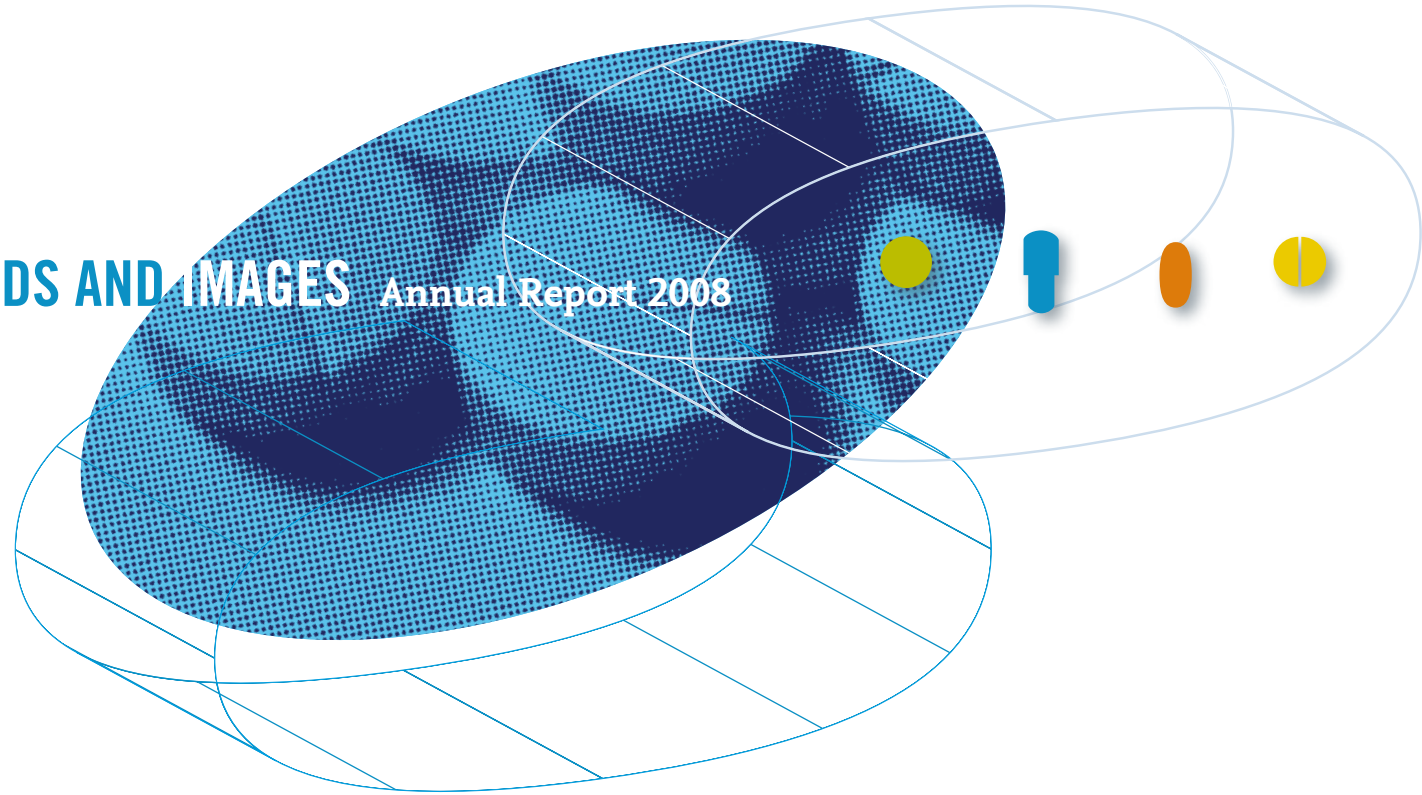
2008 IN WORDS AND IMAGES

Annual Report 2008



Federal Agency for Medicines and Health Products

A WORD FROM THE DEPUTY PRIME MINISTER AND MINISTER FOR PUBLIC HEALTH, **MRS LAURETTE ONKELINX**

Dear Reader,

I'm very pleased to present the second annual report from the Belgian Federal Agency for Medicines and Health Products (FAMHP), which was established on 1 January 2007.

The report on the Agency's first year of work was naturally focused on the establishment and transition of the organisation. This second annual report is devoted to the further development of the FAMHP, with a range of examples of the numerous positive activities which perfectly reflect the great diversity of its work.

The report alternates between descriptive articles, interviews and figures and is supplemented with more traditional elements of an annual report, such as budget and personnel details.

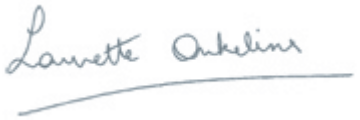
Reading the annual report makes me proud of all the hard work undertaken over the last year. This does not just include the choices made and the development of the spearheads, but also the continuing efforts made by the Agency for rapid, efficient and clear communication with the general public.

The FAMHP has opted for dialogue as a way to achieve its work; this has proved to be a well-informed choice. The Agency is actively engaged in better protection of public health and undertakes its activities in close collaboration with patients on the one hand and public health professionals, researchers, industry and the distribution sector on the other.

I sincerely hope that the FAMHP will continue to evolve at an undiminished pace.

After all, there has never been a greater need for a dynamic and target-driven public service, stringently managed, yet nevertheless transparent and professional, enjoying national and international recognition and which is, above all, able to meet the multiple demands of public health.

I hope you enjoy reading this report,



Laurette Onkelinx
Deputy Prime Minister and Minister for Public Health
Minister responsible for the FAMHP
June 2009

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MISSION, ROLE AND VALUES

MISSION

The FAMHP plays an essential role in the protection of public health, with the following mission:

"Ensuring, from development to use, the quality, safety and efficacy:

- **of medicines for human and veterinary use, including homeopathic medicines and herbal medicines, pharmacy made and officinal preparations;**
- **of health products including medical devices and accessories, and raw materials (active pharmaceutical ingredients) for the preparation and production of medicines.**

Ensuring, from collection to use, the quality, safety and efficacy:

- **of all operations involving blood, cells and tissues, which are also defined as health products.".***

* Based on the law of 20 July 2006 (B.S. - M.B. 08.09.2006) on the establishment and functioning of the FAMHP.

ROLE

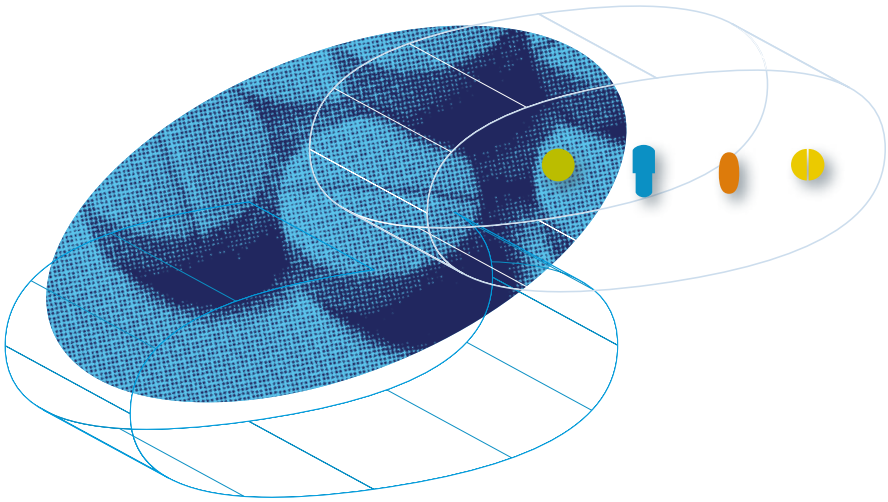
To ensure the quality, safety and efficacy of medicines and health products in clinical development and on the market.

VALUES

The values nurtured within the FAMHP are carefully selected, and form the unifying theme in our day-to-day activities:

- Professionalism
- Integrity
- Sincerity and transparency
- Comprehensiveness
- Participation.

“Your medicines and health products are our concern!”



“Installation of the FAMHP”

INSTALLATION OF THE 3 COMMITTEES

The Consultative Committee, Scientific Committee and Transparency Committee were created by the law of 20 July 2006 on the establishment and functioning of the FAMHP. These 3 committees offer direct advice to the Chief Executive Officer about the FAMHP’s functioning and how to achieve its objectives. All 3 committees are now active and held their first meetings in 2008.

SCIENTIFIC COMMITTEE

The **Scientific Committee** offers advice regarding matters for which the Agency is competent. The Scientific Committee enjoys a great deal of freedom in the context of its activities as a body of scientific expertise and coordinator for various commissions active within the FAMHP. This committee is concerned with the priorities and particular emphases of scientific evaluation and does so in order to harmonise general information about medicines and health products between the various FAMHP commissions.

June 2008: first meeting of the Scientific Committee with selection of the president and approval of the rules and regulations.

The Scientific Committee was the first FAMHP committee to have held a meeting. At that first meeting on 27 May 2008, Jean-Paul Degaute, president of the FAMHP Evaluation commission for medicines for human use, was chosen as president with a mandate of six years.

During this first meeting the Chief Executive Officer of the FAMHP, Xavier De Cuyper, welcomed and introduced every member of the Scientific Committee, meaning the presidents of the various commissions, as well as FAMHP representatives acting as observers.

Following a brief review of the legislation regarding the establishment of the Scientific Committee and the selection of the president, the members approved the rules and regulations.

November 2008: second meeting of the Scientific Committee with the selection of the vice-president and proposals for activities.

Guido van Nooten, president of the Evaluation commission for medical devices, was selected as vice-president of the Scientific Committee during the second meeting of 27 November 2009.

The following proposals regarding activities were included in the agenda:

- Evaluation of general information concerning medicines and health products;
- Exploring how clinical trials can be encouraged and proposing specific regulations for this;
- Communicating about the evaluation of active implantable medical devices: separating results and efficacy from recognition of CE marking;
- Producing quality requirements for medicines and reagents used in hospitals.

The Scientific Committee will work with to experts from the various departments and services in the Agency in order to realise these activities. The proposals reflect the diversity of the activities and responsibilities of the different FAMHP commissions. The Scientific Committee's mission consists of coordinating and harmonising activities carried out by the various FAMHP commissions with a view to guaranteeing the quality, safety and efficacy of medicines and health products. The activities proposed may involve interaction between the various FAMHP bodies; however it is not intended that the Scientific Committee should replace these.

Jean-Paul Degaute is a qualified obstetrician, physician, surgeon and specialist in Internal Medicine (July 1974). He is also a qualified University Lecturer in Medical Sciences (1993) and was head of the Department of cardiology at the Erasmus Hospital (ULB - Anderlecht) (March 2002 to 2009).

In addition to occupying an important role in the academic world, Jean-Paul Degaute has acquired a considerable amount of experience in the world of administration through his role regarding management in university, education and scientific associations:

- Member of the Higher Council for awarding physician specialist status and general practitioner training since 1987 (FPS Public Health).
- Member of the clinical toxicity and pharmacology group of the Evaluation commission for medicines for human use of the Directorate-General (DG) for Medicinal Products between 1989 and 1997 (FPS Public Health);
- Member of the Transparency commission of the DG Medicinal Products of the FPS Public Health since 1990, secretary between 1990 and 1995 and president between 1998 and 2001;
- Member of the Technical Council for Pharmaceutical Products of the RIZIV-INAMI between 1993 and 1998;
- Vice-president of the Drugs Reimbursement Commission of the RIZIV-INAMI from 2002 to the present;
- Member of the Clinical Investigation group of the National Fund for Scientific Research from 2002 to the present;
- President of the Evaluation commission for medicines for human use of the DG for Medicinal Products of the FPS Public Health from January 2005 to the present;
- President of the FAMHP Scientific Committee since May 2008.

Jean-Paul Degaute: *"The Scientific Committee is a body of scientific expertise that acts to* **coordinate** *the activities of the various commissions active within the FAMHP. My involvement in the consultation process with various Ministers' offices in preparing the establishment of the FAMHP gave me the opportunity to participate in discussions about the goals of the various committees which were in the process of being created. The presidency of the Scientific Committee appealed to me from the start because of the* **regulatory role** *of that committee in the context of the activities of the FAMHP commissions, some of which will be using a communal platform of internal experts.*
Our primary goal for 2009 is the analysis of the workings of the various commissions with the aim of harmonising and unifying working practices as much as possible. Of course, the work undertaken by the various commissions does sometimes vary greatly and anomalies that may arise from this will need to be taken into account. There will need to be regular cooperation with the various bodies of the FAMHP in order to achieve these goals. The aim of the Scientific Committee is, of course, not to replace those bodies of the organisation, but rather to develop **good collaboration** *within the agency".*

TRANSPARENCY COMMITTEE

September 2008: the Transparency Committee starts work.

The FAMHP **Transparency Committee** was established in September 2008 and offers advice on management issues. Thanks to the successful start the Committee was able to unanimously issue two important advisory notes during the first meetings.

In the first advisory note regarding the Agency's Business plan for 2008-2012 the Transparency Committee offered its support to the various FAMHP initiatives prioritising the strengthening of the FAMHP's core activities in line with its mission. This advisory note also underlines the committee's support for the development of the four spearheads chosen by the FAMHP:

- Oncology
- Vaccines
- Proactive vigilance
- Early Phase Development.

The Transparency Committee above all demands prioritisation and urgent attention to the necessary improvements required in activities concerning the provision of marketing authorisations (MA) for medicines; in particular, a thorough approach to working through the backlog of files.

In addition, the Transparency Committee also issued a positive advisory note regarding the initial budget estimate proposed for 2009. This second note requires a realistic and careful approach to both income and expenses, whilst taking into consideration the following principles:

- Budgetary balance between income and expenses;
- Improved recovery of income;
- Evolution of finances towards the "fee for service" principle;
- Realistic estimates and distribution of costs for certain projects in order to reduce their impact on the financial year.

Both advisory notes demonstrated that the Transparency Committee was taking its allocated mission seriously from its establishment. In 2009 the Transparency Committee will continue to contribute to guarantee "Good Governance" in close consultation with the Agency's management. For future years the intention is to draft the FAMHP budget in advance in mutual consultation. This will allow stakeholder representatives to contribute to ensuring the efficient use of the Agency's finances.

Representatives of the sectors contributing to the Agency's income are represented in the Transparency Committee, as well as an inspector of finances, a representative of the Minister for Public Health and the Chief Executive officer of the Agency.

The Committee is chaired by Tim De Kegel, secretary general of pharma.be. The vice-president is Marc-Henri Cornély, representative of OPHACO.

Tim De Kegel has a Master's degree in Jurisprudence (K.U. Leuven, 1998) and a Master's in Business Administration (Solvay Business School, 2000). He has been secretary general of pharma.be since 2004. Prior to that he was active in UCB Pharma, ING and the European Commission, in, for instance, The Netherlands, Spain and Singapore.
Tim De Kegel is a member of the FAMHP Consultative Committee and president of the Transparency Committee. He is also a member of the Management Committee for the "Rare diseases and Orphan medicines" Fund of the King Baudouin Foundation, as well as the Executive Board of the Anti-poisons Centre, Fost Plus and VAL-I-PAC.

Tim De Kegel: *"I've sensed a new wind of change blowing around the Agency, both within the management and amongst the staff. This is now being translated into the first results. However, enormous challenges still remain. Simplifying the registration procedures, working through the backlog of registration files, developing the spearheads, as well as developing a unit for medical devices are just some of the priorities. Members of the Transparency Committee have a significant responsibility: not only because they've accepted the mission to oversee* **good governance** *in the Agency, but also, primarily, because they have signed up to working on the* **development of an effective Agency**. *The first operational weeks of the committee have demonstrated that a high level of ambition such as this is both realistic and achievable. The collaborative advice to the Minister for Public Health regarding the Agency's business plan and budget was the first significant sign. As president I will do everything I can to ensure that the Transparency Committee continues in the same rich vein in 2009".*

CONSULTATIVE COMMITTEE

September-October 2008: installation of the Consultative Committee.

The FAMHP **Consultative Committee** was established on 24 September 2008 in the presence of the Deputy Prime Minister and Minister for Public Health, Mrs. Laurette Onkelinx. The committee advises the FAMHP on all matters relating to present or future policy: on its own initiative, at the request of the minister responsible or the Chief Executive Officer.

The Consultative Committee met for the first time in October 2008. The rules and regulations were approved and a timetable of meetings was agreed for 2009.
A comprehensive overview of the various FAMHP activities, the distribution of roles within the new structure and objectives will be presented at the first meeting in 2009 to enable the committee to act in full knowledge of the Agency's business.

In 2009, the Consultative Committee will initially attempt to arrive at joint recommendations for the FAMHP concerning proposed topics, such as transparency of information relating to medicines and health products or drafting regulations for distinguishing between medicines and products in the so-called "grey area".

Representatives of patients and consumers and from all sectors involved in products falling under the Agency's competency are represented in the Consultative Committee, as well as representatives from the relevant federal public services.

The Consultative Committee is chaired by Xavier De Cuyper, Chief Executive Officer of the FAMHP.

Xavier De Cuyper graduated in agricultural engineering in 1980 (Department of Agriculture) from the UCL Faculty of Agricultural Sciences. Prior to his appointment as Chief Executive Officer of the FAMHP, Xavier De Cuyper was active as Secretary General of the former Ministry of Agriculture and the Chief Executive Officer of the Food Safety Agency and Director General of the DG Animal - Plants - Foodstuffs at the FPS Public Health, Food Chain Security and Environment.

Xavier De Cuyper: *"My appointment as president of the Consultative Committee, as Chief Executive Officer of the FAMHP seemed logical to me given the broad mission of this committee.*
To me the Consultative Committee is the only place where all stakeholders – in the broadest possible sense – are represented. It's the only place where various interested parties are able to have a voice, and make their questions and expectations known. And there is more: the immediate interaction with other parties may create a **consensus** *which is accepted by everybody.*
The Consultative Committee also sets the direction for **protecting public health** *and produces a* **summary** *of the state of affairs within the context of the FAMHP competency domain: the competent authorities, the relevant industry, scientists, healthcare professionals and patients.*
It would be a good result if this committee was able to meet the FAMHP's expectations. After all, we expect all our stakeholders will come to this committee with their ideas for contributing to the realisation of the FAMHP. That is what is on my agenda for 2009".

Report in summary

The new FAMHP structure and procedure for appointing the management

The new FAMHP structure was approved by the Council of Ministers on 12 October 2007. The new structure was developed by the Central working group, an internal steering group composed of representatives from each of the FAMHP's departments and services. Within this new structure the operational departments were organised across 3 major pillars: The "PRE-pillar or all activities prior to the first marketing authorisation for a medicine or health product", the "POST-pillar or all activities after the first marketing authorisation of a medicine or health product" and the "INSPECTION-pillar, or all inspection and control activities". Each pillar is headed by a N-1 appointee or Director-General.

With a view to the effective implementation of the new FAMHP structure the selection procedure for the 3 N-1 appointees or Directors-General was started on 20 June 2008 by Selor. The vacancies were published in the Belgian journal of acts, orders and decrees (B.S.-M.B.) and on the Selor website (www.selor.be); applications had to be submitted to Selor no later than 22 July 2008.

The FAMHP P&O Service department was closely involved in this selection procedure for the following:

- Realisation of role descriptions;
- Development of the procedure for validation of the role descriptions by the Chief Executive Officer and subsequently by the Minister responsible;
- Development of the procedure for appraisal for salary purposes of the role descriptions by the FPS P&O;
- Compilation the dossier for the FPS P&O which organised the selection with Selor;
- Follow-up of the dossier on the basis of the reports of the selection procedures carried out by Selor;
- Preparing the appointment decisions and the publication in the Belgian journal of acts, orders and decrees.

The new organisation will become operational (see Organisation chart) as soon as the 3 N-1 appointees or Directors-General have taken up their posts at the start of 2009. Prior to this the FAMHP will continue to be organised in accordance with the previous division into 5 operational departments reflecting the life-cycle of a medicine.

Report in summary

Creation of the Mixed commission within the FAMHP

The establishment of the Mixed commission was effected by Royal decree (R.D.) on 28 October 2008 (B.S.-M.B. 19.11.2008) which determined the composition and activities of the Mixed commission; this was pursuant to article 1, paragraph 2 of the Medicines Act of 25 March 1964.

The Mixed commission is charged with offering advice about products, which in view of their characteristics taken in their entirety, fall under the definition of a medicine, as well as a definition of another product subject to other legislation. This commission offers advice regarding the files submitted in order to determine which legislation applies. This may, for instance, involve foodstuffs, cosmetics, medical devices and biocides. The final decision is made on the basis of this advice by the responsible minister or his representative.

The Mixed commission consists of a Chamber for products for human use and a Chamber for products destined for animals. The Mixed commisssion may be consulted on request by those responsible for marketing a product, on request by the relevant public services or on request by a third party. This commission is composed of representatives from the FPS Public Health (DG Animal-Plants-Foodstuffs and DG Environment), the FPS Economy, Federal Food Agency (FAVV-AFSCA) and, of course, the FAMHP. The members of the commission select a president and vice-president in accordance with the R.D. of 28 October 2008. This R.D. stipulates that the presidency is occupied by one of the members of the FAMHP and the vice-presidency by one of the members of the FPS Public Health, DG Animal-Plants-Foodstuffs.

The concrete composition of the Mixed commission will be published at the start of 2009 in the B.S.-M.B. and the commission will officially commence activities from this date. The agenda items for the first meeting will include the appointment of the president and vice-president, the drafting and approval of the commission's rules and regulations and determining the dates of meetings. The Chambers are anticipating an annual workload of around 100 files for the Chamber for products for human use and around 50 files for the Chamber for products for animals.

Special Investigation Unit (SOE-USE)

Within the FAMHP there is a Special Investigation Unit (SOE-USE) charged with combating pharmaceutical crime in general. Some examples of the areas in which it works include copying, counterfeiting, illegal trade, fraud, doping and internet fraud. This unit works "transversally" across the FAMHP inspection units.

Pharmaceutical crime includes for instance:

- Copying and counterfeiting medicines and the trade in food supplements with therapeutic indications;
- Racketeering involving narcotics and psychotropic substances in the form of medicines;
- Problems relating to the import, export and transit of medicines. In these cases, the necessary authorisations are often lacking (e.g. for production, release of batches, import, wholesale and distribution, distribution within the European Union, export, possession);
- Internet and distance selling;
- Human and veterinary doping (e.g. bodybuilding, cycling, show-jumping, pigeon racing);
- Veterinary crime relating to veterinary medicines (e.g. abuse of antibiotics);
- Crime and fraud within "Good Practices"

such as, Good Clinical Practices (GCP), Good Distribution Practices (GDP), Good Manufacturing Practices (GMP), Good Veterinary Practices (GVP);
- Borderline products and medicines without a market authorisation (MA);
- The trade in traditional medicines such as Traditional Chinese Medicines (TCM), Ayurveda and others;
- The theft of medicines and their resale on the black market.

The activities of the SOE-USE fit within the overall design of the FAMHP inspection units. The SOE-USE will also be involved in control policy, and the current demarcation with other inspection units may potentially change. The SOE-USE comprises 2 inspectors and 3 trainee inspectors. The trainees are expected to complete their training at the start of 2009. The primary objectives of the SOE-USE in the initial phase are to train these employees and to develop an infrastructure which will enable collaboration and data exchange between members. Additionally, a model will also be developed for a uniform working method for handling files, exchanging information and other tasks within the unit.

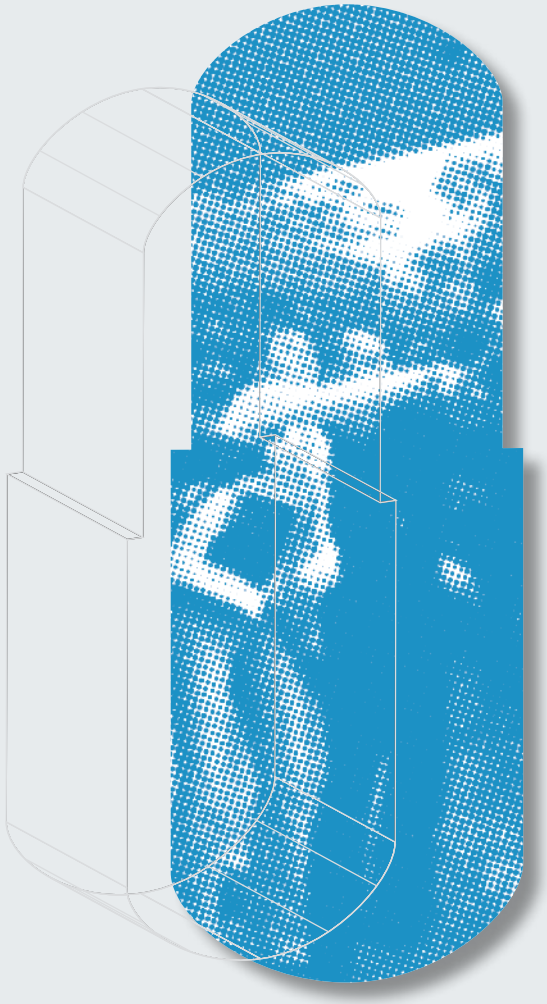
In 2008 the SOE-USE handled more than 700 files regarding illegal internet medicines and more than 100 "classic" files.

Conflict of interests and declaration of confidentiality

In the context of the FAMHP project "Transfer of values" an important initiative was set up in the course of 2008 regarding the observing and transfer of FAMHP's values and respecting its principles of professional ethics. Therefore a provision was introduced to ensure that all members of staff of the FAMHP submitted a conflict of interests declaration in accordance with the provisions of the law of 20 July 2006 concerning the establishment and functioning of the FAMHP. This allows each member of staff to declare any financial or other interests in organisations or companies falling within the FAMHP mission and obliges members of staff to inform the Agency immediately of any significant changes occurring to those interests. The FAMHP conflict of interests statement also contains a "declaration of confidentiality" providing an agreement to treat all confidential material as such. Members of all the FAMHP commissions offering advice on decisions regarding, for instance, marketing authorisation and manufacturing licences, were also required to submit a declaration to the FAMHP, as well as those external experts the FAMHP relies on for undertaking various tasks.

A modified declaration was provided to members of the Transparency Committee and the Consultative Committee, since members of these committees are representatives of bodies falling under the FAMHP mission. This declaration stipulates that signatories should observe the rules and regulations of the relevant committee and therefore consequently also those governing the activities of the FAMHP as stipulated in the law of 20 July 2006.

“Development of the FAMHP spearheads”



DEVELOPMENT OF THE 4 SELECTED SPEARHEADS

The majority of FAMHP activities are determined by law and the core activities are essential for public health. These core tasks are at the heart of the organisation and have increased unabated, primarily through the numerous changes to European legislation. Nevertheless in the context of European competition it is important to note that the FAMHP distinguishes itself from “counterparts” in other Member States in terms of its own fields of expertise. Therefore, within the autonomous Agency, in addition to the efficient execution of core tasks, a particular emphasis has been placed on the spearheads where the FAMHP wishes to excel, which in time are to be considered as the FAMHP’s visiting card in the national and European context.

The following 4 spearheads were chosen:

- Oncology (with a particular focus on cancer pain and paediatric oncology)
- Vaccines for human and veterinary use
- Proactive vigilance
- Early Phase Development.

In order to further develop the spearheads, consultations will regularly take place between the FAMHP Executive council, the coordinators for the various spearheads, the coordinator for the support services and potentially relevant contacts within the context of the Coordination committee.
The performance or evolution of each spearhead will be evaluated within the European context; this requires the introduction of quantitative and qualitative Key Performance Indicators (KPI).
Given that the optimal functioning of a spearhead is closely associated with tasks related to the FAMHP competency domains in general, a close collaboration with the operational departments will be essential.

ONCOLOGY

(with a particular focus on cancer pain and paediatric oncology)

ONCOLOGY was selected as one of the spearheads at the end of 2007 due to its significant potential for development and importance to public health; this topic will function as one of the FAMHP visiting cards in future years. Activities for the ONCOLOGY spearhead started at the outset of 2008 with the appointment of the coordinator, Sonja Beken.

VISION AND DEVELOPMENT OF THE ONCOLOGY SPEARHEAD

The development of the ONCOLOGY spearhead is intended to enable the FAMHP to function as a reference point at a national, European and international level within the domain (or within carefully selected sub-domains) of oncology (with a particular focus on treatment of cancer pain and paediatric medicines). This vision implies a close involvement with all phases of the life-cycle of these medicines.

Various strategic objectives have been identified in order to realise this vision:

- Development of an efficient virtual oncology cell (comprised of a project team and working group) including a strong team of internal experts;
- Demarcation of the sub-domains of the spearhead;
- Creation of a national, European and international scientific expertise network;
- Investment in a significant involvement for oncological medicines by:
  - Functioning as a reference point for scientific advice both nationally and within Europe;
  - Making Belgium an attractive Member State for starting clinical trials;
  - Collaborating on peer reviews of central files for obtaining marketing authorisation (MA);
  - Adopting the role of (co-)rapporteur or reference member state (RMS) for MA applications according to European procedures;

  - Developing an efficient system for oncovigilance;
  - Functioning as a reference point for specific aspects of inspection;
- Creation of a functional communication programme both internally (FAMHP) and externally (public, healthcare professionals, relevant industry, European medicines authorities);
- Active participation in national, European and international working groups, committees and scientific conferences.

THE VIRTUAL CELL OR ONCOLOGY PROJECT TEAM AND ONCOLOGY WORKING GROUP

The parties involved in the daily functioning of the spearhead have been subsumed into 2 groups: the virtual cell or oncology project team and oncology working group.

The project team or virtual oncology cell supports the daily functioning of the ONCOLOGY spearhead in the context of the various strategic objectives. In the course of 2008 various actions were identified for the realisation of the strategic objectives. The results of a domain analysis have led to a demarcation of the field of activity of the spearhead (sub-domains). In addition, an emphasis was also placed on the development of a working method (frequency and planning of subsequent meetings, reporting systems) and potential internal and external communication means.

The working group is by definition a more extended, interdisciplinary group working across areas, which is comprised of members of the project team and members of the Committee for Medicinal Products for Human Use (CHMP), Committee for Advanced Therapies (CAT), Paediatric Committee (PDCO) (including the president), PharmacoVigilance Working Party (PhVWP), Scientific Advice Working Party (SAWP) and the Coordination Group for Mutual Recognition and Decentralised Procedure, human (CMDh). Work is being undertaken on scientific aspects associated with the files and knowledge management within the domain; this is being carried out on the basis of monthly meetings which were started in the last quarter of 2008. Advice can be requested at any stage from the Department for Proper Use of Medicines (BUM) of the FAMHP and from members of the Efficacy Working Party (EWP), Safety Working Party (SWP), Biosimilar Medicinal Products Working Party (BMWP), Blood Working Party (BWP) and Quality Working Party (QWP).

DEMARCATION OF THE SUB-DOMAINS OF THE ONCOLOGY SPEARHEAD

A thorough inventory and benchmarking exercise have demonstrated that careful selection of the sub-domains will be required in order to develop a European profile. Selection of sub-domains will primarily have an influence on the involvement in the evaluation of scientific advice (national and European) and Pediatric Investigation Plans (PIP), and will certainly affect the provision of marketing authorisations via European procedures (central - CP, decentralised - DCP and mutual recognition procedure - MRP), as well as the further optimisation of the national network of external experts and the development of internal expertise.

Taking into consideration the predominance of both requests for scientific advice in the European context as well as the central MA system in the field of solid tumours and the specialisation of oncologists who are part of the national network, it is advisable that the ONCOLOGY spearhead concentrates on (adult) solid tumours in the start-up phase. However, the domain of "(adult) solid tumours" is still very broad. Account should also be taken of experiences already acquired and therefore the tough competition at the CHMP level from European Member States such as Denmark, France, The Netherlands, Germany, Sweden and the United Kingdom, particularly in respect of "significant" solid tumour indications such as breast, colorectal and lung cancer.

Proposals for specific sub-domains may be formulated taking into account the CHMP "pipeline", the relevant industry, and existing internal and external expertise. However, this choice needs to be reviewable at any stage, taking into account scientific progress, advice from SAWP, PDCO, CAT, Committee for Orphan Medicinal Products (COMP) and CHMP, as well as the interests of the relevant industry, the aims of the National Cancer Plan set out by Mrs. Laurette Onkelinx, Deputy Prime Minister and Minister for Public Health, and the available internal and external expertise.

It is abundantly clear that it is strategically advisable to limit the selection to 3 sub-domains in the start-up phase:

- Sub-domain 1: Neuro-oncology;
- Sub-domain 2: Advanced Therapies for oncological indications;
- Sub-domain 3: Pediatric oncology.

THE SITUATION IN BELGIUM

The objectives for the ONCOLOGY spearhead are anchored with the 32 initiatives in the National Cancer Plan. The FAMHP has been closely involved in the round table discussions preparing for the publication of the National Cancer Plan ("Treatment and care" of 18 February 2008 and "Research and innovative therapies" of 25 February 2008) and the introduction of the Cancer Plan on 10 March 2008.

The FAMHP's contribution to the various initiatives which directly link in to the inherent responsibilities of the Agency was submitted to Minister Onkelinx's office through an "FAMHP Memorandum regarding the National Cancer Plan". This memorandum describes in detail the various relevant projects within the ONCOLOGY spearhead, the anchoring of the various initiatives in the National Cancer Plan, as well as the budgetary implications. A business plan was drawn up for the ONCOLOGY spearhead for 2009 which is closely associated with the FAMHP contribution to the National Cancer Plan and takes into consideration the different strategic objectives.

FUTURE PERSPECTIVES

The FAMHP not only grants permission to start clinical trials; the Agency is also responsible for following-up, monitoring and evaluating trials. This is undertaken through a close collaboration

with the existing Ethics Committees via the Clinical Trial Task Force (CTTF), an informal structure established in 2003 under the FAMHP mission. Currently, a project to establish a "Scientific – technical council" in the context of the CTTF is being discussed, which would act as a discussion forum between the relevant FAMHP department and the Ethics Committees.

In the context of the National Cancer Plan and the FAMHP spearhead policy a scientific subgroup for oncology should be established within the CTTF in order to discuss critical aspects of clinical oncology research in adults and children at an advanced scientific level. Encouraging clinical trials and the inherent evaluation of applications for these trials, as well as the creation of a scientific subgroup for oncology, means that the FAMHP will need to have the necessary autonomy to attract the essential expertise for this relatively complex domain from the point of concept of innovative medicines.

Currently, Belgium is not involved as (co-)rapporteur for centralised procedures (CP) for registration of oncological medicines. However, the FAMHP is involved in the evaluation of medicines for the treatment of cancer pain and anti-emetics for use during chemotherapy. The significant involvement of the FAMHP in the activities of the PDCO will now require a similar involvement of Belgium in the registration of paediatric oncological medicines, which will require additional efforts by the FAMHP in the short term. In the context of the ONCOLOGY spearhead there also needs to be an additional focus on the effective marketing of generic oncological medicines which in turn will lead to a diversification of therapeutic options for those associated healthcare professionals. In order to enable this the FAMHP intends to develop an extensive external national, European and international scientific network (within the academic world, relevant industry, experts from other competent authorities) via the ONCOLOGY spearhead. The first contacts have taken place and further efforts are being planned following the demarcation of the sub-domains in the ONCOLOGY spearhead. Within the FAMHP the necessary expertise is being developed, administrative support provided and a standardised working method for an internal/external evaluation team is being created.

The aim is within the start-up phase (2009) to acquire some initial involvement in the centralised procedures (CP) for registration of oncological medecines within the selected sub-domains. This involvement will be actively supported through the work of an oncologist as a new replacement member of the CHMP. In addition, the FAMHP will also develop an active profile in providing MA for generic oncological medicines. The needs in terms of budget and personnel have been summarised in the business plan and the FAMHP memorandum regarding the National Cancer Plan.

The development of an efficient system for oncovigilance is being considered in the context of the project "Proactive pharmacovigilance" by the Belgian Centre for Pharmacovigilance

(BCGH-CBPH), which is part of the FAMHP. The project started at the outset of 2008 and aims to record a larger number of adverse effects determined by healthcare professionals and to ensure a better quality of reporting of these adverse effects. Due to the complexity of pharmacovigilance in the context of cancer treatment, there are currently no specific provisions in terms of follow-up. The treatment of cancer requires complex therapies where various techniques are employed (including radiation therapy, computer tomography or CT, and surgery). This creates difficulties for the evaluation and coding of adverse effects. The evaluation of oncological adverse effects (as well as the evaluation of the Periodic Safety Update Report – PSUR, Annual Safety Report - ASR, Suspected Unexpected Serious Adverse Reaction - SUSAR) requires a coordinated approach, in a similar way in which the clinical treatment of cancer requires a multi-disciplinary approach (R.D. 21 March 2003); this includes pharmacists, physicians, oncologists and other associated physician specialists. A rigorous and standardised evaluation methodology needs to be introduced in this context.

Cancer treatments are complex and affect all the FAMHP's competency domains: medicines, blood, tissue, medical material, medical devices and obligations in the context of research programmes. Pharmacovigilance is a very important part of the problems associated with oncological vigilance and is not just limited to a single activity. It therefore seems advisable to allocate the activities in the context of oncological vigilance to a specialist team, where the work and competencies are not solely restricted to pharmacovigilance. The shortage of physicians in the FAMHP is a significant limiting factor for the introduction of new evaluation methods. Filling this gap needs to be a priority. There also needs to be collaboration with academic cancer specialists and an urgent review of existing methods of collaboration.

The development of the ONCOLOGY spearhead is therefore an ambitious project with a view to introducing:

- A specific policy to engage every healthcare professional active in the fight against cancer to report more adverse effects and events;
- A standard methodology for collecting and evaluating oncological reports;
- An archive based on the available IT tools;
- Modified training programmes and information;
- A highly visible and high quality reference centre for oncology information within the FAMHP.

The implementation of this strategy will now need to be worked out completely. It is, however, a complex project with a significant number of questions still outstanding, and therefore a pilot phase will be introduced in the first instance.

There is an urgent need for targeted information to physicians regarding, amongst other things, the anticipated adverse effects of oncological medicines; this is directly associated with the oncological vigilance project and falls within the context of a greater involvement of physicians in the process of cancer treatment. The FAMHP would like to develop this further in collaboration with the Belgian Centre for Pharmacotherapeutic Information (BCFI-CBIP).

Sonja Beken received her Master's degree in Biological Sciences from the VUB in 1993. She completed her doctorate in Pharmaceutical Sciences at that university in 2000 with research in the field of in vitro pharmacotoxicology. During this period she was also employed as a researcher for the Belgian Platform for Alternative Methods (BPAM). Her primary fields of expertise are (in vitro) toxicology and metabolisation and alternative methods for animal trials.

Sonja Beken was appointed in February 2001 as a senior, non-clinical evaluator to the former General Pharmaceutical Inspectorate (AFI-IGP), which subsequently became the DG Medicinal Products of the FPS Public Health, and is now the FAMHP. In this role she is involved in the evaluation of non-clinical data that are part of applications for marketing authorisation (MA) for medicines (human and veterinary, national and European) and providing scientific advice (national and European). In March 2004 she was appointed as coordinator for the Unit of non-clinical evaluators of the former DG Medicinal Products, which is now the FAMHP.

Sonja Beken is a member of the EMEA Safety Working Party (SAWP). She is also a member of the Scientific Advisory Committee of the European Centre for the Validation of Alternative Methods (ECVAM) and, at a Belgian level, of the Professional Ethics Committee of the FPS Public Health. Since January 2008 she has been the coordinator for the ONCOLOGY spearhead.

Sonja Beken: *"The "FAGG-AFMPS 2008" project chose ONCOLOGY as a spearhead given its significant potential for development and significant importance to public health. ONCOLOGY is intended to act as a visiting card for the FAMHP in future years. This choice implies that we, as the FAMHP, will profile ourselves in a relatively new domain of expertise and therefore that we will need to start from scratch to develop an active involvement within the full lifecycle of an oncological medicine. The realisation of the ONCOLOGY spearhead can only happen within the context of a favourable political, social and scientific environment. The fight against cancer is high on the national and European political agendas and the development of oncological medicines is enjoying an enormous boom. The combination of developing cross-cutting internal interaction mechanisms and external networks means the job of a coordinator can be extremely challenging.*

A series of inventories and benchmarking exercises already undertaken have demonstrated that a careful choice of sub-domains is required within ONCOLOGY in order for the Agency to be able to gain importance at a European level. This choice will guide the FAMHP's involvement in scientific advice, and the evaluation of the "Paediatric Investigation Plans" (PIP) and centralised procedures (CP) for marketing authorisation, as well as the further optimisation of the national network of external experts and the development of internal expertise. The availability of a solid national and international scientific network (academic world, relevant industry, experts from other competent authorities) which is representative of the sub-domains, will allow us to function as a reference point for scientific oncological advice, to act as (co-)rapporteur or reference member state (RMS) for assessing marketing authorisation (MA) applications for important products via European procedures and to be actively involved in the evaluation of PIP. In the (middle to) long term we also hope to play an active role in relevant international committees, working groups, seminars and conferences, as well as in collaboration with the EARLY PHASE DEVELOPMENT spearhead, to make Belgium an attractive Member State for organising clinical trials in the field of oncology.".

VACCINES

VACCINES FOR HUMAN USE

VACCINES was also selected as one of the spearheads at the end of 2007 due to its significant potential for development and importance to public health; this topic will function as one of the FAMHP visiting cards in future years.

The FAMHP's work involving vaccines dates back to the end of the 90s. The experts of the Belgian delegation in the CPMP (now the CHMP - Committee for Medicinal Products for Human Use) of the EMEA were appointed as rapporteurs for important vaccines such as Tritanrix HepB (vaccine against diphtheria, tetanus, whooping cough and hepatitis B in newborns), Prevenar (conjugate vaccine against pneumococcus for newborns) and Infanrix Hexa and Penta (vaccine against polio, diphtheria, tetanus, whooping cough, hepatitis B and Haemophilus influenza type b – hexa). Expertise in this field has significantly grown in recent years. Belgium put its name forward as much as possible as candidate for both the evaluation of applications for marketing authorisation (MA), as well as the assessment of scientific advice at both national and European level.

DESCRIPTION OF THE DOMAIN

Vaccinology is a poorly defined field in medicine. Vaccinologists are drawn from a number of different disciplines, the most important of which are epidemiology of infectious agents and immunology. These two disciplines are inextricably linked. A vaccine can only be produced on the basis of epidemiological knowledge and although vaccinology used to be a purely empirical science in earlier times requiring no knowledge of immunology, this state of affairs would be unthinkable today. No vaccines could be developed these days without knowledge of immunology.

The VACCINES spearhead is focused solely on the development of medicines against infectious agents. The so-called therapeutic vaccines or the treatment of cancers through antibodies do not fall within this mission and can be found in the ONCOLOGY spearhead.
The expertise required for evaluating these immunotherapies is different to that required for conventional vaccines. Where there is a relationship between infection and cancer (as is the case for the hepatitis B virus and liver cancer, Human Papilloma Virus and cervical cancer) then these vaccines do fall within the spearhead policy for the VACCINES and ONCOLOGY domains.

VACCINES ARE "IMPORTANT" MEDICINES

Vaccines are part of our fundamental medical armoury and rest on the principle of "prevention is better than cure". These days children in Belgium are vaccinated against 13 different infectious agents. This basic medicine is a very cheap form of medicine if we compare prevention with the cost of curative medicine. Furthermore, the administration of vaccines is the only way to eradicate a disease, as for instance has happened in Europe with diseases such as smallpox and polio.
There is, additionally, a very important ethical aspect: vaccines save lives in many cases and this is certainly the case in developing countries, where there are too few means available to offer proper "curative" medicine.

VACCINES ARE ALSO VERY "CHALLENGING" MEDICINES

These days new vaccines are high technology products. There is no compromise allowed in terms of quality. Vaccines need to be produced by the book; they are, after all, used to treat healthy newborns, children, adolescents, adults and the elderly. The risk to this target group has to be extremely small. This stands in stark contrast to for instance, oncology patients, where a medicine needs primarily to be effective. In addition, vaccines also require a long-term follow-up: are vaccines still effective and even safe 5 or 10 years after the first clinical trials? There is a growing wealth of unfounded and non-scientific criticism based on prejudice that also needs to be considered. Continuous follow-up of all literature regarding vaccines is necessary in a world where there is unfounded criticism.

FUTURE PERSPECTIVES

Within European legislation a new application for MA submitted to the EMEA needs to be assessed by the team with the "best available expertise". This means there is a given amount of competition between the competent medicines authorities in the various European Member States for evaluating files such as these. Expertise in vaccines is limited in Europe. There are seven Member States investing in these matters. It is the FAMHP's intention to develop a pioneering role within this group. The reason behind this ambition is certainly not obvious: the competent medicines authorities in other Member States have the same ambition and vaccinology is, in epidemiological terms, a very broad domain, ranging from the prevention of neonatal pathology to hospital infections to sexually transmitted diseases. However, the development of an academic expertise network should be able to offer some guarantees to these challenges. And there is more: there is also the development of vaccines for developing countries. A good collaboration with our academic centres for tropical medicine will be crucial here. There is a large number of so-called vaccine projects in the pipeline for developing countries, which are also requesting our expertise. The development of an academic network is a priority. At this moment in time the FAMHP already has contacts with various university centres in Belgium and concrete collaborative links have been established to intensify this collaboration.

The provision of scientific advice at the level of the EMEA has been a particular success in recent years. The Belgian delegation for this consists of two effective members and one deputy. The presidency of the Scientific Advice Working Party (SAWP) is also represented by a Belgian expert. Companies developing vaccines have also managed to find their way to "London" (EMEA) for scientific advice. The Belgian delegation is attempting to play an important role in this process by putting its name forward as candidate for evaluating vaccine applications.

The further development of a national framework for formulating scientific advice is an important aspect in preparing European advice. This offers the companies involved the opportunity to discuss their applications in a less formal way with the regulators. On the basis of the Royal decree (R.D.) the FAMHP will develop a national framework for scientific advice, to offer companies the opportunity to discuss "early" questions with the regulators in a less formal way.

Given the complex nature of the files for acquiring MA, the majority of companies opt for a centralised procedure (CP), even although this is currently not compulsory for vaccines. Currently this is only compulsory for biotechnological vaccines. This offers the opportunity to all national delegations to put themselves forward as candidate for evaluating a new vaccine, and this is how in recent years the Belgian delegation has been awarded various rapporteurships.

If the FAMHP is looking to play a pioneering role in this process, we will need to go beyond the current state of affairs and look towards the latest developments. It is therefore critically important to keep up-to-date with the literature and to follow new developments in this specific area. Four scientific meetings have been planned for the academic year 2008-2009, organised by FAMHP employees and external experts. The first took place in September 2008 and considered a highly promising technology: "reverse vaccinology". Around 30 researchers participated in this meeting. It is the intention to organise more of these meetings in the future to consolidate the expertise network and to further develop the scientific knowledge in vaccinology and share this within the scientific network.

Pieter Neels is a physician (UA, 1985). He started his career as a general practitioner (1986-1994) in Berchem (Antwerp). In 1994 his research interests led him to the pharmaceutical industry (Byk Belga: a small subsidiary of what is now Altana). In this role he was responsible for clinical trials in Belgium. In 1997 he was recruited by the then General Pharmaceutical Inspectorate (AFI-IGP), later the DG Medicinal products of the FPS Public Health, and now the FAMHP, as senior evaluator for clinical aspects of applications for marketing authorisation (MA) for medicines in the field of cardiac, renal, and gastro-intestinal diseases. In 2002 vaccines were added to this list. In 2001 Pieter Neels was appointed as a member of the CPMP (now CHMP - Committee for Human Medicinal Products) of the EMEA and became rapporteur for a number of files MA-submitted via the centralised procedure (CP). In 2002 he had to take over the portfolio for MA-applications for vaccines from a colleague. That year saw Pieter Neels getting the vaccinology "bug" and he is currently (co-)rapporteur for more then 20 files.

Pieter Neels has also been involved in numerous scientific advisory notes for vaccines both at a national and a European level. Pieter Neels was invited as rapporteur for important European vaccine files onto the Vaccine Working Party (VWP), which is a group of experts meeting 6 times per year at the EMEA to discuss vaccines. In 2008 he was elected as vice-president to this working group. The World Health Organisation (WHO) has asked Pieter Neels in the last 4 years to participate in various discussion forums on MA for vaccines as a very great deal of scientific information is being generated for the new vaccines falling under his role as rapporteur.

Pieter Neels: *"Originally I thought vaccines were boring, but once bitten it opened up a whole new world of interesting research for me. Vaccines are still being developed empirically to some extent. There is a clear need for epidemiological and immunological data, but … we can't go anywhere without testing the vaccine in the field! We know that certain vaccines work. However, there are some vaccines where we don't know how they work. That's the real challenge for me. An additional factor that makes working with vaccines so interesting to me is the wide variety in this area. Bacteria, viruses and even parasites: All infectious agents are being chased by people who believe a vaccine can be produced against these causes of disease. An additional factor is that money, lots of money has been made available for vaccination of children in developing countries, by, for instance, GAVI, Bill & Melinda Gates foundation, Wellcome, Novartis trust. This stimulus has enabled various important and interesting projects for which there were insufficient funds in the past.*
The aim of our spearhead is to become a major player within vaccinology for providing MA around the world. Previous initiatives have meant that Belgian authorities are already known as significant contributors in this context, however we need to invest in order to 1 maintain this position and 2 develop it further; the domain is very broad and most of the know-how is already present in Belgian universities. This means that the development of this academic network is extremely important. The FAMHP should be considered as the national and international coordination point, as a reference where you can find answers to questions about vaccines throughout the entire vaccine lifecycle: development, MA and pharmacovigilance. This last point is of enormous importance: vaccines are associated with all types of bizarre, non-proven problems; therefore our job is also to play a pioneering role in this process to gather evidence that can tell us whether registered vaccines are safe or not and take the right decisions when required.".

VACCINES FOR VETERINARY USE

The field of immunological medicines for veterinary use is very broad, yet at the same time also highly specific. In 2008 marketing authorisations (MA) for vaccines for veterinary use accounted for 22% of the total MA issued for veterinarian medicines.
In contrast to curative therapeutic treatments, vaccines enjoy the benefit of being able to prevent certain diseases or at the very least being able to limit the effects of disease (reduction of clinical symptoms and/or transfer of the specific pathogen to other animals). Vaccines are the only alternative against the majority of viral illnesses.

VACCINES, IMPORTANT MEDICINES IN VETERINARY SCIENCE

Vaccines for veterinary use are intended to combat a very large number of diseases caused by different types of micro-organisms. Around 160 pathogens can be combated via the vaccination of various target animals (e.g. dogs, cats, cattle, pigs, chickens, horses); these mostly involve viruses and bacteria, but also include protozoa, helminths and fungi. Various modes of administration exist for vaccines for veterinary use: we distinguish between injectable vaccines and products for oral, nasal, oculo/nasal or in ovo administration.
Some vaccines for veterinary use are particularly important in combating regulated pests, zoonoses (for instance, rabies) or certain highly infectious and dramatic diseases for livestock farms that are under epidemiological supervision and subject to health regulations (e.g. bird flu, classic swine fever, foot and mouth disease, bluetongue, Aujeszky's disease, Marek's disease, Newcastle disease, Rabbit Hemorrhagic Disease (RHD), myxomatosis).

In addition to acquiring the desired protection through active immunisation, there is also passive protection of animals via vaccination of the mother. Although vaccines for veterinary use mostly fall under the so-called "classic" vaccines category (=inactivated or weakened), these days increasingly more vaccines are being made by companies through genetic manipulation (genetic engineering). Some so-called "marker" vaccines allow vaccinated animals to be distinguished from infected animals. These vaccines are particularly useful in the context of pathogen eradication campaigns.

Other important aspects are also taken into consideration in addition to the safety, quality and efficacy of the vaccine for the targeted animal species: safety of the user (the individual administering the vaccine), safety of the consumer eating the animal product (some vaccines require a specific waiting time before slaughter) and environmental safety. This applies in particular to the case of genetically modified organisms (GMO), which are covered by a specific evaluation procedure.

During the evaluation of applications for MA of vaccines for which there is only a limited market (for instance, a less significant target animal and/or low frequency disease), account needs to be taken of the "Minor Use/Minor Species" (MUMS) aspect as defined in the relevant European guideline.

In addition to vaccines there are also other immunological medicines, such as immunoglobulins and serums, immunomodulators and medicines destined for immunocastration.

Therefore, immunological medicines are enormously important in veterinary medicine. Furthermore, the veterinary vaccine industry has a strong presence in Belgium, similar to other internationally recognised experts in these products. It is therefore absolutely right and proper for veterinarian immunological products to be included in the FAMHP's activities under the VACCINES spearhead.

DEVELOPMENT OF THE VACCINES SPEARHEAD FOR VETERINARY USE

Various strategic targets have been set which need to be realised prior to the VACCINES spearhead for veterinary use being considered as efficient. A vaccines for veterinary use project team was established to support the daily activities of the spearhead in line with the defined strategic objectives. The team was assembled according to the competencies and responsibilities of the spearhead. The coordinator works alongside the heads of the experts, file managers and inspectors at he FAMHP.

The FAMHP also intends to extend the expertise network both internally (through recruitment and continuing development), as well as externally. The FAMHP Veterinary medicines Unit is already working with various faculties of veterinary medicine, relevant organisations (e.g. the Veterinary Agrochemical Research Centre – CODA-CERVA, the scientific institute of public health - WIV-ISP, the federal food agency – FAVV-AFSCA, the FPS Public Health and the Belgian centre for pharmacotherapeutic information – BCFI-CBIP). A significant number of contacts have already been made in order to strengthen the links between the Veterinary medicines Unit and the outside world and these will continue to be fostered in the future.
On 19 May 2008 an agreement was signed between the Agency and CODA-CERVA. The latter has been designated as having expertise as an "Official Medicines Control Laboratory", recognised by the FAMHP and the European Directorate for the Quality of Medicines (EDQM), for the monitoring of immunological products for veterinary use prior to marketing authorisation for the Belgian market.
This agreement provides for an enhanced collaboration between the two institutions in the evaluation of quality data in applications for MA or associated amendments (variations) for vaccines for veterinary use, "Good Manufacturing Practices" inspection (GMP) and post-marketing reviews (monitoring by the FAMHP on samples taken).
CODA-CERVA recruited two scientific researchers for this in September and October 2008 who will be exclusively involved in this process. The consultative committee, which structures and evaluates the collaboration between the two organisations, met for the first time following the agreement in 2008. At the first meeting the modalities for collaboration between the two organisations were determined and realisations assessed.

ROLE OF THE FAMHP IN THE EUROPEAN CONTEXT

The Belgian representatives in the Committee for Medicinal Products for Veterinary Use (CVMP) have – out of a total of 56 products – assumed the (co-)rapporteurship for 20 immunological products. This qualifies Belgian members as some of the most active members of the CVMP for immunological products. Belgium is also actively represented in the Immunologicals Working Party (IWP) and the Pharmacovigilance Working Party-Veterinary (PhVWP-V). The intention is to continue to strengthen this collaboration within committees, working groups, seminars and national and international conferences in the future.

One of the strategic objectives the FAMHP has set itself in the field of VACCINES for veterinary use is the development of a national and international network where the academic world, as well as relevant industry and experts from other Member States are represented.
In 2008 the Belgian members of the CVMP took on the role of (co-)rapporteur 4 times for acquiring MA for veterinary medicines via a centralised procedure (CP), and one case of a referral procedure. The adoption of rapporteurships for vaccines for veterinary use via CP, via mutual recognition procedures (MRP) and via decentralised procedures (DCP) is one of our priorities. In 2008 Belgium acted as reference member state (RMS) for 1 veterinary vaccine and agreements were also entered into for Belgium to act as RMS for another 4 DCP for vaccines for veterinary use in the near future.

FUTURE PERSPECTIVES

The FAMHP intends to significantly increase its involvement in the lifecycle of immunological medicines for veterinary use by providing scientific advice, evaluating applications for clinical trials in Belgium, adopting (co-)rapporteurships for CP, MRP and DCP for MA of vaccines for veterinary use and developing pharmacovigilance and inspection activities.
Scientific advice regarding vaccines for veterinary use is almost exclusively dealt with at a European level by the Scientific Advice Working Party-Veterinary (SAWP-V). Although the Belgian CVMP member was previously involved as coordinator for formulating scientific advice, no Belgian representatives were invited as a member of the SAWP-V in 2008. The intention is to change this in 2009 with a view to developing the spearhead.
The FAMHP is working on an implementing decree delineating the framework for clinical trials with veterinary medicines in Belgium. A shortage of experts within the FAMHP for the quality of vaccines section is a limiting factor in adopting the role of RMS/(co-)rapporteur; this problem needs to be solved in the future in order to strengthen Belgian involvement in Europe and in order to evaluate the numerous analytical variations of vaccine files within the delimited timeframe, at both national and European level.

Within pharmacovigilance, the intention is to develop an autonomous and effective Belgian centre for veterinary pharmacovigilance in collaboration with other European centres for pharmacovigilance (for instance with Germany for immunological products).

Finally, the FAMHP intends to develop a functional programme for internal (FAMHP) and external communication (public, healthcare professionals, medicines sector, EMEA, national medicines authorities).

Frédéric Descamps is a veterinarian by training (Ulg), but quickly developed an interest in infectiology in the broadest sense. He completed his doctorate shortly after his studies attempting to understand the pathogenesis of infections with microsporum canis (cause of tinea in cats, dogs and humans). Amongst other things, his thesis explored the immune response against a protease caused by this fungus; this was expressed in recombinant form, which was tested as a potential vaccine. At the end of 2003 Frédéric Descamps was appointed as (preclinical and clinical) evaluator to the former DG Medicinal Products of the FPS Public Health, now the FAMHP. His role primarily involves assessing files regarding vaccines and antibiotics for veterinary use. In June 2007 he was appointed deputy member of the Committee for Medicinal Products for Veterinary Use (CVMP) and since March 2009 he has also been a member of the Scientific Advice Working Party-Veterinary (SAWP-V) of the EMEA.

Frédéric Descamps: *"Vaccines for veterinary use are, in my opinion, an exciting and varied domain, in which I have particularly developed a significant amount of theoretical, as well as practical expertise. Thanks to my role as coordinator for the VACCINES for veterinary use spearhead, I'm more involved at a European level, particularly via the CVMP and SAWP-V. The same goes for the FAMHP and the Veterinary medicines Unit. An important detail is that the FAMHP has already acquired an excellent reputation in the field of vaccines for veterinary use, thanks to the work that has been delivered by Paul-Pierre Pastoret and Bruno Urbain, its representatives in the CVMP. It is now important to continue along this road by ensuring (co-) rapporteurships for European (centralised – CP and decentralised - DCP) procedures and scientific advice. Ideally I would prefer the various types of requests (for instance, MA, variations, inspections, derogations to specifications, complaints) regarding vaccines for veterinary use always to be handled in an efficient and scientifically coherent manner, all within the statutory delimited timeframes. This requires a great deal of effort in terms of coordination between numerous departments, services and units of the FAMPH on the one hand and our various partners on the other. The end goal being that the FAMHP becomes recognised on both a national and international level as the reference point for vaccines for veterinary use."*.

PROACTIVE VIGILANCE

The aim of proactive vigilance is to establish a series of actions to prevent adverse events and adverse effects associated with the use of medicines and health products. Proactive vigilance includes pharmacovigilance of medicines for human and veterinary use, materiovigilance (for medical devices for human and veterinary use), haemovigilance (for human blood and blood components) and biovigilance (for human cells and tissues).

THE VISION FOR THE PROACTIVE VIGILANCE SPEARHEAD

The choice of PROACTIVE VIGILANCE as spearhead indicates to external partners (patients, healthcare professionals, relevant industry, political world, government and other national and international authorities) that the FAMHP wants to become a recognised player in the prevention and monitoring of adverse effects and adverse events associated with the use of medicines for human and veterinary use and health products (blood, cells and tissues, medical devices) throughout the entire lifecycle of the products.

Healthcare professionals and consumers of medicines and health products need to be made aware of the utility and obligation (in the case of materiovigilance and haemovigilance) of reporting adverse effects and adverse events associated with the use of medicines and health products to the FAMHP. Furthermore, the report form should be made easy to complete and send to the FAMHP. The system should enable information to be collected about certain categories of medicines and health products if required (=targeted monitoring).

It is also important to produce qualitative evaluations about vigilance information (for instance through the use of case reports, Periodic Safety Update Reports - PSUR, Annual Safety Reports-ASR), enabling the correct, scientifically based decisions to be made in a coherent way. In addition, there also needs to be effective communication about vigilance to both the public and healthcare professionals. In this age of the internet the speed of the information stream is an increasingly important factor in the eyes of the public and care providers. There is therefore also a need to be able to combine rapid, qualitative information.

DEVELOPMENT OF THE PROACTIVE VIGILANCE SPEARHEAD

Awareness campaigns will be required to make healthcare professionals and consumers of medicines and health products aware of the need to contribute to the vigilance programme by reporting any adverse effects and events occurring after medicines and health products have been taken or used. The awareness campaigns regarding pharmacovigilance for medicines for human use, which have been programmed in the context of the “Active pharmacovigilance” project (see Vigilance) were started in 2008 and will continue to be developed. The FAMHP will raise awareness amongst pharmacy students attending

the various Belgian universities through a presentation on this subject. The Agency intends to expand this further to all medical, pharmacy and dental students at a later stage.

A simple guide for veterinary pharmacovigilance has been published on the FAMHP website; together with the associated reporting form this has also been sent to all veterinarians and pharmacists. In 2008 a number of presentations were also made to faculties of veterinary science and regional veterinary associations. Similar presentations will also be organised in 2009.

Although the reporting of adverse events involving medical devices for human and veterinary use (materiovigilance) is compulsory, in reality very little is reported to the FAMHP. The awareness campaigns will therefore need to be continued and intensified.

In the area of haemovigilance the FAMHP Centre for Haemovigilance presented its second annual report, "Haemovigilance in Belgium – Annual Report 2007" in October 2008 to all blood establishments and hospitals, prior to publishing it on the FAMHP website. A similar campaign is now undertaken annually.

Other awareness campaigns involving biovigilance will be provided in the future, in particular the presentation of the annual report. At the start of 2008 forms and user guides were sent to managers of cell and tissue banks in order to encourage voluntary reporting in expectation of the national transposition of the relevant European directive which made reporting of adverse effects and adverse events to the competent authorities compulsory. The basic European directive was transposed into law in December 2008.

There are currently a number of ongoing projects aimed at enabling reports of adverse effects associated with the consumption of medicines for human use ("Active pharmacovigilance" project) and haemovigilance reports to be notified online in the future. The intention is to extend this to pharmacovigilance for medicines for veterinary use, materiovigilance and biovigilance.

At the end of 2007 the FAMHP initiated a programme for specific monitoring of new medicines ("black triangle" – symbol included in the BCFI-CBIP annotated drugs formulary – Gecommentarieerd Geneesmiddelenrepertorium – Répertoire Commenté des Médicaments) with the aim of encouraging healthcare professionals to report adverse effects of medicines with a new active substance to the FAMHP. The specific monitoring of new medicines with a "black triangle" is logical given that their safety profile by definition is less well known than that of medicines that have been on the market for some time. This principle of targeted monitoring may furthermore also be applied to pharmacovigilance of medicines for veterinary use and health products; however a more effective reporting system will need to be developed first.

The first steps were taken for medicines for veterinary use in the context of treatment of “blue tongue”. The information sent to veterinarians now asks for them to report any adverse effects determined using a form provided.
Proactive vigilance requires the available expertise within the FAMHP to be enhanced in order to be able to carry out high quality analyses for the vigilance information. This is required, amongst other things, in the context of pharmacovigilance of vaccines (for human and veterinary use) and oncology (medicinal products for human use). This initiative is part of the global mission of the Agency which includes a specific project where the intention is to further develop the internal and external expertise.

The prevention of adverse effects and adverse events attributable to the use of medicines and health products is closely linked with information for healthcare professionals and the public regarding the risks associated with the use of medicines and health products. The FAMHP regularly publishes reports on its website regarding vigilance problems.

The feasibility of distributing more information about the safety of using medicines and health products is also being considered (for instance, the publication of risk management plans).
Furthermore, the collaboration between the BCFI-CBIP and FAMHP regarding the distribution of information about pharmacovigilance of medicines for human and veterinary use will also be continued.

FUTURE PERSPECTIVES

Thanks to the introduction of a proactive vigilance policy within the FAMHP via the PROACTIVE VIGILANCE spearhead, the safety profile of medicines and health products will be better known, thereby also promoting safer use of these products.
Currently priority is focused on the awareness campaigns for healthcare professionals which are intended to promote the utility and importance of reporting pharmacovigilance of medicines for human and veterinary use. The reporting of adverse effects and adverse events will also need to be encouraged at the same time through the development of an online reporting system. The initial results of the “Active pharmacovigilance” project have been very encouraging given that the number of reports received by the FAMHP has more or less doubled between 2007 and 2008.

Thierry Roisin is a pharmacist (UCL - June 1988). He has worked for the government throughout his entire career: in December 1988 he started work at the General Pharmaceutical Inspectorate (AFI-IGP), later the DG Medicinal Products of the FPS Public Health, now the FAMHP. Having been responsible for the management and evaluation of pharmacovigilance files for a considerable period of time, he was appointed in 2004 as head of the Vigilance Department of the DG Medicinal Products, now the FAMHP. Since 1995 Thierry Roisin has been involved in producing articles regarding pharmacovigilance for the Belgian Centre for Pharmacotherapeutic Information (BCFI-CBIP). Finally, since 1999 he has lectured on pharmaceutical law to pharmaceutical science students at the UCL.

Thierry Roisin: *"Given my experience in the context of my activities in the field of pharmacovigilance and haemovigilance I'm convinced that a proactive vigilance policy will have a positive influence on public health. I regard this as the logical outcome of better prevention of adverse effects and adverse events associated with the use of medicines and health products.*
The expertise currently available in the FAMHP needs to be extended further, and cooperation with external experts needs to be strengthened. Awareness campaigns and efficient reporting instruments are an absolute must in encouraging healthcare professionals and consumers of medicines and health products to provide more and more useful information in the context of pharmacovigilance. My own target is for our external partners to view the FAMHP as a reference centre in the field of prevention and monitoring of medicines and health products.".

EARLY PHASE DEVELOPMENT

There is still a significant need for developing better medicines in a number of domains. For instance, in the case of many types of cancer, "orphan diseases" (rare diseases), chronic diseases and certain infectious diseases which are being tested with chemical medicines and often vaccines as well. It is also evident that there is a need for clinical trials in early phase development.
The EARLY PHASE DEVELOPMENT spearhead is intended to guide these types of clinical trials in Belgium in the best possible conditions and naturally we also hope to receive applications for early phase trials for the two other selected spearheads: ONCOLOGY and VACCINES.
The occurrence of severe, unexpected adverse reactions in an early phase trial will in most cases mean that development will be stopped. However, it is the intention to apply the PROACTIVE VIGILANCE principle to the early development stage. Chemical medicines can continue to be improved for instance in the area of selective action, metabolism, and reduction of adverse reactions. The mechanisms of some more innovative chemical medicines are still unknown or too little is known about them. These medicines may provide a new therapeutic approach for diseases which currently cannot be treated adequately. Biotechnological medicines, cell and gene therapy open up possibilities for improved or totally new types of treatments. Given that these domains are relatively new, this will require changes within the FAMHP, development of knowledge and the opportunity for consulting external experts more frequently. A primary aim of the FAMHP is that the testing of new medicines, even in early phase trials, occurs as safely as possible.

The FAMHP should be able to play a role in this by:

- The professional evaluation of applications submitted for clinical trials;
- The development of procedures for guiding applications and monitoring trials (Suspected Unexpected Serious Adverse Reaction - SUSAR, inspections, standards for units conducting clinical trials);
- Provision of scientific advice to sponsors and researchers regarding products and conducting trials (in consultation with Ethics Committees and if necessary with external experts);
- Participating in developing international guidelines which also include new preclinical models (particularly for medicines with a highly specific mechanism of action which cannot be fully tested on animals);
- Preparation for internationalisation of clinical trial applications for some diseases and for early phase trials;
- Maintaining core knowledge within the FAMHP which can be expanded and transferred.

EARLY PHASE DEVELOPMENT OF MEDICINES

Before a medicine's safety and efficacy can be tested in large groups of patients in late phase II trials and ultimately in phase III trials, the appropriate dose needs to be determined firstly in healthy volunteers and patients. This entails investigating the safety and efficacy of increasing doses of the product and the pharmacokinetics in phase I and early phase II trials. In a number of cases researchers will determine firstly for humans whether there is any value in undertaking full development of a product; this will be done in so-called explorative trials or phase o trials. Although the distinction between the various phases of medicines research is not always very evident, particularly in early trials where this is a continuous process, it is still possible to produce a description of early phase development.

The following studies are considered to be early phase trials in the development of a medicine:

- All studies where a product is being administered for the first time to humans;
- Explorative studies;
- Phase I studies intended to determine the dose, safety and initial pharmacokinetic data in humans, even where this is not the first trial with humans;
- Phase II trials to determine the active therapeutic doses and the Maximum Tolerated Dose (MTD) in patients.

Trials to determine enzyme induction or inhibition, pharmacodynamic or pharmacokinetic interactions with other medicines, as well as evaluating the pharmacokinetics in specific patient populations or evaluating adverse effects, such as QT effects (effect on cardiac rhythm), are all phase I trials. These studies will normally not be considered to be early phase trials in this context, except where this concerns explorative trials.

THE SITUATION IN BELGIUM

Relatively speaking a large number of trials are carried out in the early phases of the development of medicines in Belgium. The number of early phase trials is per capita one of the highest in Europe. Since the publication of the guideline trials for conducting explorative studies in Belgium, in mid June 2007, 25 applications for conducting these clinical trials have been submitted to the FAMHP. In the course of 2008 there were at least another 99 early phase trials of which 43 trials being carried out for the first time in humans, 164 phase I trials (including those not falling under the definition of an early phase trial), 176 phase II trials and 223 phase III trials. The database currently does not always allow a distinction to be made between early phase trials as defined above and later phases. However, the figures do clearly show that there is a considerable number of early phase trials. There are 7 units in Belgium actively undertaking phase I clinical trials and a number of early phase trials are being conducted in centres where there is expertise in specific clinical areas. Given the large number of early phase clinical trials being carried out, the FAMHP has to be able to manage applications for these clinical trials quickly and efficiently. Furthermore, the Agency intends to take a leading role in producing guidelines for these early phase trials.

CONSULTATION WITH THE ETHICS COMMITTEES

Applications for clinical trials in Belgium are evaluated by an Ethics Committee or Ethics Committees and the FAMHP. The Ethics Committee is primarily concerned with the ethical and medical aspects, and is the body that has to provide explicit authorisation to allow a clinical trial to start. The FAMHP is concerned with the evaluation of preclinical and quality aspects of a trial. It is, however, clear that although the Ethics Committees and the FAMHP arrive at their decisions independently, there is potentially a considerable amount of overlap between the interpretation of preclinical and medical aspects. Therefore, organising consultation between both of these bodies for specific trials is also one of the short-term goals. It would also be advisable to have a more general consultation platform in the long term. The FAMHP R&D (research and development) Department has already put a considerable amount of work into fostering collaborations like this with the Ethics Committees. It is evident that the introduction of an electronic consultation platform and opportunities for teleconferencing will be an essential link in this process.

TIME LINES

The law of 7 May 2004 relating to experiments on the human person in Belgium provides that any objections from the FAMHP need to be submitted within a maximum of 28 days following the validation of applications for clinical trials. If no comments have been received within this timeframe, it is tacitly assumed that the FAMHP has approved the commencement of the clinical trial. For phase I studies, and therefore the large majority of early phase trials, the statutory time limit amounts to just 15 days. It is an absolute priority to ensure that the rapid and expert processing of these applications is guaranteed. This goal has been realised in previous years and this needs to be maintained in the future through the use of straightforward procedures. It may be particularly useful in early phase trials to organise meetings with the company involved in order to solve any confusion and problems interactively. There is a need, particularly for early phase trials, to provide some flexibility to allow protocol amendments based on the initial findings in humans. The monitoring of substantial amendments needs to occur in a timely manner in order to guarantee this level of flexibility.

REQUIREMENTS FOR INITIATING CLINICAL TRIALS

An application for initiating a clinical trial should satisfy the requirements stipulated in the ICH M3 document for preclinical data and those determined in the relevant European quality directive. In a large number of cases the applicable standards are clear, although it is sometimes necessary to allow scientifically determined deviations, which are characteristic of the product and/or the early phase of development of the product. Likewise, when these guidelines are reviewed, as is currently the case with the ICH M3, doubt may arise whether it is advisable to follow the current guidance or whether it is better to follow the new, but as yet unapproved, guidelines. A Royal decree (R.D.) is being drafted in order to solve this lack of clarity in advance; this decree will provide the opportunity for requesting scientific advice. Advice such as this will significantly improve the opportunities for conducting clinical trials of medicines in the early phases of development.

EXPLORATIVE TRIALS

It is important that the most promising products are identified so that available means (such as time, trial animals, working time, money) can quickly be concentrated on further development of these products. The best policy is for the development of less promising medicines to be stopped quickly, resulting in fewer means being fruitlessly expended. One of the bottlenecks in this early phase of development is often not knowing whether the medicine will actually have the desired effect in humans or whether the pharmacokinetics is appropriate to achieve therapeutic aims in humans and in a number of cases there are various candidate medicines where it is unknown which product has the most chance of achieving the intended therapeutic action in humans. Often in the early phases the available quantity of the product is relatively limited. Before large-scale production is started it may also be useful to determine whether the particular product is worth the investment. Explorative (phase 0) trials are required in order to make the right choice both quickly and with little expenditure. There is a Belgian guideline which provides a general framework for submitting requests for conducting trials such as these. This guideline is incidentally very similar to that currently under discussion in the review of the ICH M3. The practical application and continuing guidance based on experiences acquired will remain an important core area in future years within early phase development and it may very well be that experiences in explorative studies will have an effect on classic phase I trials. Monitoring of various developments in this field will be a significant challenge for the EARLY PHASE DEVELOPMENT spearhead.

REASONS FOR NOT APPROVING EARLY PHASE TRIALS IMMEDIATELY

Preclinical data have to sufficiently demonstrate that there is a reasonable chance of a therapeutic effect. It is very important for the initial dose, maximum dose and duration of treatment (for an early phase trial normally not longer than and for an explorative study certainly not longer than 14 calendar days) to be adequately justified. The choice of trial animal for the preclinical experiments also requires justification. It is evident that a study cannot be started whenever there are insufficient quality guarantees. Finally, the preclinical data themselves may also give reason for concern. One or more significant commentaries will be provided in these cases. The company will then have one month to respond. In the majority of cases this answer will be sufficient and the study can then be started. Sometimes it can be useful to organise a meeting between the company and the FAMHP in this phase, although this needs to remain an exception to the general rule.

SHORT TERM DEVELOPMENTS

The application of Good Manufacturing Practices (GMP) in the early phases of development of a medicine needs to be adopted as a priority on both the national and European level. Currently, there are only European stipulations in existence for this area. However, these stipulations are not applicable in practice in their current form

for early phase trials. This is because the active product could be produced in a pilot laboratory or because sometimes more manipulation of the product is required in phase I research units in comparison to medicines that are tested in later phases, which would allow work to take place within an environment appropriate to production norms for medicines with marketing authorisation (MA). A text is being prepared within the FAMHP in collaboration with various parties concerned which will enable a realistic approach to be adopted. This should enable inspections to be initiated regarding the application of GMP and Good Clinical Practice (GCP) standards within clinical trials, which is seen as being a priority. These inspections form part of the FAMHP mission.

Other products may also be used in clinical trials with new medicines to stimulate a response in the body against which the effect of the new product can then be determined. In some cases a baseline therapy is provided with other medicines or medicines are provided to counter potential adverse effects or replacement therapy needs to be introduced if it appears during the trial that the new agent does not have an adequate therapeutic effect on the patient or there are too many adverse effects. In most cases this does not cause too many problems if medicines are being used with an MA. However, if a medicine is being administered for which there is no MA, a minimum number of quality standards need to be put in place and a minimum guarantee needs to be provided through the animal tests conducted or existing experience with humans, suggesting that the medicine will not lead to unacceptable effects in trial participants. There are still improvements to be made in terms of legislation and agreements in this area at a national, European and even global level.

VOLUNTARILY HARMONISED PROCEDURE

The Clinical Trial Facilitation Group (CTFG) is a collaborative effort to facilitate and harmonise clinical trials in Europe. Within the CTFG agreements have been made for various competent authorities to voluntarily arrive at a common evaluation for applications for clinical trials whenever this involves multicentre trials with participating centres from different Member States. Although early phase trials mostly involve only a single centre (monocentre), multicentre trials may be required in the case of, for instance, orphan diseases or where there are few non-treated patients available. Trials such as these are a good source of pilot projects for testing a European evaluation procedure.

Walter Janssens completed his veterinary training at the UA in 1975. He was a research assistant at this university until 1979 (Department of Internal Medicine, Physiopathology and Pharmacology section) and research assistant and appointed scientist to the National Fund for Scientific Research (NFWO) at the K.U. Leuven until 1983 (Centre for Thrombosis and Vascular Research). He obtained his doctorate at the UA in 1980. Between 1984 and 2001 he was employed as a researcher in the Discovery Department at Janssen Pharmaceutica, with interests in general pharmacology and particularly cardiovascular and gastrointestinal pharmacology and migraine; this post allowed him to acquire experience in numerous aspects around the early development of medicines. From 2002 he was active in the scientific institute for public health (WIV-ISP) in the field of toxicology and the safe use of industrial chemicals. Since May 2006 he has worked as a senior preclinical evaluator at the then DG Medicinal Products of the FPS Public Health, now the FAMHP, where he is involved in the evaluation of preclinical data which are part of applications for clinical trials and in providing scientific advice. He is coordinator for the EARLY PHASE DEVELOPMENT spearhead and participates in the activities of the Scientific Advice Working Party (SAWP) of the EMEA when he deputises as a member.

Walter Janssens: *"EARLY PHASE RESEARCH IN THE DEVELOPMENT of medicines has to be safe: a number of quality requirements need to be satisfied and a number of preclinical data need to be available in order to demonstrate adequately that the safety of participants can be guaranteed for a given dose and length of exposure, before new potential drugs can be tested in humans.*
The development of a medicine is a continuous process where the finetuning of the chemical–pharmaceutical process and the preclinical and clinical tests both occur in parallel and influence each other. It is clear that quality standards and preclinical data need to be adapted to the phase of clinical development. This last principle has been recognised in the relevant directives. If standards are too strict, then early phase research becomes virtually impossible and the discovery and development of new medicines will be severely impeded. However, if standards are set too low, the safety of trial participants could not be sufficiently guaranteed. Finding the right balance is a fascinating process that links closely to my earlier work. Starting up and maintaining collaborations between the numerous parties involved, such as the relevant industry, phase I centres, Ethics Committees, inspectors and other European Member States, which is necessary to enable a realistic approach and flexibility regarding new developments is an exciting and fascinating enterprise. Different departments and staff within the FAMHP have their roles to play. The evolution of the EARLY PHASE DEVELOPMENT spearhead requires an ad hoc approach with cooperation between various experts rather than pursuing "continuous activity". This is also an exciting experience.".

Report in summary

International relations (IR) Unit

At the start of March 2008 an International relations (IR) Unit was created at the FAMHP through the appointment of an IR coordinator. The aim in establishing this unit is to organise the FAMHP's activities within the context of international relations by coordinating internal and external exchange of information and defending the Belgian position to national and international authorities. We intend to utilise this to produce coherent communication with national and international authorities and in formalising the Belgian position; this will offer policy makers the opportunity to take evidence-based decisions with an eye on the international context.
In the first instance, a full inventory of all of the FAMHP's contributions to international forums was created in order to arrive at a system with the provision of mandates regarding the positions to be taken by the FAMHP. During 2008 the IR Unit was also involved in the preparation and progress of the European benchmarking exercise (BEMA). Preparations were also started for the Belgian presidency in the second half of 2010.

BEMA: European benchmarking exercise of September 2008

The Heads of Medicines Agencies (HMA) have decided to organise a benchmarking exercise between all the medicines authorities of the different European Member States. Following the medicines authorities in London and Bonn it was the Belgian FAMHP's turn at the end of September 2008 to be visited by the three assessors. The aim of this exercise is for all medicines authorities to exchange information, knowledge and expertise in the field of organisation, assessment, pharmacovigilance and inspection (vision, policy and decision-making aspects). The FAMHP IR Unit is responsible for coordinating this. In the first instance, the FAMHP "BEMA team" had to answer a standard questionnaire, and then had to go through a self-evaluation process. Secondly, the 3 recognised assessors (recognised in France, Portugal and The Netherlands, respectively) visited our Agency to focus on a number of points raised in the questionnaire. We are already able to say following the first debriefing that a number of major points were identified within the FAMHP, for instance, our approach to risk management or risk analysis. However, the assessment team's visit also identified a number of weak points, such as the lack of a comprehensive system for guaranteeing quality. The FAMHP was already aware of the lack of this system and work is currently being undertaken to harmonise procedures. A global evaluation will ultimately only be possible once the FAMHP has been provided with the full report; this is expected to arrive at the beginning of 2009.

Report in summary

Project Management Office (PMO)

Six key factors were determined in the course of 2007 reflecting the FAMHP's vision and ambition:

- Recognition at national, European and international level
- Informing the public optimally
- Developing transversality (collaboration across the various departments and services) within the organisation
- Developing partnerships with the healthcare sector
- Realising and establishing a learning organisation culture
- Performing basic tasks in a professional manner.

The vision and ambition, key factors and strategic objectives need to transform our Agency in the mid-to-long term into an effective organisation, a well-oiled machine. A number of concrete projects have been listed in order to achieve these strategic objectives to improve and facilitate the functioning of the organisation. The Program Management Office (PMO) Unit is coordinating the entire process. The PMO Unit was established at the end of 2007 to safeguard the coordination, planning, monitoring and communication of the numerous projects within the FAMHP.

A number of projects have already been realised in 2008; for instance, the online publication of the database of medicines authorised in Belgium, as well as Twister (implementation of computerised P&O processes) and the improved induction of new staff; other projects have made significant progress and will be completed by the start of 2009. These projects include the FAMHP's website, Cartophar (digital cartography of retail pharmacies) and the "Information about the FAMHP" project which has already provided a number of concrete publications (including the three monthly @ctua and the first annual report 2007).

The PMO Unit will continue its work in 2009 and further develop the various activities started up in 2008.
Particular attention will be paid to a number of projects which manifestly and urgently need to "progress" in order to record some convincing results, to allow the Agency to achieve its goals. Every successful project does not only mean a satisfactory achievement for the project leader and his team, it affects the entire FAMHP as well.

Business plan 2008-2012

The FAMHP proposed its draft Business plan for 2008-2012 during the course of September 2008. It is the Agency's intention that this first business plan meets, as far as possible, the government's expectations as formulated in the act creating the Agency. Within the limits of its competency domains the FAMHP has a lasting responsibility for the maximum protection of public health. However, the FAMHP also intends to be an effective public service and a fully fledged partner to the numerous players in the medicines and health product fields, all of whom supported the establishment of the Agency. This means that all of the FAMHP's staff activities need to be coherent and transparent.

The Business plan for 2008-2012 will be transformed into a concrete annual operational plan grouping all intended activities by department/service. The implementation of the new structure and launch of an organisation with realistic ambitions form crucial phases in the intended improvements within the context of realising the Agency's mission, as many have suffered from a lack of stability and under-financing in previous years. The business plan therefore intended to prioritise strengthening the various teams, managing

the backlog, as well as IT and organisational improvements. Secondly, priority will also be given to a system which will allow us to assess our activities on the basis of our strategic and operational objectives. The same will also apply to the provision of a framework for the management of all of the changes that will be introduced as part of this plan. Independently of these priorities and without waiting for them to be realised in full, a number of projects have already been started to transform and achieve the Agency's strategic objectives by 2012 in concrete terms.

The intention here is for us to concentrate on the future of the FAMHP, including within a European and international context.

“FAMHP fields of competency”

FIELDS OF COMPETENCY

The FAMHP is the competent authority in the field of quality, safety and efficacy of medicines and health products.
The Agency works together with healthcare professionals, the relevant industry, academic centres and other competent authorities at a national and international level to guarantee the rational use of medicines and health products required by the public.

In terms of **research and development** (R&D) the FAMHP is responsible for the evaluation, granting of authorisation, monitoring and inspection of clinical trials involving medicines and health products. The Agency also provides scientific advice.

In terms of **registration** or the **granting of marketing authorisation (MA),** the FAMHP is charged with the evaluation of new applications for registration or marketing authorisation (MA) of a medicine or applications for amendments to existing MA.

In terms of **vigilance**, the FAMHP monitors the adverse effects associated with the use of medicines and health products through the collection of information. The Agency collates reports, evaluates these and takes measures, if required.

In terms of **production and distribution**, the FAMHP grants authorisations, recognitions and certificates and reviews whether medicines and health products comply with existing regulations regarding manufacturing processes, distribution, dispensing, import and export. The Agency also monitors (the preparation of medicines) pharmacies and combats illegal practices.

In terms of **proper use** the FAMHP ensures that all parties involved have access to the relevant information to allow medicines to be used in a rational and safe manner. The Agency is also responsible for monitoring advertising for medicines and health products.

R&D (RESEARCH AND DEVELOPMENT)

The R&D (research and development) Department of the FAMHP is responsible for the evaluation and approval of clinical research activities from the first "use" (concept) to very extensive trials with medicines being developed and undertaken by universities and other research centres, as well as the relevant industry.

In general the R&D (research and development) Department safeguards the quality and safety of trial medicines being used in clinical trials, and does so in collaboration with the Ethics Committees. The protection of participants in clinical trials and reliability of the data generated are the fixed, primary goals, as well as the promotion and optimisation of the development process to allow innovative medicines to be quickly accessible to patients.

The department's core tasks are as follows:

- The validation, evaluation and approval of applications for clinical trials;
- Monitoring of approved clinical trials through evaluating and approving amendments, and by monitoring adverse effects or lack of efficacy;
- Collating relevant scientific expertise and making this available to the FAMHP.

In addition, the department also handles applications for making the medicines available for compassionate use programmes and medical need programmes.

Finally, the department is also responsible for providing national scientific and technical regulatory advice and positioning this advice in the European context. This is guaranteed in a number of ways, including a representative from the team attending the EMEA Scientific Advice Working Party (SAWP).

CONCRETE REALISATIONS IN 2008

The Belgian representation in the European working groups was further expanded in 2008. Belgium plays an active role within the Clinical Trial Facilitation Group (CTFG) or sponsoring at the level of the Heads of Medicines Agencies (HMA) and the FAMHP is responsible for the secretariat of the CTFG. A workshop on Early Phase Development was organised by the R&D (research and development) Department in October 2008, mandated by the CTFG.

The FAMHP R&D (research and development) Department also plays a role in a number of European projects. This, for instance, includes the project around the Voluntary Harmonised Procedure (VHP), which will start in 2009; the consultation in the area of Non-Investigational Medicinal Products (NIMP) and substantial amendments.

A number of collaborative partnerships have been optimised internally within the FAMHP, including the handling of reports of unexpected adverse effects and the start of the Good Clinical Practices (GCP) inspections.

Furthermore, the department also set out in 2008 to improve collaboration with other

relevant parties. A number of points for improvement regarding the submission of applications for clinical trials were discussed in various workshops together with a number of sponsors of clinical trials. This resulted, amongst other things, in the publication of circular 528, intended to clarify various aspects regarding the submission and handling of applications for clinical trials.

A transversal working group was established to address the problems regarding declarations of trial medicines located in Belgian companies. Representatives of the R&D (research and development) Department and the Production & Distribution Department of the FAMHP, as well as the relevant industry are present in this group.

There has also been close collaboration with Ethics Committees. In 2008 4 information sessions were organised for fully recognised Ethics Committees to discuss elements of harmonisation and improvements to the current situation. A great amount of preparation has also been focused on the creation of a scientific/technical council which will function as a scientific consultation platform.

The last noteworthy fact is the development of a helpdesk for national scientific/technical advice, which on the one hand involved preparations for the statutory basis of this service, and on the other involved the development and testing of the procedures and documents. The intention is for this to start in 2009.

Some figures

In 2008, there was a significant increase observed in the number of applications for clinical trials and amendments (changes to an existing file) and of the percentage of phase I trials. The absolute number of non-commercial ("academic") trials remained stable.

The provision of scientific advice and the assessment of compassionate use programmes and medical need programmes were all new in 2008 and were handled within the predetermined timelines.

	2007	2008	Increase
Original applications/complete applications for clinical trials	560	633	13 %
Amendments/changes to original applications	1.214	1.504	23 %
Proportion of phase I trials out of the total number of applications	24 %	26 %	2 %
Non-commercial ("academic") trials	7 %	7 %	unchanged
Applications handled within the legally provided timeframe (15-28 calendar days)	95 %	97 %	2 %
Scientific advice	-	41	
Compassionate use programmes	-	4	
Medical need programmes	-	37	

Report in summary

Belgian network for paediatric clinical trials

The FAMHP organised on 24 June 2008 a debate and a workshop for establishing a national network for paediatric clinical trials.

In accordance with the European regulation (art. 44) the intention is for the EMEA with the support of the Paediatric Committee (PDCO) to develop a European network consisting of national networks and specific centres of expertise and to offer these to the relevant industry after accreditation. The aims of this network are on the one hand to significantly improve the care of children and their families by striving for quality and safety of clinical trials and making medicines available as quickly as possible through an effective coordination and maximum participation, and at the same time to avoid unnecessary clinical trials in children.
Networks such as these have already been established in neighbouring countries (Germany and France) and The Netherlands launched the Medicines for Children Research Network (MCRN) on 9 September 2008.

Professor Ramet, president of the Belgian Association for Paediatric Medicine (BVK-SBP) has taken the initiative in establishing a steering group where paediatricians active in clinical trials are represented alongside the FAMHP, the Ethics Committees, hospital pharmacists, the relevant (pharmaceutical) industry and the Clinical Research Organisations (CRO); the aim is to produce a project plan, including financial aspects, within a timeframe of 6 months. The creation of an inventory of all the centres and researchers already active in this domain in Belgium and the identification of opportunities for Belgium and training needs are the first priorities.

Clinical Trial Task Force (CTTF)

The Clinical Trial Task Force (CTTF) is an informal consultative body where various stakeholders are represented. This consultative body comprises representatives of the Minister for Public Health, the FPS Public Health, the Ethics Committees, the Consultative Committee for Bioethics and various sponsors involved in the implementation of the law of 7 May 2004 on experiments on the human person.
The problems and points for improvement concerning the implementation of this act are discussed at meetings. There is no formal mission, but in general terms the CTTF mission consists of guaranteeing and optimising the law of 7 May 2004.

Advanced Therapy Medicinal Products (ATMP)

Since 30 December 2008 the regulation of the European Parliament and of the Council of 13 November 2007 concerning advanced therapy medicinal products has been applicable. Specific regulations have been stipulated in this document concerning the granting of authorisations, monitoring and pharmacovigilance for Advanced Therapy Medicinal Products (ATMP). ATMP refers to medicines for gene therapy, cell therapy or products arising from tissue manipulation. ATMP are subject to a centralised procedure (CP) for acquiring marketing authorisation (MA) in order to utilise the expertise of all European experts. Furthermore an expert committee, the Committee for Advanced Therapies (CAT), was established within the EMEA; Bruno Flamion and Claire Beuneu represent the Agency within that committee.

A transversal working group has been established within the FAMHP which is responsible for the coordination of this matter and the introduction of the new regulations in practice. This consultation process arrived at the following decisions:

- Potential conflicts between the new regulation and current Belgian legislation will be identified and modified where required;
- A list will be compiled of ATMP that have been authorised according to a national procedure (NP) for MA in Belgium;
- The circumstances will be determined in which ATMP fall under article 28.2 of the regulation. This article stipulates that MA is not required for ATMP being prepared according to an individual medical prescription for a given patient within a hospital. “Non routine” preparations such as these continue to fall under the responsibility of the prescribing physician. The regulation states that production, quality and pharmacovigilance standards need to be determined for these products;
- The progress of Good Manufacturing Practices (GMP)/Good Clinical Practices (GCP) for ATMP will be monitored;
- A management strategy for scientific advice for ATMP will be prepared and a procedure drafted to avoid overlap with the activities of the CAT;
- Stakeholders will be identified and information gatherings planned in the course of 2009 with the aim of explaining the implementation process, sharing ideas and obtaining feedback from the relevant industry.

The results of these decisions will become apparent in the course of 2009. The FAMHP is preparing itself to face the challenge that management of these medicines will present in the future.

MARKETING AUTHORISATION

The FAMHP's Marketing authorisation Department is responsible for evaluating new applications and requests for amendments to existing marketing authorisation (MA) with a view to granting authorisation for marketing a medicine or health product. The evaluation is based on current standards and guidelines on the quality, safety and efficacy of medicines and health products.

The department consists of four entities, namely:

- Medicines for human use;
- Homeopathic and herbal medicinal products;
- Medical devices;
- Medicines for veterinary use.

MEDICINES FOR HUMAN USE

Since the Agency was established on 1 January 2007 there has been enormous pressure on the Marketing authorisation Department to deal with applications for MA for medicines for human use.

Between December 2007 and November 2008 147 % more applications were closed. This comprises 6.258 applications for obtaining an MA or variations in 2008 compared to 2.527 in 2007.

2008 was also the year of the stabilisation of working methods and the electronic system for submission and approval of medicines applications, MeSeA.

Regarding medicines for human use, the backlog in handling the applications in terms of dispatching was fully cleared in 2008, and a system based on the risk analysis for handling minor changes (type IB) was introduced.

This year the Marketing authorisation Department also introduced the inactivation procedure, the light MA and the unique registration number.

The variation principles were further developed and the project regarding the management of the variation table was completed.

HOMEOPATHIC AND HERBAL MEDICINAL PRODUCTS

All **homeopathic medicines** sold on the Belgian market need to be notified to the FAMHP. There are two registration procedures for marketing homeopathic medicines in Belgium: the simplified procedure and the full procedure after which an MA is granted. Currently there are various ongoing registration procedures and procedures for obtaining an MA. Each new homeopathic medicine which has not already been notified needs to be authorised/registered before it can be marketed.

The Evaluation commission for homeopathic medicines for human and veterinary use met 10 times in 2008.
The commission dealt with:

- Monitoring of the test phase
  - 113 assessment reports of module 3 as well as responses to questions;
  - Drafting of a standard commentary regarding the "No Assay threshold";
  - Proposing a format for submitting module 5 details for both the simplified and the full procedure.
- Preparing for interaction with:
  - The Homeopathic Medicinal Products Working Group (HMPWG), particularly for the "First Safe Dilution" (FSD) project and the "Justification of homeopathic use" project for which Belgium is acting as rapporteur, as well as for the stability theme;
  - The European Directorate for the Quality of Medicines (EDQM), Homeopathic Manufacturing Methods (HMM) group, for the general monograph on preparation methods for homeopathic raw materials and deconcentration;
  - The handling of requests for modification of notifications.

The Homeopathic and Herbal Medicinal Products Unit participated in 2 meetings of the HMPWG at a European level; Belgium is acting as rapporteur for the "FSD" and "Justification of homeopathic use" projects.

In accordance with the Royal decree (R.D.) of 14 December 2006 there are three procedures for issuing of an MA or registration for **herbal medicinal products**: the full procedure, the "Well Established Use" procedure and a third, specific procedure for traditional herbal medicines as stipulated in article 43 of that decree.

At the start of 2008 an autonomous commission was established: the Evaluation commission for Herbal Medicines.
The commission met 6 times and dealt with the following:

- The first applications for Traditional Use registration (TU);
- The TU notification project;
- The interaction with the "Grey area" consultation platform regarding health claims and the safety of botanicals in the food sector;
- Preparation of scientific advice;
- The link with activities of the Committee on Herbal Medicinal Products (HMPC) via the preparation of monographs by experts and monitoring of the applications relating to health claims.

In December 2008 the Homeopathic and Herbal Medicinal Products Unit also published circular 533 regarding the notification of traditional herbal medicines. Finally, a specific database was developed for this.

MEDICAL DEVICES

The European directives regarding medical devices are referred to as the New Approach Directives. Products may be commercialised without the intervention of a competent authority. The conformity inspection at the manufacturer's is undertaken by a third party (a notified body) who issues a CE certificate. This certificate allows the manufacturer to include the CE conformity marking on the relevant products. Medical devices with a CE marking can move freely within the European Union (EU).

Therefore, on the basis of these European directives the FAMHP is principally charged with supervising the market by monitoring incidents (materiovigilance) and by inspecting manufacturers, distributors and retailers established on Belgian territory. International cooperation is essential given the free movement of goods and there is a necessity for Belgium to participate in meetings between competent authorities and in European working groups.
The FAMHP is also responsible for the notification and supervision of the notified bodies established on Belgian territory. There are two of these organisations in Belgium: Apragaz and SGS Belgium.
Finally, the FAMHP also provides authorisations for clinical evaluations of critical products.

Some figures

Meetings:

- National
  - 7 meetings of the Evaluation commissions;
  - 5 meetings of the consultation platform;
  - 12 meetings of the "Grey area" consultation platform;
  - 12 meetings of the Technical Council for Implants;
- International
  - 19 European meetings.

Inspections of:

- Beauty products;
- Distributors;
- Pharmacies;
- Manufacturers.

Projects:

- Proactive materiovigilance is aimed at encouraging users to report incidents, for instance through the use of an online reporting system;
- Improvement of market supervision;
- Working through the backlog, particularly for the notifications of class I manufacturers.

Progress realised in 2008

The realisation of projects and clearance of the backlog are dependent on available personnel. The personnel specifically recruited for inspections in the context of medical devices are currently being trained. Their presence will promote market supervision but will only be effective once they become operational. Various information campaigns were organised in the wholesale distribution sector and the European directive has been transposed into Belgian law.

The table below demonstrates the number of applications processed.

	2007	2008	Increase
Tax declarations	582	656	13 %
Notifications for distribution	209	134	-36 %
Export certificates	745	729	-2 %
Clinical trials	27	32	19 %
Bespoke manufacturer notifications	13	14	8 %
Class I manufacturer notifications	96	64	-33 %
Materiovigilance	636	805	27 %

VETERINARY MEDICINES

Regarding the **granting of MA** for veterinary medicines we have noted:

- A reduction in the backlog despite a significant rise in the number of newly submitted applications for obtaining an MA. The number of applications closed was
- 45 % higher than the number of applications submitted;
- The Evaluation commission for medicines for veterinary use evaluated 28 % more reports for national procedures (NP) for obtaining an MA in respect of 2007. The number of applications managed for Mutual recognition procedures (MRP) and decentralised procedures (DCP) for obtaining an MA remained approximately stable;
- Four applications were evaluated for temporary authorisation to use a vaccine against blue tongue serotype 8 for the vaccination campaign against blue tongue;
- The Veterinary medicines Unit carried out an active campaign to profile itself as a reference member state (RMS);
- A database for clinical trials was realised;
- The development of the VACCINES spearhead for veterinary use was instigated and included:
  - The publication in @ctua in October 2008;
  - The drafting of the collaborative protocol with CODA-CERVA;
  - The adoption of the RMS-ship for a DCP for obtaining an MA for a vaccine;
  - The adoption of 4 (co-)rapporteurships for the CP for vaccines and 1 rapporteurship for a referral procedure for a vaccine.

Some figures

Meetings:

- 11 plenary meetings of the Evaluation commission for medicines for veterinary use;
- 11 meetings of the Bureau of the commission.

The number of applications closed:

- 507 applications, NP;
- 24 applications, MRP;
- 20 applications, DCP.

(Co-)rapporteurships:

- During 2008 Belgium was RMS in the context of 9 different procedures for obtaining an MA. 2 of these were started in 2008;
- During 2008 Belgium was active as (co-)rapporteur in 3 CP and 1 referral procedure.

Clinical trials processed by the Veterinary medicines Unit:

- 31 applications.

In the area of **pharmacovigilance** of medicines for veterinary use we noted:

- The start of a policy of proactive vigilance for medicines for veterinary use including:
  - Active promotion by sending a guide to pharmacovigilance and a European reporting form to veterinarians and retail pharmacists;
  - The organisation of a roadshow on the pharmacovigilance theme for veterinarians in Flanders and Wallonia;
  - Providing a presentation regarding pharmacovigilance of medicines for veterinary use at a BRAS workshop in December 2008;
  - The development of an active collaboration with the BCFI-VET-CBIP-VET for the Folia veterinaria.
- The organisation of a "Eudravigilance" training programme in collaboration with the EMEA for the associated national industry in April 2008.
- The management of adverse effects in the context of the vaccination campaign against blue tongue serotype 8 and collaboration with the FAVV-AFSCA for this campaign.
- The implementation of the first pharmacovigilance inspection for medicines for veterinary use in December 2008.

Some figures

- In January 2008 23.000 guides and reporting forms were sent to veterinarians and pharmacists;
- Organisation of 10 roadshows in Flanders, 11 in Wallonia; a total audience of 1000 veterinarians was reached in this way.

Report in summary

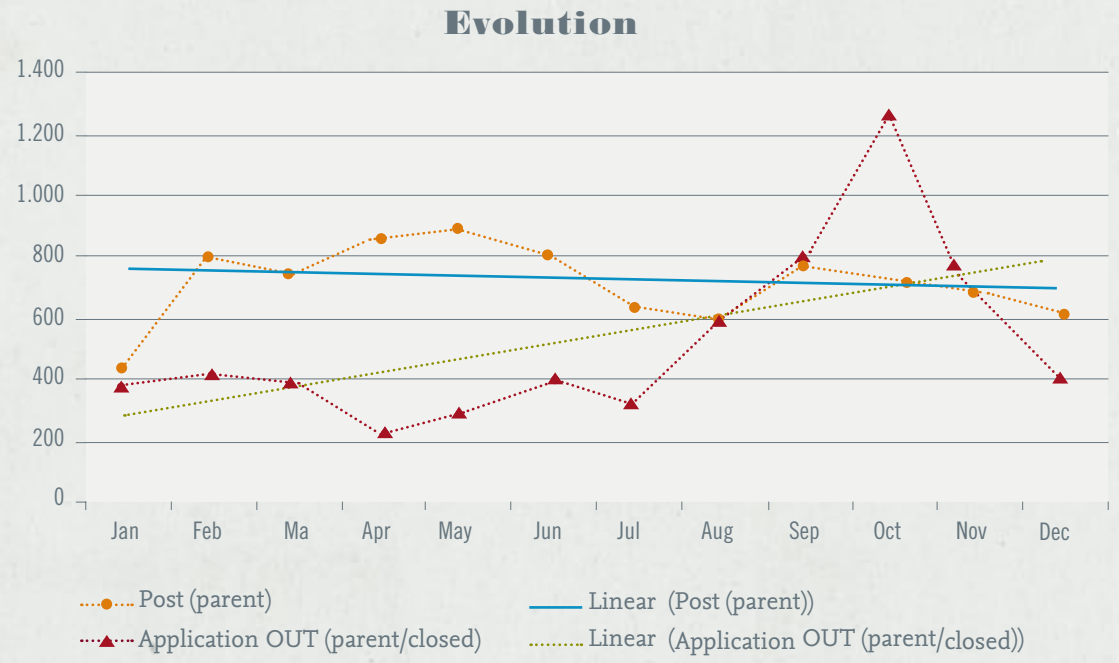
Introduction of a unique Belgian registration number

The FAMHP started to introduce a unique Belgian registration number in June 2008. This project ensures that every medicine with marketing authorisation (MA) in Belgium will have a unique registration number. Each medicine now will have a single number that will remain unchanged throughout the life of the product, whereas before a medicine could have had a number of different registration numbers which could change frequently. The unique registration number consists of the code "BE" followed by a unique 6-digit combination created using an automatic tool. The unique registration number is issued upon granting of an updated MA.

Working through the backlog

• **Medicinal products for human use**

The monthly number of applications submitted remained constant in 2008. The number of applications closed per month increased continuously and by the second half of 2008 exceeded the number of applications submitted. The clearance of the backlog is continuing at a good rate.



• Veterinary medicines Unit

For the fifth year in a row the number of applications closed for obtaining marketing authorisation (MA) within the Veterinary medicines Unit has exceeded the number of new applications submitted. The reduction of the historical backlog is gaining momentum. This is attributable to the synergistic effect of a number of activities undertaken within the Veterinary medicines Unit, such as:

- The effect of the so-called MRP-like procedure which was started in 2007;
- Establishing strict priorities for evaluation;
- A significant strengthening of the unit with 1 evaluator (end of 2007), 1 file manager (end of 2007) and an administrative assistant (June 2008);
- The collaboration with the CODA-CERVA for the evaluation of the quality applications for vaccines.

This has resulted in an increase in the number of applications processed of 81 % in respect of 2007, despite the fact that the number of new applications also increased significantly in 2008. The number of applications closed in 2008 was 45 % higher than the number of applications submitted. This means that the Veterinary medicines Unit has managed to work through a considerable amount of its historical backlog.

	2007	2008	Increase
Number of submitted applications - IN	829	1.138	37 %
Number of closed applications - OUT	915	1.654	81 %
OUT versus IN	+ 86	+ 516	500 %

VIGILANCE

The Vigilance Department's mission is to supervise the safety of medicines for human use (pharmacovigilance), blood and labile blood components of human origin (haemovigilance) and of human cells and tissues (biovigilance). This mission incorporates the collection of information, evaluation of this information and acting on this by taking measures if required.

The department's principal tasks are:

- Collecting and evaluating individual reports of adverse effects originating from marketing authorisation (MA) holders and healthcare professionals;
- Collecting and evaluating periodic reports in the area of pharmacovigilance (Periodic Safety Update report - PSUR) and safety reports regarding clinical trials (Annual Safety Report - ASR) of medicines authorised in Belgium;
- Managing and evaluating applications for five-yearly renewals (RQ) of MA approved via the national procedure (NP);
- Participating in activities in the context of European pharmacovigilance;
- Distributing information in the area of pharmacovigilance for the attention of healthcare professionals and the public;
- Implementing measures proposed after evaluation of pharmacovigilance data;
- Collecting and evaluating information about severe adverse events associated with the collection, testing, processing, storage and distribution of blood or blood derivatives, which may have an effect on the quality and safety of these products;
- Collecting and evaluating information about severe adverse reactions in blood donors and recipients of blood derivatives;
- Implementing measures proposed after the evaluation of haemovigilance data;
- Authorisation of blood establishments, cell and tissue banks;
- Determining prices for blood derivatives, cells and tissues.

CONCRETE REALISATIONS IN 2008

Since the end of 2007 healthcare professionals have been asked to pay particular attention to incidents and adverse effects occurring in respect of medicines for human use that are based on new active substances (medicines identifiable with the "black triangle"); this is referred to as targeted monitoring. These are by definition less familiar medicines for which it is very important to collect data to better evaluate their safety profile. The list of relevant medicines can be consulted on the FAMHP website.

In 2008 the first pharmacovigilance inspections of MA holders took place. The aim of these inspections is to assess whether the pharmaceutical companies are acting in line with the relevant legislation regarding pharmacovigilance. There is a further monitoring of whether the companies concerned have a system for pharmacovigilance at their disposal to allow them to efficiently identify concerns and act appropriately when safety problems occur with a particular medicine.

In October 2008 the second annual report of the FAMHP's Centre for Haemovigilance, "Haemovigilance in Belgium - Annual Report 2007" was presented to blood establishments and hospitals; the report was also published on the FAMHP website. This report offers an overview of the reports, most important findings and recommendations regarding haemovigilance.

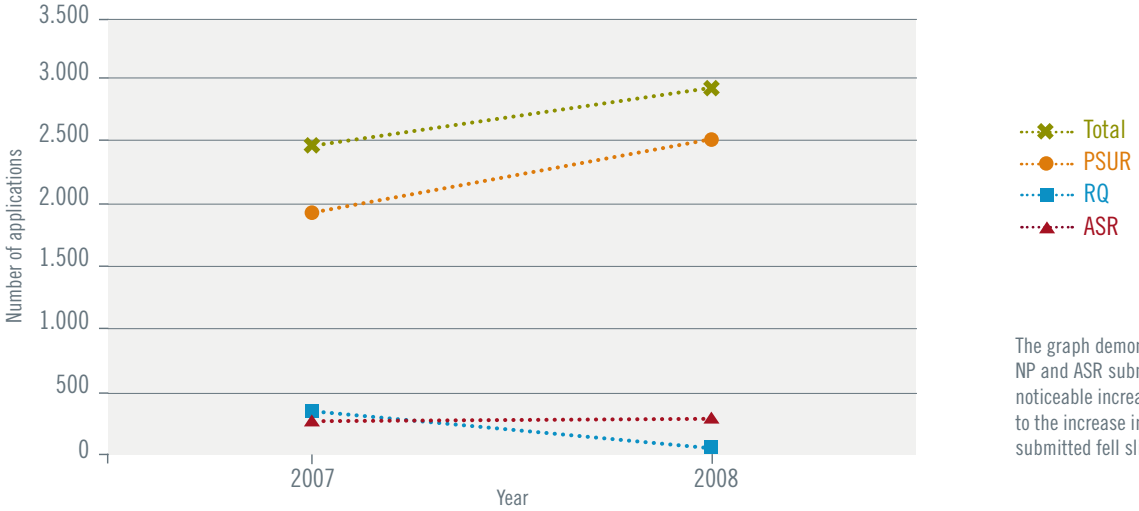
The reporting of severe adverse effects in donors and recipients of cells and tissues, as well as serious adverse effects occurring between the time of donation and distribution of cells and tissues will become compulsory during 2009. In anticipation of this the management of cell and tissue banks are being asked - on a voluntary basis - to start reporting incidents such as these to the FAMHP from 7 March 2008.

Some figures

The table below shows some figures relating to the FAMHP'S vigilance tasks.

	2007	2008	Increase
Individual reports of adverse effects from MA holders and care providers	4.350	4.125	-5 %
• Yellow forms, originating directly from healthcare professionals		616	
• From consumers via Test-Aankoop - Test-Achat		175	
Reports of reactions and incidents in haemovigilance	848	782	-8 %
• From hospitals	314	267	-15 %
• From blood establishments	534	515	-4 %
Pharmacovigilance inspections	-	14	
Hearings	-	6	
Inspections in context of blood, cells and tissues	-	110	

Evolution in the total number of applications for "pharmacovigilance" submitted for evaluation to the FAMHP BCGH-CBPH



The graph demonstrates the evolution in the number of PSUR, RQ of MA granted via NP and ASR submitted to the FAMHP BCGH-CBPH for evaluation. There has been a noticeable increase in the total number of applications to be evaluated, particularly due to the increase in the number of PSUR and ASR submitted. In contrast, the number of RQ submitted fell slightly as - in principle - an MA holder now only needs to submit one RQ.

Report in summary

Project "Active pharmacovigilance"

In January 2008 the FAMHP's Belgian Centre for Pharmacovigilance of medicines for Human use (BCGH-CBPH) launched the "Active pharmacovigilance" project. Currently, this project is part of one of the four FAMHP spearheads: PROACTIVE VIGILANCE.
The aim of the project is to improve knowledge of the safety profile of medicines. This is possible thanks to an increase in the number of reports to the BCGH-CBPH of adverse effects by healthcare professionals and thanks to an improvement in the quality of these reports. Participants in the project have been asked to systematically report all severe, unexpected and/or suspected adverse effects to the BCGH-CBPH, including adverse effects occurring in exceptional situations. This concerns vulnerable groups of people, such as children, pregnant women or breastfeeding women and the elderly; following the administration of vaccines, after the first administration of an "original" or "generic" medicine and following the incorrect use of a medicine.

The following campaigns were undertaken in 2008 in order to publicise the project and increase the number of reports and improve their quality:

- Announcement of the project in the Folia Pharmacotherapeutica of January 2008, on the websites of the FAMHP, the Belgian Centre for Pharmacotherapeutic Information (BCFI-CBIP) and various professional organisations and medical pharmaceutical committees;
- Distribution of a brochure explaining the project; the brochure was distributed in a supplement to the Folia Pharmacotherapeutica of April 2008;
- Correspondence with physicians and pharmacists who had reported one or more adverse effects in the previous years (February 2008);
- Realisation of an electronic newsletter "VIG-NEWS" which is sent to participants in the project (since May 2008). This newsletter contains recent reports about pharmacovigilance from various sources (for instance, the FAMHP, BCGH - CBPH, Food and Drug Administration - FDA, EMEA, scientific publications), a report focusing on a particular class of medicines, as well as practical information concerning pharmacovigilance (for instance, definitions, questions and answers - FAQ);
- Regular publications of articles regarding pharmacovigilance in specialist journals;
- Organisation of awareness campaigns about pharmacovigilance aimed at universities, hospitals and various associations of physicians and pharmacists;
- An individualised and more detailed file to be sent to individuals reporting events in response to each report; this file contains a summary of the evaluation of the report by the BCGH-CBPH working group and the documentation that has served as the basis for this.

The first phase of the project consisted of obtaining the cooperation of a group of approximately 200 healthcare professionals (general practitioners, specialist physicians, retail pharmacists and hospital pharmacists, including clinical pharmacists). The predetermined goals had already been exceeded by the end of April 2008.

At the end of 2008 there were 324 healthcare professionals actively participating in the project. The participants are distributed as follows:

- 52 % physicians, of which 27 % were general practitioners and 25 % physician specialists
- 48 % pharmacists, of which 25 % were hospital pharmacists and 23 % retail pharmacists

The total number of reports directly sent by healthcare professionals to the BCGH-CBPH (via the "yellow form") has more or less doubled since the project was started, with approximately 600 reports in 2008. In addition, half of the total number of yellow forms received by the BCGH-CBPH originated from project participants.

The "Active pharmacovigilance" project has been a great success with healthcare professionals and appears to tap into a real need. The FAMHP hopes that thanks to this project pharmacovigilance will become better integrated into daily clinical practice.

Working through the backlog - Vigilance

• Five-yearly renewal (RQ)

In the context of the FAMHP project "backlog" the Vigilance Department succeeded in 2008 in closing a considerable number of applications for five-yearly renewal (RQ) for marketing authorisation (MA) via the national procedure (NP). In comparison to 2007 the total number of applications still being processed has dropped by almost 30 %.

• EudraVigilance

Since April 2008 the FAMHP has been able to upload reports of adverse effects into the European EudraVigilance database. For technical reasons the electronic reports from the period between 2005 and April 2008 could not be uploaded any earlier. In 2008 an action plan was created in order to work through the backlog that had arisen. Each report of an adverse effect is now processed in two phases. For the first phase "preparing" the electronic report approximately 60 % of the backlog has been removed. The second phase consists of correcting and sending the definitive report to the European EudraVigilance database.

PRODUCTION & DISTRIBUTION

The Production & Distribution Department's mission is, in the interests of public health, to safeguard the availability of quality medicines and health products to patients, to ensure the conformity of manufacturing, import, large-scale distribution and dispensing of medicines and health products to current regulations, standards, guidance, directives, guidelines and international agreements, to combat illegal practices and fraud and to carry out inspections of blood, cell and tissue banks.

The department is divided into 3 units: **Unit I, Unit II** and **Unit III**.

Unit I's principal tasks are:

- Inspections of retail pharmacies, hospital pharmacies and medicinal stocks at veterinarians;
- The retail pharmacies registry and the secretariat of the Commission for the establishment of retail pharmacies;
- The granting of licences for retail pharmacies;
- The secretariat of the Commission for the recognition of pharmacists - clinical biologists.

Unit II is principally concerned with:

- Inspections of the pharmaceutical industry, recognised laboratories, blood, cell and tissue banks and inspections regarding medical devices;
- Dealing with quality problems (Rapid Alert System - RAS);
- The secretariat of the Advisory commission;
- Dealing with the non-availability of essential medicines for Belgian patients;
- Administrative sampling of medicines and follow-up;
- Recognition of qualified persons;
- Granting of authorisations for the manufacture, import, export and large-scale distribution of medicines;
- Granting of certificates for good manufacturing practices (GMP) for medicines;
- Contributing to the EUDRA GMP database;
- Provision of export declarations and certificates;
- Overview and monitoring of stocks of medicines stockpiled in the context of terrorism and influenza epidemics.

Unit III has two principal tasks:

- Monitoring of the legal trade in specially regulated products (narcotics or psychotropic substances, precursors, hormonal and anti-hormonal products, anabolics and anti-infectious agents);
- To combat pharmaceutical crime (counterfeit, falsification, illegal trade, fraud, doping, internet fraud). This task is undertaken by the Special Investigation Unit (SOE-USE), a transversal unit within the inspection units (Unit I, Unit II).

In addition to these 3 units the Production & Distribution Department also houses the secretariat of the Belgian Pharmacopoeia commission.

The secretariat of the Belgian Pharmacopoeia commission is charged with:

- Contacts with the secretariat of the European Pharmacopoeia commission;
- The development of a Therapeutical Magistral Formularium (TMF-FTM);
- The realisation of the Good Officinal Practices guide;
- Compiling a list of medicines that need to be stocked at all times in sufficient quantities for the public in retail pharmacies and hospital pharmacies;
- Licensing of raw materials used by retail pharmacists.

Depending on the type of activity the Production & Distribution Department works in close collaboration with medicines authorities of the other Member States, the European Commission, the EMEA, the Council of Europe, the United Nations, the Pharmaceutical Inspection Cooperation Scheme (PIC/S), the International Narcotic Control Board (INCB) and the Permanent Forum on International Pharmaceutical Crime (PFIPC).

CONCRETE REALISATIONS IN 2008

In addition to the daily activities (inspections, granting of licences/authorisations/certificates, RAS) the Production & Distribution Department also focused efforts in 2008 on gradually solving the backlog of Dutch language establishment applications and transfer applications for retail pharmacies. Additionally, the backlog in respect of raw materials used by retail pharmacies was also tackled.

Work was also undertaken in terms of the organisation of inspections of medicinal stocks at veterinarians and a roadshow around this topic for stakeholders.

In 2008 inspections were started in the context of monitoring the medical devices market and themed inspections of retail pharmacies were continued.

The Production & Distribution Department also assumed responsibility for inspections in the context of granting authorisation renewals to blood establishments, cell and tissue banks in collaboration with the Vigilance Department.

The Production & Distribution Department is charged with organising Good Clinical Practice/GCP inspections and pharmacovigilance inspections; in 2008 a risk analysis was carried out in order to create planning for these inspections.

The Production & Distribution Department also made progress in the area of simplifying the administrative procedures associated with the regulations for establishment applications, transfers of retail pharmacies and the registry of pharmacies.

In order to optimise collaboration with a number of our stakeholders protocols were concluded between the FAMHP and the scientific institute of public health (WIV-ISP), the federal food agency (FAVV-AFSCA), the Veterinary Agrochemical Research Centre (CODA-CERVA) and the federal agency for nuclear control (FANC-AFCN) in order to delineate the responsibilities of all parties concerned.

A protocol has been established between the FAMHP and the Federal Police regarding the trade in precursors and illegal drug production.

Finally, in 2008 the Special Investigation Unit (SOE-USE) started its work. This unit is charged with combating pharmaceutical crime and is of extreme importance given the significant increase in the number of cases of counterfeits.

Some figures

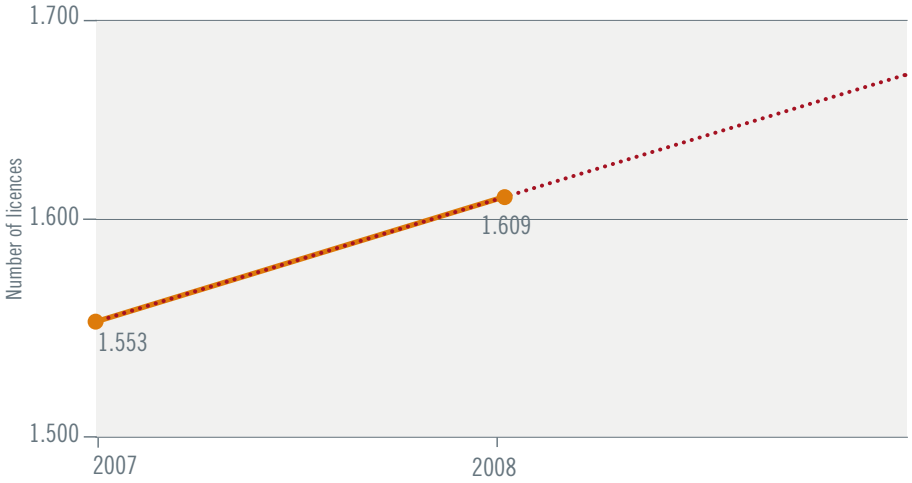
	2007	2008	Increase
Number of **inspections** in			
Retail pharmacies	733	951	29 %
Hospital pharmacies	89	84	- 5 %
Medicinal stocks at veterinarians	54	134	148 %
Pharmaceutical companies			
GMP	69	84	22 %
GDP	68	145	> 100 %
Medical devices (manufacturers; distributors; retailers; care providers; hospitals; medicinal stocks at veterinarians; trade fairs)	-	59	90 %
Number of **official reports** drawn up by inspectors concerning			
Retail pharmacies	86	134	55 %
Hospital pharmacies	3	9	200 %
The pharmaceutical industry	12	12	-
Narcotics and psychotropic substances			
Number of inspections of stock and accounts at manufacturers, wholesalers-distributors, importers and exporters (Fr)	316	297	- 6 %
Number of licence reviews			
Import (Fr)	318	383	20 %
Export (Fr)	49	38	-22 %
Number of inspections of stock and accounts at manufacturers, wholesalers-distributors, importers and exporters (NI)	212	249	17 %
Number of licence reviews	513	537	5 %
Import (NI)	118	87	- 26 %
Export (NI)			
Applications for **import / export licences**	7.514	7.701	2 %
Average period for obtaining a licence: 5 days, unchanged			
Narcotics forms	600.000	600.000	-
Average period for sending a narcotics form: 8 days, unchanged			
Precursors			
Activities licences to market participants	88	81	- 8 %
Import/export authorisations			
Export	200	189	- 5 %
Import	11	17	54 %
Number of pre-export notifications	280	189	- 32 %
Intra-community trade	1.224	1.517	24 %
Suspect orders and transactions	53	52	-2 %

	2007	2008	Increase
Hormones and antibiotics			
Number of new licences (NI)	116	98	- 15 %
Renewals (NI)	99	69	- 30 %
Extension of certificates (NI)	119	124	- 4 %
Number of new licences (Fr)	56	52	- 7 %
Renewals (Fr)	60	45	- 25 %
Extension of certificates (Fr)	39	60	53 %
Export			
Granting of GMP certificates	1.653	1.481	- 10 %
Granting of certificates of pharmaceutical products	3.181	2.730	-14 %
Granting of certificates of medical devices	734	725	-1 %
Granting of other certificates (e.g. certified copies, analysis reports)	276	353	28 %
Average period for obtaining a certificate 14 days in 2007/12 days in 2008			
Export declarations	149	196	31 %
Declaration of toll manufacturing activity	63	114	80 %
Rapid alerts of quality Total number, of which 56 originating in Belgium, 85 from Europe: 46 class 1, 69 class 2, 12 class 3, 8 unclassified, 6 fraud/counterfeit; 129 for medicines for human use, 9 for medicines for veterinary use, 2 for raw materials and 1 for IMP	150	141	-6 %
Licences 14.12.06 and 30.06.2004			
Total number of new applications		41	
Total number of applications for amended licences		274	
Stable situation in comparison with 2007, except for a 33 % increase in amendments of licences for medicines for human use			
Total number of applications for variations to the Advisory commission			
Total number of urgent applications	24	16	- 33 %
Total number of applications processed according to normal procedure	72	114	38 %

	2007	2008	Increase
Commission for the establishment of retail pharmacies; French language chamber			
Total number of applications	52	48	- 8 %
Total number of decisions	55	42	- 23 %
Registry of pharmacies: Fr			
Closed applications		442	
Commission for the establishment of retail pharmacies; Dutch language chamber			
New applications	66	59	-12 %
Ministerial decisions	97	92	-5 %
Registry of pharmacies: Nl			
Closed applications		189	
Pharmacopoeia commission			
Number of Belgian meetings	26	29	11 %
Number of European meetings			
Expert groups: number of meetings in which Belgian experts participated	32	33	3 %
European meeting			
Commission meetings	3	3	-
Number of raw materials approved in the context of the R.D. of 19.12.1997 regarding raw materials used by retail pharmacists	148	364	146 %
Number of monographs approved in the context of the R.D. of 19.12.1997	29	10	- 5 %
Special Investigation Unit			
Number of files: infringements to the R.D. of 12.04.1974		12	
Number of files: other infringements to medicines regulation		18	
Assistance to public prosecutors and number of opened files		101	
Number of postal packages inspected		736	
Recognition of pharmacists-biologists			
French language chamber:			
Total number of new training plans	10	10	-
Total number of approvals issued	8	7	- 12 %
Dutch language chamber:			
Total number of new training plans	7	14	100 %
Total number of approvals issued	5	6	20 %
Recognition of qualified persons			
Total number recognised	27	31	15 %
Number of files waiting (problems in terms of curriculum)		12	
Total number of rejections doubled in comparison with 2006 through an increase in requirements			

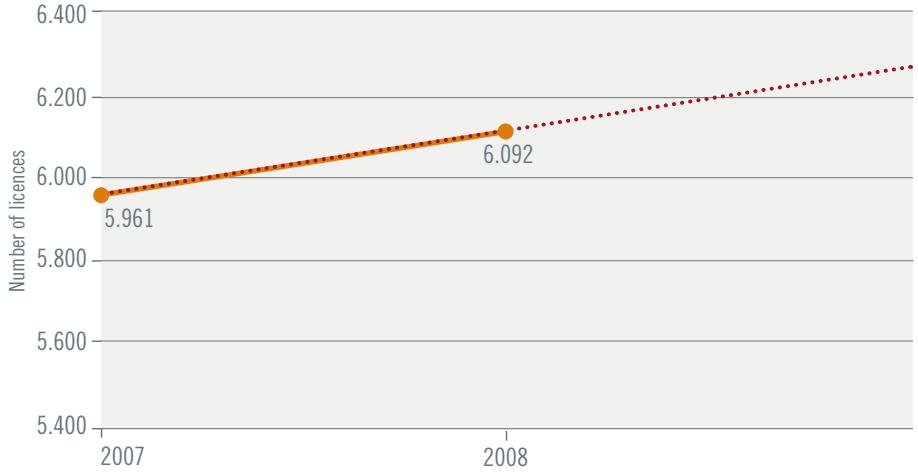
NARCOTICS AND PSYCHOTROPIC AGENTS

Manual import and export licences



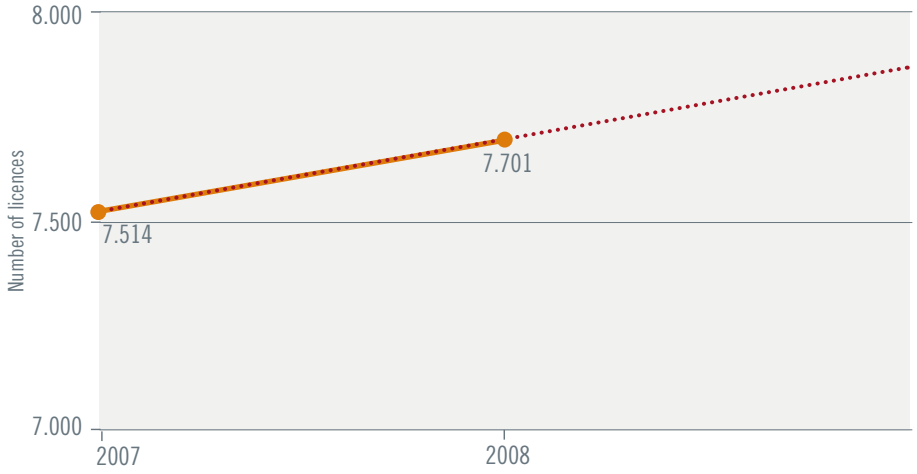
Since 2002 the number of applications for manual import and export licences has followed the trend line with approximately 1.600 manual licences. We noted that applications increased despite a small reduction in 2007 compared to the increase between 2004 and 2006, and that more than 1.600 applications were submitted (1.609) in 2008. The trend line clearly reflects a linear increase.

Automatic import and export licences



Since 2002 the number of applications for automatic import and export licences has followed the trend line and that number is increasing constantly. In 2008, 6092 applications were submitted. The automatic (computerised) requests are processed manually.

Import and export licences (total)



This figure reflects the two previous figures and demonstrates the same trend, that is an annual increase from 350 to 400 applications since 2002. 2008 is following the same upward trend with 7.701 licences as a result.

Report in summary

Backlog - Production & Distribution

• Commission for the establishment of retail pharmacies, Dutch language chamber

On 1 January 2007 the FAMHP had 325 uncompleted files regarding applications (in Dutch) on the basis of the establishment regulations. Above all, the "new opening" applications (and the renewals of these) appeared to be problematical given that the applications dated back to 1981. This concerned 250 old files where closing was difficult.
On 8 July 2008 the R.D. of 12.06.08 appeared in the Belgian journal of acts, orders en decrees (B.S. - M.B.) amending the previous R.D. of 25.09.1974. This amendment may apply to the simplification of the procedure regarding the admissibility of files, amongst other things. The R.D. of 19.09.08 regarding the appointment of members of the Establishment commission appeared in the B.S. - M.B. on 14 October 2008. This allowed two Chambers to operate to remove the backlog of Dutch applications. There were still 203 old files to be processed in 2008.

• Raw materials used by retail pharmacists

After dealing with the backlog in terms of raw materials used by retail pharmacists within the context of the FAMHP "Backlog" project, measures were taken to standardise the management of applications for obtaining marketing authorisation (MA) based on an existing Pharmacopoeia or on existing monographs from pharmaceutical companies. Firstly, procedures were drawn up including a description of the timeframe for the various processing stages of the applications, amongst other things. Secondly, at the end of June 2008 new letters with explanations of the procedure to be followed and the approved timeframes were sent to pharmaceutical companies whose applications were contributing to the totality of the backlog. At the same time in agreement with the companies it was decided to reset the counters to zero again and to apply this to all levels of the processing chain of an application (e.g. the Pharmacopoeia secretariat for raw materials, experts, subcommissions).
Since then and up to the present time all applications based on monographs from pharmaceutical companies are processed according to the different timeframes determined in the procedure. Furthermore, all applications based on existing monographs submitted in 2008 have been processed.

Inspection of medicine stocks at the veterinarians

In 2008, 2 inspectors - veterinarians were appointed to the "Inspection" Unit of the Production & Distribution Department of the FAMHP; 3 more are in training. The task of these inspectors consists primarily of monitoring medicinal stocks at veterinarians.

Various roadshows were organised in order to inform the FAMHP stakeholders about this new activity within the FAMHP and to provide a coherent explanation of recent regulations regarding medicines for veterinary use and the distribution of these products in particular; the roadshows were organised for and in collaboration with the veterinarian professional organisations. In the Dutch speaking region of the country 8 roadshows were presented; 11 were presented in the French speaking region. Opportunities for questions were offered at the end of the presentations. These roadshows were evaluated by the attendees and received a particularly high score; the roadshows also received a lot of coverage in the trade press and have led to a list of questions and answers (FAQ) which is discussed and added to at each presentation.

Risk analysis for the planning of Good Clinical Practices (GCP) inspections

In addition to the unannounced inspections following, for instance, complaints or alerts requiring a specific approach, in terms of Good Clinical Practices (GCP) inspections, we distinguish between the following aspects:

- Focus on clinical trials via the various parties involved (for instance, sponsor of the clinical trial, companies/establishments involved in the realisation of clinical trials);
- Systematic quality monitoring of the management of clinical trials for those involved.

When developing a plan a choice has to be made between an inspection at the level of those involved and/or at the level of the clinical trial(s).

At the level of those involved the risk factors that need to be taken into consideration are those regarding the research sites themselves. Given that the number of those involved is high and the investigator (the person administering the product to the patient) is the only individual who knows the patient, he is the first port of call regarding aspects of public health.

These risk factors are:

- First in human studies; the risks here are at a maximum given the lack of knowledge of the molecule at a human physiology level;
- Hazards associated with galenic form; for instance, the injectable form takes precedence over an oral form;
- The therapeutic domain; the ONCOLOGY and VACCINES domains were chosen in the context of the FAMHP's spearheads and their importance in the context of current progress in the medical world;
- The size of the study population; the larger the population being studied the greater the statistical risk;
- The paediatric population; this choice reflects the vulnerability of this category and the current priority given to this category at a European level.

PROPER USE OF MEDICINES - BUM

The safety and efficacy of medicines and health products are closely associated with the correct use of these products. In order to promote proper use of medicines, both healthcare professionals and patients/consumers, as well as those organisations involved in healthcare need to have easy access to objective, appropriate and up-to-date information.

The Department of Proper Use of medicines (BUM) ensures that all parties concerned have access to the necessary information to allow each individual to judge for themselves and in their own interests what the most appropriate position is to adopt regarding a rational and safe use of medicines and health products.

The most important tasks of the BUM Department are:

- Information provision regarding medicines;
- Supervising advertising and promotional activities for medicines and monitoring information campaigns making reference to medicines.

CONCRETE REALISATIONS IN 2008

The BUM Department collects and distributes relevant information about medicines and health products. The department is responsible, amongst other things, for the management of the database of authorised medicines in Belgium; this has been available on the FAMHP website since March 2008. This database is an important tool used by the FAMHP departments/services in the context of their activities as well as by the BUM Department itself in order to answer the numerous questions posed by healthcare professionals, patients/consumers, relevant industry or other national or foreign authorities.

Healthcare professionals need to be encouraged to promote the rational use of medicines.
In this respect it is important that they have access to objective and constantly up-to-date information in order to adapt their practices to the principles of Evidence Based Medicine.
In this context the FAMHP supports provision of pharmacotherapeutic information to care providers and has concluded partnerships with independent organisations providing objective information about medicines (for instance the Belgian Centre for Pharmacotherapeutic Information – BCFI-CBIP and Project Farmaka, not-for-profit organisations). This process needs to take into consideration the expectations of healthcare professionals in terms of information content on the one hand, and the ease of access and consultation of the data on the other.

It is also essential for rational and safe use of medicines that the information in advertising agrees with the elements approved of when the marketing authorisation (MA) for the medicine was granted. Healthcare professionals when making a therapeutic choice should not be influenced by elements that are not associated with the characteristics of the medicine.
Therefore, each advert for a medicine for human use destined for use by the general public is checked prior to publication. Radio and television advertisements are provided with a licence after advice from the Commission for the supervision of advertising of medicines for human use or after notification to the FAMHP for the other media.

In order to regulate the quality and relevance of messages to the public, a prior licence is required for radio and TV information campaigns about human health and illness which refer directly or indirectly to medicines. This licence is normally issued by the Minister responsible following advice from the Commission for the supervision of advertising for medicines for human use.

In 2008, additional attention was paid to advertising for medicines in the written press for healthcare professionals.

In terms of premiums and benefits, since 1 January 2007 there has been a requirement to request a prior licence when a pharmaceutical company or company selling medical devices wishes to pay the costs of a healthcare professional participating in a scientific gathering including at least one overnight stay.
As provided in the legislation the authorisation procedure for these licences was entrusted to a recognised institution: Mdeon. Mdeon, which works very closely with the FAMHP, published a report of its activities at the end of 2008 and handed a copy of the report from its external auditors to the Agency.
Recognition of Mdeon was extended for a further year on the basis of these documents.

In 2008 the BUM Department continued its provision of information to the pharmaceutical companies, companies producing medical devices, healthcare professionals and healthcare institutions in the context of the legislation regarding premiums and benefits, which has been in force since 2007.

Furthermore, the BUM Department started inspections in 2008 in the field of medical-pharmaceutical conferences in Belgium in order to monitor the implementation of the legislation and the conformity of the advertising messages distributed at such events.

The BUM Department also has a "contact point" available for anyone with information concerning any potential infringements of the statutory requirements for advertising. The information collected is processed by the FAMHP inspectors who will open an investigation to assess whether or not there has been an infringement and who, were necessary, will take appropriate measures.

Some figures

	2007	2008	Increase
Monitoring of advertisements aimed at the public at large			
Radio and television advertisements			
Commission for the supervision of advertising of medicines: number of meetings	16	16	-
Number of licence requests for advertisements	61	77	26 %
Number of licence requests for information campaigns	7	4	-43 %
Other media			
Number of notifications	276	301	9 %
Other reviews			
Total number of files opened after suspicion of infringement		200	
article 9 of the law of 25 March 1964		125	
article 10 of the law of 25 March 1964		65	
article 12 of the law of 25 March 1964		3	
other		7	
Number of files opened after complains	75	101	35 %
article 9 of the law of 25 March 1964		66	
article 10 of the law of 25 March 1964		26	
article 12 of the law of 25 March 1964		2	
other		7	
Number of official reports	11	17	54 %
article 9 of the law of 25 March 1964		14	
article 10 of the law of 25 March 1964		2	
article 12 of the law of 25 March 1964		1	
Number of warnings	27	89	266 %
article 9 of the law of 25 March 1964		57	
article 10 of the law of 25 March 1964		31	
article 12 of the law of 25 March 1964		1	
Number of files dismissed		52	
article 9 of the law of 25 March 1964		28	
article 10 of the law of 25 March 1964		23	
article 12 of the law of 25 March 1964		1	
Number of files transferred to other establishments		19	
article 9 of the law of 25 March 1964		12	
article 10 of the law of 25 March 1964		2	
other		5	
Number of files still open		23	
article 9 of the law of 25 March 1964		14	
article 10 of the law of 25 March 1964		7	
other		2	

Report in summary

Online database of all medicines with marketing authorisation (MA) in Belgium

Since 20 March 2008 the database of all medicines authorised in Belgium has been available on the FAMHP website. This database is the culmination of all the work invested in creating, modifying, adapting, and where necessary preparing the database for publication in four languages (French, Dutch, English and German).
The database of all medicines authorised in Belgium consists of two components: the data regarding medicines for human use with an MA, registration or authorisation for parallel import and the data regarding medicines for veterinary use with an MA, registration, authorisation for parallel import or temporary authorisation for use. These databases contain all types of useful information regarding authorised medicines such as the name of the medicinal product, pharmaceutical form, packaging, marketing authorisation holder, registration number, date of first authorisation, the type of authorisation, composition of the active substance(s), method of administration and whether or not the medicine is being sold in Belgium. The target animals are also recorded for the veterinary medicinal products.

e-MED or the project involving the electronic prescription of medicinal products and the FAMHP "Authentic Medicines Source"

As in our daily lives, innovations in information technology are also playing an increasing part in healthcare.
For instance, electronic prescription of medicinal products is an excellent method for exchanging and processing patient details electronically. Electronic prescription leads to a noticeable improvement in the quality of the prescription, better management of potential errors and administrative simplification for both care providers and patients.

The e-MED project, which was intended to develop a coherent plan of approach to enable electronic prescription of medicinal products, has followed a successful course and achieved its original goals at the end of 2008. The e-MED project was started in 2007 on instructions from the RIZIV-INAMI, the FAMHP and FPS Public Health. The project leader, Johan Van Calster, developed the project, under the supervision of a steering group consisting of leading officials from the relevant public services and the Crossroads Bank for social security, with a working group consisting of representatives of all stakeholders involved and the various subgroups which were specifically focused on legal aspects, organisation and ICT aspects, the Authentic Medicines Source, the budgetary impact, all of which was applied to both hospitals and the ambulant sector.

Electronic prescription, which will function via the e-Health platform, relies on various sources known as authentic sources. These databases contain validated and up-to-date data necessary for electronic prescription. For instance, there is an "Authentic Medicines Source". The FAMHP's specific contribution is to guarantee access to the "Authentic Medicines Source" for both hospitals and the ambulant sector. It is expected that this authentic source will provide all the necessary elements for a prescription, as well as a correct and sufficient supply of medicines.
The data in this source need, of course, to agree with those that have been approved or determined by the competent authority for marketing authorisation – MA (FAMHP), price (FPS Economy) and reimbursement modalities (RIZIV-INAMI), respectively.

As part of its partnership with the Agency, the Belgian Centre for Pharmacotherapeutic Information (BCFI-CBIP) has developed a medicines database of commercialised medicines. This information has been included in software packages being used by physicians when managing their patient files. The FAMHP has expanded the existing convention with the BCFI-CBIP for further development of the existing databases towards an "Authentic Medicines Source" that meets the requirements for use in electronic prescriptions in hospitals and the ambulant sector. This authentic source should also offer prescribers the opportunity to access a reference database for "assistance" or support in writing a rational and safe prescription.
This development of the "Authentic Medicines Source" and the reference database has been financed by the RIZIV-INAMI on the basis of the "RIZIV-FAMHP convention."

“FAMHP Personnel and budget”

PERSONNEL

In 2008, the service level agreement (SLA) with the FPS Public Health for human resources management came to an end. Since 1 June 2008 the P&O Service has been developed into an autonomous service. The service is responsible for HR management and organisational developments within the FAMHP. The most important task is to strive towards optimal efficiency in respect of work undertaken and the professional development of every member of staff and the organisation as a whole.

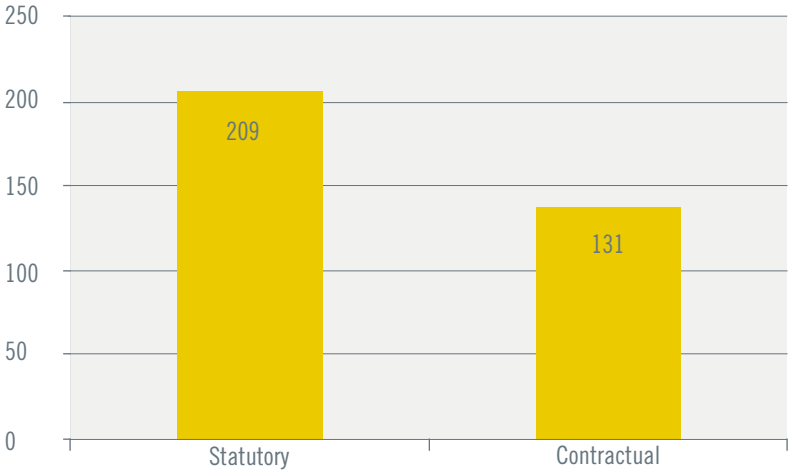
A NUMBER OF FOCUS POINTS FOR 2008

- eHR twister;
  In the course of 2008 Twister was developed in collaboration with the ICT Service for the management of personnel files. In terms of full autonomy for the P&O Service, there was a need for an integrated IT solution to personnel management such as this. The system is specifically designed for staff of the P&O Service and has been operational since midway through 2008. The first phase of the application consisted of various components such as basic details, assignment, financial matters, skills and competencies, basic reporting and organisational development. A second phase was developed in the course of 2008 involving an expansion of the system to enable tailored reporting. Expansions in terms of monitoring sickness absences are also envisaged, amongst other things.
- The trial project “Telework” was started;
- In 2008 the P&O Service was in the middle of a process of change. The implementation of the new organisation chart as envisaged for the start of 2009 requires the P&O Service to develop a definition of its future role in terms of the expectations from the 3 Directorates-General and other departments and services, to implement the 1 % reduction imposed for personnel expenditure and to further develop the strategic decision to convert the FAMHP into a “learning organisation”. The P&O Service’s task is primarily focused on developing a modern human resources policy. A project was started in collaboration with a consultant in order to assess what is required for this. The conclusions were submitted to the Executive Council at the end of 2008 and choices will need to be made regarding the future.
- In the following years efforts will also continue to be expended on dealing with the requirement to evolve the P&O Service from an administrative partner (focus on personnel management) into a business partner in order to realise our strategic goals.

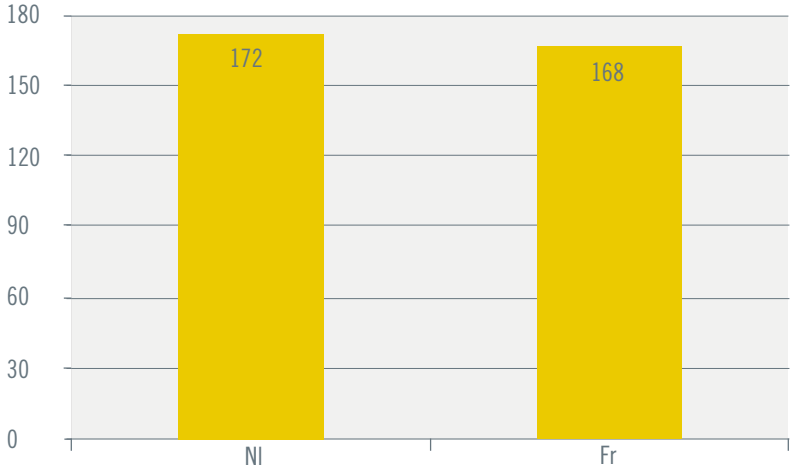
SOME FIGURES FOR 2008

At the end of 2008, there were 102 more staff employed at the FAMHP than when it was established on 1 January 2007. The figures (see page 74 and 75) provide more information about the FAMHP staff.

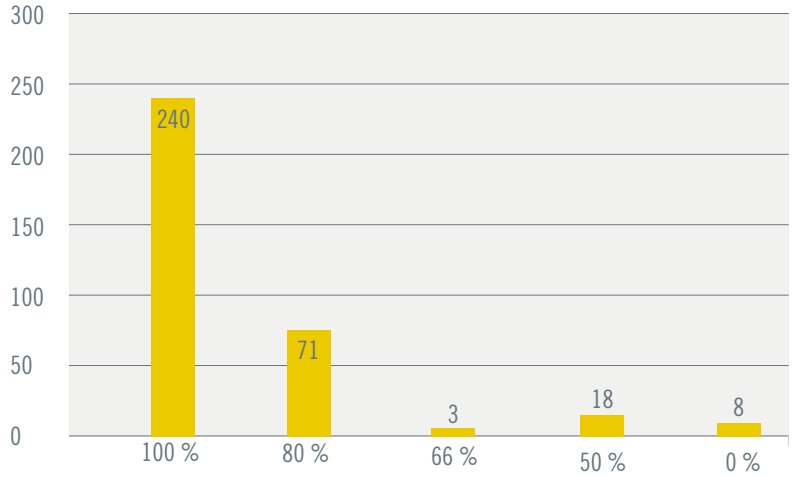
Distribution contractual-statutory



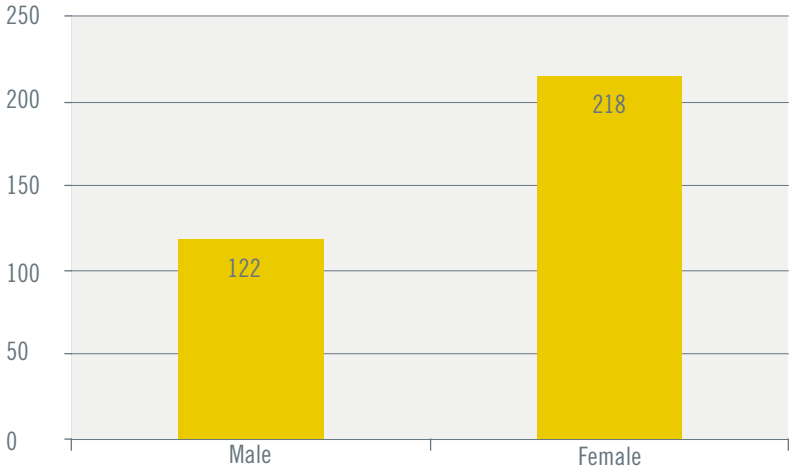
Distribution NI-Fr



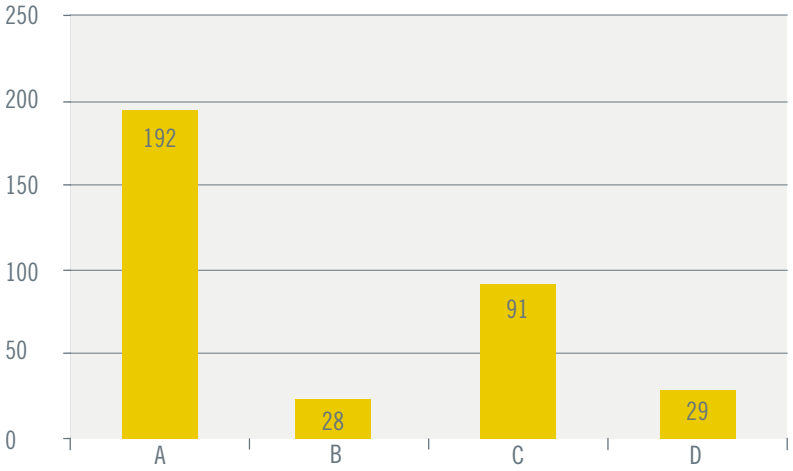
Distribution fulltime-equivalent



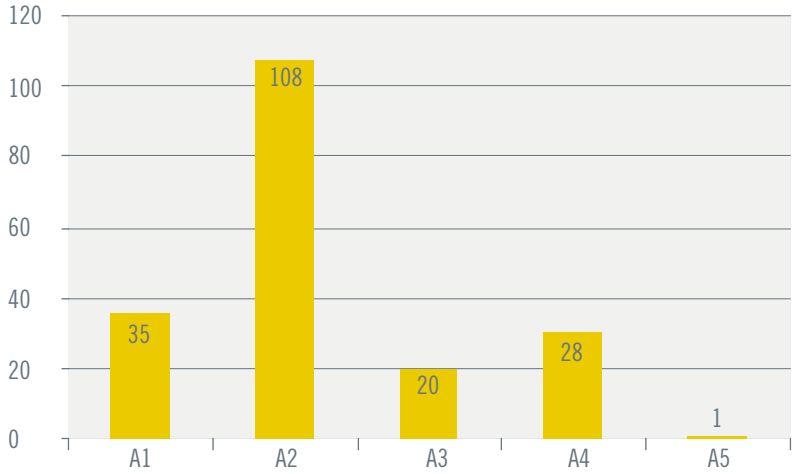
Distribution male-female



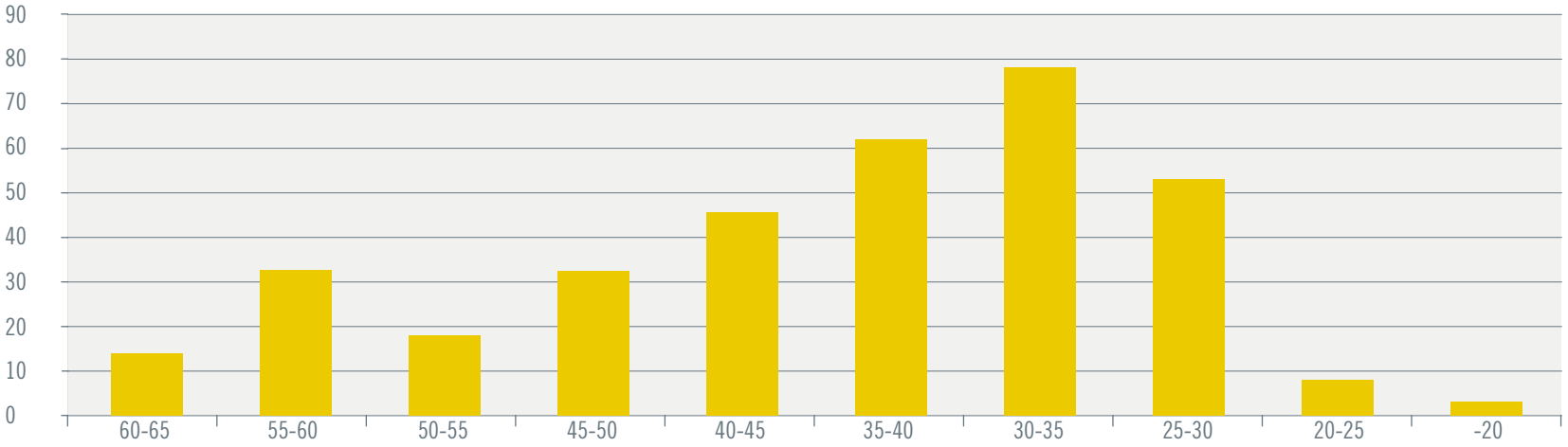
Distribution across levels



Distribution across level A



Age



Report in summary

Trial project "Telework"

The trial project "Telework" started in 2008.
10 % of the staff at that time (30 persons) had the option of applying. The choice of candidates was split into 4 main categories:

- Personnel working with MeSeA;
- Personnel from the support services who were frequent users of electronic data from the FAMHP to which they had access;
- Personnel from operational departments not (or barely) working with MeSeA;
- Clinical and non-clinical evaluators.

Furthermore, the sample also consisted of an equal number of French and Dutch-speaking staff, staff who had opted to telework a fixed or variable number of days per month.

The aims of this trial project are to derive guidelines to regulate teleworking using knowledge of the current state of affairs, e.g.:

- To determine roles that are compatible with teleworking;
- To estimate IT needs (hardware and software) and to ensure effective IT services in the various working environments;
- To create a monitoring system by:
  - Determining measurement tools to evaluate work produced;
  - Developing a procedure describing how the teleworker can be reached (by e-mail alone or via e-mail and telephone).

Integration day within the FAMHP

The first "Integration day for new FAMHP staff" took place on 17 June 2008. Around 40 new staff who started work between 1 October 2007 and mid-May 2008 participated in this event. The aim of this integration day was to clarify the general role of the various departments/services of the FAMHP in an interactive way. There was an opportunity for questions at the end of each presentation.
The second "Integration day for new FAMHP staff" took place on Friday 28 November 2008 for the 32 new staff who started work between mid-May and mid-November 2008.
All interested FAMHP staff will have the opportunity to participate in the next "Integration day".

Information and Communication Technology (ICT)

The realisations of the ICT Service have concentrated primarily on computerisation and simplification of internal administrative procedures, the development of electronic transactions, synergy with external partners and compliance with European guidelines regarding electronic submission and evaluation of applications for obtaining marketing authorisation (MA). The ICT Service of the FAMHP employed partners from the private sector and public sector for a number of these realisations.

The ICT Service provided for the following, amongst other things:

- Strengthening of the technical platforms of the MeSeA system and extensive user testing with a view to system migration;
- Installation of the necessary computer material in the context of the trial project "Telework";
- Functional analysis of the reports of adverse effects in the context of the "Active pharmacovigilance" project;
- Completion and publication of the "Nees" guide;
- The success of the "central repositories" test phase of the EMEA;
- The start-up of the database project "Authentic Medicines Source" in the context of the e-MED project; this took place in collaboration with the Belgian Centre for Pharmacotherapeutic Information (BCFI-CBIP);
- The computerisation of clinical trials for veterinary medicines and scientific and technical advice;
- Technical support for the improvement of the FAMHP image and online communication;
- Further renewal of the computer systems.

A study was also conducted regarding the ICT transition, the term we use to refer to the move away from the current situation of the FAMHP ICT Service. This represents a transition from a service which in terms of infrastructure is still dependent on the ICT Service within the FPS Public Health to an autonomous ICT Service.

The purpose of the study was to evaluate the possibilities for developing to a position of complete autonomy. The ICT transition programme was started in 2008. The Agency and the FPS Public Health have concluded a "best effort ICT" agreement to safeguard the continuity of the ICT services during the transition period.

BUDGET

The main tasks of the Budget & Management control (B&Mc) Service consist of:

- Compiling and monitoring the annual budget;
- Recording income and expenditure and compiling the annual accounts;
- Paying invoices.

SOME ELEMENTS OF THE BUDGET

The 2008 FAMHP budget, approved by Parliament, amounted to 46,403,505 euros in income and 46,386,265 euros in expenditure. Income includes the government grant (17,631,098 euros), paid via the FPS Public Health, and the organisation's own income from the application of various laws and regulations. This includes income from the Agency's reserves estimated at 1,080,000 euros.

DISTRIBUTION OF INCOME FOR 2008

After the closure of the accounts for the year, the income for 2008 came to a total of 49,705,200 euros. This reflects an improvement by 7.12 % of our income in comparison with the budget submitted; the difference relates entirely to the organisation's own income.

The generated income consists of 32,050,200 euros of our own income and 17,655,000 euros of granted funds. Our own income represents 64 % of the total income; the granted funds therefore represent 36 %.

In 2008, the organisation's own income included the balance of 785,035 euros from the exceptional contribution 2007 allocated in connection with the establishment of the Agency by articles 241 and following the programme law of 27 December 2006. This contribution was calculated on the basis of the turnover for medicines (according to the RIZIV-INAMI definition) for 2007 and has not been renewed since.
The analysis of the FAMHP's own income (see graph) shows that 35 % of it comes from taxes and 65 % from fees for service. These taxes are, depending on the various items of applicable legislation and regulations, collected on the basis of the number of packages of medicines and raw materials sold or on the basis of the turnover generated from medical devices. In terms of the FAMHP's own income there is also the special fee from the EMEA to pay for the FAMHP's activities at European level amounting to 3,387,930 euros. There is one other fee that is notable for its intended purposes, since the "clinical trial" contribution (2,114,473 euros) will serve not just to cover the Agency's costs for these trials, but also plays a large role in the financing of Ethics Committees.

As far as taxes are concerned it should be pointed out that the tax on packaging, the so-called "30 centimes and 15 centimes", represented an amount of 3,137,148 euros or 28 % of taxes. However, the most significant tax was the so-called "50 centimes" tax on packaging; this represented 4,028,919 euros or 36 % of taxes. This last tax is not used in the financing of the Agency, but goes in its entirety towards the permanent monitoring of medicines.

DISTRIBUTION OF EXPENDITURE FOR 2008

Expenditure for 2008 amounted to 41,692,475 euros of which 17,393,511 euros was committed to personnel costs (statutory and contractual staff), corresponding to 42 % of expenditure.
Payment of the subsidy for financing NAT blood tests represented another significant item of expenditure of 9,082,342 euros or 22 %.
Two other important expenditure items were the costs incurred in control and analysis assignments for medicines and IT expenditure. These costs amounted to 4,855,342 euros and 2,497,297 euros, respectively or 12 % and 6 %.

REGISTRATION OF TRANSACTIONS AND ACCOUNTING PRINCIPLES

Since the creation of the FAMHP, the B&Mc Service has performed double accounting. As well as complying with legal requirements, this also makes it possible to bring more transparency to the different incoming and outgoing financial flows, bringing more clarity to the financial functioning of the FAMHP for the various stakeholders. All items of income and expenditure are collected within the same IT system so that generating the accounting statement is simple and the statement can be consulted directly.

For its expenditure in 2008 the FAMHP had a total of 4,110 invoices. These invoices are checked and entered into the accounting system after approval. The system automatically (after a double digital signature) performs the payment within the month via the "Isabel" payment system.

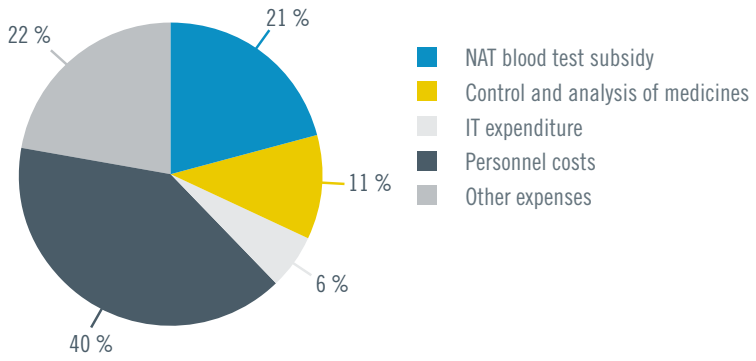
The FAMHP's own income for 2008 came from 19,300 payments into 7 bank accounts, into each of which specific income is paid. The accounts are for payments received from the EMEA, R&D, medicated animal feed, taxes on the number of packages and an account for miscellaneous fees.

After cash has been received, it is booked as income under the correct turnover entry. The turnover is then debited against the fee for each submitted service application. In 2008 this involved booking 17,128 virtual sales in the "computerised day books". Data input happens manually. Information about the bookings, such as the reconciliation of fees and the corresponding service applications, is mainly obtained from the MeSeA system, more specifically through verification of the "public inbox payment tracking". Account allocation data that is not included in MeSeA is communicated by conventional means using the administrative forms and financial folders of the Agency's different departments and services.

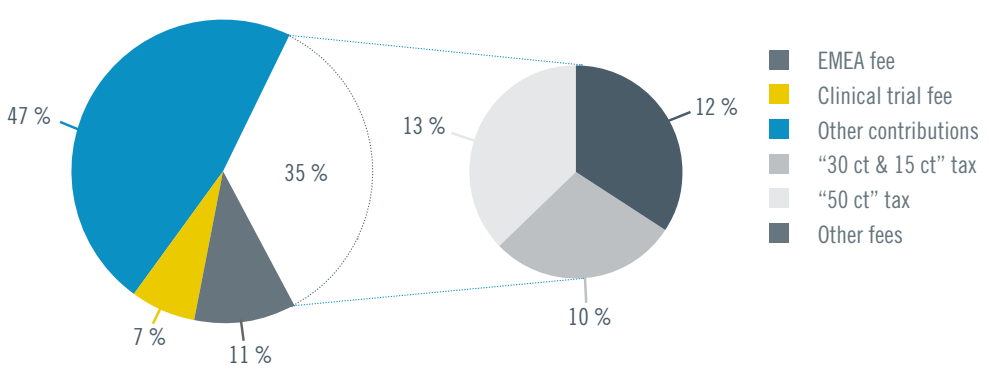
The Agency's budget for 2008 in euros

	Budget	Actual
Income		
Grant	17,631,098	17,655,000
Own income	28,772,407	32,050,200
Total	46,403,505	49,705,200
Expenditure		
Cost of labour and social charges	18,974,421	16,641,914
Other personnel costs	792,000	751,597
Non-ICT operating costs	13,305,792	12,654,504
ICT operating costs	2,950,000	2,186,846
Non-ICT capital expenditure	75,000	64,821
ICT capital expenditure	400,000	310,451
NAT blood test subsidy	9,889,052	9,082,342
Total	46,386,265	41,692,475

FAMHP expenditure 2008



FAMHP Income 2008 (excluding grant)



Report in summary

Launch @ctua

The FAMHP Communication Service launched the first @ctua on the last working day of 2007. @ctua is a three-monthly electronic information bulletin from the FAMHP. The primary focus of the newsletter is the FAMHP stakeholders, but it is also intended for any interested parties. The topics included in @ctua include FAMHP current affairs, competencies, spearheads and the new organisational structure. @ctua is available on the FAMHP website in Dutch and French.

First FAMHP day

On 30 May 2008 the Communication Service organised the first FAMHP day for all FAMHP staff. Team building, meeting people and group spirit were the central themes of the day in a relaxed atmosphere. The "Brussels Upside Town" hike was an informal event with the primary aim for people to get to know their colleagues a little better and improve mutual involvement between staff.
The results of the satisfaction survey demonstrated that a large majority of participants rated the first FAMHP day as good (44 %) to very good (36 %). Staff particularly enjoyed meeting other team members. The primary aim of the team building exercise was perceived by 46 % of staff as developing better communication and by 43 % as experiencing an enjoyable event together, which means the original purpose of the event was achieved! Around 92 % would like another team building exercise to take place and 77 % thinks this is best done annually. On the basis of these exceptionally positive comments it was decided to organise an annual team building activity.

First visit of the Deputy Prime Minister and Minister of Public Health, Mrs Laurette Onkelinx, to the FAMHP and presentation of the first FAMHP annual report

On Wednesday 24 September 2008 the Minister of Public Health, Mrs. Laurette Onkelinx, established the third and final FAMHP committee: the Consultative Committee. This committee offers the Agency advice on its own initiative, or at the request of the Minister responsible or the Chief Executive Officer. It may formulate advice about any matters relating to the policies being followed or to be pursued by the FAMHP. This committee consists of representatives of patients and users, of all sectors who are involved in the matters under the Agency's mission, as well as representatives from the relevant federal public services.

The Chief Executive Officer of the Agency, Xavier De Cuyper, took the opportunity of the establishment of this committee to present the FAMHP's first "annual report": **A MEDICINES AGENCY UNDER CONSTRUCTION – Annual report 2007**. 2007 was a transition year for the FAMHP. The first "annual report" therefore focused development and transition. The report provided the reader with brief summaries of the new Agency's mission and vision and also introduced the most significant activities. At the same time the projects started in 2007 and the Agency's achievements so far were also described. The projects discussed enable the Agency to offer a high quality service to patients and all partners in terms of the following main aims:

- To develop a dynamic and efficient public service thanks to the autonomy acquired and a transparent and professional management;
- To develop into an organisation with national and international reputation;
- To become a learning organisation able to respond to public demands in terms of public health.

The FAMHP's ambition is primarily to turn the slogan, **"Your medicines and health products are our concern"** into a reality.
The 2007 "annual report" is available on the FAMHP website in Dutch, French and English.

A FEW WORDS FROM THE CHIEF EXECUTIVE OFFICER

The Federal Agency for Medicines and Health Products (FAMHP) was established almost two years ago. The establishment of the Agency was an important step towards creating an efficient and modern public service. The organisation received greater levels of autonomy in terms of finance and management, which should allow the Agency to respond more optimally in the future to stakeholder expectations on the one hand and those of the public on the other.

The year 2008 was the first phase in the transformation or switch to a new structure. The 3 committees of the FAMHP have been created and the selection procedure for the 3 Directors-General initiated. The introduction of the new structure, arranging the Agency's activities logically across the three Directorates-General or pillars, will be continued into 2009 as previously planned.

In 2008, action plans were approved for the 4 chosen spearheads which will act as the visiting card in the future.

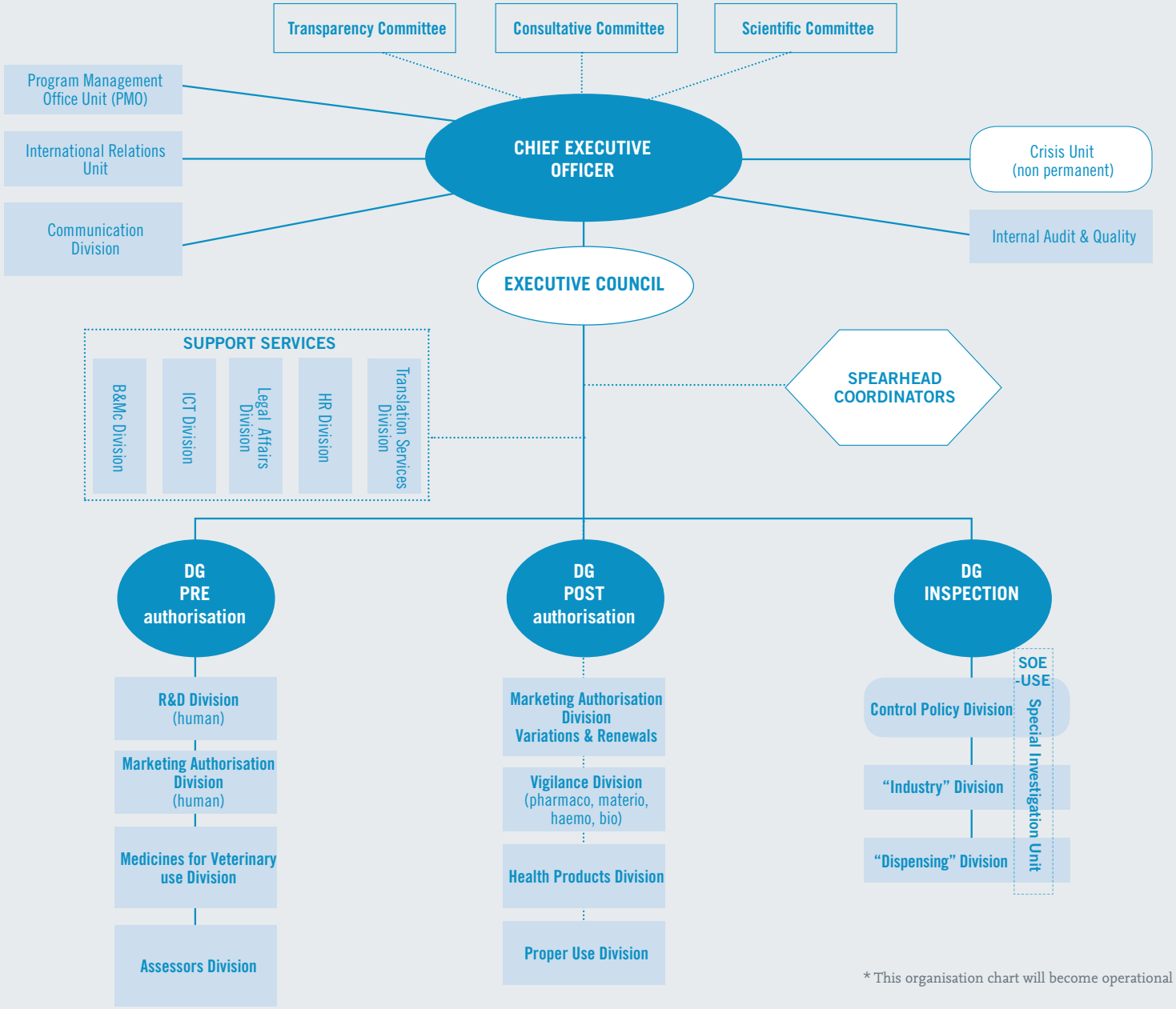
Additionally, numerous projects were started and further developed both within and by the FAMHP. A number of those projects are now in the final stages and will offer excellent prospects for the coming years.

The Belgian Federal Agency for Medicines and Health Products, although it is still undergoing significant developments, will seize every opportunity to ensure higher levels of quality and improve its performance. The anticipated report from the European evaluators following the benchmarking exercise (BEMA) carried out at the FAMHP in 2008 will undoubtedly prove to be an asset for the Agency in this respect.

I would like to take this opportunity to thank everybody for actively contributing to the demonstrable progress in our collective ambitions.

Xavier De Cuyper,
Chief Executive Officer of the FAMHP

ORGANISATION CHART*



* This organisation chart will become operational at the start of 2009

FAMHP COMMISSIONS AND CONSULTATION PLATFORMS IN 2008*

DG PRE AUTHORISATION	DG POST AUTHORISATION	DG INSPECTION
FAMHP COMMISSIONS		
• Evaluation commission for active implantable medical devices • Evaluation commission for homeopathic medicines • Evaluation commission for medical devices • Evaluation commission for medicines for human use • Evaluation commission for medicines for veterinary use • Evaluation commission for traditional herbal medicines • Pharmacopoeia commission	• Evaluation commission for active implantable medical devices • Evaluation commission for homeopathic medicines • Evaluation commission for medical devices • Evaluation commission for medicines for human use • Evaluation commission for medicines for veterinary use • Evaluation commission for traditional herbal medicines	• Advisory commission that is consulted e.g. in cases of non-availability of medicines • Commission for the approval of institutions assigning preliminary approvals for scientific events • Commission for the establishment of retail pharmacies and chambers of appeal (French language chamber and Dutch language chamber) • Commission for the recognition of pharmacists-clinical biologists • Commission for the supervision of advertising for medicines for human use
NATIONAL CONSULTATION PLATFORMS WITH PUBLIC SERVICES AND INSTITUTIONS		
• BAPCOC (with FPS Public Health) • Board for biosafety (with WIV - ISP and the Biosafety and Biotechnology Service) • Consultation platform with FANC-AFCN • Consultation platform with FAVV - AFSCA, FPS Public Health and Public Health Minister's office • "Grey area" consultation platform (with FPS Economie, FPS Public Health and FAVV - AFSCA) • Professional Ethics Committee (with FPS Public Health - DG Animals - Plants - Foodstuffs) • Strategic unit/RIZIV - INAMI	• BAPCOC (with FPS Public Health) • Consultation platform with FANC-AFCN • Consultation platform with FAVV - AFSCA, FPS Public Health and Public Health Minister's office • e-MED (electronic prescription of medicines) (with FPS Public Health and RIZIV - INAMI) • "Grey area" consultation platform (with FPS Economie, FPS Public Health and FAVV - AFSCA) • Guidance committee of the network of medical-pharmaceutical committees • Interdepartmental committee of experts on blood, organs, cells, tissues and embryos (with FPS Public Health, KCE, RIZIV - INAMI and WIV - ISP) • Interdepartmental network on "information society services" (with FPS Economy) • Strategic unit/RIZIV – INAMI • Unavailability of medicines (with RIZIV - INAMI) • Working group on blood of the Belgian Federal Supreme Health Council • Working group on cells, tissues and organs of the Belgian Federal Supreme Health Council	• Consultation platform with FANC-AFCN • Consultation platform with FAVV - AFSCA, FPS Public Health and Public Health Minister's office • DGO - SCM guidance committee (with APB and OPHACO) • e-MED (electronic prescription of medicines) (with FPS Public Health and RIZIV - INAMI) • "Grey area" consultation platform (with FPS Economie, FPS Public Health and FAVV - AFSCA) • Guidance committee of the network of medical-pharmaceutical committees • ICVV – CICSA • Influenza (in cooperation with external partners) • Interdepartmental committee of experts on blood, organs, cells, tissues and embryos (with FPS Public Health, KCE, RIZIV - INAMI and WIV - ISP) • Inter DG drugs (with FPS Public Health) • Mdeon board of management • Non-availability of medicines (with RIZIV - INAMI) • Potassium iodide tablets campaign (with FPS Interior Affairs) • Provincial medical commissions (with FPS Public Health) • Strategic unit/RIZIV – INAMI
CONSULTATION PLATFORMS WITH FAMHP STAKEHOLDERS		
• Clinical Trial Task Force (CTTF) • Consultation platform FAMHP - Industry • TOR • V-amazone	• Consultation platform FAMHP - Industry • Consultation platform FAMHP – Medical devices • TOR • V-amazone	• Consultation platform FAMHP – APB and OPHACO • Consultation platform FAMHP – Medical devices • Consultation platform FAMHP – Hospital pharmacists

* Free translations and explanations

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LEGAL CONTEXT OF THE FAMHP*

- **Regulations governing organisation, functioning and activities of the FAMHP: see www.fagg.be - www.afmps.be**
- **New legislative elements: Laws, Royal Decrees (R.D.), ministerial decisions (M.B. - A.M.) and circulars published in 2008**

LAWS PUBLISHED IN 2008

- Law of 19 December 2008 regarding various stipulations in healthcare - B.S.-M.B. 31.12.2008:
  - Chapter XIV - Federal Agency for Medicines and Health Products.
  - Section 1. Amendments to the Law of 25 March 1964 regarding medicines (art. 81-83).
  - Section 2. Amendments to the Law of 7 May 2004 regarding experiments on the human person (art. 84).
  - Section 3. Amendments to the Law of 20 July on the establishment and functioning of the Federal Agency for Medicines and Health Products (art. 85).
- Law of 19 December 2008 on the acquisition and use of human tissue for medicinal purposes in humans or scientific research - B.S.-M.B. 30.12.2008.
- Programme law (I) of 22 December 2008 - B.S.-M.B. 29.12.2008:
  - Title VII - Public Health. Chapter 2 - Federal Agency for Medicines and Health Products.
  - Section 1. Amendments to the Law of 25 March 1964 regarding medicines (art. 171).
  - Section 2. Amendments to the royal decree no. 78 of 10 November 1967 on the practice of the healthcare professions (art. 172).
  - Section 3. Amendments to the Law of 22 February 1998 on social stipulations (art. 173-174).
  - Section 4. Amendments to the Law of 12 of August 2000 on social, budgetary and various stipulations (art. 175-177).
  - Section 5. Amendments to the Law of 20 July 2006 on the establishment and functioning of the Federal Agency for Medicines and Health Products (art. 178-180).
  - Section 6. Amendments to the Law of 21 December 2007 on various stipulations (I) (art. 181).
- Law of 24 July 2008 on various stipulations (I) - B.S.-M.B. 07.08.2008:
  - Title X, Public Health – Chapter IV. Federal Agency for Medicines and Health Products.
  - Section 1. Amendments to the Law of 25 March 1964 regarding medicines (art. 102-104).
  - Section 2. Amendments to the Law of 7 May 2004 regarding experiments on the human person (art. 105-108).
  - Section 3. Amendments to the Law of 20 July 2006 on the establishment and functioning of the Federal Agency for Medicines and Health Products (art. 109).
  - Section 4. Amendments to the Law of 6 July 2007 on medically assisted reproduction and destination of excess embryos and gametes (art. 110).
  - Section 5. Amendments to the royal decree no. 78 of 10 November 1967 on the practice of the healthcare professions (art. 111).

ROYAL DECREES AND MINISTERIAL DECISIONS PUBLISHED IN 2008

- R.D. of 14 February 2008 establishing the registered offices, organisation and functioning of the FAMHP - B.S.-M.B. 14.03.2008.
- R.D. of 17 March 2008 determining the conditions under which the FAMHP works with other institutions of the State - B.S.-M.B. 11.04.2008.
- R.D. of 16 April 2008 on the grant awarded to the FAMHP - B.S.-M.B. 16.05.2008.
- R.D. of 1 June 2008 permitting the vaccine for veterinary use against Japanese encephalitis - B.S.-M.B. 09.06.2008.
- R.D. of 12 June 2008 on establishing pharmacies - B.S.-M.B. 08.07.2008.

* Free translations and explanations

- R.D. of 30 June 2008 on the grant awarded to the FAMHP - B.S.-M.B. 18.07.2008.
- R.D. of 21 August 2008 on the award of a subsidy to blood establishments of 2008 - B.S.-M.B. 26.09.2008.
- R.D. of 21 August 2008 amending the R.D. of 25 September 1974 on the opening, transfer and merger of retail pharmacies - B.S.-M.B. 03.10.2008.
- R.D. of 18 September 2008 amending the R.D. of 30 March 1976 for a contribution intended to finance the monitoring of medicines and assignments resulting from the implementation of the Law of 25 March 1964 on medicines - B.S.-M.B. 21.10.2008.
- R.D. of 28 October 2008 establishing the composition and functioning of the Mixed Commission and implementing article 1, paragraph 2 of the Law of 25 March 1964 on medicines - B.S.-M.B. 19.11.2008.
- M.B.-A.M. of 31 October 2008 establishing the price of certain types of tissue of human origin - B.S.-M.B. 14.11.2008.
- R.D. of 17 December 2008 amending the R.D. of 19 October 1978 on regulations regarding retail pharmacies and medicine stocks in care institutions - B.S.-M.B. 23.12.2008.
- R.D. of 17 December 2008 on the monitoring undertaken by the FAMHP - B.S.-M.B. 23.12.2008.

CIRCULARS PUBLISHED IN 2008

- 11.01.2008: **circular 503**, to holders of a marketing authorisation or a registration. For the attention of those responsible for pharmaceutical information. Transfer of samples of medicines for human use: reporting of details to the Federal Agency for Medicines and Health Products (FAMHP).
- 30.01.2008: **circular 500**, for the attention of retail pharmacists, marketing authorisation holders for wholesale trade in medicines and wholesale distributors. Dental medicines.
- 27.02.2008: **circular 513**, to manufacturers, importers, distributors and marketing authorisation holders or registration holders for medicines. To manufacturers, importers and distributors of medical devices. Scientific events with at least one overnight stay. Reminder of the requirement to have this reviewed by Mdeon.
- 02.2008: **circular 512**, to presidents of the Ethics Committees. Outstanding payments to the Ethics Committees (years 2004-2005). Indexation of amounts to be paid for experiments. Details for the interactive website. Activity reports 2007.
- 03.2008: **circular 515**, to presidents of Ethics Committees. Amendments to the list of Ethics Committees with full authorisation.
- 02.04.2008: **circular 514**, for the attention of hospital pharmacists. Outsourcing of magistral preparations
- 08.04.2008: **circular** + registration requests regarding wholesale distributors, to holders of marketing authorisation for wholesale in medicines with a statutory public service obligation (wholesalers – distributors). By application of article 272 of the R.D. of 14 December 2006 on medicines for human and veterinarian use.
- 21.04.2008: **note 518**, to professional practitioners in the healthcare sector. Scientific events with at least one overnight stay. Reminder of the requirement to have this reviewed by Mdeon.
- 03.05.2007: **circular 490** + application form MA + Guidance on the e-submission of renewal of a national Marketing Authorisation to holders of marketing authorisation for a medicine for human use. All those with responsibilities in terms of pharmacovigilance (medicines for human use).
  The new medicines legislation coming into effect: most important amendments in terms of pharmacovigilance of medicines for human use:
  1. Renewal of a national marketing authorisation.
  2 Periodic safety reports for medicines approved according to national, MRP, DCP and centralised procedures.
  + 21.03.2008: **addendum to circular 490**, synchronisation of time schedule for submitting periodic safety reports of medicines (human use) containing the same active substance (national, decentralised or mutual recognition procedure) in the context of the European "PSUR work sharing" project.
- 28.04.2008: **circular 519**, to all marketing authorisation holders for medicines with active ingredients in the form of a mesilate, (di-)isethionate, tosylate or besilate. Request to assess the risk of potential contamination of medicines with mesilate esters and associated components.

- 16.05.2008: **circular 523**, to directors of tissue and cell banks. Inspection of cell and tissue banks.
- 09.06.2008: **circular 522** + Simplified MA + checklist for closing file, to all marketing authorisation holders for medicines for human use. Simplified marketing authorisation (MA) for medicines for human use. Unique national registration number for medicines for human use.
- 09.06.2008: **circular 521**, Applicants for marketing authorisation (MA) for medicines for human use. Inactivation of files in the closure phase.
- 29.07.2008: **circular 524**, for the attention of hospital directors and directors of cell and tissue banks. Procedure regarding application to authorise or extend authorisation of a cell and tissue bank.
- 12.08.2008: **circular 525**, for the attention of directors of blood establishments (BE) and directors of cell and tissue banks. Clarification of age limits (version August 2008).
- 01.11.2008: **circular 528** to sponsors of clinical trials. Update and clarification regarding the submission and processing of requests for clinical trials.
- 11.2008: **circular 527**, to manufacturers of research medicines. Notification of research medicines.
- 12.12.2008: **circular 520**, to marketing authorisation (MA) holders of medicines for human and veterinary use. Inspections regarding pharmacovigilance. Update of information regarding pharmacovigilance (human and veterinary).
- 15.12.2008: **circular 533** and explanatory note + notification form, for the attention of companies marketing products based on plants and herbal medicines. Reporting details of traditional herbal medicines and products based on plants conforming to the definition of traditional herbal medicines.
- 16.12.2008: **circular 535**, to holders of marketing authorisation for wholesale trade in medicines. Increase in taxes/contributions owed per package.
- 16.12.2008: **circular 534**, to holders of marketing authorisation for wholesale trade in medicines and wholesale distributors. Increase in taxes/contributions owed per package.
- 16.12.2008: **circular 531** to sponsors of clinical trials. Payment for applications for clinical trials.
- 17.12.2008: **circular 532**, to marketing authorisation (MA) holders or registration holders for medicines for human and veterinary use. Risk management programme – Approval of the "additional risk-limiting activities" by the national governments.

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The electronic version of this annual report 2008 is available on the FAMHP website
(www.fagg.be - www.afmps.be)

LIST OF ABBREVIATIONS AND DEFINITIONS

@ctua	Electronic newsletter of the FAMHP to its stakeholders
AFI	General Pharmaceutical Inspectorate, later DG Medicinal Products of the FPS Public Health, now FAMHP
APB	Algemene Pharmaceutische Bond - Association Pharmaceutique Belge: the coordinating federation of the Belgian professional associations of independent retail pharmacies
art.	Article
ASR	Annual Safety Report
ATMP	Advanced Therapy Medicinal Products
B&Mc	Budget and management control
BAPCOC	Belgian Antibiotic Policy Coordination Committee
BCFI-CBIP	Belgian Centre for Pharmacotherapeutic Information
BCGH-CBPH	Belgian Centre for Pharmacovigilance for medicines for human use
BEMA	Benchmarking European Medicines Agencies
BMWP	Biosimilar Medicinal Products Working Party
BPAM	Belgian Platform for Alternative Methods
BRAS	Belgian Regulatory Affairs Society
B.S.-M.B.	Belgisch Staatsblad - Moniteur belge : Belgian journal of acts, orders and decrees
BUM	Proper use of medicines
BVK-SBP	Belgian Association for Paediatric Medicine
BWP	Blood Working Party
Cartophar	Digital cartography of retail pharmacies
CAT	Committee for Advanced Therapies
CE	Marking that companies are required to display on products falling within the scope of the New Approach Directives – European conformity marking
CHMP	Committee for Medicinal Products for Human Use (ex CPMP)
CIBE	Public sector tailored communication
CMDh	Co-ordination Group for Mutual Recognition and Decentralised Procedures, human
CODA-CERVA	Centrum voor Onderzoek in Diergeneeskunde en Agrochemie - Centre d'Etudes et de Recherches Vétérinaires et Agrochimiques: Veterinary Agrochemical Research Centre
COMP	Committee for Orphan Medicinal Products
CP	Centralised Procedure
CRO	Clinical Research Organisation
ct	Centimes
CT	Computed Tomography
CTFG	Clinical Trial Facilitation Group – A collaborative group established to facilitate and harmonise the organisation of clinical trials in Europe
CTTF	Clinical Trial Task Force – Informal consultation regarding clinical trials
CVMP	Committee for Medicinal Products for Veterinary Use
DCP	Decentralised Procedure
DG	Directorate-General
DGO-SCM	Dienst Geneesmiddelenonderzoek - Service de Contrôle des Médicaments: medicines control laboratory of APB
e.g.	Exempli gratia – For instance
e-Health	Secure platform for electronic data exchange within the Belgian healthcare sector
e-MED	Project concerning the electronic prescription of medicines
ECVAM	European Centre for the Validation of Alternative Methods
EDQM	European Directorate for the Quality of Medicines
EMEA	European Medicines Agency
EU	European Union
EWP	Efficacy Working Party
FAGG - AFMPS	Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten - Agence Fédérale des Médicaments et des Produits de Santé = FAMHP
FAMHP	Federal Agency for Medicines and Health Products = FAGG / AFMPS
FANC - AFCN	Federaal Agentschap voor Nucleaire Controle - Agence Fédérale de contrôle nucléaire : federal agency for nuclear control
FAVV - AFSCA	Federaal Agentschap voor de Veiligheid van de Voedselketen - Agence Fédérale pour la Sécurité de la Chaîne Alimentaire: the federal food agency
FAQ	Frequently Asked Questions
FDA	Food and Drug Administration
FPS	Federal Public Service
FSD	First Safe Dilution
GCP	Good Clinical Practices
GDP	Good Distribution Practices
GMO	Genetically Modified Organism
GMP	Good Manufacturing Practices
GVP	Good Veterinary Practices
HMA	Heads of Medicines Agencies
HMM	Homeopathic Manufacturing Methods
HMPC	Committee on Herbal Medicinal Products
HMPWG	Homeopathic Medicinal Products Working Group
HR	Human Resources
ICH	International Conference on Harmonisation
ICT	Information and Communication Technology
ICVV-CICSA	Interdepartementale Coördinatiecel voor de controle van de Voedselveiligheid - Cellule de Coordination Interdépartementale pour le Contrôle de la Sécurité Alimentaire : interdepartmental coordination unit for the control of food security
INCB	International Narcotics Control Board
IR	International Relations
IWP	Immunologicals Working Party
KCE	Federaal Kenniscentrum voor de Gezondheidszorg - Centre Fédéral d'Expertise des Soins de Santé : Belgian health care knowledge centre
KPI	Key Performance Indicator
MA	Marketing authorisation
MD	Ministerial decision
MCRN	Medicines for Children Research Network – Dutch network to stimulate, facilitate and conduct efficient high quality, relevant and safe medicines research in Dutch children
Mdeon	Mdeon is the common professional ethics platform created for the associations of doctors, pharmacists, the pharmaceutical industry and the medical devices industry
MeSeA	Medicines electronic Submission and electronic Approval
MRP	Mutual Recognition Procedure
MTD	Maximum Tolerated Dose
MUMS	Minor Use Minor Species
NAT	Nucleic Acid Testing
NFWO	National Fund for Scientific Research
NP	National procedure
no.	Number
OPHACO	Vereniging der Coöperatieve apotheken van België - Office des Pharmacies Cooperatives de Belgique : Belgian professional association of cooperative retail pharmacies
Orphan disease	Orphan disease or rare disease
P&D	Production and distribution
P&O	Personnel and organisation
PDCO	Paediatric Committee
PFIPC	Permanent Forum on International Pharmaceutical Crime
pharma.be	General association of the Pharmaceutical Industry (AVGI), a not-for-profit organisation established to promote the interests of the pharmaceutical industry in Belgium
PhVWP	PharmacoVigilance Working Party
PhVWP-V	PharmacoVigilance Working Party, Veterinary
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIP	Pediatric Investigation Plan
PMO	Program Management Office
PSUR	Periodic Safety Update Report
QT-effect	Effect on cardiac rhythm
QWP	Quality Working Party
R&D	Research and development
RAS	Rapid Alert System
R.D.	Royal decree
RIZIV-INAMI	Rijksinstituut voor ziekte- en invaliditeitsverzekering - Institut national d'assurance maladie-invalidité: national institute for sickness and invalidity insurance
RMS	Reference Member State
RHD	Rabbit Hemorrhagic Disease – Virus in rabbits
RQ	Renouvellement quinquinal : five-yearly renewal
SAWP	Scientific Advice Working Party
SAWP-V	Scientific Advice Working Party, Veterinary
Selor	Government recruitment agency
SLA	Service Level Agreement
SOE-USE	Speciale Onderzoekseenheid - Unité Spéciale d'Enquête : special investigation unit
SUSAR	Suspected Unexpected Serious Adverse Reaction
SWP	Safety Working Party
TCM	Traditional Chinese Medicines
TMF-FTM	Therapeutic Magistral Formularium
TOR	Technisch Overleg Registratie - concertation technique en matière d'enregistrement: technical consultation platform for registration
TU	Traditional Use
Twister	Implementation of computerised P&O processes
UCL	Université catholique de Louvain: Catholic university of Louvain – French language university
ULB	Université Libre de Bruxelles: Free University of Brussels – French-language university
V-amazone	Consultation platform on veterinary medicines
VWP	Vaccine Working Party
Vzw - asbl	Vereniging zonder winstoogmerk - association sans but lucrative : non-profit association
WHO	World Health Organisation
WIV-ISP	Wetenschappelijk Instituut Volksgezondheid – Institut Scientifique de Santé Publique : scientific institute of public health

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