



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Annual report 2011

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Overview of the Agency's contribution  
to science, medicines and health in the  
European Union

Adopted by the Management Board on 22 March 2012



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 (EU) 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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## *Note on annexes*

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## Foreword by the Chair of the Management Board

"A year of significant challenges, but also one of substantial progress."



**Sir Kent Woods**  
Chair of the  
Management Board  
since June 2011

**It is my great pleasure to introduce this annual report, the first during my tenure as Chair. The report provides an impressive record of the work achieved by the Agency's staff and its European experts throughout 2011.**

It has been a year of significant challenges, but also one of substantial progress towards improving public health through the regulation of medicines. It will be remembered in particular for the work done in preparation for some major pieces of European legislation – arguably the greatest change to the regulatory framework of the Agency since its foundation. With the adoption of the Falsified Medicines Directive in June, the agreement in December on an implementation plan for the pharmacovigilance legislation and the preparatory work for a revision of the Clinical Trials Directive, a firm foundation has been laid for the continuation of this far-reaching legislative programme in 2012 and beyond.

Within the Agency's core areas of business, the report demonstrates a steady progression of activity. The direction of travel was set at the beginning of the year with the publication of the Agency's 'Road map to 2015'. We have seen a welcome expansion of the involvement of civil-society representatives in the Agency's business, and progress has also been made on transparency issues and conflicts-of-interests guidelines for scientific committees. The launch of the European Union Clinical Trials Register opens a further avenue for transparency and public accessibility in the domain of medical research. I would also like to direct attention to the data on public-health benefits of new medicines and new indications recommended for approval in 2011. This is a rich illustration of the practical contribution the Agency makes to providing better medicines for Europe.

Looking further afield, I was also pleased to see significant progress made on developing international collaborations. Examples include the Agency's agreement with the U.S. Food and Drug Administration (FDA) on: sharing resources in the inspections of manufacturing sites; pilot programmes for parallel assessment in certain areas; and joint working through the Transatlantic Taskforce on Antimicrobial Resistance.

Later in the year, I was pleased to welcome Professor Guido Rasi to the Management Board as the Agency's new Executive Director. I have worked closely with Guido for several years as a colleague in the European medicines regulatory network. I know that he will bring vision and energy to his new role, together with the spirit of collaborative working which is such a strength of the network. The Management Board is also extremely grateful to Andreas Pott for his leadership and hard work during his tenure as Acting Executive Director for much of 2011.

I would additionally like to extend thanks to my colleagues on the Management Board for the support I have received as Chair. All of them have crowded diaries and heavy responsibilities elsewhere. To make best use of their time, we will be adjusting the pattern of Board meetings in 2012.

Finally, I can record that a major milestone for the Agency was reached in August, when the lease was signed for the Agency's new premises at 25 Churchill Place. This is an essential step in what has been a very comprehensive and well-executed accommodation project ('Project 2014'). With its future base secured, the Agency can look forward with confidence, serving its key public-health role in the regulation of human and veterinary medicines in Europe and maintaining strong partnerships with other agencies around the world.

# Introduction by the Executive Director

"Once again, the Agency has shown it is capable of overcoming major challenges."



**Guido Rasi**  
Executive Director  
since November  
2011

The year 2011 was a challenging year, but once again the European Medicines Agency has shown it is capable of overcoming major challenges. The Mediator case in France, delays in the budget-discharge process, issues surrounding conflicts of interests of former staff and experts, and delays in the appointment of a new Executive Director for the Agency - all of these had a major impact on the Agency's reputation and created a challenging environment for the Agency to operate in.

Despite the difficult climate, when I arrived in November 2011, I found a well-managed, functioning organisation with a dedicated staff that was yet again able to deliver on its core business activities and priorities set out in its work programme and 'Road map to 2015'. Much of the credit for this goes to Andreas Pott, who served as Acting Executive Director for almost a year, and to the Agency's senior management group, as well as to the whole staff of the Agency. They ensured that the Agency remained on course throughout this eventful year. Credit also goes to the national competent authorities: their scientific expertise and contribution is the fundamental basis on which the Agency's success is built.

During 2011, the Agency saw continuously high levels of activities in almost all its business areas. There was a slight increase in the number of applications for initial marketing authorisations for medicines for human use, from 91 applications in 2010 to 100 applications in 2011. We have positively noted that most of this increase is due to applications received for new medicines. The number of these rose by over 40%, from 34 in 2010 to 48 in 2011.

The number of applications received for initial marketing authorisation for veterinary medicines declined slightly, which is likely due to the delayed impact of global recession and the consolidation seen in recent years in the sector. The rise seen in veterinary scientific advice is a healthy sign that interest remains high in bringing innovative veterinary products to the market through the centralised procedure.

Significant advances were made in terms of transparency: in March 2011, the European Union (EU) Clinical Trials Register went live. The launch of this database was welcomed by patients', consumers' and healthcare professionals' organisations as an important step towards increasing the transparency of medical research and facilitating availability of information about clinical trials taking place.

Later in the year, the Agency launched a new database of European experts. The database is part of the Agency's approach to handling conflicts of interests, and allows the public to access each expert's declaration of interests online.

Nowhere was the impact of the Agency's much more proactive approach to transparency experienced more dramatically than in relation to the Agency's handling of requests for access to documents. During the course of the first full year of operation of the new access-to-documents policy, the Agency released more than 1,000,000 pages in response to requests.

Many of the transparency measures implemented anticipate changes that will be introduced with the new pharmacovigilance legislation. Preparation for this new piece of legislation was one of the main priorities for 2011. Owing to the commitment of the Agency and the whole of the EU medicines regulatory system, preparations progressed according to plan, although an ever-evolving budget situation required the readjustment of some priorities.

Looking back at the year 2011, I would like to congratulate my staff and all of the European experts who work with the Agency. It is an honour for me to present their achievements to the Agency's Management Board.

# Highlights of the year 2011

## January

- European Medicines Agency publishes final 'Road map to 2015'.

## February

- New version of EudraGMP allows access to information from all Member States.
- Agency hosts global animal-health conference on availability of veterinary medicines.
- Agency releases first clinical biomarker qualification for public consultation.
- Agency launches strategy on medicines for older people.

## March

- Agency and FDA launch pilot program for parallel assessment of quality-by-design applications.
- Agency announces process improvement of core business procedures.
- Launch of the EU Clinical Trials Register.

## April

- First stakeholder forum on the implementation of the new pharmacovigilance legislation.

## June

- First meeting of expert group on the replacement, reduction and refinement of the use of animals.
- First positive opinion for paediatric-use marketing authorisation.

## July

- Legislation on falsified medicines adopted.
- New strategy on combating antimicrobial resistance published.

## August

- Lease for new office space signed.

## September

- Launch of the updated European experts database.

## October

- Management Board appoints Guido Rasi as new Executive Director.

## November

- Plans for business continuity during the London 2012 Olympics agreed.
- Guido Rasi starts mandate as Executive Director.

## December

- Formalisation of interaction with healthcare professionals.
- Agency and FDA agree programme to rely on each other's manufacturing-site inspections.

# 1. The European Medicines Agency and the world

## 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 its scientific committees, working parties, scientific advisory groups and related groups.*

### Preparation for new legislation

#### **Implementation of the new EU pharmacovigilance legislation**

One of the Agency's main priorities for 2011 was to prepare for the implementation of the new EU pharmacovigilance legislation. This new piece of legislation is the biggest change to the Agency's legal framework since its establishment. The management and coordination of this complex project required intensive engagement and consensus-building with partners in the EU medicines system, particularly with the national competent authorities. Although the complexity of the planning process was increased by an evolving budgetary situation which led to changing priorities, the Agency achieved a number of milestones throughout the year:

- Establishment of a governance structure that brings together all experts from all relevant disciplines from the Agency and the national competent authorities. Further to a request from the Heads of Medicines Agencies (HMA), their involvement in the project will be further strengthened in 2012.
- Timely publication of the legal notice and detailed guidance on submission of medicinal product information under Article 57. Following feedback received during the consultation phase, the Agency is now working with industry stakeholders on a staggered implementation of the Article 57 requirements.
- Timely delivery of the Agency's technical contributions to the European Commission's Implementing Measures.
- Agreement of a strategy for EudraVigilance and EU Telematics Controlled Terminology by the Agency's Management Board. A fall-back scenario was prepared in case the budgetary situation would not allow for the implementation of the strategy agreed by the Board.
- Agreement of the 2012 implementation plan using prioritisation criteria by both HMA and the Management Board in December 2011.
- Preparation of more than 15 reflection papers to orientate policy and strategy on the implementation, for discussion within the governance structure.
- Establishment of stakeholder fora to discuss implementation of the legislation with the key stakeholder groups. The Agency held three one-day-long meetings, which received unanimously positive feedback.

#### **Antifalsification legislation**

The new legislation on falsified medicines was published on 1 July 2011. Preparation for the implementation of the legislation started with the establishment of a cross-Agency task force, development of a project plan, drawing up of information and communications technology (ICT) requirements and initial estimates of human, financial and ICT resource requirements.

The work in 2011 focused on the preparation of formats for certificates and related information of registration of wholesale distributors and of active pharmaceutical ingredient (API) importers and/or manufacturers in the EU database. In addition, the existing guidance on good distribution practice was revised to incorporate requirements of the new legislation. Stakeholders were consulted on the revision.

### **Clinical trials legislation**

The European Commission plans to put forward, in 2012, a legislative proposal to revise the Clinical Trials Directive 2001/20/EC. The Agency provided its comments to the European Commission on a concept paper on the revision of the clinical trials legislation. The paper outlines potential approaches on how to address some of the key concerns about the Clinical Trials Directive.

### Operating the EU incident management plan

The Agency operates an EU incident management plan to ensure that emerging issues in relation to the safety of human medicines are managed proactively and in a coordinated manner across the EU medicines network, thus preventing that incidents develop into crisis situations.

The workload in relation to this activity increased significantly in 2011. A total of 16 emergency issues were discussed by the Incident Review Network. Of these, 3 related exclusively to centrally authorised medicines, 4 involved both centrally and nationally authorised medicines and in 9 cases only nationally authorised medicines were concerned.

In a significant number of cases (5) the issue related to quality defects.

Work will now start on reviewing the mandate and the composition of the Incident Review Network, based on the lessons learned from the pilot. The concept of the incident management plan will be defined in detail in a specific module of the good pharmacovigilance practice guideline, to allow full implementation of the procedure. Proposals will be made at the February 2012 Heads of Medicines Agencies meeting.

### Implementation of the policy on handling of conflicts of interests

New rules on how the European Medicines Agency handles conflicts of interests of scientific experts entered into force on 30 September 2011. The new rules provide for a more proactive approach both in identifying potential conflicts of interests and in searching for alternative experts.

A major building block for the implementation is the update of the Agency's experts database and the new online list of experts, which were launched to coincide with the Agency's new policy on handling of conflicts of interests. The updated database contains the names of approximately 5,000 experts. By the end of the year, new forms for declaring interests (updated in accordance with the new rules) were received and published for more than half of the nominated experts (54%). The declarations of experts who have not yet submitted or signed their forms will continue to be received and published over the coming months, so that all experts have a valid and signed declaration of interests published on the Agency's website. Involvement in the Agency's activities is subject to the availability of a signed declaration of interests form and assessment of declared interests for the concerned activity.

### Application of the 3Rs in the regulatory testing of human and veterinary medicinal products

In September 2011, the Agency established an ad hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products (JEG 3Rs). The group is composed of representatives from the scientific committees and expert working groups, nominated on the basis of their particular expertise in this specialised field. The mandate of the group is to promote best practice in the implementation of the 3Rs in regulatory testing of medicinal products and to facilitate full and active cooperation with other European groups working in the 3Rs area.

### Preparation for future enlargement

#### **Instrument for Pre-accession (IPA) programme**

The Agency, through the IPA programme, provides assistance for the involvement of Croatia, the former Yugoslav Republic of Macedonia, Turkey, Albania, Bosnia and Herzegovina, Montenegro, Serbia and Kosovo (under UNSC Resolution 1244/99) in its activities. The IPA programme supports the participation of nominated representatives of the countries concerned in selected meetings and training courses as observers.

In June 2011, as part of the programme, the Agency organised a two-day conference in Zagreb, Croatia, titled 'Reinforcing patient safety in Europe'. Supported by the European Commission, the conference was organised in

collaboration with the Croatian Agency for Medicinal Products and Medicinal Devices, HALMED. A total of 223 delegates attended the conference, including almost 100 representatives from the pharmaceutical industry.

In September 2011, a new two-year contract was signed with the European Commission to facilitate the continuity of the programme up to 2013. During the previous programme, 649 delegates from countries covered by the IPA programme attended a total of 144 meetings as observers.

#### **Pre-accession linguistic check for Croatian**

In January 2011, the Agency, together with the Croatian national competent authorities, started a pre-accession linguistic checking process for product information in the Croatian language. This procedure aims to facilitate the phasing-in of Commission decisions on centrally authorised medicines once Croatia joins the EU on 1 July 2013.

### Meetings at the European Medicines Agency

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

A total of 542 meetings were held at the Agency. The number of meetings has decreased slightly over recent years, owing to the increase in virtual meetings. The total number of delegates coming to the Agency remained stable, at 8,486.

In 2011, the number of reimbursed meetings decreased by 5% in comparison with 2010. However the number of reimbursed participants increased slightly, by 0.5%.

A delegate questionnaire was launched in May 2011. The results indicated that 95% of delegates were satisfied or very satisfied with the support provided by the Agency.

**Table 1.**

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	95%

## 1.2. European cooperation

### Data collection on sales of veterinary antimicrobials within the EU – the ESVAC project

The Agency launched the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project at the end of 2009, following a request from the European Commission to develop a harmonised approach to the collection and reporting of data on the use of antimicrobials in animals from the Member States. The collection of data on the sales of veterinary antimicrobials is important as the use of any antimicrobial brings with it the risk of the development of resistance.

In September 2011, the Agency published its first report on sales of veterinary antimicrobial agents for the period 2005-2009 in the Czech Republic, Denmark, Finland, France, the Netherlands, Norway, Sweden, Switzerland and the United Kingdom. For the first time, data on sales of antimicrobials, normalised for animal populations according to harmonised demographic data, could be compared across nine European countries.

ESVAC is currently collecting detailed and standardised data for 2010 from up to 20 countries; the report will be published during 2012. The reports are being used by risk assessors and risk managers in Member States to inform antimicrobial policy and responsible use of antimicrobials. The Agency is currently discussing with the European Centre for Disease Prevention and Control (ECDC), the European Food Safety Agency (EFSA) and the EU Reference Laboratory for Antimicrobial Resistance integrated use and reporting of data on consumption of, and resistance to, antimicrobial agents in humans, animals and food in the European Union.

## Transatlantic Taskforce on Antimicrobial Resistance (TATFAR)

The Transatlantic Taskforce on Antimicrobial Resistance was established in 2009 at the annual summit between the EU and US presidencies. The purpose of the taskforce is to identify urgent antimicrobial-resistance issues that could be better addressed by intensified cooperation between the US and the EU within the following key areas:

- appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities;
- prevention of both healthcare and community-associated drug-resistant infections;
- strategies for improving the pipeline of new antimicrobial drugs.

In September 2011, TATFAR published a report with 17 recommendations in these key areas where future cooperation would prove fruitful. Those recommendations in which the Agency is involved are listed below.

### Human medicines:

- The FDA and the Agency discussed ways to facilitate the use of the same clinical-development programme to satisfy regulatory submissions of applications for new antibiotics to both authorities. Reflections on this issue are included in the current Agency guideline on development of antibacterials.
- Establishment of regular meetings between the FDA and the Agency to discuss common issues in the area of antibacterial drug development and regulation.

### Veterinary medicines:

- Collaboration on ongoing and future projects that relate to the collection of data on sales and use of veterinary antimicrobials in food-producing animals, such as ESVAC (see above).
- Collaboration on the implementation of recently developed guidelines on risk assessment for foodborne antimicrobial resistance as prepared by Codex Alimentarius.
- Enhanced information-sharing on approaches to promote appropriate use of antimicrobials in veterinary communities.

## Working with health technology assessment bodies

The Agency has no direct role in the health technology assessment (HTA) process; however, recognising the need for cooperation with HTA bodies to enable better decision-making by all players who have a role in making medicines available to patients, the Agency has started working together with these bodies in recent years on three main areas:

- improving the information available on centrally authorised medicines in European public assessment reports (EPARs);
- improving the information available on orphan drug designation;
- early-stage drug development.

In terms of improving the information available on centrally authorised medicines, the Agency has progressed its collaboration with the European Network for Health Technology Assessment (EUnetHTA), a body representing the HTA bodies from across Europe. Following the gathering of requirements from HTAs on how information on the benefits and risks of a medicine should be included in the EPAR to make a better contribution to relative-effectiveness assessments by HTA bodies, the Agency revised its EPAR template, which was in use all through the year. The Agency and EUnetHTA are currently reviewing their experience with the new template with a view to further refining requirements and fine-tuning the template as necessary.

The Agency has also initiated work with EUnetHTA on improving the exchange of information regarding orphan-drug-designation outcomes.

In terms of early-stage drug development, the Agency is engaging with HTA bodies through its scientific advice process to converge the advice given to companies on the development of a medicine from regulators and HTA bodies wherever possible. A joint scientific advice procedure was introduced in 2010. Uptake of the joint procedure of the Agency and HTA bodies accelerated during 2011, with 9 procedures being completed by the end of the year, with a further 1 ongoing.

### 1.3. International cooperation

*The growth in the Agency's international activities mirrors the increasing globalisation of pharmaceutical activities, in particular the growth of clinical-trial activity in countries outside the EU, increasing reliance on starting materials manufactured in developing countries, and associated concerns about ethical considerations and counterfeit operations. There is a strong public-health need to ensure that these activities are properly monitored. The Agency is therefore strongly committed to international cooperation, both on a bilateral and a multilateral basis.*

#### Bilateral cooperation with non-EU countries

The Agency has bilateral confidentiality arrangements (CAs) with the U.S. Food and Drug Administration (FDA), Health Canada (HC), the Japanese Pharmaceutical and Medical Devices Agency (PMDA) / Ministry of Health Labour and Welfare (MHLW) and the Australian Therapeutic Goods Administration (TGA). A more limited arrangement is in place with Switzerland's Swissmedic. Interactions with these regulatory authorities continued to intensify in 2011, with increasing exchanges of information on product-related activities, but also development of new cluster activities, in particular with the FDA.

In addition, the Agency continued to support the European Commission's work with China, India and Russia on issues related to medicines.

#### Multilateral activities

The Agency cooperates with authorities from many other countries within a variety of multilateral frameworks, including the International Conference on Harmonisation for pharmaceuticals for human use (ICH) and for veterinary use (VICH), the World Health Organization (WHO), the Council of Europe, the Organisation for Economic Cooperation and Development (OECD), Codex Alimentarius, the World Organisation for Animal Health (OIE) and the European Free Trade Association (EFTA). These multilateral activities are an important part of the Agency's international strategy, as they create synergy between the Agency and its international partners.

The Agency made progress with regard to international standardisation activities. ISO standards were agreed for individual case safety reports (ICSR) for the identification of medicinal products (IDMP). Major progress was made on a new guideline on periodic safety-update reports.

There was close liaison with the WHO on a number of ongoing Article 58 procedures. This type of procedure allows the Agency, in cooperation with the WHO, to give scientific opinions on medicinal products that are intended exclusively for marketing in non-EU countries.

#### Capacity-building activities

The Agency is engaged in a number of capacity-building activities. A successful basic training course for good-clinical-practice (GCP) inspectors and an international GCP-inspection workshop were held at the Agency in March 2011 and October 2011, respectively. Participants came from many countries, both within and outside the EU. These activities form part of the Agency's commitment to capacity building for GCP inspectors internationally and to the creation of an international network of GCP inspectors.

Within the framework of the ICH Global Cooperation Group, the Agency supported training activities in countries such as Malaysia and Singapore.

The Agency also contributed to an international paediatric medicines network initiative, helping to improve the availability of paediatric medicines worldwide, and in this context provided expertise to the WHO and countries outside the EU.

The Agency has been identified as one of the key stakeholders for the provision of technical and regulatory affairs expertise for the Eastern African Countries (EAC) regulatory capacity-building project. The implementation of this project, due to be launched in March 2012, will be coordinated by the WHO and the New Partnership for Africa's Development (NEPAD).

## Resource-sharing activities

The Agency is involved in a number of international activities that are aimed at resource sharing, particularly in relation to good manufacturing practice (GMP) and good clinical practice (GCP) inspections and, since April 2011, quality-by-design (QbD) concepts. Based on the experience gathered during the pilot project, the joint GMP and GCP activities are now moving to operational programmes.

## Mutual-recognition agreements

Mutual-recognition agreements (MRAs) on good manufacturing practice allow EU authorities to rely on GMP inspections performed by other regulators, the waiving of batch-testing of products on entry into the EU, and information-sharing on inspection-related information and quality defects. The EU has MRAs in place with Australia, New Zealand, Canada, Japan and Switzerland.

Switzerland, Canada, Australia (veterinary) and New Zealand (human) are now connected to EudraGMP. Work is ongoing with Japan, Australia (human) and New Zealand (veterinary) to ensure that they are also connected.

## 1.4. Communication, provision of information and transparency

*The EU 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.*

## Strengthening communication on medicines evaluated by the Agency

### **Increase in communications activities**

Communication of product-related information following the monthly meetings of the Committee for Medicinal Products for Human Use (CHMP), as well as communication on emerging issues, saw a substantial increase in 2011. These activities also include the coordination of messages across the EU medicines network.

### **Improving product information**

A multidisciplinary exercise took place to increase the quality and the readability of package leaflets. Patients and consumers, healthcare professionals, pharmaceutical industry and clinical research organisations specialised in user testing were involved. The exercise resulted in a new template that puts emphasis not only on the risks of taking the medicines but also on the benefits the patients can expect (e.g. symptom relief, timing of the improvement), and also gives concrete recommendations on the conditions of use of the medicine concerned. In parallel, initiatives were undertaken within the European medicines network to strengthen the quality of information presented in summaries of product characteristics.

## Integration of civil-society representatives in the Agency's activities

The trend of increasing involvement of civil society representatives in the Agency's work continued in 2011.

### **Progress with involvement of patients' and consumers' organisations in the Agency's work**

Significant progress was made in terms of the Agency's interaction with patients' and consumers' organisations. In addition to their statutory involvement in the Agency's Management Board and some of its scientific committees, representatives of patients' and consumers' organisations are now involved at various levels of the Agency's work, including in scientific advisory group meetings and meetings of the Pharmacovigilance Working Party. The latter is preparing the ground to integrate patients as members of the Pharmacovigilance Risk Assessment Committee that will be established in July 2012 as part of the new pharmacovigilance legislation.

Patients also participate in the review of Agency documents, including package leaflets for new medicines prior to authorisation, European public assessment report summaries, question-and-answer documents and press releases on safety issues. In a paper titled 'The role of patients as members of the EMA Human Scientific Committees' (EMA/351803/2010), the added value of patients has been described as bringing "a unique and critical input based on their real-life experience of being affected by a disease and its current therapeutic environment".

In October 2011, the Agency published revised criteria to be fulfilled by patients' and consumers' organisations involved in Agency activities. The revised criteria clarify the transparency requirements with regard to the organisations' funding sources.

#### ***Involvement of patient representatives in scientific advisory group (SAG) meetings***

The Agency concluded a one-year pilot of involving patient representatives in SAG meetings with the publication of an outcome report at the end of December 2011.

The report states that the pilot project enabled patient representatives to become integrated in confidential discussions at the Agency and contribute their views. It concludes that the inclusion of the patient viewpoint adds robustness to the output of the meetings and enriches the overall evaluation of the benefits and risks of medicines.

SAGs are groups of European experts brought together by the Agency's committees to provide advice in connection with the evaluation of specific types of medicines or treatments. During the pilot phase, which ran from October 2010 to October 2011, 22 patient representatives took part in a total of 18 SAG meetings on human medicines.

Following the success of the pilot, the Agency will continue to invite one or two patient representatives to SAG meetings where their input is likely to be suitable and beneficial.

#### ***Formalisation of interaction with healthcare professionals***

On 15 December 2011, the Agency's Management Board adopted a framework for interaction and criteria to be fulfilled by healthcare professionals' organisations to be involved in the Agency's activities. The Agency has been interacting with healthcare professionals since it was founded in 1995, but the new framework for interaction aims to make this relationship more structured and complete. As part of its implementation, the Agency will transform its Healthcare Professionals' Working Group (HCPWG), which has been meeting since 2006, into a working party with links to all scientific committees dealing with human medicines.

**Table 2.**

<b>Key performance indicator</b>	<b>Target</b>	<b>Outcome</b>
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 4 weeks of the Commission decision	80% of marketing authorisations granted	73%
Percentage of EPAR summaries in a language understandable to the public, published together with the EPAR	90% of EPARs	100%
Percentage of withdrawal question-and-answer (Q&A) documents published at the time of the next appropriate CHMP monthly report	90% of Q&A documents	90%
Percentage of refusal Q&A documents published at the time of the CHMP opinion	90% of Q&A documents	100%

#### **Launch of the EU Clinical Trials Register**

The Agency launched the EU Clinical Trials Register (<https://www.clinicaltrialsregister.eu/>) on 22 March 2011. The online register gives public access to information on interventional clinical trials for medicines authorised in the 27 EU Member States and Iceland, Liechtenstein and Norway. The database also allows the public to search for information on clinical trials authorised to be conducted outside the EU if these trials are part of a paediatric investigation plan.

The launch of the database was welcomed by patients' and consumers' organisations as an important step in increasing transparency of medical research and facilitating the availability of information about clinical trials taking place in Europe.

In September 2011, the EU Clinical Trials Register was recognised by the WHO as one of the primary registries for its International Clinical Trials Registry Platform (ICTRP), a web-based portal that allows access to a wide range of information from different clinical-trial registers from across the world. Recognition as a primary registry by the WHO is also an endorsement of the importance of the EU Clinical Trials Register for potential clinical-trial participants, as well as for sponsors, researchers, ethics committees and policymakers.

The information contained in the EU Clinical Trials Register will become available through the ICTRP in early 2012.

### Launch of a database of clinical studies in children completed before 2007

In October 2011, the Agency published a new database containing information on studies of medicines authorised in the European Union that were carried out in children and completed before the Paediatric Regulation came into force in 2007.

The database allows users to search for information on the studies' names and aims, the medicines studied and the ages of patients included. For a subset of studies, documents summarising the study's results are also available.

### Launch of online European experts list

By the end of September 2011, the Agency launched its new online list of European experts. The list includes all European experts who have been nominated by the national competent authorities to form part of the network of European experts and who have submitted an electronic declaration of interests. These declarations are also made publicly available.

The launch of the online list, with access to declarations of interests, is a major building block of the Agency's policy on the handling of conflicts of interests of its scientific experts, which aims at protecting the Agency's scientific opinion-making processes from the influence of any improper interests.

### EudraVigilance access policy

The EudraVigilance access policy for medicines for human use was published, albeit with a revised implementation plan as a result of the evolving budgetary situation. A stepwise implementation is foreseen, starting with the publication of pre-produced monthly reports for centrally authorised medicines, in the first half of 2012. The next phases, up to 2015, will also see a gradual increase in transparency for nationally authorised medicines, as well as access by pharmaceutical industry, sponsors and research organisations to the EudraVigilance Datawarehouse and Analysis System (EVDAS).

In the meantime, all requests for access to data from EudraVigilance are being handled by a dedicated team at the Agency, which saw a significant increase in the requests received.

### Transparency policy

The comments received on the Agency's draft transparency policy during the public consultation exercise in 2010 were reviewed. The main findings from the consultation exercise form the basis for the next steps of the project. These will be tailored to fit with the transparency provisions of the new pharmacovigilance legislation.

The HMA/EMA guidance document on the identification of commercially confidential information and personal data within the structure of the marketing authorisation dossier (release of information after the granting of a marketing authorisation) was released for a three-month public consultation period on 1 June 2011. Comments on this guidance were discussed with the HMA/EMA group in October and December 2011.

## EPAR usability project

The European public assessment report (EPAR) usability project aims to increase the transparency and the quality of the information contained in EPARs, as well as to streamline and simplify the EPAR process. In 2011, measures recommended previously were implemented in the EPARs. These include the publication as part of the EPAR of divergent scientific opinions, assessment of paediatric studies, outcome of applications for extension of indication and a new annex to the CHMP opinion, as well as a review of the structure of the report.

## Access to documents

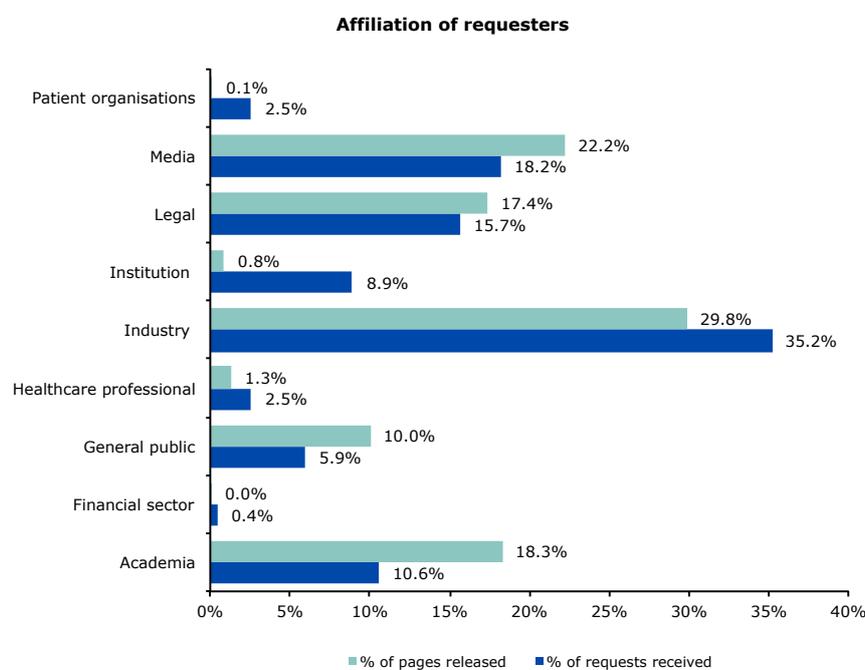
This was the first year of the operation of the Agency's 2010 policy on access to documents. This had major impact: the number of requests increased by 92% in 2011 compared to previous years. The number of pages released increased dramatically. The Agency released over 1,000,000 pages in 2011. This is more than 143 times as many as in 2010.

With a view towards improving the way access-to-document requests are handled and processed, the Agency launched a new project that is intended to help it cope with the ever-increasing number of requests. The 'Ask EMA' project is looking at reactive publication first and will consider proactive publication in the next phase of the project.

**Table 3.**

	2009	2010	2011
Total number of requests received	108	108	207
Total number of appeals	8 (7.4%)	7 (6.5%)	18 (8.7%)
Total number of pages released	7,603	7,080	1,019,138

**Figure 1.**



## 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 work of the Agency's Innovation Task Force and CHMP working parties, 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 that shorten 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 from the Agency's SME Office.*

### SME Office

The year 2011 was an extremely active one for the SME Office, not only in terms of its core activities of providing assistance to small and medium-sized enterprises (SMEs), but also in terms of reviewing and discussing with stakeholders the experience with the SME initiative in its sixth year of operation.

#### *Companies assigned SME status*

In 2011, the number of companies assigned SME status by the Agency increased by 34% compared to 2010. Currently, 679 SME companies are registered, with requests from a further 80 companies under review by the end of 2011.

The geographic distribution of companies remained similar to previous years, with the highest proportion of companies being based in the United Kingdom, France, Germany, Sweden and the Netherlands. There was an increase in the number of micro-sized companies (i.e. companies with fewer than 10 employees) in 2011, with around 41% of all registered companies now falling into this category. Approximately one quarter (23%) of the registered SMEs were created during 2008-2011 and around 17% are academic spin-offs.

Of the assigned companies, the large majority (73%) are developing medicines for human use; 6% are developing medicines for veterinary use; 7% of companies are developing products for both human and veterinary use and 14% are regulatory consultants.

#### *Review of experience with the SME initiative*

A survey was launched in March 2011 to obtain detailed feedback on the SME initiative, five years following its implementation. It also aimed to gather information on how successful (or not) the measures introduced to support SMEs have been, and to identify current and future challenges faced by SMEs in the pharmaceutical sector.

A roundtable-meeting with stakeholder organisations was held on 3 October 2011 to present the results of the survey and discuss the challenges identified, as well as those reported by SMEs.

#### *Simplified SME assignment process*

In October 2011, the Agency introduced a simplified process for handling requests from companies that wish to register as micro, small or medium-sized enterprises. The new process is expected to reduce the administrative burden on companies and speed up the SME assignment/renewal process. Improvements include: a move to electronic-only submissions; introduction of an ownership checklist to improve accuracy of submissions; a risk-based approach to the Agency's review process, reducing the number of submissions that need to be checked; and replacement of formal SME qualification documents with electronic versions.

## Availability of veterinary medicines – minor uses/minor species (MUMS)/limited markets

The criteria for providing free scientific advice in relation to the development of products indicated for MUMS/limited markets were amended in 2009 with the introduction of the new MUMS/limited markets policy on 1 September 2009. This has provided an incentive for developing such products and an increase in the number of scientific advice applications for this type of product has been noted.

The number of requests for MUMS/limited markets applications continued to increase, with 21 applications received in 2011. A detailed analysis was published in October in an annual report on the second year of operation of the policy (EMA/680110/2011).

**Table 4.**

Requests for MUMS/limited markets classification	2009 <sup>1</sup>	2010	2011
Requests received	8	23	21
Requests classified as MUMS	8	18	18
Requests not classified as MUMS	0	5	3
Requests classified as MUMS with financial interest	3	12	8
Requests classified as MUMS without financial interest	5	6	10
Requests for immunologicals	4	5	3
Requests for pharmaceuticals	1	13	16
Requests for others, e.g. biotech, antivirals	3	5	2

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

## Cooperation in research projects

### *Innovative Medicines Initiative (IMI)*

The IMI-funded 'EU Protect' project, designed to improve methodologies in pharmacovigilance, was effectively coordinated. Reasons for the slow progress with the EU Protect work package on benefit/risk were reviewed and dealt with.

Building on the success of the EU Protect project management function, Agency-wide coordination of input into the IMI is now being consolidated.

### *DISCONTTOOLS*

The DISCONTTOOLS project, funded by DG Research as part of the European Technology Platform for Global Animal Health (ETPGAH), started in 2008 and aims to stimulate the delivery of new or improved veterinary diagnostics, vaccines or pharmaceuticals in order to improve our ability to control animal diseases. Stakeholders include representatives from universities, research institutes, chief veterinary officers, vets, pharmaceutical industry and the World Organisation for Animal Health (OIE). The Agency provides regulatory input to the working groups on disease prioritisation, gap analysis and technology evaluation. To date, approximately 50 sets of disease information have been placed on the public website ([www.discontools.eu](http://www.discontools.eu)). The original project will be coming to a successful conclusion in 2012, but is expected to be extended and will end with a conference in late 2013 on the results achieved.

It is foreseen that several of the DISCONTTOOLS projects supported by the European Technology Platform for Global Animal Health will ultimately lead to product development opportunities that may be eligible for support under the Agency's MUMS/limited markets scheme.

## Medicines for use in the elderly

On 18 February 2011, the CHMP adopted its geriatric medicines strategy. The strategy represents a key step forward in the Agency's commitment towards responding to its changing environment, as set out in its 'Road map to 2015'. Against the background of an ageing population in the European Union, it aims to ensure that medicines used by older people are of high quality and are studied appropriately in the older population, both before and after authorisation. It also aims to improve the availability of information for older people on the use of medicines.

In May 2011, as part of the implementation of this strategy, the Agency's CHMP established the Geriatric Expert Group (GEG) to provide scientific advice on issues related to the elderly.

## 1.6. Methodology and outcomes-assessment projects

*The Agency has established a programme aimed at evaluating outcomes of regulatory action on Agency stakeholders and public health in general. The programme also aims to provide methodologies for a more detailed justification of benefit-risk assessments done by the Agency's committees.*

### Measuring effectiveness of risk-management plans

The Agency identified medicines for which the regulatory actions undertaken in the past to address safety issues will be evaluated. Calls for tenders were finalised for the following medicines: iostretinoin, bisphosphonates, rosiglitazone, pioglitazone and oral contraceptives.

In addition, the Agency performed an evaluation of the effectiveness of risk-management measures implemented by marketing-authorisation holder between 2006 and 2010. A paper is under development and is expected to be submitted to a peer-reviewed journal in the first half of 2012.

### Gap analysis of outcome measures for paediatric clinical trials

The gap analysis of outcome measures for paediatric clinical trials is under way. A report comparing clinical endpoints and other outcome measures between the paediatric population and adults has started.

### Benefit-risk assessment methodologies

The Agency has made headway with its project on benefit-risk methodologies. The project is intended to move regulators from 'implicit' decision-making to explicit decision-making through gradual adoption of benefit-risk methodologies and tools.

The conceptual phase for this project was finalised in 2011 with the successful conclusion of 'field tests' of the most appropriate models in five national competent authorities. In the next phase, the Agency will be moving towards implementation, with the initiation of a number of pilot projects over the next year.

### Impact of emerging science

The Agency prepared a draft report on the impact of science on marketing authorisations in the period 2007-2010 as a follow-up to the CHMP think-tank report. As part of this report the Agency reviewed all medicines authorised in the time period that are considered innovative or were developed using innovative methodologies.

## 1.7. Corporate governance

*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.*

## Implementation of ERP system (SAP)

In October 2011, the human resources module of the Agency's Enterprise Resource Planning (ERP) system went live. The chosen platform, SAP, had already been used successfully in the Agency's ERP Financial Stream project. The system is expected to bring new levels of operational efficiency and reduce bureaucratic processes, by avoiding redundancies, automation of certain human resources processes and improved records-management for historical data.

## Project 2014

On 9 August 2011, the Acting Executive Director Andreas Pott signed a 25-year lease agreement with Canary Wharf Group plc for office space in a new building on the Canary Wharf estate in London. The Agency plans to move in 2014, when the leases on its current premises expire.

The new building, currently under construction by Canary Wharf Group, will be located at 25 Churchill Place. The Agency will lease the basement, promenade, ground and first nine office floors in the 20-storey tower.

On 18 July 2011, the President of the European Parliament, Jerzy Buzek, informed the Agency of his agreement on the relocation of the Agency, following a favourable opinion from the Committee on Budgets.

The new building will enable the Agency to improve the efficiency of its use of space, reducing the overall floorspace rented and its annual expenditure. The Agency hopes to cover the costs of relocation with the savings that these reductions will bring over the first ten years of its tenancy.

## Preparation for the London 2012 Olympic Games

The Agency has put in place a series of measures expected to manage the impact of the London 2012 Olympic Games on its operations. The Olympic Games, running from 29 July to 12 August 2012, and the Paralympic Games, running from 29 August to 9 September 2012, will involve events at venues across London and the United Kingdom. The huge number of spectators, tourists and people using the transport system and hotels will mean that London will be significantly busier than usual.

Meetings at the Agency held in the period prior to the Olympic Games between late June and July are expected to be severely affected by these disruptions. The Agency has therefore decided that meetings of its scientific committees and working parties during this period will be held at the offices of other European regulatory authorities, held virtually or cancelled.

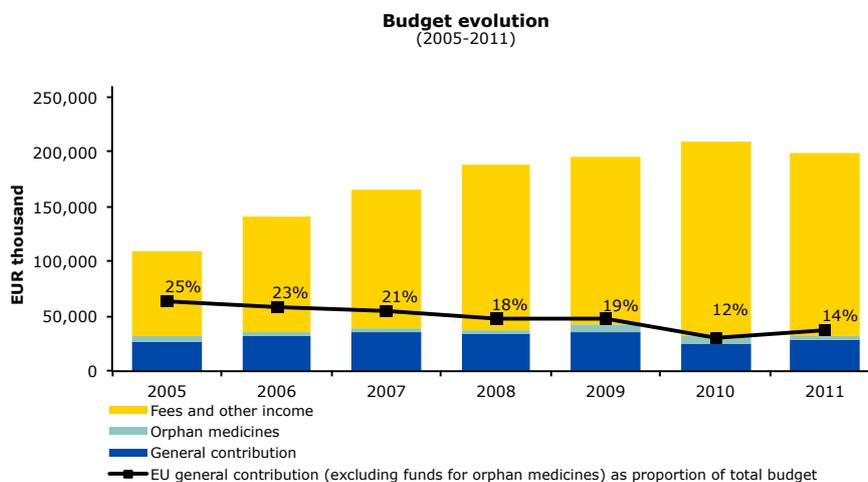
Meetings, including the first meeting of the new Pharmacovigilance Risk Assessment Committee, will take place at the European Commission; others will be held in Malta, Germany, the Netherlands and Sweden.

**Table 5.**

Key performance indicator	Target	Outcome
Budget implementation	Minimum of 95% implementation rate	96.74% of expenditure appropriation implemented
Staff recruitment (long-term positions)	4% vacancy rate by year end	3%
Testing of business-continuity arrangements	Annual test ensuring involvement of different staff members each year	Postponed

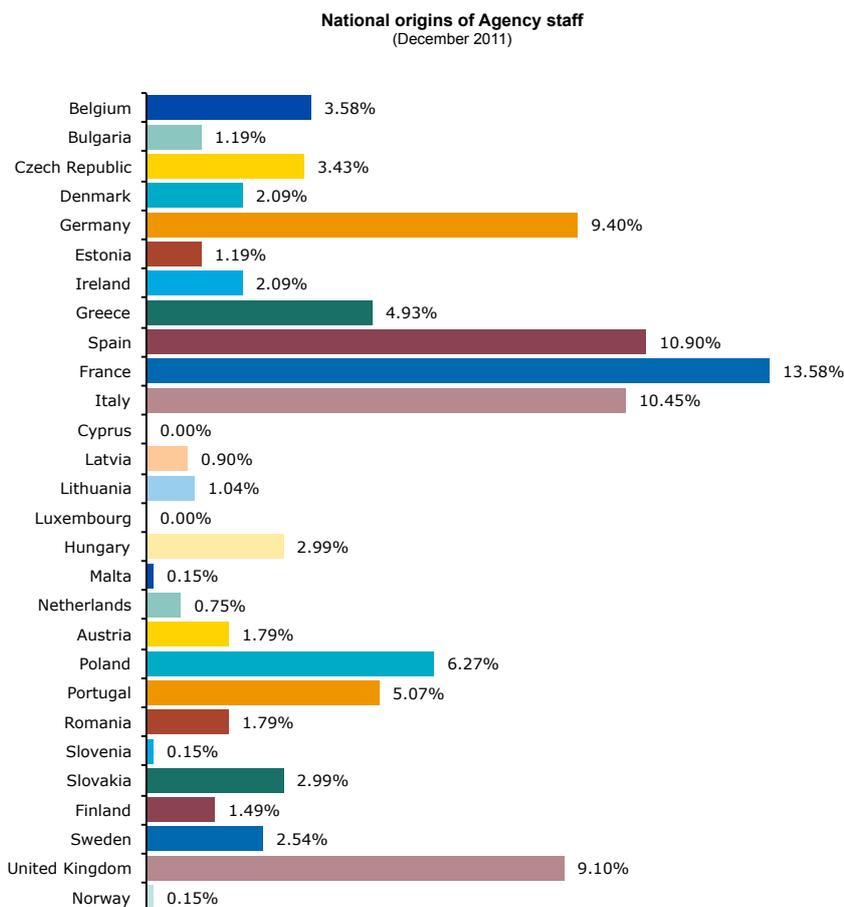
## Budget

Figure 2.



## Staffing

Figure 3.



## Dealing with resource constraints – Operational Excellence

The Agency has launched an 'Operational Excellence' initiative across its business activities. This initiative addresses the Agency's need to further strengthen its operations to achieve efficiency gains. The initiative responds to the fact that the Agency is currently in a phase of zero growth due to economic pressures and responds to the changing environment in which it operates. It aims to reduce the complexity of the administrative burden and to support further efficiency improvements, and encompasses a revised approach to business operations, ICT governance and the management of information held by the Agency.

It must be emphasised, that, as the Agency is currently in a phase of zero growth and due to economic pressures across the entire EU regulatory network, a number of aspirations in the 'Road map to 2015' cannot be addressed with the current resources available. Efforts will nonetheless continue to be made to improve efficiency and achieve resource savings.

The Operational Excellence initiative supports the Agency in achieving its goals by:

- saving resources without compromising on quality;
- re-engineering processes and reallocating resources to deliver on core activities;
- improving efficiency to better handle workload;
- demonstrating European best practice.

The success of all of the Agency's activities to implement the road map is dependent on continuing support from the EU regulatory network, as well as on ensuring that the activities outlined complement those outlined in the Heads of Medicines Agency's strategic plan.

## Improving information-management at the Agency

Version 3 of SIAMED, covering both human and veterinary centralised-procedure activities, was delivered in 2011. It enhances the management of initial marketing authorisations, post-authorisation procedures and pre-submission activities; it also improves data quality, procedure templates, reports and product-information management.

SIAMED is the central information system supporting the Agency's core activities. It allows not only to track product and procedural information during the lifecycle of a medicine, but also to produce template letters, reports and statistics. This information is now easily retrievable, especially where public access to information is concerned.

Among the most important assets of the Agency are the information it receives from external stakeholders and the information it provides to the public. Managing the information as an asset and strengthening the data quality is essential to support the Agency's scientific activities efficiently.

## 2. Medicines for human use

### 2.1. Orphan-medicinal-product designation

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

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

Figure 4.

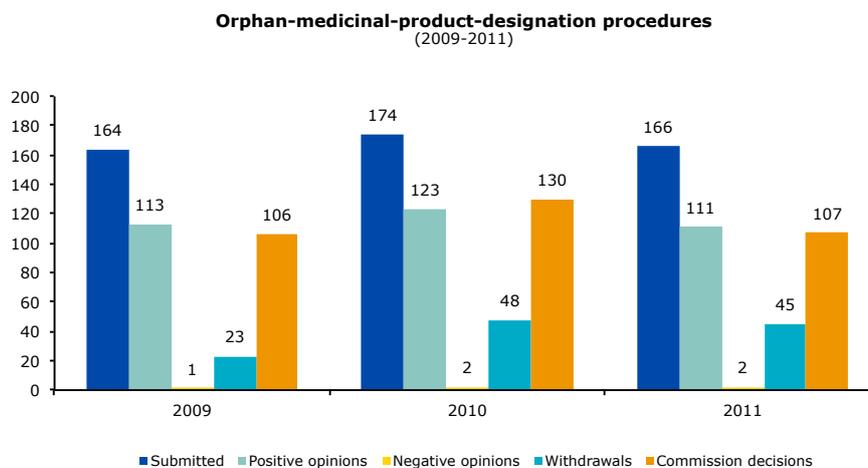


Figure 5.

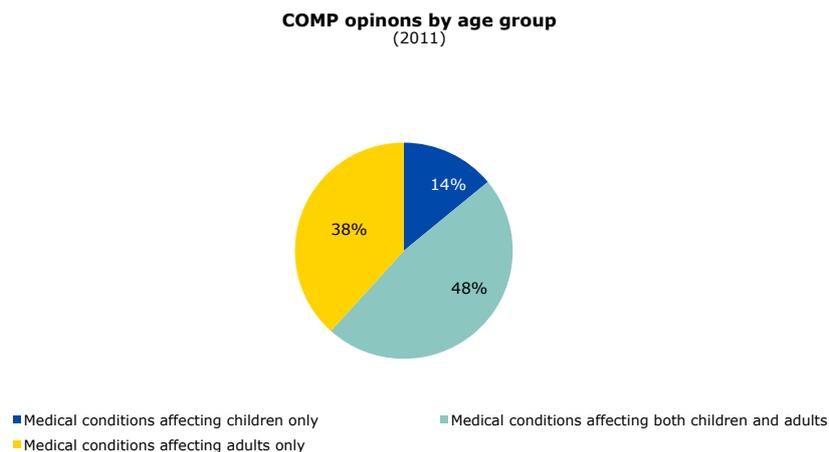


Figure 6.

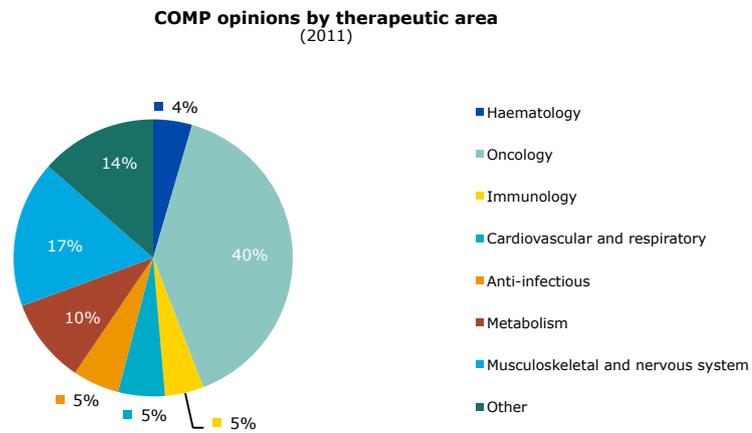


Figure 7.

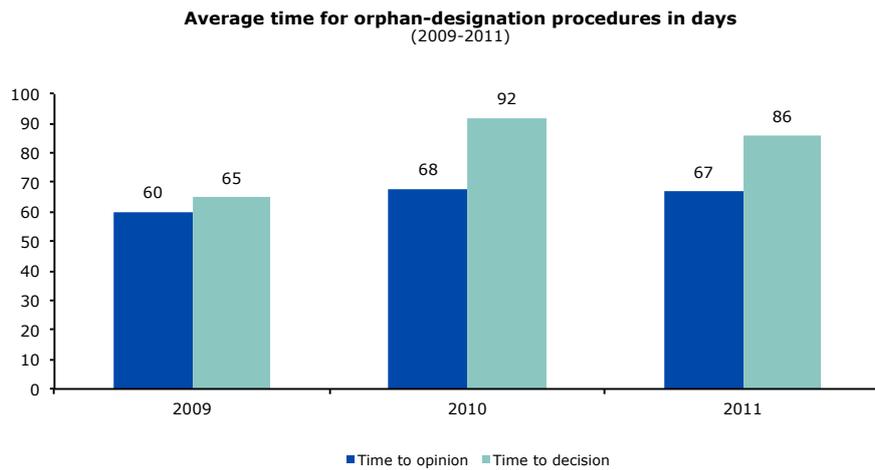
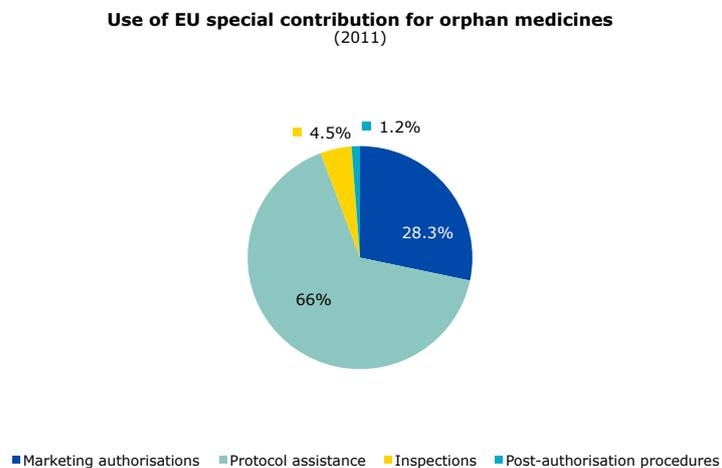


Figure 8.



**Table 6.**

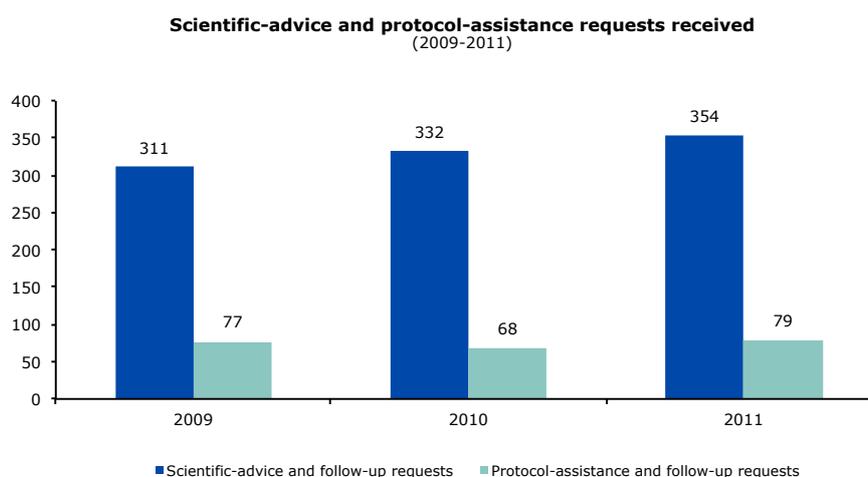
Key performance indicator	Target	Outcome
Percentage of applications reviewed within 90-day time frame	100%	100%
Percentage of summaries of COMP opinions published within one month of the European Commission's decision on designation	90%	100%
Percentage of public assessment reports (on review criteria) published within one month of the European Commission's decision on marketing authorisation	80%	100%

## 2.2. Scientific advice and protocol assistance

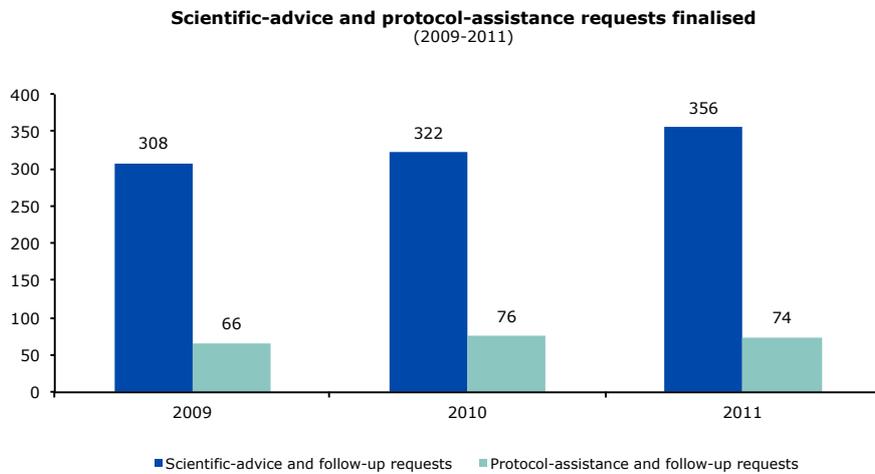
*The Agency provides scientific advice and protocol assistance to sponsors during the research and development phase of medicinal products. Scientific advice is considered as a means to facilitate and improve earlier availability of medicinal products to patients and healthcare professionals, and as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

### Stable increase of activities

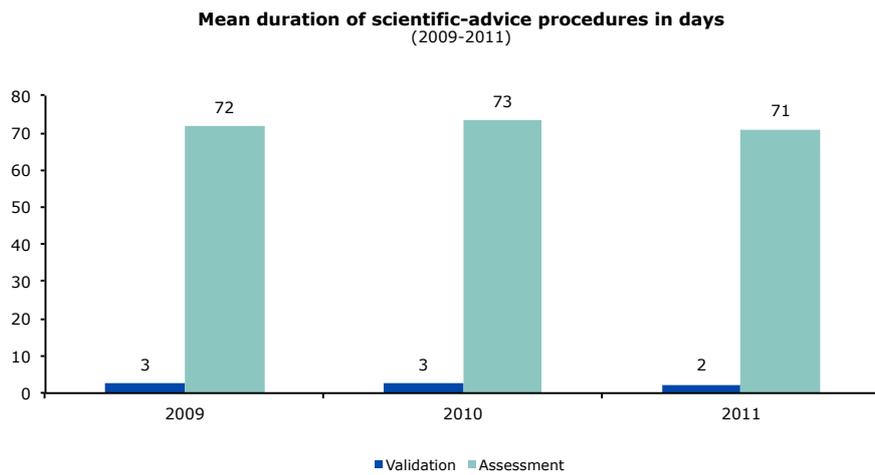
- Sixty-two per cent of requests for scientific advice and protocol assistance related to chemicals and 38% to biologicals.
- Thirty-one scientific-advice requests related to similar biological medicines, compared to 15 requests in 2010.
- Eight requests were for parallel scientific advice with the FDA.
- The number of joint scientific-advice requests with health technology assessment bodies increased; by the end of the year, 7 procedures were completed.
- As in previous years, the therapeutic area with the highest number of requests received was oncology, followed by central nervous system conditions, metabolic and alimentary tract conditions, general anti-infectives and blood products.

**Figure 9.**

**Figure 10.**



**Figure 11.**



**Figure 12.**

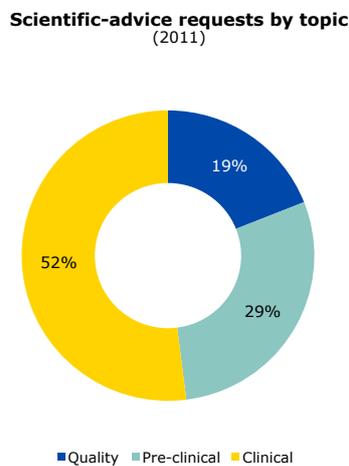


Figure 13.

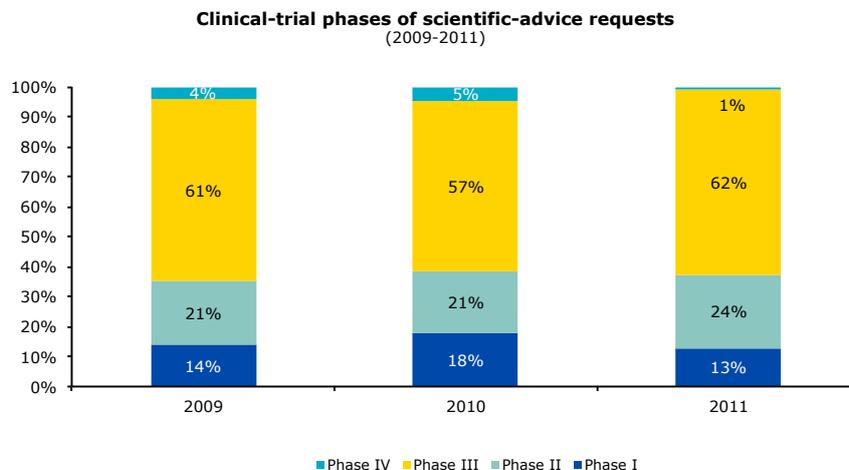
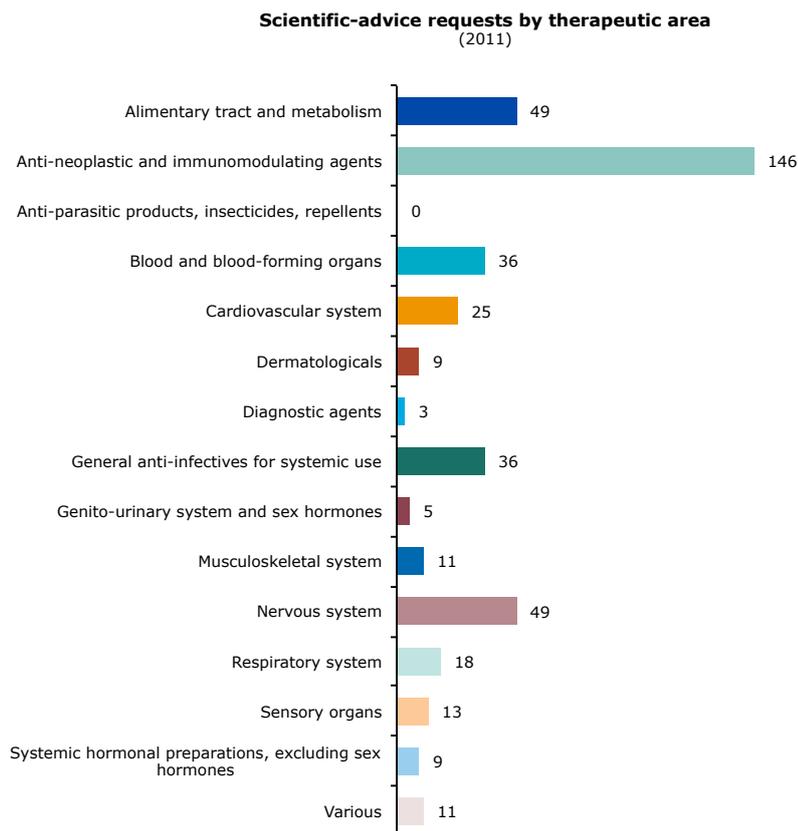


Figure 14.



## Biomarkers

In February 2011, the Agency released the first qualification opinion for a clinical biomarker for use in humans for public consultation. Throughout the year the Agency released a total of 4 qualification opinions for biomarkers, relating to Alzheimer's disease or pre-dementia.

Biomarkers are tests that can be used to follow body processes and diseases in humans and animals. They can be used to predict how a patient will respond to a medicine or whether they have, or are likely to develop, a certain disease. On request, the Agency can give an opinion on the qualification of the use of a biomarker, to indicate its acceptability for a specific use in pharmaceutical research and development.

**Table 7.**

Key performance indicator	Target	Outcome
Scientific-advice (SA) and protocol-assistance (PA) requests evaluated within the procedural time frame	100% of requests	99%
External experts involved in procedures	30% of SA and PA requests	15% of SA and PA requests
Percentage of marketing-authorisation applications for new technology products having received scientific advice/protocol assistance	50% of applications	57% of applications

## 2.3. Initial evaluation

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

### Increase in applications received for new medicines

- The Agency received a total of 100 applications for initial evaluation for human medicines, including 1 application for an opinion for a medicine intended for use outside the EU (Article 58 opinion), the second application for a paediatric-use marketing authorisation (PUMA) and 2 advanced-therapy medicinal products (ATMPs), including the first application for re-registration of an ATMP that was legally on the market in the EU before 2009.
- The number of applications for new medicines (non-orphan) increased by over 40%, from 34 to 48.
- The number of applications received for generics, hybrids, etc., has decreased as a result of tighter restrictions imposed on duplicate applications.

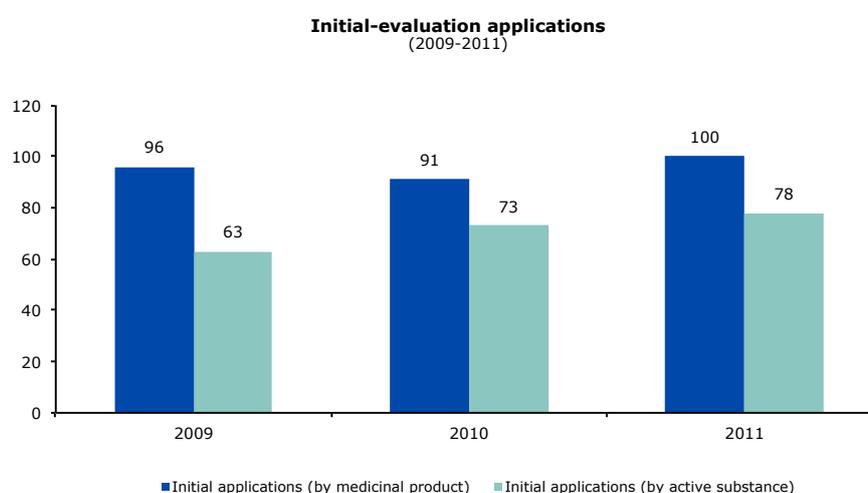
**Figure 15.**

Figure 16.

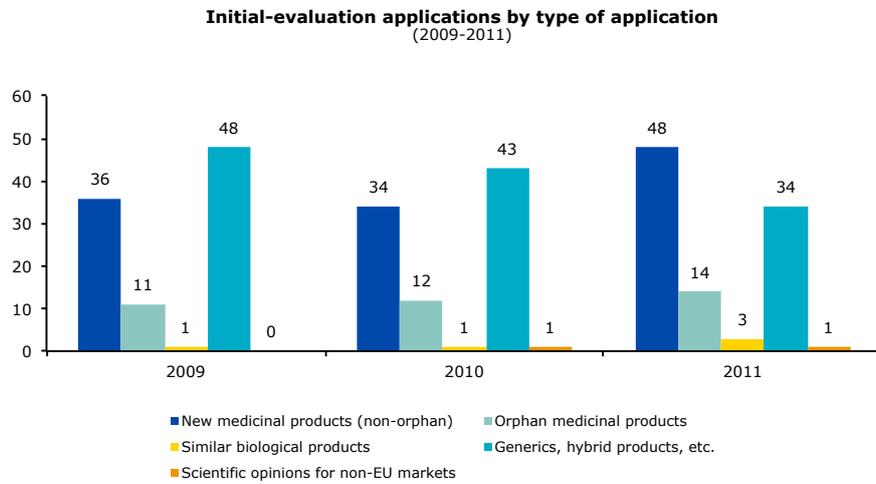
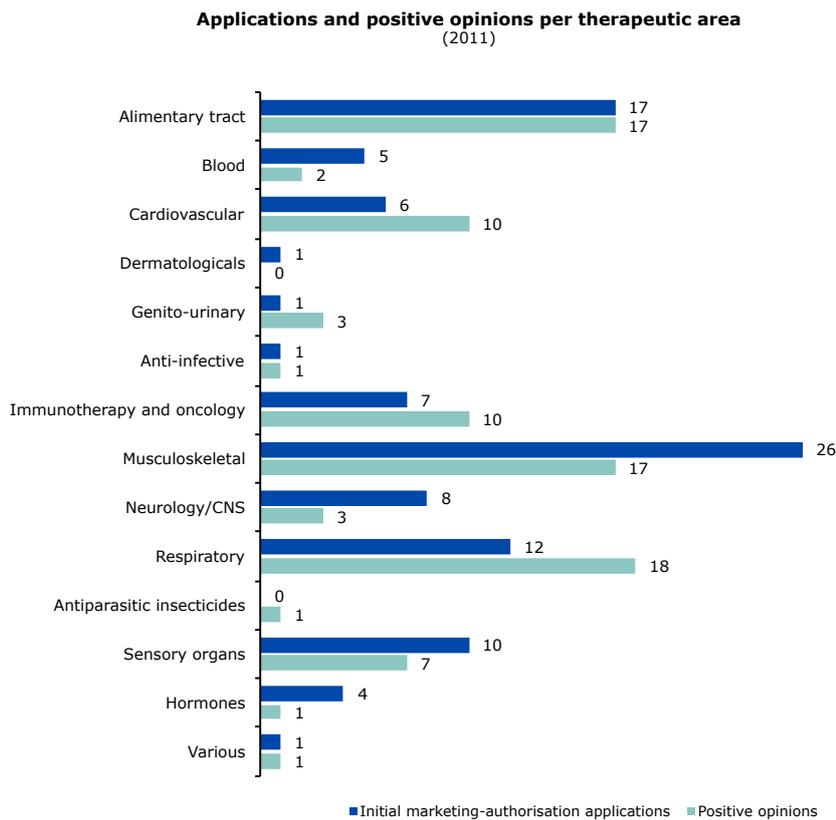


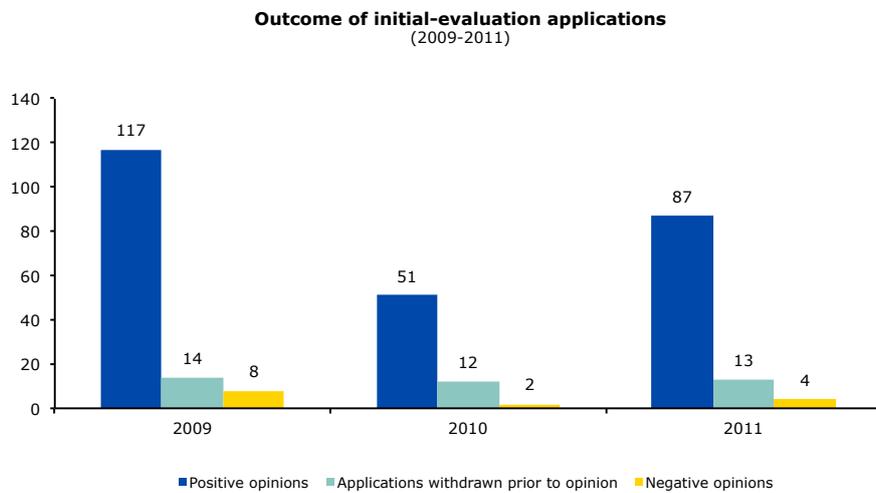
Figure 17.



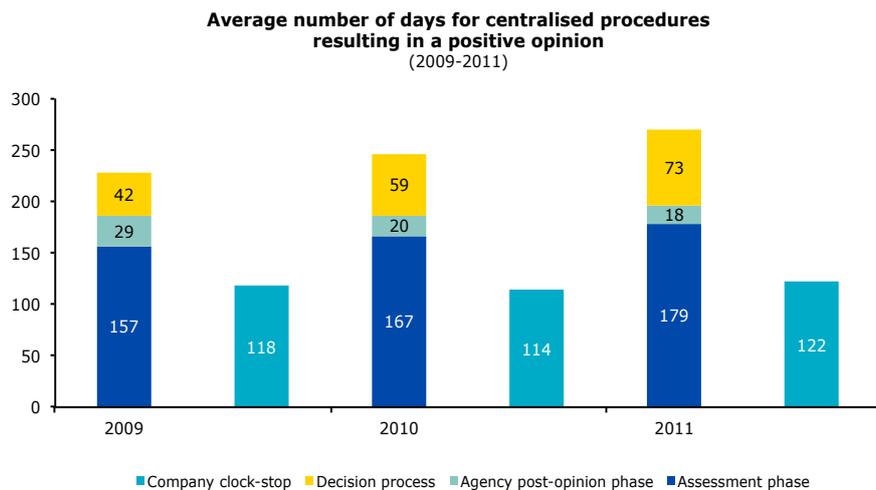
## Opinions adopted

- A total of 91 opinions were adopted, including 4 negative opinions.
- The CHMP adopted the first opinion for a paediatric-use marketing authorisation (PUMA) for a medicine (Buccolam).
- Re-examination of opinion was requested for 5 medicines; by the end of the year, 4 re-examination procedures were finalised.
- The average assessment time for the CHMP was 179 days. This is longer than in previous years and possibly due to the larger number of complex applications for new active substances.

**Figure 18.**

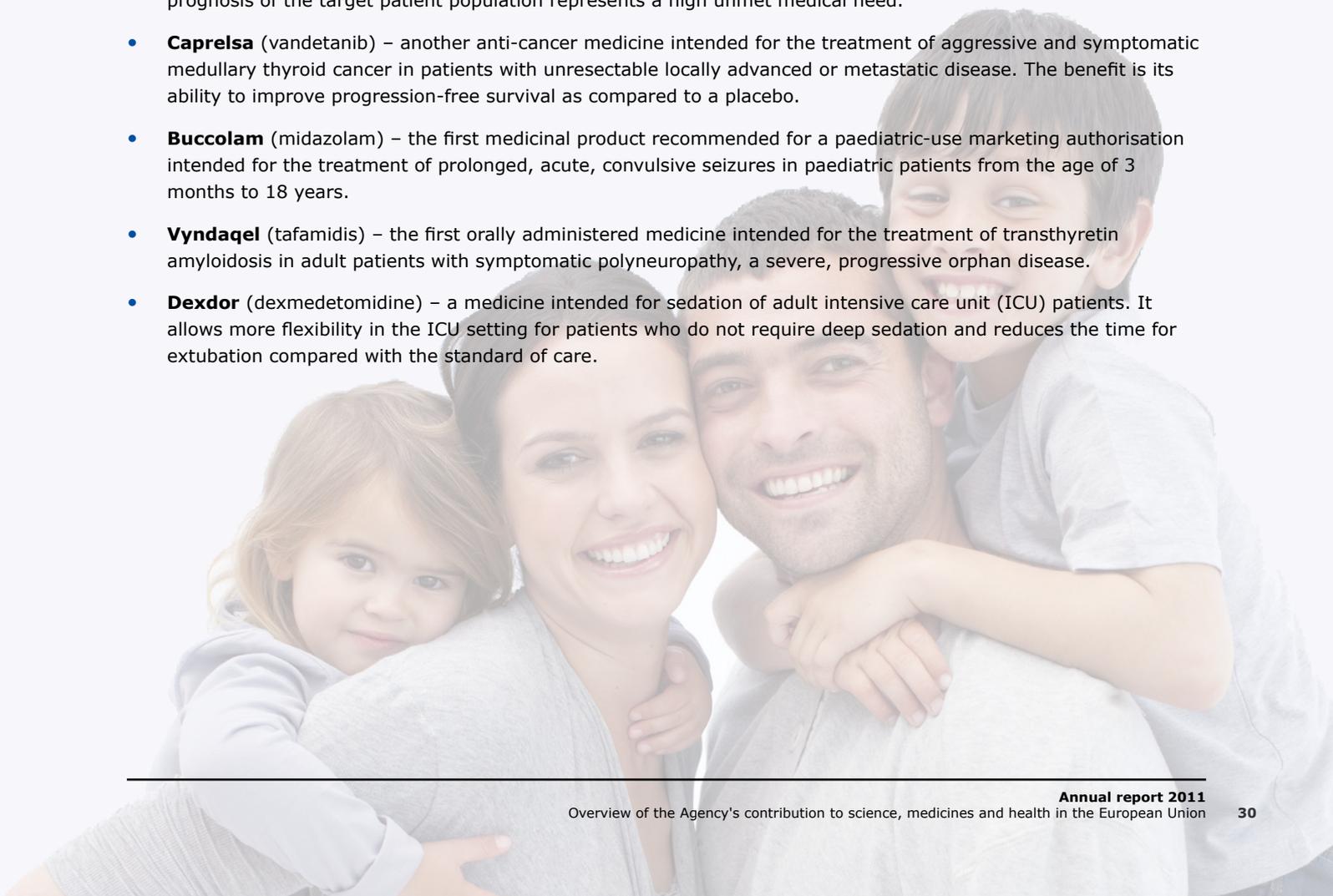


**Figure 19.**



## Public-health benefits of medicines recommended for approval in 2011

- **Eurartesim** (dihydroartemisinin/piperaquine phosphate) – the first medicinal product recommended for the treatment of uncomplicated *Plasmodium falciparum* malaria.
- **Dificlir** (fidaxomicin) – a first-in-class macrocyclic antibiotic intended to treat adults with *Clostridium difficile* infections, also known as C. difficile-associated diarrhoea, characterised by inflammation of the gut and severe diarrhoea.
- **Vibativ** (telavancin) – an antibacterial medicinal product intended for the treatment of adults with nosocomial pneumonia, known or suspected to be caused by methicillin-resistant *Staphylococcus aureus* (MRSA).
- **Victrelis** (boceprevir) and **Incivo** (telaprevir) – two first-in-class medicines for the treatment of chronic hepatitis. Both directly inhibit the replication of the hepatitis-C virus in hepatitis-C-virus-infected host cells.
- **Vepacel** – a vaccine intended for the prevention of H5N1 subtype of influenza A in either a pre-pandemic or pandemic situation in adults aged 18 years and older.
- **Zelboraf** – a novel protein-kinase inhibitor as a first-in-class treatment for patients suffering from metastatic or unresectable melanoma with BRAF V600 mutations.
- **Votubia** (everolimus) – an orphan medicine intended for the treatment of patients aged 3 years and older with subependymal giant-cell astrocytoma associated with tuberous sclerosis complex.
- **Mercaptopurine** (mercaptopurine monohydrate) – an orphan medicine intended for the treatment of acute lymphoblastic leukaemia in adults, adolescents and children. This medicine has been formulated as a suspension, which provides better accuracy and ease of administration, especially when used in small children.
- **Zytiga** (abiraterone acetate) – an anti-cancer medicine with a novel mechanism of action, which is intended, in combination with prednisone or prednisolone, for the treatment of metastatic castration-resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen. The poor prognosis of the target patient population represents a high unmet medical need.
- **Caprelsa** (vandetanib) – another anti-cancer medicine intended for the treatment of aggressive and symptomatic medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. The benefit is its ability to improve progression-free survival as compared to a placebo.
- **Buccolam** (midazolam) – the first medicinal product recommended for a paediatric-use marketing authorisation intended for the treatment of prolonged, acute, convulsive seizures in paediatric patients from the age of 3 months to 18 years.
- **Vyndaqel** (tafamidis) – the first orally administered medicine intended for the treatment of transthyretin amyloidosis in adult patients with symptomatic polyneuropathy, a severe, progressive orphan disease.
- **Dexdor** (dexmedetomidine) – a medicine intended for sedation of adult intensive care unit (ICU) patients. It allows more flexibility in the ICU setting for patients who do not require deep sedation and reduces the time for extubation compared with the standard of care.



## Peer-review for generic medicines

The Agency implemented an internal peer-review process for marketing-authorisation applications for generic medicines, with a focus on bioequivalence. By the end of the year, the internal process was fully operational. A proposal to extend the peer-review process to the CHMP was presented to the Committee and is expected to be adopted very soon.

**Table 8.**

Key performance indicator	Target	Outcome
Percentage of applications evaluated within the regulatory time frame of 210 days	100% of applications	98.9%
Percentage of accelerated-assessment applications evaluated within the regulatory time frame of 150 days	100% of applications	100%
Percentage of plasma-master-file applications evaluated within the regulatory time frame	100% of applications	100%
Percentage of opinions sent to the European Commission within the regulatory time frame of 15 days	100% of applications	100%

## 2.4. Post-authorisation activities

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

### Significant increase in applications received

- The number of variation applications received continued to increase significantly in 2011, with a marked change in distribution by variation type. This trend was already seen in 2010.
- This is due to the implementation of the revised variations legislation in 2010, which changed the default 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. Consequently, the number of type-II variations has continued to decrease.
- The new classification also resulted in more detailed identification of individual variations. This has contributed to the overall increase in variations.

**Figure 20.**

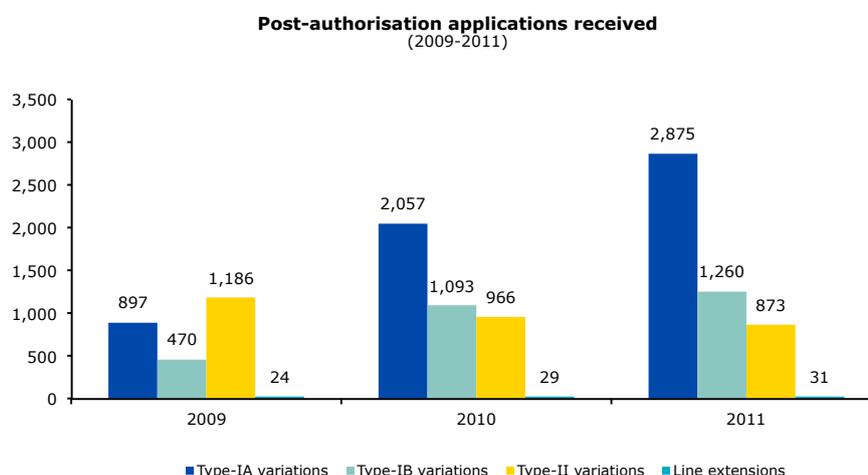
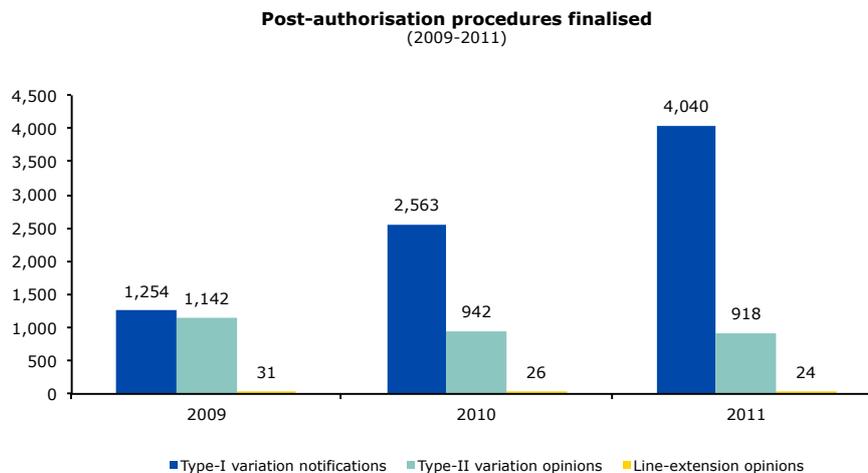


Figure 21.



### Public-health impact of positive opinions for new indications in 2011

The CHMP adopted 38 (including 3 duplicate) positive opinions recommending new indications or the broadening of patient populations for approved indications, providing additional treatment options for patients.

The medicines concerned include:

- **Afinitor** (everolimus): treatment of patients with unresectable or metastatic, well- or moderately differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease;
- **Alimta** (pemetrexed): monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy;
- **Avastin** (bevacizumab): first-line treatment in combination with capecitabine of patients with metastatic breast cancer in whom treatment with other chemotherapy options, including taxanes or anthracyclines, is not considered appropriate (positive opinion after re-examination); and in combination with carboplatin and paclitaxel, front-line treatment of advanced (FIGO stages III B, III C and IV) epithelial ovarian, fallopian tube, or primary peritoneal cancer;
- **Erbix** (cetuximab): treatment of patients with epidermal growth factor receptor (EGFR)-expressing, KRAS wild-type metastatic colorectal cancer as first line in combination with FOLFOX;
- **Herceptin** (trastuzumab): treatment of patients with HER2-positive early breast cancer ... in combination with neoadjuvant chemotherapy followed by adjuvant Herceptin therapy, for locally advanced (including inflammatory) disease or tumours > 2cm in diameter; and treatment of patients with HER2-positive early breast cancer in combination with adjuvant chemotherapy consisting of paclitaxel or docetaxel following adjuvant chemotherapy with doxorubicin and cyclophosphamide, or consisting of docetaxel and carboplatin;
- **Retacrit** (epoetin zeta): reduction of allogeneic blood transfusions in adult non-iron-deficient patients prior to major elective orthopaedic surgery;
- **Soliris** (eculizumab): atypical haemolytic uraemic syndrome (aHUS);
- **Tarceva** (erlotinib): first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer with EGFR-activating mutations;
- **Baraclude** (entecavir): treatment of adult patients with chronic hepatitis B virus infection and decompensated liver disease;
- **Cervarix** (human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed)): extension to subjects from the age of 9 years for the prevention of premalignant cervical lesions and cervical cancer causally related to certain oncogenic human papillomavirus (HPV) types;

- **Prevenar 13** (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)): active immunisation for the prevention of invasive disease caused by *Streptococcus pneumoniae* in adults aged 50 years and older;
- **Prezista** (darunavir): treatment of HIV infection in adults who have been previously treated with antiretroviral therapy to the 400mg strength;
- **Synflorix** (pneumococcal polysaccharide conjugate vaccine (adsorbed)): increase in upper age limit for children from 2 to 5 years of age;
- **Carbaglu** (carglumic acid): treatment of hyperammonaemia due to isovaleric acidaemia, methylmalonic acidaemia and propionic acidaemia;
- **Levemir** (insulin detemir): extension of lower age range from 6-17 years to 2 years and above;
- **Onglyza** (saxagliptin): in combination with insulin (with or without metformin), when this regimen alone, with diet and exercise, does not provide adequate glycaemic control;
- **Revatio** (sildenafil): orphan use to include paediatric patients aged 1 to 17 years with pulmonary arterial hypertension;
- **Xarelto** (rivaroxaban): treatment of deep vein thrombosis (DVT) and prevention of recurrent DVT and pulmonary embolism (PE) following an acute DVT in adults; and prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors;
- **Corlentor** and **Procoralan** (ivabradine): treatment of chronic heart failure;
- **Galvus, Jalra** and **Xiliarx** (vildagliptin): monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance;
- **Pradaxa** (dagibatrán): prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation;
- **Enbrel** (etanercept): extension of lower age range in polyarticular juvenile idiopathic arthritis (JIA) from 4 to 2 years; and extension of lower age range in paediatric plaque psoriasis from 8 to 6 years;
- **Humira** (adalimumab): treatment of juvenile idiopathic arthritis in patients aged 4 to 12 years;
- **INOmax** (nitric oxide): treatment of peri- and post-operative pulmonary hypertension related to heart surgery;
- **Kiovig** (human normal immunoglobulin): treatment of multifocal motor neuropathy;
- **Remicade** (infliximab): extension of approved indication for severe Crohn's disease to patients with moderately to severely active disease.

## Review of variations processes

Following the implementation of the new Variations Regulation in 2010, the Agency initiated a review of the processes it operates. As part of this exercise, the Agency performed a gap analysis with a specific focus on the classification process of variations. An expert group was convened and the revision of the classification guideline is now underway.

The Agency also developed an action plan for streamlining and minimising administrative and procedural tasks.

**Table 9.**

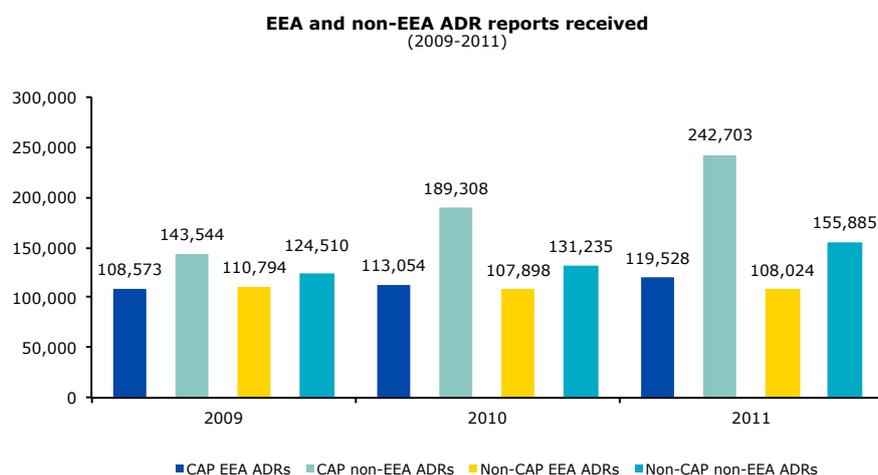
Key performance indicator	Target	Outcome
Percentage of applications for post-authorisation procedures evaluated within the regulatory and procedural time frame	100% of applications	94% for Type IA 96% for Type IB 100% for Type II
Percentage of Agency recommendations on classification of variations delivered within the legal timeframe	100% of applications	N/A
Percentage of grouping and worksharing procedures completed within the procedural timeframe	100% of applications	100%

Key performance indicator	Target	Outcome
Submission of outcome reports for post-authorisation commitments to applicants/marketing-authorisation holders within two weeks of the CHMP meeting	90% of reports	85%
Percentage of applications meeting the legal time frame of 27 days for the linguistic post-opinion check	100% of applications	79%

## 2.5. Pharmacovigilance and maintenance activities

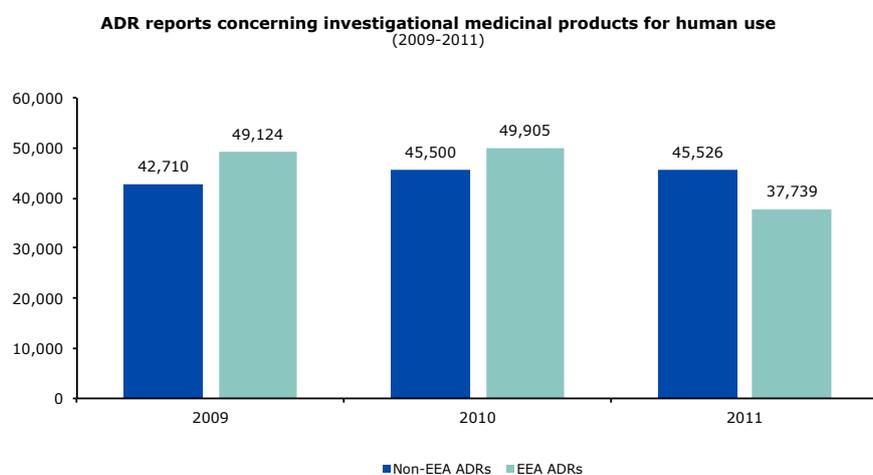
Pharmacovigilance covers the science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADRs) or any other drug-related problem. This includes the management of suspected ADRs in the pre- and post-authorisation phases, periodic safety-update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

**Figure 22.**



Note: CAP = centrally authorised product; EEA = European Economic Area; ADRs = adverse drug reactions.

**Figure 23.**



## Classification of post-authorisation measures

The Agency has started an exercise to classify all recommended post-authorisation measures into their appropriate legal framework. The first implementation phase started in June 2011. An Advisory Group on Classification of Post-Approval measures (CPAG) was set up to provide advice to rapporteurs and Agency staff for (re-)classification of potential post-authorisation measures, so-called ex-follow-up-measures (ex-FUMs) to the initial marketing authorisation. The second phase started in November for post-authorisation activities.

The next steps of this exercise are a dedicated training course for assessors, to be held in 2012, and the establishment of a system for monitoring compliance. Possibilities for enforcing regulatory actions will be further investigated.

## EudraVigilance

Throughout the year, the Agency worked closely with sponsors, marketing-authorisation holders and Member State competent authorities to improve the quality of the data submitted to the EudraVigilance database. Major steps of this initiative included the entry into force of the new business rules, the data-cleaning activities performed on the EudraVigilance data by the Agency's service provider (Kinapse), and the introduction of a process of cooperation with the pharmacovigilance inspectors of the Member State competent authorities to provide them with the results of the Agency's analyses of the quality of data in EudraVigilance.

Around 70,000 duplicate cases were removed or flagged for removal from EudraVigilance during 2011 and 141,216 reported medicinal product terms were recoded against the EVMPD.

## Monitoring of pharmacovigilance compliance

Drafting of a compliance-monitoring strategy is under way and is expected to be finalised in the first half of 2012. Key concepts of this have already been considered in the ongoing development of the good vigilance practice.

## European signal-management initiative

Work on the European signal-management initiative progressed. Phase 1 of a nine-month pilot phase aimed at assessing the sharing of signals within the European medicines network using the European Pharmacovigilance Issues Tracking Tool (EPITT) started on 1 May 2011.

The creation of an electronic reaction-monitoring report (eRMR) led to significant efficiency gains in the signal-monitoring process. Preparations are now under way to extend the scope of the signal-detection activities to include non-centrally authorised products and also provide eRMRs for nationally authorised medicines.

A half-year report on signal-detection activities was presented to the Management Board in December 2011. The second half-year report is expected to be presented in June 2012.

**Table 10.**

Key performance indicator	Target	Outcome
Percentage of risk-management plans (RMPs) peer-reviewed by the Agency as part of the assessment of the initial marketing-authorisation application	90% of applications	100%
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	90% of applications	100%
Percentage of individual case safety reports reported electronically for centrally authorised medicines	100%	100%
Percentage of centrally authorised medicines monitored at least monthly by the signal-detection group	100%	100%

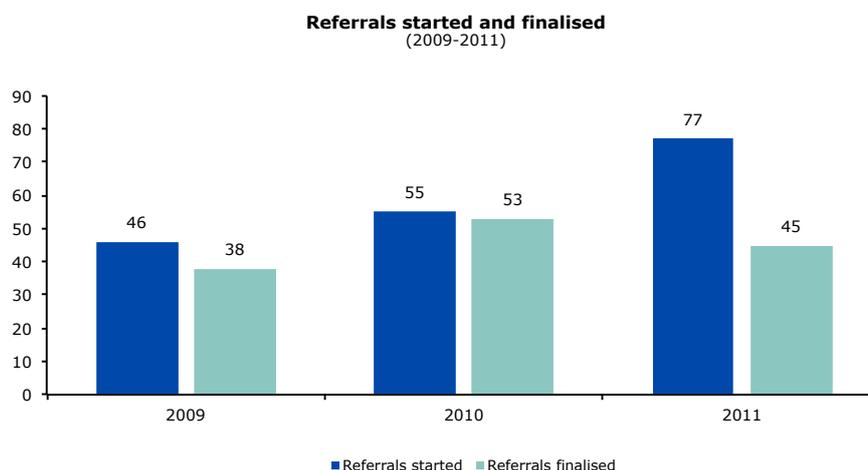
## 2.6. Arbitration, Community referrals and opinions on any scientific matter

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

### Major increase in referral activities

- In the post-Mediator environment, there was a major increase in referral activities, due to the increased sensitivity both at Member State and European Commission level with regard to emerging safety issues. In 2011, 77 new referral procedures were started, compared to 55 in 2010.
- The diversity and complexity of referral procedures increased, too. There was a high number of unexpected quality or good manufacturing practice (GMP)-related referrals. A number of procedures also had an impact on the supply to patients of the medicines concerned, and required coordination of a complex network of stakeholders to ensure that patients most in need continued to have access to treatments. Managing the referral procedures often involved scientific advisory groups (SAGs), expert meetings and multiple interactions with the Commission.
- The high workload required that focus be maintained on the management of ongoing and new referral procedures. As a consequence, a number of key performance indicators could not be met in 2011. These related to the provision of translations to the European Commission on day 27 and the publication of scientific conclusions two weeks after the Commission decision.
- Taking into account increasing difficulties in terms of supply of medicinal products in the context of referral procedures, a draft strategy paper regarding product-supply interruptions and shortages consequent to GMP non-compliance and/or manufacturing failures/quality defects was prepared and presented to the Management Board in December 2011. An implementation plan will be introduced in 2012.

**Figure 24.**



### Procedures of high public-health interest in 2011

Among the referral procedures with a high public-health interest were:

- review of Pandemrix and its possible association with narcolepsy;
- review of Multaq because of concerns over liver, lung and cardiovascular adverse events;
- review of the manufacture of Baxter's peritoneal dialysis solutions over potential presence of endotoxins in some batches;

- review of pioglitazone-containing medicines over possible risk of bladder cancer;
- review of medicines manufactured at Ben Venue Laboratories to deal with shortcomings in quality assurance;
- review of Octagam to lift the suspension of the marketing authorisations from 2010;
- review of Revlimid because of concerns over a higher number of new cancers.

### Preparation for implementation of Article 107i of the new pharmacovigilance legislation

The new pharmacovigilance legislation introduces a new procedure to safeguard public health. As this will have considerable impact on the Agency's referral procedures, significant efforts were made to prepare for this new 'urgent Union procedure', so that when the pharmacovigilance legislation enters into force in July 2012, all necessary processes are in place to run the new procedure.

### Monitoring the implementation of the Article 29 paediatric procedure

To date there have been only a very small number of Article 29 paediatric referral procedures. It was agreed that more experience should be gathered.

**Table 11.**

Procedure type	Started in 2011	Finalised in 2011
Article 6(12) of Commission Regulation (EC) No 1084/2003	2	0
Article 6(13) of Commission Regulation (EC) No 1084/2003	0	0
Article 13 of Commission Regulation (EC) No 1234/2008	1	1
Article 31 of Directive 2001/83/EC	10	7
Article 36 of Directive 2001/83/EC	5	3
Article 5(3) of Regulation (EC) No 726/2004	7	3
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	2	2
Article 29(4) of Directive 2001/83/EC	2	4
Article 30 of Directive 2001/83/EC	6	4
Article 29 of Regulation (EC) No 1901/2006	0	0
Article 20 of Regulation (EC) No 726/2004	42	21
<b>Totals</b>	<b>77</b>	<b>45</b>

**Table 12.**

Key performance indicator	Target	Outcome
Percentage of arbitration and referral procedures evaluated within the legal time frame	100%	100%
Publication of question-and-answer documents for Community-interest referral procedures (Art. 31, 36, 107(2)) and Art. 20 procedures at the time of the CHMP opinion	100%	100%

Key performance indicator	Target	Outcome
Publication of the CHMP opinion and assessment report for Article 5(3) procedures at the time of the CHMP opinion	100%	0% None of the 3 procedures were published at the time of the CHMP Opinion; delays occurred due to high workload and discussions with the WHO on the product
Publication of the CHMP opinion and assessment report for referrals other than Art. 5(3) procedures no later than 2 weeks following the Commission decision	100%	0% None of the 26 procedures were published no later than 2 weeks following the Commission decision; delays occurred due to high workload
Opinion annexes (translations) sent to the European Commission within the legal timeframe (27 days post opinion)	100%	58% For 21 out of 50 procedures, delays occurred due to high workload, when several marketing-authorisation holders were involved in the translation process for a class review, for translations in case of suspension or withdrawal and due to late submission of translations when small companies were involved

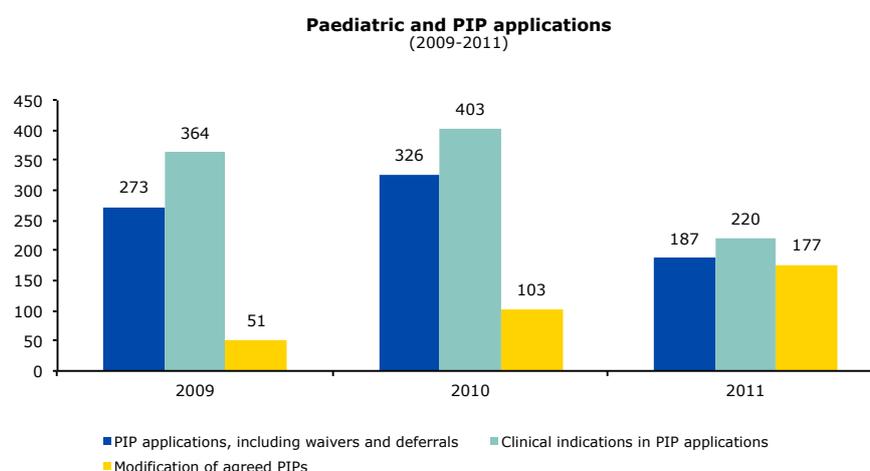
## 2.7. Medicines for children

*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).*

### Numbers of PIP applications lower, following 2010 peak

- The number of PIP applications was lower in 2011, following the peak seen in 2010, as a result of 115 applications received in that year for allergen products that became subject to a marketing authorisation in Germany.
- Modifications to PIPs continued to increase by 49% over the previous year.

**Figure 25.**



## Guidance for conduct of paediatric medicines development

Children are not small adults. The Agency therefore set out to develop specific guidance for the development of medicines for children, taking into account the specific physical, metabolic and psychological processes peculiar to growth from birth into adulthood. In May 2011, the Agency released its draft 'Guideline on pharmaceutical development of medicines for paediatric use' (EMA/CHMP/QWP/180157/2011) for consultation. In addition, 2 model PIPs in the area of oncology were drafted and 1 for pandemic influenza is currently under revision.

## Network coordination group for Enpr-EMA

The Agency achieved major progress with Enpr-EMA, the network of research networks, investigators and centres with recognised expertise in performing clinical studies in children, which aims to foster high-quality ethical research on quality, safety and efficacy of medicines to be used in children.

Following agreement of an organisational structure for the network in 2010, the Agency published a full list of the networks that applied for Enpr-EMA membership in January 2011, indicating those that met all of the criteria and those that needed to provide further clarification or did not yet qualify in January 2011. In March 2011, during its third workshop, the Enpr-EMA coordinating group was established. The operational centre of Enpr-EMA, the group is responsible for the network's long- and short-term strategy. Its tasks include: facilitating access of the pharmaceutical industry to paediatric clinical study centres and experts; identifying new networks to include in Enpr-EMA; and developing common educational tools for children and parents, to increase their willingness to take part in clinical trials.

## European Court of Justice confirmed the Agency's decision to refuse a paediatric waiver

In December 2011, the General Court of the European Union issued a judgment on the first legal action regarding the Paediatric Regulation, stating that the European Medicines Agency acted appropriately when it rejected the application for a paediatric waiver for a diagnostic agent. The Court concluded that, in keeping with the Paediatric Regulation, the Paediatric Committee was allowed to require studies supporting the use in children beyond the indication proposed by the applicant.

**Table 13.**

Key performance indicator	Target	Outcome
Number of PIP or waiver opinions and decisions established within legal time frame	100%	99.6% (1 opinion was sent one day after the legal deadline)
Percentage of Agency decisions on paediatric investigation plans/waivers published within 6 weeks of the decision	95%	98.5%
Expert workshops on specific diseases/therapeutic areas	3 meetings	3 meetings

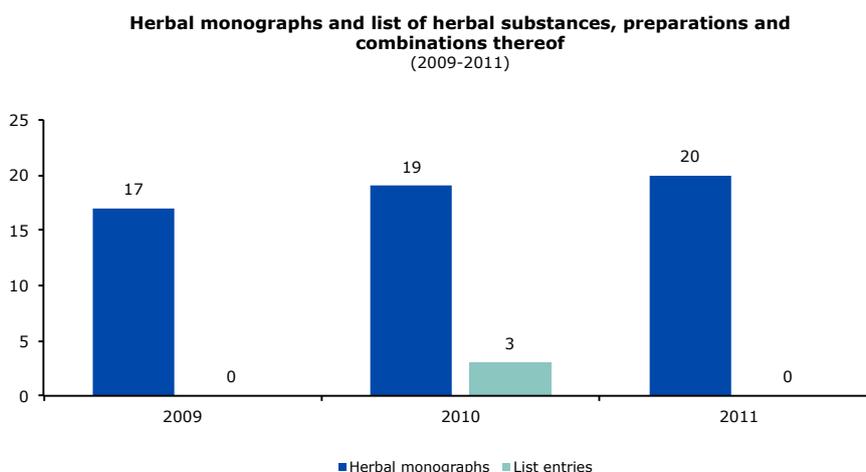
## 2.8. Herbal medicinal products

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

### Stable level of activities – list entries below expectations

- The transition period for applicants to register traditional herbal medicinal products that were already on the market on the date of entry into force of the Herbals Directive in April 2004 ended on 30 April 2011. The Agency participated in a number of awareness-raising events, including one organised by Members of the European Parliament.

- Twenty-one draft Community herbal monographs were released for public consultation and 20 final monographs were approved. In addition, 2 final and 5 draft public statements on assessment work that could not lead to the establishment of a monograph were published.
- Despite a forecast of 10, no list entries were released or finalised in 2011 because there were no suitable genotoxicity data and the HMPC could not find an alternative solution for this issue.
- A revision to the HMPC meeting model was agreed and implemented as of May 2011. The Committee now meets before the Working Party on Community monographs and Community list (MLWP). This allows rapporteurs and peer-reviewers more time to finalise documents to highest quality standards.

**Figure 26.**

### Uptake of the traditional-use registration scheme

The Agency published two reports on the uptake of the traditional-use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States. The data included in the reports show that there was an increase in the uptake of the scheme, particularly over the past two years.

## 2.9. Advanced therapies and other emerging therapies and new technologies

*The Agency supports 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.*

### Number of ATMP applications lower than forecast

- The number of ATMP applications is lower than originally forecast at the start of the implementation of the ATMP Regulation, as most ATMPs are put under the national 'hospital exemption' scheme.
- No applications for certification of quality and non-clinical data from SME applicants were received.
- Twelve requests for scientific recommendations on advanced-therapy classification were submitted and an equal number of scientific recommendations were adopted. However, the number of new requests for classification is lower than expected.
- Data on ATMPs legally on the market were collected and analysed. A report on the analysis of and the experience with the implementation in the transitional period foreseen in Article 29 of Regulation 1394/2007 is being prepared.

- The Agency and the Committee for Advanced Therapies are currently collaborating in an exercise exploring the possibility for the international harmonisation of requirements for cell therapies (including stem-cell products).

### Evaluation of combined ATMPs

An exercise to consolidate and streamline consultation and interactions with notified bodies for medical devices for the evaluation of combined ATMPs was successfully completed. Procedural advice on the evaluation of these combined products and the consultation of Notified Bodies was adopted and published in February 2011.

### CAT workshop

In October 2011, the Committee for Advanced Therapies (CAT) held a workshop together with the European Society of Gene and Cell Therapy. This was the first workshop organised in cooperation with a learned society. The workshop brought together industry, academia and regulators to discuss how to progress the development of advanced-therapy medicinal products. It addressed specific issues related to both gene-therapy and cell-based medicinal products.

**Table 14.**

Key performance indicator	Target	Outcome
Percentage of applications handled by the CAT within the procedural time frame (allowing adoption of the opinion by the CHMP within the legal time frame of 210 days)	100% of applications	100%
Scientific recommendations on advanced-therapy classification provided within the legal time frame	100% of requests	100%
Certification of quality and non-clinical data issued within the procedural time frame	100% of requests	N/A for 2011 (no applications received)

## 2.10. 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.*

### Modification of the Agency's framework for working parties

Following the adoption of a reflection paper on working parties, adopted by the CHMP in 2010, the Agency's new framework for working parties was implemented and applied to all new and existing working parties and drafting groups in 2011, and a new coordination group was put in place. The revised framework aims at improving efficiency and avoiding overlapping and unnecessary competition between working parties. A report with an analysis of the new working-party structure is under preparation and will be presented to the CHMP during 2012.

### Optimising the functioning of scientific advisory groups

The CHMP concluded in 2011 that the system for scientific advisory groups is working well and that at present there is no need for a change.

## Interaction between committees

Work on a procedure for interaction between the CHMP and the PDCO started in June 2011, with a first meeting between the secretariats and preparation of a draft document, which is still being discussed.

### 2.11. 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.*

#### Core activities

- Four MRP and 18 DCP initial applications and 5 applications for type-II variations were referred to the CMDh in 2011.
- Agreement was reached for 4 MRP and 4 DCP referrals for initial applications (2 of the 4 MRP referrals were referred to the CMDh in 2010) and for 4 referrals for type-II variations.
- Two MRP and 3 DCP initial applications were referred to the CHMP for the adoption of an EU-wide scientific opinion under Art. 29(4) of Directive 2001/83/EC, as amended (1 of the 2 MRP referrals was referred to the CMDh in 2010), as were 4 applications for type-II variation under Art. 13 of Commission Regulation (EC) No 1234/2008.
- With regard to work-sharing for the assessment of paediatric studies submitted according to Art. 45 and Art. 46 of the Paediatric Regulation, 55 active substances under Art. 45 and 34 submissions of paediatric studies under Art. 46 were processed. Twenty-seven public assessment reports according to Art. 45 and 17 public assessment reports according to Art. 46 were published on the CMDh website.
- With regard to the revised Variations Regulation, 14 requests for recommendations according to Art. 5 were received. For 7 of these, the CMDh gave recommendations; 6 procedures were closed at an early stage, as the variations were not considered to be unforeseen; 1 procedure was withdrawn.

#### Specific objectives

##### *Preparation for the new pharmacovigilance legislation*

The new pharmacovigilance legislation will significantly change the role of the CMDh. Much effort was therefore put into preparing for the entry into force of the new legislation in July 2012. An implementation plan for the activities of the CMDh and the secretariat was drafted and is currently under discussion.

## 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.*

#### Continued interest in 2011

- The Agency is keen to promote early applications for scientific advice in relation to the development of veterinary medicines.
- The number of applications has more than doubled in recent years and the increase in applications also continued in 2011, particularly from SME applicants. The availability of the minor uses/minor species (MUMS) scheme has been widely publicised with the veterinary pharmaceuticals industry and an increasing number of applications were received for products not intended for authorisation via the centralised procedure. This reflects the industry's increasing understanding that the procedure is also applicable to other routes of authorisation.
- Ten out of 26 (38%) of scientific-advice requests received in 2011 came from SMEs. One of these was reviewed in parallel with the U.S. Food and Drug Administration. This is a slight increase on 2010, where 33% of scientific-advice requests were received from SMEs.
- Demand for scientific advice with respect to the submission of applications for innovative veterinary medicines through the centralised procedure continued to increase. This included a number of medicines containing active substances of biological origin, such as cytokines and novel vaccines.

**Figure 27.**

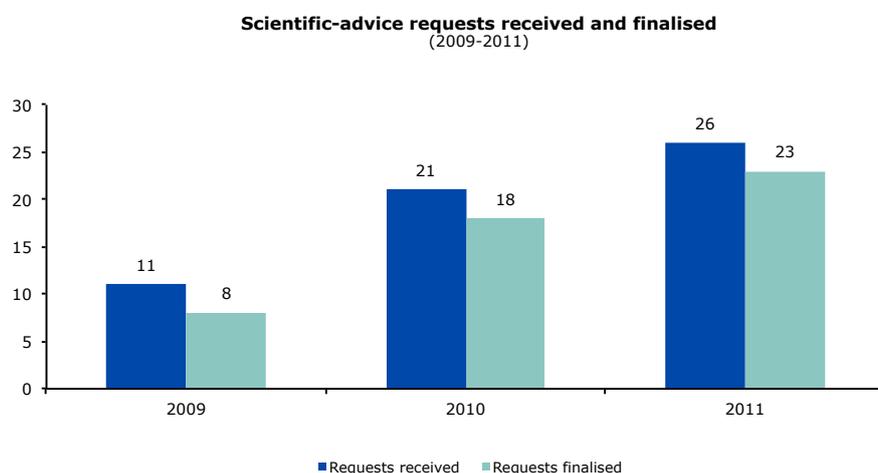


Figure 28.

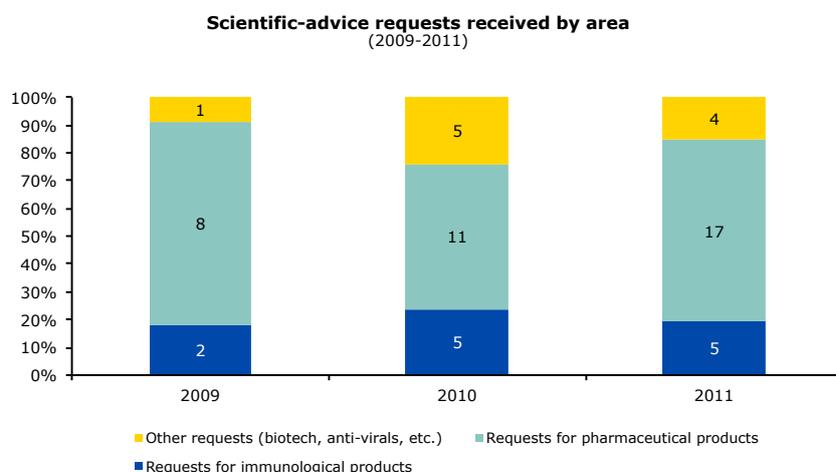


Table 15.

Key performance indicator	Target	Outcome
Scientific-advice requests evaluated within the procedural time frame	95% of applications	100% of applications

## 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.

### Decline of applications compared to the previous two years

- In recent years, around 20% of new applications were requests for authorisation under exceptional circumstances for vaccines against epizootic diseases of livestock, particularly against avian influenza and bluetongue. With the availability of authorised products against avian influenza and bluetongue, and no new outbreaks or known risk of an outbreak of an epizootic disease of livestock at present, only 1 further application for a vaccine against an epizootic disease was submitted in 2011.
- While the Agency's measures regarding the development of products for MUMS/Limited markets have been very successful so far in terms of requests for classification and free scientific advice, together with incentives for development, the impact on applications for authorisation will take some time to feed through into applications for marketing authorisation, with 3 positive opinions for new products and 1 new application received in 2011.
- Applications for generic versions of centrally authorised veterinary medicines continue to be limited due to the small number of active substances with the necessary commercial potential.
- The current economic situation has started to have an apparent impact on the decisions of companies to register new products.

Figure 29.

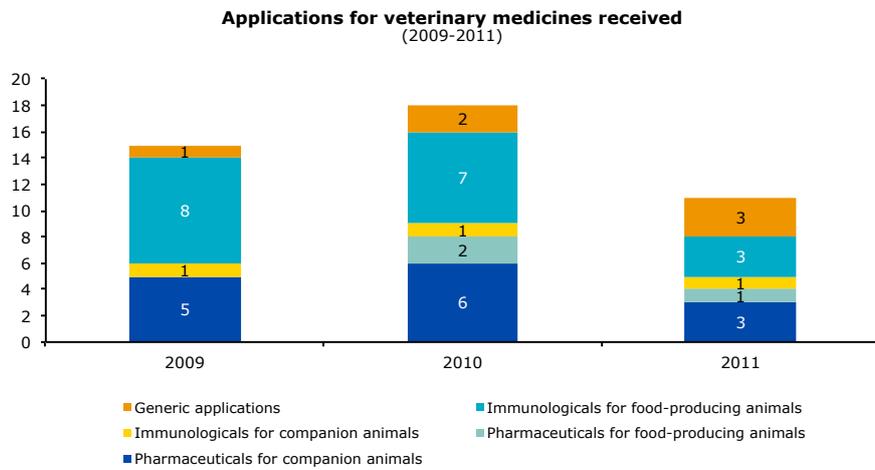


Figure 30.

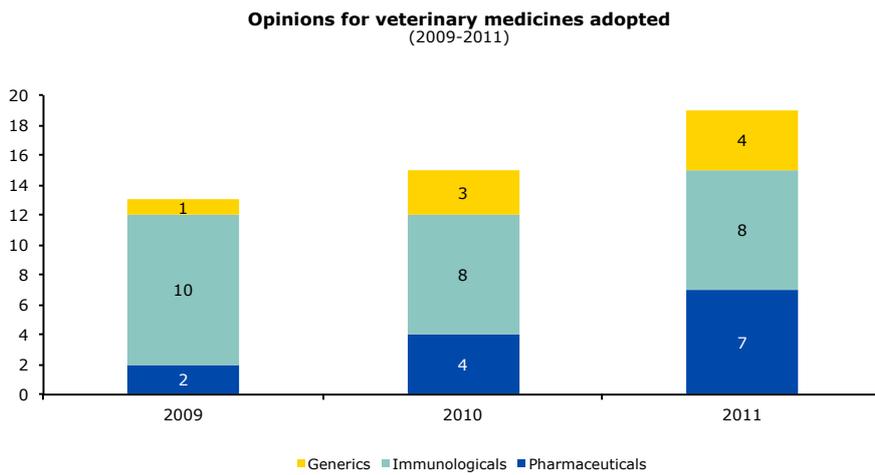
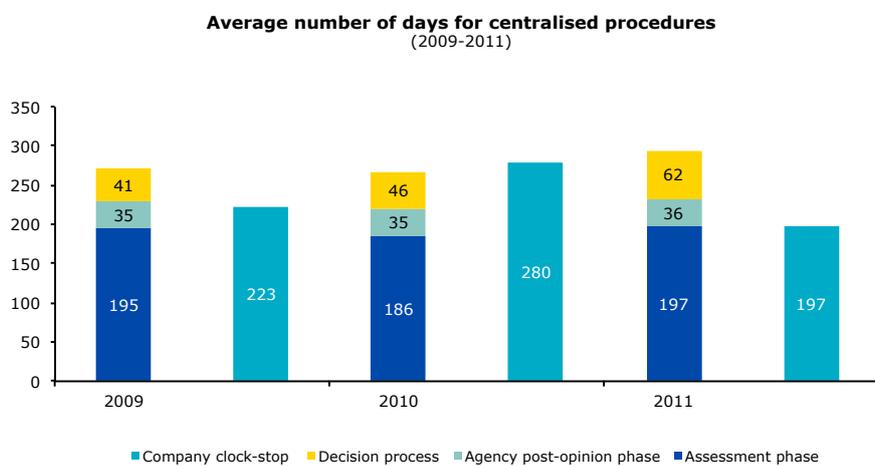


Figure 31.



### Animal-health impact of medicines recommended in 2011 for marketing authorisation

Veterinary medicines that received a positive opinion for authorisation included:

- 4 vaccines against bluetongue disease, to protect cattle or sheep against clinical signs and to reduce or prevent transmission of serotypes 1 and 8 of this virus; authorisation of these vaccines at EU level is a great advantage for the Union as it 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;
- 1 vaccine against Leishmania infection in dogs and 1 vaccine for immunisation against West Nile disease in horses; both these vaccines are intended to combat animal diseases previously only seen in warmer climates, but which possibly have spread to some EU countries as a result of global warming;
- 3 medicines for the treatment of parasitic infections in domestic pets; novel products for this kind of infection remain a priority area for the companion-animal sector due to relaxation of the rules on movement of pets within the EU;
- 1 medicine against parasitic infections in cattle;
- 2 new antibiotic medicines, one for use in companion animals, the other in pigs and cattle;
- various vaccines against specific diseases in chickens, rabbits, dogs and horses;
- 1 medicine for control of post-operative pain in dogs;
- 1 medicine for the treatment of bone fractures in dogs.



**Table 16.**

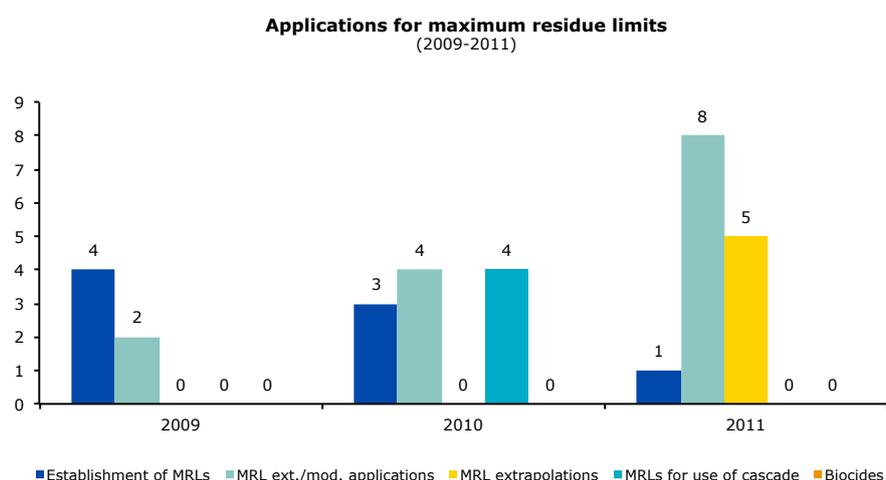
Key performance indicator	Target	Outcome
Percentage of products evaluated within the regulatory time frame of 210 days	100% of applications	100% of applications

### 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 medicine can be authorised, an evaluation of the safety of residues must be carried out. The Agency recommends maximum residue limits (MRLs) for pharmacologically active substances used in veterinary medicines, to provide for the safe use of foodstuffs of animal origin, including meat, fish, milk, eggs and honey.

#### Increase in extension opinions

- There was a 50% increase in the number of MRL-extension applications compared to 2010, indicating the welcome interest of the pharmaceutical industry in extending the use of existing veterinary products to new species.
- The number of applications for new molecules, however, remained low, with only 1 application submitted in 2011.
- The first requests for extrapolation of existing MRLs to a different food commodity were received. This is based on Article 27 of the new MRL Regulation, which provides for Member States and the Commission to request extrapolations from previously established MRLs. More such requests can be expected in the future.
- Although the new MRL Regulation gives the Agency the competence to recommend MRLs for pharmacologically active substances intended to be used in biocidal products to be used in animal husbandry, no applications have yet been received.

**Figure 32.**

#### MRLs for biocides

The draft guideline on risk-characterisation and assessment of maximum residue limits for biocides was finalised for release for consultation after intense work in cooperation with the European Commission services and representatives of national competent authorities responsible for the authorisation of biocides.

## Extrapolation of MRLs

The work on further development of the approach for extrapolation of maximum residue limits from one animal species to other animal species and/or food commodities was initiated to provide the scientific grounds for recommendations for extrapolations in accordance with the requirements of the new MRL Regulation (Article 5 of Regulation 470/2009).

**Table 17.**

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

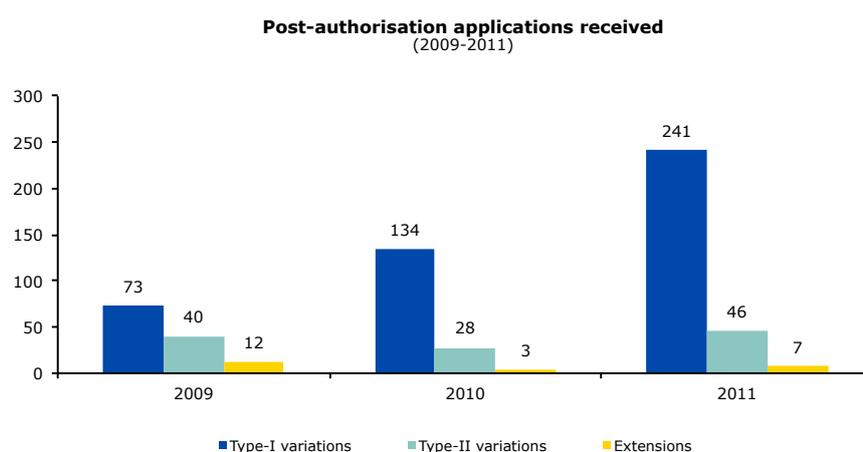
## 3.4. Post-authorisation activities

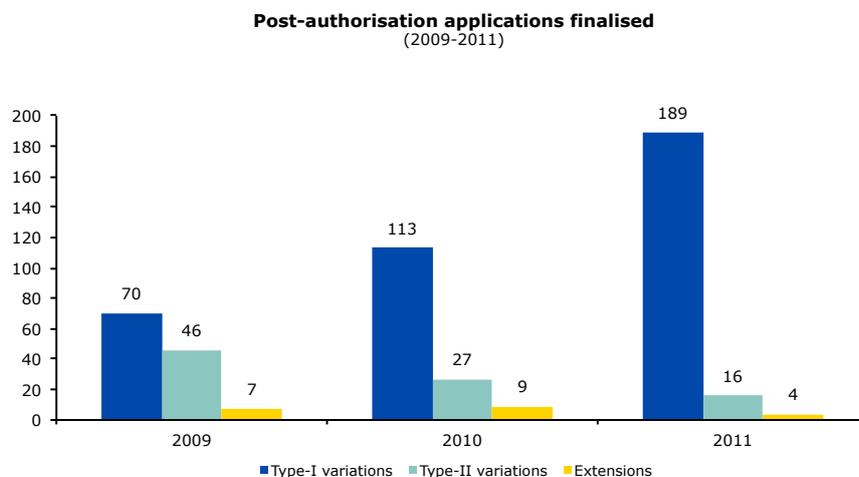
*Post-authorisation activities relate to variations, line extensions and transfers of marketing authorisations. Variations to marketing authorisations can concern either minor (type-I) or major (type-II) changes.*

### Last year's trend continues

- The trend reported in 2010, with the number of type-I variations increasing considerably and the number of type-II variations reducing – probably a result of downgrading of some variations to type IB, and the change of the default classification from type II to type IB – continued during the first half of 2011. However, during the second half of 2011 the number of type-II variations increased, bringing the total close to the level seen before the new Variations Regulation entered into force.
- The number of type-I variations again exceeded predictions: 241 type-I variations were submitted in 152 applications, compared to 134 variations in 96 applications submitted in 2010. The number of type-II variations increased to 2009 levels, with 46 applications (compared to 28 in 2010 and 40 in 2009).
- Further streamlining of the handling of post-authorisation applications, and in particular type-II applications, was put in to practice during 2011.

**Figure 33.**



**Figure 34.**

### Keeping post-authorisation guidance up to date

Standard operating procedures (SOPs) relating to type-IA and IB variations and grouping were published in 2011. The SOP on type-II variations is expected to be finalised in the first quarter of 2012. The public post-authorisation guidance is kept up to date on a regular basis.

**Table 18.**

Key performance indicator	Target	Outcome
All post-authorisation procedures processed in accordance with legal requirements	100% of applications	>99% 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 2011, to ensure that post-authorisation monitoring and effective risk-management are continuously applied to veterinary medicines throughout the EU.*

### Continuous increase in activities

- The number of adverse-event and human-reaction reports concerning centrally authorised veterinary medicinal products increased by 10% compared to 2010. This is consistent with the increase in number of centrally authorised veterinary medicines.
- Of the 4,888 reports received in 2011, 4,629 related to suspected adverse reactions in animals and 259 to reactions in humans following exposure to veterinary medicines.
- The EudraVigilance (EVVet) database contains more than 67,000 adverse-event reports related to veterinary medicines authorised within the EU. Of these, 45,000 occurred within the EU and 22,000 outside the EU.

Figure 35.

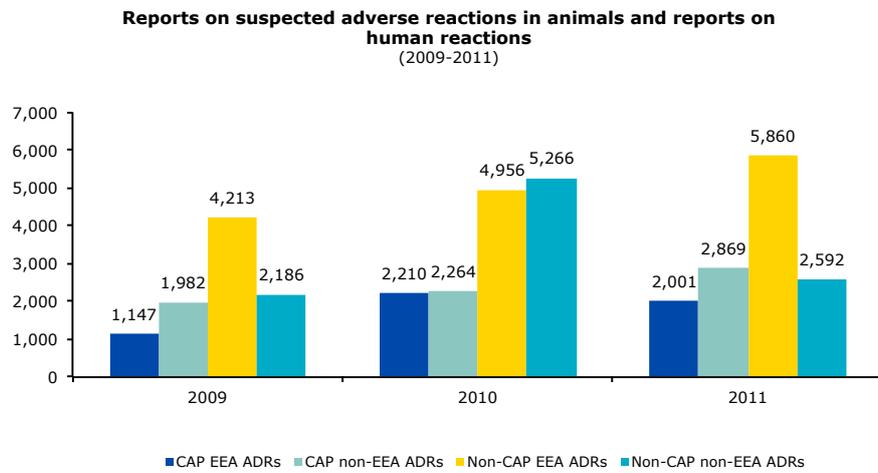


Figure 36.

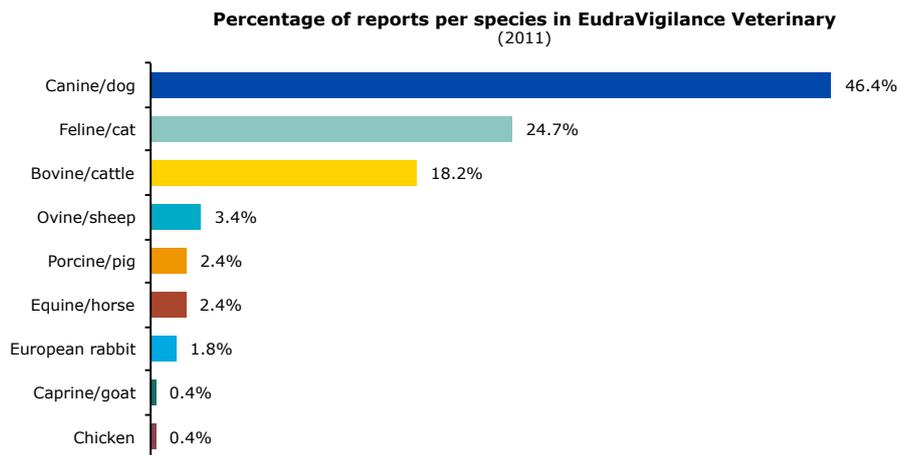
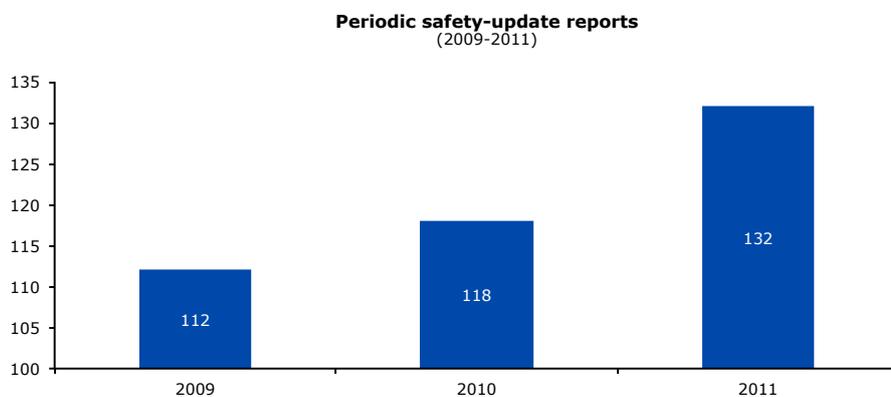


Figure 37.



### Progress with signal-detection

A new surveillance procedure for centrally authorised medicines was implemented, involving a risk-based approach and signal-detection using the electronic tools in the EudraVigilance Veterinary Data Warehouse. The procedure also represents a more effective use of expertise, by giving the main responsibility for surveillance to the CVMP Pharmacovigilance Working Party.

### Progress with EudraVigilance Veterinary

The further development of EudraVigilance Veterinary through the EVVet 3.X project progressed in accordance with planning and reached the development phase following completion of inception and elaboration.

Good progress was made populating the EudraVigilance Veterinary product database, with eight Member States having transmitted product data, mostly via direct transfer to the EudraPharm database.

**Table 19.**

Key performance indicator	Target	Outcome
Percentage of PSURs evaluated within the established time frame	80%	88%
Percentage of suspected adverse reaction (SAR) reports monitored within the established time frame	100%	100%

## 3.6. Arbitration, Community referrals and opinions on any scientific matter

*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).*

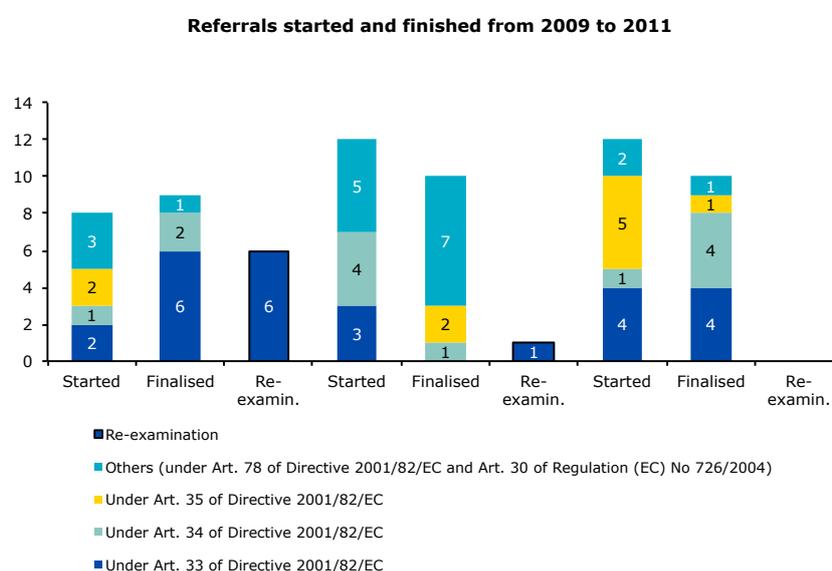
*Referrals relating to other issues are also processed by the CVMP, including requests by the Executive Director of the Agency for an opinion on a scientific matter (Article 30 of Regulation (EC) No 726/2004) and requests for the opinion of the Agency by the European Commission on an urgent matter (Article 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).*

### Stable level of referral procedures

- The number of referrals submitted (12) in 2011 was consistent with the forecast.
- The CVMP concluded a total of 10 referral procedures in 2011.
- The Community interest referrals received under Article 35 of Directive 2001/82/EC concerned either veterinary medicines containing antimicrobials or issues related to concerns regarding residues of veterinary medicines.

**Table 20.**

Procedure type	Started in 2011	Finalised in 2011
Article 33(4) of Directive 2001/82/EC	4	4
Article 34 of Directive 2001/82/EC	1	4
Article 35 of Directive 2001/82/EC	5	1
Article 78 of Directive 2001/82/EC	1	1
Article 30(3) of Regulation (EC) No 726/2004	1	0
<b>Totals</b>	<b>12</b>	<b>10</b>

**Figure 38.**

### Animal-health impact of referral opinions

Nearly all of the referrals considered by the CVMP in 2011 and for which the CVMP made recommendations were related to veterinary medicinal products containing antibiotics. This reflects the high concern throughout the regulatory network on this class of medicines.

Among the types of antibiotics considered were all medicines indicated for food-producing species containing systemically administered (parenteral and oral) 3rd and 4th generation cephalosporins. The CVMP recommended restrictions of indications and the addition of appropriate warning sentences to the summary of product characteristics for these medicines, as well as the contraindication of any use of these medicines in poultry.

Other opinions on referrals regarding antibiotics included products containing doxycycline and a number of products containing potentiated amoxicillin.

### Strategy for harmonising summaries of product characteristics (SmPCs)

The joint CVMP/CMDv Task Force on Referrals and Harmonisation made steady progress in developing a strategy for SmPC harmonisation under the future revised veterinary legislation and on prioritisation of referrals. The Heads of Medicines Agencies supported the continuation of the work as proposed by the Task Force, and finalisation of the strategy is foreseen for 2012.

**Table 21.**

Key performance indicator	Target	Outcome
Percentage of arbitration and referral procedures managed within the legal time frame	100% of procedures	100% of procedures
Adoption of CVMP opinions by the European Commission	100% of opinions	100% of opinions

### 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.

#### Antimicrobial resistance

The Agency and the CVMP, together with its Scientific Advisory Group on Antimicrobials (SAGAM), again devoted much effort in 2011 to activities aimed at minimising the risks of antimicrobial resistance arising from the use of veterinary medicinal products.

- The CVMP adopted a revised 'CVMP strategy on antimicrobials 2011-2015' (EMA/CVMP/287420/2010). The strategy seeks to promote the continued availability of effective antimicrobials for use in animals, while at the same time acting to minimise risks to animals or man arising from their use, and sets out intentions for direct action by the Committee during the next 5 years.
- On the basis of recommendations from the SAGAM, the CVMP finalised a reflection paper on meticillin-resistant *Staphylococcus pseudintermedius* (MRSP), mainly in companion animals in the EU, and another on the use of macrolides, lincosamides and streptogramins (MLS) in food-producing animals, as well as a concept paper on the use of pleuromutilins in food-producing animals.
- Progress was achieved with the Agency's project to coordinate at a European level the collection by Member States of harmonised data on use in the EU of antimicrobials in food-producing species and companion animals (ESVAC), as described in Section 1.2 of this report.

#### Interaction with other scientific committees of EU institutions, in particular EFSA

The CVMP maintained close working relationships with a number of other scientific committees of the EU institutions, to ensure consistency of assessment approaches and scientific opinions, and exchanges of information. Notably, there were numerous exchanges with the panels of the European Food Safety Authority (EFSA).

### 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, in accordance with the approved rules of procedure.*

#### Mutual-recognition and decentralised procedures

A total of 230 mutual-recognition (MR) and decentralised (DC) procedures were finalised in 2011, compared to 160 in 2010. Similarly to last year, the majority of new marketing-authorisation applications were for abridged applications (mainly generics), accounting for nearly 80% of all MR/DC procedures. Full, new applications under Article 12(3) accounted for around 20% of MR/DC procedures.

Eighteen referrals to the CMDv under Article 33(1) of Directive 2001/82/EC were started in 2011: 5 were concluded through agreement at the CMDv; 13 could not be resolved and were consequently referred to the CVMP for further arbitration.

### Harmonisation of product information

The CMDv's focus in 2011 was on driving forward the development of initiatives to harmonise the summaries of product characteristics (SmPCs) of older products that are authorised on a national basis and have not benefited from a harmonised assessment through MR or DC procedures. The two key milestones were the conclusion of the first phase of the CMDv's pilot (voluntary) SmPC harmonisation procedure and the development of guidance to effect the transfer to MR status of national marketing authorisations after a CVMP referral procedure (under Article 34 of Directive 2001/82/EC).

### Review of packaging and labelling requirements

Towards the end of 2011, the CMDv and a major industry stakeholder initiated extensive discussions on packaging and labelling in order to contribute to the Commission's review and simplification of current requirements. These discussions will continue into 2012, and the secretariat will provide support by hosting a workshop in the first quarter of the year. Also in the area of packaging, as a result of extension discussions during 2011, the product information ('QRD') templates were harmonised between the CMDv and CVMP.

### Implementing the variations legislation

The CMDv continued to support the practical aspects of implementing the Variations Regulation (Commission Regulation (EC) 1234/2008) relating to grouping and worksharing procedures. In particular, the CMDv developed an informal worksharing procedure to allow harmonised assessment between Member States of variations affecting products authorised on a national basis. This greatly reduces the workload for industry.

### New working groups

Two new CMDv working groups were created: one to discuss the Commission's ongoing review of the EU regulatory framework for veterinary medicines, and the other to discuss borderline medicines, i.e. medicines that are difficult to classify as belonging to a specific regulatory framework.

### Guidance on commercially confidential information

The secretariat initiated a working group of Agency and CMDv colleagues to prepare a guidance document, similar to the one developed for marketing authorisations for human medicines, that outlines the principles for commercially confidential information (CCI) and the protection of personal data (PPD) within the dossier for veterinary marketing-authorisation applications.

## 4. Compliance and inspections

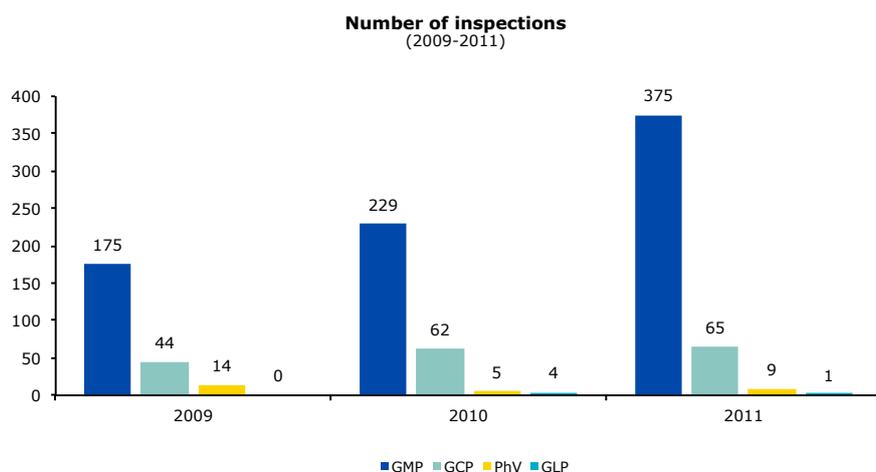
The Agency coordinates the verification of compliance with the principles of good manufacturing practice (GMP), good clinical practice (GCP) and good laboratory practice (GLP), with pharmacovigilance (PhV) obligations and with certain aspects of the supervision of authorised medicinal products in use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

### Inspections

#### More inspections than forecast

- The number of GMP inspection requests (375) exceeded the forecast (245). Several factors contributed to this increase, including an increase in active pharmaceutical ingredient (API) inspections and an unusual number of 'for cause' inspections, owing to significant quality or GMP problems at multi-product sites which involved both finished products and APIs.
- The numbers of GCP and PhV inspections were also both slightly over target (65 and 9 inspections versus the target of 58 and 8 inspections). The number of GLP inspections was below the target for 2011 (1 inspection versus the target of 2 inspections).

Figure 39.



### 4.1. Manufacturing and quality compliance

#### Quality-defect reports

##### Number of reports continues to rise

- Quality-defect reports rose by 38% compared to 2010, continuing the trend of recent years, during which an unusual number of complex cases involving significant GMP and/or quality issues with impact on the safety and supply of the medicines concerned were handled.
- The Agency started a project to explore root causes of quality defects. The outcome of this work will be available in 2012.
- A strategy paper regarding product supply interruptions and shortages consequent on GMP non-compliance and/or manufacturing failures/quality defects was prepared and presented to the Management Board in December 2011. An implementation plan will be introduced in 2012.

Figure 40.

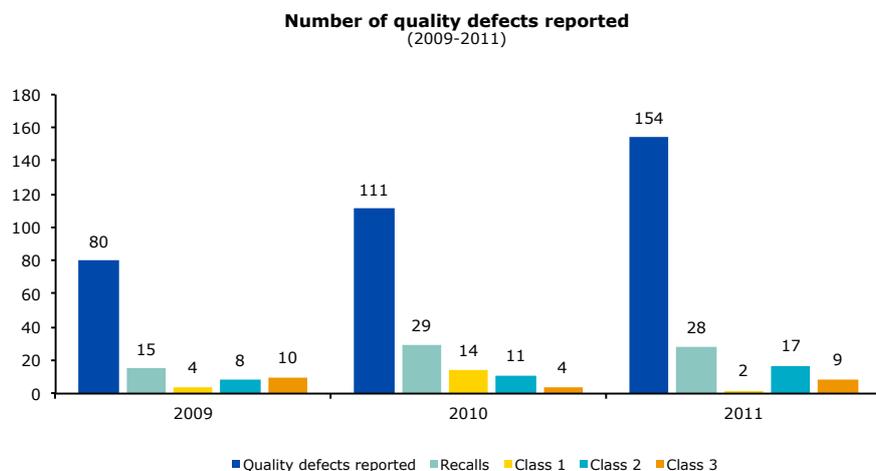
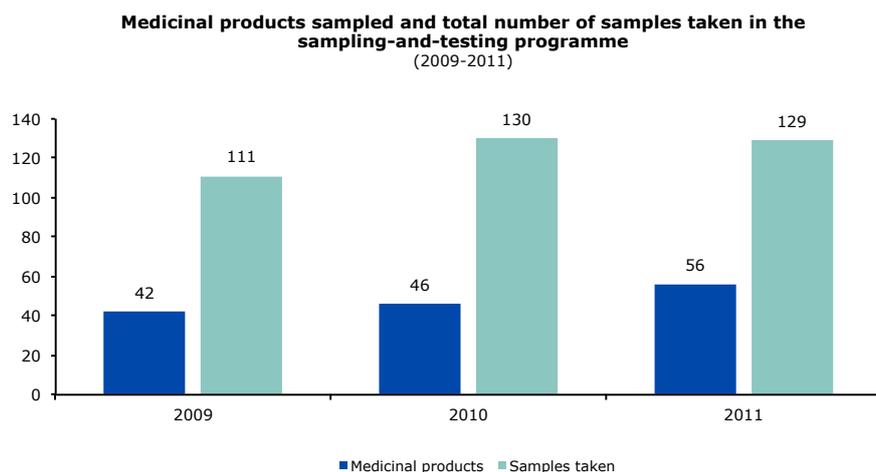


Figure 41.



### Enhanced collaboration on international GMP agreements with international partners

Information-sharing on API inspections with Australia and the United States was extended from the limited number of Member States in the pilot project to all Member States, and EudraGMP is now being used as a central repository for information exchange. Discussion is under way on how to extend participation in the existing scheme to other international partners. The terms of reference are being revised to accommodate this. A significant expansion of the number of participants will require that changes be made to the way the scheme is managed.

With respect to GMP inspections in the EU and the US, collaboration with the FDA continues, with a number of joint inspections contributing to confidence-building. The Agency and the FDA agreed on extending collaboration to reliance upon information from the other partner when certain criteria are met. This will become operational in 2012. The FDA has access to EudraGMP.

### Strategy on sampling and testing of generic medicinal products

A pilot strategy on the handling of generics within the sampling-and-testing programme was trialled in 2011 with clopidogrel. Lessons from this exercise will be considered in 2012 and will inform the future development of a procedure.

## Checking of packaging and labelling of centrally authorised products

Samplers are now undertaking routine checks of packaging and labelling of all centrally authorised products included in the sampling-and-testing programme.

**Table 22.**

Key performance indicator	Target	Outcome
Management of inspections within the legislative time frame	100% of inspections	100%
Number of products in the sampling-and-testing programme for centrally authorised products actually tested	52	56

## 4.2. Clinical and non-clinical compliance

### Operation of the international network of GCP-inspection services

A list of international contact points has been established. Information on opportunities to participate in Agency training courses and in GCP inspections as observers is shared within the network, when applicable.

The Agency organised GCP-inspection training activities as outlined under 'Capacity-building activities' in Section 1.3.

### Agency/FDA GCP initiative

The successful pilot phase of the joint Agency/FDA GCP initiative was concluded in March 2011, and a report on this initiative, highlighting the targets achieved, was published in August 2011. Following agreement among the Agency, GCP inspectors of the Member States and the FDA, the pilot has now been extended into a long-term operational phase.

## 4.3. Clinical-trials support

### Strategy for the acceptance of clinical trials conducted in third countries

The 'Reflection paper on ethical and GCP aspects of clinical trials for human medicines conducted outside of the EU/EEA and submitted in marketing-authorisation applications to European regulatory authorities' (EMA/121340/2011) was endorsed by the Agency's Management Board in December 2011.

### Risk-based quality-management in clinical trials

The GCP Inspectors Working Group (IWG) and the Clinical Trials Facilitation Group (CTFG) subgroup finalised their draft reflection paper on risk-based quality-management in clinical trials. The paper, after being endorsed by the GCP IWG and CTFG plenary groups, was released for public consultation in August 2011. It marks an important contribution to widespread international discussion on the adoption of more proportionate and risk-based approaches to the regulation and conduct of clinical trials.

### Support to Clinical Trials Facilitation Group (CTFG) activities

The Agency continues to support the organisation of the CTFG plenary meetings held on its premises.

The Agency provided training to CTFG members on the use of the EudraCT Datawarehouse, to help them in the preparation of EudraCT reports of their concern. Ad hoc EudraCT reports are also prepared by the Agency's staff to address particular requests from CTFG members.

The Agency developed a procedure on the interaction between it (mainly the CHMP) and the CTFG in cases where a suspension, revocation or withdrawal of a medicine has an impact on planned or ongoing clinical trials.

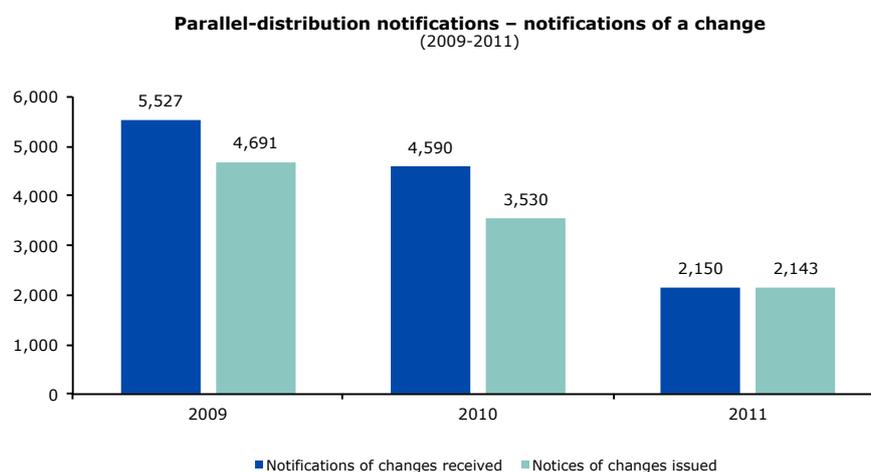
### EudraCT development

EudraCT version 8.0 was launched in March 2011 after some delays. The database now contains important additional functionality, as well as an updated clinical-trial application form, and serves as the information source for the public EU Clinical Trials Registry.

The EudraCT full data warehouse was launched in September 2011. It is expected that data-quality control and use of data from EudraCT will support the clinical-trial supervision process and that the new reporting possibilities offered by the data warehouse will facilitate policy development.

## 4.4. Parallel distribution

**Figure 42.**



### Process improvement

Process improvements introduced in the handling of parallel-distribution requests have allowed the Agency to handle almost all (96.6%) notifications within their target time frame.

### Electronic submission

More than 95% of parallel distributors are using electronic submission. This almost paperless system has resulted in a much more efficient and consistent outcome.

### Pilot to check product information

A pilot to check product information of centrally authorised medicines by parallel distributors was started with the UK Medicines and Healthcare products Regulatory Agency (MHRA). MHRA inspectors take photos of medicines to be released and send them to the European Medicines Agency for regulatory checking. A total of 74 samples corresponding to 11 parallel distributors were checked. Many critical deficiencies were identified, one of them resulting in the suspension of a manufacturing licence and three of them in a batch recall. A significant improvement in the quality of data submitted by the UK parallel distributors has been noted since the project started.

Discussions with six other EU Member States are underway to extend this project in 2012.

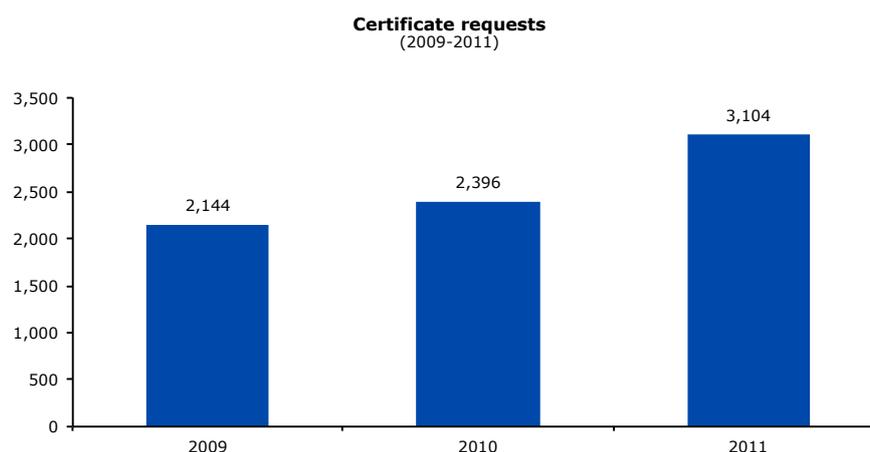
**Table 23.**

Key performance indicator	Target	Outcome
Percentage of initial notifications checked for compliance within the regulatory time frame: paper submission validation and regulatory check 35 days	80%	96.6%
Number of parallel-distributed products sampled on the EU market checked for compliance with the notices issued by the Agency	20 products	74

## 4.5. Certificates

### *Unexpected increase*

The number of certificate requests received was 22% higher than forecast. Due to the unexpected higher workload, the turnaround time for requests was 10.4 days, which – although longer than the 7.4 days achieved in 2010 – is almost in line with the target turnaround of 10 days.

**Figure 43.**

### Urgent procedure

A new urgent procedure for issuing certificates of medicinal products in 48 hours was approved by the Management Board at the end of 2011, and will start in 2012.

## 5. Information and communications technology (ICT)

### 5.1. Implementation and operation of ICT in support of internal activities

Table 24.

Project	Performance in 2011
<b>Resource-management projects</b>	
Launch of the financial module of the enterprise resource system	Launched in January 2011
Launch of the human resources module of the enterprise resource system	Launched in October 2011
<b>Improving management of processes</b>	
Launch of SIAMED II to support procedure and workload management	Launched in October 2011
Electronic signatures	This project could not be started in 2011; it is scheduled to start in early 2012
Electronic workflows for publication	This project was not started in 2011
System to support plasma-master-file applications	Delivered in December 2011
<b>Improving quality of data input, processing and management</b>	
Launch of electronic application form (EAF) for applications for initial marketing authorisations and variations	Development of most forms was completed in 2011; all forms will be launched in 2012, following a pilot
Improvements to systems supporting electronic submissions	The next version of the eCTD review tool (EiY 3.1) was launched in September 2011; vision documents for electronic submission and a central repository of eCTD files were created
Enterprise information architecture	No progress was made; this project was subsumed into the Operational Excellence initiative
Pilot for the unique product identifier	Progress was made in defining the business processes using unique product identifiers; the pilot was not started
Update of the Eudra Common Directory	This project was suspended in late 2010 to allow improvements to the business processes underpinning the information-management of organisations and individuals in ECD to be investigated
<b>Implementation of legislation</b>	
Document register	A project to deliver the document register was started by the end of 2011
Implementation of tracking support	This was not started in 2011
Register of experts' declarations of interests	Public version launched in September 2011

## 5.2. EU telematics

**Table 25.**

<b>Project</b>	<b>Performance in 2011</b>
<b>Improved communication</b>	
Publish a new version of the telematics website for the European medicines network in Q2	This was not started in 2011
Implement the Management Board Telematics Committee strategy for increasing use of virtual meetings technology by Q4	Over 50% of the Management Board Telematics Committee meetings are virtual; other groups, including TIGs, have also increased their usage of virtual technology for TIGs
Review the governance structure of EU Telematics by Q3	A study to review the governance structure of EU telematics is ongoing and is scheduled to be completed in March 2012
<b>Efficient and interoperable platform</b>	
Make available a first iteration of partially ISO-compatible medicinal products and substances database within EUTCT by Q2	A first iteration has yielded a consolidated and confirmed scope, high-level requirements and technical architecture
Next version of the Eudra Common Directory available in Q4	This project was suspended in late 2010 to allow improvements in the business processes underpinning the information-management of organisations and individuals in ECD to be investigated
Launch a revised data warehouse offering business intelligence functionality on EudraVigilance Human data by Q4	This project was suspended to give priority to implementation of the new pharmacovigilance implementation
Launch a data warehouse offering business intelligence functionality on EudraCT data by Q3	Launched in September 2011
<b>Efficient telematics systems that are fit for purpose</b>	
Complete EV data management (backlog) 100% by Q4	This is ongoing
Implement EV data-access policy by Q4	The system implementing the EV data-access policy was delivered in December 2011; work on a dedicated website in all EU languages will finish in Q2 of 2012
Progress implementation of new legislative functionality in EV (human), the data warehouse and the eSubmission systems	Implementation of Article 57 of Regulation (EU) No 1235/2010 was progressed and will be made available in Q1 2011
EudraCT version 8.x: new CTA Paediatrics Protocol, EU Clinical Trials Register and delivering increased electronic communication between registries and other stakeholders by Q3	The new CTA Paediatrics Protocol and the EU Clinical Trials Register were delivered in March 2011
EudraCT version 9: Complete analysis and design, and deliver a first prototype by Q4	The high-level analysis of EudraCT 9 was completed in 2011
<b>Improved capacity for performance measurement</b>	
Implement automated key performance indicators by Q4	Automated key performance indicators for ICT processes and activities are now in production and can be accessed by all staff members who request access

<b>Project</b>	<b>Performance in 2011</b>
<b>Increasing the Agency's contribution to international regulatory activities</b>	
Improved assimilation of EU requirements leading to a coherent EU position	IDMP – European position agreed in May 2011 CTR&R – European requirements formalised in December 2010
ISO ICSR (individual case-safety report) standard available by Q2	ICSR standard published December 2011
RPS (regulated product submission) release 3 ballot package available by Q4	RPS is currently in draft for trial use; much vocabulary work needs to be undertaken after testing before this standard will be made normative; earliest publication in Q1 2013
Test results of CTR&R (clinical trial registration and results) draft standard for trial use satisfactory for EU requirements by Q2	CTR&R earliest test results in Q3 2012
ISO IDMP (identification of medicinal products) standard available by Q4	Standard scheduled to be published in June 2012
<b>Objectives for assuring the coherent technical implementation of legislation</b>	
<b>Interoperability of systems</b>	
EUTCT: All Telematics systems using at least 10% of their necessary CTLs in Q4	Six EU telematics systems and one corporate system consume CTLs from EUTCT; on average, each system uses 8 CTLs from EUTCT
EUTCT: 70% of national competent authorities (NCAs) using at least one list from EUTCT in Q4	This target has not been met; NCAs from four Member States are using lists from EUTCT; at least three other NCAs are currently looking into making use of lists
<b>Redundant input of information</b>	
EAF (Electronic Application Form) in production for initial applications and variations in Q2	Development of most forms was completed in 2011; all forms will be launched in 2012, following a pilot
<b>Increased efficiency of pharmacovigilance activities</b>	
Tools supporting improved data for the identification of medicinal products in place in Q2	Priority was given to the implementing Article 57 of Regulation (EU) No 1235/2010
<b>Increased transparency, communication and provision of information</b>	
EudraPharm: publishing medicinal product information from 55% of NCAs in Q4	Currently, 17% of NCAs have provided medicinal product information to EudraPharm; the uptake of EudraPharm has been slowed down by the implementation of Article 57 of Regulation (EU) No 1235/2010

Table 26.

<b>Key performance indicator</b>	<b>Target</b>	<b>Outcome</b>
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

**Table 27.**

<b>Severity rating</b>	<b>Description</b>	<b>Resolution time**</b>	<b>Target</b>	<b>Outcome</b>
1. Critical	Users are unable to use the system	3 hours	80%	None logged
2. Severe	The system is operational but severely restricting use	1 business day	80%	100%
3. Important	The system is operational, but one or more functions are restricted	10 business days	80%	100%
4. Minor	The system is operational and no functions are restricted	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.

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**Annual report 2011**

Overview of the Agency's contribution to science, medicines and health in the European Union  
EMA/MB/977044/2011

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