, operation of procedures shortening regulatory timeframes, stimulation of applications for products intended for non-EU markets in the context of cooperation with the WHO, support to veterinary pharmaceutical companies developing products indicated for minor uses/minor species (MUMS)/limited markets, contribution to the implementation of action plans arising from the Heads of Medicines Agencies' Taskforce on Availability of Veterinary Medicinal Products and the Community Animal Health Strategy.

Small and medium-sized enterprises operating in the human and veterinary pharmaceutical sectors are often innovative companies that can notably benefit from the pooling of scientific expertise at EU level. Regulations (EC) No 726/2004, (EC) No 1394/2007 and Commission Regulation (EC) No 2049/2005 make provisions for incentives in the form of fee reductions or deferrals and administrative assistance by the Agency's SME Office.

Regulatory support to innovative drug development

Good progress was made in 2010 with a number of initiatives to promote innovative drug development.

The Agency received nine scientific advice requests on new methodologies for drug development, a 4.5-fold increase over 2009. A procedure was established by the end of the year.

The Agency participated in a number of projects related to the Innovative Medicines Initiative and Critical Path (C-Path) activities. These included SAFE-T, a project dealing with qualification of translational biomarkers, and EMTRAIN, the European Medicines Research Training Network.

PROTECT

Good progress was made with the Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium (PROTECT) project. 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 31 public and private partners.

A grant agreement was signed in February 2010 and pre-financing was received and distributed among the partners. A multilayer project coordination and management system was put in place, providing for efficient and reliable operation and implementation of the project. Following collection of financial statements from the project partners and receipt of progress reports from the work packages, the Agency finalised the annual report for the Innovative Medicines Initiative Joint Undertaking.

European Medicines Agency/CHMP think-tank exercise on innovation

The Agency/CHMP think-tank exercise was nearing completion by the end of 2010. All outstanding actions in the plan were addressed and closed off over the course of 2010. The Agency is now finalising a report for publication during 2011.

Agency input to European activities for medicines used in geriatric populations

The Agency developed a detailed proposal for initiatives aimed at ensuring that medicines are adequately tested in the elderly. The plan was sent to the CHMP for agreement by the end of the year. During the year, the Agency made progress in establishing contacts with recognised learned societies in the field.

Promoting scientific advice for medicines for minor uses and minor species (MUMS)/limited markets

Following amendment of the procedure in 2009, uptake of scientific advice by companies developing veterinary medicines for minor uses and minor species (MUMS)/limited markets increased significantly in 2010. Eight out of 21 scientific-advice requests received were for MUMS. Twenty four requests for classification of a product intended as a MUMS/limited-market product were received, indicating receipt of further scientific-advice requests in the future.

SME Office

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.

The work of the Agency's SME Office has been recognised widely by stakeholders. In 2010, the SME Office was awarded the Mediscience award for 'Most significant contribution to mediscience sector'.

Other achievements in 2010:

- The Agency received 102 requests for administrative assistance, 9 more than in 2009.
- 251 requests for qualification as an SME were received, 25% more than expected. 272 requests for renewal of SME status were received.
- A total of 495 decisions with regard to qualification for or renewal of SME status were concluded.
- By the end of 2010, the Agency launched the SME registry, to facilitate and promote interaction among SMEs. The database provides information on companies that are registered as SMEs with the Agency. The registry is intended to give a more complete picture of the registered SMEs in Europe and to support their growth in the EU through partner search and cooperation.

1.6. Methodology and outcomes-assessment projects

Activities of the Agency in this area focus on developing the capacity for performing assessments of specified regulatory outcomes and methodologies to aid regulatory decisions on the benefits and risks of medicines.

Advancing regulatory science

The Agency plays a key role in the development and application of regulatory science, which covers all areas of science that are used in the assessment of the quality, safety and efficacy of human and veterinary medicines throughout their lifecycle, as well as the scientific areas used in regulatory decision-making.

In November 2010, the Agency announced the launch of a collaborative research project with the Massachusetts Institute of Technology (MIT), focusing on enhancing regulatory science in pharmaceuticals. Specific questions addressed by this project include the adaptation of the current regulatory requirements to support the efficient development of safe and effective drugs, incorporation of patient preferences into regulatory decision-making, implementation of 'staggered' and 'progressive' approaches to drug approval, and improving the fulfilment of post-marketing regulatory requirements.

The year ended with a conference on regulatory science. This event, hosted by the Agency, gave stakeholders an opportunity to discuss what role the Agency can play to best support regulatory science.

Methodology for benefit-risk assessment

The Agency strives to make its opinions on the balance of benefits and risks as consistent and transparent as possible. A three-year project on benefit-risk methodology was begun in early 2009, aiming to identify decision-making models that can be used in the Agency's work. The project is carried out in cooperation with experts in decision theory from the London School of Economics and Political Science (LSE) and with the University of Groningen.

Two of the five work packages were finalised in 2010. These cover description of the benefit-risk assessment models already being used in the EU regulatory network and assessment of the suitability of the current tools and processes used in benefit-risk assessments. Work to field-test the most appropriate models identified in the earlier stages of the project in five European medicines regulatory agencies began in September 2010.

Effectiveness of risk-management plans

The Agency finalised a report on the effectiveness of the measures put in place by marketing authorisation holders as part of risk-management plans in 2006 and 2007. The final report, 'Effectiveness of risk-minimisation measures as reported by marketing-authorisation holders', was published.

Impact of scientific advice on the outcome of marketing-authorisation applications

The Agency set up a detailed methodology for reviewing the impact of scientific advice on the outcome of marketing-authorisation applications for human medicines, product by product. A report was finalised and published in the January 2010 edition of the Journal of Clinical Pharmacology.

In addition to the projects mentioned, Agency staff participated in scientific projects relating to the Agency's core activities. A comprehensive list of publications by staff, members of the scientific committees and working parties is available as an Annex to this report.

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-resources management; business and financial management; health and safety and environmental policies; and business-continuity planning.

Organisational structure

The implementation of the new organisational structure of the Agency was completed in 2010. The new structure has been put fully in place following the establishment of a new Sector for Product Data Management and the appointment of Jean-Claude Brival as new Head of Sector.

Operational excellence, 'OpEx@EMA'

There has been growing interest in operational excellence ('OpEx') initiatives in both public and private sectors over the past decade. While the private sector is looking to increase profitability, the Agency looks for increased efficiency and improved service to its stakeholders.

Adopting an operational-excellence programme addresses the needs of the Agency to respond to the changing environment in which it operates. The operational-excellence programme's objective is to strengthen the Agency with a structured business-driven approach, to further improve efficiency and effectiveness and reduce the complexity of the administrative burden in the area of new marketing-authorisation applications.

It also recognises that processes rely on people and further addresses mutual expectations, relevant skills, roles and responsibilities. Finally, the programme will work with the operating structure from an end-to-end-process perspective, to better support the Agency's capabilities to deliver and support sustainable results. Consultation at the national competent authorities and other European agencies has started.

Competence-development among staff

Much effort was again devoted to developing the competence of the Agency's staff, and the Agency now offers a comprehensive range of courses to its staff. Following the launch of an internal scientific-training programme, a number of training sessions on issues such as biomarkers, statistics and clinical-trials methodology were organised.

In addition, the Agency is also looking at technology-based learning applications, and completed a pilot for the development of appropriate e-learning courses.

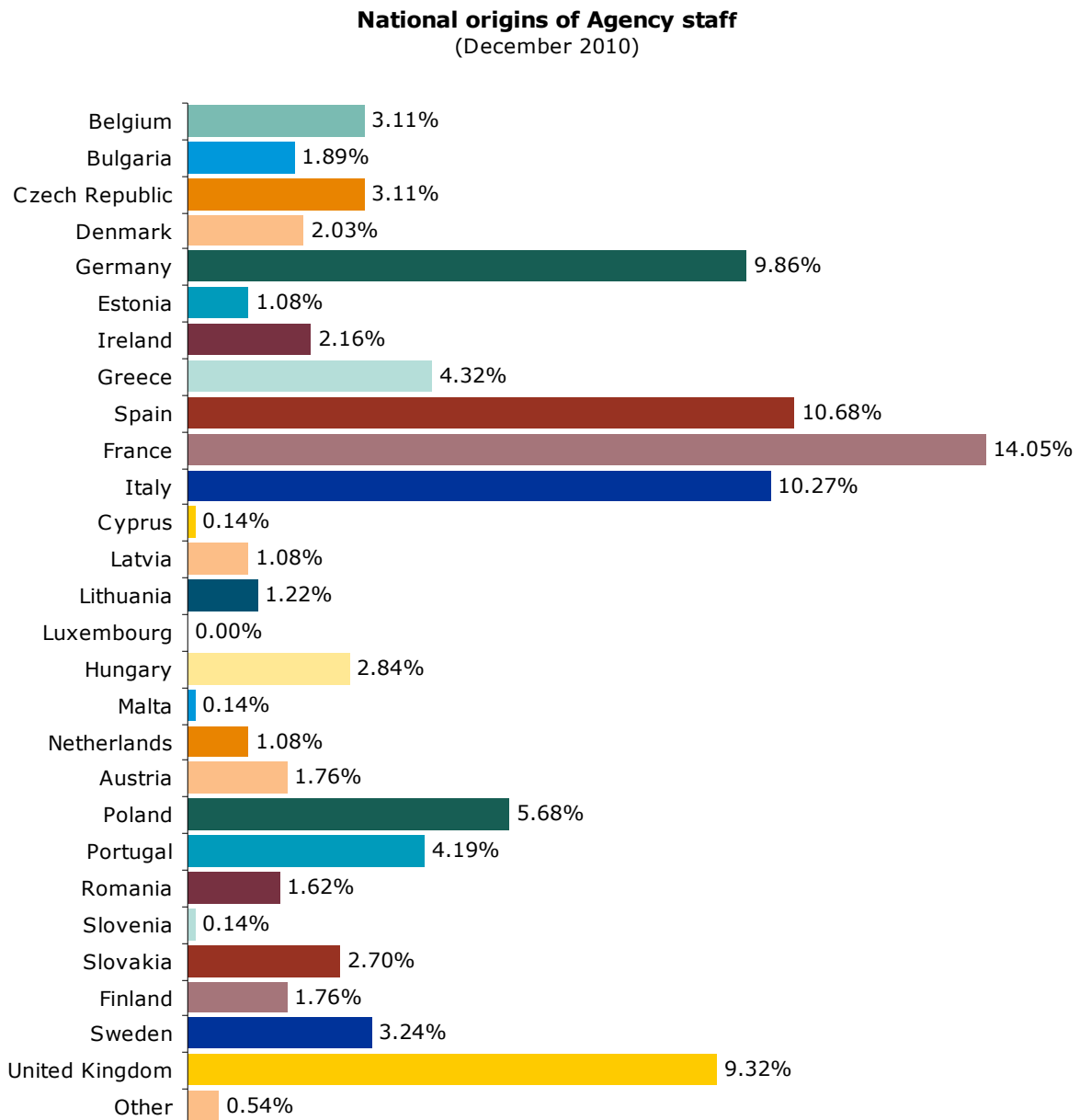
Staff management and recruitment

The establishment plan for 2010 foresaw a total of 567 temporary-agent posts in 2010. 96% of these posts were occupied by the end of the year. In addition, there were 97 contract agents and 98 other staff, including interims, contractors, trainees and national experts.

A total of 90 selection procedures were carried out in 2010. The majority were related to recruitment of contract agents.

French staff members represent the largest group in terms of national origins, followed by Spain, Italy, Germany and the United Kingdom.

Figure 2.



Enterprise-resource planning

The implementation of an Agency-wide enterprise-resource-planning system for the Agency's financial transactions (SAP FIN) was a major activity in 2010, with its implementation on track by year's end.

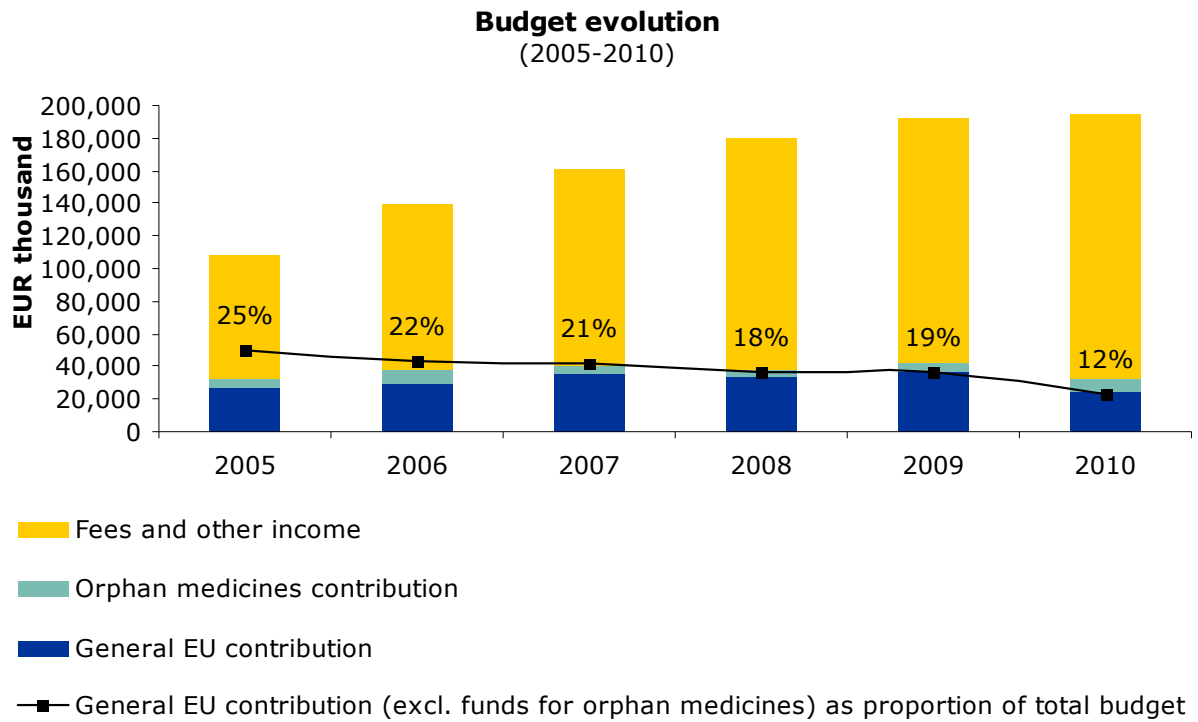
Accommodation planning

In preparation for the expiry in 2014 of the lease for the Agency's current premises at 7 Westferry Circus, in London, the Agency explored a variety of options for its future accommodation, taking into account potential future needs. A feasibility study on office premises for the Agency after 2014 was carried out and presented to the Management Board. A final decision is expected during the first quarter of 2011.

Budget

The Agency's total budget for 2010 was EUR 208,387,000, of which 18.7% derived from the general EU contribution to the Agency's budget.

Figure 3.



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

- Interest in the orphan-designation process remains high. A total of 174 applications for orphan designation were submitted in 2010 – a 6% increase over the previous year.
- The COMP adopted 123 positive opinions. Two applications received a negative opinion. A relatively high number of applications (48) were withdrawn prior to the adoption of an opinion.
- 78 of the 174 applications received were designated in parallel with the U.S. FDA.
- A total of 66 medicines that were recommended for orphan designation in 2010 were intended for the treatment of children.
- A third of COMP opinions were for medicines intended for use in cancer treatment.
- The average time taken to evaluate applications was 68 days, an eight-day increase compared with 2009.
- For 2010, a special contribution of €4.5 million, reinforced by €3.7 million financed by the Agency's surplus from 2008, totalling €8.2 million was granted, of which €1.2 million were used for fee reductions granted in 2009, leaving €7.0 million for fee reductions in 2010. The Agency processed requests for designated orphan medicinal products totalling €6,742,800.

Figure 4.

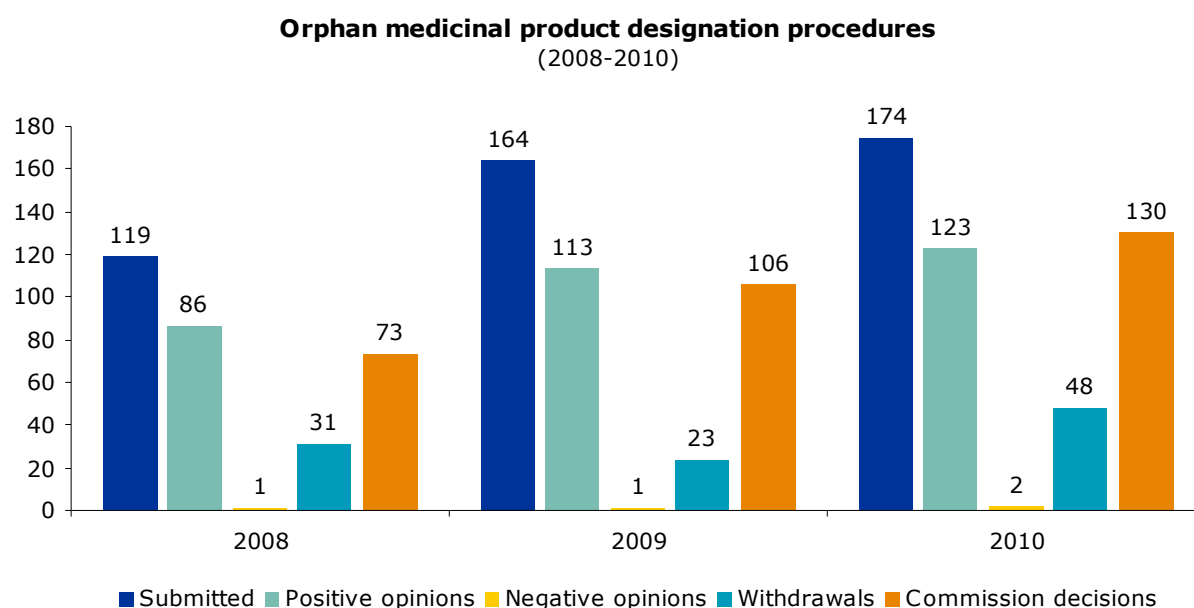


Figure 5.

Percentages of designated orphan medicinal products for the treatment of children and adults (2008-2010)

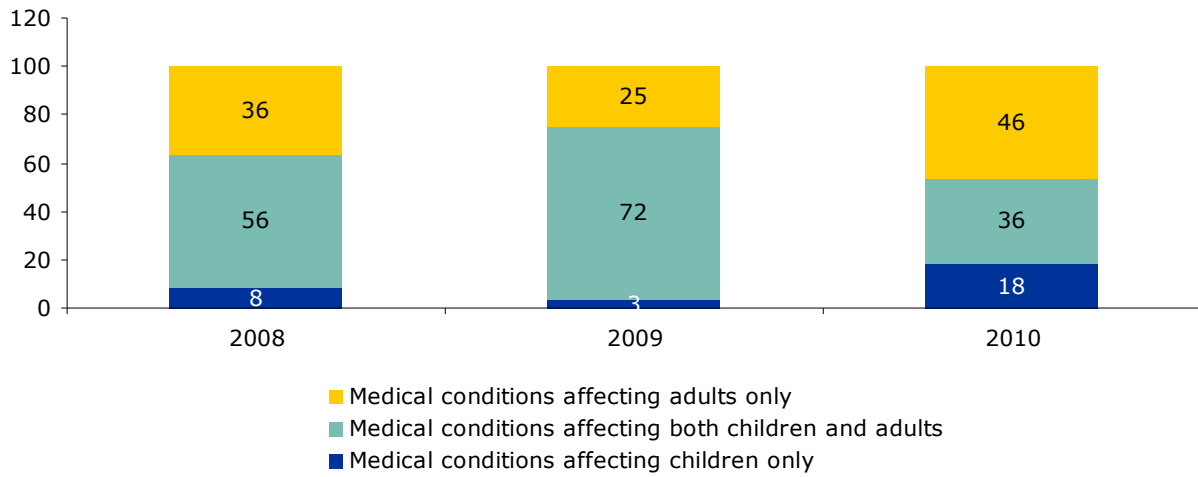


Figure 6.

COMP opinions by therapeutic area (2010)

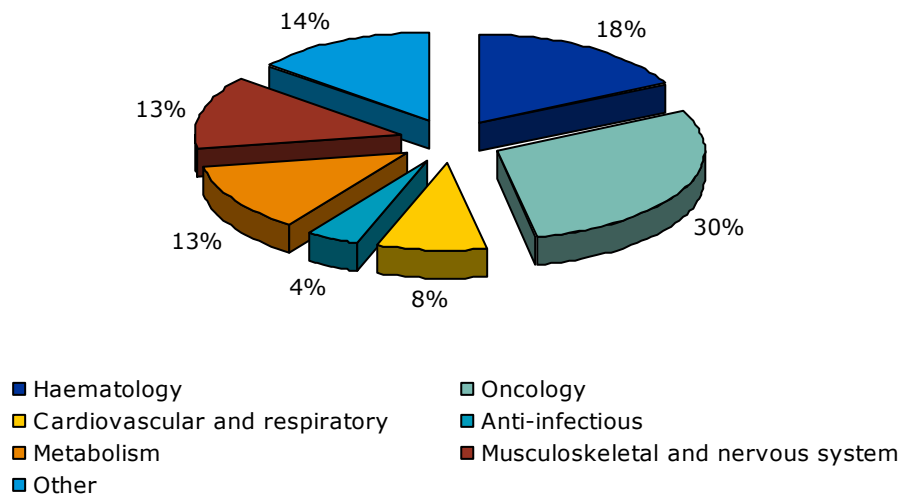


Figure 7.

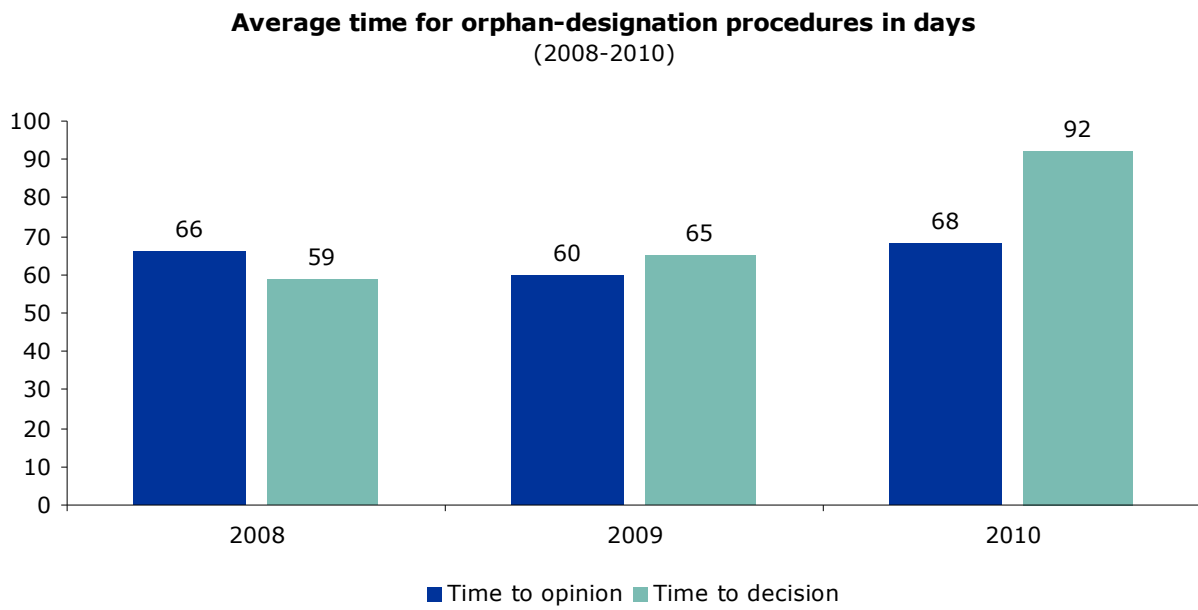
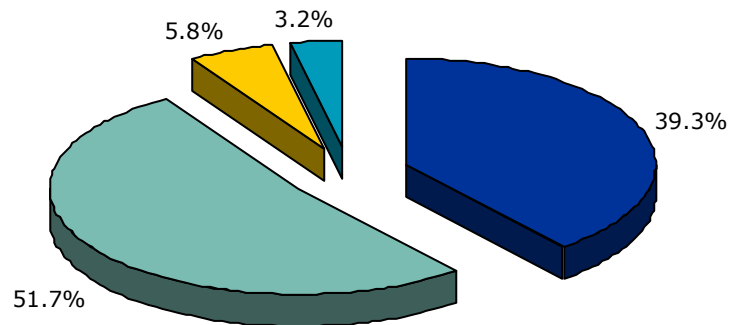


Figure 8.

Use of EU special contribution for orphan medicines
(2010)



■ Marketing authorisations ■ Protocol assistance ■ Inspections ■ Post-authorisation procedures

Specific objectives

Ten years of the COMP

- 2010 was the tenth year of the orphan regulation in the EU. To mark the anniversary, the Agency held a two-day conference on 3 and 4 May 2010, with representatives from the European Parliament, the European Commission, international and European regulatory agencies, members of the Committee for Orphan Medicinal Products (COMP), patient groups, health professionals, and the pharmaceutical industry. The conference was part of the Agency's reflection process on the impact the Orphan Regulation has made so far in the field of rare diseases and on future opportunities and challenges.

Increased communication

- In September 2010, the Agency published the first of its 'review of orphan designation' documents, summarising the COMP's position on whether the orphan designation for a medicinal product that is receiving marketing authorisation should be maintained or revoked. The first review document concerned Vpriv (velaglucerase alfa), which was authorised for the treatment of Gaucher disease on 26 August 2010. The COMP concluded that Vpriv's orphan designation could be maintained.
- The COMP's recommendation to the European Commission on the publication of data on clinical trials for rare diseases was postponed due to delays in the launch of the EU Clinical Trials Register.

Key performance indicator	Target	Outcome
Percentage of applications reviewed within 90-day timeline	100%	93%. 9 out of 123 delays occurred due to the extension of the COMP meetings and a lack of quorum.
Percentage of summaries of COMP opinions published within one month of the European Commission's decision on designation	90%	97%
Percentage of public assessment reports (on review criteria) published within one month of the European Commission's decision on marketing authorisation	80%	100%

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 332 requests for scientific advice in 2010, 7% more than in 2009.
- The number of requests for protocol assistance for orphan-designated medicines decreased slightly to 68, following a peak of 77 requests in 2009.
- 32 of the scientific-advice requests received related to medicines for children; 20 scientific-advice requests related to advanced therapy medicinal products.
- The parallel scientific advice procedure with the U.S. FDA was used for four requests.
- A total of 398 scientific-advice and protocol-assistance requests were finalised in 2010.
- The timeline for the delivery of scientific advice and protocol assistance has remained stable over a number of years. In 2010, the mean duration was 73 days.
- As in previous years, the therapeutic area with the highest number of requests received was oncology, followed by central-nervous-system conditions and anti-infectives.
- The Agency received 9 requests for qualification of biomarkers. The qualification process is a new, voluntary, scientific pathway leading to either a CHMP qualification opinion or advice on innovative methods or drug development tools.

Figure 9.

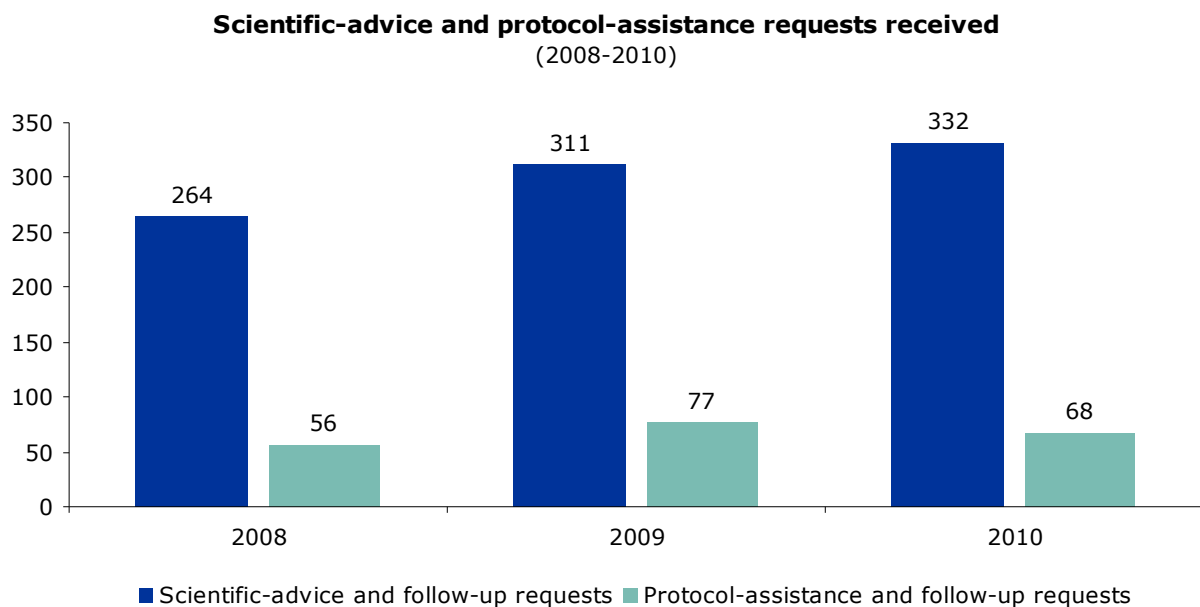


Figure 10.

Scientific-advice and protocol-assistance requests finalised
(2008-2010)

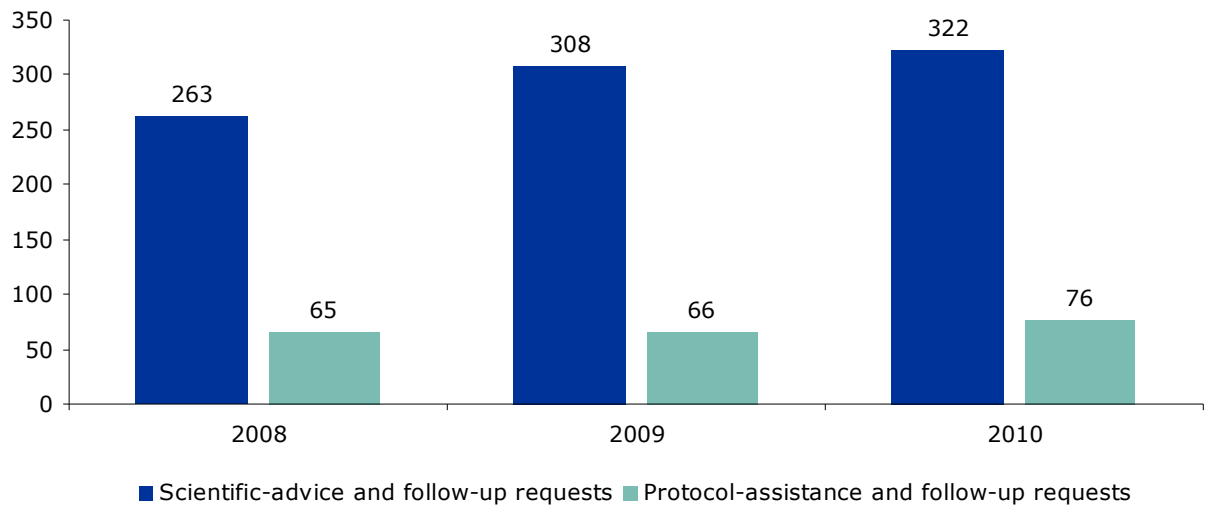


Figure 11.

Mean duration of scientific-advice procedures in days
(2008-2010)

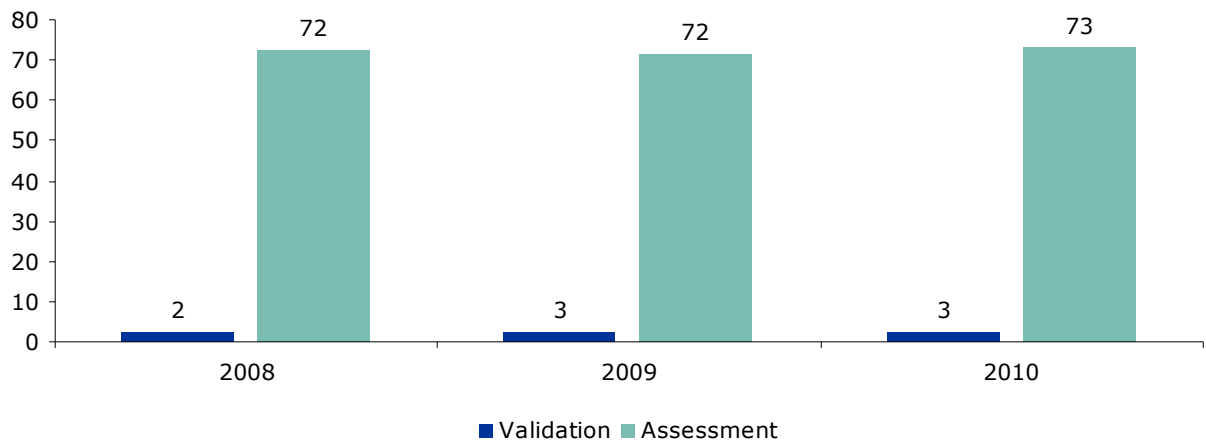
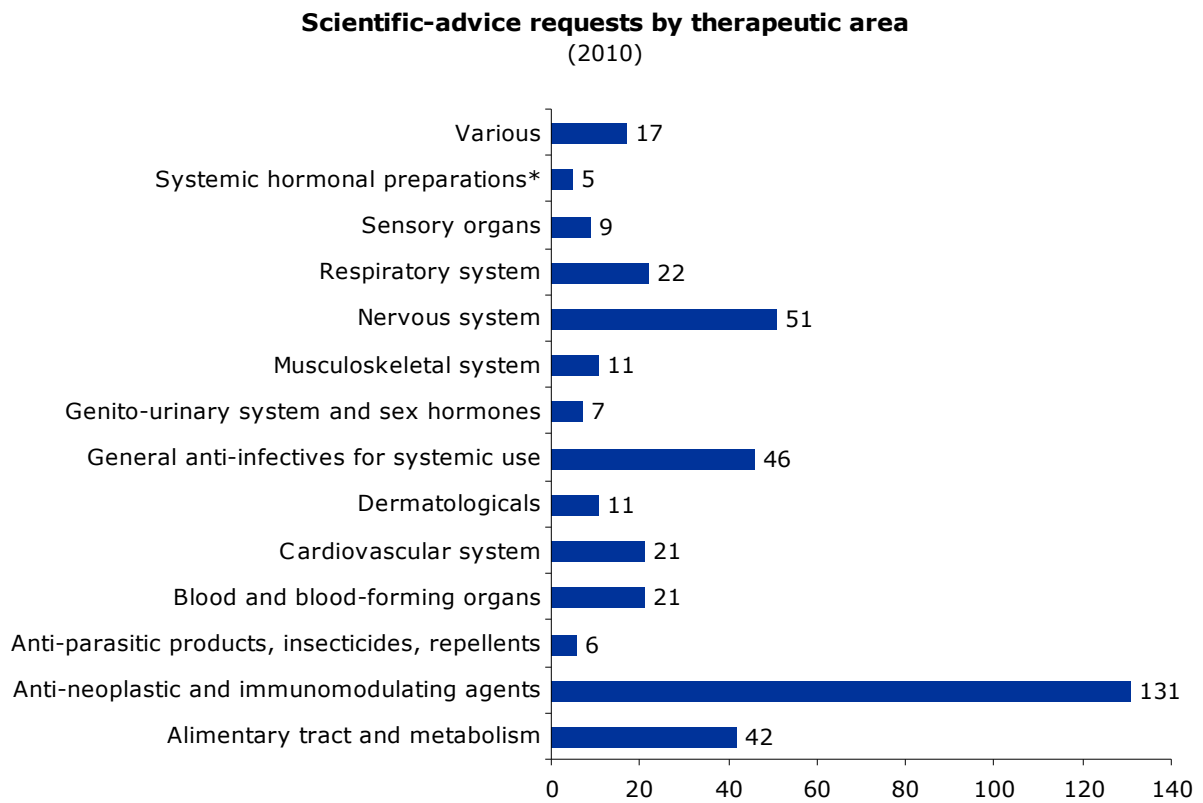


Figure 12.



* Excluding sex hormones.

Figure 13.

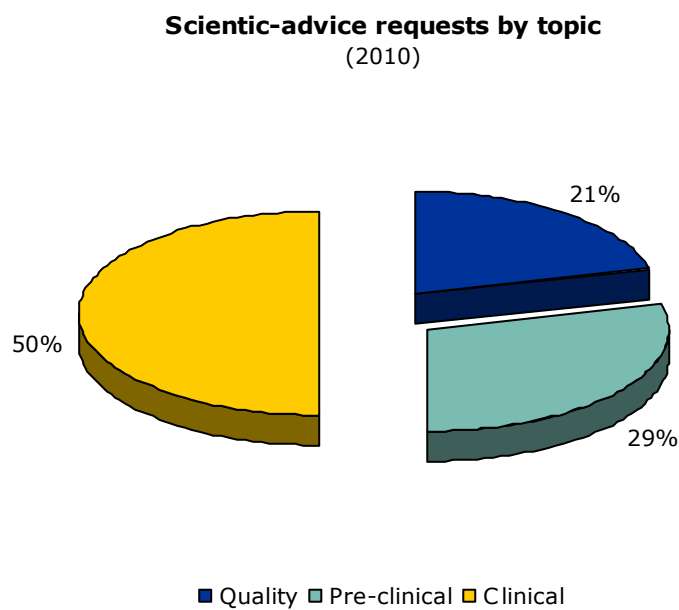


Figure 14.

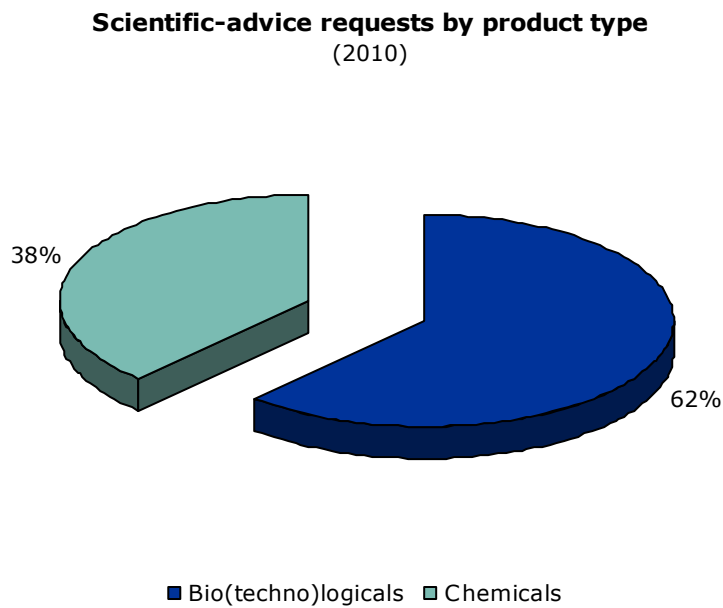
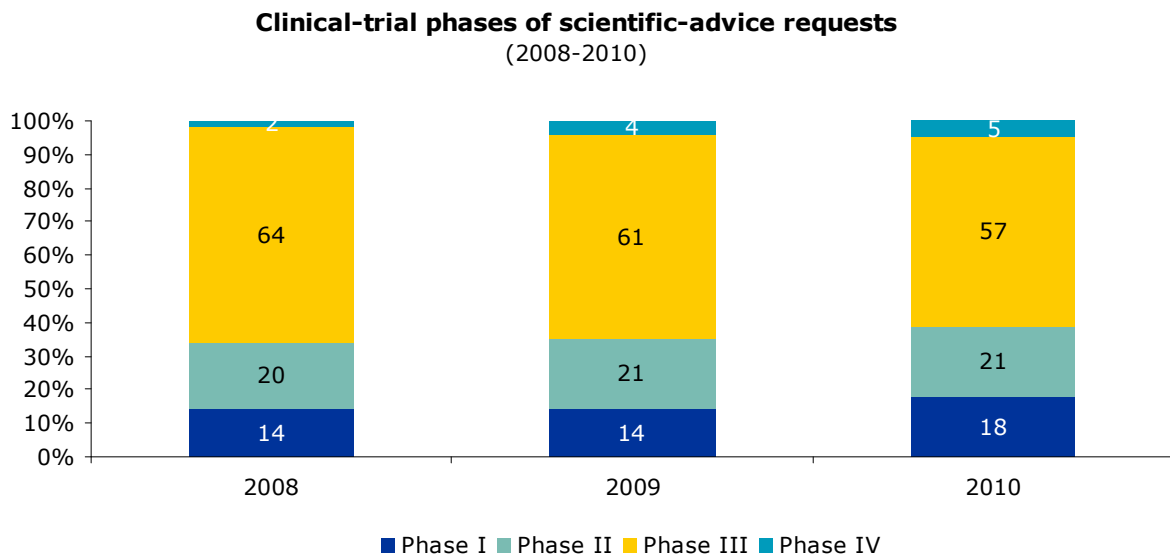


Figure 15.



Specific objectives

Supporting development of high-quality data on advanced therapy medicinal products (ATMPs)

- The scientific-advice procedure was promoted on the Agency's website, through regulatory workshops and in briefing meetings as a tool for SMEs to prepare for the advanced-therapies-certification procedure. The procedure foresees scientific evaluation by the Committee for Advanced Therapies (CAT) of quality and (where available) non-clinical data for ATMPs under development by SMEs. However, no applications for certification were submitted to the Agency in 2010.

Re-assessment of biomarker-qualification procedure postponed

- The re-assessment of the qualification procedure for biomarkers introduced in January 2009 was postponed because the critical number of requests needed for re-assessment of the procedure had not yet been reached.

Key performance indicator	Target	Outcome
Scientific-advice and protocol-assistance requests evaluated within the procedural timelines	100% of requests	99.5%
External experts involved in procedures	40% of SA and PA requests	38%

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 2010, the Agency received a total of 91 applications for marketing authorisation for human medicines, including 1 for a scientific opinion for a medicine intended for use outside the EU.
- Excluding multiple applications, this relates to 73 applications by active substance. Compared to 2009, this is a decrease of 5% in the total number of applications but an increase of 16% in terms of applications by active substance.
- Of the 91 applications received, 46 related to new medicines; 12 of these were for orphan-designated medicines.
- Almost half (43) of all applications received in 2010 were for generic medicines or hybrid and informed-consent applications. One application was received for a similar biological medicine.
- The Agency received the first application for a paediatric-use marketing authorisation (PUMA).
- Musculoskeletal disorders was the therapeutic area in respect of which most applications were received (24), followed by medicines intended to treat respiratory diseases and alimentary-tract disorders.

Figure 16.

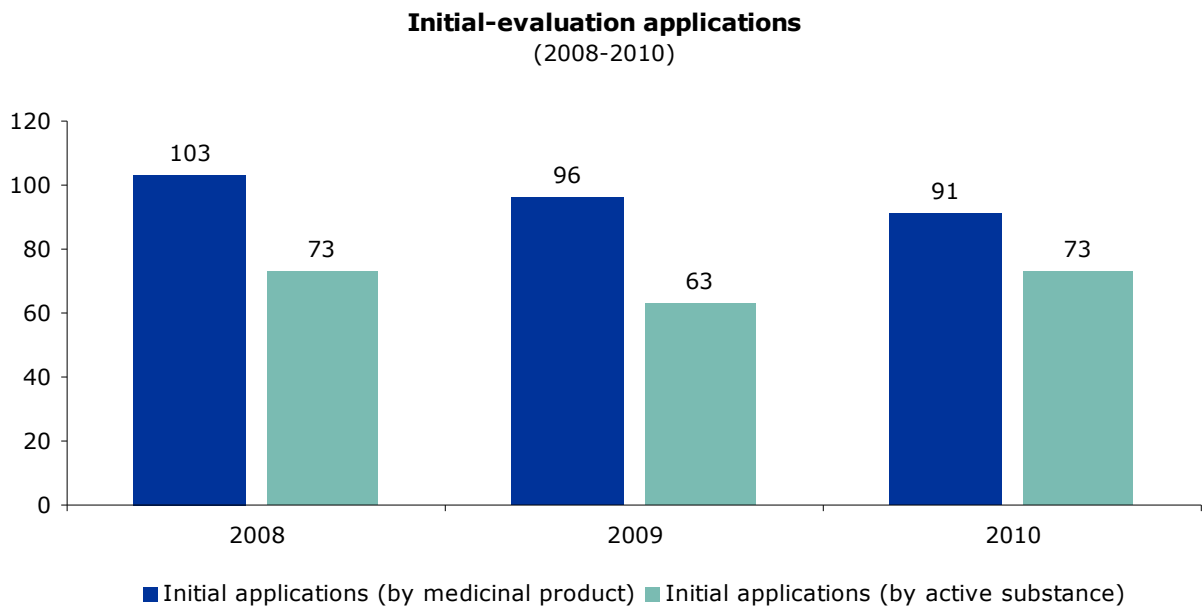
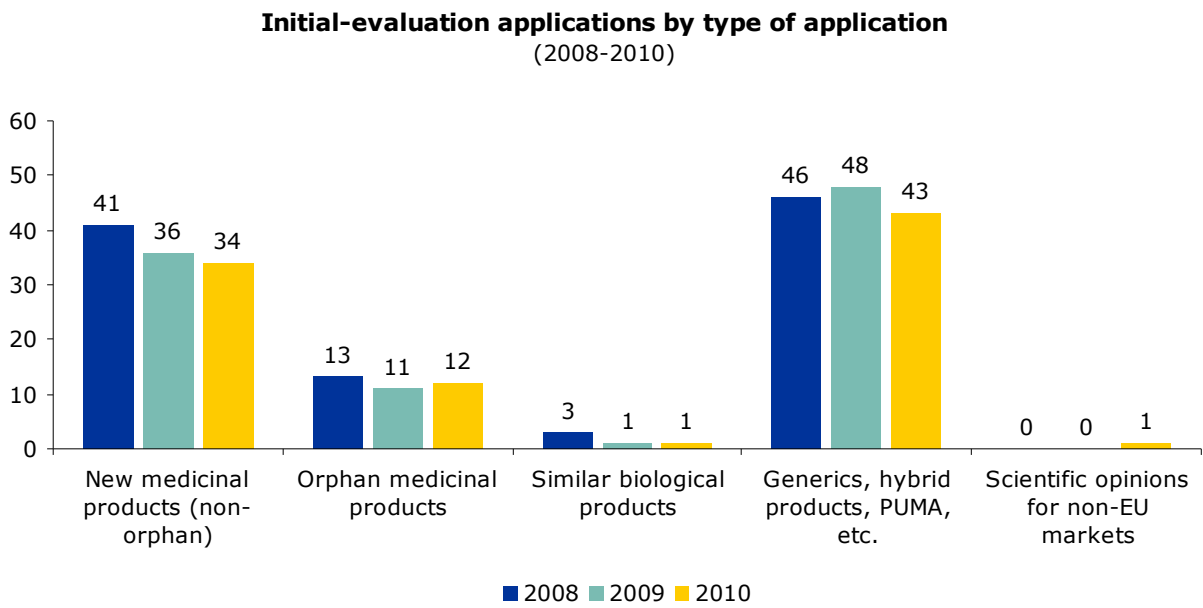


Figure 17.



Opinions adopted

- The Agency adopted a total of 53 opinions in 2010 – a sharp drop compared to the record number of 125 opinions adopted in 2009.
- Of the opinions adopted, 6 were for new orphan medicines. Out of 47 opinions for non-orphan medicines, 20 were for new medicines and 26 for generic or hybrid medicines and informed-consent applications. One opinion was adopted recommending a similar biological medicine for approval.
- Fifty-one applications received a positive opinion, 2 applications received a negative opinion. Applications for 12 medicines were withdrawn before the CHMP adopted an opinion.
- The CHMP finalised 3 re-examination procedures.
- The CHMP took an average of 167 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 114 days.

Figure 18.

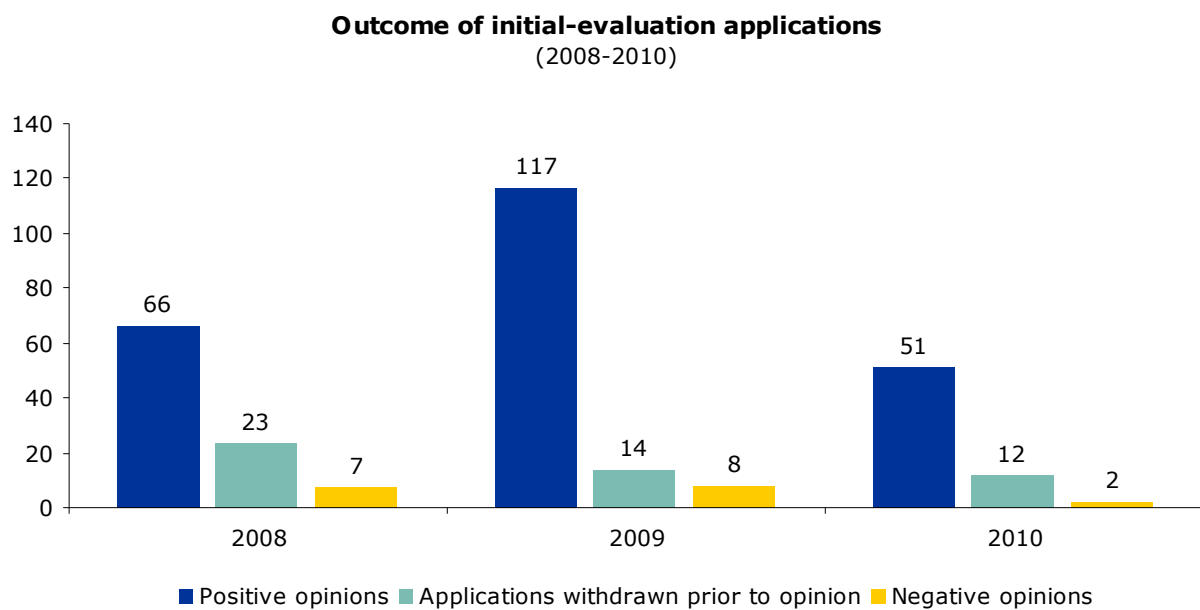
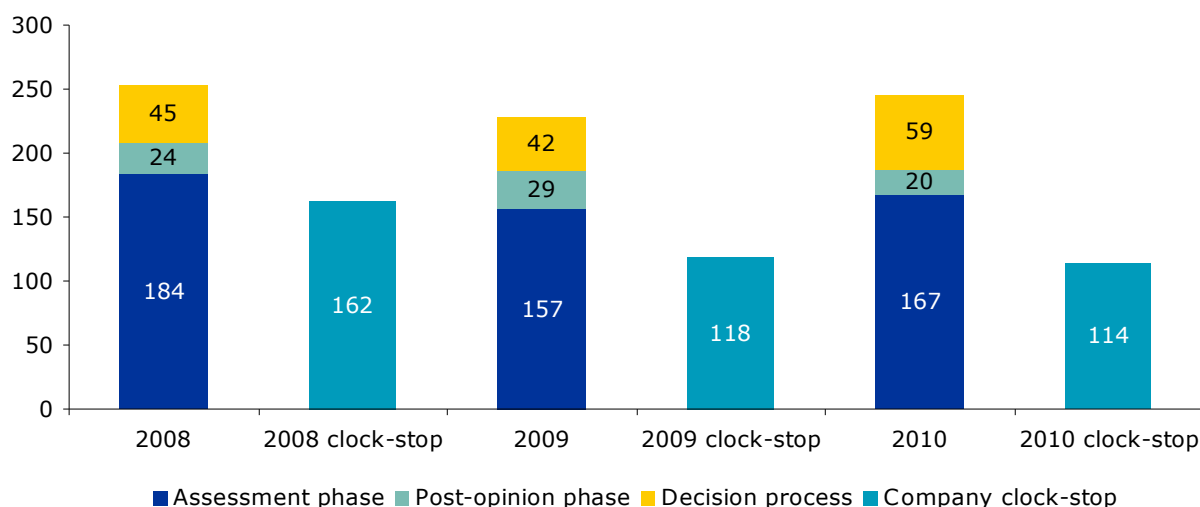


Figure 19.

**Average number of days for centralised procedures - positive opinions
(2008-2010)**



Public-health benefits of medicines recommended for approval in 2010

Medicines of notable public-health interest that received a positive opinion from the CHMP in 2010 included:

- The fourth and fifth influenza H1N1 pandemic vaccines intended for the prophylaxis of influenza in an officially declared pandemic situation.
- A new H5N1 mock-up pandemic-influenza vaccine intended for the prevention of influenza during an officially declared pandemic situation (a mock-up pandemic vaccine is not intended for stockpiling, but can be used to speed up the availability of a final vaccine in the event of a pandemic, once the pandemic strain has been identified).
- Prepandemic influenza vaccines intended for immunisation against the H5N1 subtype of the influenza A virus.
- A nasally administered influenza vaccine intended for the prophylaxis of influenza in children.
- A diagnostic agent intended as pharmacological stress agent for radionuclide myocardial perfusion imaging.
- A designated orphan medicine produced using recombinant DNA technology, intended for the treatment of angioedema attacks. It is extracted from the milk of rabbits that have had a gene (DNA) inserted, which makes them able to produce the human protein in their milk.
- A designated orphan medicine intended for the treatment of Gaucher disease. The product is of major public-health interest in the light of the shortage of the authorised medicine for the treatment of this disease.
- Designated orphan medicines intended for the treatment of pulmonary conditions; one for suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in cystic fibrosis, and another for idiopathic pulmonary fibrosis.

- A designated orphan medicine intended for the treatment of inborn errors in primary bile acid synthesis due to enzyme deficiencies.
- A designated orphan medicine intended for the treatment of patients with chronic lymphocytic leukaemia.
- A medicinal product intended for maintenance treatment of severe chronic obstructive pulmonary disease associated with chronic bronchitis in adult patients as add-on to bronchodilator treatment, presenting an oral treatment with a new mode of action.
- A medicinal product intended for the treatment of moderate to severe manic episodes associated with bipolar I disorder, and another for the treatment of schizophrenia.
- A medicinal product intended for the treatment of a musculoskeletal condition known as Dupuytren's contracture, presenting a non-surgical alternative.

Specific objectives

Improving the quality of assessment reports

- In line with its objective to reinforce the regulatory and scientific consistency and transparency of the CHMP's opinions on initial evaluation, all applications started in 2010 underwent improved documented quality-control in line with agreed criteria.

More detailed assessment of clinical data relating to the elderly

- As part of its strategy to ensure that medicines are adequately tested in elderly patients, the Agency achieved its target that 50% of applications started in 2010 should have a more detailed assessment of clinical data relating to geriatric populations and adequate reporting. The Agency introduced a monitoring system to check the inclusion of assessment of data in the elderly in rapporteurs' and co-rapporteurs' assessment reports.

Improved consistency in the assessment of identical applications for generic products between procedures at Agency and national level

- The Agency published an updated guidance document, as well as an explanatory question-and-answer document, for industry, marketing-authorisation holders and assessors on generic and hybrid applications.

Key performance indicator	Target	Outcome
Percentage of applications evaluated within the regulatory timeline of 210 days	100% compliance	96%
Percentage of accelerated assessment applications evaluated within the regulatory timeline of 150 days	100% compliance	100%
Percentage of opinions sent to the European Commission within the regulatory timeline of 15 days	100% compliance	100%
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, extension of marketing authorisations and transfer 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 variation and extension of marketing authorisations received in 2010 increased significantly, by almost 61%: a total of 4,145 applications were received, compared to 2,577 in 2009. The distribution by variation type also changed markedly compared to 2009. This is due to the implementation of the revised variations legislation, which changed the default variation from type II to type IB and introduced a new classification that resulted in the downgrading of variations from type II to type IB and type IA. The new classification also resulted in more detailed identification of individual variations that has contributed to the increase.
- The new variations legislation introduced new procedures for grouping and work-sharing. In 2010, the Agency received 111 applications for work-sharing procedures, 482 grouping applications and 41 applications for multi-product type-IA groupings.
- Adopted post-authorisation opinions and notifications also rose significantly, by 61% compared to the previous year. This also included opinions on 58 work-sharing applications, 339 grouping applications and 31 multi-product type-IA grouping applications.
- A total of 45 applications for an extension of the authorised indications or a broadening of the patient population for authorised indications were submitted. By the end of the year, the CHMP had adopted 25 opinions, giving new treatment options to patients.
- A total of 559 periodic safety-update reports (PSURs) were received in 2010 – a 32% increase compared to 2009. By the end of the year the review was concluded for 548 reports.

Figure 20.

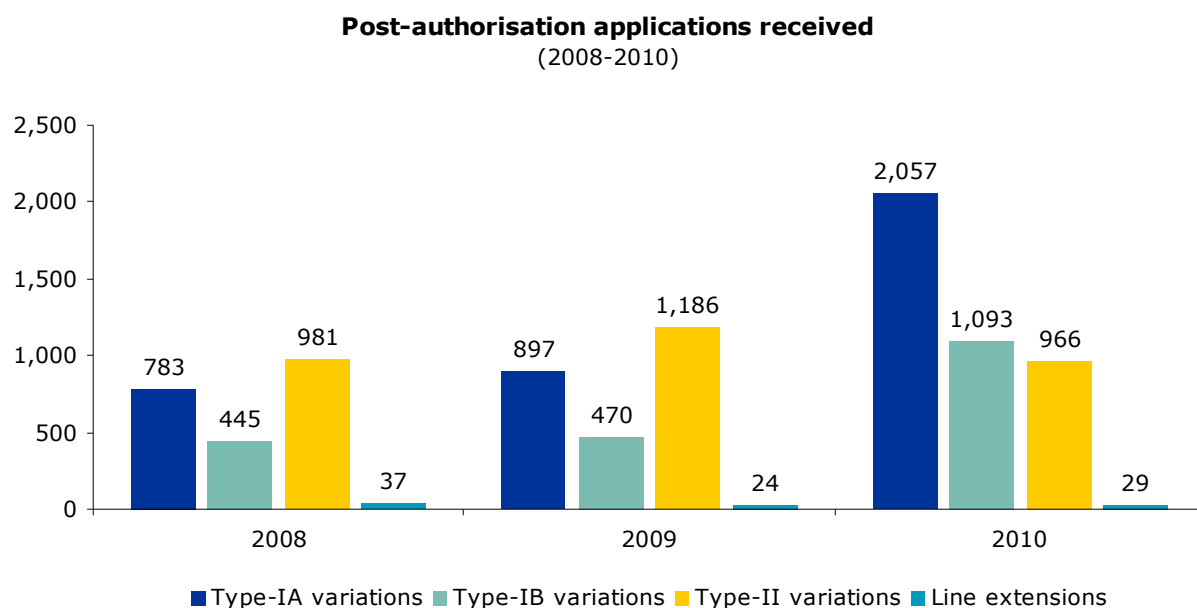


Figure 21.

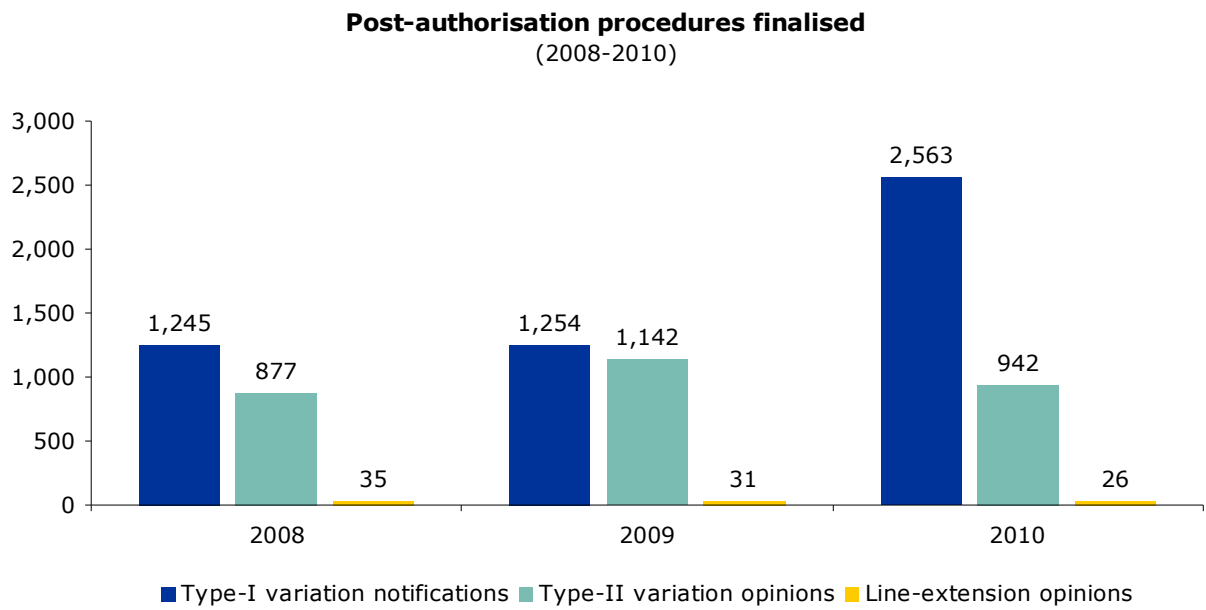
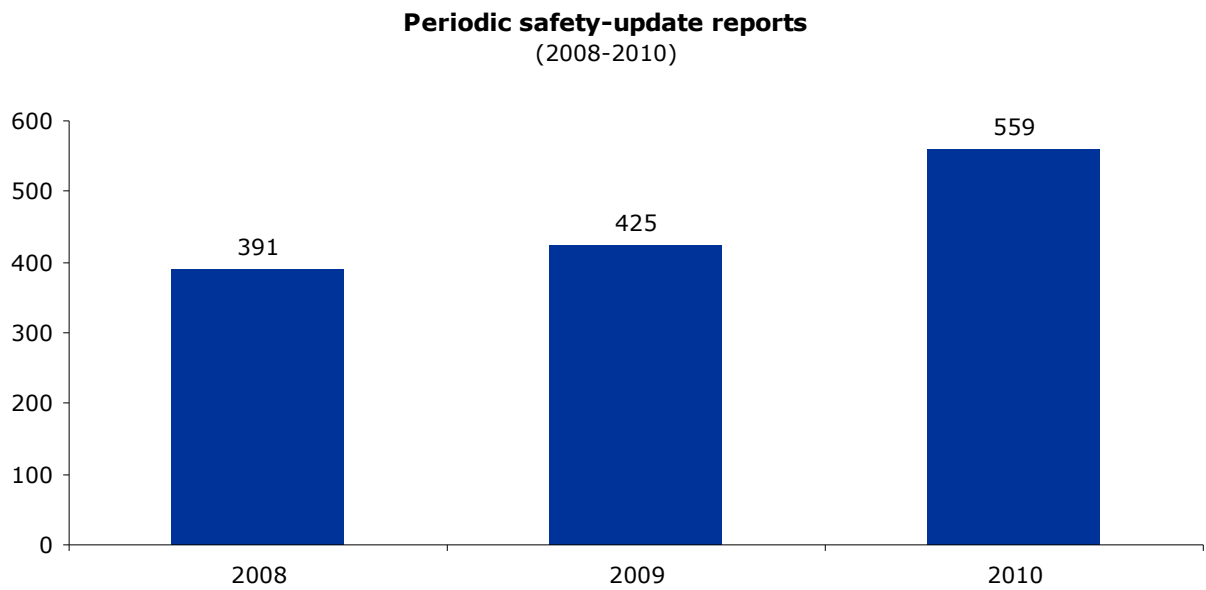


Figure 22.



Public-health impact of positive opinions for new indications in 2010

Compassionate use

The first 2 positive opinions under the European rules on compassionate use were adopted. They related to new intravenous formulations of authorised antiviral products used to treat critically ill patients with a life-threatening condition due to pandemic or seasonal influenza.

Positive opinions for new indications

The CHMP adopted 25 (including 4 duplicate) positive opinions recommending new indications or the broadening of the patient population for approved indications, providing additional treatment options for patients.

These new indications included:

- Cholestagel (colesevelam): combination treatment with ezetimibe, with or without a statin, in adult patients with primary hypercholesterolaemia, including familial hypercholesterolaemia.
- Tyverb (lapatinib): treatment of patients with breast cancer whose tumours overexpress HER2 (ErbB2), in combination with an aromatase inhibitor in postmenopausal women with hormone receptor-positive metastatic disease, not currently intended for chemotherapy.
- Tarceva (erlotinib): maintenance treatment in patients with locally advanced or metastatic non-small cell lung cancer with stable disease after four cycles of standard platinum-based first-line chemotherapy.
- Reyataz (atazanavir): treatment of HIV-1 infected paediatric patients above 6 years of age.
- RoActemra (tocilizumab): reduction in the rate of progression of joint damage and improvement in physical function, when given in combination with methotrexate.
- Orencia (abatacept): treatment of moderate to severe active rheumatoid arthritis in patients who responded inadequately to previous therapy with one or more disease-modifying antirheumatic drugs including methotrexate or a TNF alfa inhibitor.
- Taxotere and Docetaxel Winthrop (docetaxel): adjuvant treatment, in combination with doxorubicin and cyclophosphamide, of patients with operable node-negative breast cancer eligible to receive chemotherapy according to internationally established criteria for primary therapy of early breast cancer.
- Byetta (exenatide): treatment of type-2 diabetes mellitus in combination with thiazolidinedione (with or without metformin).
- Gardasil and Silgard (human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed)): prevention of premalignant genital lesions, cervical cancer and external genital warts in mid-adult women, from 26 to 45 years of age.
- Arixtra (fondaparinux sodium): treatment of acute symptomatic spontaneous superficial vein thrombosis of the lower limbs without concomitant deep vein thrombosis.
- M-M-RVAXPRO (measles, mumps and rubella vaccine live): vaccination of healthy children from nine months of age under special circumstances, in accordance with official recommendations or when early protection is considered necessary.
- Viread (tenofovir disoproxil): treatment of chronic hepatitis B in adults with decompensated liver disease.

- Mabthera (rituximab): treatment of follicular lymphoma patients responding to induction therapy; and a second change in indication regarding improvement in physical function and reduction in the rate of joint damage when given in combination with methotrexate.
- Tasisign (nilotinib): treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukaemia in the chronic phase.
- Invega (paliperidone): treatment of psychotic or manic symptoms of schizoaffective disorder.
- Lucentis (ranibizumab): treatment of visual impairment due to diabetic macular oedema.
- Sprycel (dasatinib): treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukaemia in the chronic phase.
- Sutent (sunitinib): treatment of unresectable or metastatic, well-differentiated pancreatic neuroendocrine tumours with disease progression in adults.
- Plavix, Iscover and Clopidogrel Winthrop (clopidogrel): prevention of atherothrombotic and thromboembolic events, including stroke, in adult patients with atrial fibrillation who have at least one risk factor for vascular events and who cannot take vitamin K antagonist therapy.
- Simponi (golimumab): adult patients with severe, active and progressive rheumatoid arthritis (RA) not previously treated with methotrexate; and reduction in the rate of progression of joint damage in all RA populations.

Negative opinions for new indications

The CHMP adopted 1 negative opinion recommending the refusal of extension of indication. For Avastin (bevacizumab), the CHMP concluded that the medicine's benefits do not outweigh its risks as first-line combination therapy with capecitabine in patients with metastatic breast cancer.

Specific objectives

Strengthening quality assurance for major changes to the marketing authorisation

- As part of its drive to improve the quality of the assessment reports, the Agency started the implementation of a system at the level of the CHMP to allow for peer-review of assessment reports relating to major changes to the marketing authorisation. The project was started in 2010 and is ongoing. This is based on the positive experience gained with CHMP peer-review during the initial evaluation phase.

Key performance indicator	Target	Outcome
Percentage of type-IA variations completed within the legal timeframe	100% compliance	85%
Percentage of type-IB variations completed within the legal timeframe	100% compliance	95%
Percentage of type-II variations completed within the legal timeframe	100% compliance	100%
Percentage of Agency recommendations on classification of variations delivered within the legal timeframe	80% compliance	82%

Key performance indicator	Target	Outcome
Percentage of grouping and worksharing procedures completed within the procedural timeframe	100% of applications	100%
Submission of outcome reports for post-authorisation commitments to applicants/MAHs within two weeks of the CHMP meeting	90% of reports	86% (2,323 reports were handled; 2,030 were on time)
Percentage of applications meeting the legal timeline of 27 days for the linguistic post-opinion check	100% of applications	70% (350 out of a total of 497 were on time; 101 were 1-3 days late; 46 were more than 3 days late)

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, ICSRs), periodic safety-update reports (PSURs), risk-management plans (RMPs) 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 2010, 541,495 individual case-safety reports relating to authorised medicines were received – an 11% increase over the previous year.
- The Agency received 95,405 reports of suspected unexpected serious adverse reactions (SUSARs) relating to medicines used in clinical trials – an increase of 4% over the previous year.
- All risk-management plans (90) submitted for initial applications and all (55) submitted for variations or line extensions resulting in a significant change to the marketing authorisation were peer-reviewed.

Figure 23.

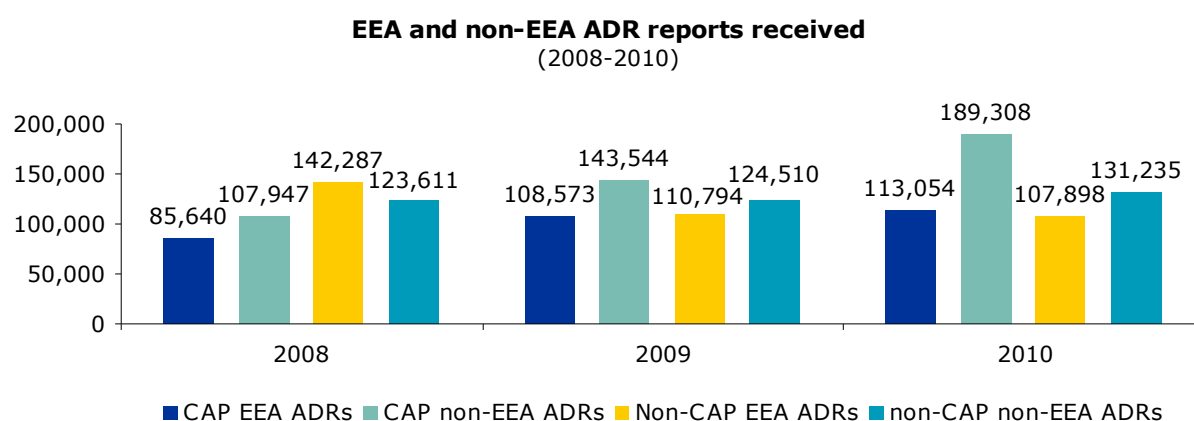
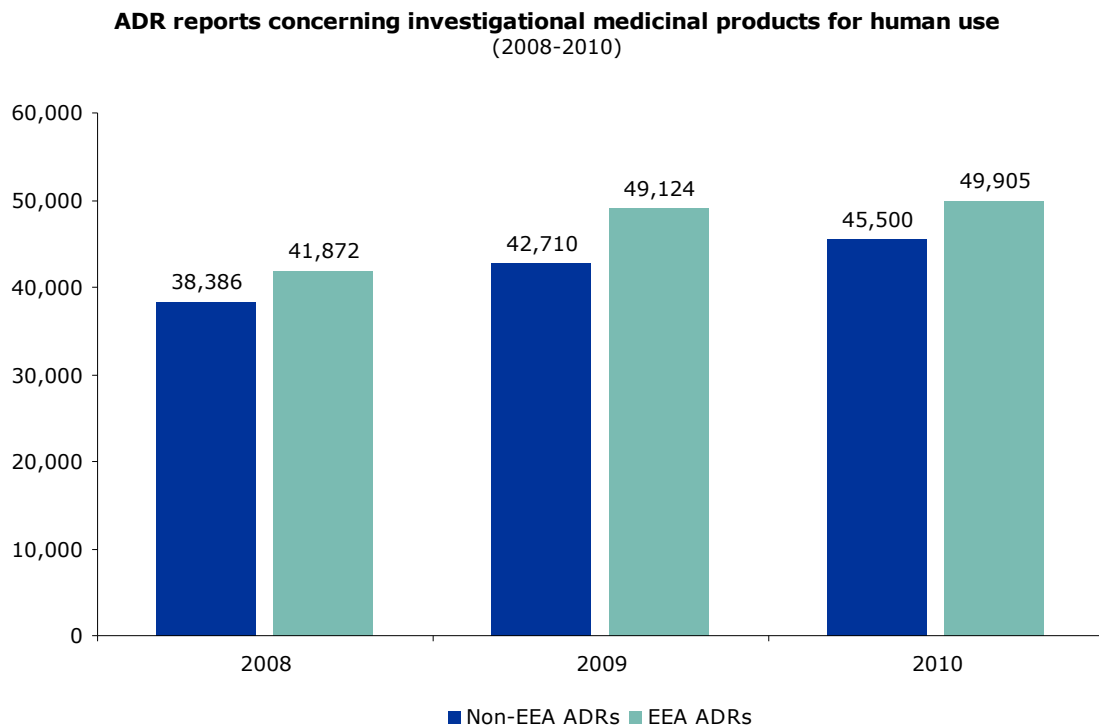


Figure 24.



Specific objectives

European Risk Management Strategy (ERMS)

- The Agency continued its contribution to the ERMS. The updated work plan was presented to the Heads of Medicines Agencies in April 2010. Work on preparing for an annual report and the next work plan was started.

European Incident Management Plan

- A report on the operation of the EU Incident Management Plan was prepared and presented to the Heads of Medicines Agency in July 2010, together with recommendations and an extension of the pilot phase.

Risk management

As part of the outcome assessment of risk-management plans, the report on the effectiveness of risk-minimisation measures was finalised (see also section 1.6).

Signal detection

The Agency continued the intensive monitoring of centralised vaccines and antivirals used in the 2009 H1N1-influenza pandemic. This included analysis and validation of safety data and production of initially weekly (and from March 2010 onwards, biweekly) pandemic safety updates for publication until August 2010.

The 2009 EudraVigilance-Human Status Report was endorsed by the Management Board for publication in October 2010. The report describes signal detection and the Agency's activities in relation to

EudraVigilance-Human in 2009. The report also covers signal-management activities, including information about the use of the EU Pharmacovigilance Issues Tracking Tool (EPITT), responses to queries from stakeholders and influenza-pandemic-related activities.

EudraVigilance

- A retrospective individual case-safety report (ICSR) data-quality-improvement exercise in EudraVigilance began, following selection of a service provider through a tender procedure.
- A detailed EudraVigilance project plan for 2010 to 2013 was prepared and approved by the EudraVigilance Steering Committee in February 2010, to ensure a coordinated development of the system in line with the expectations of medicines regulatory agencies and the need to support public-health protection, and in preparation for the new pharmacovigilance legislation.

In anticipation of the implementation of the EudraVigilance access policy, processes and procedures were being put in place to respond to the challenge that the new policy will have on resources and expertise.

The number of requests for data and data analysis from EudraVigilance received from stakeholders rose continuously throughout 2010. Timely responses were delivered in liaison with requesters to address very diverse scientific queries.

EU Pharmacovigilance Issues Tracking Tool (EPITT)

The first development phase of EPITT was concluded in 2010, including the integration of the tracking and monitoring of risk-management plans in EPITT. Currently, there are 250 Member State users of the system, with regular training sessions provided to them. An extension of licences and features to further extend the number of users was requested. EPITT is very well received by the Member States.

Collaboration with DG Research on publicly funded drug-safety research

- Working with the European Commission's DG Research to identify drug-safety-research priorities, the CHMP adopted a list of prioritised drug-safety-research questions.
- The Agency published calls under the Seventh Framework Programme (FP7), aimed at increasing the number and quality of research projects submitted to the European Commission for funding. The Agency worked with researchers to facilitate high-quality research in response to the CHMP research question funded by the Commission.

European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

The second release of the database of research centres and data sources in the context of ENCePP was released to the public in May 2010. By the end of 2010, there were over 100 datasource entries between centres, networks and datasources.

The newly formed ENCePP steering group held several meetings, and adopted the code of conduct for ENCePP studies and the checklist of methodological standards for protocols – cornerstones of the novel 'ENCePP study' seal for independent and transparent studies. Three requests for the ENCePP seal were received in 2010.

PSUR-worksharing initiative

The Agency continued to support the Member States in their PSUR-worksharing initiative. Synchronisation lists were published in the second quarter of 2010 and will be revised on a quarterly basis.

Key performance indicator	Target	Outcome
Percentage of RMPs peer-reviewed by the Agency as part of the assessment of the initial marketing-authorisation application	80%	100% (90 out of 90)
Percentage of RMPs peer-reviewed by the Agency as part of the assessment of variations and line extensions that result in a significant change to a marketing authorisation	80%	100% (55 out of 55) of variations to extend the indication where an RMP was submitted. 100% (32 out of 32) of line extensions where an RMP was submitted.
Percentage of ICSRs reported electronically for centrally authorised medicines	100%	100%

2.6. Parallel distribution

- The number of initial parallel-distribution notifications received exceeded the forecast by more than 40%. In total, the Agency received 2,599 initial notifications in 2010 – 16% more than in 2009.
- The number of notifications of a change received by the Agency decreased by 17% compared with 2009, to a total of 4,590. This is the result of a new system to reduce the notifications of a change, which was introduced in September 2010 following consultation with stakeholders. The new system is similar to the 'do and tell' concept in the new Variations Regulation, and focuses on those changes that have a genuine impact.
- The average time taken to handle initial parallel-distribution notifications reduced significantly, from 28 days to 9 days, with a significant increase in consistency, following the launch in August 2010 of a new system for electronic submission of parallel-distribution notifications, which allows electronic checks to be made using newly installed text-verification software. The new system had been tested in a pilot phase during the first part of the year.

Figure 25.

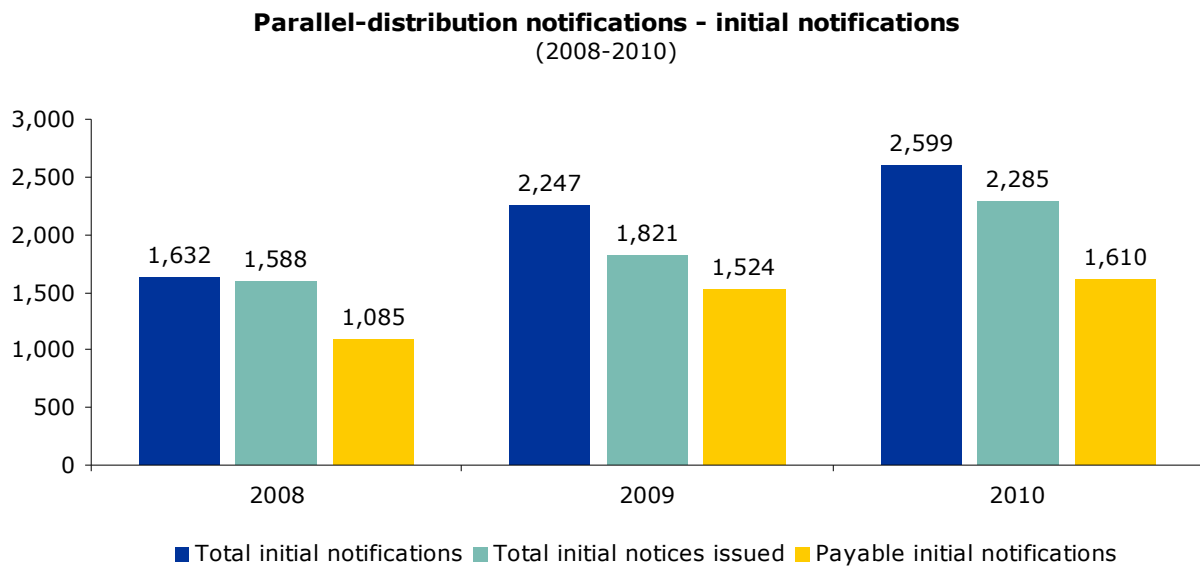
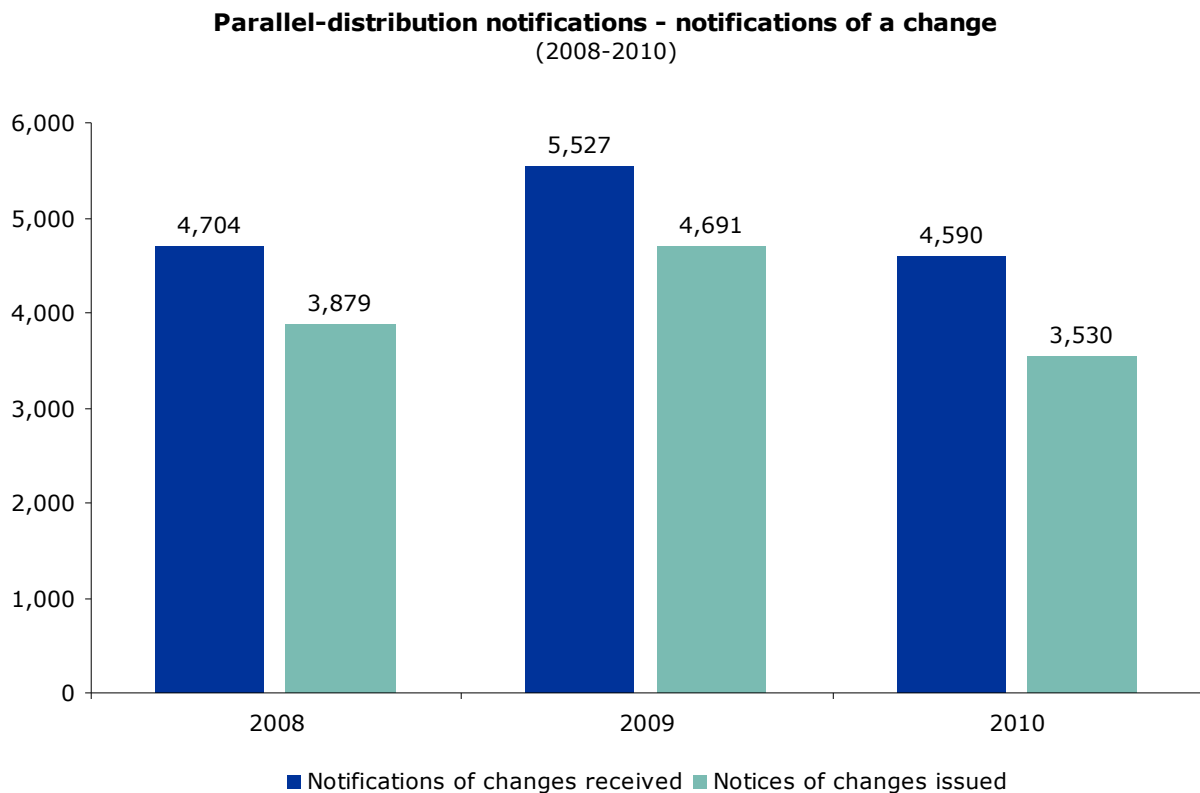


Figure 26.



Key performance indicator	Target	Outcome
Percentage of notifications checked for compliance within the regulatory timeline of 35 working days (five days for validation and 30 days for regulatory check)	70%	64%

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 Article 13 of Commission Regulation (EC) No 1234/2008) 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.

Articles 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.

Articles 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 level of activity remained high in the area of referrals. Twenty-seven new procedures were started for medicines authorised at national level and 28 review procedures were started for centrally authorised medicines.

All legal timeframes for the scientific review were complied with, including that for the publication of Q&A documents at the time of the CHMP opinion.

Some delays occurred in the transmission of translations to the European Commission, due to continuing problems with the late receipt of translations from the Translation Centre and the marketing-authorisation holders, in particular in the case of class referrals where several marketing-authorisation holders are involved.

The handling of referral procedures is becoming more and more complex, both scientifically and administratively, with an increasing number of expert meetings and scientific-advisory-group meetings that have to be organised in the context of referral procedures. In addition, a high number of marketing-authorisation holders, in particular in the case of class referrals, are involved in the procedures, increasing the administrative burden on the Agency.

For referral procedures finalised from October 2010 onwards, the CHMP assessment reports were systematically published, in addition to the CHMP conclusion, after the publication of the European Commission Decision, to increase the transparency of these procedures.

Procedures of high public-health interest in 2010

Avandia, Avandamet and Avaglim (rosiglitazone)

The review of the rosiglitazone-containing antidiabetes medicines Avandia, Avandamet and Avaglim was initiated in July 2010, following the availability of new studies questioning the cardiovascular safety of the substance. In view of the restrictions already in place on the use of rosiglitazone, the Committee could not identify additional measures that would reduce the cardiovascular risk, and therefore concluded that the benefits of rosiglitazone no longer outweigh its risks, and recommended the suspension of the marketing authorisations for the medicines in September 2010.

Avastin (bevacizumab)

The CHMP finalised a review of the use of Avastin (bevacizumab) in combination with other anticancer medicines in the treatment of metastatic breast cancer. The Committee concluded that the benefits of Avastin in combination with paclitaxel outweigh its risks, and that this combination remains a valuable treatment option for patients suffering from metastatic breast cancer. The Committee also concluded that the balance of benefits and risks of Avastin in combination with docetaxel is negative, and that this combination should no longer be used in the treatment of breast cancer.

Octagam (human normal immunoglobulin)

In September 2010, the Committee recommended the suspension of the marketing authorisations for Octagam (human normal immunoglobulin), from Octapharma GmbH, and a recall of Octagam currently on the market in Europe, because of an unexpected increase in reports of thromboembolic reactions in patients receiving the medicine, thought to be related to problems with the medicine's manufacturing process. Octagam is an intravenous solution used to strengthen the body's immune system and lower the risk of infection in patients with a weakened immune system.

Following this, the Committee began a separate review of Octagam, to allow for a scientific assessment of all available data on the safety and quality issues identified previously. This included the manufacturing process and the identification of appropriate corrective measures, and will allow for a coordinated approach across Europe on the resulting actions.

Rotarix (rotavirus vaccine, live) and Rotateq (rotavirus vaccine, live, oral)

The Committee confirmed that the oral vaccines Rotarix and Rotateq continued to have a positive benefit-risk balance, and that the presence of DNA of Porcine circovirus type 1 (PCV-1) did not present a risk to public health. Results from a very large clinical-study database, together with safety data from millions of children who had already received the vaccine, showed no safety concern with the vaccine. However, since PCV-1 should not be present in the Rotarix vaccine, the manufacturer proposed measures to manufacture the vaccine free of the virus.

Sibutramine-containing medicines

In January 2010, the CHMP recommended the suspension of the marketing authorisation for sibutramine-containing medicines, because the Committee concluded that their benefits as a weight-loss aid did not outweigh the cardiovascular risks. Sibutramine-containing medicines were authorised as Reductil, Reduxade, Zelim and other tradenames in the European Union. The review was initiated because data from the Sibutramine Cardiovascular Outcome Trial (SCOUT) showed an increased risk of serious, non-fatal cardiovascular events such as stroke or heart attack with sibutramine, compared with placebo.

Modafinil-containing medicines

In July 2010, the CHMP recommended restricting the use of modafinil-containing medicines to the treatment of sleepiness associated with narcolepsy. Doctors and patients should no longer use these medicines for the treatment of idiopathic hypersomnia, excessive sleepiness associated with obstructive sleep apnoea, or chronic shift work sleep disorder. This recommendation was confirmed in a re-examination procedure.

Topical formulations of ketoprofen

Finalising a review of topical formulations of ketoprofen, a non-steroidal anti-inflammatory drug (NSAID), the CHMP concluded in July 2010 that the benefits of these medicines continued to outweigh their risks. However, the Committee recommended that doctors should inform patients on how to use these medicines appropriately, to prevent the occurrence of serious skin-photosensitivity reactions.

Tysabri (natalizumab)

In a review of Tysabri (natalizumab) and the risk of progressive multifocal leukoencephalopathy (PML), a rare brain infection caused by the JC virus, the CHMP concluded in January 2010 that the benefits of this medicine continued to outweigh its risks for patients with highly active relapsing-remitting multiple sclerosis, but recommended further measures to manage the risk of PML.

Peritoneal dialysis solutions

The United Kingdom's medicines authority asked the CHMP for an opinion on the potential presence of endotoxins in the Baxter peritoneal dialysis solutions Dianeal, Extraneal and Nutrineal. In December 2010, the CHMP concluded that although the number of batches affected was likely to be low, current stocks should be replaced, because it was not possible to identify which bags were affected and there was a risk that patients who received peritoneal solutions containing endotoxins may develop aseptic peritonitis.

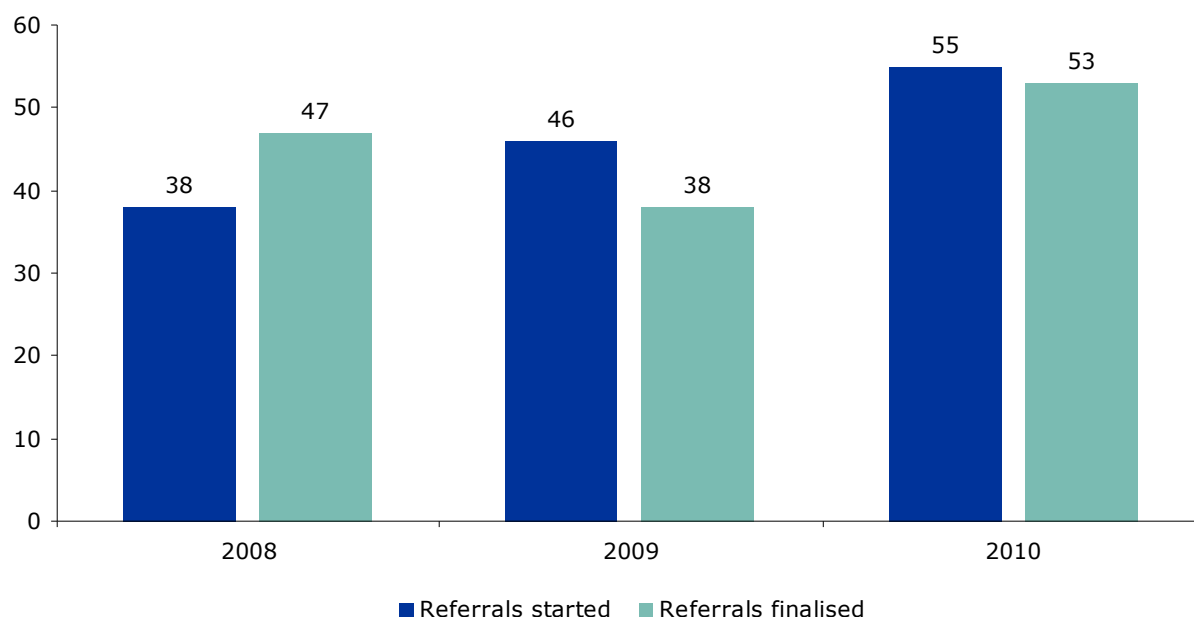
Paediatric referrals – Article 29 of Regulation (EC) No 1901/2006

In March 2010, the CHMP recommended a line-extension for Sortis and associated names (atorvastatin calcium), to add chewable tablets, a pharmaceutical formulation suitable for the paediatric population. The paediatric formulation has been developed for the treatment of hypercholesterolaemia in adolescents and children aged 10 years or older. The Committee also recommended that this indication be approved for the currently available presentations of Sortis and associated names (film-coated tablets).

In July 2010, the CHMP recommended an extension of the therapeutic indications of Xalatan eye drops and associated names (latanoprost), to include the reduction of elevated intraocular pressure in the treatment of paediatric patients with elevated intraocular pressure and paediatric glaucoma.

Figure 27.

**Referrals started and finalised
(2008-2010)**



Procedure type	Started in 2010	Finalised in 2010
Article 6(12) of Commission Regulation (EC) No 1084/2003	0	1
Article 6(13) of Commission Regulation (EC) No 1084/2003	0	1
Article 13 of Commission Regulation (EC) No 1234/2008	0	0
Article 31 of Directive 2001/83/EC	6	3
Article 36 of Directive 2001/83/EC	0	0
Article 5(3) of Regulation (EC) No 726/2004	3	1
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	3	4
Article 29(4) of Directive 2001/83/EC	6	9
Article 30 of Directive 2001/83/EC	8	13
Article 29 of Regulation (EC) No 1901/2006	1	4
Article 20 of Regulation (EC) No 726/2004	28	17
Totals	55	53

Key performance indicator	Target	Outcome
Percentage of arbitration and referral procedures evaluated within the legal timeline	100%	100%
Publication of the CHMP opinion and assessment report for Article 5(3) procedures at the time of the CHMP opinion	100%	100%

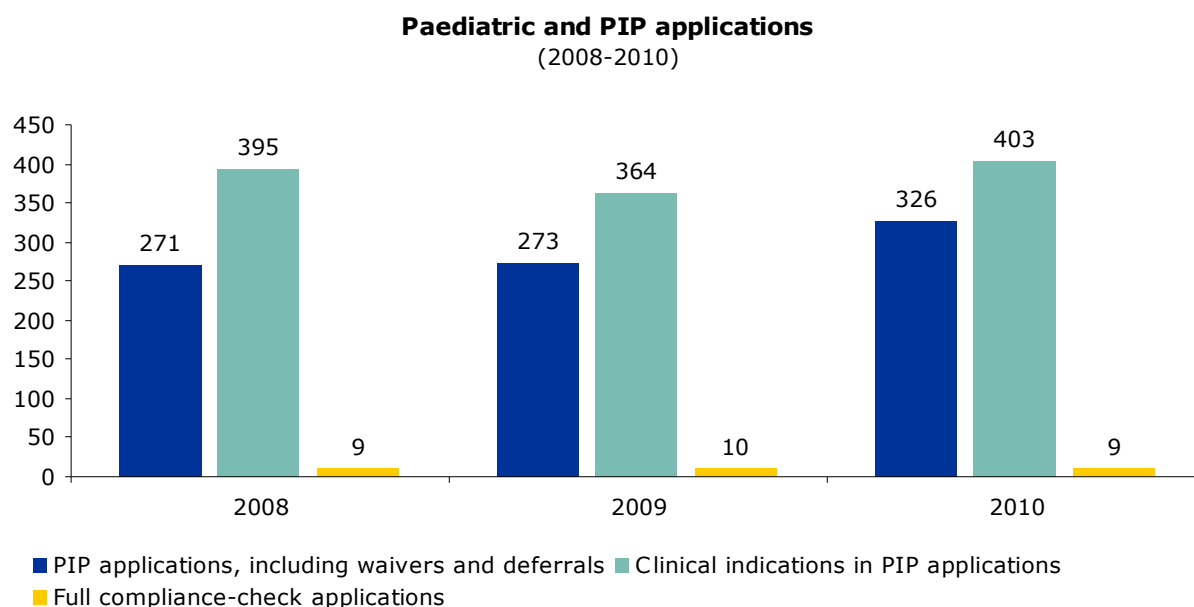
2.8. Medicines for children

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 national marketing authorisation, for new medicinal products, and in a paediatric-use marketing authorisation (PUMA) 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 2010, the Agency received applications for PIPs or waivers relating to 403 clinical indications. These correspond to 326 validated applications, an increase of 11% in terms of clinical indications and 19% in terms of applications.
- More than a third of PIP applications (115) received were for allergens, as a result of a change in German medicines legislation, which now requires a marketing authorisation for these products and consequently a PIP. By year's end, the PDCO had adopted 101 opinions.
- The number of requests for modification of an agreed PIP received was 110 – more than twice as many as forecast.
- The PDCO adopted a total of 201 positive opinions on PIPs, including potential deferrals, relating to 349 indications. An additional 52 positive opinions on full waivers and 103 positive opinions for requests to modify agreed PIPs were adopted. Eleven opinions adopted by the PDCO were negative.
- Nine requests for full compliance checks were submitted to the Agency. 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.



Specific objectives

Guidance for conduct of paediatric medicines development

- The Agency published a number of guidance documents, including revised guidance on compliance checks, which is currently out for discussion.

Improved interaction with applicants

- Interaction with applicants for PIPs/waivers improved during 2010. For 20% of applications received, the Agency held pre-submission meetings with the applicants. Further guidance on pre-submission meetings was published on the Agency's website.

Process-improvement exercise relating to handling of quality aspects started

- The Agency reached agreement on areas for improvement during 2010. Finalisation of an improvement action plan is currently under way.

Reinforced interaction between Paediatric Committee (PDCO) and Committee on Advanced Therapies (CAT) on paediatric aspects of advanced-therapy medicines

- The emphasis was on strengthening the interaction between the PDCO and the Agency's other scientific committees. A pilot for cooperation between the PDCO and the CAT was developed in the first half of 2010. By the end of the year, all 8 medicines that were identified as advanced-therapy medicines and for which a PIP/waiver application had been submitted had jointly been discussed between the two committees. The cooperation is expected to continue.

Key performance indicator	Target	Outcome
Number of PIP or waiver opinions and decisions established within legal timelines	100%	100%
Percentage of Agency decisions on paediatric investigation plans/waivers published within 4 weeks of the decision	95%	Jan-Sep 2010 (before procedure improvement): 16% within 4 weeks, 49% within 6 weeks. Oct-Dec 2010 (after procedure improvement): 51% within 4 weeks, 86% within 6 weeks.

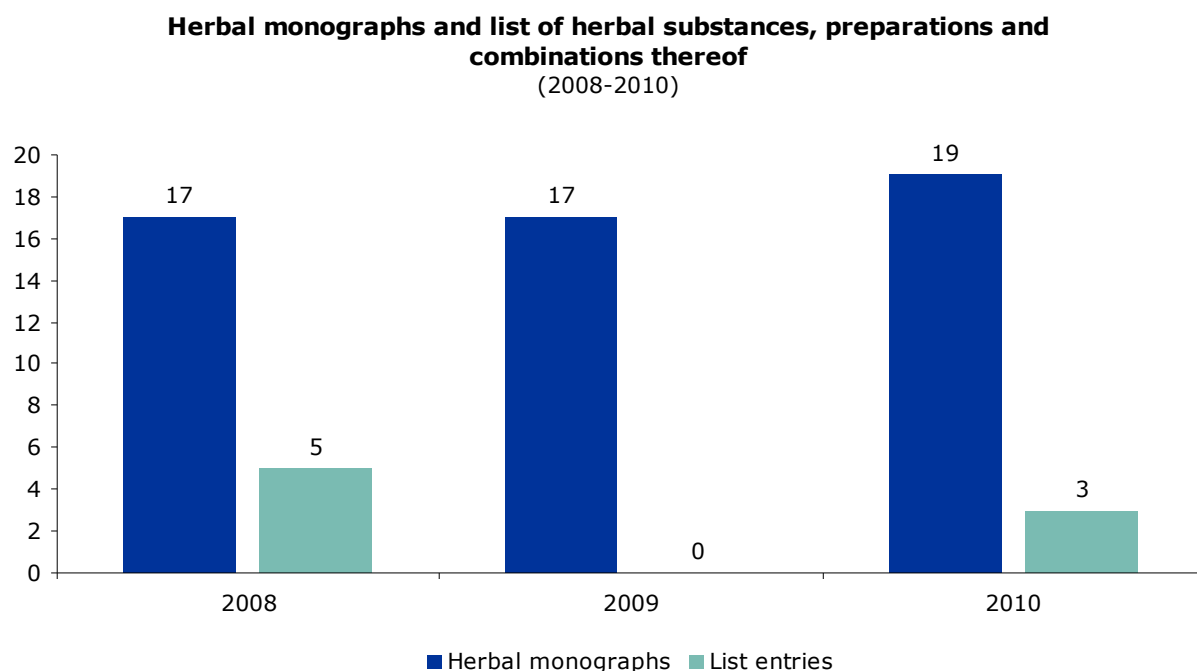
2.9. Herbal medicinal products

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; provision of scientific opinions on questions relating to herbal medicines.

Core activities

- The HMPC finalised 22 assessments of herbal substances and preparations thereof, resulting in 19 Community herbal monographs for traditional and well-established herbal medicinal products in 2010 (2 more than in 2009), and in 3 final public statements on assessment work on herbal medicines for which a Community herbal monograph could not be established.
- Twenty draft Community herbal monographs and 1 draft public statement on assessment work on herbal medicines for which a Community herbal monograph could not be established were published for public consultation.
- Three entries to the list of herbal substances, preparations and combinations thereof for use in traditional herbal medicinal products were transmitted to the European Commission, and 2 Community list entries were published for consultation.

Figure 29.



Action plan for herbal medicines for 2010 and 2011 published

The HMPC secretariat prepared an action plan for herbal medicines for 2010 and 2011, to address a number of difficulties currently encountered in this field, which was adopted by the Management Board and the Heads of Medicines Agencies.

Key performance indicator	Target	Outcome
Number of Community herbal monographs (finalised/published for consultation)	40 (20/20)	19 monographs finalised. 20 monographs published for consultation. 3 public statements finalised.

Key performance indicator	Target	Outcome
		1 draft public statement released for consultation.
Number of Community list entries (finalised/published for consultation)	10 (5/5)	3 transmitted to the European Commission. 2 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 (ATMPs), 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. The main tasks of the Committee for Advanced Therapies (CAT), established by the Regulation, are to provide in relation to advanced-therapy medicinal products: draft opinions to the CHMP on the evaluation of marketing-authorisation applications; specific expertise and advice to the European Medicines Agency, CHMP and/or the European Commission; input on the certification of quality and non-clinical data; input on scientific recommendations on classification and on CHMP scientific advice. Other emerging therapies and new technologies that are outside the scope of the Regulation are also covered in this strategic area.

The year 2010 was the second year of operation of the Agency's Committee for Advanced Therapies (CAT). 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.

Core activities

- An ATMP application for Cerepro was withdrawn after re-examination of the negative opinion.
- One new ATMP application was submitted in 2010.
- Some applications foreseen for 2010 were postponed to 2011 by the applicants, or will no longer be submitted.
- The number of marketing-authorisation applications for ATMPs legally on the market in the EU Member States is expected to be less than originally predicted (about 20 products), as some of these ATMPs will be put under national 'hospital exemption' schemes, meaning that no application has to be submitted to the Agency.
- The first opinion on the certification of experimental data generated for an ATMP under development by an SME was issued by the CAT, relating to the suspension of mononuclear cells for acute myocardial infarction and chronic ischaemic heart disease.
- The CAT adopted 27 scientific recommendations on the classification of medicines as ATMPs. The number of classification requests submitted in 2010 was 19.
- The CAT provided feedback to the Scientific Advice Working Party on 15 scientific-advice requests for ATMPs, and to the Paediatric Committee on 1 paediatric investigation plan for ATMPs.
- The activities of the former CHMP working parties on cell-based products and on gene therapy were integrated into the operations of the CAT.

Specific objectives

CAT work programme 2010-2015

The CAT prepared a work programme for 2010-2015, to help bring more advanced-therapy medicines to the market. The CAT aims to contribute to an environment that encourages the development of ATMPs. The work programme sets out a proactive approach for the CAT, in which training and early dialogue with relevant stakeholders play a central role. It also tasks the CAT with looking at how the current regulatory framework can be made more accessible for SMEs, academia, patient groups, hospitals, charity foundations and trusts developing ATMPs.

Procedural advice on the interaction with notified bodies when developing combined medical devices and ATMPs was prepared, and its adoption is foreseen for the beginning of 2011.

Key performance indicator	Target	Outcome
Percentage of applications handled by the CAT 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	100%

2.11. Scientific committees, working parties and scientific advisory groups

The Agency has five scientific committees related to medicines for human use. These are the Committee for Medicinal Products for Human Use (CHMP), the Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Paediatric Committee (PDCO) and the Committee for Advanced Therapies (CAT). The work of the scientific committees is supported by standing working parties, scientific advisory groups and ad-hoc expert groups. It is the role of the Agency's secretariat to ensure appropriate coordination between committees and working parties.

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 for human use. 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 2010, each of them lasting 4 days.

Dr Eric Abadie was re-elected in June 2010 as CHMP Chair and Dr Thomas Salmonson as Vice-chair. Both will serve for a second 3-year term.

An extraordinary CHMP meeting via teleconference was organised in March 2010 to discuss Rotarix, as the unexpected presence of DNA of a non-disease-causing viral strain in batches of this oral vaccine raised concerns for public health.

The April 2010 meeting of the CHMP was also held partly as a teleconference, as a consequence of worldwide air travel disruptions caused by a volcanic ash cloud.

In September 2010, an extraordinary CHMP meeting (partially via teleconference) took place to review Avandia, Avandamet and Avaglim (rosiglitazone-containing medicines), following reports of an increase in the risk of cardiovascular problems with rosiglitazone.

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 2010, with each meeting lasting up to 2 days.
- In May 2010, the COMP secretariat organised a conference to mark the 10th anniversary of the COMP and the orphan medicines legislation.

Committee on Herbal Medicinal Products (HMPC)

The HMPC establishes Community herbal monographs. Other core tasks include the establishment of a draft 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 well-established use and traditional herbal medicinal products laid down in the Member States, and helps to further integrate herbal medicinal products into the European regulatory framework.

- The HMPC met 6 times in 2010, with each meeting lasting up to 1½ days.

In November 2010, Dr Werner Knöss was elected as new HMPC Chair and Prof. Ioanna Chinou was re-elected as Vice-chair for a 3-year term.

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 the European network of paediatric research.

- The PDCO met 12 times in 2010, with each meeting lasting up to 3 days.
- Six workshops on specific paediatric topics were held in 2010.

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 SMEs, and the provision of recommendations on the classification of ATMPs.

- The CAT met 11 times in 2010, with each meeting lasting 1½ days.

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. Eighteen SAG meetings took place in 2010.

- A total of 19 new CHMP concept papers were initiated by the Agency's working parties in 2010 – more than twice as many as forecast. In addition, 20 new CHMP guidelines were initiated in 2010, following stakeholder consultation on respective concept papers.
- By the end of the year, 5 new concept papers had been released for public consultation.
- Twenty-two new CHMP guidelines were adopted.

Specific objectives

Interaction of the CHMP with the PDCO and CAT

Discussions between the CHMP and both the PDCO and the CAT are well established and well advanced. Adoption of detailed procedures for interaction will be concluded in 2011.

Consultation of interested parties during development of clinical guidelines

The Agency established criteria to identify appropriate interested parties, such as academia, learned societies, healthcare professionals and patients, for consultation on guidelines during their development process. Guidelines were systematically disseminated to interested parties during 2010. A total of 52 guidelines were sent to 1,564 interested parties. This means that for each guideline an average of around 30 representatives of interested parties were consulted.

Modification of the Agency's framework for working parties

Following a review of the structure of the working parties carried out as part of the CHMP's 2008-2010 work plan, the Agency introduced a number of changes to the organisation of its working parties, designed to improve transparency, reduce duplication of work between working parties, and ensure the scientific competence of, and active contribution from, all working-party members.

Changes included: replacement of the Efficacy Working Party with a number of temporary working parties with more specific therapeutic fields of expertise; establishment of drafting groups to draw up

and review guidelines that do not fall within the remit of existing working parties; establishment of a Coordination Group to coordinate the activities of the working parties and drafting groups.

More information is available in a reflection paper on working parties, and in the mandate, objectives and rules of procedure for the temporary working parties and drafting groups, available [here](#).

Optimising the composition and availability of SAG experts

The Agency implemented actions agreed with the CHMP on the composition and availability of experts for SAGs, their governance and policy. By the end of 2010, the core membership for 5 out of 6 SAGs was increased and the mandates of all SAGs were revised.

2.12. 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 subgroups/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 (SmPC) harmonisation lists, the CMDh supports the entry of such products into the EU market.

Core activities

The CMDh met 11 times in 2010, with each meeting lasting up to 2½ days. The CMDh's April meeting was mainly held via teleconference, due to travel disruptions caused by a volcanic ash cloud.

A full report on CMDh activities in 2010 is available [here](#).

- The Agency's CMDh secretariat coordinates the 60-day referral to the CMDh procedure, including communication with applicants, organisation of oral explanations, monitoring compliance with the relevant timetable and communication of the outcome of 60-day procedures to interested parties in the CMDh press release.
- The number of new applications submitted in 2010 via MRP (313) decreased by 4% compared to 2009. The number of new applications submitted in 2010 via DCP (1,599) increased by 15% compared to 2009.
- A total of 1,777 MRP and DCP applications were finalised in 2010, an increase of 6% compared to 2009. The number of new applications finalised via MRP (325) in 2010 decreased by 14% compared to 2009, while the number of applications finalised via DCP increased by 11% to 1,452.
- Fourteen MRP applications and 3 DCP applications were referred to the CMDh in 2010.
- For 5 MRP and 2 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.
- Statistical information on applications under the MRP and the DCP was provided by the Agency and presented in the monthly CMDh press releases. Also, six-monthly and annual statistics were published on the CMDh website.

Variations legislation

- The CMDh received 38 requests for recommendations in accordance with Article 5 of the Variations Regulation (Reg. 1234/2008). Twenty-nine recommendations were given by the CMDh, 5 procedures were not started and 2 were withdrawn.
- Forty-six requests for worksharing procedures including MRP/DCP products were received.

Specific objectives

Improving the functioning of the CMDh

A best-practice guide on administrative and organisational issues for CMDh activities was finalised.

A paper on the interaction between the CHMP and CMDh was prepared.

Implementation of the revised Variations Regulation

- A number of work instructions were drafted to take account of changes introduced by the new Variations Regulation. These included a procedure on providing advice on unclassified variations, a procedure on the 60-day referral procedure for variations, and a procedure on variation worksharing.

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

- The number of scientific-advice requests considerably exceeded predictions. 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 almost a doubling of the number of applications received. Following the positive trend seen in 2009, the increase of scientific-advice requests is now expected to stabilise, in line with the numbers of marketing-authorisation applications submitted for veterinary medicines.
- Uptake of the procedure continued to be 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 and 33% in 2010 were from SMEs.
- An increase in applications for medicines not intended to be authorised via the centralised procedure was also seen, reflecting increased awareness by the pharmaceutical industry that such products are eligible for scientific advice from the Committee for Medicinal Products for Veterinary Use (CVMP).

Figure 30.

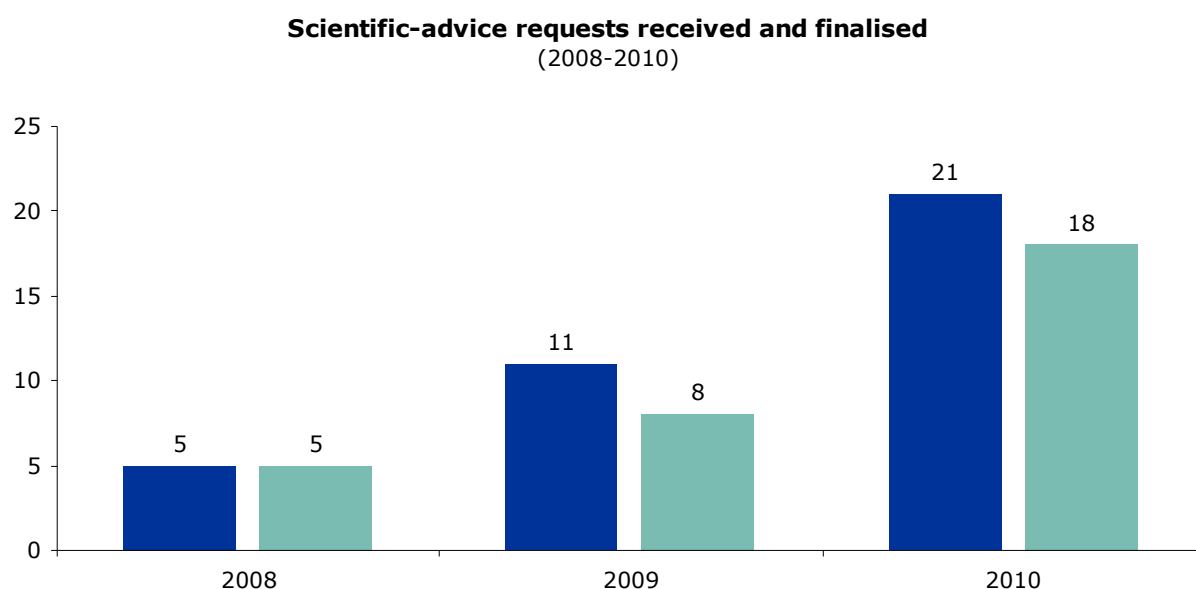
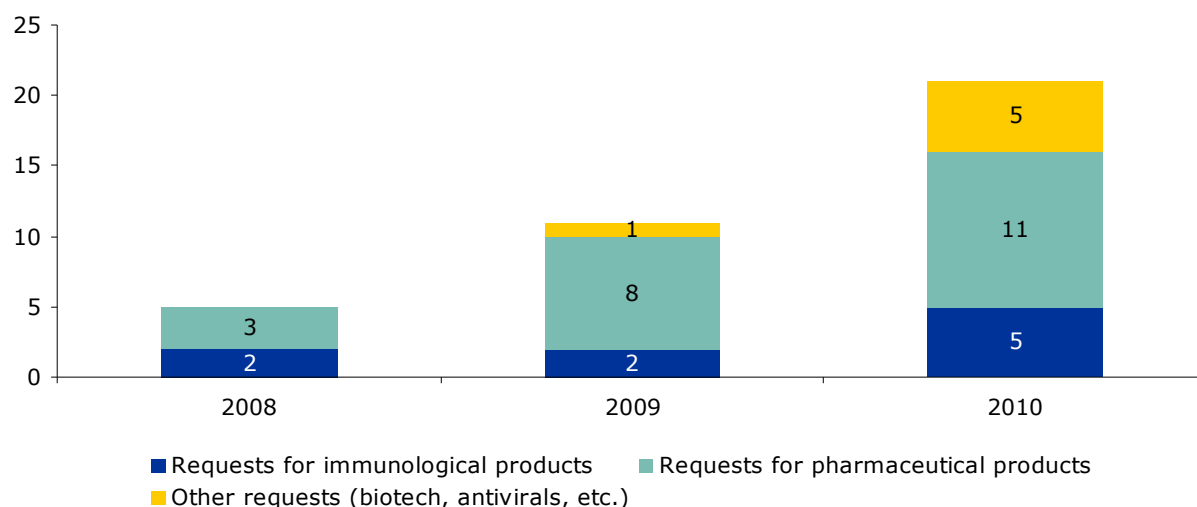


Figure 31.

**Scientific-advice requests received by area
(2008-2010)**



Specific objectives

Scientific advice for medicines for MUMS/limited markets

- The criteria for providing free scientific advice in relation to the development of products indicated for minor uses and minor species (MUMS)/limited markets were amended in 2009. The MUMS/limited market policy came into force on 1 September 2009, with the possibility to request classification of a product intended as a MUMS/limited-market product by the CVMP. This policy provides an incentive for developing such products. The number of requests for classification received in 2010 was 23.
- Many of these will result in requests for scientific advice at some stage in the development process. In 2010, 8 out of 21 scientific-advice applications had been the subject of a MUMS classification request, thus contributing to the availability of products for MUMS and limited markets.

Requests for MUMS/limited markets classification	2009¹	2010
Requests received	8	23
Requests classified as MUMS	8	18
Requests not classified as MUMS	0	5
Requests classified as MUMS with financial interest	3	12
Requests classified as MUMS without financial interest	5	6
Requests for immunologicals	4	5
Requests for pharmaceuticals	1	13
Requests for others, e.g. biotech, antivirals	3	5

¹ The MUMS/limited market scheme only entered into force in September 2009.

Scientific advice for non-centralised medicines

- A new category of scientific advice was also introduced in 2009, whereby applicants can request confirmation of the general data requirements for an application in line with the adopted MUMS data guidelines. The increased workload in 2010 was addressed by increasing the number of members of the Scientific Advice Working Party for Veterinary Medicines (SAWP-V) from 14 to 16, to ensure the availability of coordinators to assess applications.

Promoting awareness of the scientific-advice procedure

- The provision of scientific advice in parallel with the U.S. 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.
- Potential applicants were advised at industry meetings and conferences of the incentives on offer and of the advantages of requesting scientific advice at an early stage in product development, in particular for novel products. The number of requests has increased substantially, with an 80% increase for 2010.
- Specific emphasis was placed on informing potential applicants for medicines for MUMS/limited markets about the incentives available. By the end of 2010, 8 out of the 21 scientific-advice applications received were for medicines for MUMS/limited markets.

Key performance indicator	Target	Outcome
Scientific-advice requests evaluated within the procedural timelines	100% 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 Committee for Medicinal Products for Veterinary Use (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

- The predicted continued increase in applications for new products was confirmed, with a total of 18 initial applications being received. Judging by letters of intent received from applicants, this trend is expected to continue in 2011.
- 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 recently, in particular, bluetongue) continued. Five of the opinions adopted by the CVMP in 2010 concerned authorisations for vaccines under exceptional circumstances: 4 bluetongue-virus vaccines and 1 vaccine against *Coxiella burnetii*. However, now that several bluetongue vaccines have been authorised, it is expected that this trend will slow or cease in 2011.
- For full new applications, an equal number of applications for new products concerned vaccines and pharmaceuticals.

- With the exception of 1 vaccine application for a product intended for dogs, all other applications for vaccines were intended for food-producing species.
- The majority of new applications for pharmaceuticals were for products intended for companion animals, but 2 applications concerned products intended for food-producing species.
- Only 2 applications submitted for new veterinary medicines concerned generic products, and these were intended for food-producing species.

Animal-health impact of medicines recommended for marketing authorisation

The Agency continued to give positive opinions for authorisation under exceptional circumstances of vaccines against bluetongue disease. Vaccines were authorised to protect cattle and sheep against clinical signs, and to reduce or prevent transmission of serotypes 1, 2, 4 and 8 of this highly variable virus. Authorisation at EU level makes vaccines immediately available for use as part of national and transnational disease-control campaigns against this highly virulent and contagious disease of domestic livestock.

The Agency also gave a positive opinion for authorisation under exceptional circumstances of a vaccine to reduce the shedding of *Coxiella burnetii* by infected cattle and goats. An extensive outbreak of this bacterial disease, which is the causative agent of Q fever in man, occurred in the Netherlands in 2009. The CVMP therefore considered it appropriate to recommend that the product be authorised on the basis of a positive benefit-risk balance while further studies are carried out to determine more precisely the efficacy in goats.

Novel products for the treatment of ectoparasites, mainly fleas, in domestic pets remain a priority area for the companion animal health sector, and two products of this type were authorised in 2010.

Figure 32.

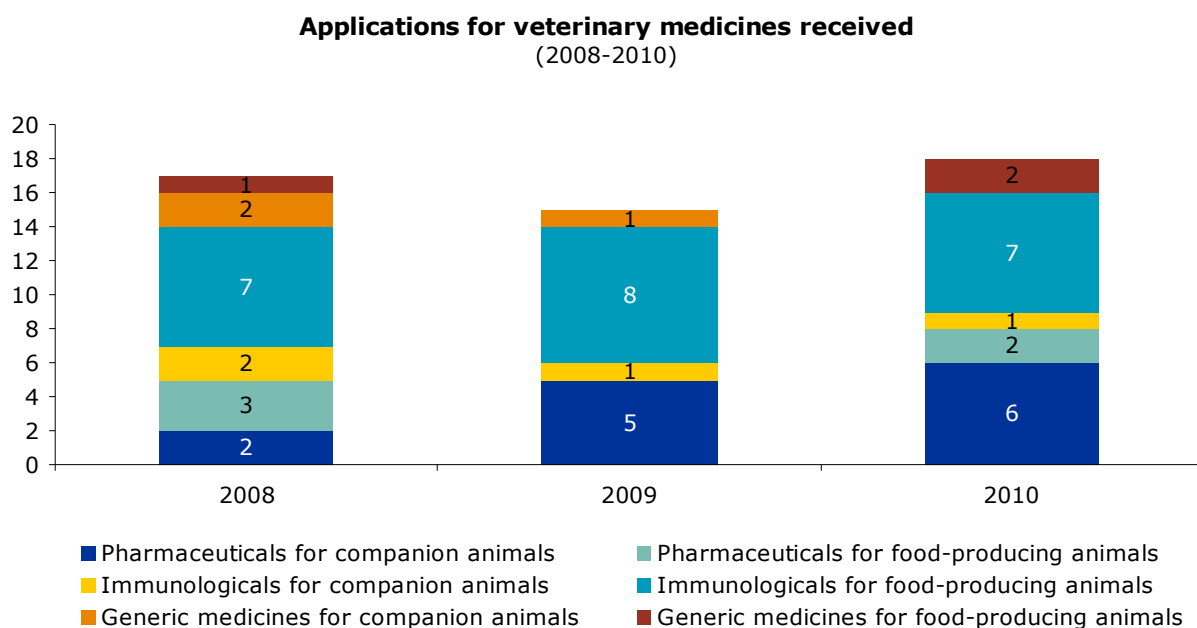


Figure 33.

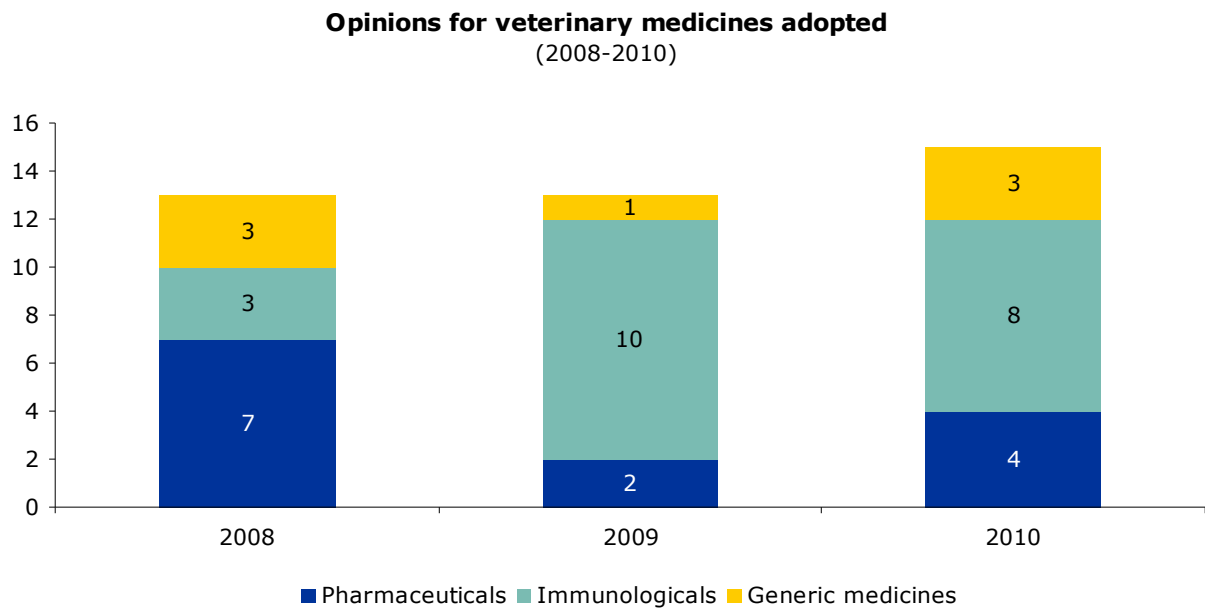
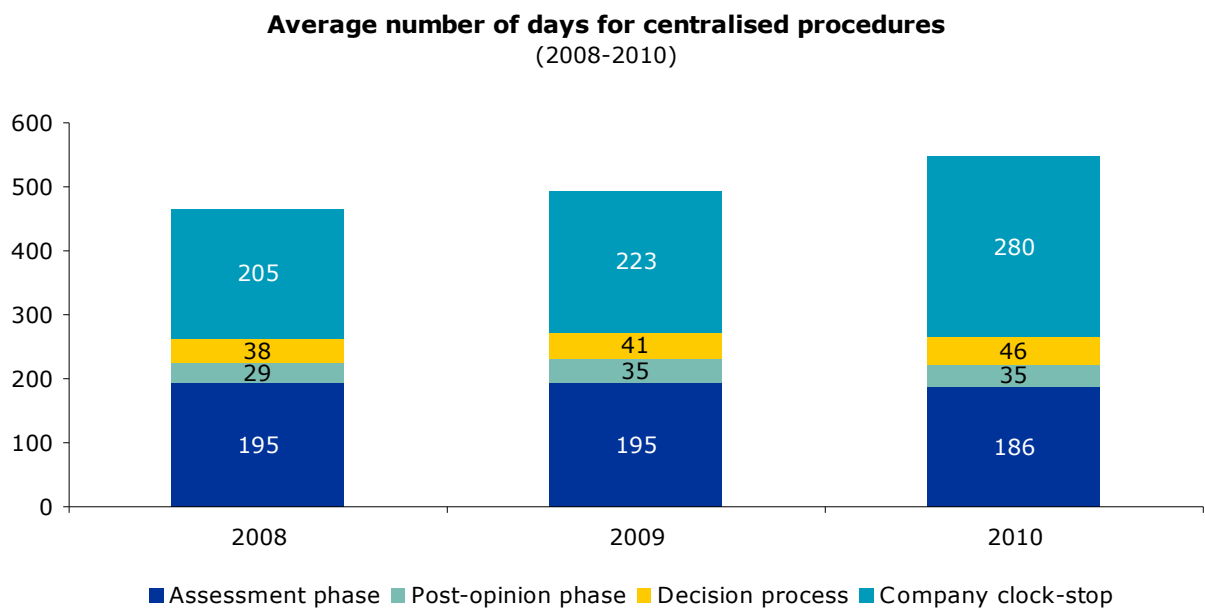


Figure 34.



Specific objectives

- The CVMP initiative of peer-reviewing assessment reports as part of the quality-assurance system was strengthened, following the review of a pilot phase with a major revision of the peer-review procedure in early 2010. The process was confirmed as a permanent system. It was extended and is now applied for initial applications, extensions, major variations, MRL applications and referrals. In 2010, 91% of assessment reports produced by the CVMP were subject to peer review, exceeding the target of 80%.

- The CVMP, based on the work of its task force for the review of veterinary legislation, provided in July 2010 responses to the Commission consultation, including proposals for improving the efficiency and effectiveness of authorisation procedures for veterinary medicinal products within the EU.
- The authorisation through the centralised procedure of vaccines against epizootic diseases of livestock was actively promoted, resulting in the receipt of 3 applications for vaccines against bluetongue disease and adoption of marketing authorisations for 2 bluetongue vaccines. In addition, the CVMP finalised and published requirements for multistrain dossiers in March 2010.
- The CVMP gave a positive opinion for authorisation under exceptional circumstances of a vaccine against Q fever in cattle and goats, in July. This is intended as an important tool in controlling the current epidemic of this zoonotic disease of major public-health significance in some Member States.

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

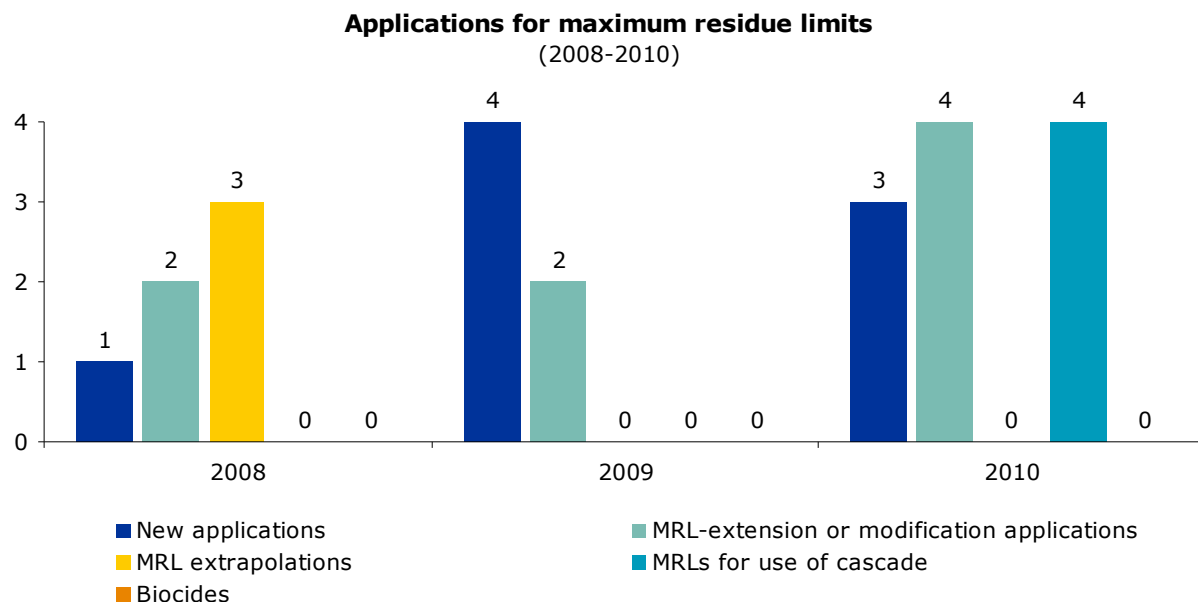
The use of veterinary medicinal products in food-producing animals may result in the presence of residues in foodstuffs obtained from treated animals. Before a veterinary medicinal product can be authorised, an evaluation of the safety of residues must be carried out. The Agency establishes maximum residue 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

- Applications for the establishment of new maximum residue limits remained at a low but constant level, confirming that each year a few new molecules for use in food-producing animals are developed. A slight increase in the number of MRL-extension applications was noted, signalling that existing products are being developed for use in new species.
- In 2010, the Agency received and validated 3 new applications for MRLs.
- The number of requests for MRL-extension applications was 4 – an increase of 50% over 2009.
- The new MRL Regulation provides specific emphasis on extrapolations, and allows Member States and the European Commission to submit requests to the Agency without payment of fees.
- The Regulation also provides for applications by the Commission, Member States and interested parties for the establishment of MRLs for substances used under the so-called 'cascade'. Currently, 4 applications are awaiting further clarification from the Commission on the most appropriate legal basis to use for approval of MRLs.
- Under the new MRL Regulation, the Agency became responsible for substances included in biocidal products used in animal husbandry, for which MRLs should be established in accordance with Directive 98/8/EC. While procedures for cooperation with the competent authorities for biocides are being set up, no such applications have been received yet.

- The Agency adopted 5 opinions on MRLs: 2 for the establishment of new MRLs, 1 relating to the extension or modification of existing MRLs, and 2 for MRLs for use under the cascade.

Figure 35.



Specific objectives

- Further good progress was made on implementing the new MRL Regulation (Regulation 470/2009), adopted in June 2009, and it is envisaged that a draft for the revision of Volume 8 of 'The rules governing medicinal products in the European Union', on establishment of MRLs, can be submitted to the European Commission in 2011, once clarification on the procedure regarding biocides for use in animal husbandry has been agreed.
- As part of this, the Agency also submitted reflections to the European Commission on an alternative approach for the modification of standard withdrawal periods for veterinary medicines used under the cascade. The Agency is currently awaiting the Commission's response before progressing further.
- 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 2 Codex MRLs in this context during 2010.

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

- The number of type-I variations greatly exceeded predictions, with the number of applications received in 2010 almost doubling (134, compared to 73 in 2009). The number of type-II variations, however, reduced even further than had been foreseen, due mainly to the new Variations Regulation, under which many variations were downgraded to type IB and the default classification was changed from type II to type IB.
- Much effort was put into ensuring consistent application of the new classification requirements, and that appropriate grouped variations were processed.
- A further streamlining of the handling of post-authorisation applications, in particular type-II applications, was developed during 2010 and will be put into practice in 2011.

Figure 36.

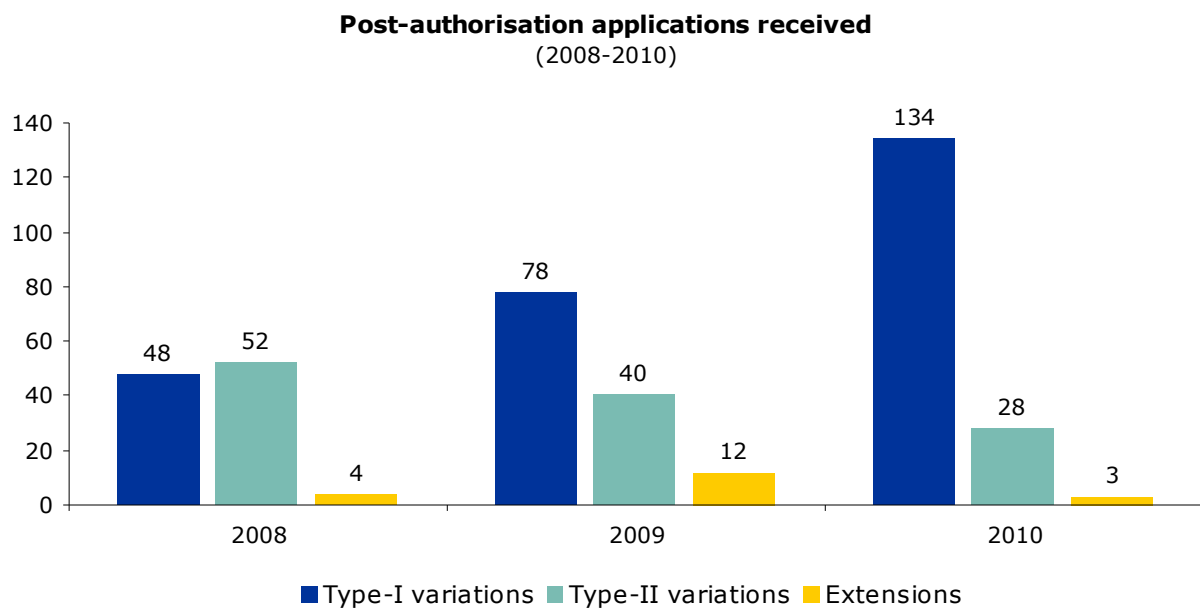
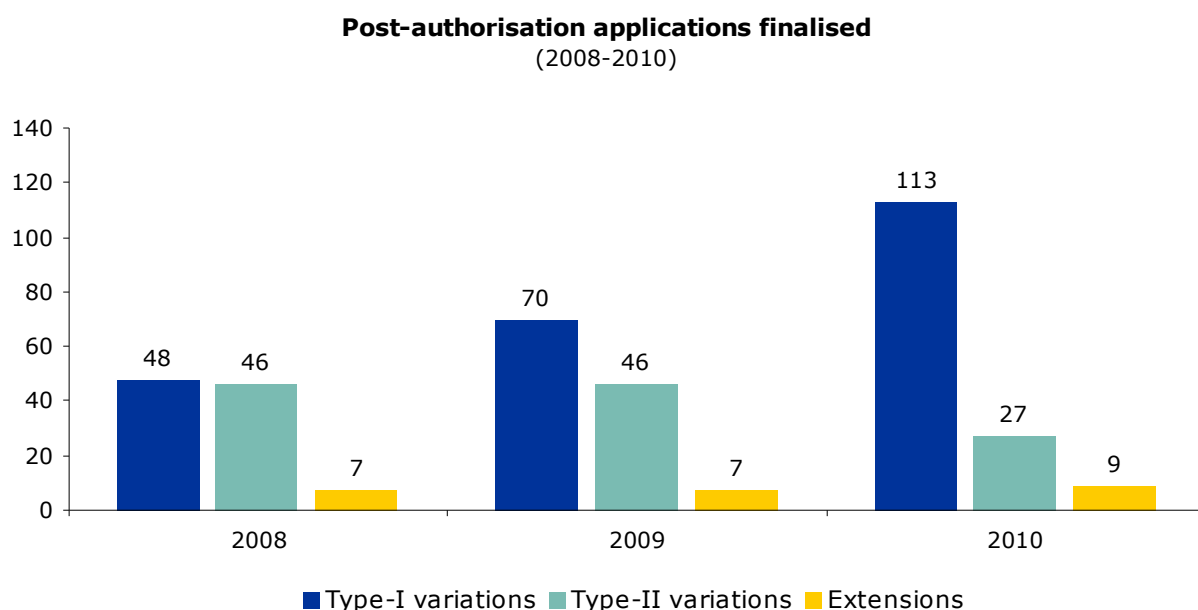


Figure 37.



Specific objectives

- The completely revised post-authorisation guidance was published in December 2010. Work continues on the revision of the standard operating procedures.

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	100% of applications

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

- The number of serious-adverse-event and human-reaction reports concerning centrally authorised veterinary medicinal products has increased continuously over recent years, and the number of reports received in 2010 exceeded the estimated 40% increase (forecast 4,000) to 4,474.
- Of these reports, 4,250 related to suspected adverse reactions in animals and 224 to reactions in humans following exposure to a veterinary medicinal product.

- Of the 4,250 reports of suspected adverse reactions in animals, 2,812 concerned companion animals (mainly dogs and cats) and 1,438 concerned food-producing animals (mainly cattle, pigs and sheep).
- The number of safety-update reports received, 118, was lower than forecast, due to the withdrawal by the marketing-authorisation holders of 4 products.
- The EudraVigilance (EVVet) database contains more than 50,000 adverse-event reports (up from 33,000 in 2009 and 23,000 in 2008), of which 36,000 occurred within the EU and 14,000 outside the EU. Those outside the EU related to veterinary medicinal products authorised within the EU.
- The majority of reports in the EVVet database relate to companion animals, mainly dogs and cats. The number of reports for food-producing animals is relatively low, with the highest percentage of reports in cattle, mainly due to targeted reporting in the previous years related to the use of bluetongue-virus vaccines in the EU.

Figure 38.

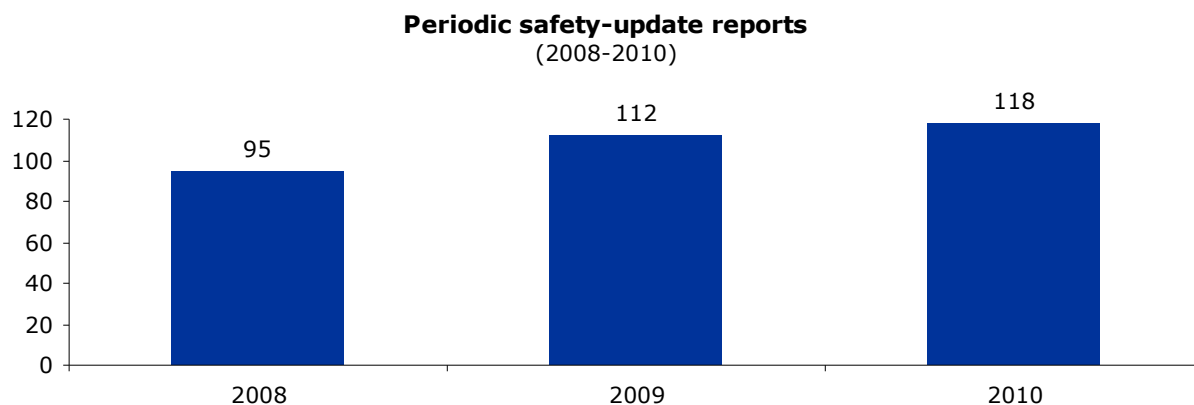
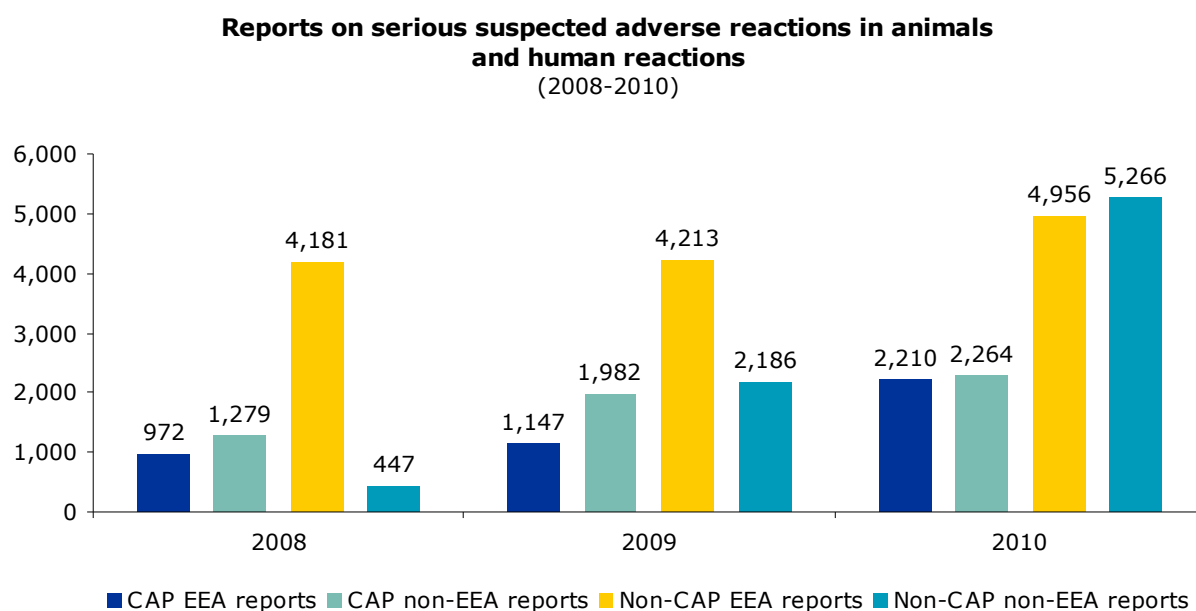


Figure 39.



Specific objectives

International harmonisation

- A major milestone was reached in 2010 with the adoption of a suite of internationally harmonised guidelines on pharmacovigilance reporting under Veterinary International Conference for Harmonisation (VICH), after several years of development. Work at VICH level on electronic reporting, led by a group of technical experts, will continue, with the aim of ensuring harmonised implementation of all related pharmacovigilance guidelines.

Update of Volume 9B

- Volume 9B of the revised 'Rules governing medicinal products in the European Union' was finalised by the Pharmacovigilance Working Party (PhVWP-V) and subsequently endorsed by the CVMP. The document has been sent to the European Commission.

Progress with EudraVigilance Veterinary

- The EVVet 3.X project was launched to modernise and simplify data input, to implement international standards and the access policy, and to include a new tracking facility that will allow results from data analyses performed on EVVet data to be exchanged and stored. The vision document and high-level project plan were concluded and a Technical Advisory Group, which includes representatives from industry, was set up to gather business specifications.
- Activities relating to product-data transfer from Member States' product databases to the EudraVigilance Veterinary product database continued.
- The finalisation of the policy on access to EudraVigilance Veterinary was delayed until December 2010, due to ongoing discussions between the Agency, the EU Ombudsman and the European Data Protection Supervisor in relation to the protection of personal data. The implementation will be stepwise, with access for the general public to static reports of summarised data foreseen for 2012.

Progress with signal detection

- Following the full implementation of the EudraVigilance Veterinary Data Warehouse in 2009, the tools for signal detection were optimised by a pilot group of the PhVWP-V to establish the Agency's surveillance role within the EU, initially with emphasis on centrally authorised products.
- The draft recommendation document for the basic surveillance of EudraVigilance Veterinary data was finalised and published for public consultation. Following the end of the consultation in November 2010, the comments are being considered and the finalisation of the recommendation is foreseen for the first quarter of 2011.

Key performance indicator	Target	Outcome
Percentage of PSURs evaluated within the established timelines	80%	93%* 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 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).

Referrals relating to other issues are also processed by the CVMP, including requests by the Executive Director of the Agency for an opinion on a scientific matter (Article 30 of Regulation (EC) No 726/2004) and requests for the opinion of the Agency by the European Commission on an urgent matter (Article 45 of Regulation (EC) No 726/2004). Referrals can also be initiated by Member States when measures are considered necessary as a result of the evaluation of pharmacovigilance data (Article 78 of Directive 2001/82/EC).

Core activities

- The Agency dealt with a high volume and large variety of referrals in 2010, which saw a relatively high percentage of harmonisation referrals (Article 34) being submitted.
- A significant proportion of referrals related to authorisation of generic products. Authorisation of generics is more complex for veterinary medicines than for human medicines, due to a number of additional factors that need to be considered, including consumer protection and the use of the same product in different species.
- The 12 referrals submitted in 2010 were consistent with the forecast. The CVMP concluded a total of 11 referral procedures during the year.
- The referrals related to a variety of matters based on Articles 33, 34 and 78 of Directive 2001/82/EC and Articles 30 and 45 of Regulation (EC) No 726/2004.
- Of the referrals received and finalised in 2010, 7 related to veterinary medicinal products containing antimicrobial substances, reflecting the ongoing high level of concern within the EU that such products be authorised with appropriate conditions of use.

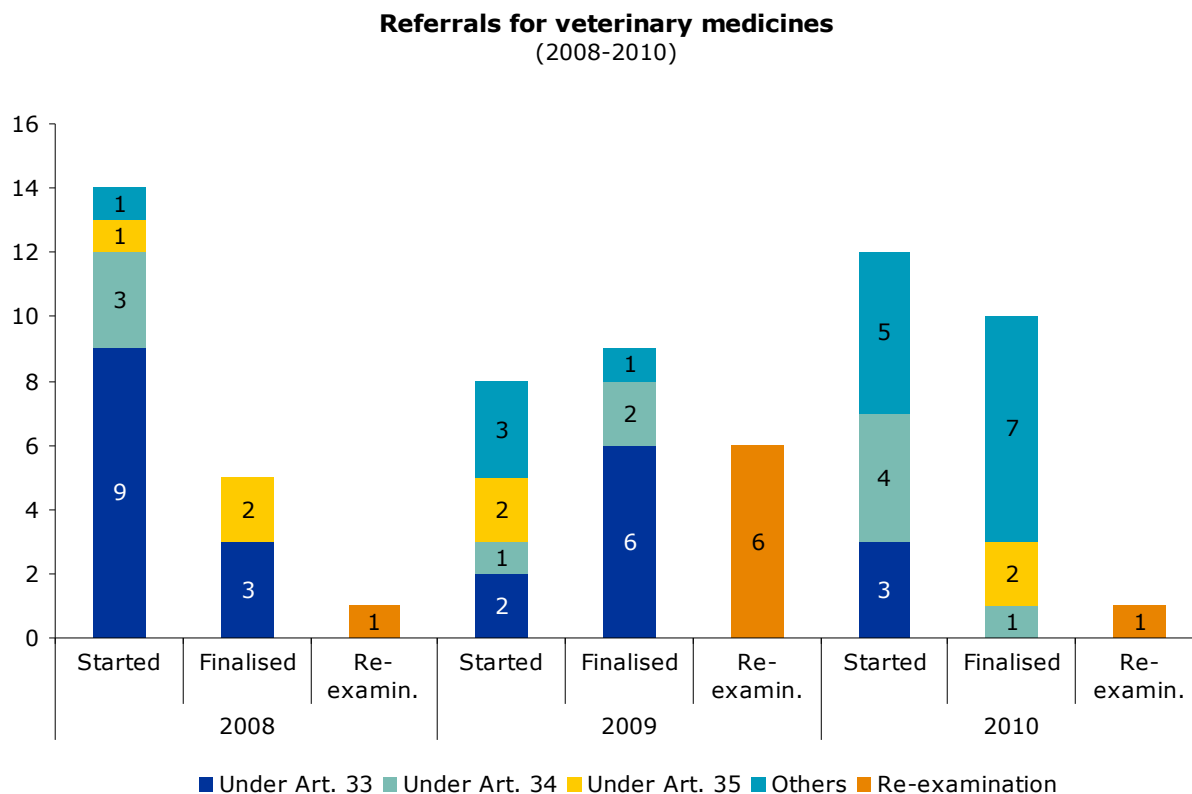
Animal-health impact of referral opinions

Many of the referrals considered by the CVMP in 2010 related to veterinary medicinal products containing antibiotics, reflecting the high concern throughout the regulatory network over this class of actives. A range of antibiotics for administration by a variety of routes were referred to the CVMP to ensure that the instructions for use were harmonised throughout the EU and represent the latest scientific thinking as to how to minimise the risks associated with the development of antimicrobial resistance. Among the types of antibiotics referred were all products indicated for food-producing species containing quinolones and fluoroquinolones, products intended for administration in drinking water containing doxycycline or those containing colistin, and a number of intramammary products containing potentiated amoxicillin.

An urgent referral on the basis of pharmacovigilance (Article 78 of Directive 2001/82/EC) led to the suspension of a vaccine against bovine virus diarrhoea, due to the identification of an association between vaccination of dams and the occurrence in their calves of the condition 'bovine neonatal pancytopenia', resulting in uncontrolled bleeding following minor trauma. The aetiology of the

condition is multifactorial and the vaccines were suspended until the marketing-authorisation holder can clarify and resolve the involvement of the vaccine.

Figure 40.



Specific objectives

- The joint CVMP/CMDv Task Force on referrals has made steady progress in developing a strategy for SPC harmonisation and criteria for prioritisation of referral procedures and harmonisation. The Task Force has also contributed to the comments from the CVMP to the Commission's consultation on the veterinary legislation review. A strategy document for referrals and harmonisation, including proposals regarding prioritisation, is being prepared for subsequent consideration by the Commission and Heads of Medicines Agencies. Finalisation of the document is foreseen for 2011.

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 its routine work relating to the adoption of opinions on the authorisation of veterinary medicines, the CVMP was active in the areas described below.

Activities relating to antimicrobial resistance

- The Agency and the CVMP, together with its Scientific Advisory Group on Antimicrobials (SAGAM), again devoted much effort in 2010 to activities aimed at minimising 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 the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals in the European Union: development of resistance and impact on human and animal health'. The document also includes recommendations aimed at minimising the development of resistance. The recommendations place further emphasis on the need for prudent use of antimicrobials, to avoid them being used unnecessarily. Macrolides are a group of antimicrobials that are of high importance for animal health, and it is important, for both animals and humans, that resistance is minimised.
- The CVMP adopted an opinion on an Article 35 referral concerning all veterinary medicinal products authorised in the EU containing (fluoro)quinolones, recommending risk-management actions to be included in the product information for these products. This referral was initiated in 2009 by the European Commission to ensure the inclusion in the product literature of all (fluoro)quinolone-containing veterinary medicines in the EU of warning statements regarding prudent use, in line with the recommendations of the CVMP.
- On the basis of recommendations from the SAGAM, the CVMP adopted and published a reflection paper on meticillin-resistant *Staphylococcus pseudintermedius* (MRSP), a prominent new risk to companion animals in the EU. MRPS is not a direct concern for human health, but might become an indirect risk, as treating animals might favour the transfer of resistance to other pathogens of relevance to man.
- The CVMP provided technical support to the European Commission on its involvement in the Codex Alimentarius Intergovernmental Task Force on Antimicrobial Resistance, which finalised its recommendations for a methodology for risk assessment and risk management in relation to food-borne antimicrobial-resistant microorganisms.
- Major progress was achieved in 2010 with the Agency's project to coordinate at European level the collection by Member States of harmonised data on use in the EU of antimicrobials in food-producing species and companion animals (ESVAC), with a pilot involving 10 Member States being launched. The project also adopted a template to be followed by Member States to collect data on consumption of veterinary antimicrobials in a harmonised manner. Training on collecting data was provided for Member States.

Immunologicals

- The CVMP, with the support of its Immunologicals Working Party, finalised several new guidance documents on marketing-authorisation requirements for immunologicals. Of particular note were guidance documents on multi-strain dossiers for inactivated vaccines against avian influenza,

bluetongue and foot-and-mouth disease, and reflection papers on the control of the active substance in the finished product for immunological veterinary medicinal products and the demonstration of a possible impact of maternally derived antibodies on vaccine efficacy in young animals.

Liaison with other scientific committees and EU institutions

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

Minor uses and minor species (MUMS)/limited markets

- Since the establishment in September 2009 of the new incentives scheme for the development of veterinary medicinal products for minor uses and minor species (MUMS)/limited markets, the scheme has been taken up successfully by companies. In total, 23 requests for classification for MUMS/limited markets were submitted to the CVMP in 2010. For 18 of these requests, the products complied with the criteria for MUMS/limited markets and were classified accordingly, with 12 qualifying for financial incentives, the remaining only for reduced data requirements.

Working parties and scientific advisory groups

- The working parties of the CVMP continued to be very active during 2010, developing or updating a wide range of guidelines and guidance documents, where appropriate, to implement the revised Annex I of Directive 2001/82/EC. The updating of existing CVMP guidelines was completed, where appropriate.
- Focus-group meetings and workshops involving external stakeholders were organised on the topics of environmental risk assessment, the fate of veterinary medicinal products in manure, and pharmacovigilance.

Interested parties

- The CVMP held a meeting with interested parties within the margins of a plenary Committee meeting, and had further interactions with interested parties through an info day, organised by the Agency with IFAH-Europe, and through consultation on guidelines.

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 (CMDv) and its subgroups/working groups.

- The year 2010 was characterised by many wide-ranging discussions on divergent interpretations of legislation by Member States, particularly with regard to variations and generics. These and other points, such as national validation requirements and various questions from industry, were addressed by the CMDv with significant support from the secretariat.
- In the area of packaging and labelling, harmonisation was achieved between CMDv product-information templates and the Agency's QRD templates through discussion at the vet break-out sessions of the QRD group.

- A substantial review and revision of CMDv best-practice guides and guidance documents was carried out in 2010. This was driven partly by the need to incorporate the provisions of the new Variations Regulation, and partly to harmonise practices with CMDh with regard to MRP and DCP. Work began on 3 important new documents on duplicate applications, informed-consent applications, and CMDv recommendations on transfer to MRP of national MAs involved in an Article 34 referral following a positive Commission Decision.
- CMDv discussed extensively the implementation of Commission Decisions for Article 34 and 35 referrals. The importance of maintaining the harmonisation achieved by such referrals has been identified as a new issue, as has the need to harmonise the different approaches of Member States in implementing these types of decision.
- The current level of referrals is expected to continue, and may increase. The primary grounds for CMDv referrals under Article 33(1) in 2010 was disagreement on the approach taken by applicants to demonstrate bioequivalence, reflecting the upward trend in the number of generic applications being submitted. These accounted for approximately 75% of all MR/DC procedures in 2010.
- A pilot procedure for the CMDv's voluntary SPC harmonisation scheme started in Q3 2010, and the first step of the procedure (harmonisation of the SPC) is expected to be completed in Q2 2011. The subsequent steps, for standardisation of the quality part of the dossier and transfer of the MAs to MRP status, should then follow.
- Implementation of the new Variations Regulation resulted in additional responsibilities for the Group (e.g. Article 5 – recommendation on unforeseen variations and worksharing procedures).
- The CMDv maintained close working relationships in 2010 with the European Commission and interested parties, to ensure consistency and relevant exchanges of information.

4. Compliance and inspections

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

Similarly, the Agency coordinates inspections of blood establishments within the framework for plasma-master-file (PMF) certification, as well as communications and actions by Member States in response to suspected quality defects and counterfeit medicines where centrally authorised products are concerned.

4.1. Inspections

Core activities

- In 2010, a total of 300 inspections were carried out – an increase of almost 30% compared to 2009.
- There were 229 GMP, 62 GCP, 5 PhV and 4 GLP inspections.
- All inspections were handled within the legal timelines.

The number of suspected quality defects reported in 2010 compared to 2009 was significantly higher. A number of high-profile manufacturing failures occurred, with increasing international involvement, demanding considerable resources from the Agency. This also involved significant support for the EU regulatory network in cases involving nationally authorised products.

The Agency will be initiating a detailed root-cause analysis of quality defects in 2011.

Product shortages, in some cases linked to manufacturing failures, are increasingly becoming a source for concern.

Significant progress in completing the data in EudraGMP was made, with major transfers of records to the system from France, Italy, Denmark, Poland and Spain, resulting in a significant increase (around 60%) in data population. Transfers from Austria, Germany and The Netherlands are in progress. Austria decided in Q4 to use XML, and therefore has to validate the transfer.

The 'Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials' was finalised and published.

A draft 'Reflection paper on guidance for laboratories that perform the analysis or evaluation of clinical trial samples' was released for consultation.

Figure 41.

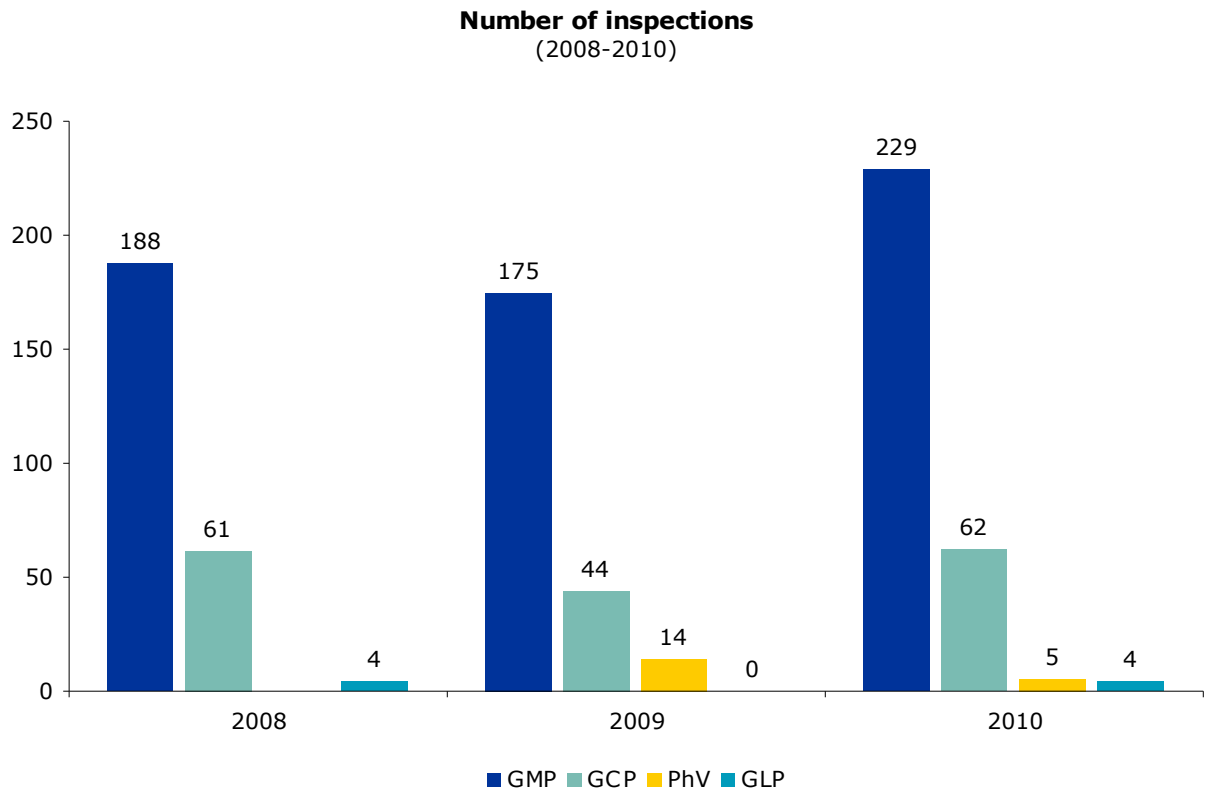
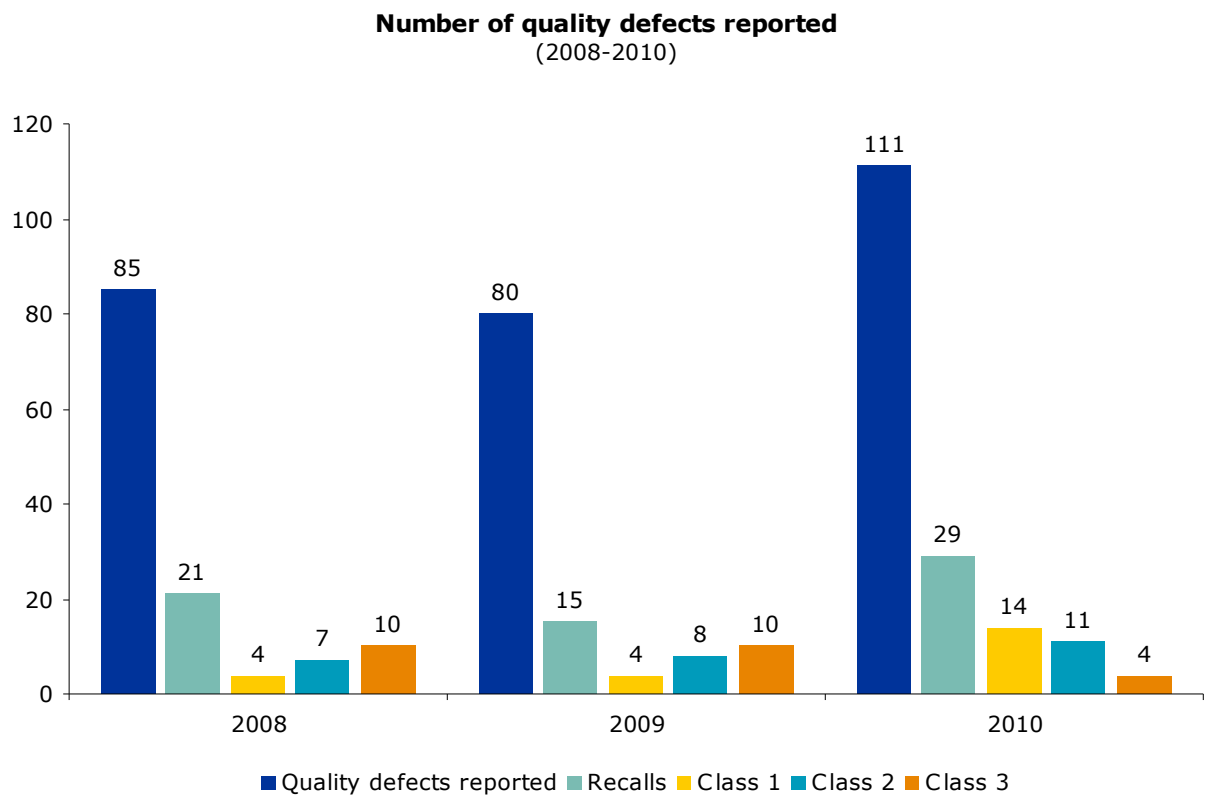


Figure 42.



Specific objectives

Pilot projects on joint GMP and GCP inspections

The pilot projects on joint GMP and GCP inspections with the U.S. FDA were very successful.

Seven joint and 5 observed GCP inspections were carried out, and many exchanges of information, teleconferences and 2 meetings took place, relating to inspections and to GCP procedures and policies.

The initial target for joint GMP pre-authorisation inspections with the U.S. FDA (5 joint inspections with FDA on dosage forms) was considered to be unrealistic for 2010. Following an amendment of the terms of reference to include post-authorisation joint inspections, an exchange of information on possible candidates for joint post-authorisation inspections in 2011 began.

Discussion on cooperation in the area of pharmacovigilance inspections commenced.

An interim report on the International API Inspection Pilot Programme was published in September 2010, and the pilot was completed in December 2010. The commitment of the participants in the pilot programme to this initiative is unquestionably strong, and there is an essential public-health incentive to collaborate on inspections of API manufacturers worldwide. The initiative involves the Agency and the inspectorates of France, Germany, Ireland, Italy and the United Kingdom, as well as the European Directorate for the Quality of Medicines and HealthCare (EDQM) from the Council of Europe, the U.S. Food and Drug Administration and the Australian Therapeutic Goods Administration (TGA).

Pharmacovigilance inspections

The development of processes in the area of pharmacovigilance inspection progressed well in 2010. A joint meeting of pharmacovigilance inspectors and assessors was held, and a draft procedure on actions to be taken after the completion of a pharmacovigilance inspection was prepared and will be further developed in 2011, in the context of preparing for the implementation of the new pharmacovigilance legislation.

Following preliminary discussions held with the U.S. FDA, pharmacovigilance inspections were included in the 2011 programme, with the aim of starting a pilot project similar to those for GMP and GCP inspections.

The Pharmacovigilance Inspectors Working Group held a training course for pharmacovigilance inspectors, which was organised and hosted by the Belgian authorities, in conjunction with the Agency.

Strategy on acceptance of clinical trials conducted in third countries

A reflection paper on ethical and GCP aspects of clinical trials conducted in third countries submitted in marketing-authorisation applications in the EU was released for consultation. A workshop with participants from across the globe was held as part of the consultation process on 6-7 September 2010. In this context, an international workshop of GCP inspectors, with delegates from Europe, Africa, Asia and the Americas, took place on 8 September 2010, to initiate a discussion on the creation of an international network of GCP inspectors.

People attending this workshop were also invited to attend the EU GCP IWG training course, held on 3-5 November 2010. Delegates from the following countries outside the EU attended this course: Bosnia and Herzegovina, former Yugoslav Republic of Macedonia, Montenegro, Switzerland, Turkey, Canada, Ghana, Indonesia, Japan, Kenya, Republic of Korea, Nigeria, South Africa, United Republic of Tanzania, and the USA.

The report 'Clinical trials submitted in marketing-authorisation applications to the EMA: Overview of patient recruitment and the geographical location of investigator sites' was revised to include data from marketing applications submitted in 2009. The report, 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.

Key performance indicator	Target	Outcome
Management of inspections within legislative timelines	100% of inspections	100% for GCP, GMP and PhV

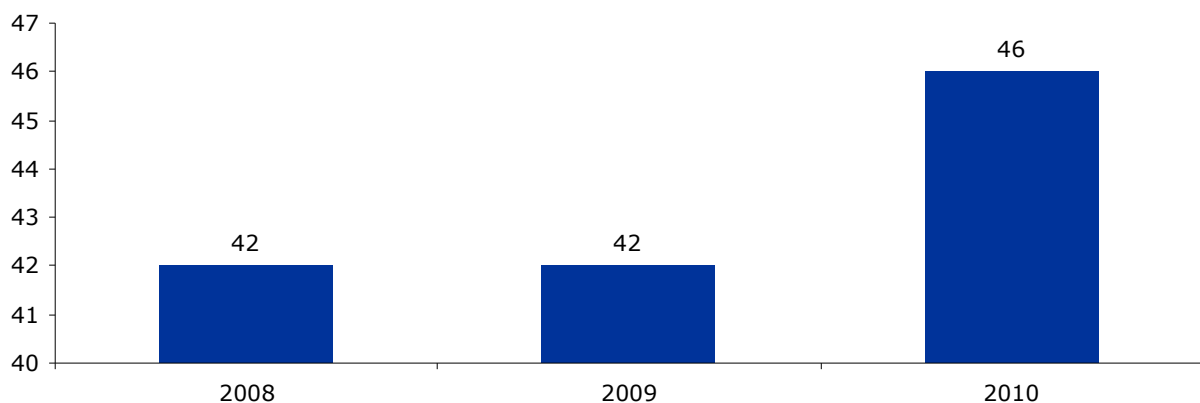
4.2. Sampling and testing

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 2009 was successfully concluded and the 2010 programme was brought close to completion.
- Parallel-distributed products were included in the programme.
- Reflecting on experience gained in the field of human medicines, a risk-based approach to sampling and testing was introduced for veterinary medicines.
- Forty-six medicinal products were tested – 3 more than planned.

Figure 43.

Medicines included in the sampling-and-testing programme (2008-2010)



Key performance indicator	Target	Outcome
Percentage of planned products (43) actually tested	95% of planned products	106% (46 products)

4.3. Implementation of the Clinical Trials and GCP Directives

- The Agency continued to provide support to the Clinical Trials Facilitation Group (CTFG). Six face-to-face meetings and 8 teleconferences were held in 2010. A subgroup on standard report designs was established.
- The Agency, CHMP, Heads of Medicines Agencies and the CTFG agreed a plan of action to improve the link between the assessment of marketing-authorisation applications in the centralised procedure and the approval and supervision of clinical trials at the level of the Member States.
- The preparation of a reflection paper on risk-based quality-management in clinical trials was initiated.
- The launch of EudraCT Version 8 and the related EU Clinical Trials Register was delayed. The challenges of converting the database to its current structure to support this and future developments, and additional difficulties encountered in data migration and testing of the software, meant that the release was delayed until March 2011.

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.

The table below gives an overview of projects planned and performance in 2010.

System or process	Performance in 2010
EudraVigilance	
EV Vet 3, requirements-gathering phase	Requirements-gathering is incomplete, as the relevant inception- and elaboration-phase artefacts (3 iterations planned in 2010) have been completed but not signed off.
EV Human, access policy	The whole suite of EudraVigilance projects were re-planned at the end of 2009, in the context of the implementation of the pharmacovigilance legislation and of a revised planning roadmap agreed at the EudraVigilance Steering committee in February 2010. This set of functionalities is therefore now planned for May 2011.
EV Vet, access policy	As a consequence of the re-planning of the EudraVigilance suite of projects, in the context of the implementation of the pharmacovigilance legislation for human medicinal products, this set of functionalities has also been deferred.
Eudra Data Warehouse, finalisation of inclusion of medicinal products for human use in the updated datawarehouse.	The pilot implementation was completed. Phase 2 – full implementation for human medicinal products – is in progress, but was held back by the complexities to be taken into account in planning for the integration of IDMP in the context of the new pharmacovigilance legislation, and by a lack of resources to complete the business-analysis aspects of the exercise.
EV data management (backlog)	The contract with the service provider was put into place, and the set-up phase completed, in the fourth quarter of 2010. Work on the backlog had begun by the end of the year.
EudraCT	
Release of versions 8 and 8.5	Release of version 8 was postponed to Q1 2011, due mainly to technical difficulties encountered in migrating data from the existing database into the enlarged database that is the foundation of version 8.
E-Application form	
E-Application Form project	Difficulties in reaching consensus on the implementation of the Variations Regulation, taken together with delays in business analysis and technical errors in dealing with a new technology, resulted in the need to review the project in the third quarter of 2010. The forms are planned to go into pilot in mid-2011.
eCTD	
eCTD for all marketing authorisation applications	The full implementation of eCTD for all applications for marketing authorisation to the Agency was achieved. This is expected to increase the efficiency of the centralised procedures.

System or process	Performance in 2010
ICT support to communication and provision of information	
Light Authoring Tool, PIM Review System, Data Validation Engine for centrally authorised medicines	Following discussion of the business case for and the allocation of resources to PIM, it was decided that development of the PIM Review System should be continued to the end of March 2011. A decision to stop the project was taken in the first quarter of 2011.
Migration of centrally authorised products	A formal guide to migration of products was delivered in mid-2010. This activity was then suspended pending the decision on the project as a whole, and in consequence of the delay in likely availability of the review system into 2011.
Reference Data Model V3	Version 3 of the Reference data model was published across the Network on time. The first review was complete as at the end of 2010, but further detailed analysis remains necessary.

5.2. Implementation and operation of corporate IT

This activity area includes:

- defining the ICT strategy of the Agency in line with the Agency's road map;
- providing 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;
- delivering information systems required to support the Agency's corporate business processes;
- delivering information systems as defined in the EU telematics strategy for use by the European medicines network, pharmaceutical industry, healthcare professionals and the general public;
- promoting and facilitating the European medicines network and public administrations, in collaboration with the European Commission;
- promoting and facilitating the provision of information on medicinal products to citizens and enterprises.

In addition, a specific emphasis has been put on business and ICT alignment, business project and change management in order to:

- ensure consistent business involvement in projects;
- support the benefit-cost balance;
- manage resources limitation by aligning projects with each other, eliminating redundancy and duplication.

System or process	Performance in 2010
Enhancing and developing ICT systems supporting efficient conduct of the Agency's core business	
Siamed II	The planned implementation of support for the processing of marketing-authorisation applications has been rescheduled for delivery in mid-2011, because the complexity of the main functionality (timetabling, procedure-tracking, etc.) was underestimated at the outset.
Enterprise resource planning system	The development of the Agency's enterprise resource planning system was on track in terms of timing and scope. The project was slightly over budget. Preparations were made for the go-live of the financial module; blueprinting for human resources modules was completed.
Agency information architecture and enterprise information management projects	On the basis of an assessment of the deliverables from phase I, the approach was reconsidered over 2010. Initiation of phase II, focused on the business rather than ICT, occurred at the end of the year.
New system to plan, manage, document and evaluate GXP inspections	A reduced corporate GXP module on GCP/PhV was developed and is working successfully, with some fixes to be done during the maintenance phase. The reduction was due to the lack of budget and the extra iteration needed for the critical issues on the GMP module.
Improving operation of Eudra and corporate-IT user-support	
Service level agreements	Service level agreements for Eudra and corporate-IT user-support were created and agreed with the business in the first quarter of 2010. Services complied with the agreed definitions.
Metrics and monthly reporting to management	Metrics were created. From the second quarter of 2010, reports were created and circulated on a monthly basis.
Incident management	A standard operating procedure for ICT maintenance was created to support the Agency's business-continuity planning.

Key performance indicator	Target	Outcome
Telematics and corporate-IT systems availability measured against Agency working hours	98%	Over 99%

Eudra Service Desk - meeting of service level agreements per system/priority level

Severity rating	Description	Response time*	Target	Outcome	Resolution time**	Target	Outcome
1. Critical	Users are unable to use the system.	30 minutes	90%	100%	3 hours	80%	None logged
2. Severe	The system is operational but severely restricting use.	1 hour	90%	100%	1 business day	80%	100%

Severity rating	Description	Response time*	Target	Outcome	Resolution time**	Target	Outcome
3. Important	The system is operational, but one or more functions are restricted.	1 day	90%	100%	10 business days	80%	100%
4. Minor	The system is operational and no functions are restricted.	3 days	90%	100%	120 business days	80%	100%

* Response time means the time within which the Service Desk will inform the user what it is intending to do to resolve the problem.

** Resolution time means the time within which the support team (1st, 2nd & 3rd-line) should resolve the problem and close it.